Heart and kidneys: Renal denervation as therapy for hypertension

Technical aspects and complications

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The procedure

- Percutaneous procedure via the lumen of the renal artery using RF. Other modalities (ultrasound, cryoablation and perivascular delivery of neurotoxins) are being investigated
- RA angiogram is obtained to assess the anatomic suitability and to exclude significant RA stenosis.
- Each RA should have a diameter of ≥4 mm and a length of ≥ 20 mm to allow adequate application of RF energy and a sufficient number of RF ablation treatments (n ≥ 4)
- The treatment catheter is introduced through a 6-9 F guiding catheter into the RA and placed distally before the first branch of the RA under to ensure stable contact with the vessel wall.
- Discrete low energy RF ablations are then applied from distally to proximally within each RA

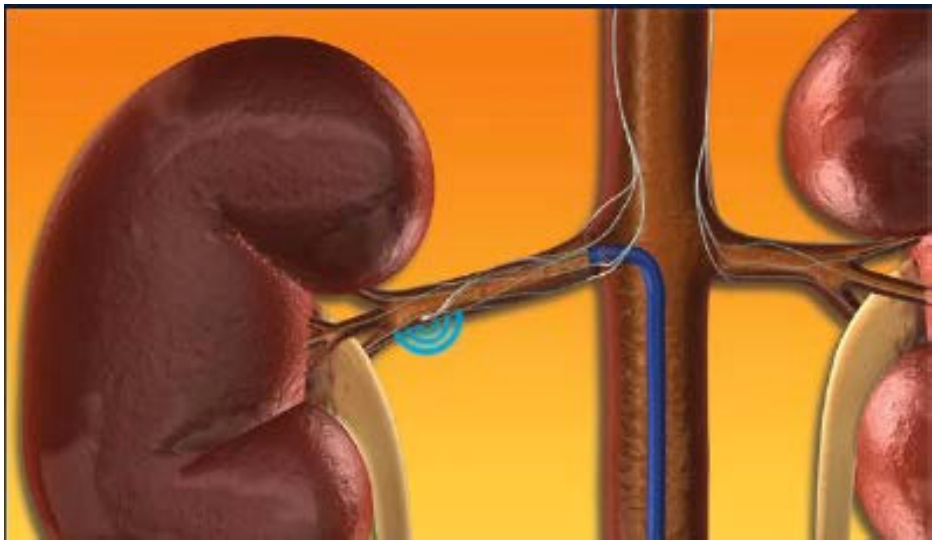
Periprocedural managment

Pain management: The ablation procedure is typically accompanied by diffuse visceral nonradiating abdominal pain which does not persist beyond the RF energy application and needs to be managed by intravenous analgesic and anxiolytic/sedative medication. Vital signs should be monitored during the procedure.

Systemic anticoagulation and anti-platelet therapy: Prior to the procedure, appropriate systemic (target ACT 200-250 sec).

Peri-procedural anti-platelet therapy may be advisable: 250 mg of acetylsalicylic acid during the procedure and 75-100mg/d for up to 4 weeks after RDN has been suggested.

Simplicity ™



Consist of an endovascular catheter (6Fr), dispersive electrodes, foot switch, power cable and a generator

Ablative time per renal artery: 600”

EnligHTN ™

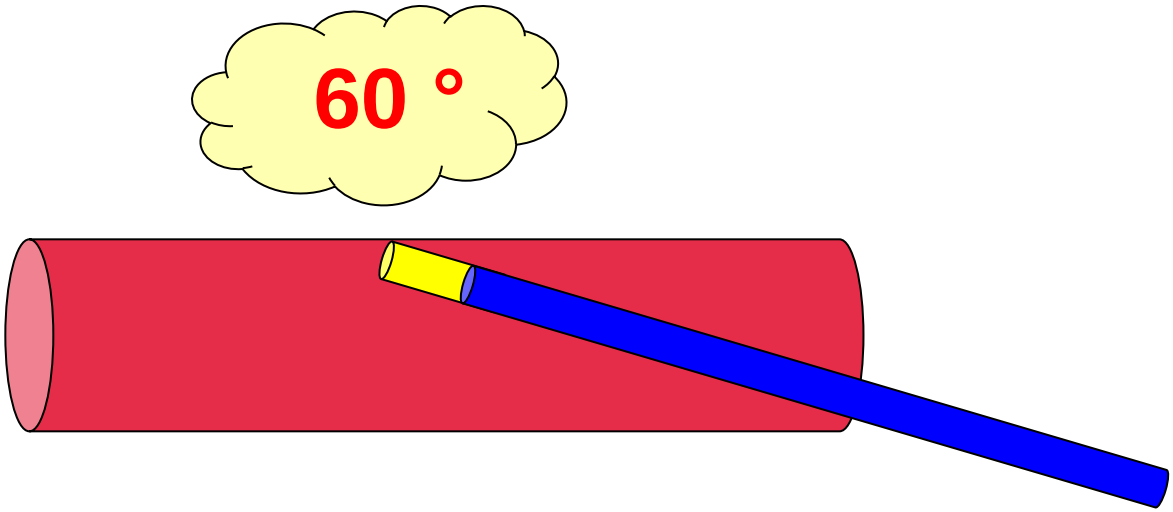
EnligHTN Renal Artery Ablation Catheter

EnligHTN Guiding Catheter (Coming Soon)

EnligHTN RF Ablation Generator

Consist of an endovascular catheter (8 Fr) with nitinol basket, 4 electrode per basket

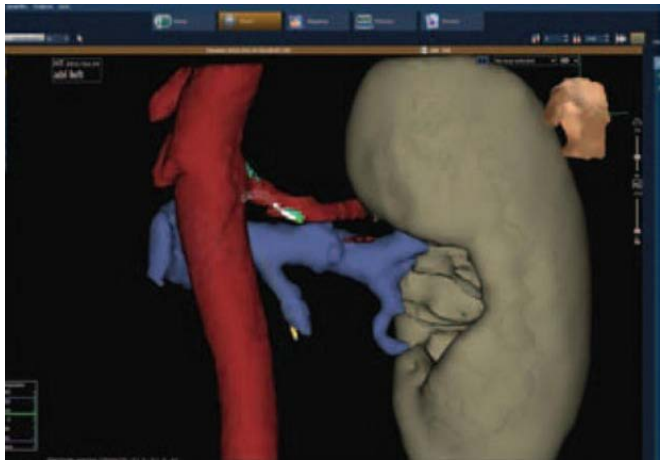
Ablative time per renal artery: 90”

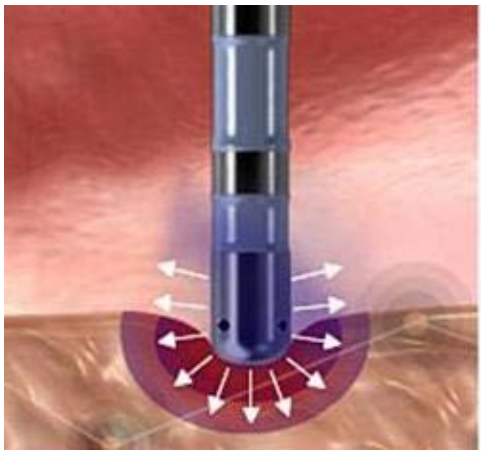


The Problem is…RF may damage the vessel wall and ultimately results into atherosclerosis progression

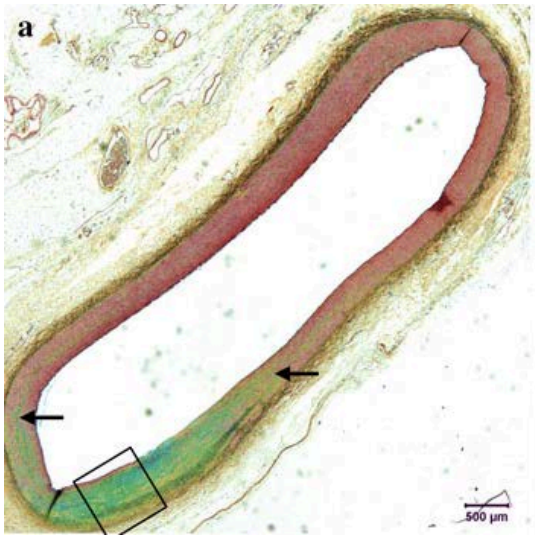
Calhoun et al. *Circulation* 2008

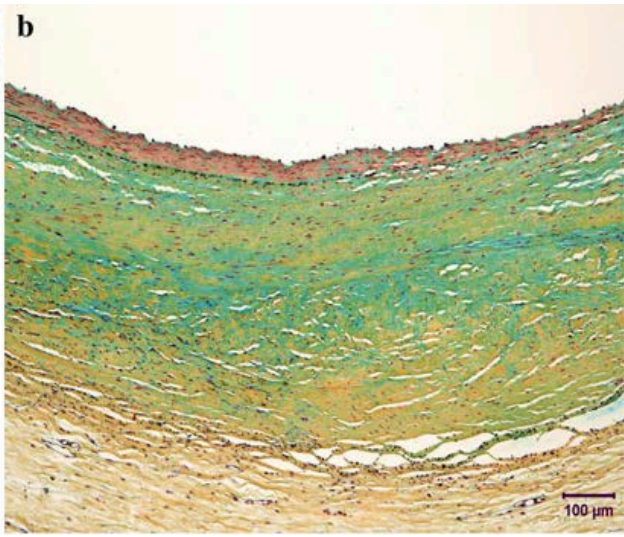
The elevated temperature has to create a vessel wall injury



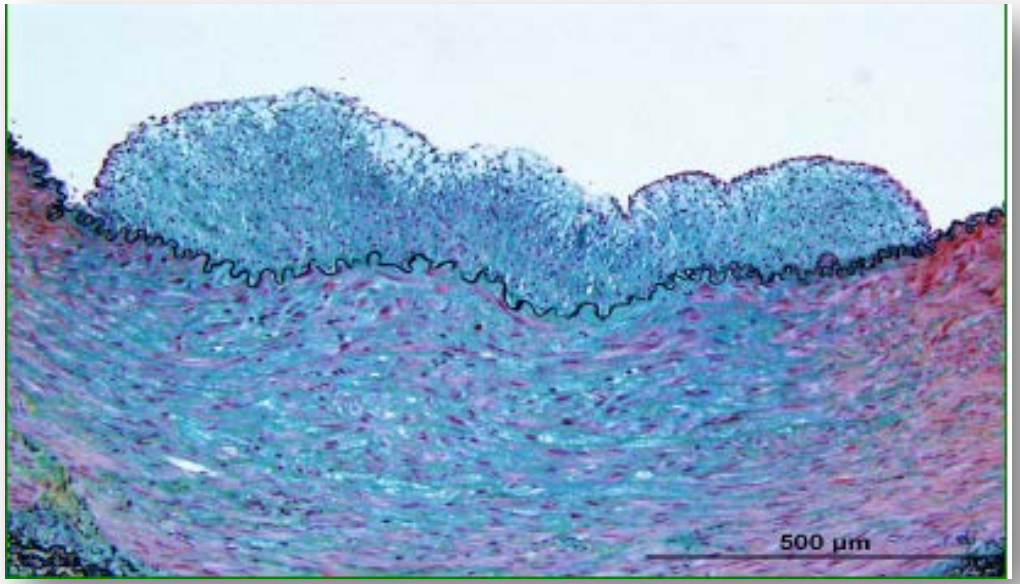


Which is consequence of this vessel wall injury?





Rippy et al. Clin Res Cardiol 2011



?

"…Neointimal thickening is uncommonly observed in animals even in the presence of severe injury to media…"

Virmani R, Oral presentation, TCT 2012

Symplicity HTN-1: 3-Yrs Follow-up

81 patients with 6-month renal CTA, MRA or duplex

- No vascular abnormalities at any site of RF delivery
- One progression of a pre-existing stenosis unrelated to RF treatment (stented without further sequelae)
- One new moderate stenosis which was not hemodynamically relevant and not treated

Expanded results presented at the Transcatheter Cardiovascular Therapeutics Annual Meeting 2012 (Schlaich, M.)

Simplicity HTN -2

- No serious device or procedure related adverse events (n=52)

- 6-months renal imaging (n=43)
  - No vascular abnormality at any RF treatment site
  - 1 MRA indicates possible progression of a pre-existing stenosis unrelated to RF treatment (no further therapy warranted)

Safety evaluation at 6 months

Symplicity HTN-2 Investigators. Lancet. 2010;376:1903-1909.

Non critical ostial Left Renal artery stenosis……

Procedural success at day 1

Clinical success at 1 months

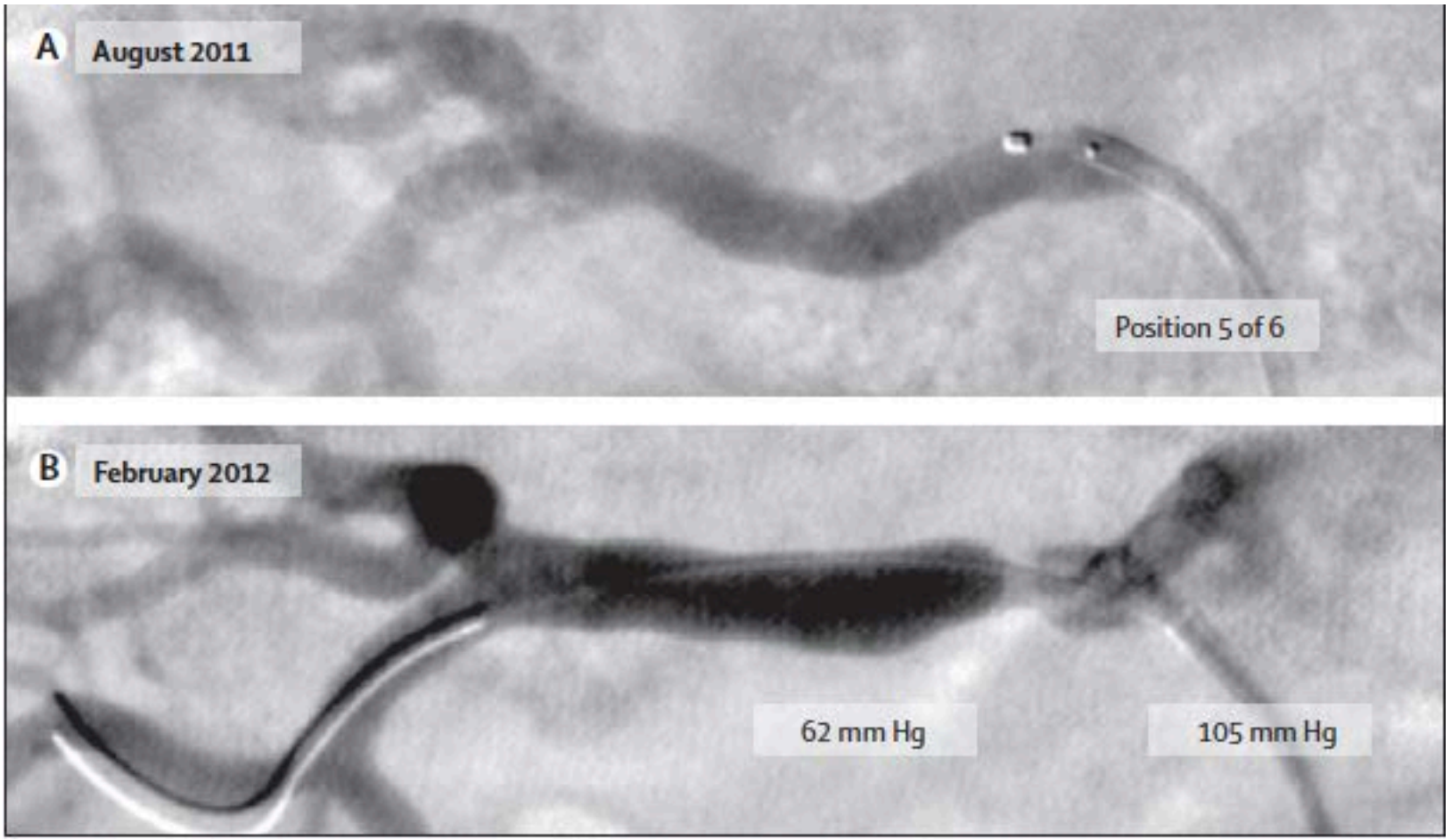
Clinical success at 6 months

Uncontrolled hyperthension and PE at 12 months

…..at 12 months there was a critical stenosis…....

Secondary rise in blood pressure after renal denervation

Oliver Vonend, Gerald Antoch, Lars Christian Rump, Dirk Blondin

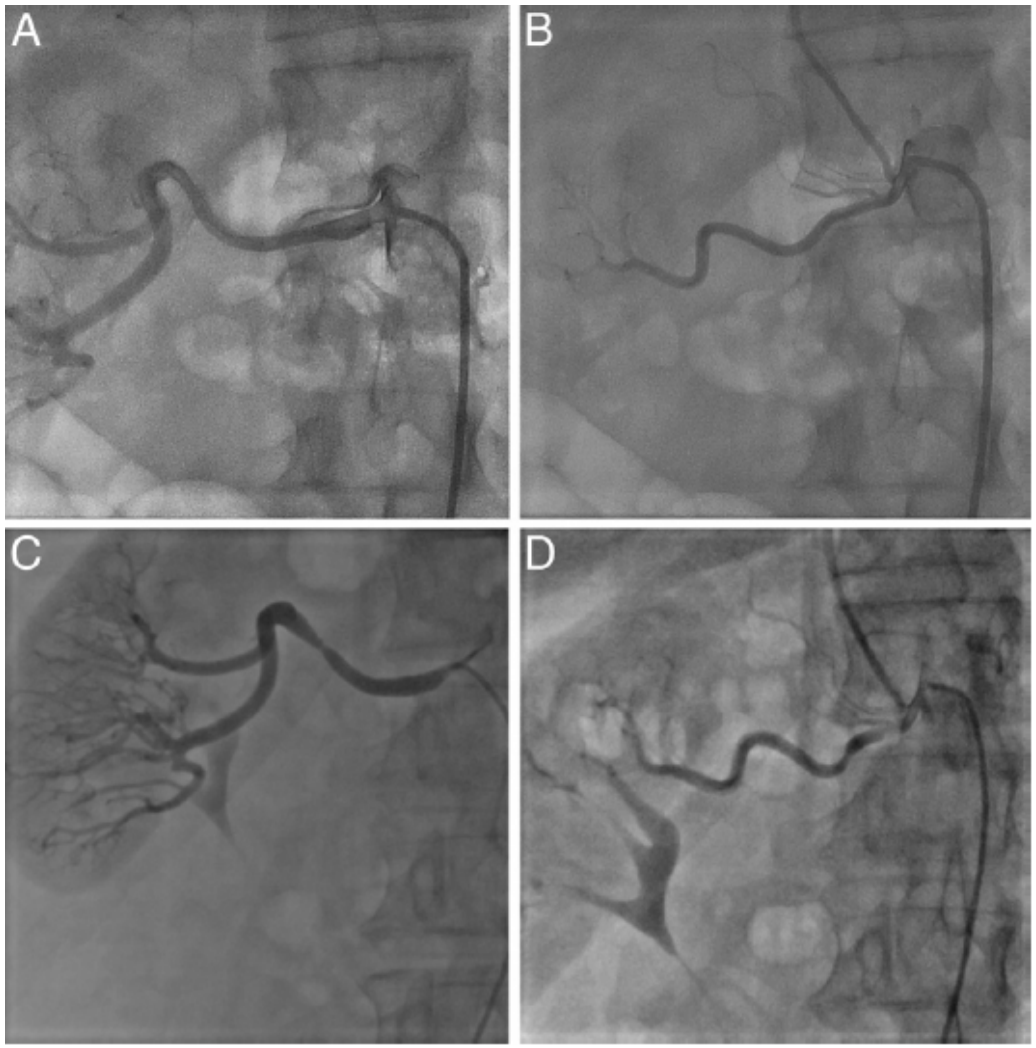


Lancet 2012

Renal Artery Stenosis After Renal Sympathetic Denervation

Post RADN

5 Months

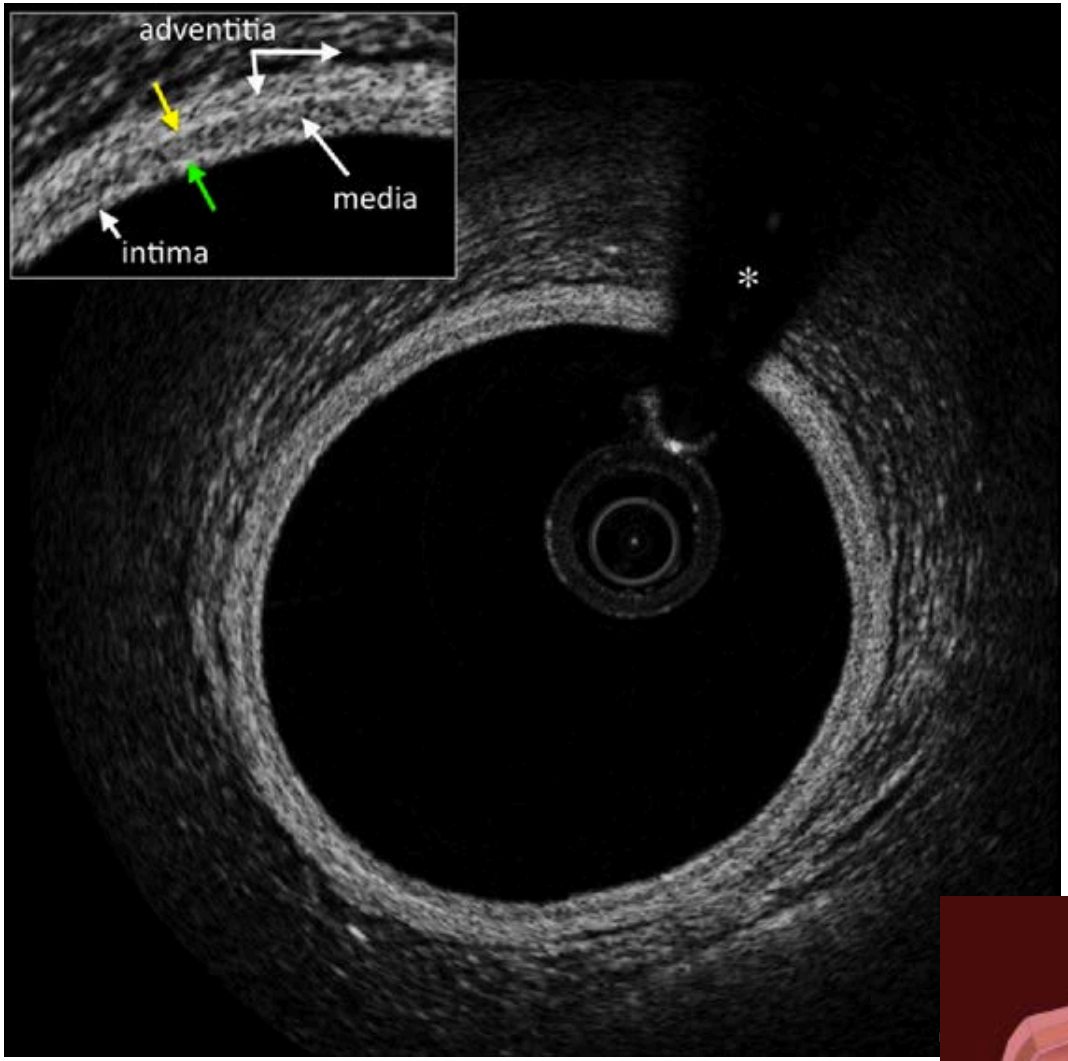


J Am Coll Cardiol 2012

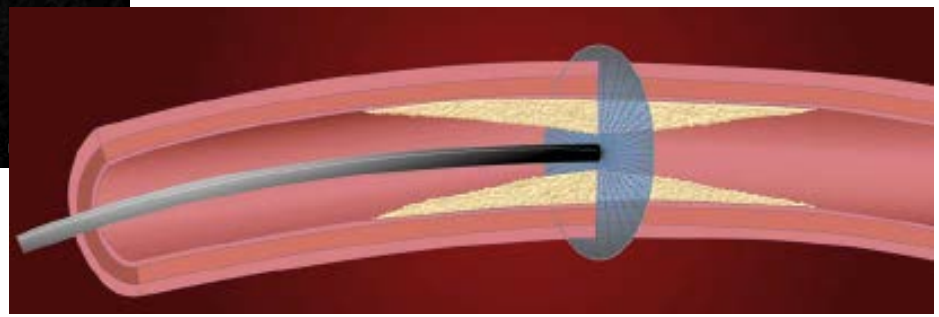
Key question:

How can we evaluate the vessel wall integrity after RADN?

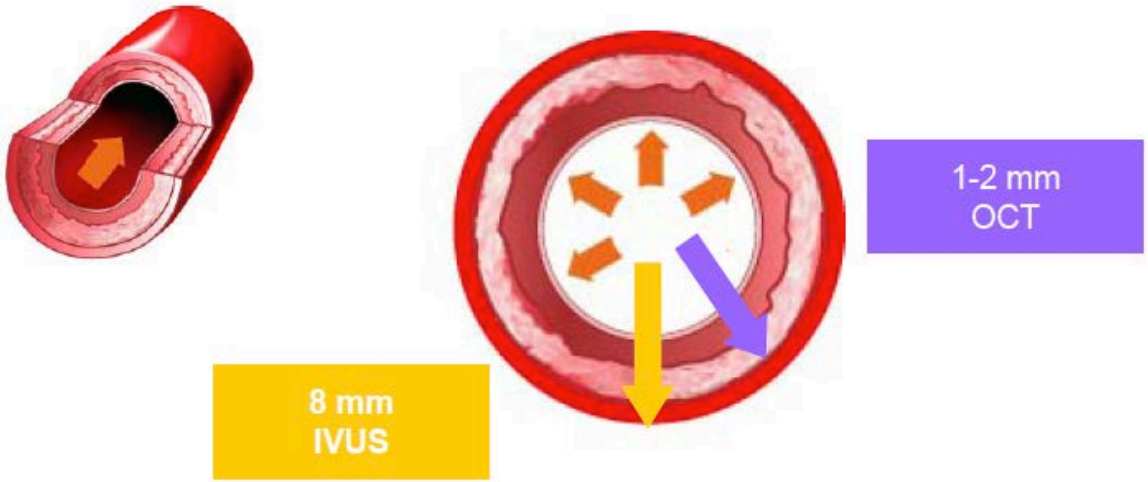
OCT

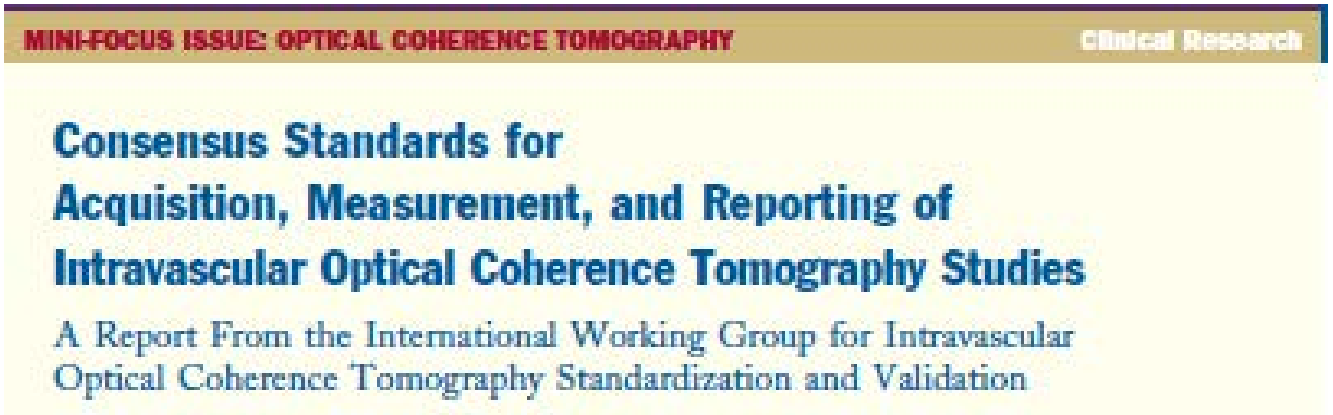


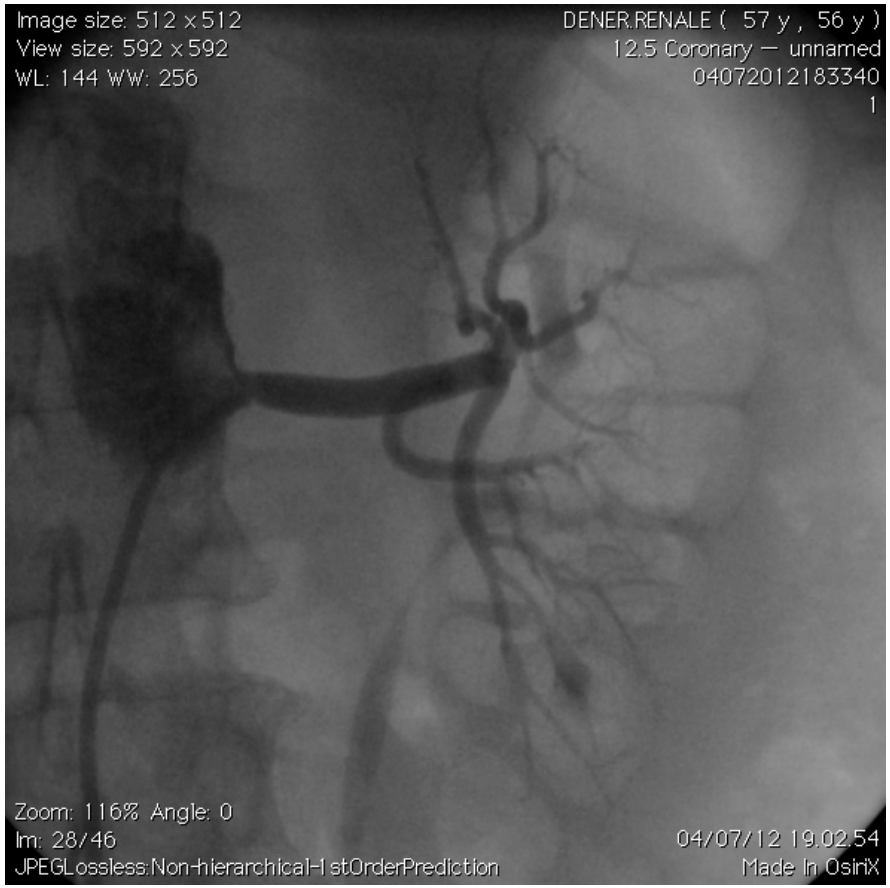
Optical Coherence Tomography is a technique for obtaining live morphology images at higher resolution (10 µm).

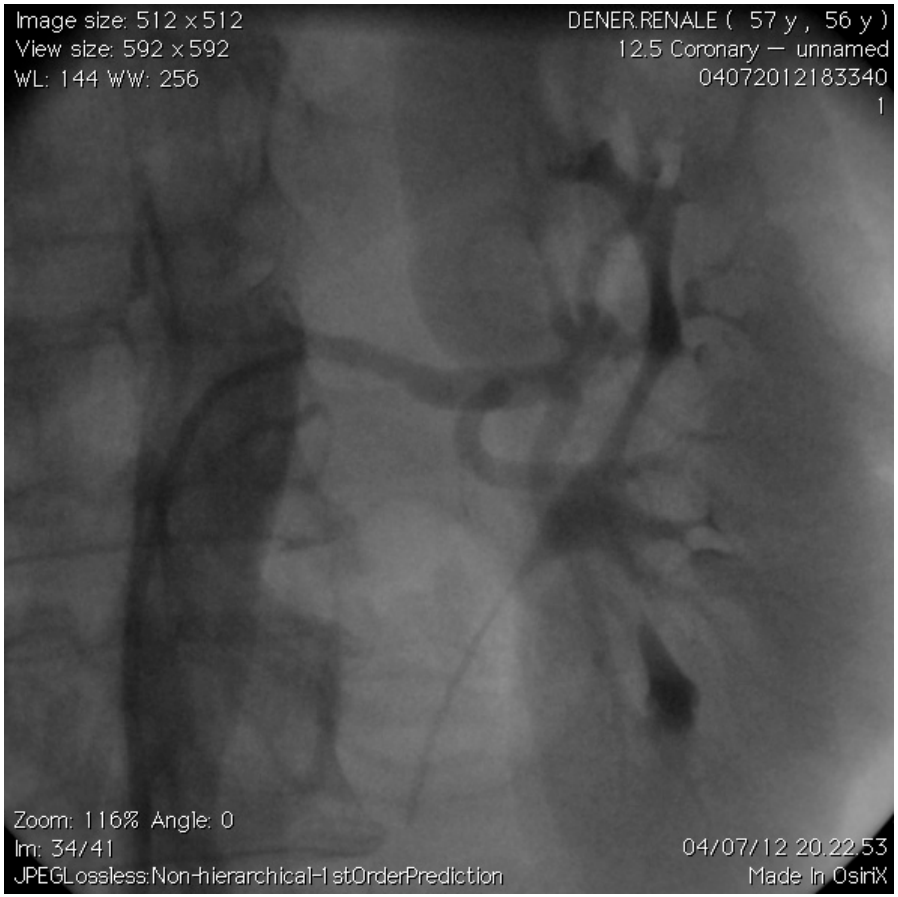


Compared to IVUS it has an higher resolution but it is limited to imaging 1 to 2 mm below the surface in biological tissue



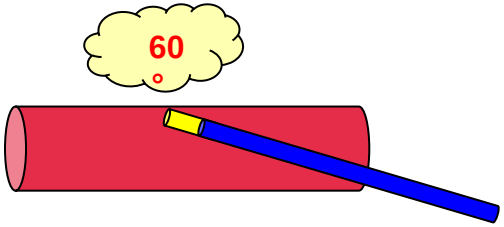


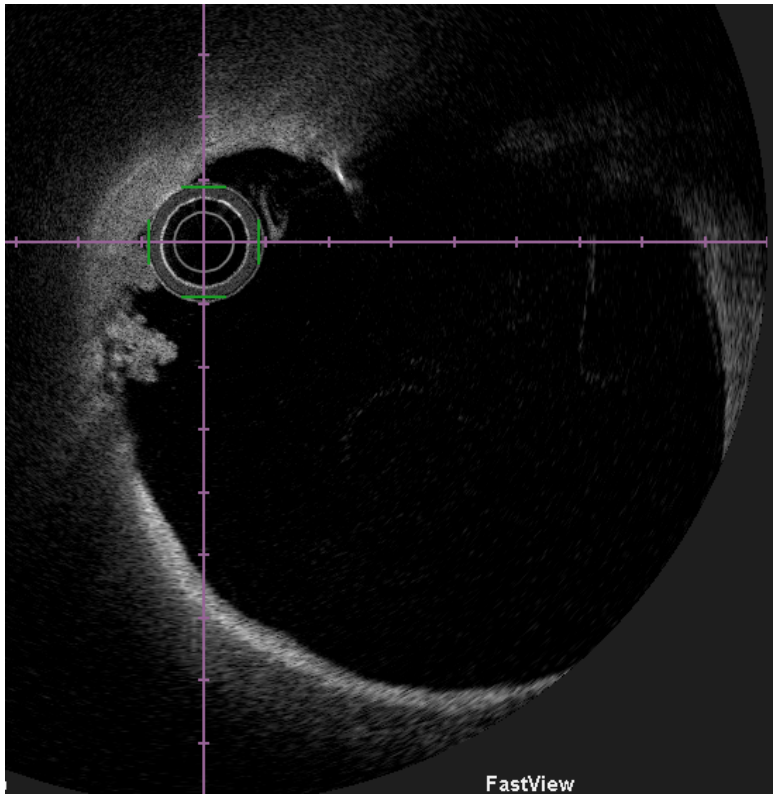


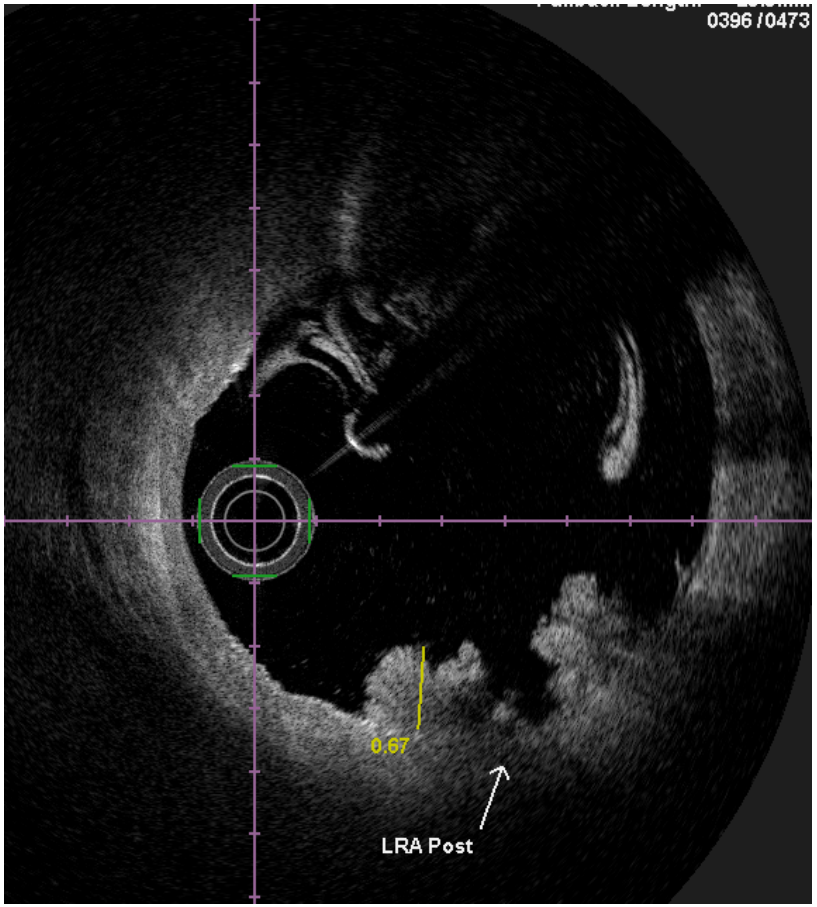


…it is a spasm it will disappear with time!!!!

….I’m not sure !





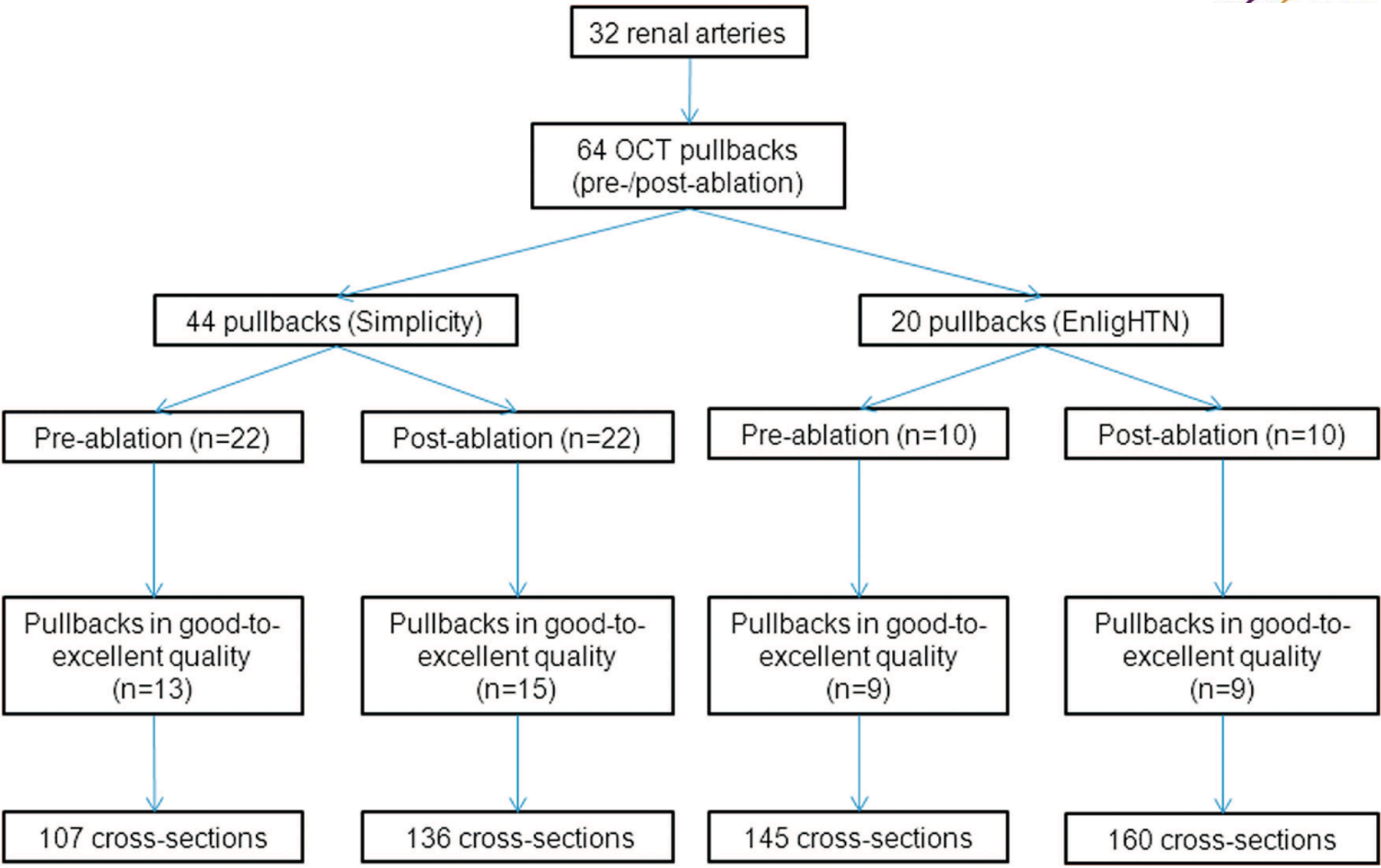


European Heart Journal
doi:10.1093/eurheartj/eht141

FASTTRACK CLINICAL RESEARCH

Vascular lesions induced by renal nerve ablation as assessed by optical coherence tomography: pre- and post-procedural comparison with the Simplicity™ catheter system and the EnligHTN™ multi-electrode renal denervation catheter

Templin et al. *European Heart Journal* 2013



Templin et al. *European Heart Journal* 2013

OCT Findings

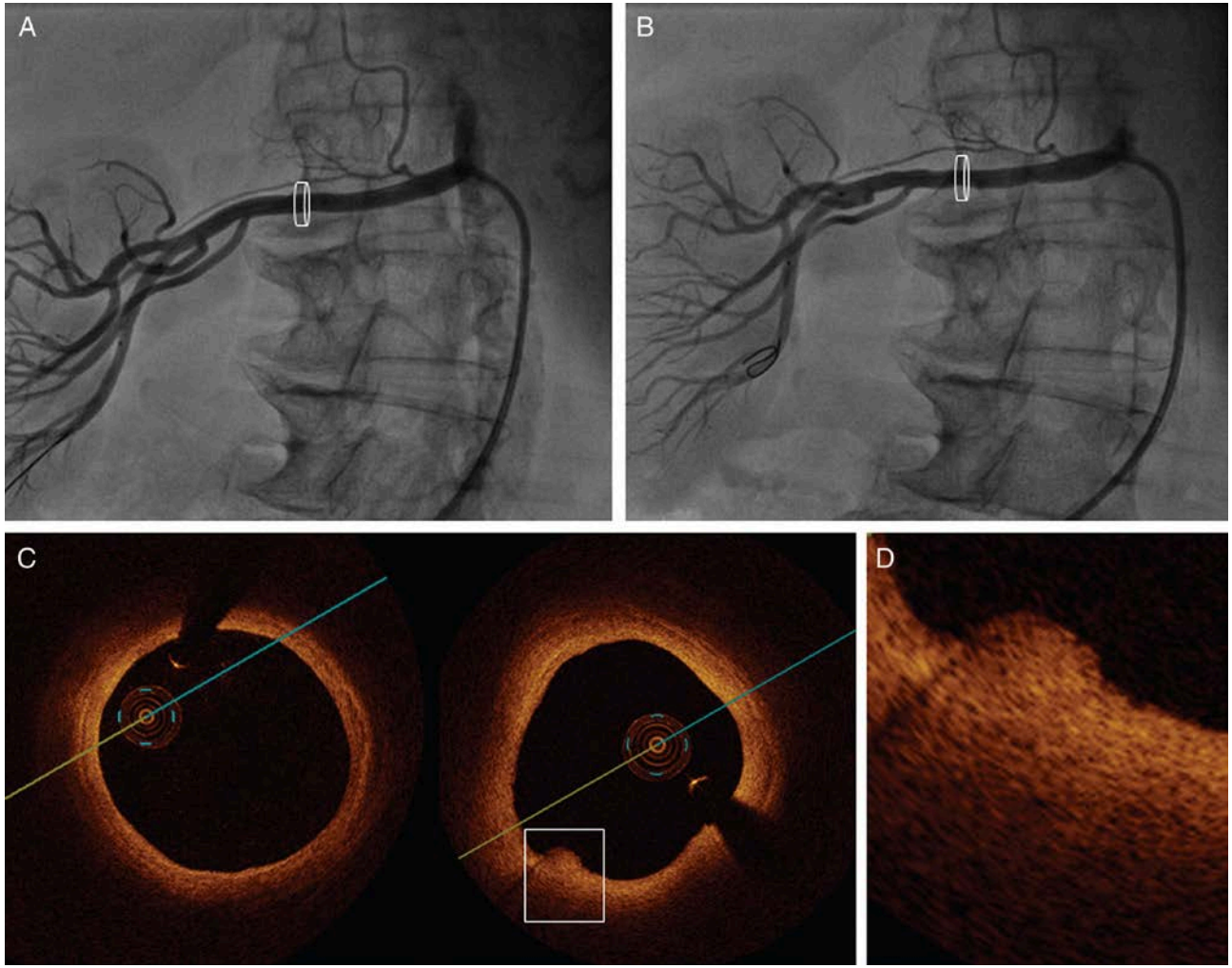
15 pts Simplicity

9 pts EnligHTN

	Before RNA, pullbacks (*n* 5 22)	After RNA, pullbacks (*n* 5 24)	*P* value
Oedema, *n* pullbacks (%)	10 (45)	23 (96)	, 0.001
Oedema in total	14	72	
Oedema per RA	0.58 ± 0.83	3.0 ± 2.0	, 0.001
Thrombus, *n* pullbacks (%)	4 (18)	16 (67)	, 0.001
Thrombi in total	8	64	
Thrombi per RA	0.33 ± 0.87	2.67 ± 2.76	, 0.001
Vasospasm, *n* pullbacks (%)	0	10 (42)	, 0.001
Vasospasm in total	0	18	
Vasospasm per RA	0	0.75 ± 1.07	0.0013
Dissection/tissue disruption, *n* pullbacks (%)	0	3 (13)	0.086
Dissection/tissue disruption in total	0	5	
Dissection per RA	0	0.21 ± 0.59	0.09

Templin et al. *European Heart Journal* 2013

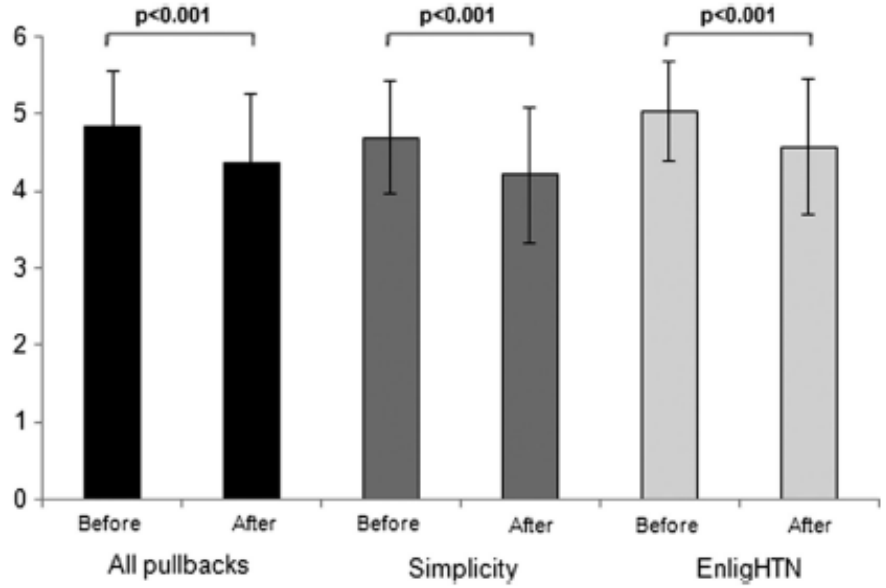
Vessel wall oedema



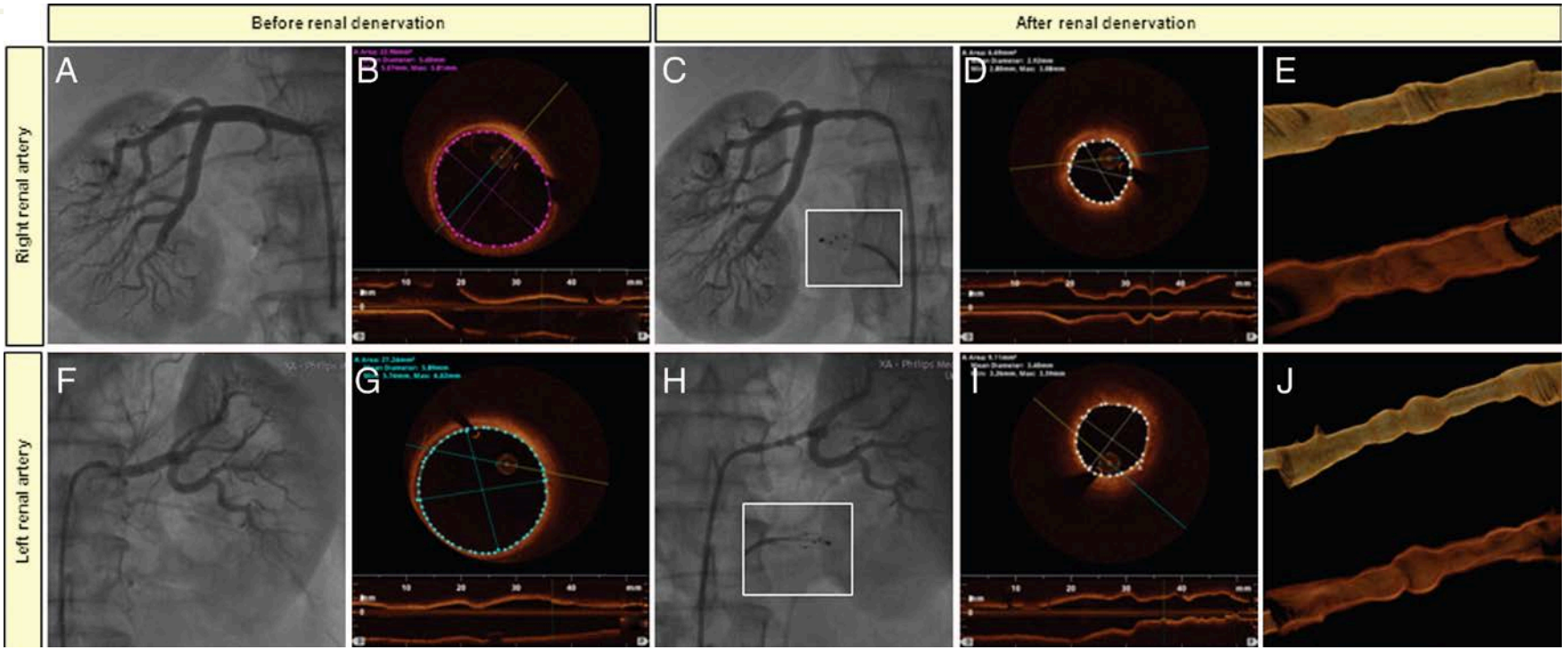
There was no significant difference in the amount of oedema between the Simplicity™ and the EnligHTN™ catheters measured per renal artery (3.1+1.9 vs. 2.3+2.0, P 0 0.35).

Templin et al. *European Heart Journal* 2013

Vessel spasm

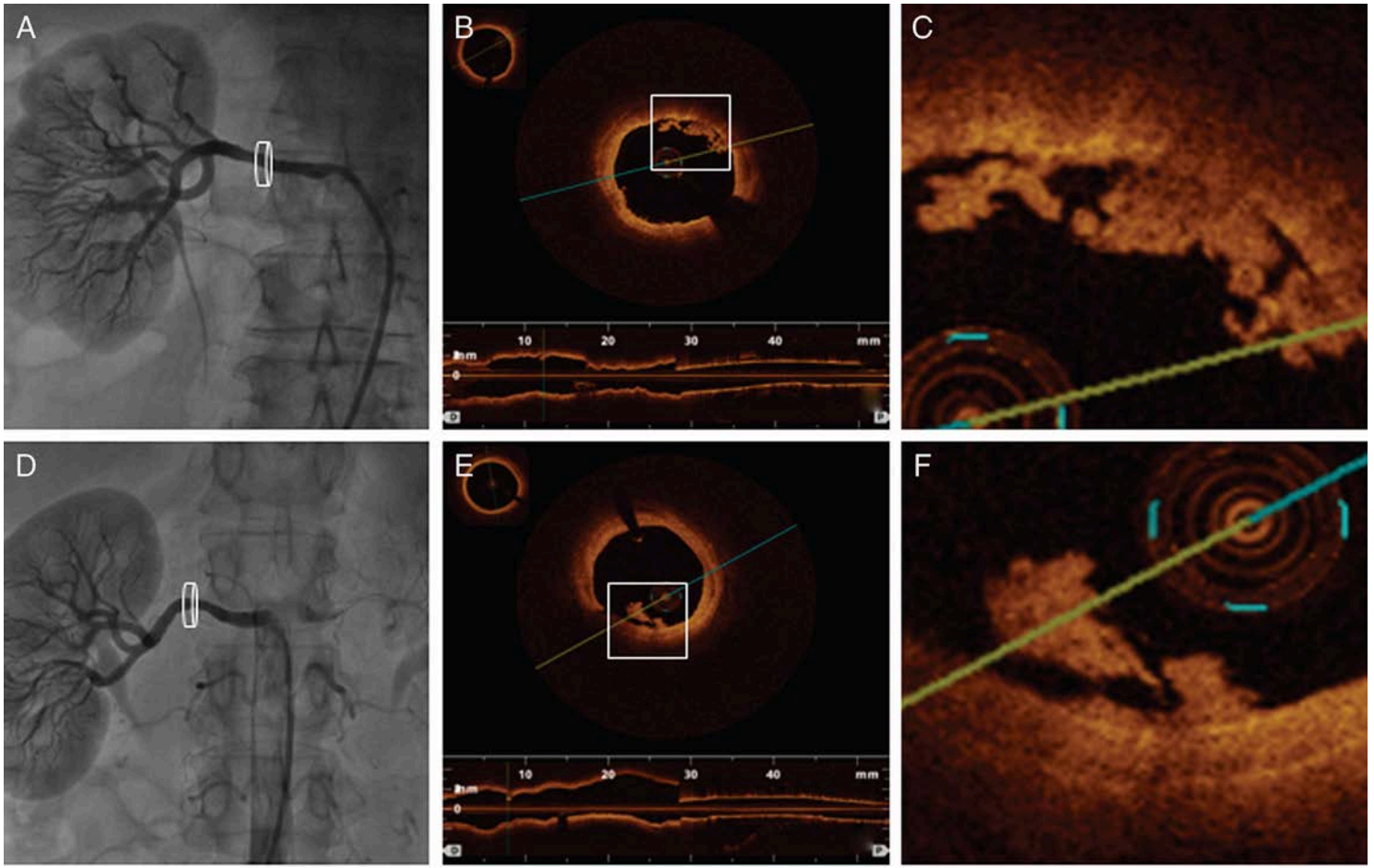


"We did not notified also any differences after the Simplicity™ and the EnligHTN™ catheters regarding the vessel spasm (40 vs. 44%, P = 0.83)"



Templin et al. *European Heart Journal* 2013

Thrombus



Templin et al. *European Heart Journal* 2013

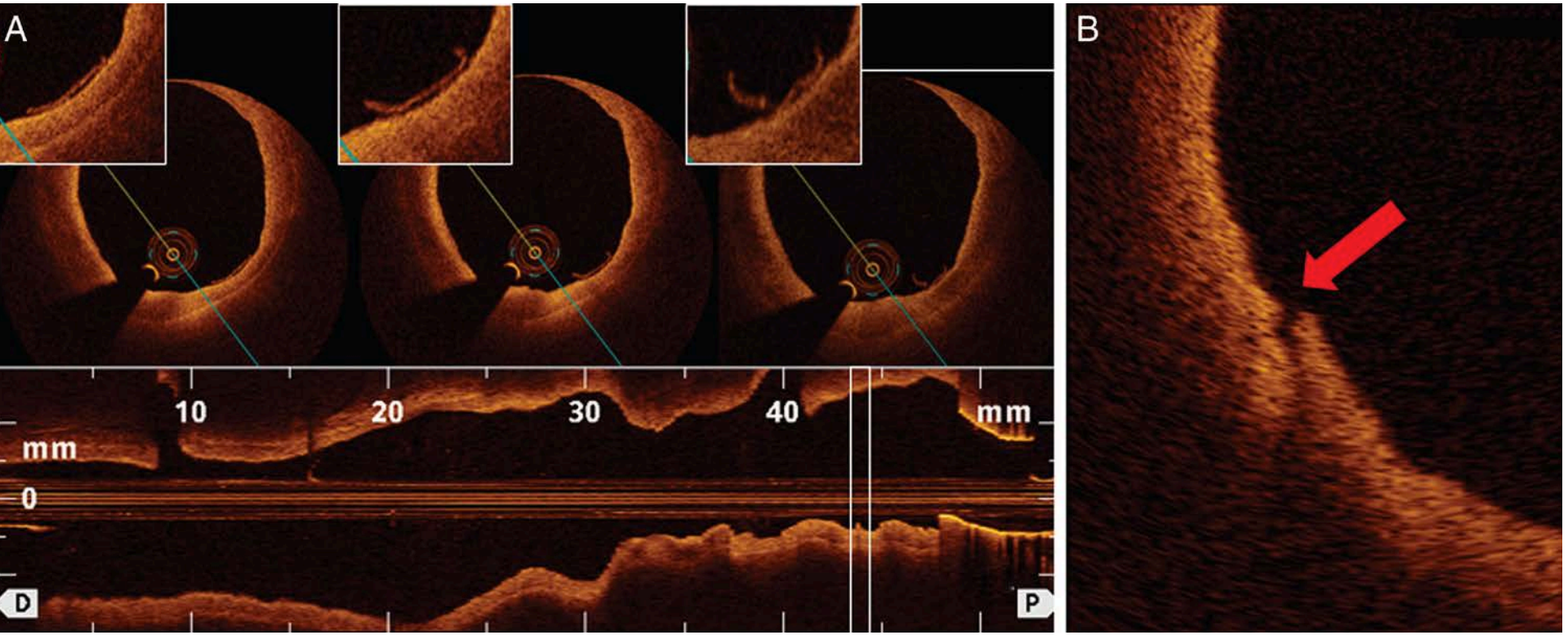
Thrombus

However,we observed a trend towards the intraluminal thrombus formation, i.e. in 89% of the cases using the EnligHTN™ catheter and in 53% with the Simplicity™ catheter-based basket ablation system (P = 0.07).

Moreover, a significantly greater thrombus load per renal artery was observed after RNA with the EnligHTN™ system compared with the Simplicity™ system (4.6+3.1 vs. 1.5+1.8, P = 0.006).

Templin et al. *European Heart Journal* 2013

Dissections

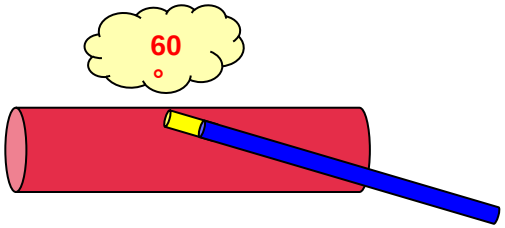


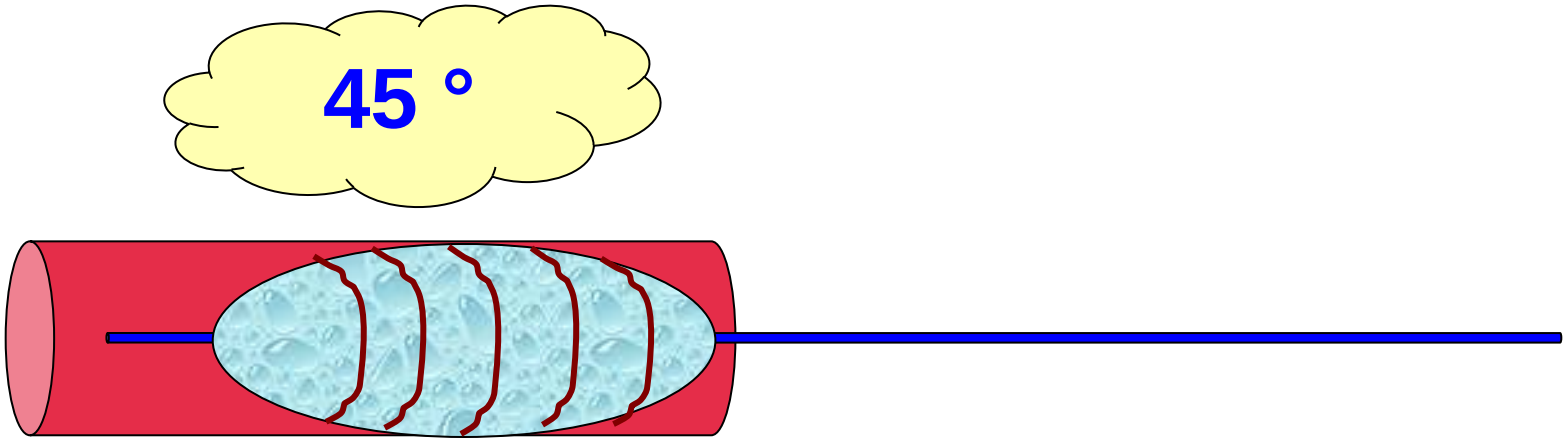
We have documented one evidence of arterial dissection after renal ablation with the Simplicity™ catheter (7%), while endothelial and intimal disruptions were observed in two patients after the EnligHTN™ catheter use (22 %) (P = 0.26)

Templin et al. *European Heart Journal* 2013

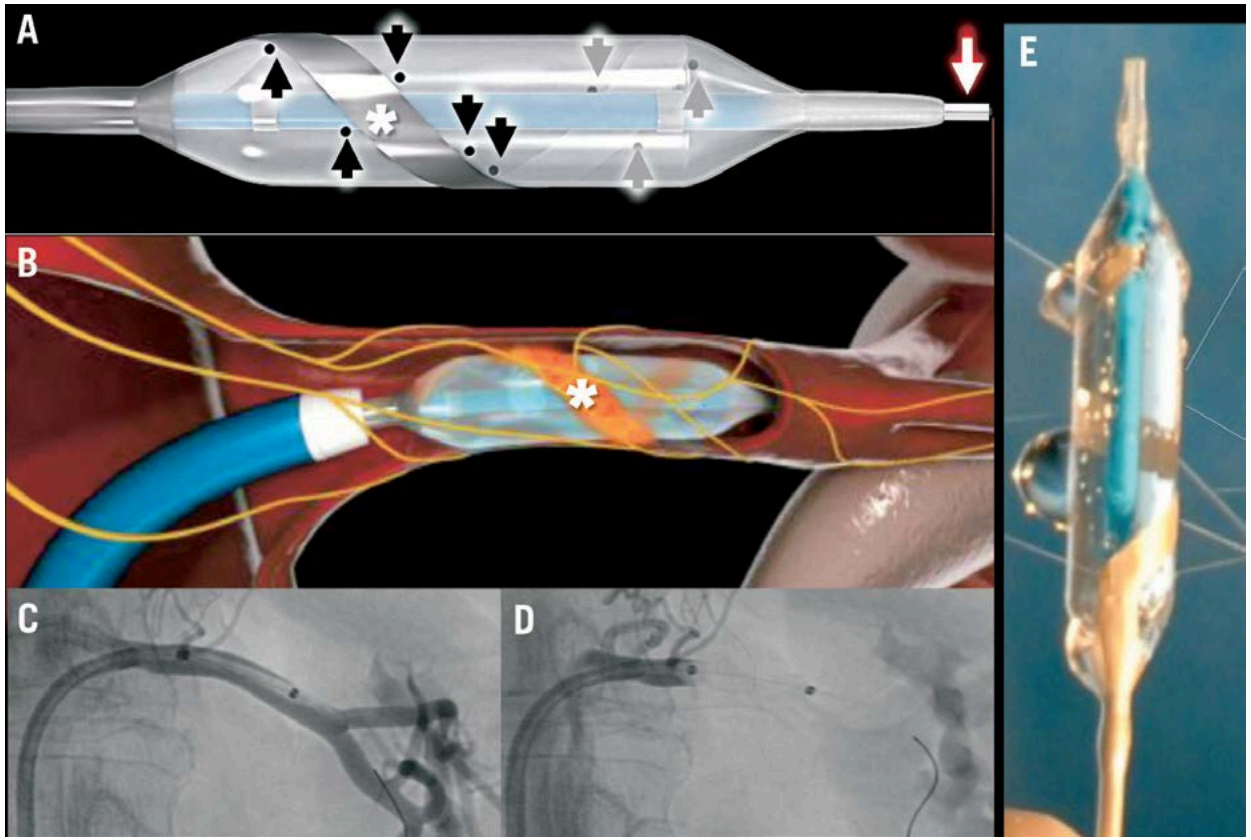
….you have to use less traumatic devices!

… you have too cool the artery!





One Shot ™



Over the wire inflatable balloon catheter, unipolar RF elctrodes on the balloon, irrigated balloon RF generator

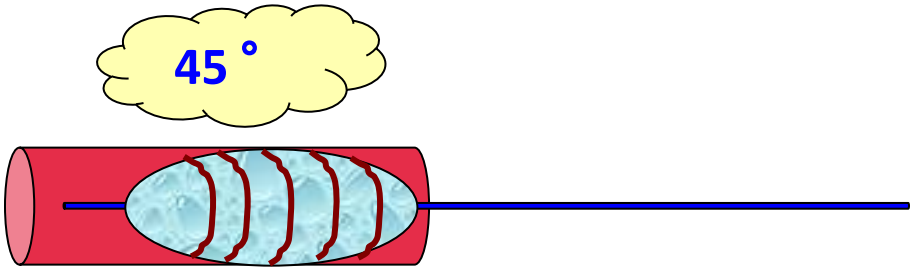
Ablative time per renal artery: 90”

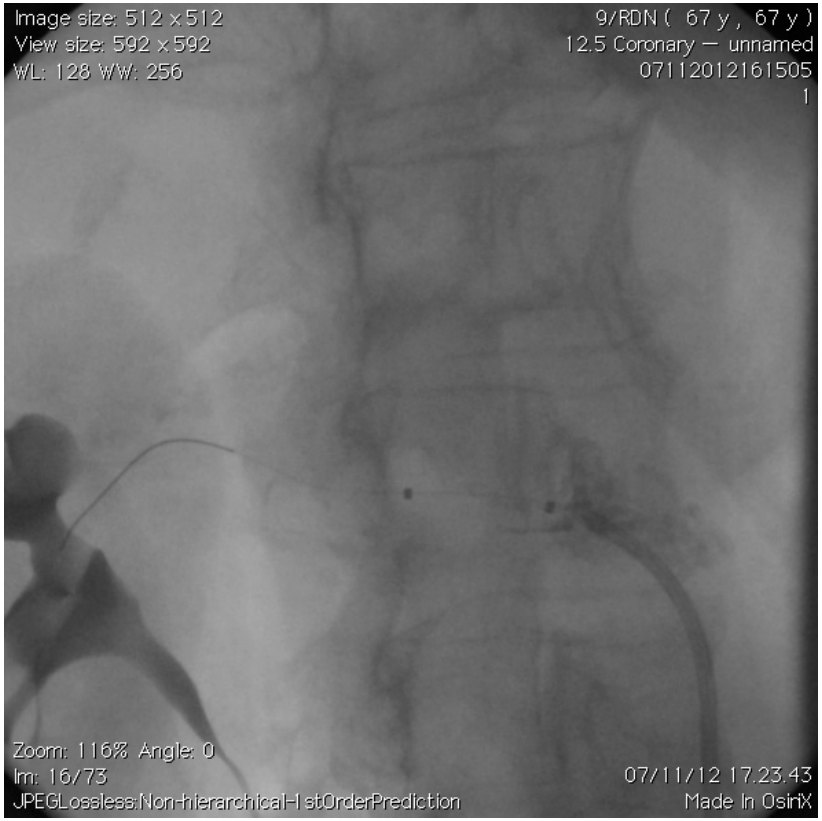
Percutaneous sympathectomy of the renal arteries: the OneShot™ Renal Denervation System is not associated with significant vessel wall injury

Eugenio Stabile[1]*, MD, PhD, FESC; Vittorio Ambrosini[2], MD; Roberta Squarcia[3], PhD; Luigi Salemme[2], MD; Grigore Popusoi[2], MD; Giovanni Esposito[1], MD; Bruno Trimarco[1], MD; Paolo Rubino[2], MD

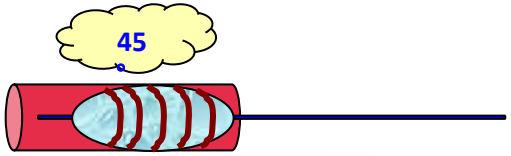
OCT Findings	***Before RADN***	***After RADN***
Number of arteries with at least one analysable pullbacks	*11*	*10*
Analysable frames per Pull backs (Mean ± SD)	*125 ± 60*	*139 ± 48*
Thrombus, pullbacks n (%)	*0*	*1 (10)*
Thrombus, in total	*0*	*1*
Thrombus, per RA (Mean ± SD)	*0*	*0.1 ± 0.32*
Dissections, n pullbacks (%)	*0*	*3 (33)*
Dissections, in total	*0*	*3*
Dissections, per RA (Mean ± SD)	*0*	*0.3 ± 0.48*

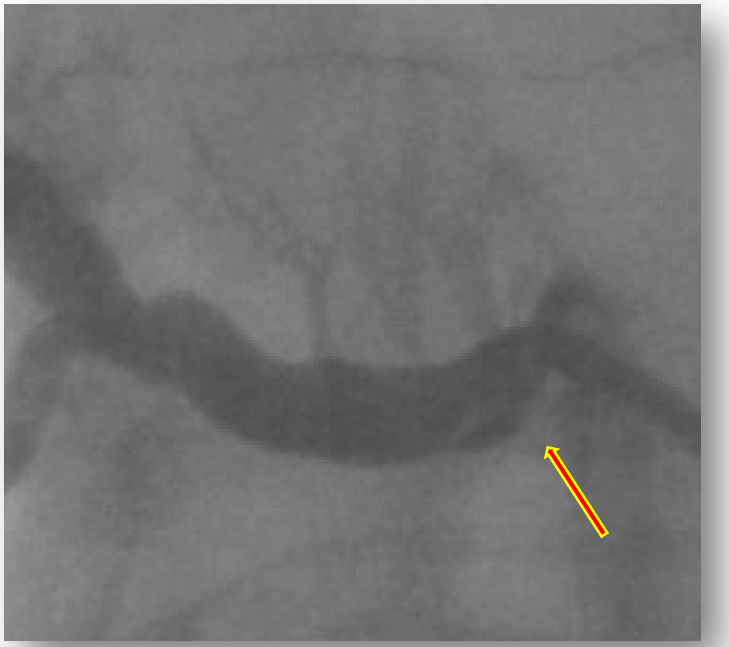
Stabile E et al. Eurointervention 2013

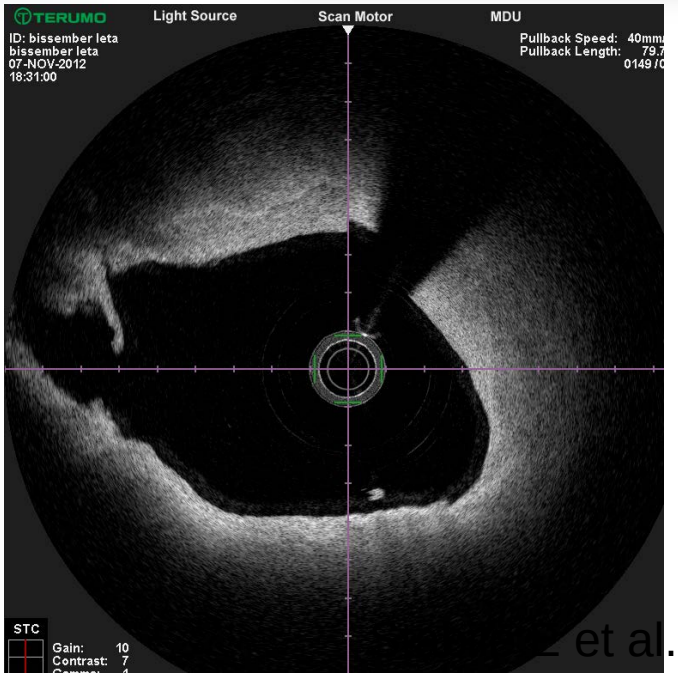




Stabile E et al. Eurointervention 2013

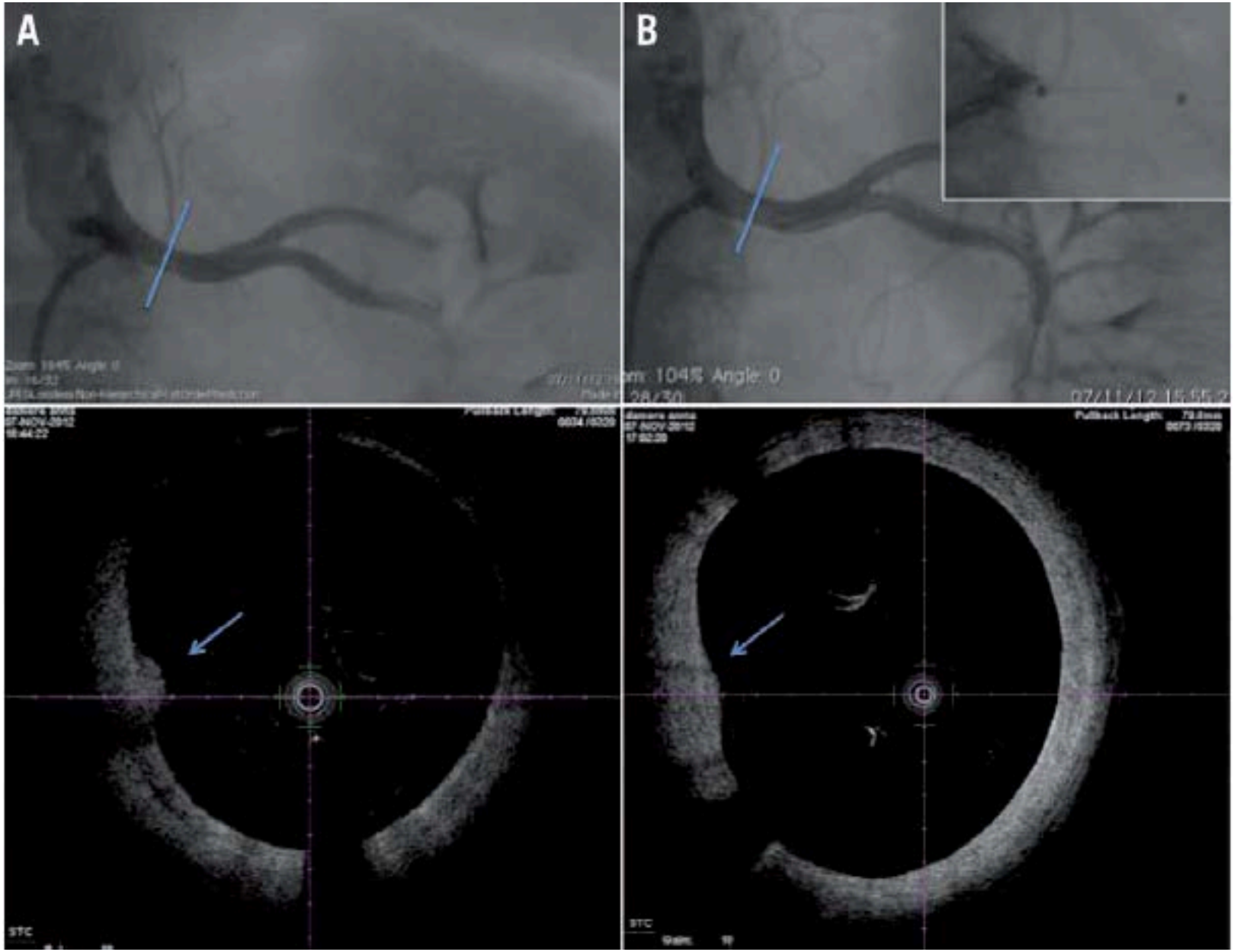






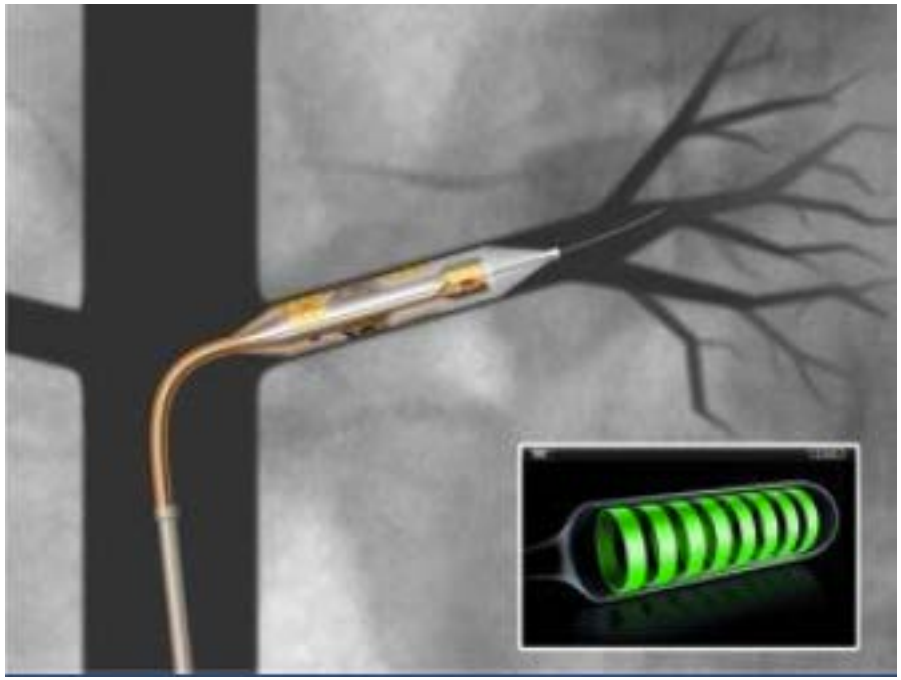
But……..

et al. Eurointervention 2013



Stabile E et al. Eurointervention 2013

Vessix V2 ™



Over the wire inflatable balloon catheter, bipolar RF elctrodes on the balloon, RF generator (recharchable)

Ablative time per renal artery: 30”

Take home messages

RADN is an effective treatment for Resistant hypertension

It can create vessel wall damage

Further studies are needed to evaluate the clinical relevance of the induced renal artery damage

Thank you!