

# Contrast FFR (cFFR)

*better than resting parameters?*

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# Disclosure Statement of Financial Interest

Within the past 12+ months, Nils Johnson has had a financial interest/arrangement or affiliation with the organization(s) listed below.

## Affiliation/Financial Relationship

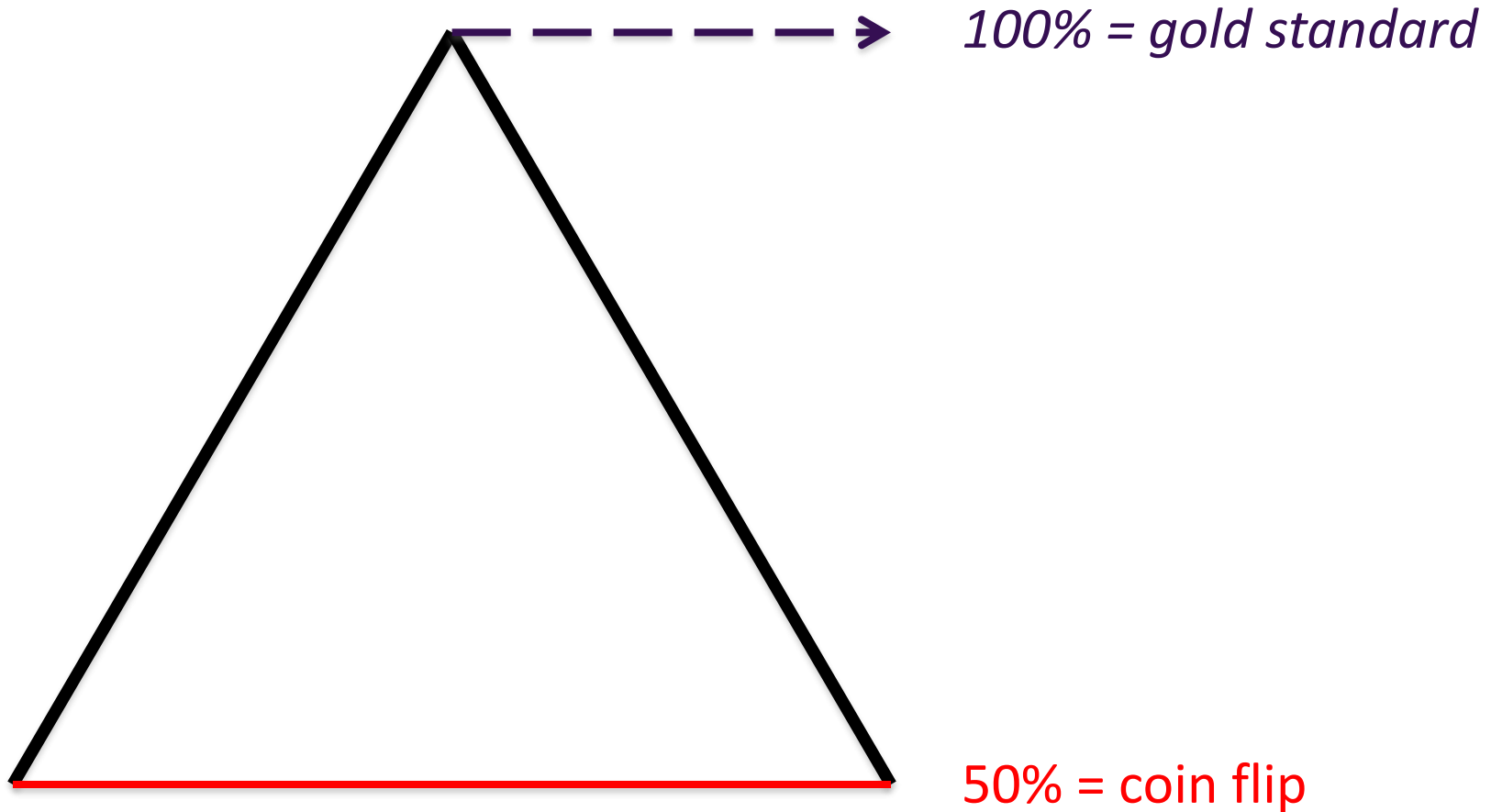
- Grant/Research Support  
(to *institution*)
- Educational organizations  
(travel support for academic meetings  
but *never honoraria*)

## Organizations (alphabetical)

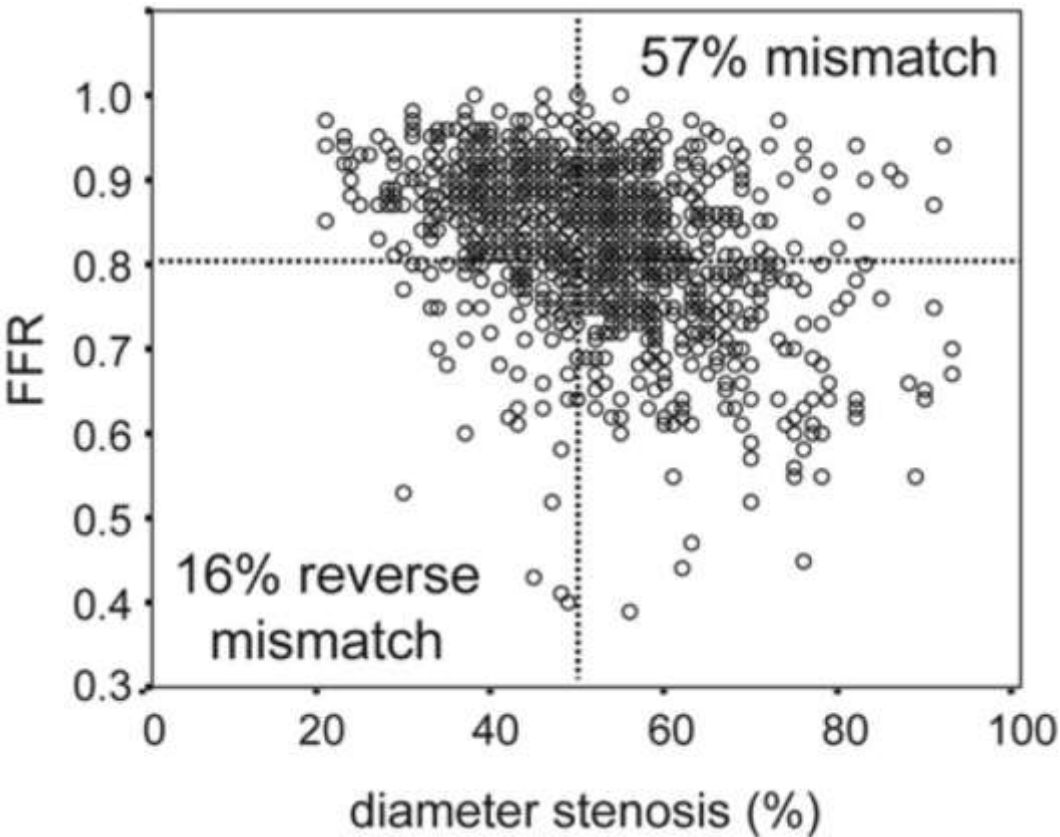
- St Jude Medical (for CONTRAST study)
- Volcano/Philips (for DEFINE-FLOW study)
- ASNC (travel award 2007)
- Canadian CPI (Montréal 2013-15)
- CRF (TCT 2012-15, CPIIS 2014)
- Emory (EPIC-SEC 2015)
- ESC (ETP physiology courses 2013-15)
- KSIC (annual meeting & IPOP 2015)
- PCR (EuroPCR 2015)
- SCAI (travel award 2010)

Nils Johnson has *never* personally received *any* money from *any* commercial company. Specifically, he does *not accept* commercial consulting, travel, entertainment, or speaking compensation *of any kind*.

# Pyramid of diagnostic accuracy



# Angiogram <70% accuracy



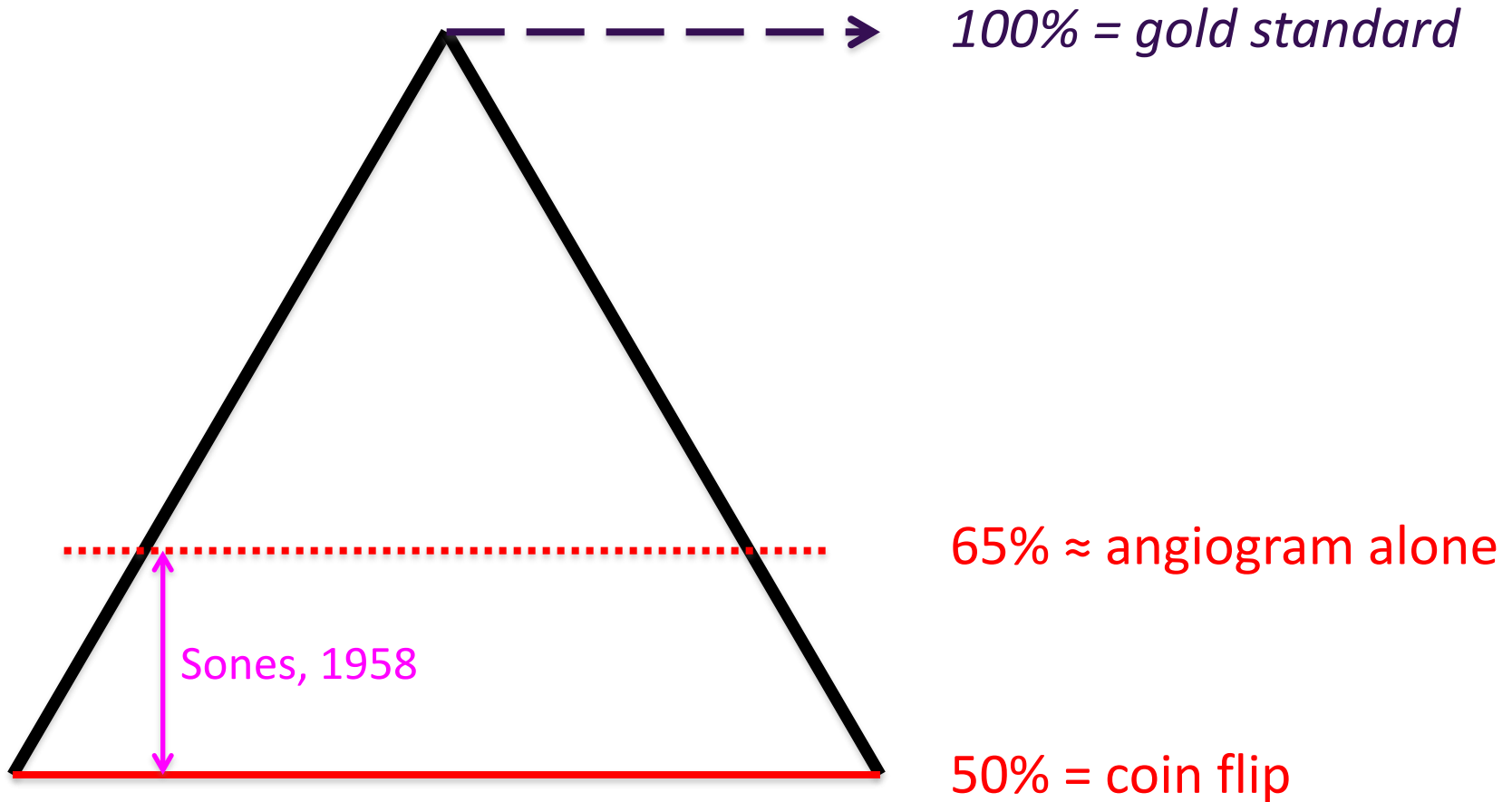
1,066 lesions with QCA  
Compared to FFR $\leq$ 0.8

•52%DS threshold

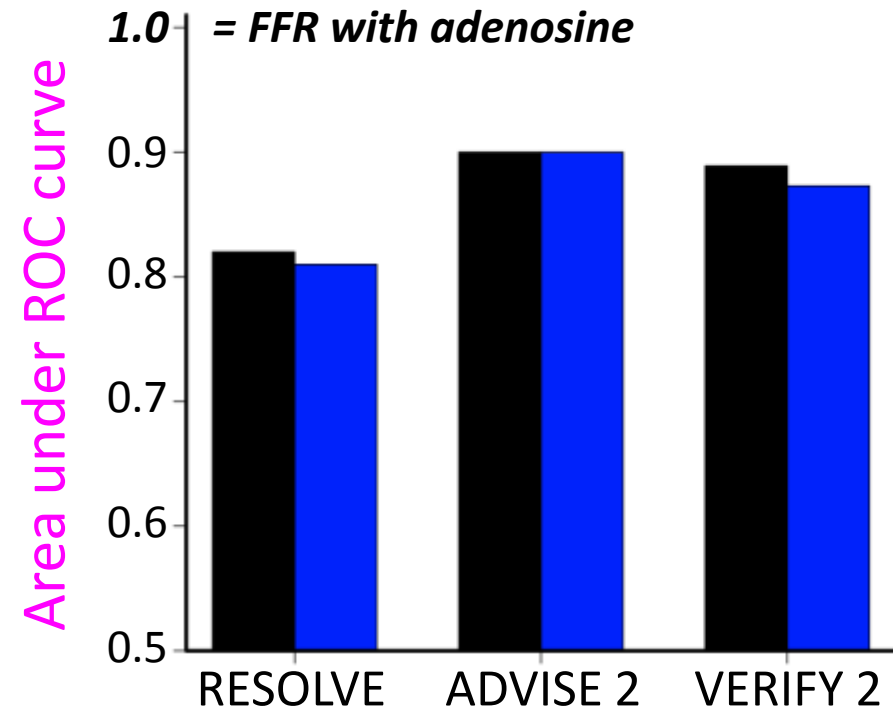
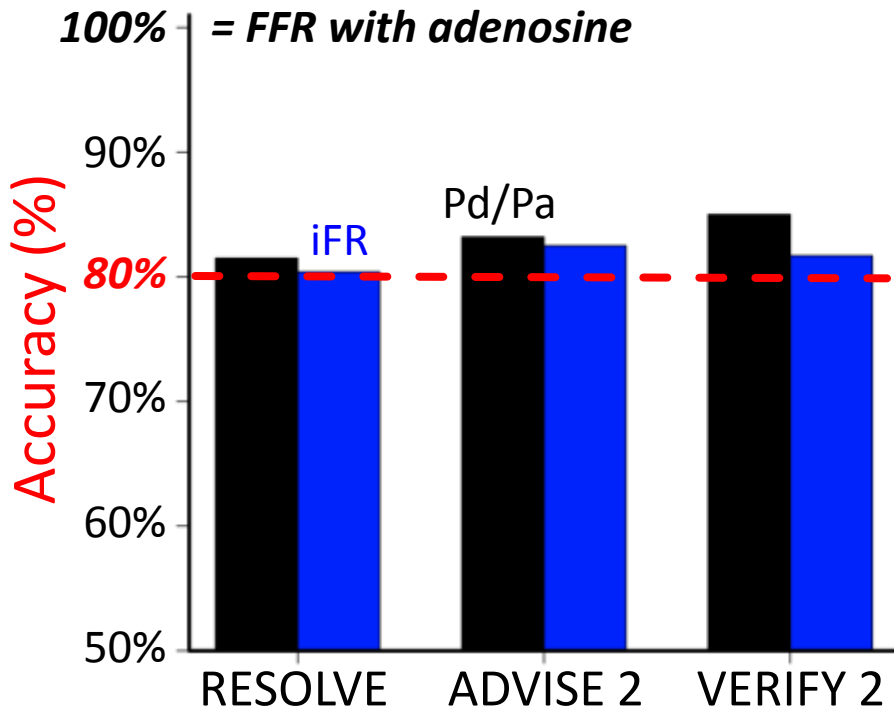
– 66% accuracy

– 0.66 AUC

# Pyramid of diagnostic accuracy



# Resting physiology $\approx$ 80% accuracy

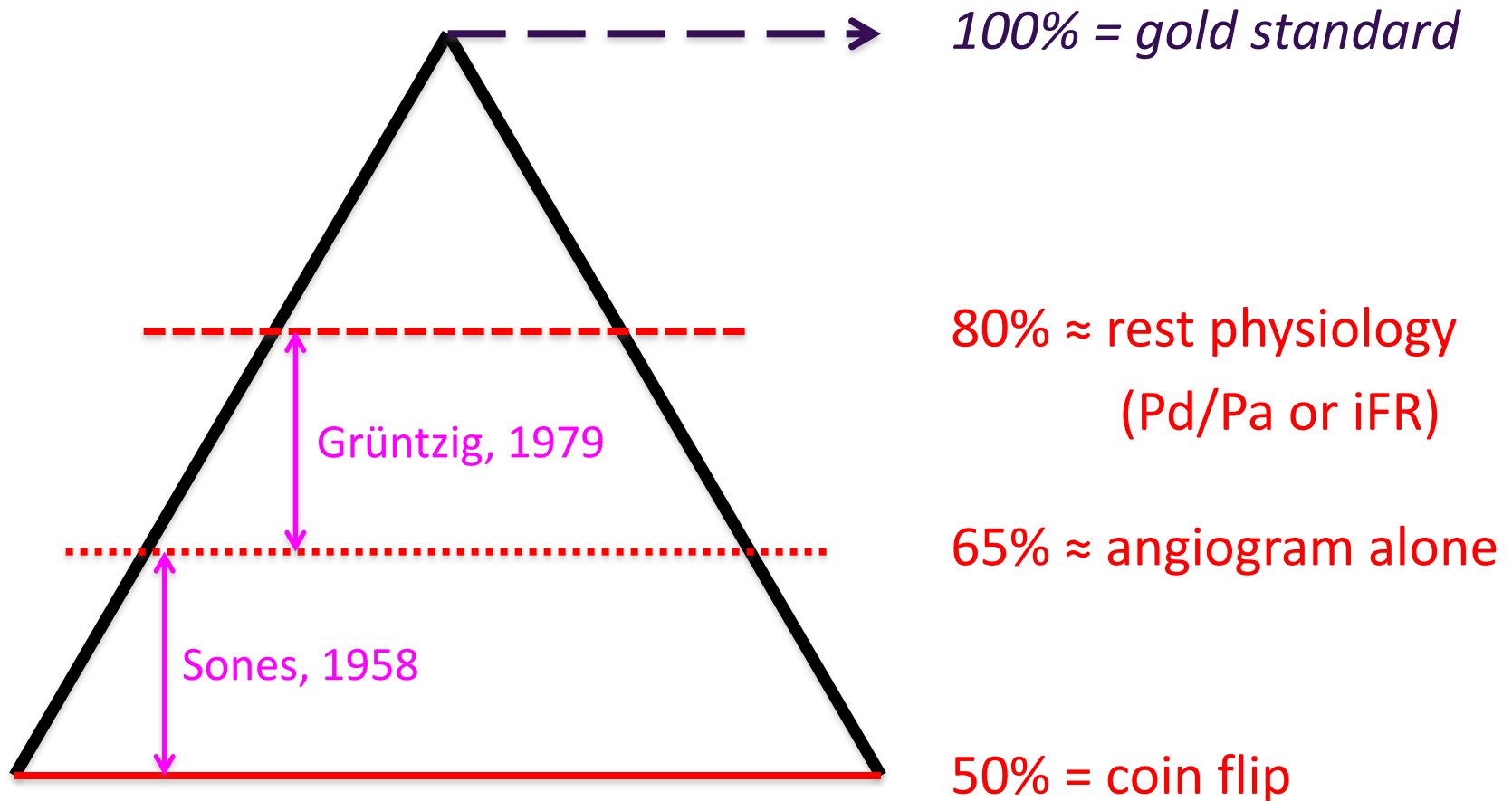


RESOLVE = Jeremias A, *JACC*. 2014 Apr 8;63(13):1253-61

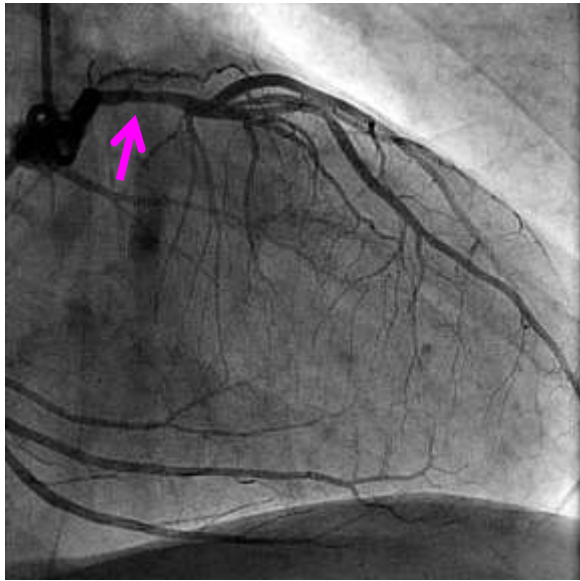
ADVISE 2 = Escaned J, *JACC Cardiovasc Interv*. 2015 May;8(6):824-33 and 834-6

VERIFY 2 = Watkins S, late-breaking clinical trial at SCAI in Las Vegas, May 30, 2014

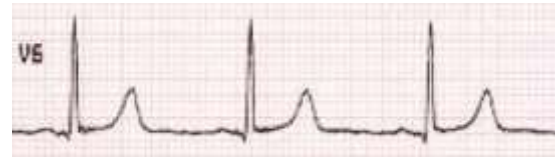
# Pyramid of diagnostic accuracy



# Clinical importance of hyperemia

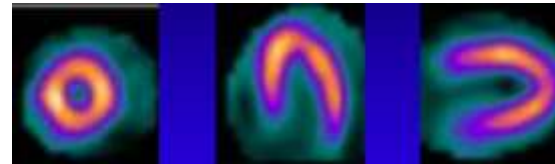


Rest



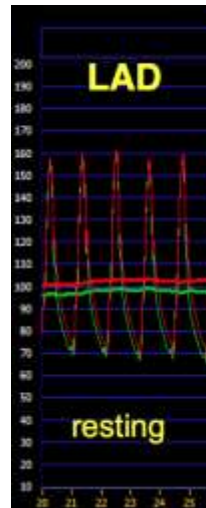
normal ECG

Rest



no defect

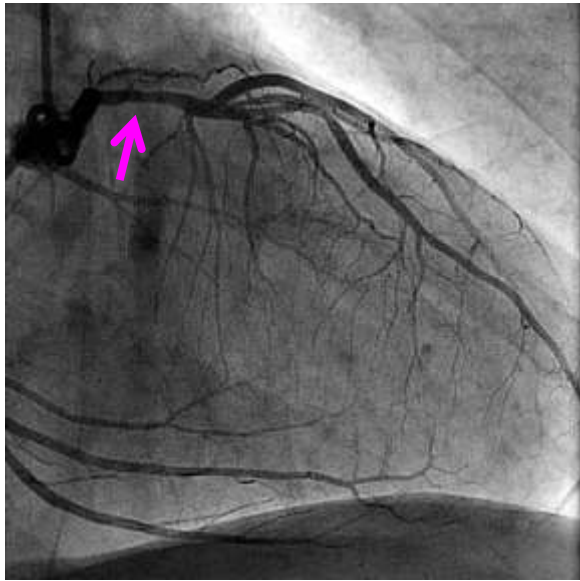
59 year-old man with  
*mild & long LAD lesion*  
and *new classic angina*



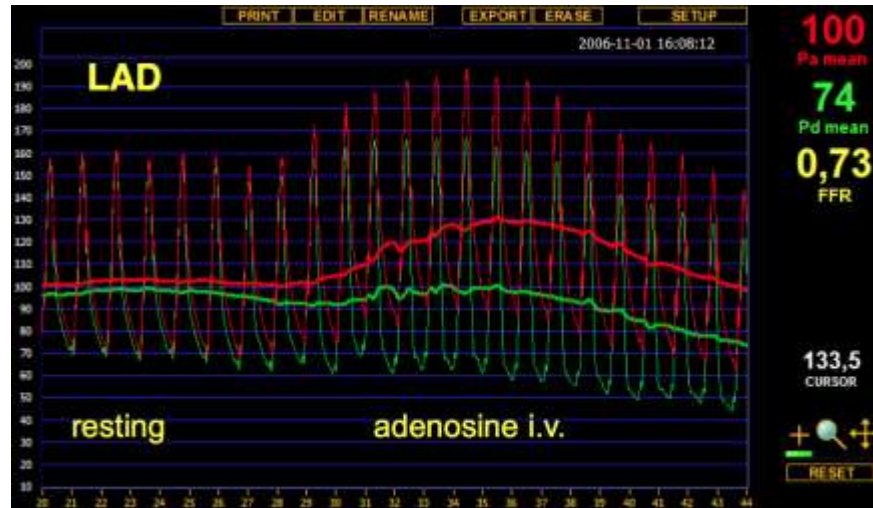
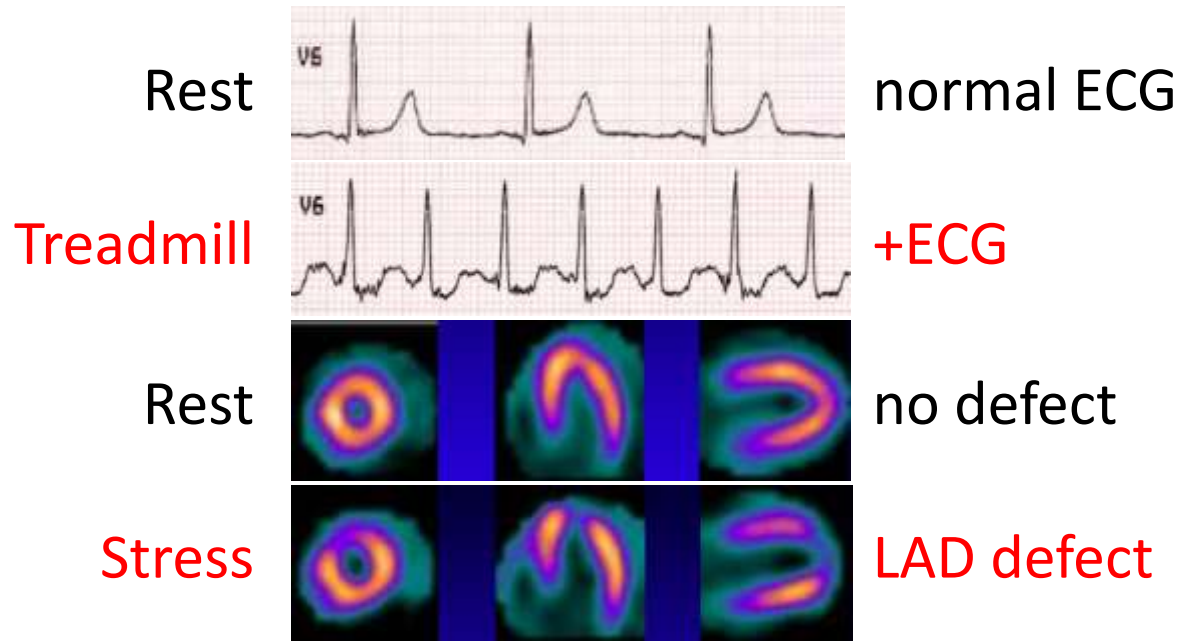
$Pd/Pa = 0.96$   
 $iFR = 0.97$



# Clinical importance of hyperemia



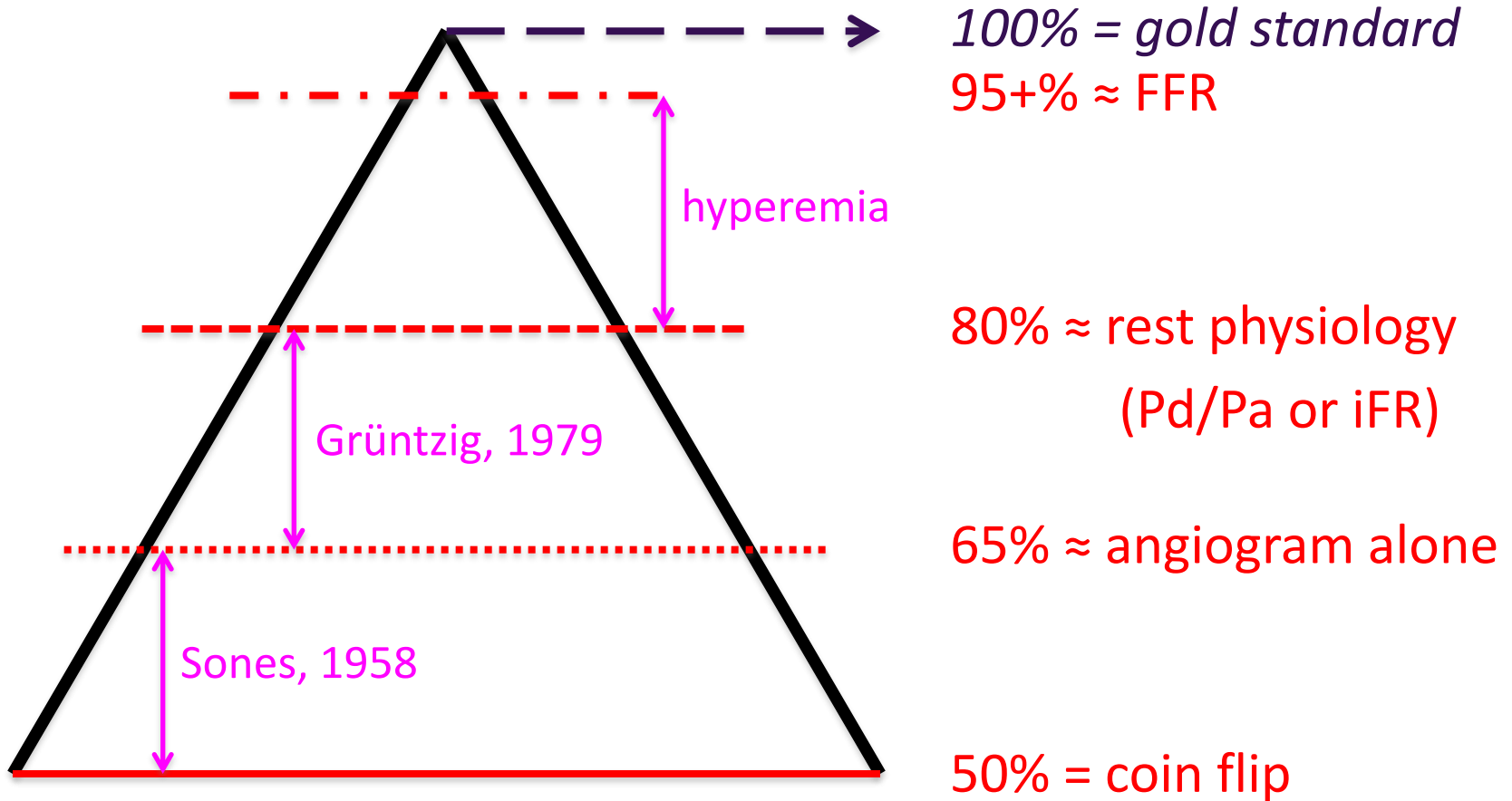
59 year-old man with *mild & long LAD lesion* and *new classic angina*



Pd/Pa = 0.96  
iFR = 0.97

FFR = 0.73

# Pyramid of diagnostic accuracy



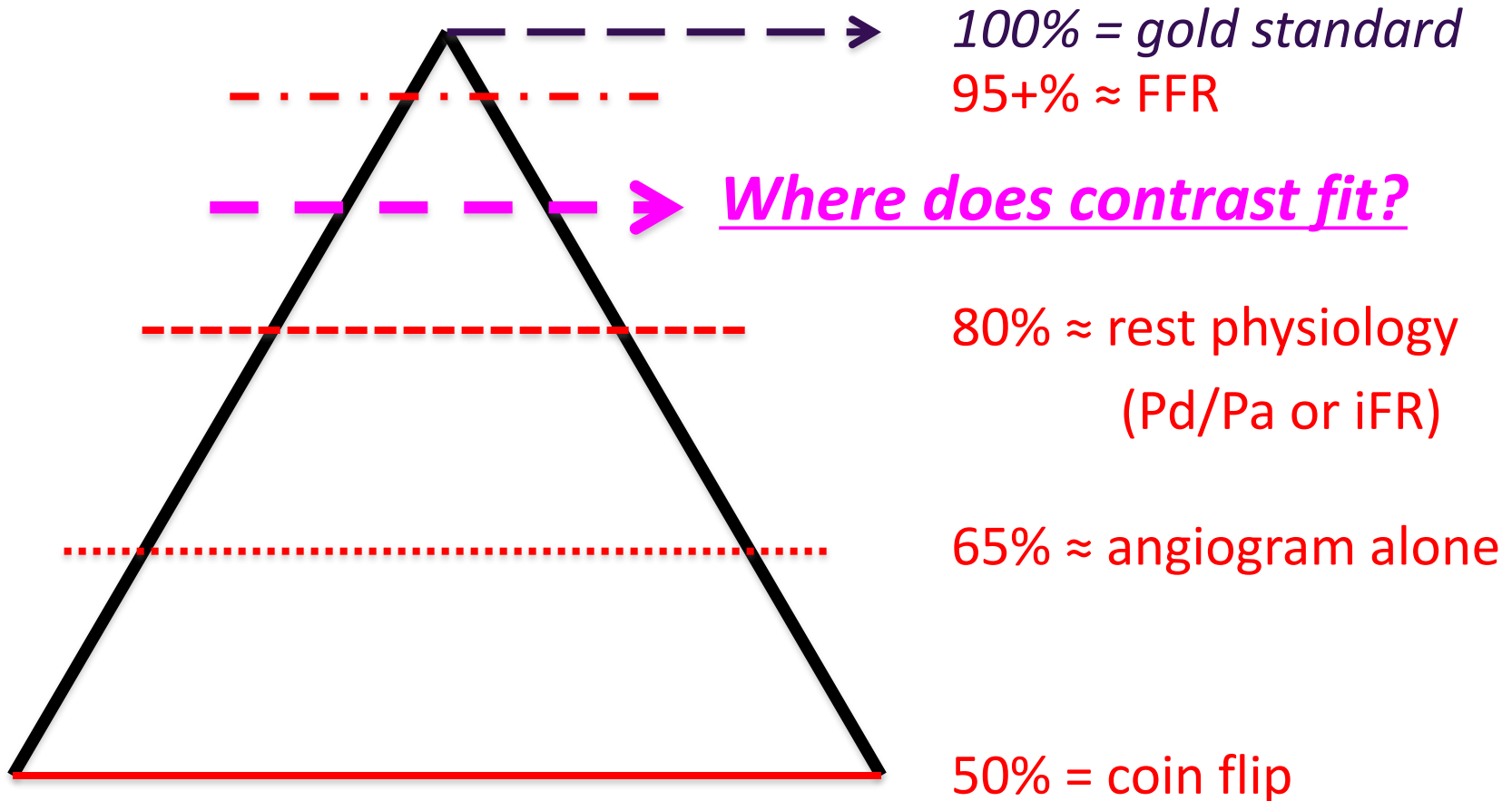
# Vasodilators in human physiology

- *contrast medium (1974, Gould KL, Am J Cardiology)*
- dipyridamole (1978, Gould KL, Am J Cardiology)
- coronary occlusion (1984, Marcus ML, NEJM)
- papaverine (1986, Wilson RF, Circulation)
- adenosine (1990, Wilson RF, Circulation)
- ATP (2003, De Bruyne B, Circulation)
- nitroprusside (2004, Kern MJ, Circulation)
- nicorandil (2006, Kang JC, Int J Cardiology)
- regadenoson (2011, Nair PK, JACC Interventions)

# Hypothesis

- Contrast FFR *provides superior agreement with FFR than resting metrics* (rest Pd/Pa or iFR)
- Primary endpoint: *diagnostic accuracy* vs FFR $\leq$ 0.8
- Secondary endpoints: *AUC by ROC, repeatability*

# Pyramid of diagnostic accuracy



# Methods

- *763 subjects* (prospective) with 1 lesion/patient
  - Any lesion fulfilling a *clinical indication for FFR*
- Hyperemic drugs
  - *IC contrast*: medium and volume *per local practice*
  - *IC adenosine*: recommended dose *100-200 µg*
  - *IV adenosine*: standard infusion rate (*140 µg/kg/min*)
- Cutoffs for comparison with FFR
  - *iFR < 0.90* (DEFINE-FLAIR), *Pd/Pa < 0.92* (RESOLVE)

# CONTRAST: participating centers

## *Belgium (Aalst)*

- *B De Bruyne*
- *E Barbato*

## *Korea*

- *BK Koo (SNUH)*
- *SJ Park (Asan)*

## *Scotland (Glasgow)*

- *C Berry*
- *K Oldroyd*

## *USA*

- *W Fearon (Palo Alto)*
- *G Chrysant (OKC)*

## *France (Lyon)*

- *G Rioufol*

## *Netherlands (Eindhoven)*

- *N Pijls*
- *F Zimmermann*

## *Sweden (Stockholm)*

- *N Witt*

## *CRF (physiology core lab)*

- *A Jeremias*
- *A Maehara*
- *M Matsumura*

## *Italy (Naples, Rome)*

- *G Esposito*
- *B Trimarco*
- *A Leone*

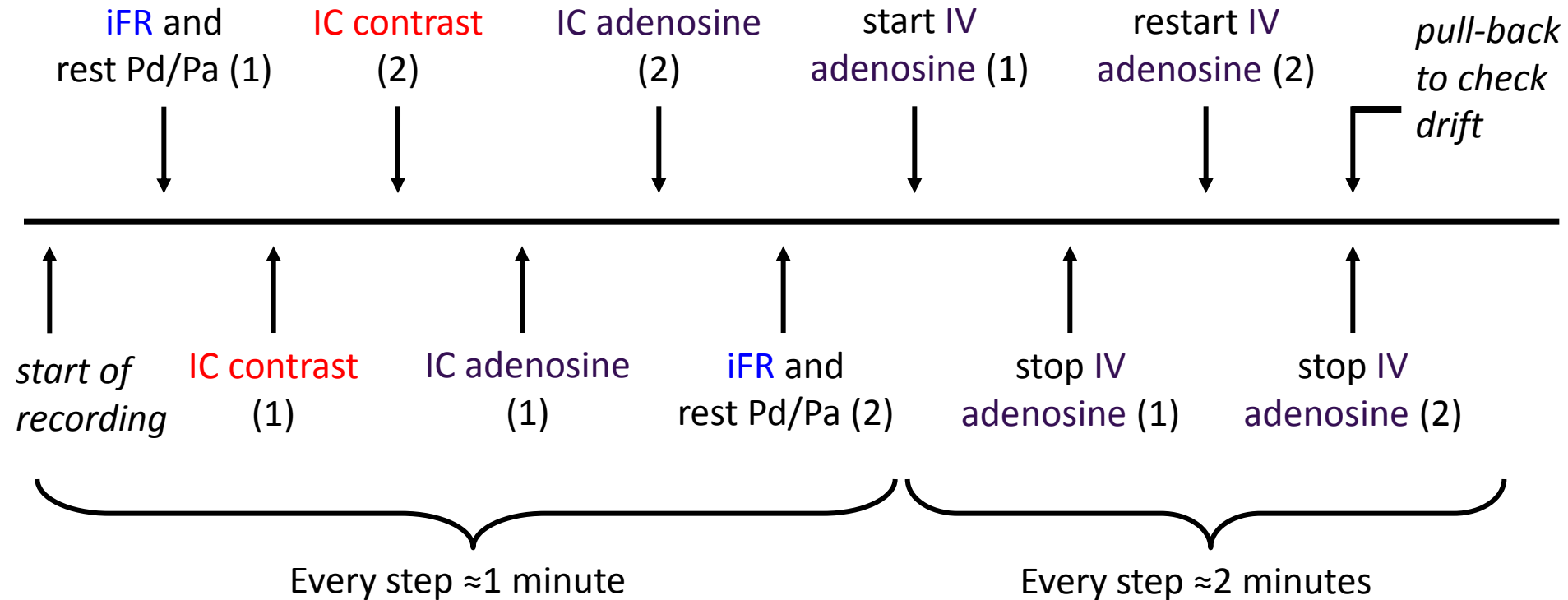
## *Portugal (Lisbon)*

- *S Baptista*

## *UT-Houston (sponsor)*

- *N Johnson*
- *R Kirkeeide*
- *KL Gould*

# Protocol



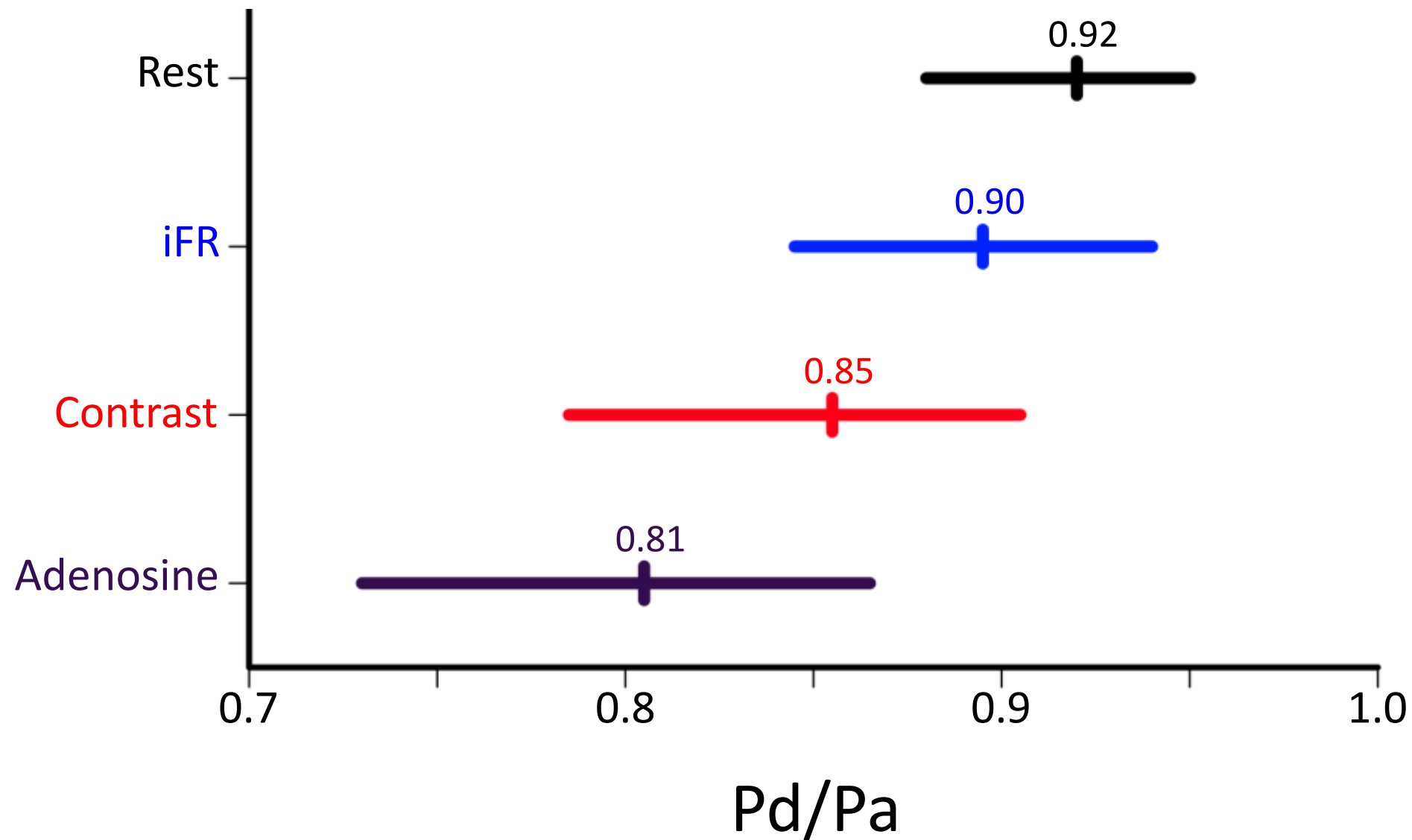
- *Tracings blinded* and their parts sent to core lab



# Results: Baseline characteristics

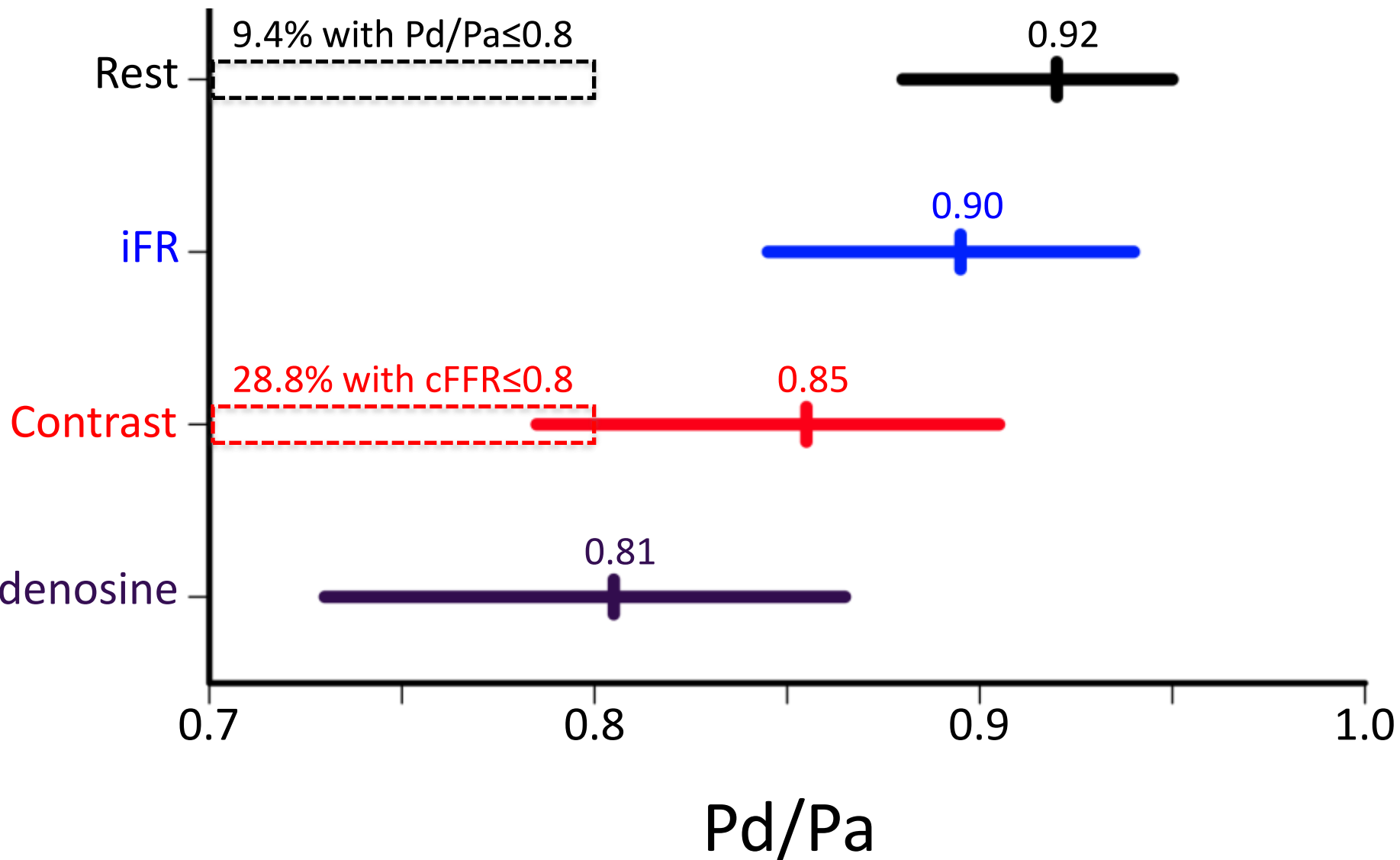
- Age  $66 \pm 10$  years, 72% male
- *10% with renal insufficiency* (eGFR<60)
- Average  *$8 \pm 2$  mL* of IC contrast, *8 different agents*:
  - iomeron (29%)
  - iodixanol (25%)
  - iohexol (14%)
  - ioversol (9%)
  - iopromide (9%)
- Exclusions by core lab
  - 10% of pressure tracings
  - *14% of ECG tracings*

# Results: Lesion physiology



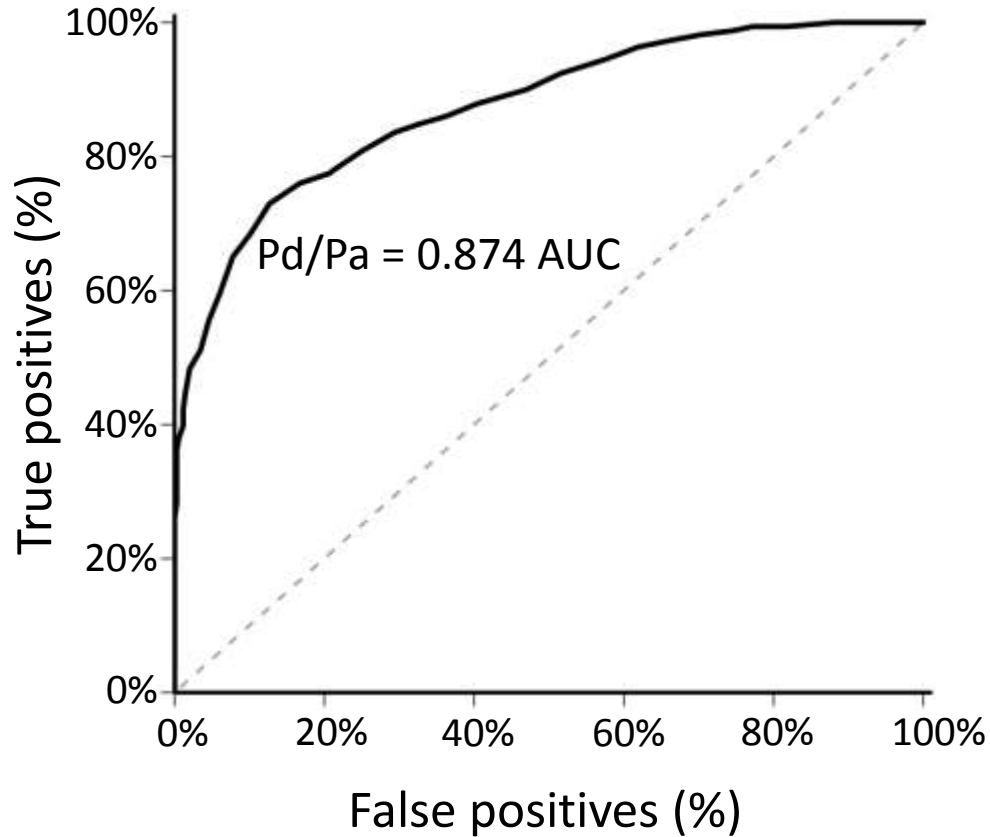
(shows median and interquartile range)

# Results: Lesion physiology



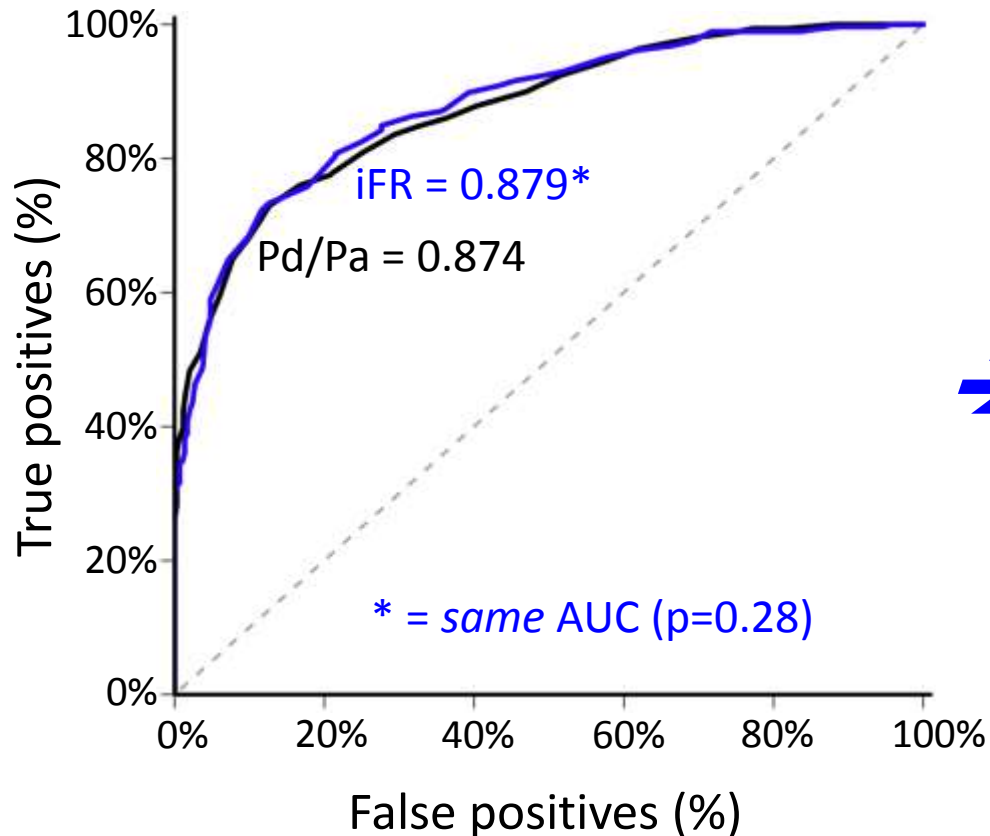
(shows median and interquartile range)

# Results: Diagnostic accuracy



Pd/Pa = 78.4% accuracy

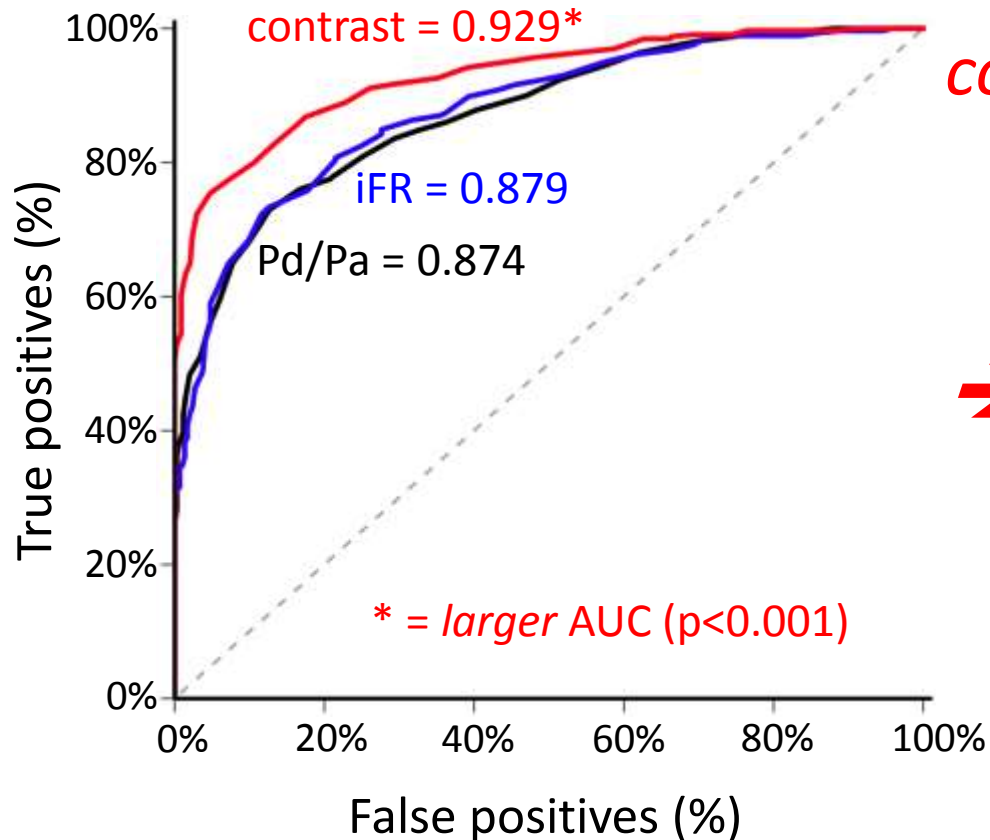
# Results: Diagnostic accuracy



iFR = 79.6% accuracy  
Pd/Pa = 78.4% accuracy  
➔ *no difference (p=0.89)*

- AUC = area under ROC curve (DeLong comparison)
- Accuracy uses  $FFR \leq 0.8$  (McNemar comparison)

# Results: Diagnostic accuracy



*contrast = 85.5% accuracy*

*iFR = 79.6% accuracy*

*Pd/Pa = 78.4% accuracy*

*→ superior accuracy (p<0.001)*

Optimal binary cutoff for *contrast FFR  $\leq 0.83$*   
(accuracy >84% for 0.83-0.85)

# Limitations

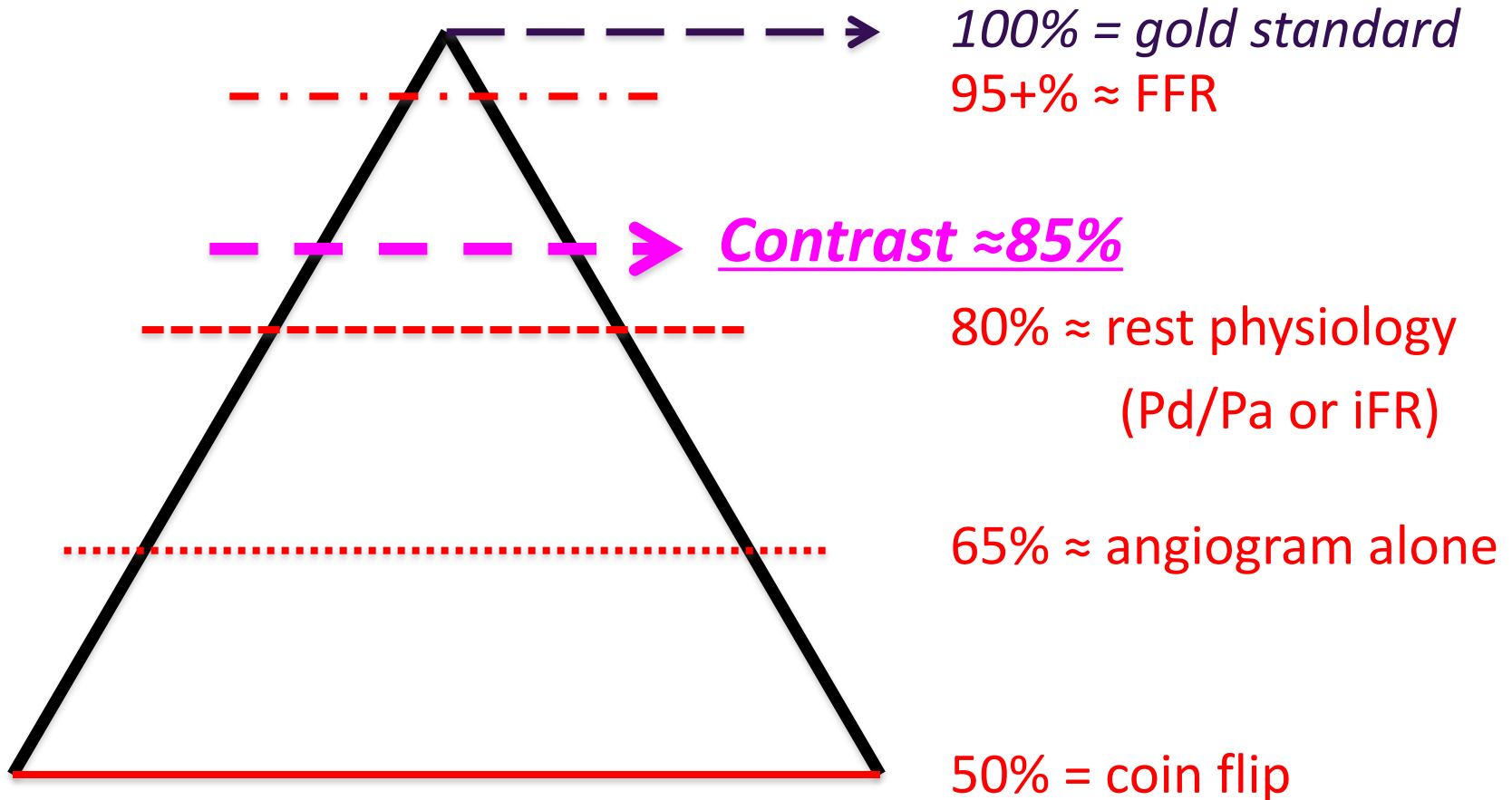
- Contrast hyperemia *too short for pull-back tracings*
  - Applies to IC adenosine too
  - Can perform serial IC bolus measurements
- No data collected on *contrast-induced nephropathy*
  - Average dose 8 mL of IC contrast for single vessel
  - Used to document pressure wire position anyway
  - *Clinical impact negligible*
- Further details for manuscript
  - Contrast *medium* and volume *dose/response*

# Conclusions

- Contrast FFR is *superior to rest Pd/Pa and iFR* for predicting FFR (using binary or hybrid approach)
- iFR and rest Pd/Pa provide *equivalent diagnostic accuracy*
- FFR with strong hyperemia (adenosine) remains the *reference standard for diagnostic certainty* (even contrast FFR only reached  $\approx 85\%$  accuracy)



# Pyramid of diagnostic accuracy



# Clinical impact

- Contrast FFR was  $\leq 0.8$  in  $\approx 30\%$  of cohort, thus confirming functional significance “for free”
- In healthcare systems in which adenosine is *prohibitively expensive* or in the *rare cases* when adenosine is contraindicated, contrast FFR:
  - Is *easy, inexpensive, and safe*
  - Displays *excellent test/retest stability*
  - Does *not depend on a specific software platform*  
(available on all pressure-wire systems) *or ECG gating* (core lab excluded 14% of ECG tracings)