The real role of renal protective devices

Michael Wholey, MD, MBA

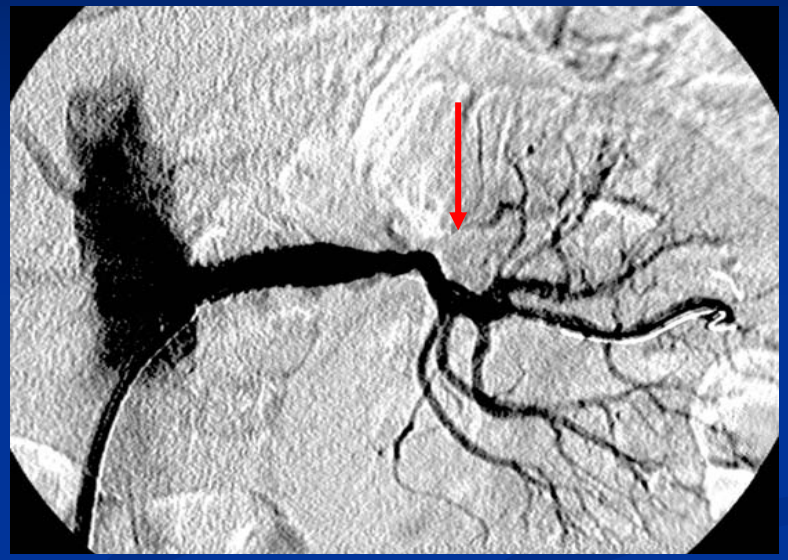
Central Cardiovascular Institute of San Antonio

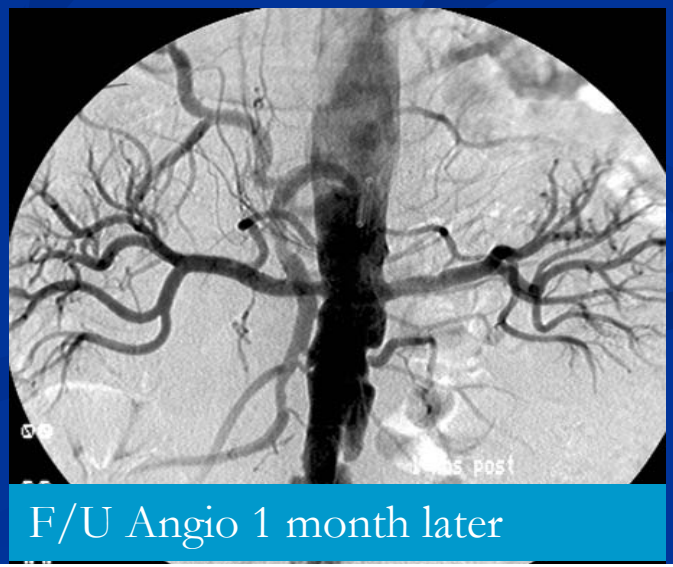
Saturday June 28 at 5:50
Session 7: Renal Artery Stenting Speaker 12:00:00 AM
Time allowed: 5 minutes

Are Embolic Related Complications from Renal Artery Stenting A Serious Problem ?

- **Immediate Procedure-Related Complications of Distal Emboli**

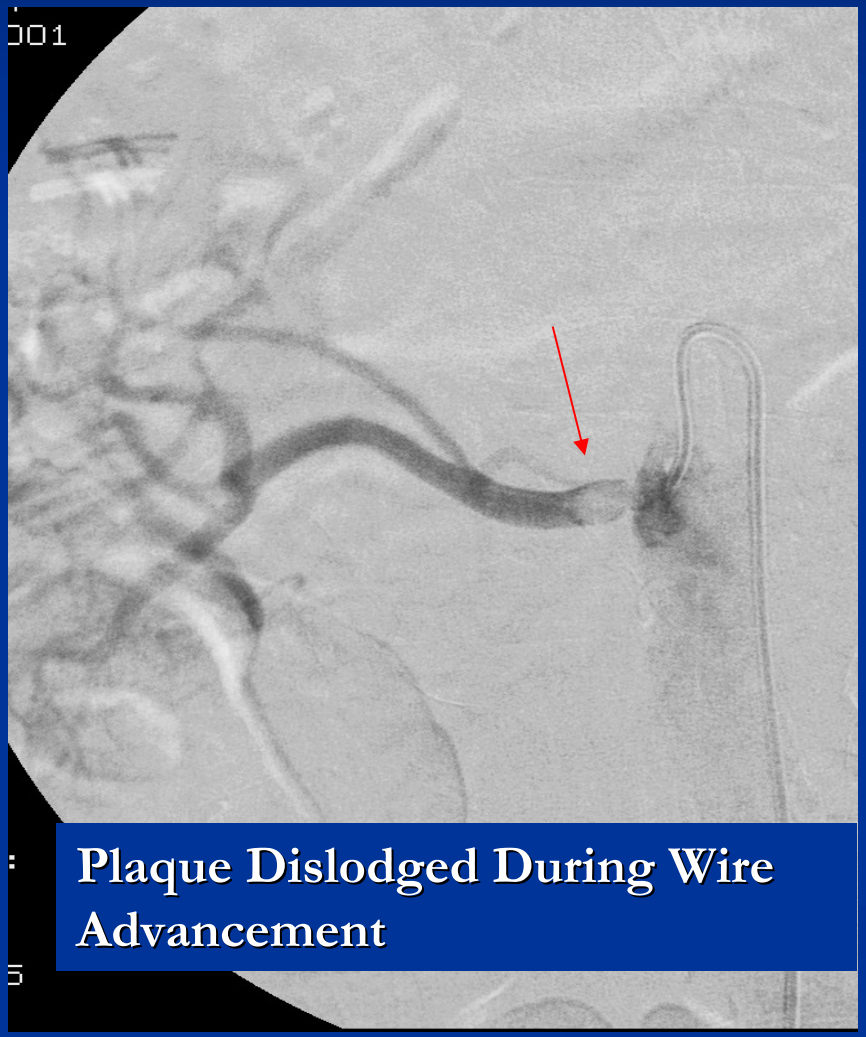
Temporary Loss of Upper Branch Immediately from Embolic Debris





F/U Angio 1 month later

Need for Embolic Protection



Plaque Dislodged During Wire Advancement

ASPIRE-2 Trial

- ASPIRE-2 study reported that embolic events occurred in 6.3% of renal stenting procedures.
  - Importantly, in-hospital clinically-evident athero-embolization occurred in only 1.4% of cases; and these were not associated with an increase in post-stent serum creatinine values or with mortality.

Are Embolic Related Complications from Renal Artery Stenting A Serious Problem ?

- **Immediate Procedure-Related Complications of Distal Emboli**
  - Not very common
  - New technology with 0.14” wires and stents, lower profile

Are Embolic Related Complications from Renal Artery Stenting A Serious Problem ?

Immediate Procedure-Related Complications of Distal Emboli

- **Rate of Worsening Renal Function and/or Hypertension following Stents**

RESULTS OF RENAL STENTING IN TREATING RAS HTN

Author	Pt. No	Cured	Improved	Stablize	Failed
Rodriguez	102	14%	59%	22%	4%
Iannone	63	4%	35%	53%	18%
Dorros	58	7%	52%	--	40%
Boisclair	33	6%	61%	33%	--
Shannon	21	29%	19%	29%	26%

RESULTS OF RENAL STENTING IN RAS RENAL DYSFUNCTION

AUTHOR	Pt No.	Improved	Stabilized	Worsened
Rees	263	34%	39%	27%
Dorros	58	28%	28%	43%
Harden	32	34%	34%	28%
Iannone	29	36%	46%	18%
Taylor	22	33%	29%	38%
Shannon	21	43%	29%	29%
Boisclair	17	41%	35%	24%

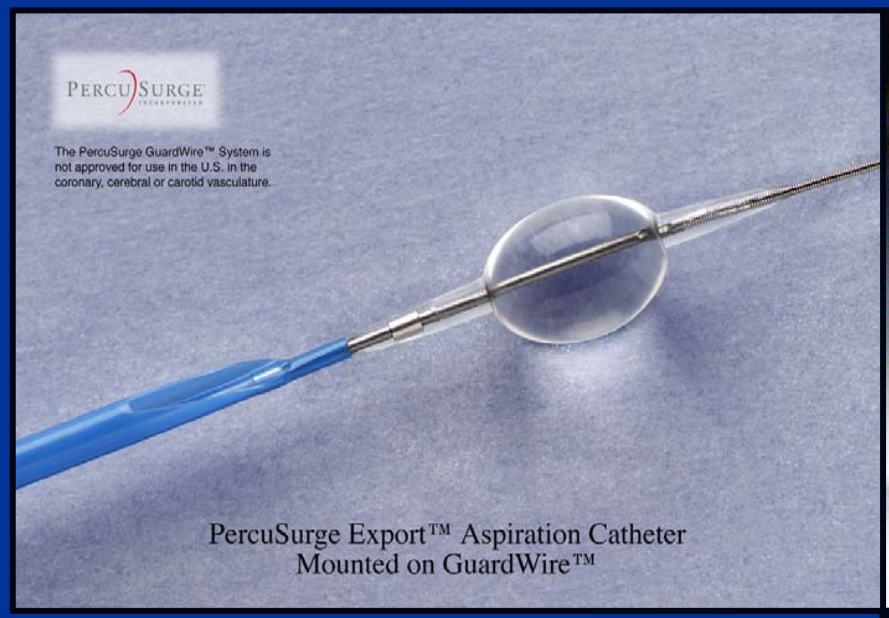
Embolic Protection during Renal Artery Stenting *Challenges*

- **Which System?**
  - Filters vs Balloon Occlusion

Distal Protection

N = 28

- Debris retrieved in all patients.
- Particles = 98.1 ± 60 (13 to 208).
- Size = 201 ± 76 μ (38 to 6,206 μ).



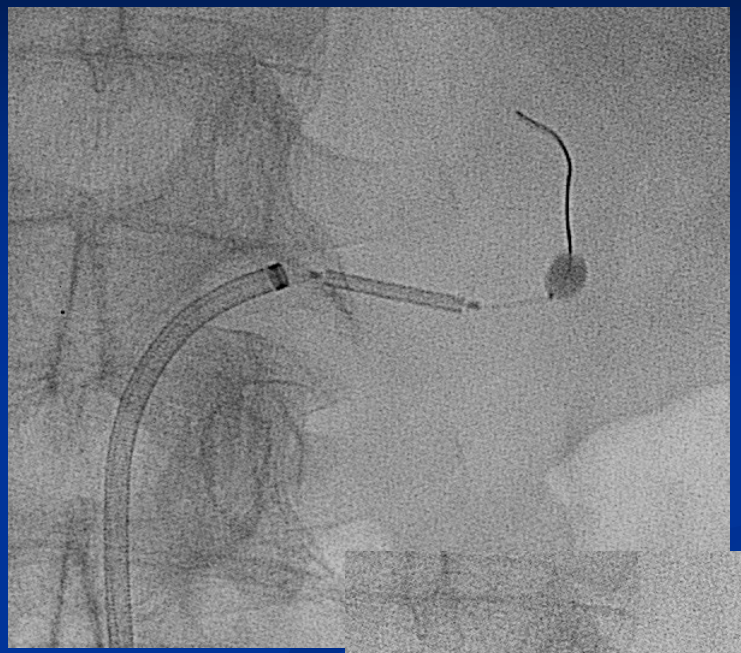
Henry M, et al; in press.

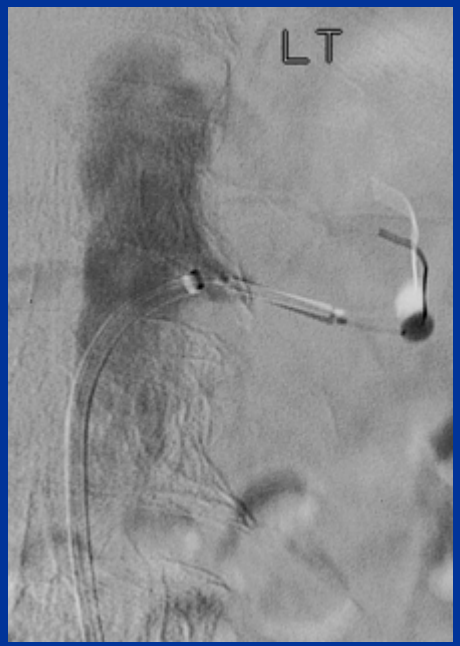
ATHEROEMBOLI DURING RENAL ARTERY ANGIOPLASTY: AN *EX VIVO* STUDY

<10 µm	500–1000 µm	>1 mm
1,265,348 ± 1,093,359	4.7 ± 1.8	1.9 ± 1.2
780,187 ± 515,886	4.0 ± 1.3	0.9 ± 0.9
942,284 ± 1,413,177	4.3 ± 2.4	1.3 ± 1.3
	3.4 ± 2.3	1.1 ± 1.1
2,987,855	**14.8 ± 6.0**	**4.8 ± 2.0**

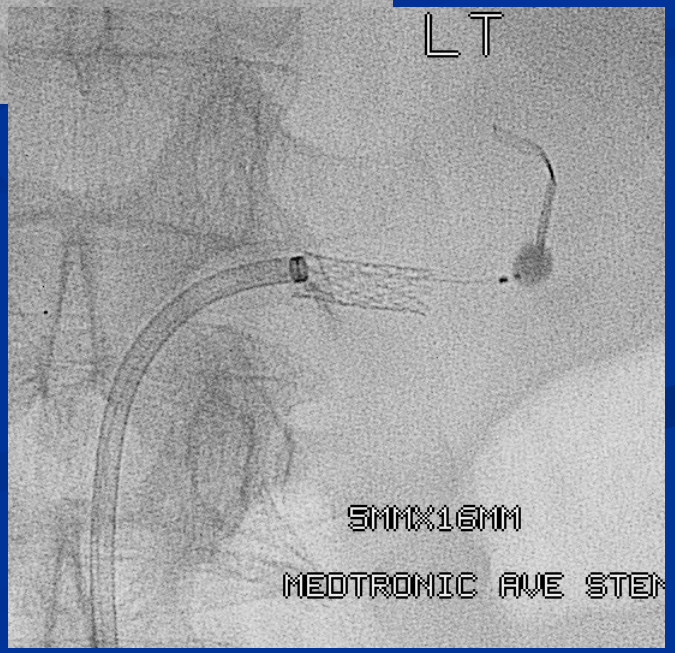
HIRAMOTO J, J VASC SURG. 2005 JUN;41(6):1026-30

PercuSurge Nightmare

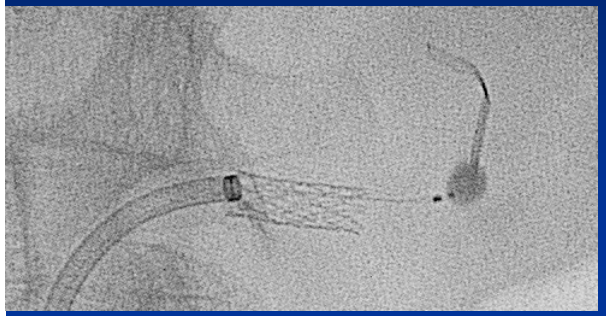


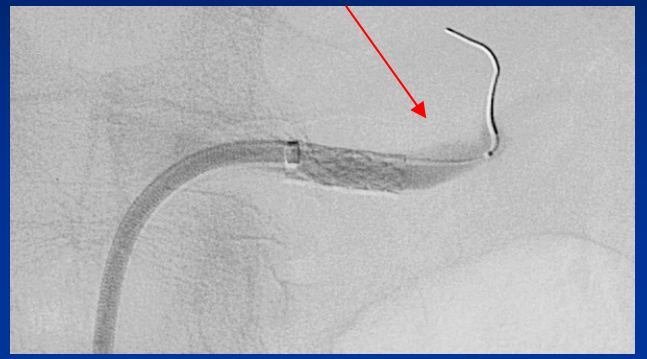


Occlusion makes it difficult to see entire lesion to stent

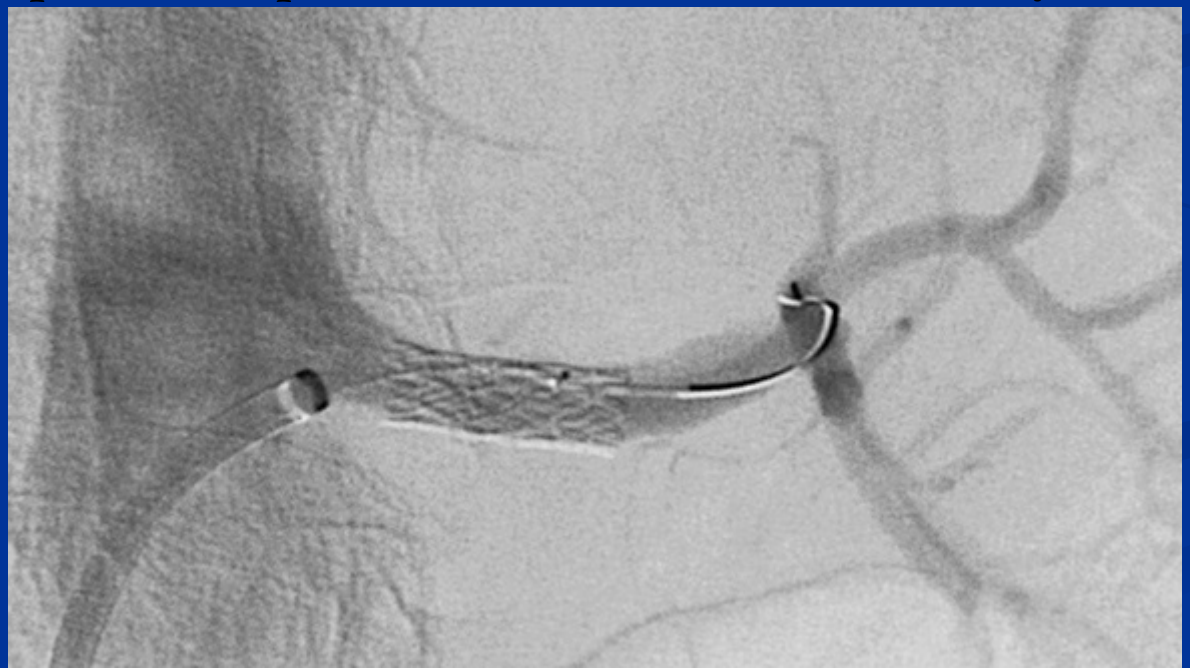


PercuSurge Nightmare





Balloon would not deflate. Had to cut off the proximal tip and let the balloon deflate slowly



<u>Dissection:</u> From stent edge or from occluding balloon

-Restenosis 6 months later

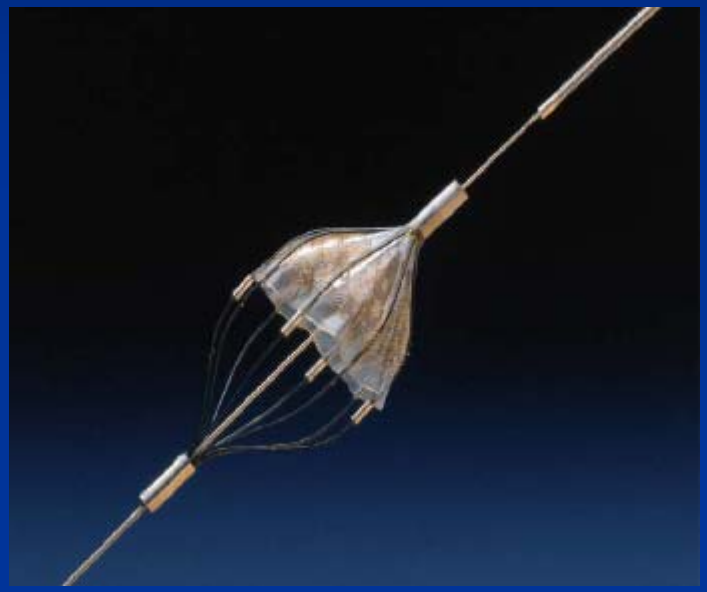
Renal Protection: Controversy

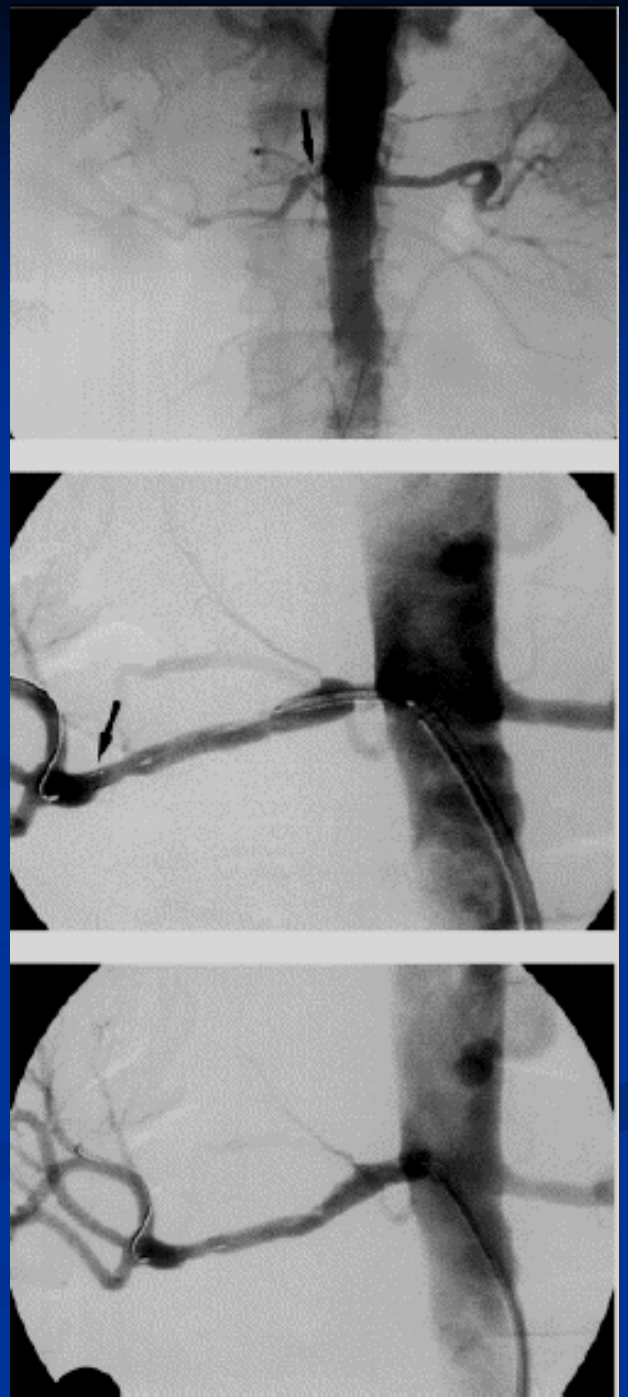
- Thomas Sos Argument: Role of cholesterol crystals
  - Slip through most filters
    - Are occlusive devices better
  - Ostial location of cholesterol
    - Emphasize importance of careful manipulation
      - Probably most important part of procedure: guide manipulation around renal artery ostium
    - Risk of causing emboli by passing distal protection past the lesion to create
    - Which is better dimension?
      - Diameter filter delivery system 3.5 Fr
      - Diameter of renal stent on 0.014" platform

Renal Protection Devices

- Occlusive
  - PercuSurge
  - Fibernet: →Will it have the same occlusive problems as above plus the risk of becoming caught in stent struts?
- Filters
  - Cordis Angioguard *-Most Experience
  - eV3 Spider
  - BSX EPI
  - Abbott Mednova

Distal Protection in RAS





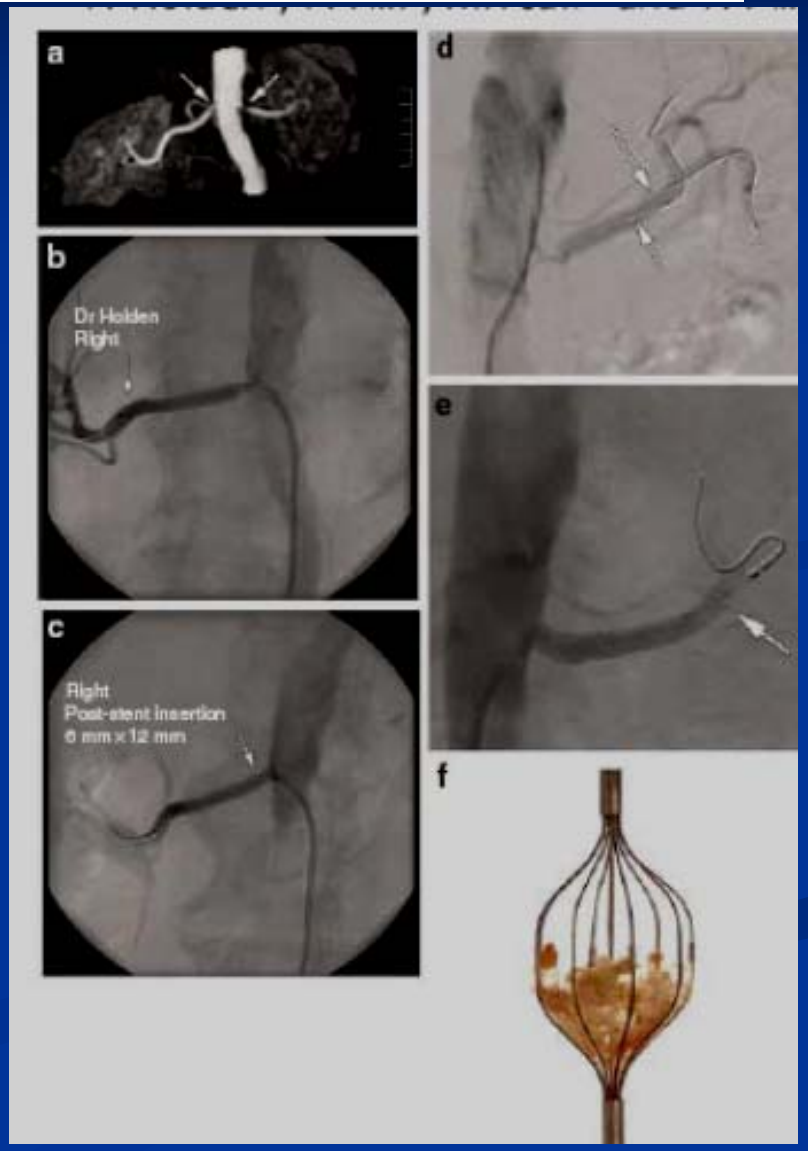
Holden A and Hill A. J Vasc Surg 2003;38:962-8.

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]

63 patients

- 83 arteries with atherosclerotic RAS
- All with CRI and deterioration in renal function within prior 6 months
- All underwent PTA/Stent with embolic protection
- Only 3% of patients had inexorable deterioration in renal function



Kidney International 2006;70:948-955.

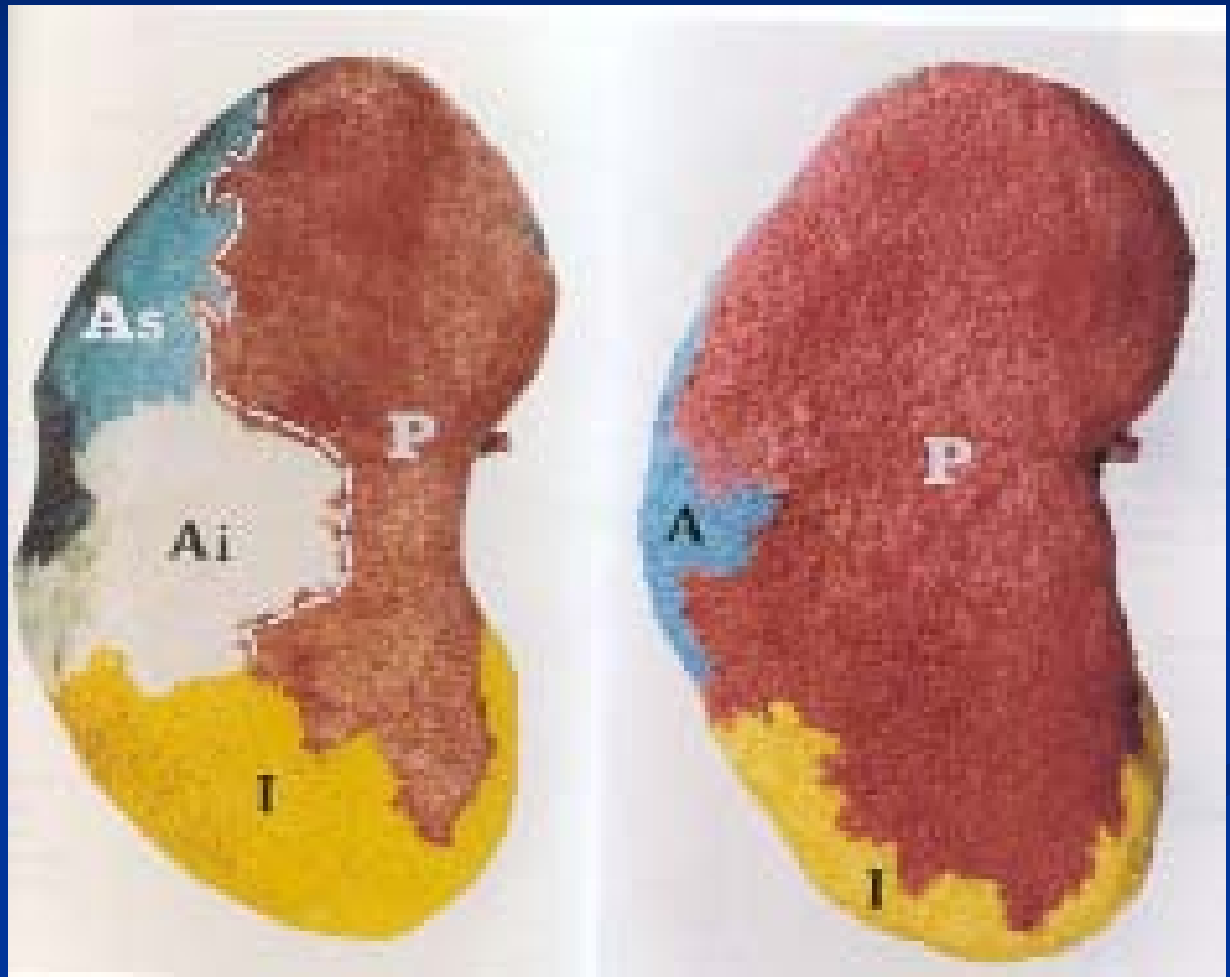
Embolic Protection during Renal Artery Stenting *Challenges*

- **Which System?**
  - Filters vs Balloon Occlusion
- **Technical Issues**
  - Ability to traverse lesion
  - Distal landing zone limited
    - early bifurcation
  - Support provided by Guidewire
    - 90+ degree angle, as opposed to “in-line” position
    - Spasm source
  - Maintenance of stable guiding catheter position
  - Risk of snagging the filter on the stent edge

Embolic Filter Issues:

- Which Vessel do you protect ?

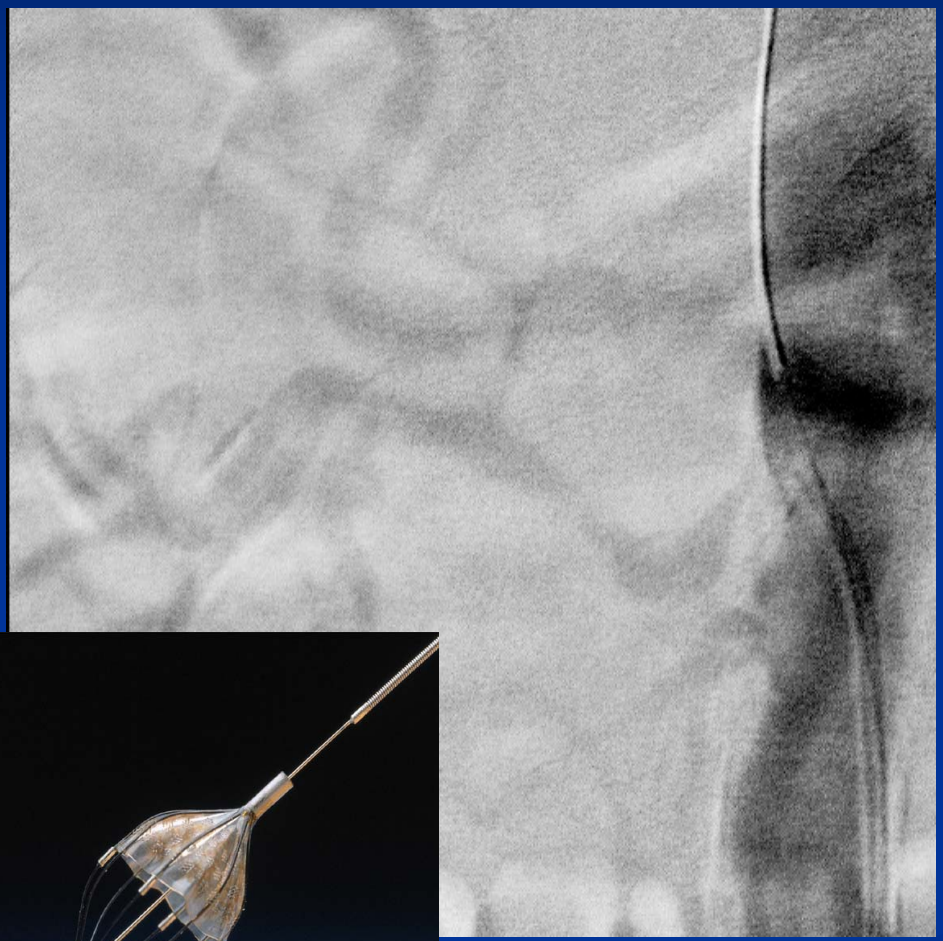
Which branch vessel needs protection the most?



Embolic Filter Issues:

Can the Filter Traverse the Difficult Lesions?

Does the System Provide Enough Support ?



Published Data

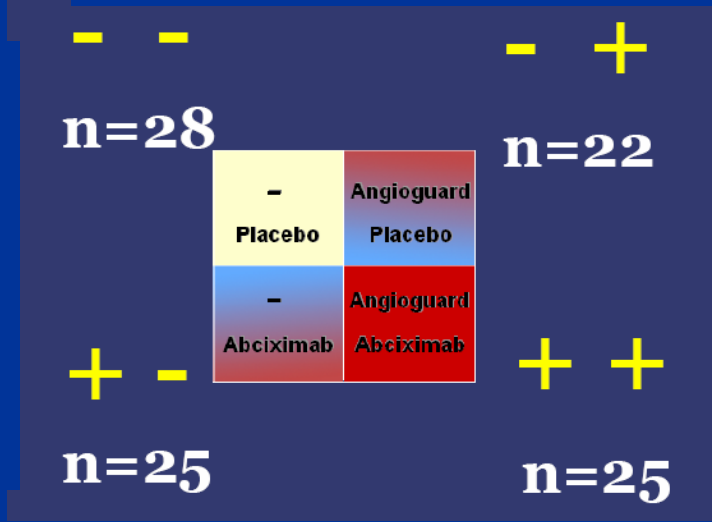
- PercuSurge Data
- RESIST
- CORAL

RESIST

Prospective, Randomized, Multi-Center Study Compaing the Safety and Efficacy of Renal Artery Stenting With and Without the Use of a Distal Protection Device and With/Without the Use of a Platelet Aggregation Inhibitor—The Trial

- 5 center randomized trial
- AngioGuard designed specifically for renal arteries
- Primary Endpoint: Single kidney GFR
- 2 x 2 design
  - +/- protection
  - +/- reopro

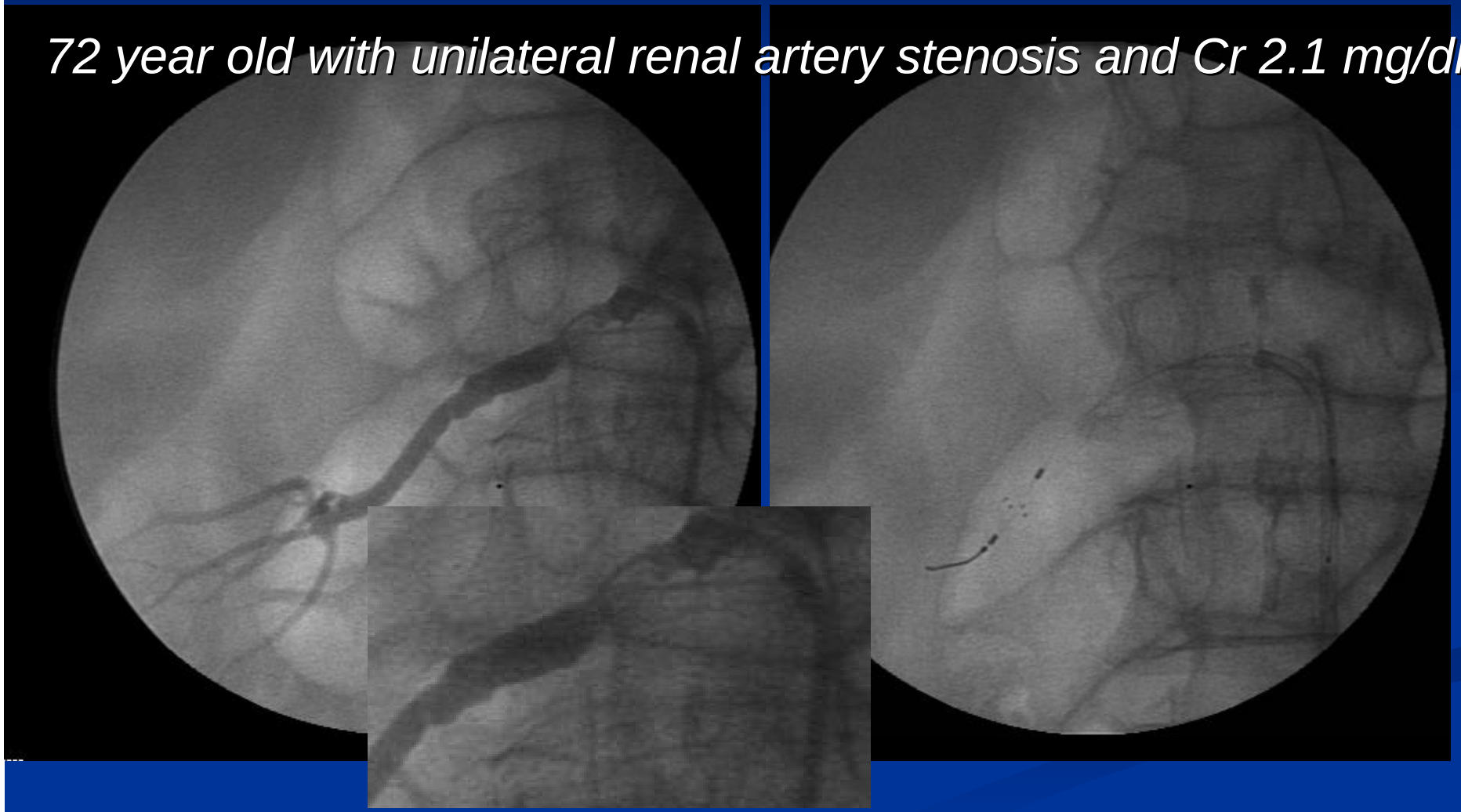
Angioguard Distal Protection



C Cooper

RESIST: initial experience

72 year old with unilateral renal artery stenosis and Cr 2.1 mg/dl



Slide courtesy of Chris Cooper, M.D.

C Cooper

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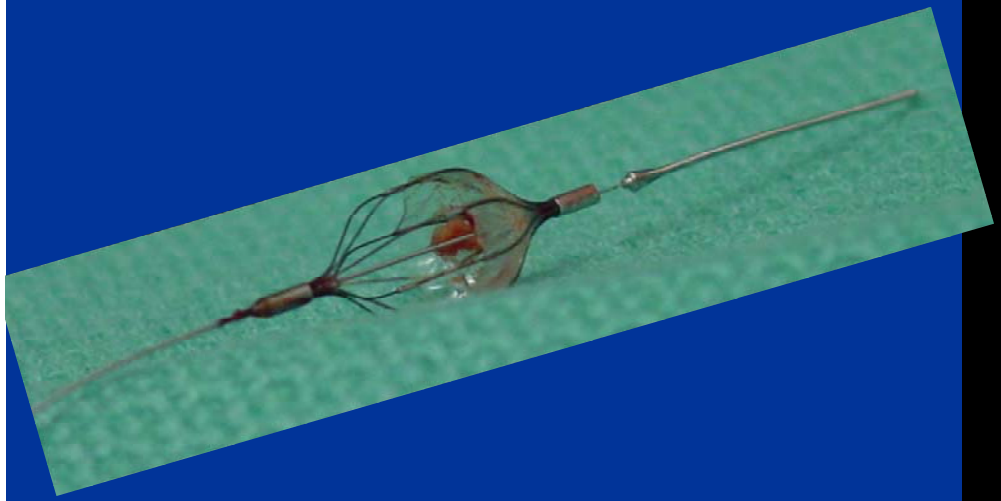
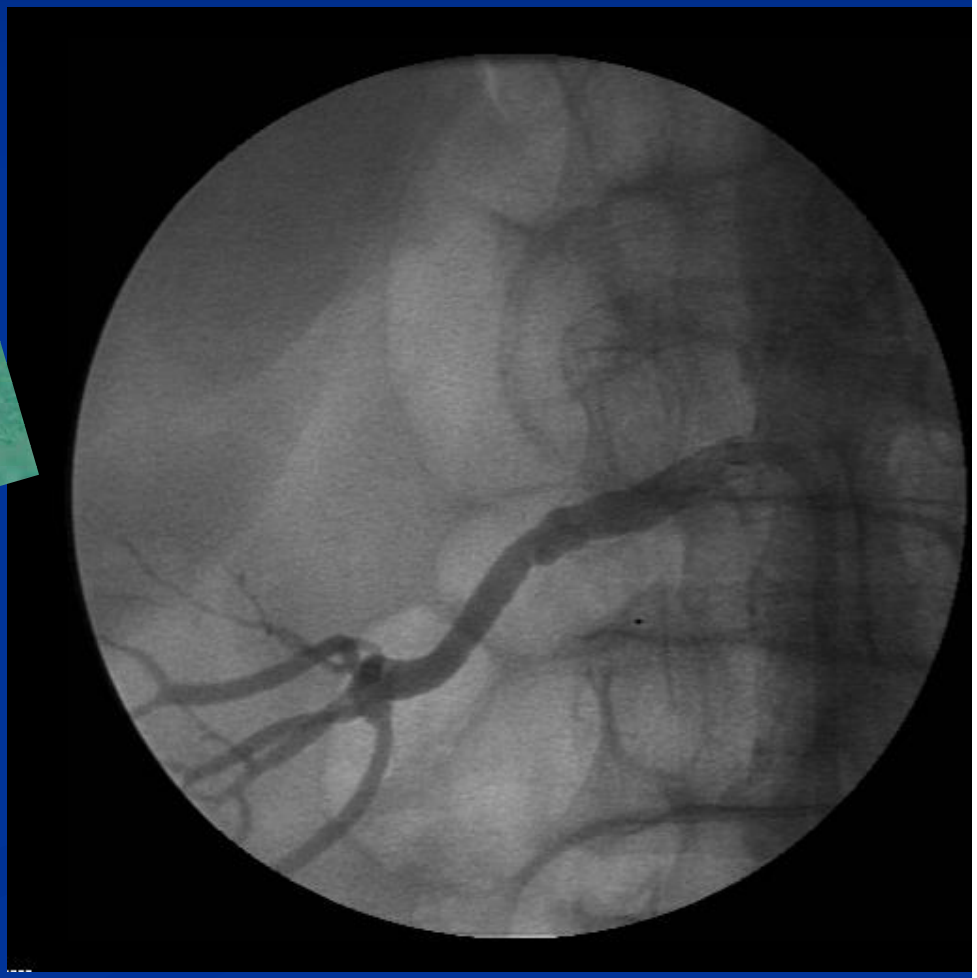
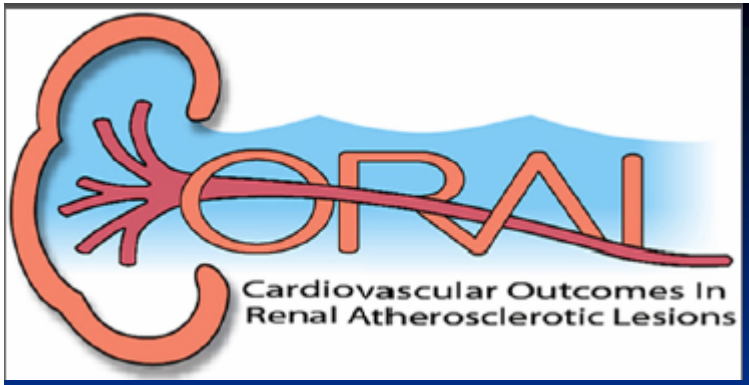




Slide courtesy of Chris Cooper, M.D.

RESIST Results

- There was a significant interaction between abciximab and embolic protection ($p < 0.05$), favoring combination treatment.
- Abciximab reduced the occurrence of platelet-rich emboli in the filters from 42% to 7% ($p < 0.01$). Major bleeding occurred in 30% of patients, although it was not significantly associated with abciximab use.



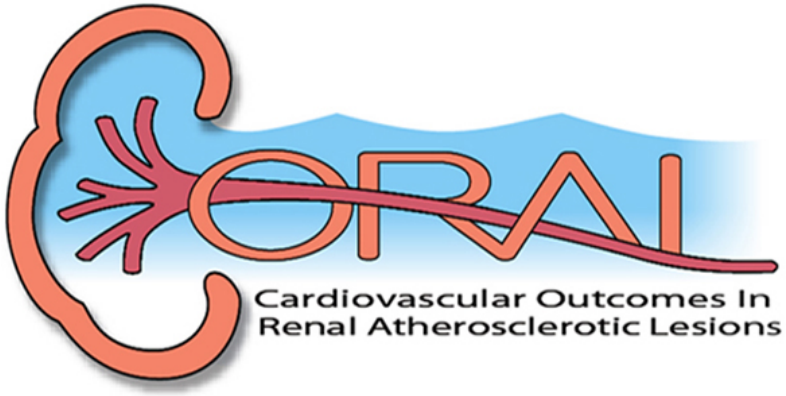
National Heart, Lung, and Blood Institute

Randomized trial sponsored by NIH

- **1,080 patients with renal artery stenosis and refractory hypertension**
- **85 Sites**
- **Up to 6 years of follow**
- **Primary Endpoint: *hard* cardiovascular and renal events**

Inclusion Criteria

- Systolic hypertension
  - ≥155 mm Hg
  - on ≥2 antihypertensive medication
- ≥1 renal artery stenosis
  - ≥60% with a 20 mm Hg systolic pressure gradient
  - ≥80% no pressure gradient required.

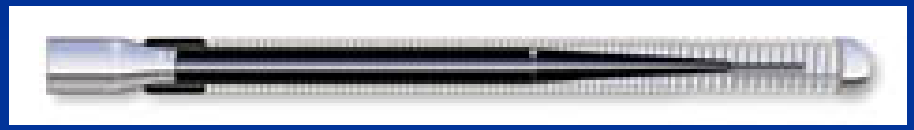


National Heart, Lung, and Blood Institute

Intervention

- Optimal Medical Therapy (OMT)
  - All receive ARB (Candesartan)
  - LDL, BP and HbA1c to guideline
- OMT plus Stent Revascularization
  - Angioguard embolic protection
  - Genesis balloon expandable stent

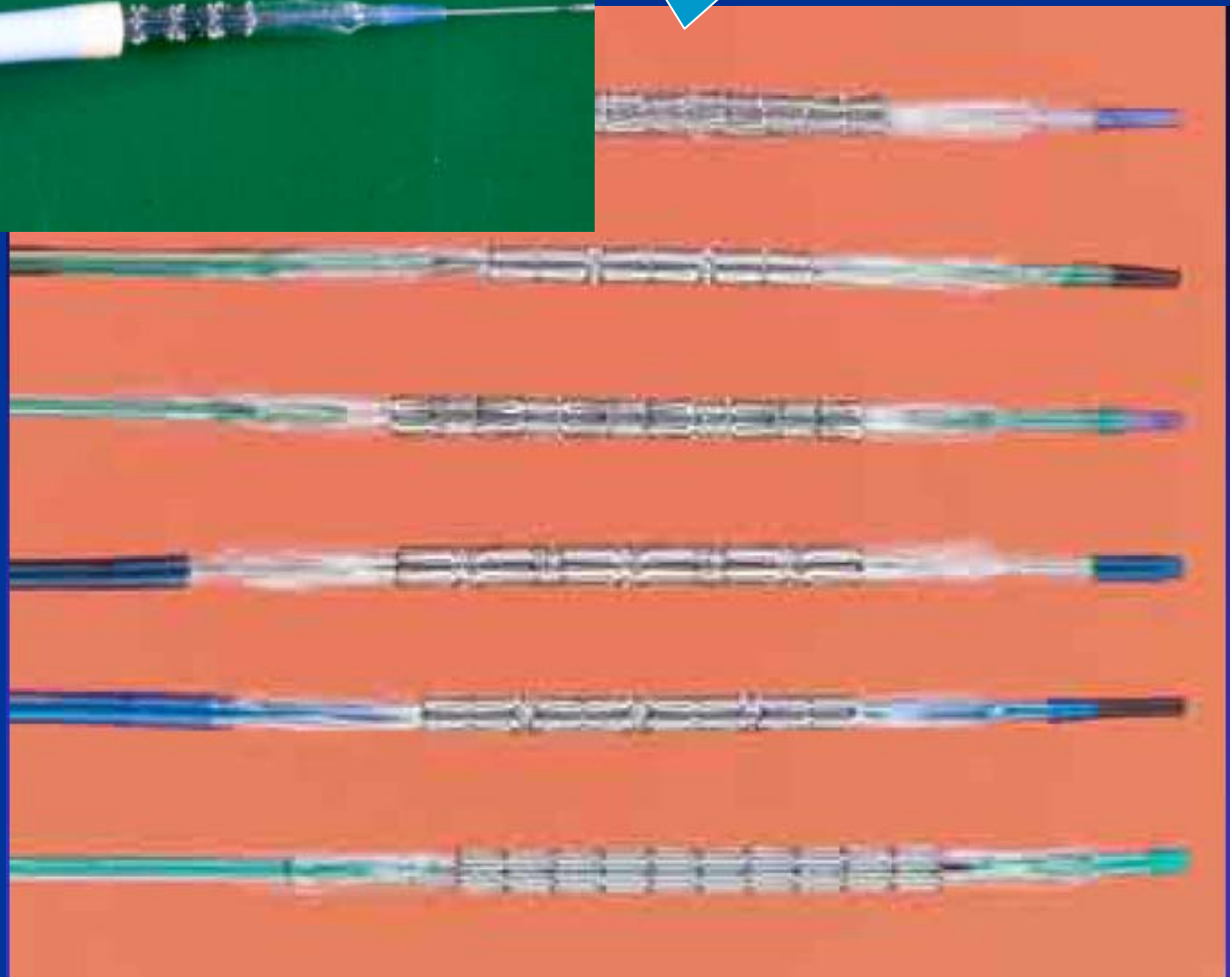
Unsung Heroes: Guidewires & Balloons



Adaptation Of 0.014” Medium And Heavy Weighted Wires

Adaptation of PTCA 0.014” Balloon Catheters

Stents: Going from 0.035” to 0.014”



Herculink Plus

Formula 414

Express SD

Genesis

Formula 418

Racer

The Future for RAS

- Distal Protection : A Reality ?
- Technology will have to improve
  - On going debate about particle size and impact
  - Will have to become less complex
- Randomized trial: expensive
- Imaging Technology identifying patients

Screening with CTA: May Determine Which Pts Need Distal Protection

Dangerous Aorta

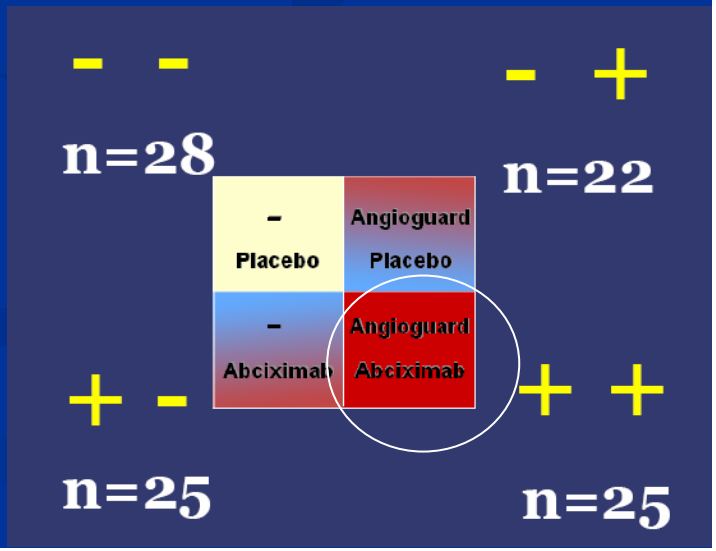
Dangerous Lesion

Conclusions

- Technology is young
  - First generation devices are promising
  - Early data limited to a few single centers
    - Trials limited: Coral pending
  - Industry and practicing physicians slightly hesitant to adopt widely

RESIST Results

- A decline in GFR was noted in patients treated with stenting alone, stenting and embolic protection, and stenting with abciximab alone
- However, with combination therapy, there was no decline in GFR ($p < 0.01$).



Increasing Role of Screening

- Role of Duplex Ultrasound of Kidneys for RAS
- Role of CTA in Diagnosing RAS
  - Good view of aorta and ostium
  - Presence of AAA
  - Plaque morphology
  - Status of distal branches with atherosclerosis
  - Pre-intervention: size of vessel, lesion length and landing zone for potential filter

RESIST Results

- Better outcome was seen with abciximab compared with placebo (0 vs. -10%; $p < 0.05$), whereas use of an EPD was not (-1 vs. -10%; $p = 0.08$).
  - There was a significant interaction between abciximab and embolic protection ($p < 0.05$), favoring combination treatment.
  - Abciximab reduced the occurrence of platelet-rich emboli in the filters from 42% to 7% ($p < 0.01$). Major bleeding occurred in 30% of patients, although it was not significantly associated with abciximab use.

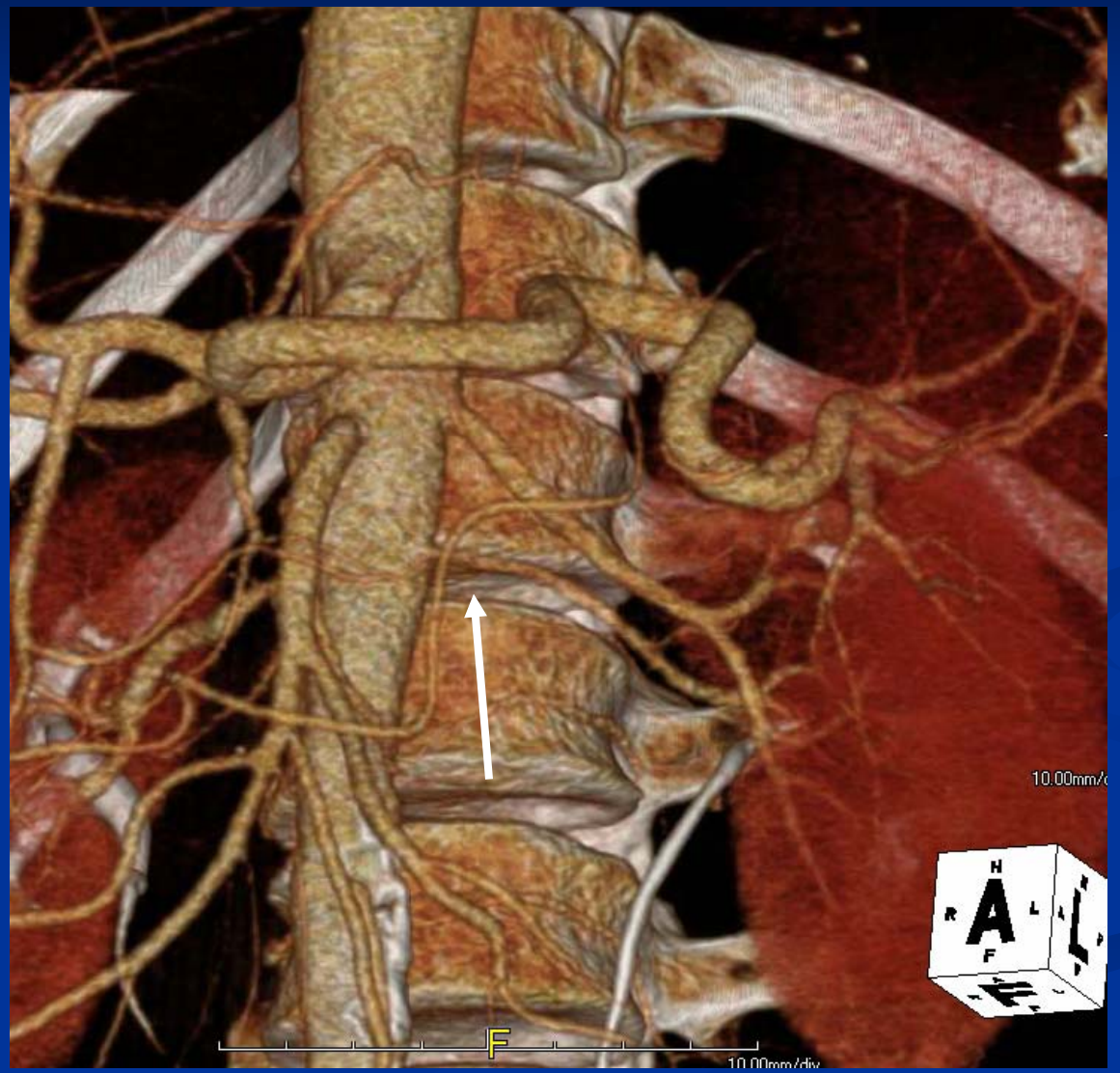
Embolic Protection and Platelet Inhibition During Renal Artery Stenting

- Randomized 100 patients undergoing renal artery stenting at seven centers to an open-label EPD, Angioguard, or double-blind use of abciximab, in a 2 x 2 factorial design.
- The main endpoint was percentage change in glomerular filtration rate (GFR) from baseline to 1 month.

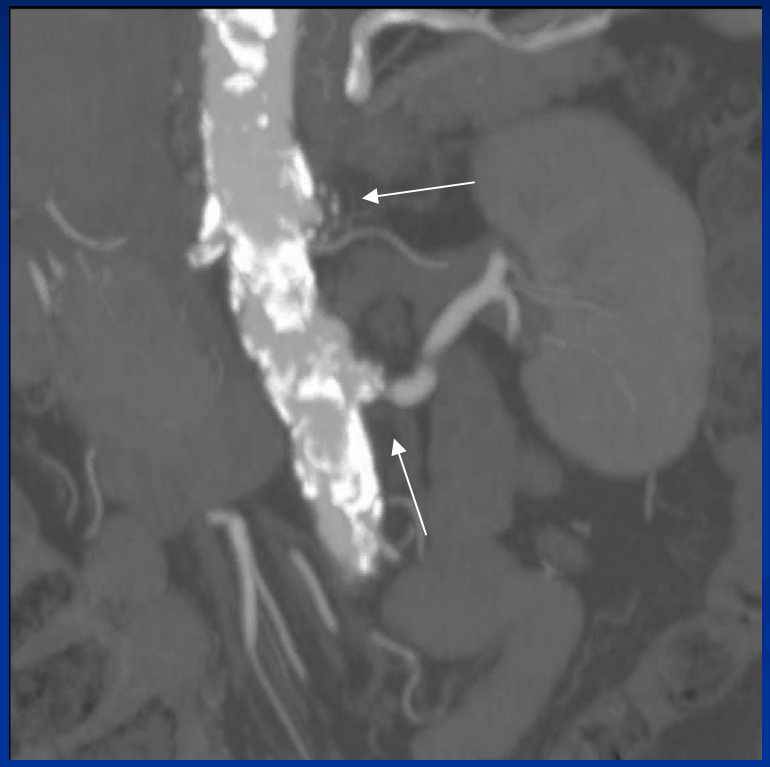
CTA in Diagnosing Renal Artery Disease

- Assess degree of renal stenosis
  - Location of stenosis
  - Lesion Pathology
    - Calcified, ulcerative, soft plaque ?
    - Other Pathology
      - Aneurysms, FMD
  - Accessory Branches
  - Look at aortic pathology

Accessory Renal Branches



Role in Diagnosing RAS



Occluded Upper Branch with disease in main left

Published Data: Individual Series

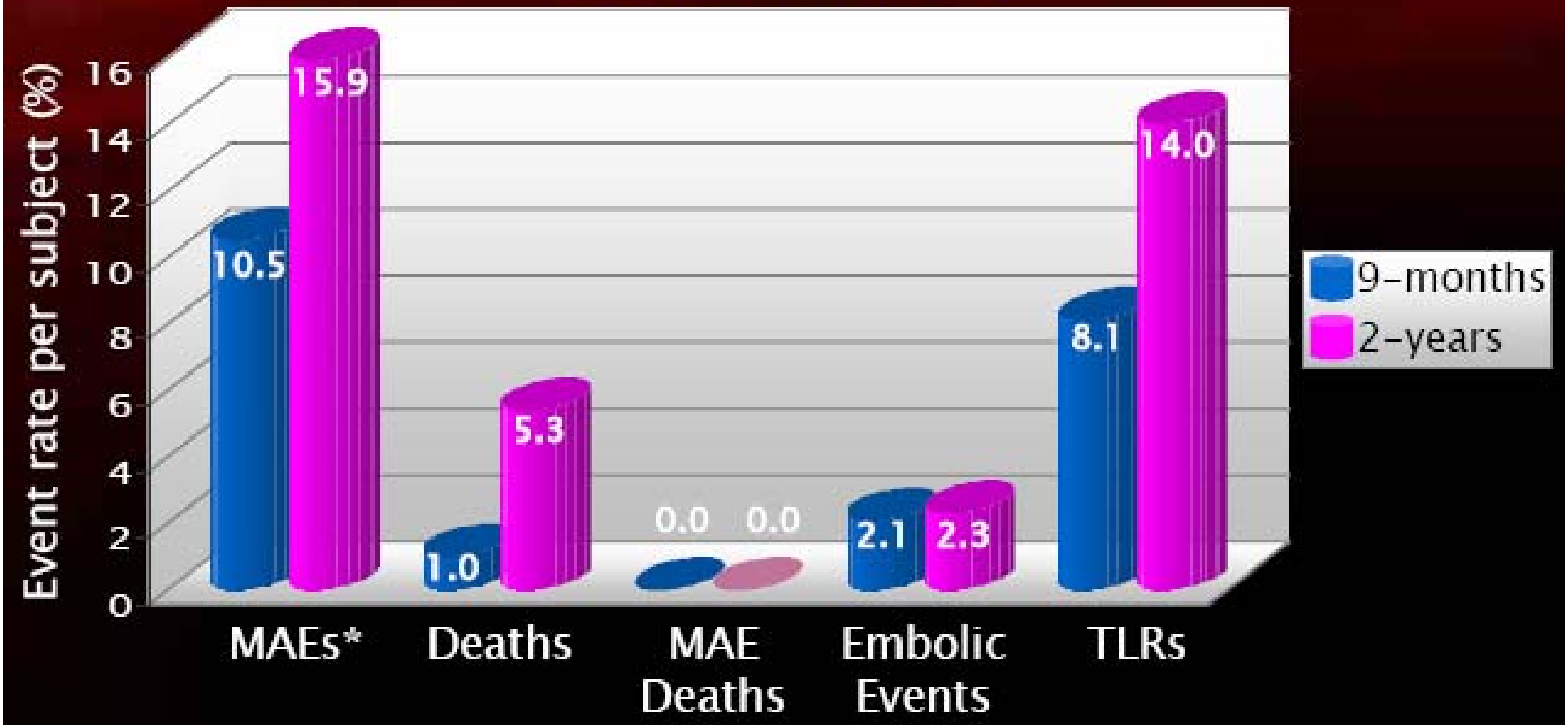
- M Henry
  - 38/60 diseased aortas
  - EPI and Percusurge
  - Tech success 98%
  - Perc debris found in 100% with mean 190 microns
  - Indications
    - Elderly
    - Bil renal disease
    - Single Kidney
    - Diabetics
    - Pts with bad renal function

Results of the Renaissance Trial

What Does It Tell Us... About Renal Stent Trial Design in 2008?

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

Major Adverse Events at 2 Years



N=100 pts

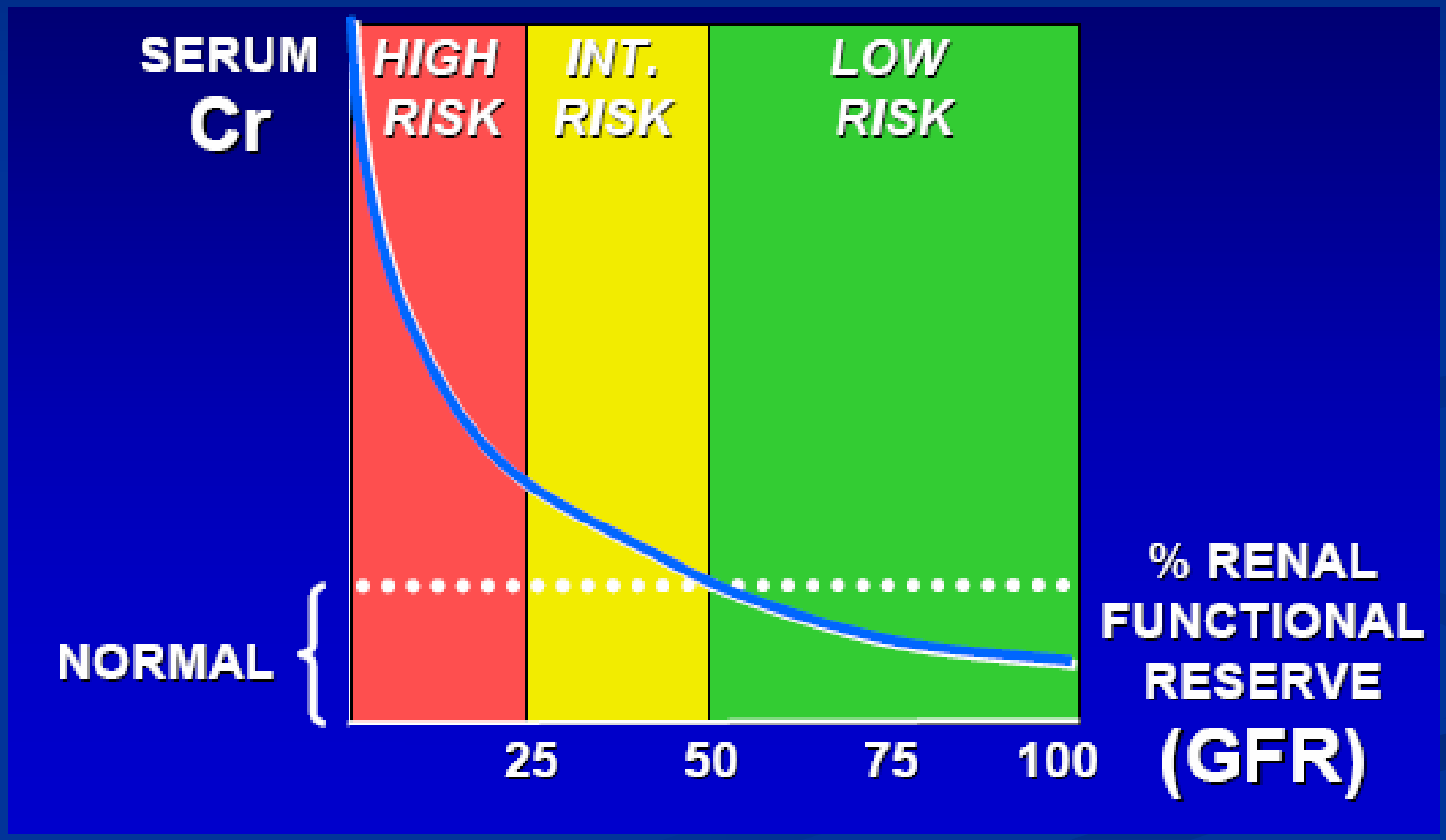
Excellent safety through 2 years

*MAE = device or procedure related death, TLR, significant embolic event causing end organ damage. Adjudicated by independent CEC.

Risk for Renal Embolization

- What is the real risk for embolization
  - Reported incidence 2-4%
  - Deterioration of renal function post stenting
    - Natural history of disease vs contrast nephropathy vs cholesterol embolization

SERUM Cr , RENAL FUNCTIONAL RESERVE (GFR) AND RISK OF INTERVENTION



Renal Stenting with and without distal protection in ischaemic nephropathy: Early Experience

RENAL FUNCTION	PROTECTION WITHOUT		WITH	
	%	#	%	#
IMPROVED	46%	0	46%	11
STABLE		0	50%	12
CONTINUE				
DECLINE	75%	15	4%	1*
ACUTE				
DECLINE	20%	4	0%	0

J VascVascSurgSurg. 38(5):962. 962--8, 2003 Nov.

Renal Protection: Controversy

- Angle of renal artery 90 degrees or more
  - Risk of filter coming back
    - Causing vessel damage
    - into the renal stent and becoming lodged
- Evidence of benefit still questionable

CORAL

- Changed the rules:
  - Filter optional
  - More sites enrolled

Atheromatous Embolization

Definition: Fragmentation and embolization of atherosclerotic debris

Spectrum

–May be clinically inapparent, if few particles embolize

–May be devastating and malignant with multiple organ systems affected

–Some organs may not initially manifest the impact of the embolization

- i.e. Renal Failure

Independent predictors of dialysis/death

–Baseline CKD

–Baseline DM

–Baseline CHF

–Acute/subacute presentation

–GI tract involvement

- ***50% reduction in dialysis/death among patients started on Statins!***

Circulation 2007;116:298-304

Primary Sources of Atheroemboli

- Ulcerated, "Shaggy" atherosclerotic aorta or peripheral arteries
- Aneurysms
  - Aorta
  - Iliac
  - Femoral
  - Popliteal
- Fibromuscular Dysplasia
- Embolic Material from Stenotic Arteries

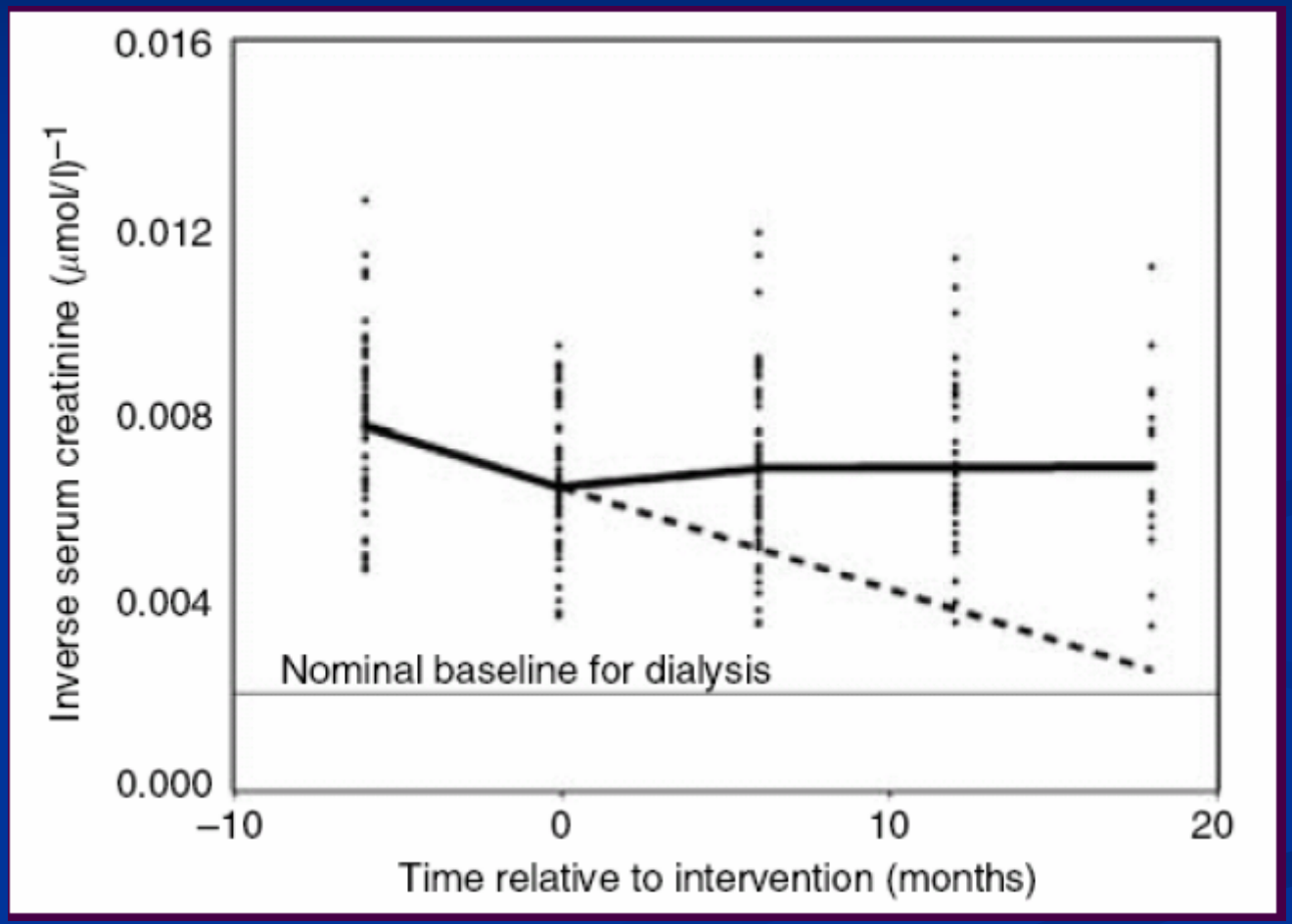
Pathology of Atheroemboli

Biopsies demonstrate arterioles with external diameter of 55-900μm

- Cholesterol crystals
  - Needle shaped in lumen or vessel wall
  - Crystals incite intense inflammatory reaction
  - Progress to fibrosis and obliteration of vessel lumen
  - Eosinophils predominate

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]



Kidney International 2006;70:948-955.

RAS and Renal Failure

AUTHORS	YEAR	PTS (n)	IMPROVED (%)	STABLE (%)	WORSE (%)
DORROS (21)	1995	69	30	48	22 *
IANNONE (28)	1996	63	36	46	18
TAYLOR (26)	1997	39	33	29	38 *
BLUM (19)	1997	68		100	
HARDEN (27)	1997	32	34	34	28 *
BOISCLAIR (45)	1997	33	41	35	24 *
PAULSEN (37)	1999	135	23	56	21 *
ISLES (44)	1999	379	26	48	26 *
RODRIGUEZ LOPEZ (38)	1999	108		95,5	4,5
HENRY (17)	1999	235	29	67	4
RUNDBACK (82)	1999	45	25	43	32
GUERRERO (41)	2002	61	19	50	31 *
ALLAQUABAND (83)	2003	22	50	23	27 *
HALLER (84)	2004	261		86	14
ZELLER (34)	2004	340	34	39	27
OVERALL		1890	25,3	53,3	21,4

- EACH MANIPULATION OF THE SPECIMENS INCLUDING SIMPLY ADVANCING THE GUIDEWIRE THROUGH THE LESION RELEASED THOUSANDS OF FRAGMENTS
- THE NUMBERS OF FRAGMENTS IN EACH SIZE CATEGORY INCREASED WITH DECREASING PARTICLES SIZE
- POSITIONING AND DEPLOYING THE STENT RELEASED AN ADDITIONAL BOLUS OF FRAGMENTS SIMILAR TO THAT RELEASED AFTER BALLOON ANGIOPLASTY

HIRAMOTO J. ET AL J. VASC.SURG 2005;41:1026-1030

ATHEROEMBOLI TYPICALLY OCCLUDE THE MEDIUM SIZED ARTERIOLES (150 TO 200 µm IN DIAMETER) AND GLOMERULAR CAPILLARIES . THE INVOLVEMENT USUALLY IS PATCHY

THE PATHOGENESIS OF RENAL FAILURE MAY BE DUE ENTIRELY TO OCCLUSION OF THESE VESSELS

BUT REACTIVE INFLAMMATION SURROUNDING THE CHOLESTEROL CRYSTALS MAY PLAY A SIGNIFICANT ROLE IN CAUSING THE LUMINAL OCCLUSION AND SUBSEQUENT RENAL FAILURE

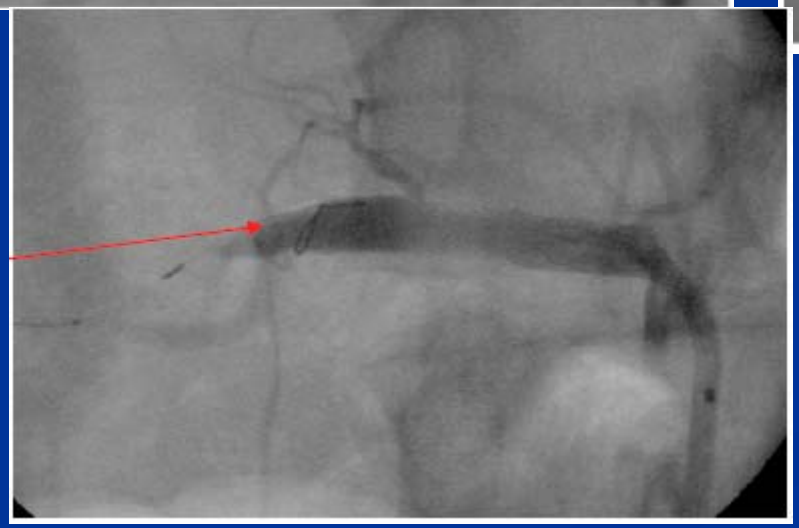
KULMANT S ET AL J.AM.SOC.NEPHROL 2001;12:1781-1787

ASPIRATED DEBRIS WITH PERCUSURGE

- VISIBLE ASPIRATED DEBRIS IN ALL PATIENTS
- PARTICLES COMPOSED OF : Atheromatous plaques, cholesterol crystals, necrotic cores, fibrin, thrombi, platelets, macrophage foam cells
- BLOOD SAMPLES ANALYSED

	MEAN PARTICLES NUMBER		MEAN PARTICLES DIAMETER (µ)	
DIRECT STENTING	11.2 ± 73.5	N.S.	190 ± 44.5	N.S.
SECONDARY STENTING	86 ± 47		210 ± 96	
ALL LESIONS	98.1 ± 60 (13 to 208)		201.2 ± 76.2 (38 - 6206)	

EPI Filter for Renal Protection



Courtesy of M Henry, MD

- 90 PATIENTS WITH ISCHEMIC NEPHROPATHY
- 106 RENAL ARTERIES
  - MILD RENAL INSUFFICIENCY : 33 (37%)
  - MODERATE RENAL INSUFFICIENCY : 48 (53%)
  - SEVERE RENAL INSUFFICIENCY : 9 (10%)
- ANGIOGUARD :94 ARTERIES
- FILTERWIRE : 12 ARTERIES

A. HOLDEN ALL THAT JAZZ 2005

MEAN FOLLOW UP : 18,2 MONTHS (2-54 MONTHS)

- IMPROVED RENAL FUNCTION : 36%
- STABILIZED : 55%
- PROGRESSIVE DECLINE : 8%
- ACUTE DETERIORATION : 1%

- **32 R.A.S. WITH PERCUSURGE**
  - RENAL INSUFFICIENCY : 92%
- **4 – 6 WEEK FOLLOW UP**
  - R.F. IMPROVEMENT : 50%
  - R.F. UNCHANGED : 50%
  - R.F. DETERIORATION : 0%

  54% OF PATIENTS WITH R.F. DETERIORATION IMPROVED
- **CONCLUSION :**
  - R.A.S. UNDER PROTECTION IS A MARKED IMPROVEMENT IN SHORT TERM R.F. RESPONSE
  - RESULTS ARE SIMILAR TO SURGICAL REVASCULARIZATION
  - PROTECTION DEVICES MAY PREVENT R.F. HARM DURING R.A.S. AS A RESULT OF ATHEROEMBOLISM

EDWARDS M.S. ET AL J.VASC.SURG. 2006;44:128-135

Embolization Protection in Renal Artery Stent Placement: Anatomical Considerations