Does Renal Artery Distal Protection Have a Role in Renal Artery Stenting?

Evolving Clinical Science

Krishna Rocha-Singh, M.D., F.A.C.C.
Director, Prairie Vascular Institute
Springfield, IL

Outcomes Of Renal Revascularization In Chronic Azotemic Renovascular Disease

Improved GFR	Stable GFR	Deterioration of GFR
25 - 30%	45 - 50%	20 - 25%
• Restoration of Blood Flow • Reversible Parenchymal Injury	• No Further Loss of Blood Flow • Stable Tissue Fibrosis	• Progressive Parenchymal Injury • Reperfusion Injury • Contrast Nephropathy • Atheroemboli

Atheroembolization

- Material impacts in small arteries, arterioles and glomeruli
- Intimal thickening and formation of giant cells
- Distal micro-infarcts and ischemic atrophy
- Becomes clinically evident 1 day to 2 months post-procedure

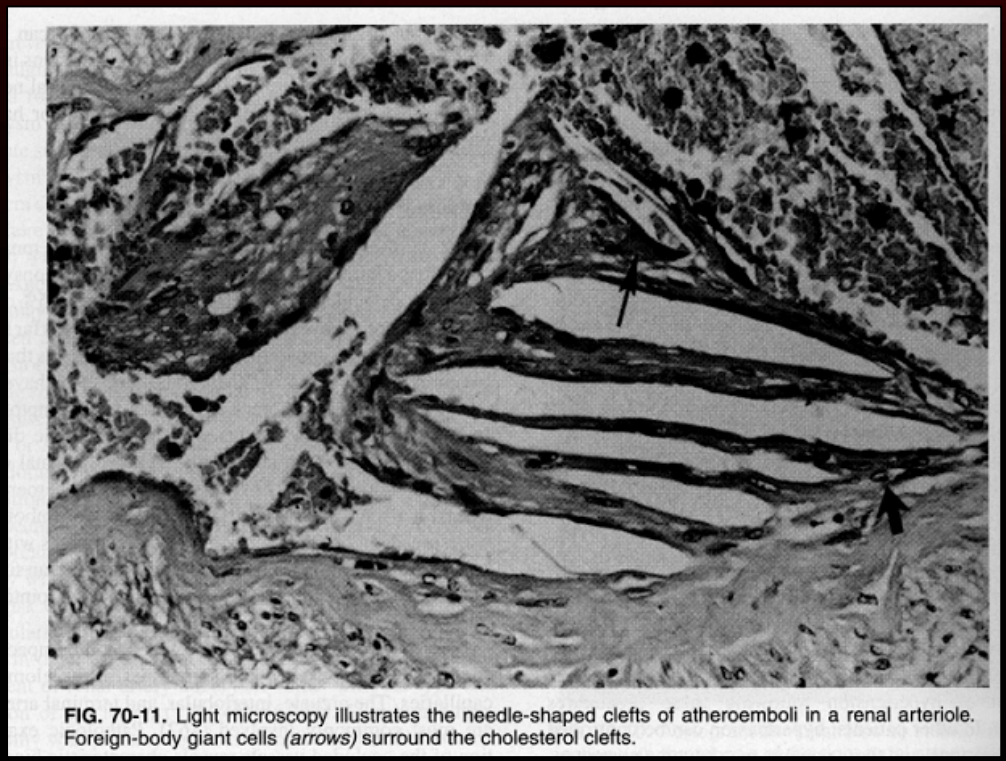
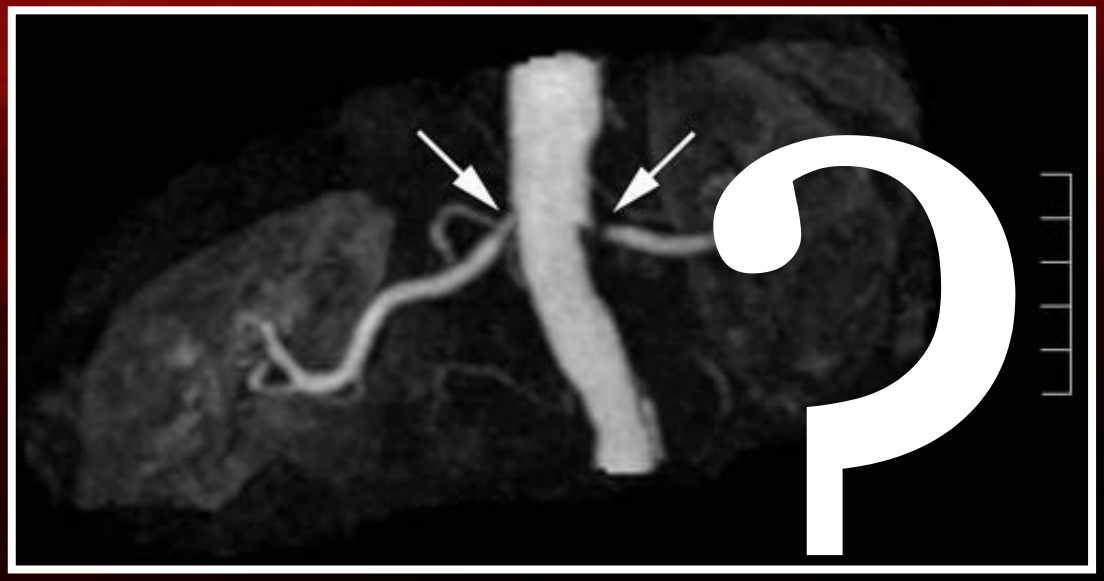


FIG. 70-11. Light microscopy illustrates the needle-shaped clefts of atheroemboli in a renal arteriole. Foreign-body giant cells *(arrows)* surround the cholesterol clefts.

From Schrier, 7th ed.

RAS



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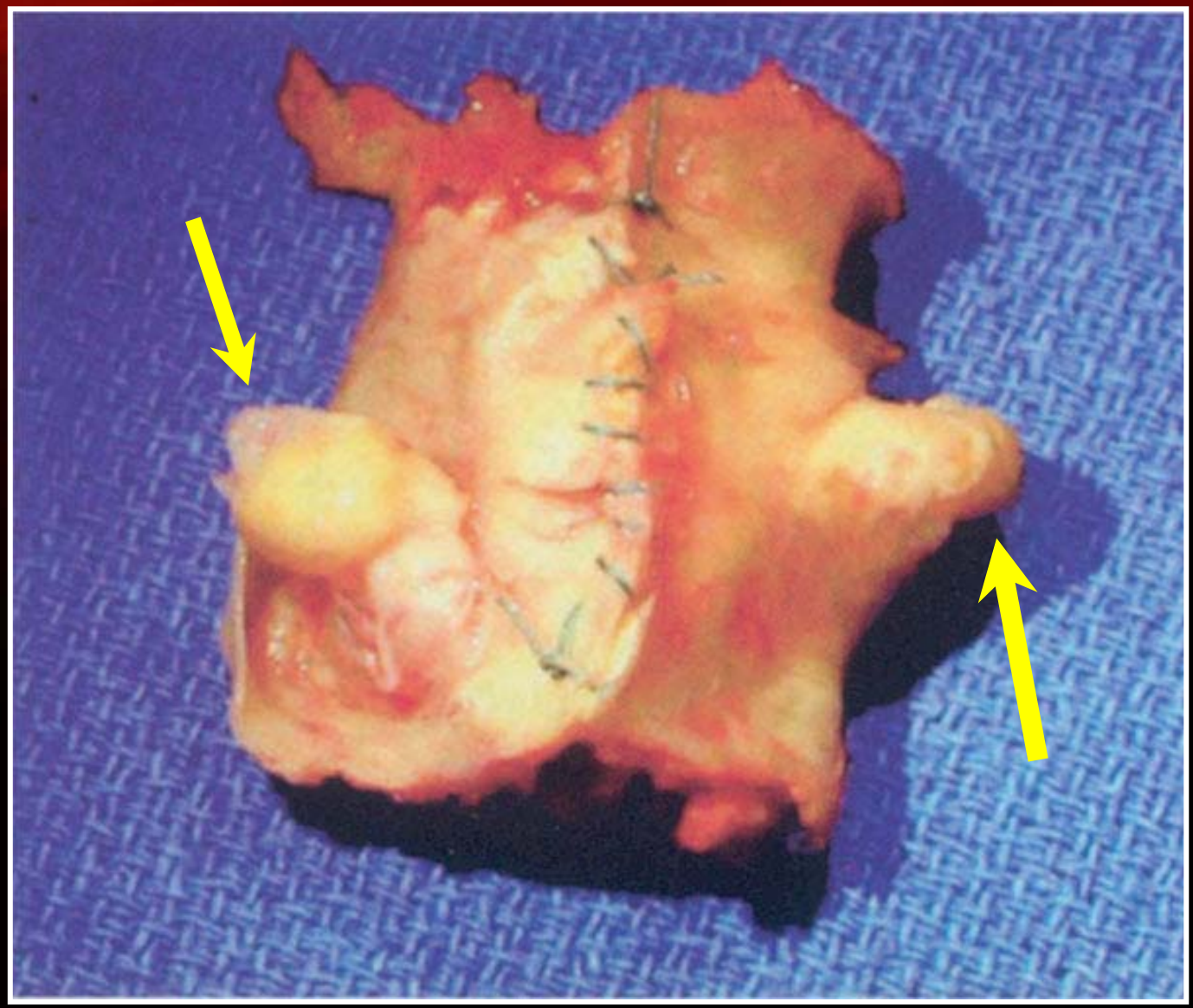
EPD

= Improved/Stabilized GFR

Aorto-renal Endartectomy Specimen



Hiromoto, JVS June ‘05

>100 µm fragments released from ex-vivo renal arteries angioplasty with stent placement

- Are atheroembolic events clinical relevant?
- If so, how is renal injury assessed?
- In what patient group?
- At what time point?
- What is the right device?

Manipulation

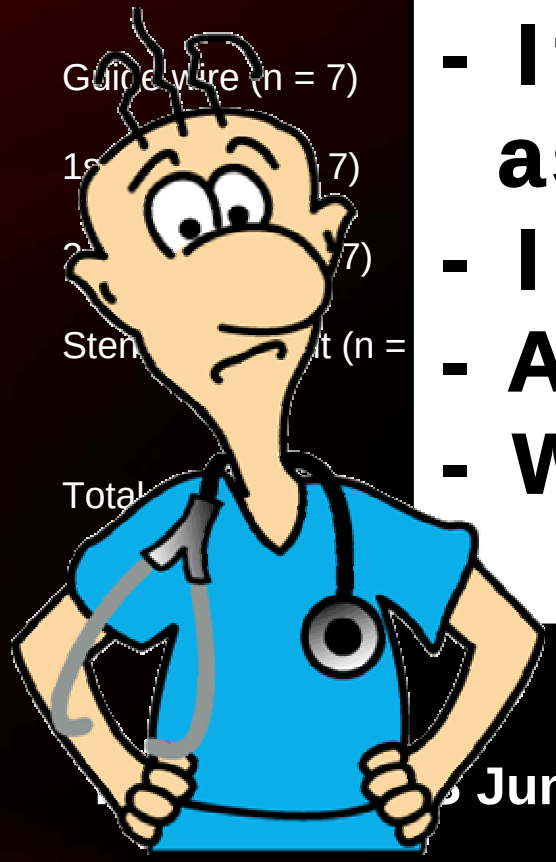
Guide wire (n = 7)

1st [illegible] 7)

2[illegible] 7)

Sten[illegible]t (n =

Total



[illegible] June '05

original article

http://www.kidney-international.org

see commentary on page 830

Renal artery stent revascularization with embolic protection in patients with ischemic nephropathy

A Holden[1], A Hill[2], MR Jaff[3] and H Pilmore[4]

[1]Department of Radiology, Auckland City Hospital, Park Road, Grafton, Auckland, New Zealand; [2]Vascular Surgery, Auckland City Hospital, Auckland, New Zealand; [3]Department of Vascular Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA and [4]Department of Renal Medicine, Auckland City Hospital, Auckland, New Zealand

- **83 arteries treated in 63 consecutive pts. All patients had baseline CRI with a documented decline in renal function over the preceding 6 mos.**
- **All patients had an identical "primary filter passage" technique and primary renal stenting**
- **All patients had a minimum 6 mos. follow up**

Holden Kidney Intern '06

The severity of the pre-intervention CRI was classified using the Kidney Disease Outcome Quality Initiative (K-DOQI)

	eGFR	n
K-DOQI 3A	41-59 ml/min	23
K-DOQI 3B	30-40 ml/min	25
K-DOQI 4	15-29 ml/min	15

44 patients (70%) were hypertensive pre-intervention

Study Design

- The primary study measures were sCr at day 1 and 6 mos. post-stenting
- The day 1 sCr: detect any acute-procedure related deterioration in renal function
- The 6 month sCr: measure renal function at a sufficient interval post-stenting to assess any sub-acute effects from atheromatous embolization

Alterations in Scr at 6 mos. were classified as follows:

Improved	SCr >20% below baseline
Progressive deterioration	SCr >20% after baseline
Stabilized	SCr within 20% of baseline

After Harden, Lancet 2000

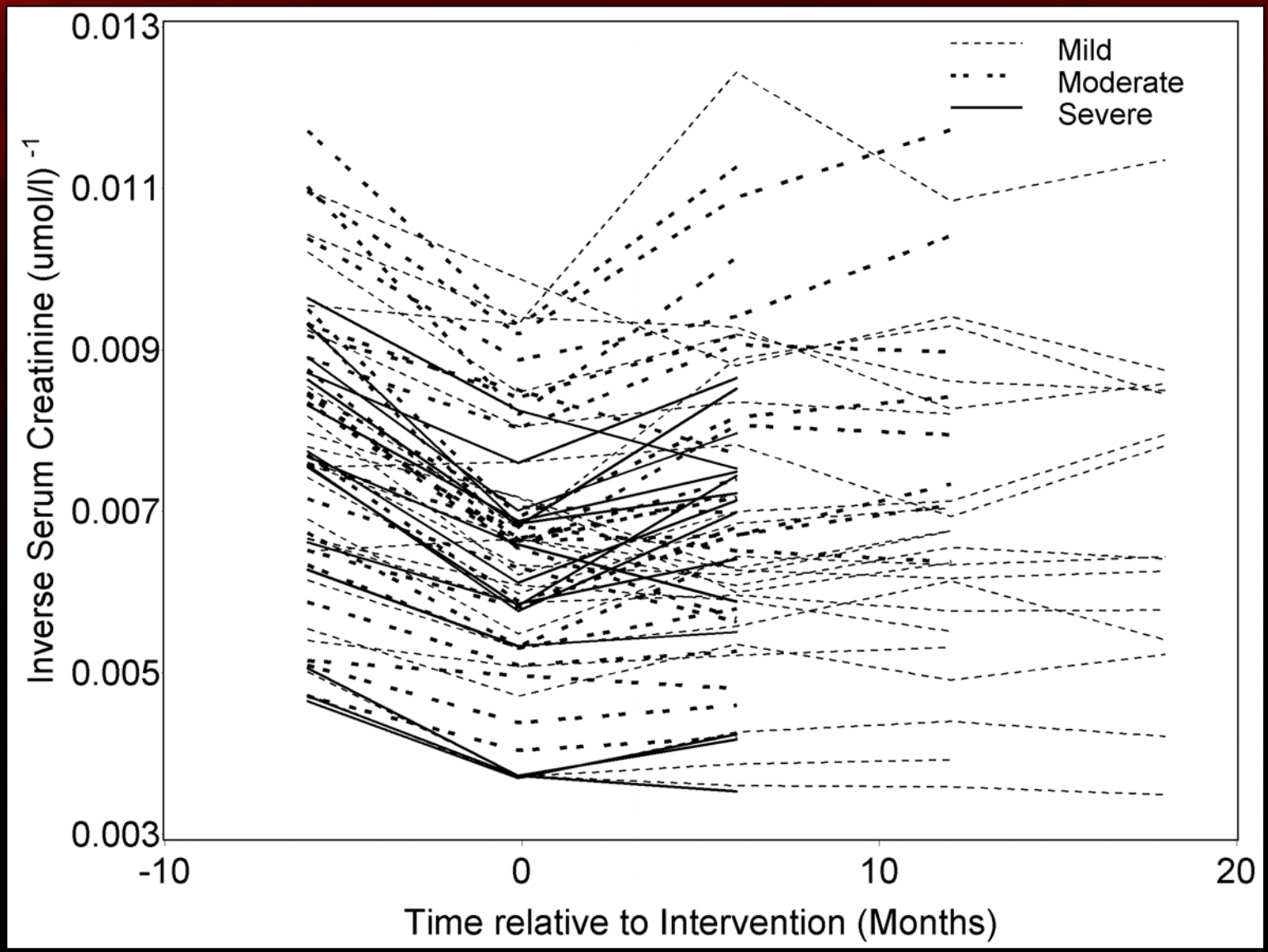
RESULTS at 6 months

Level of pre-intervention CRI

	K-DOQI 3A	K-DOQI 3B	K-DOQI 4	Total
Improved	12(52%)	8(32%)	5(33%)	25(40%)
Stabilized	11(48%)	15(60%)	10(67%)	36(57%)
Unchanged decline	0(0%)	2(8%)	0(0%)	2(3%)
Total	23	25	15	63

97% of patients had renal function improved or stabilized at 6 mos.

Regression Lines



Filter Contents

Macroscopic embolic contents present in 38/63 filters (60%)

Filter contents	Improved	Stabilized or Unchanged Decline	Total (%)
Positive	20	18	38 (60%)
Negative	5	20	25 (40%)
Total	25	38	63 (100%)

Patients with positive filter contents had significantly improved outcome (p= 0.01)

Primary Aims of the RESIST Study:

1. Determine whether embolic protection with the **AngioGuard XP Short Tip** device during stent implant ± **ReoPro** results in:
   a. Retrieval of atheroembolic material…amount
   b. Improved renal function at 1 month post-procedure
   c. Evidence of decreased injury in the kidney(s)
   d. Is it safe?

RESIST Trial

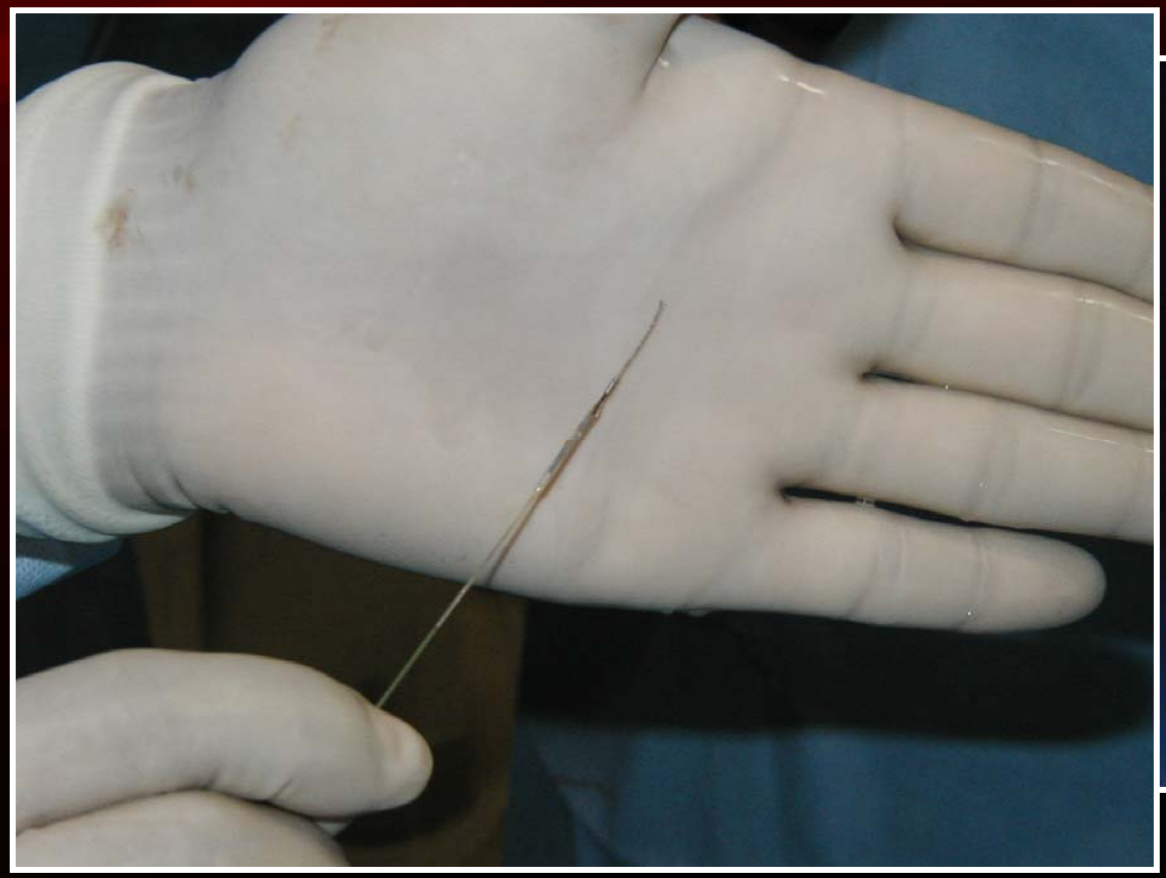
A Prospective Randomized Multicenter Study Comparing the Safety & Efficacy of Renal Artery Stenting with & without the use of a Distal Protection Device (AngioGuard) and with & without the use of ReoPro.

- **Multi-center, prospective, randomized, feasibility trial**
- **100 patients stented with PALMAZ® GENESIS® Stent**
- **50 patients randomized to stent + ANGIOGUARD™ and 50 patients to stent alone**
- **50 patients randomized to receive ReoPro**
- **Patient follow-up at 1 and 6 months**

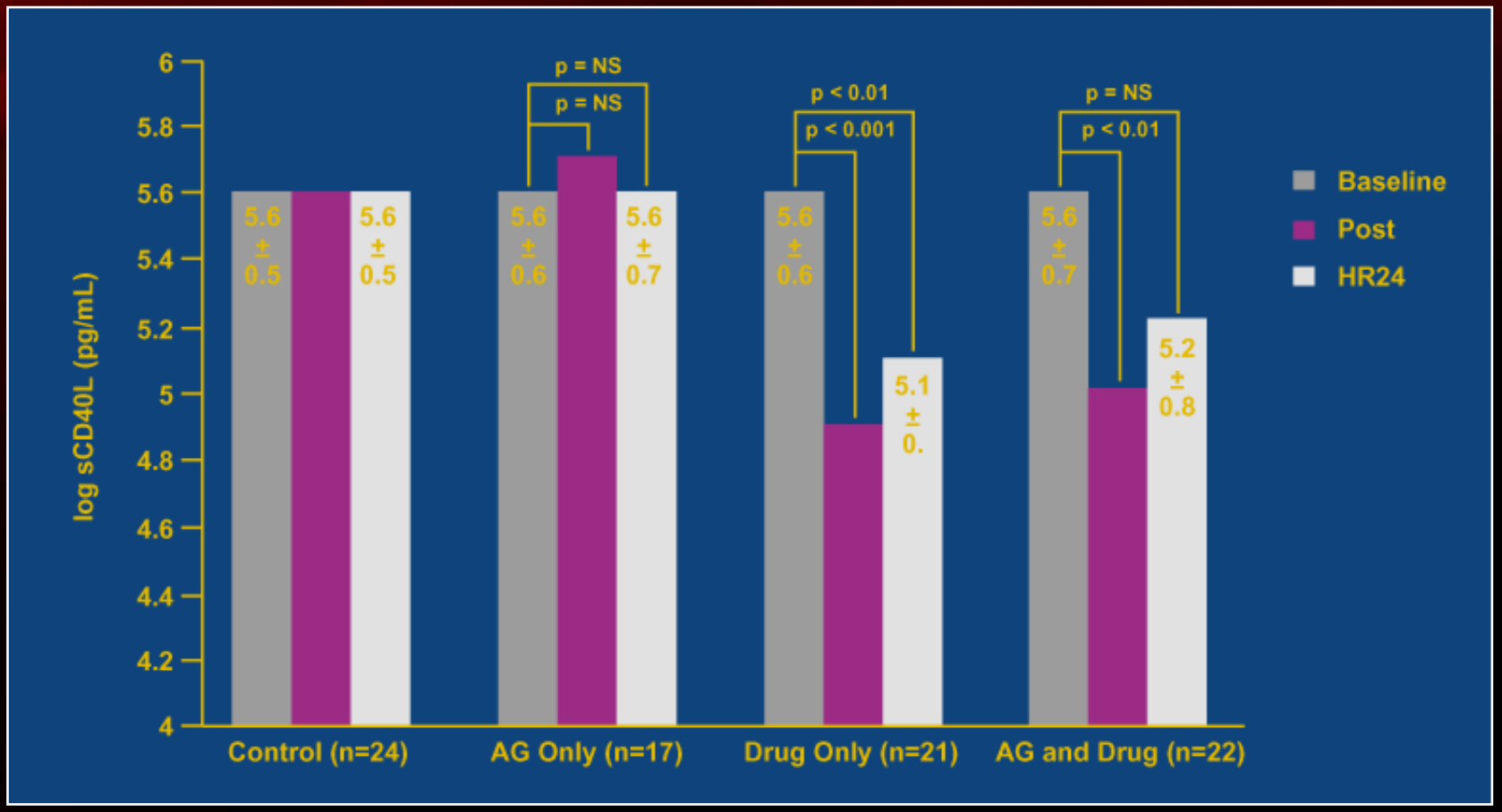
AngioGuard® Distal Protection

ReoPro Infusion	AngioGuard® Distal Protection	
	-	+
-	n=28	n=22
+	n=25	n=25

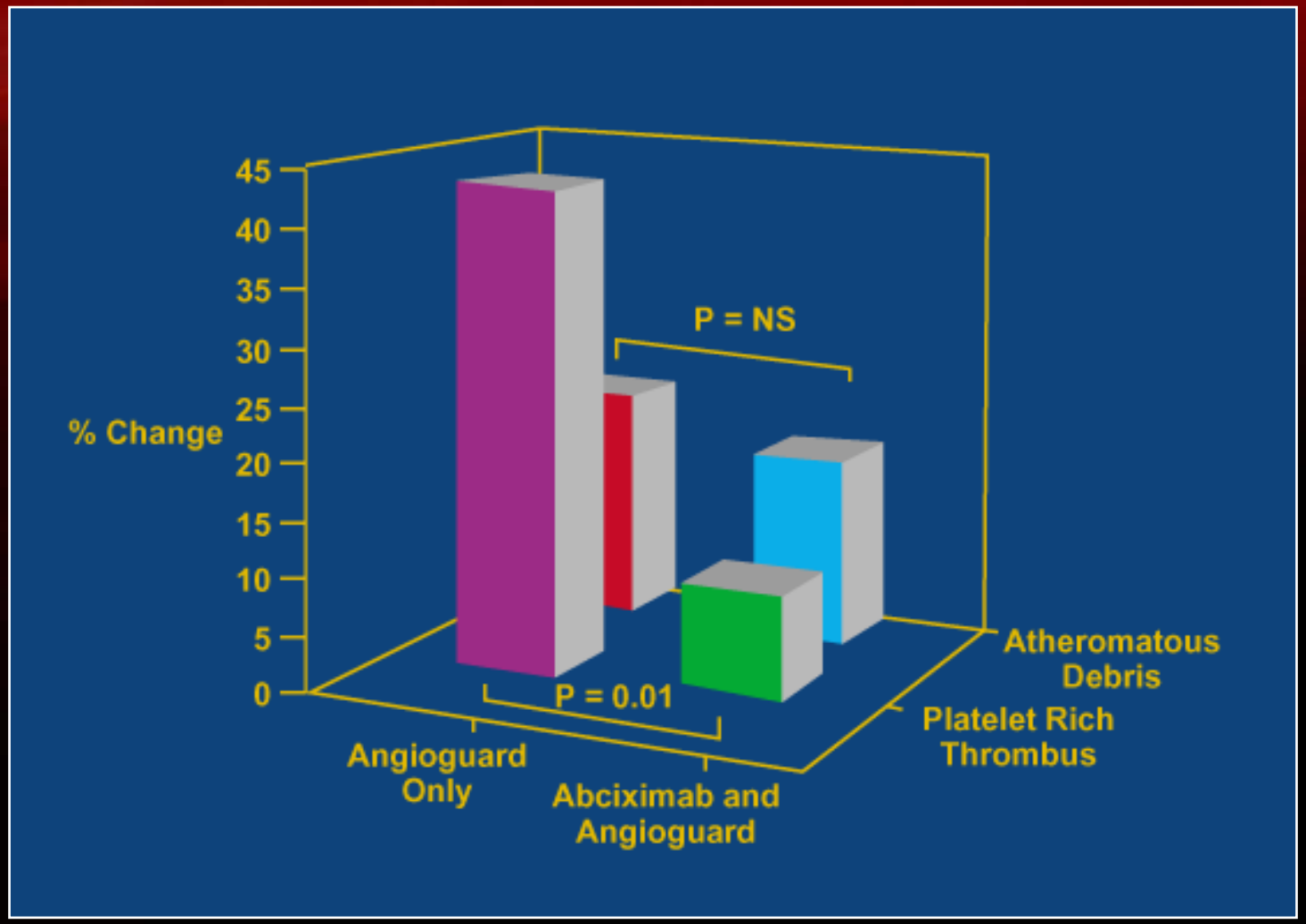
AngioGuard™ Short-Tip: RESIST Trial



RESIST Trial: Effect on Platelet Activation

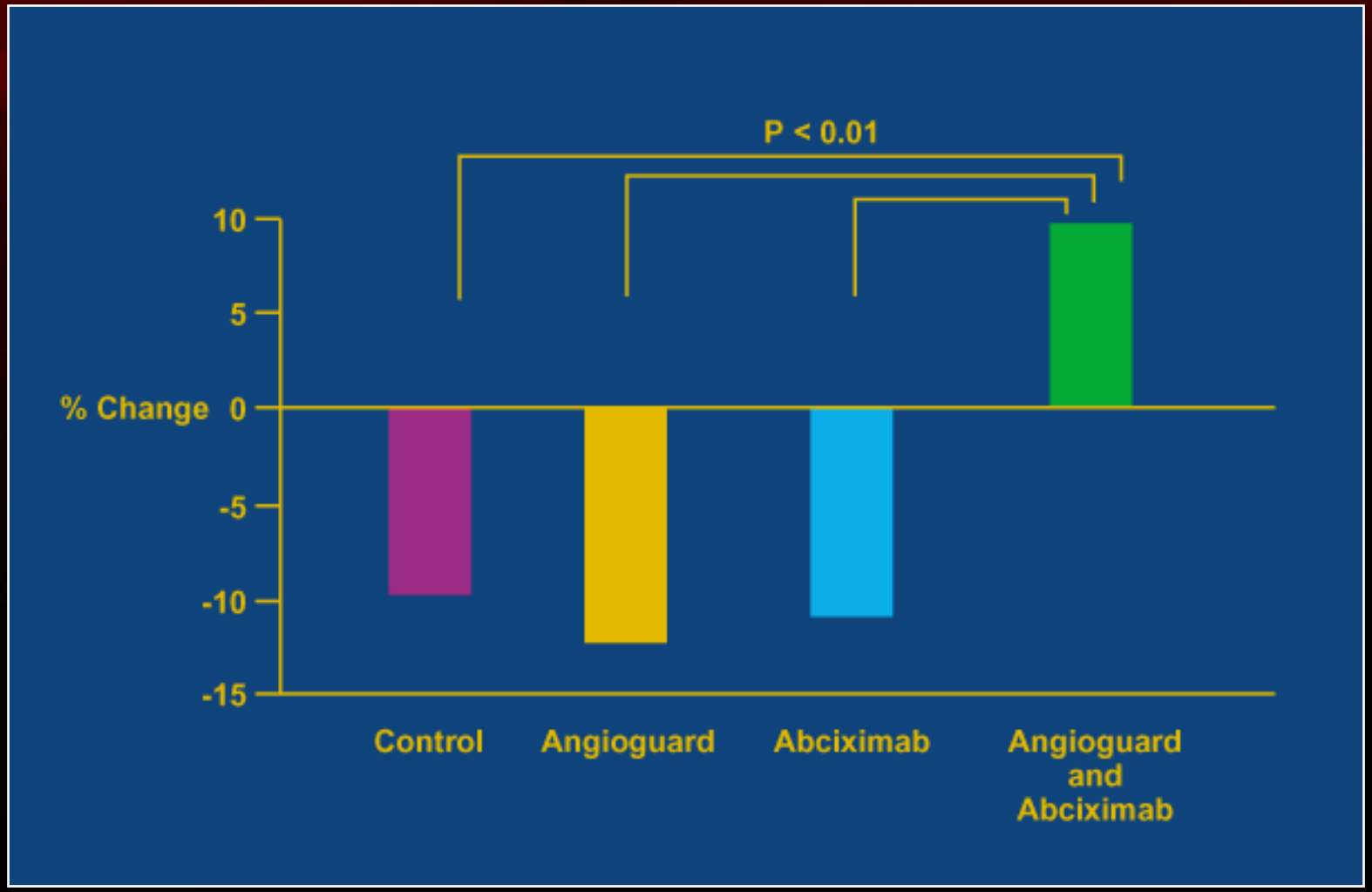


Soluble CD40 Ligand: Baseline, Post and 24 hr Post



% Patients with Platelet-Rich Thrombus and/or Visible Atheroma in Filter

RESIST Trial: Percent Change in eGFR at 1 mo.



Potential Renal Biomarkers

NEPHRON-SEGMENT	ABNORMAL FUNCT, MECHANISM TESTED	MARKER
GLOMERULUS	GFR	Serum Creatinine Creatinine Clearance Serum Cystatin C Serum β-2-microglobulin Serum Retinol-binding protein
	Basem. Membr. integrity	Collagen IV
PROXIMAL TUBULE	Substance release	Urine α-Glutathione S-Transferase (α-GST) Human Kidney Injury Molecule-1 Neutrophil Gelatinase-associated lipocalin
	Substance absorption	Urine β -2-microglobulin
DISTAL TUBULE	Substance release	π-Glutathione S-Transferase (π -GST) H-Fatty Acid-Binding Protein
COLLECTING DUCT	Papillary Function	Renal Papillary Antigen-1 (RPA-1)

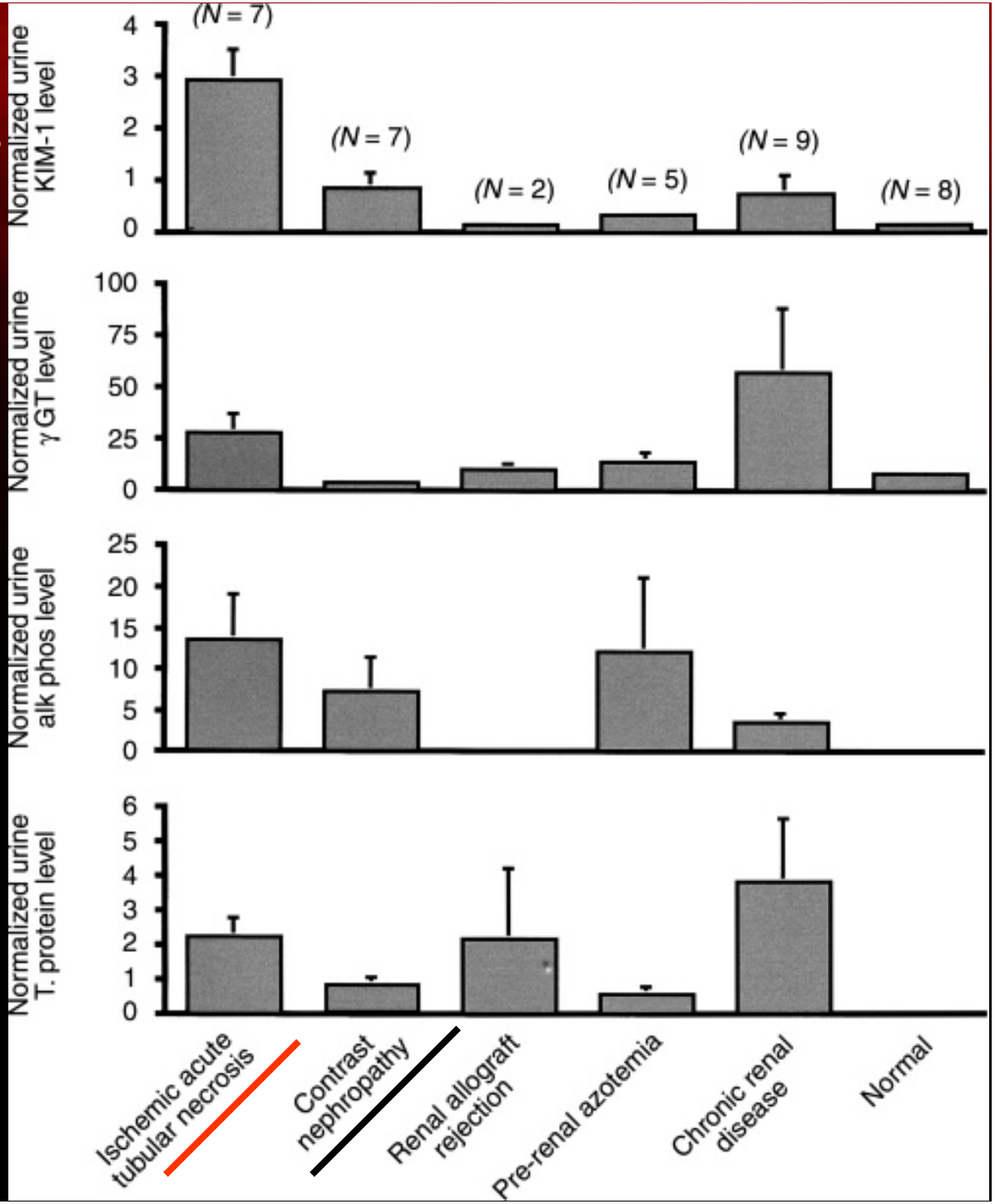
KIM-1

Kidney Injury Molecule

γGT

Alk Phos

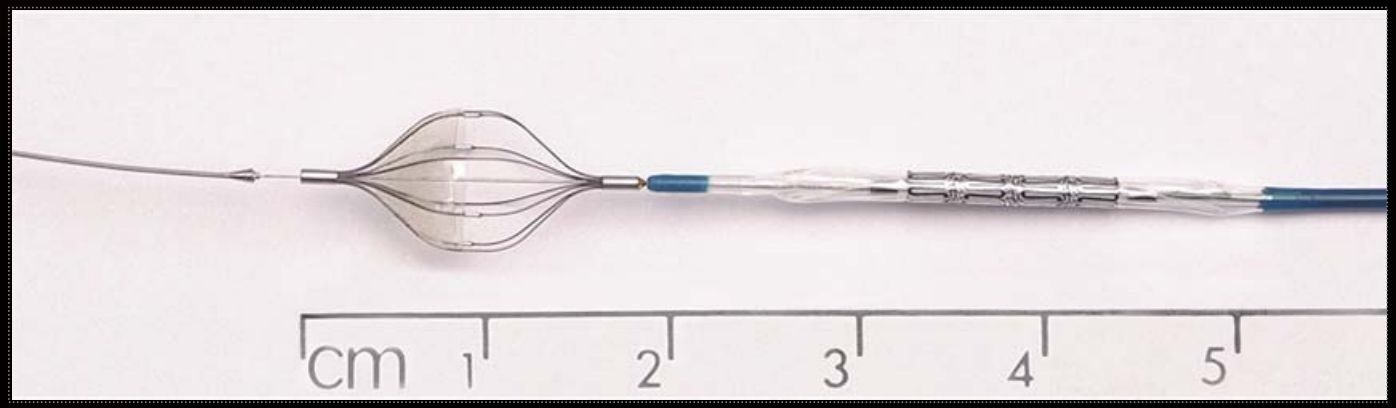
T-Protein



Kidney Int. 2002
62(1):237-44

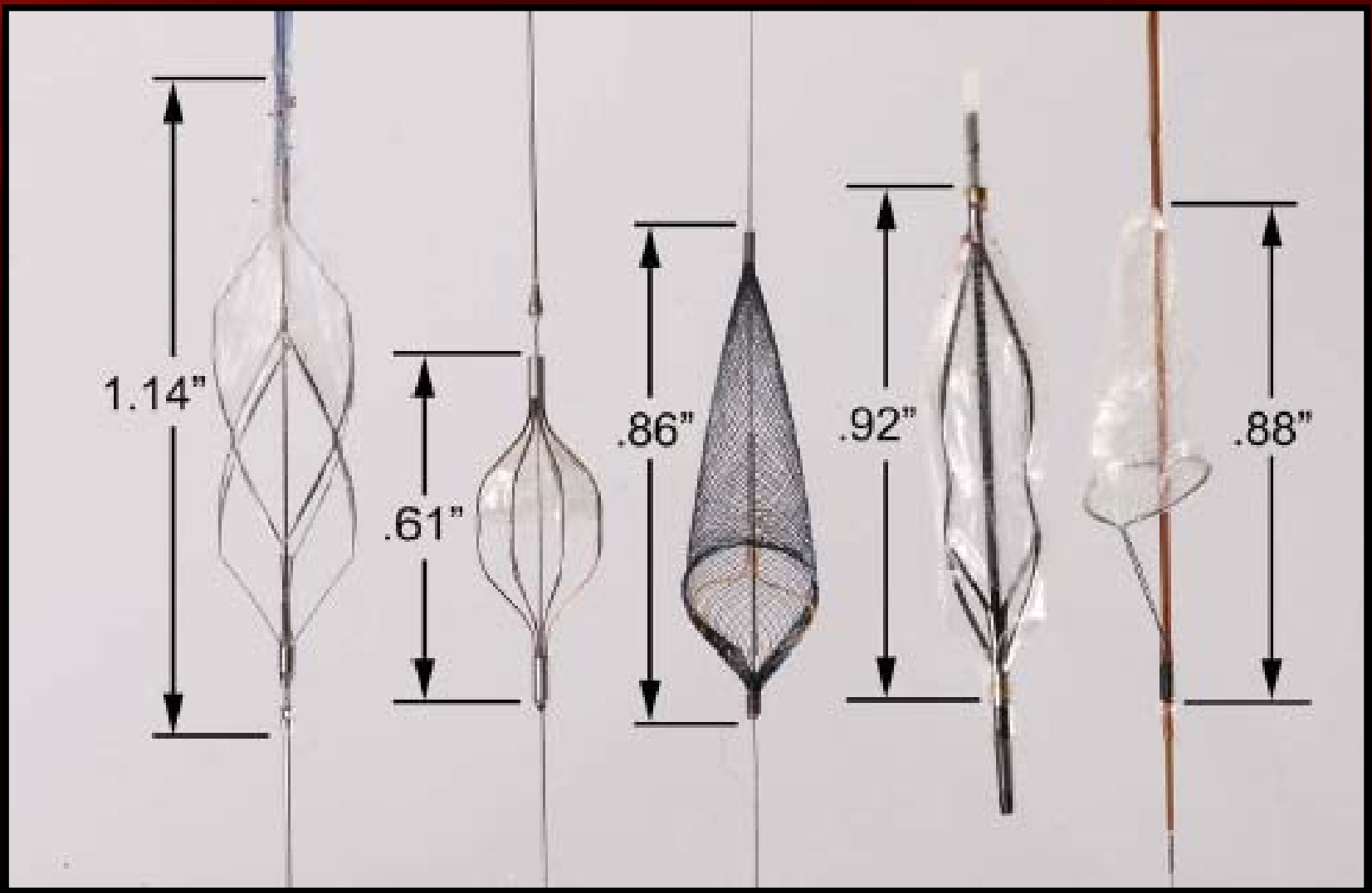
Length of stent-EPD system

- The current combined length of the filter-balloon-stent systems are between 30 and 35mm
- The main renal artery is ~40mm long in adults but early branching occurs in 20-30% of cases

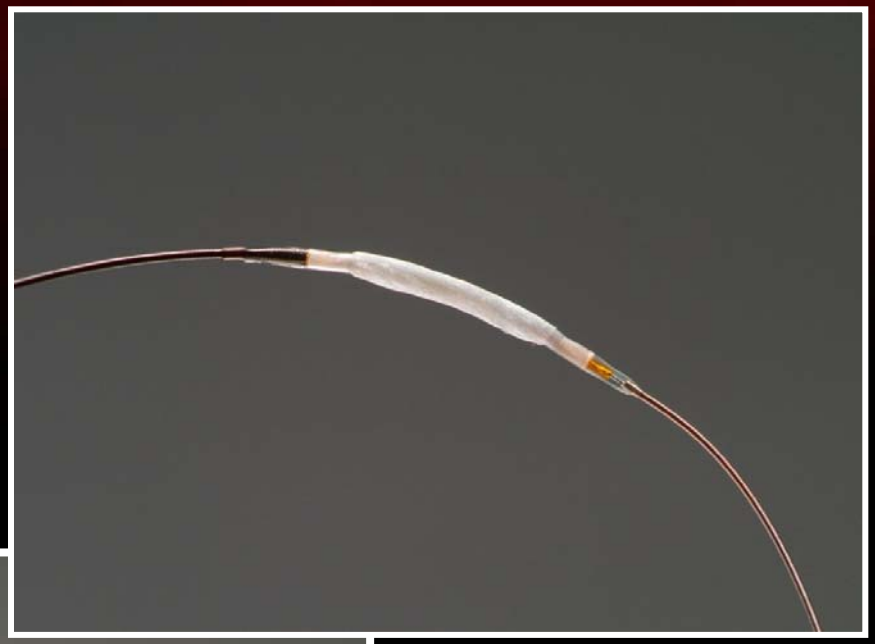


Courtesy of M.Jaff and A.Holden

Landing Zones & Filter Lengths



VIVA III Trial: FiberNet EPD



CONCLUSIONS

- **Protected renal artery stenting with a distal filter is technically feasible…most of the time**
- **Embolic protection *appears* to impact renal preservation in pts. with IN…RCTs are needed**
- **The potential role of platelet activation in the pathophysiology of atheroembolization and progressive renal dysfunction requires further study**
- **Renal-specific markers of injury are needed**
- **A renal-specific EDP system is needed**