Unmet needs in TAVI: My sweet dreams

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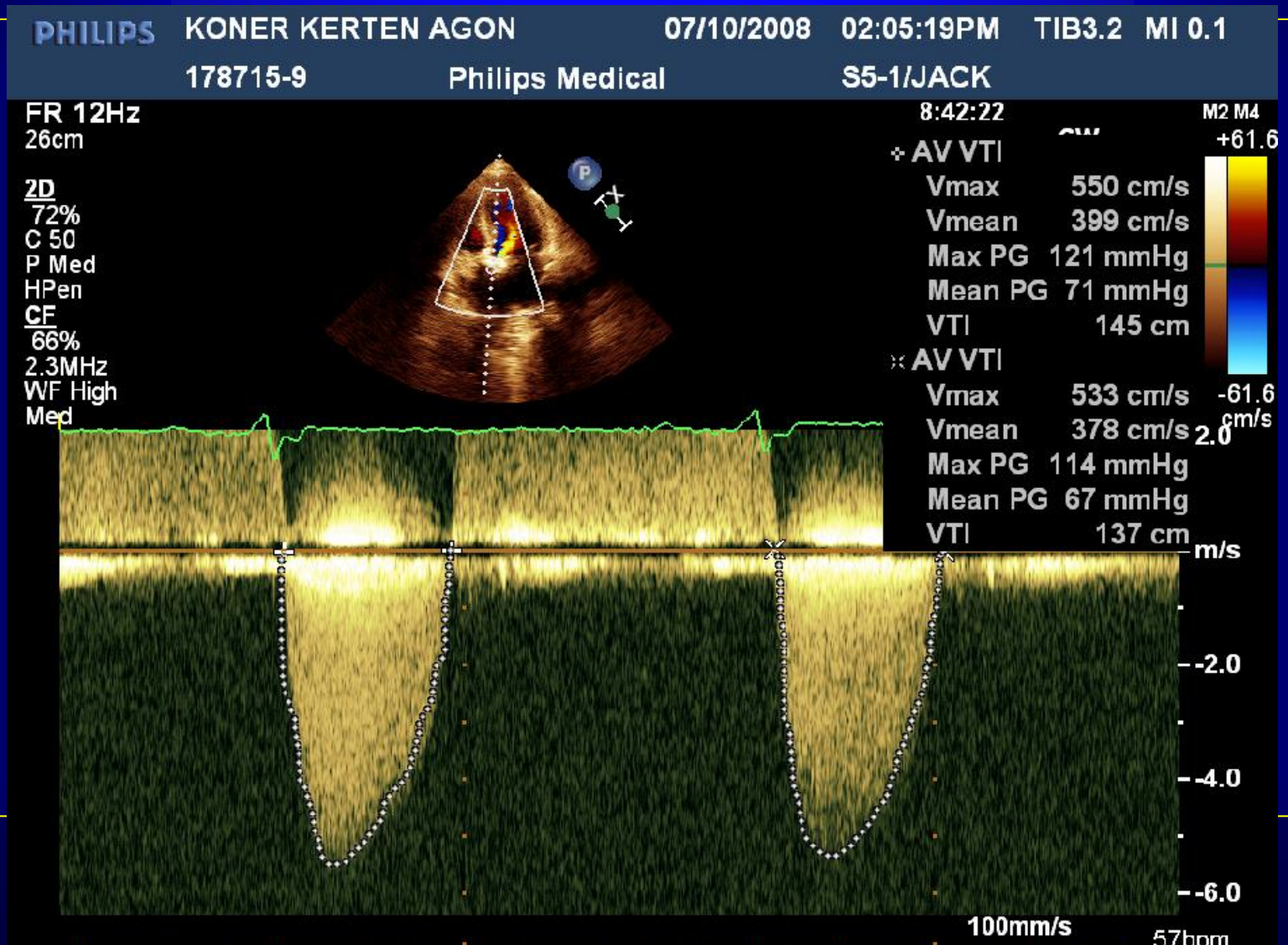
Case Presentation

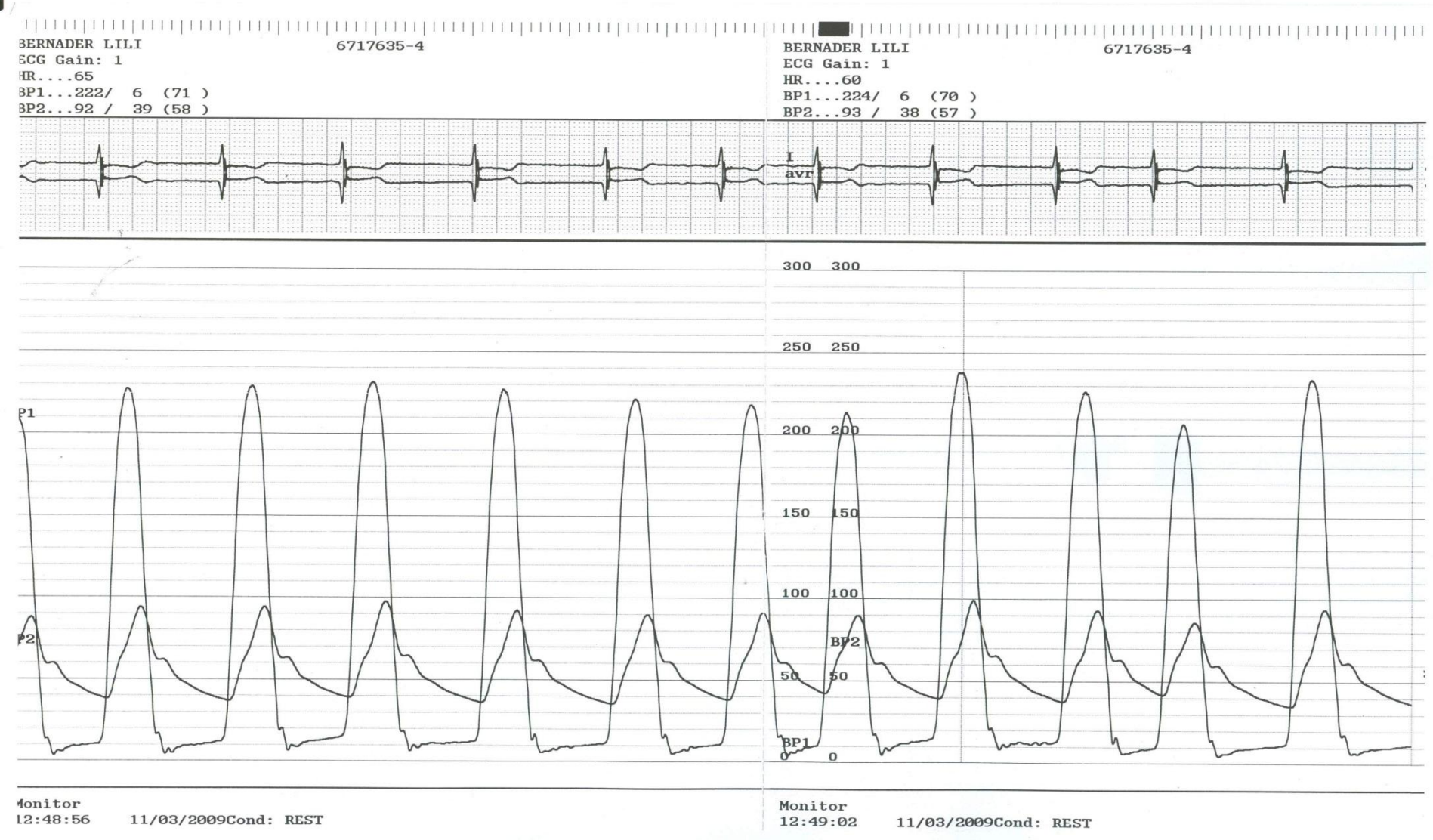
- E.K. 85 y-old male
- HTN
- Hypercholesterolemia
- Obesity
- Rec. pulmonary edemas → SOB – NYHA class III

Echocardiography

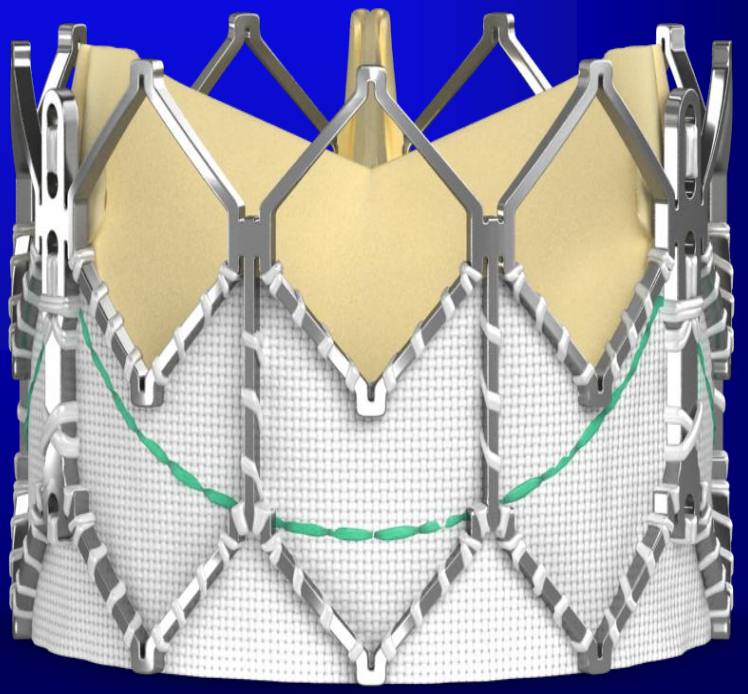
Echocardiography



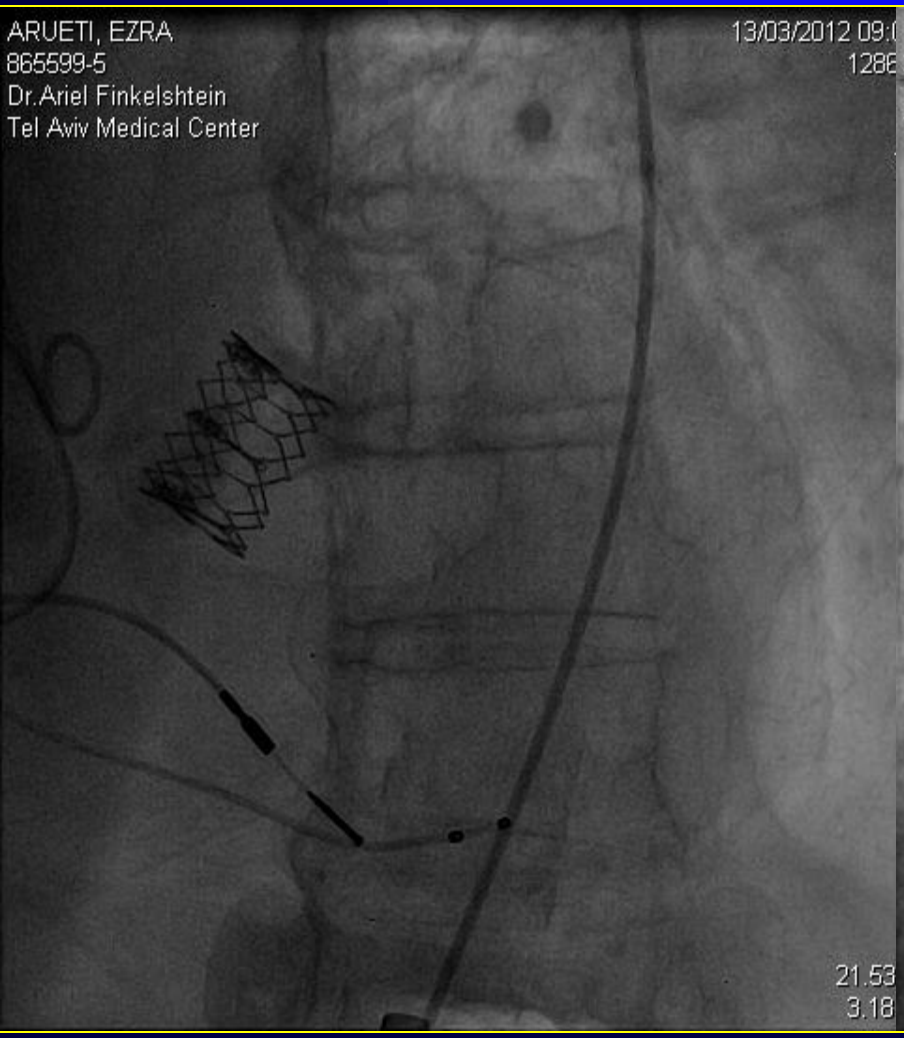
Hemodynamics-before

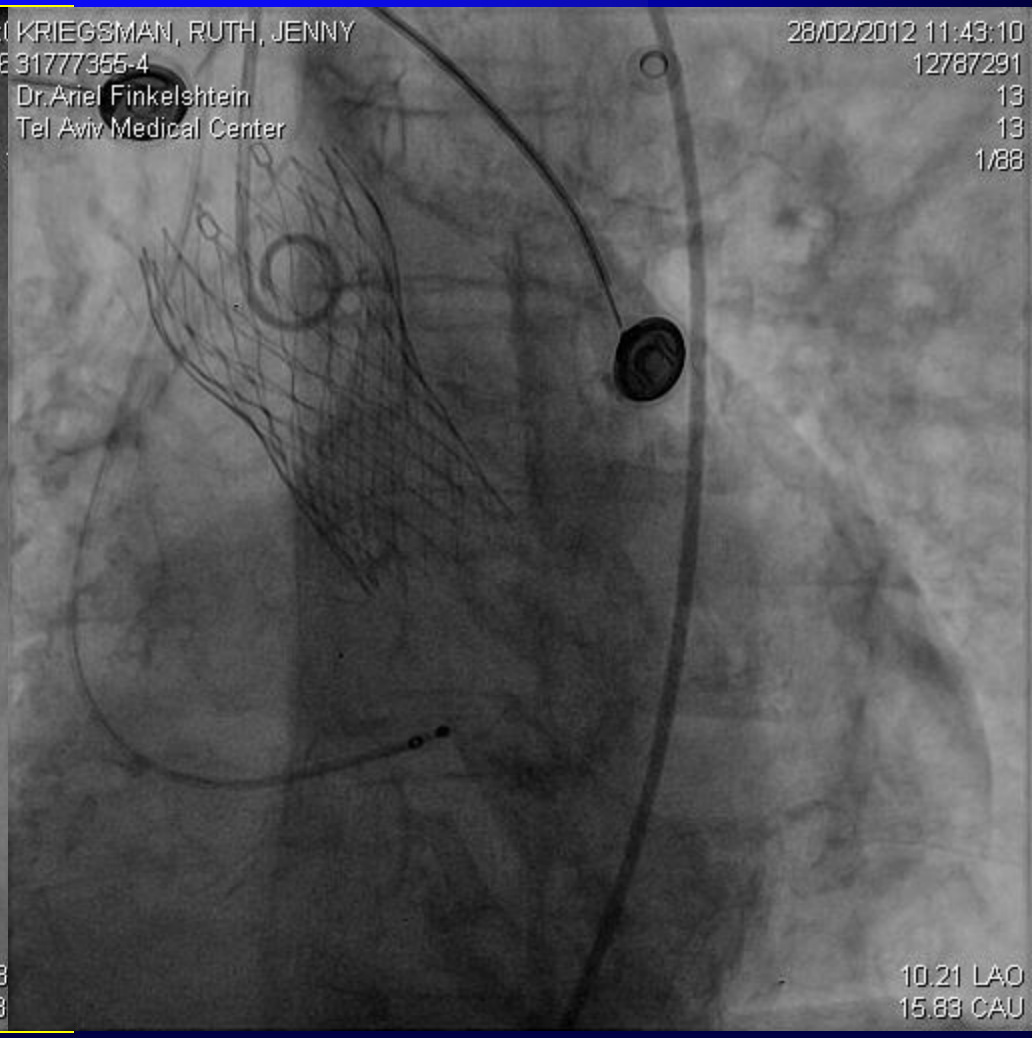


Current Generation Devices: That's what we have, that's what we have to win with…



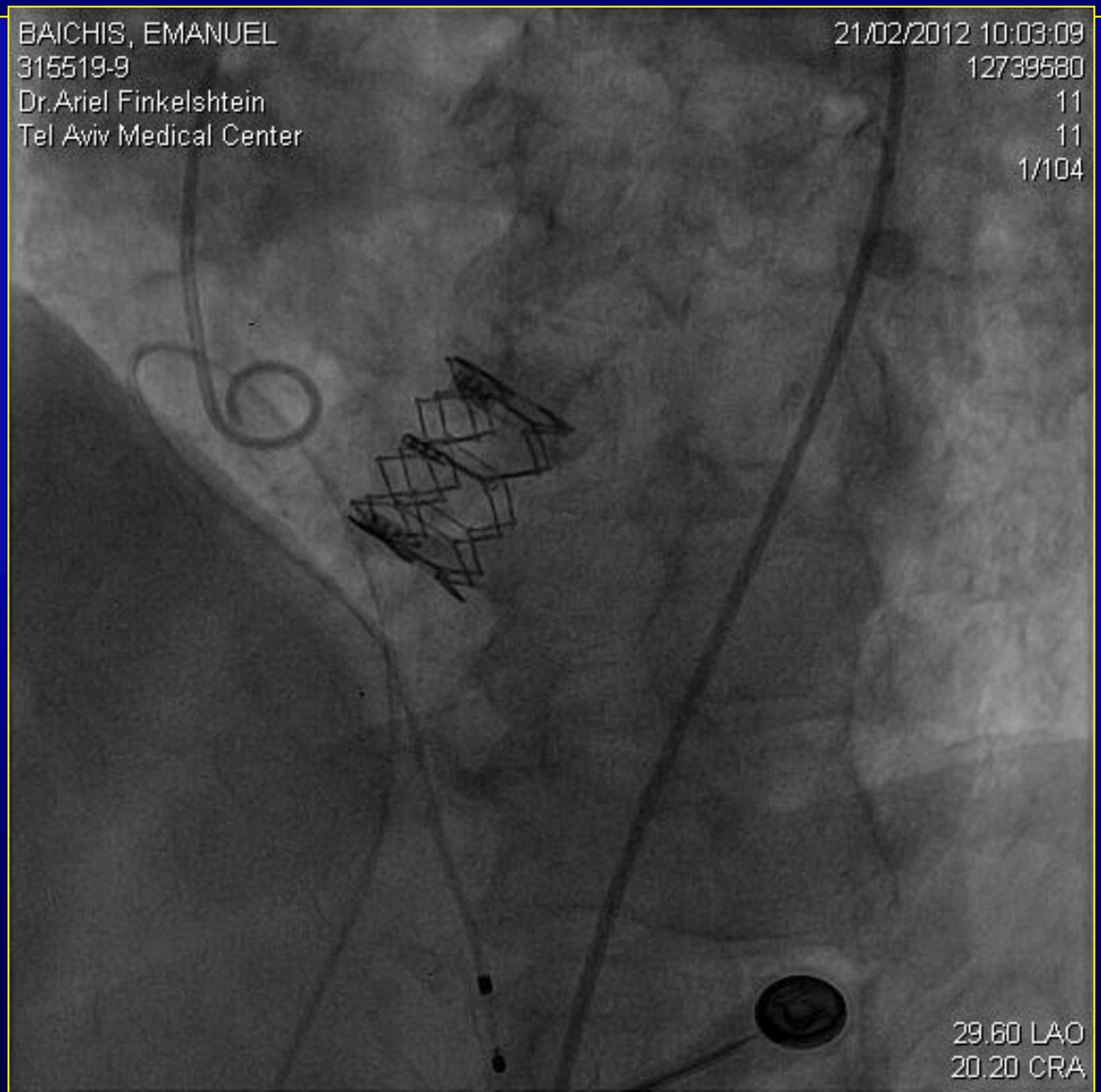
Well, the vast majority looks like that





BUT SOME WILL NOT…

Like this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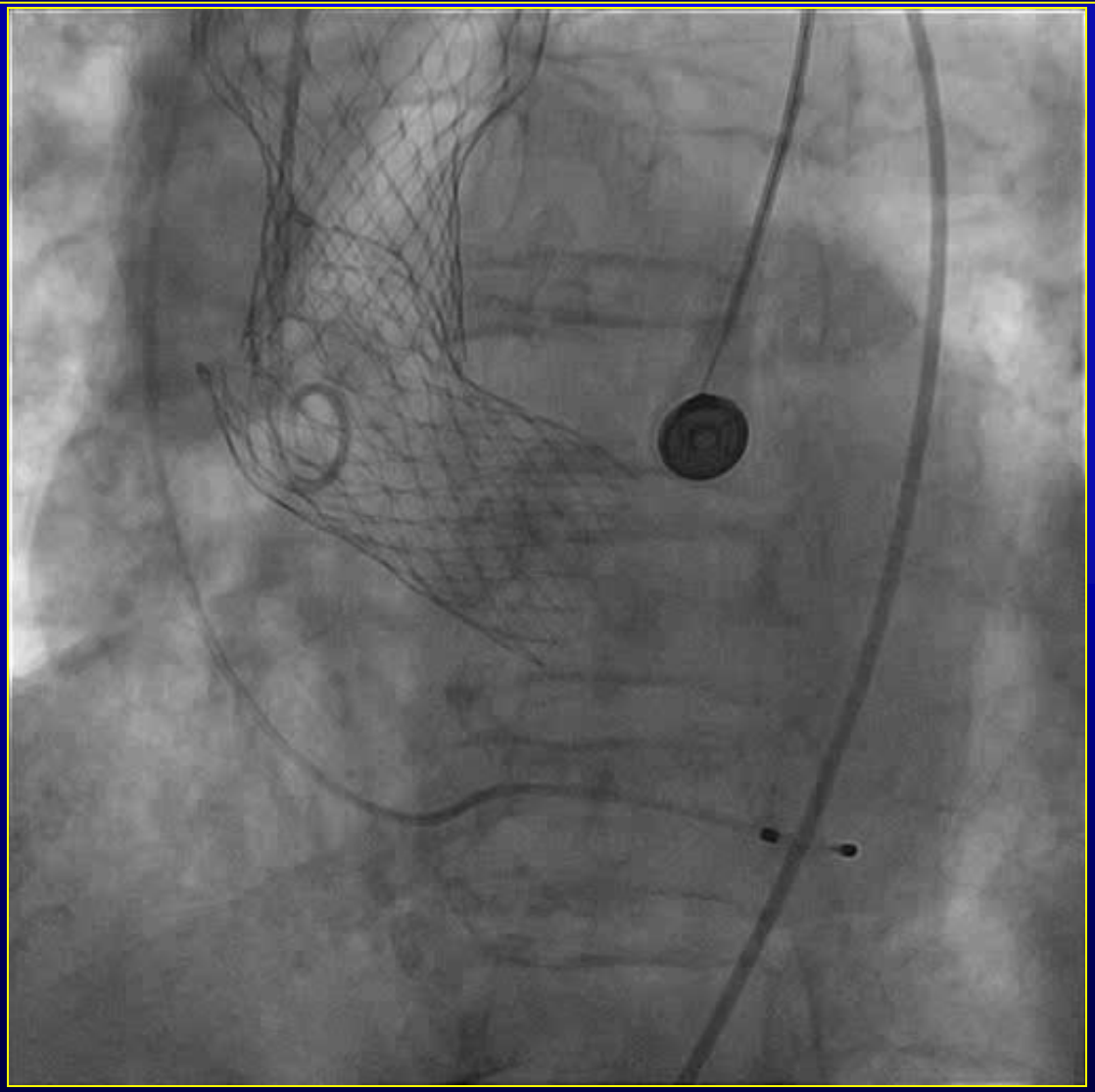
And this



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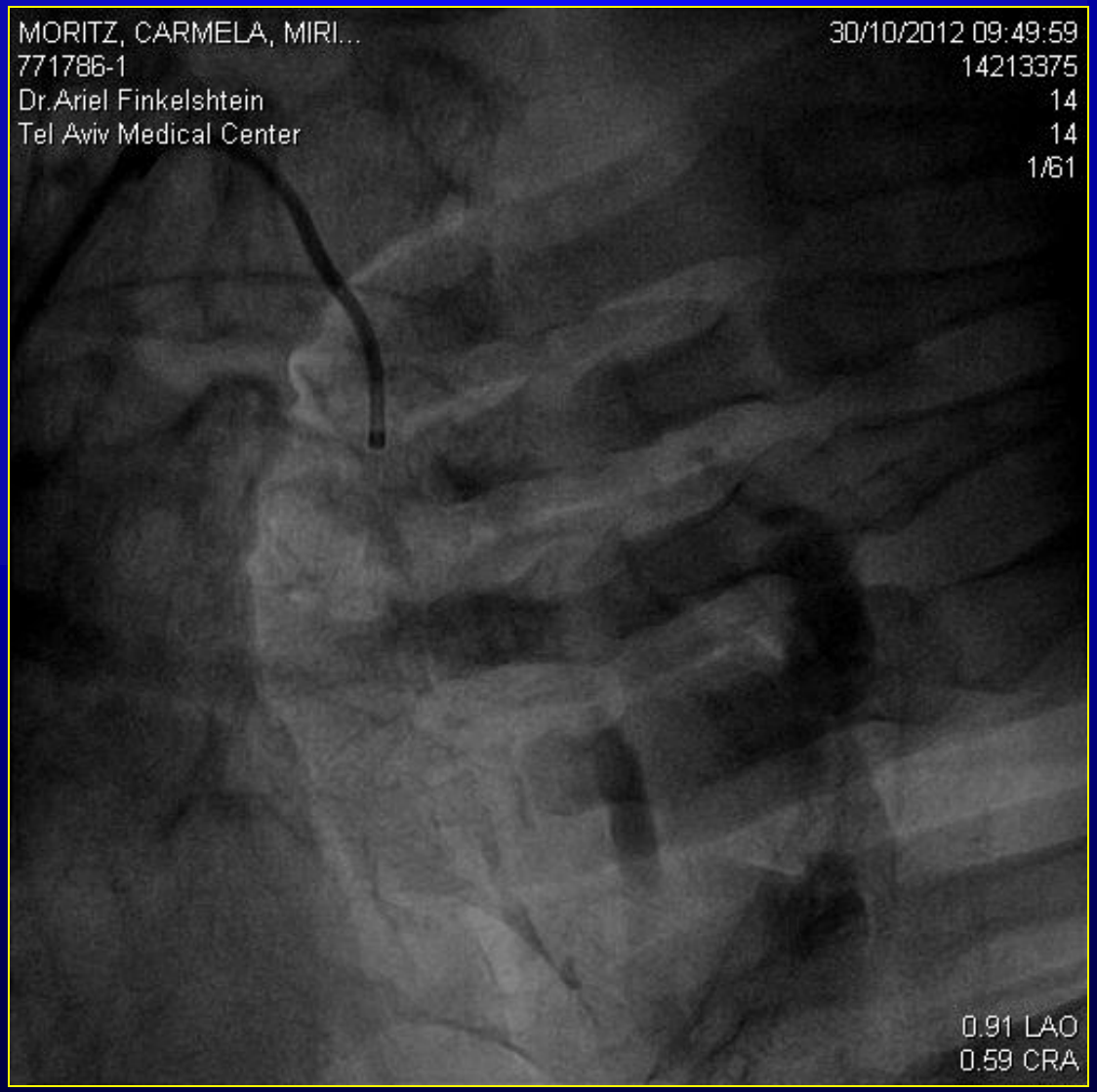
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TAVI Technologies: My main problems

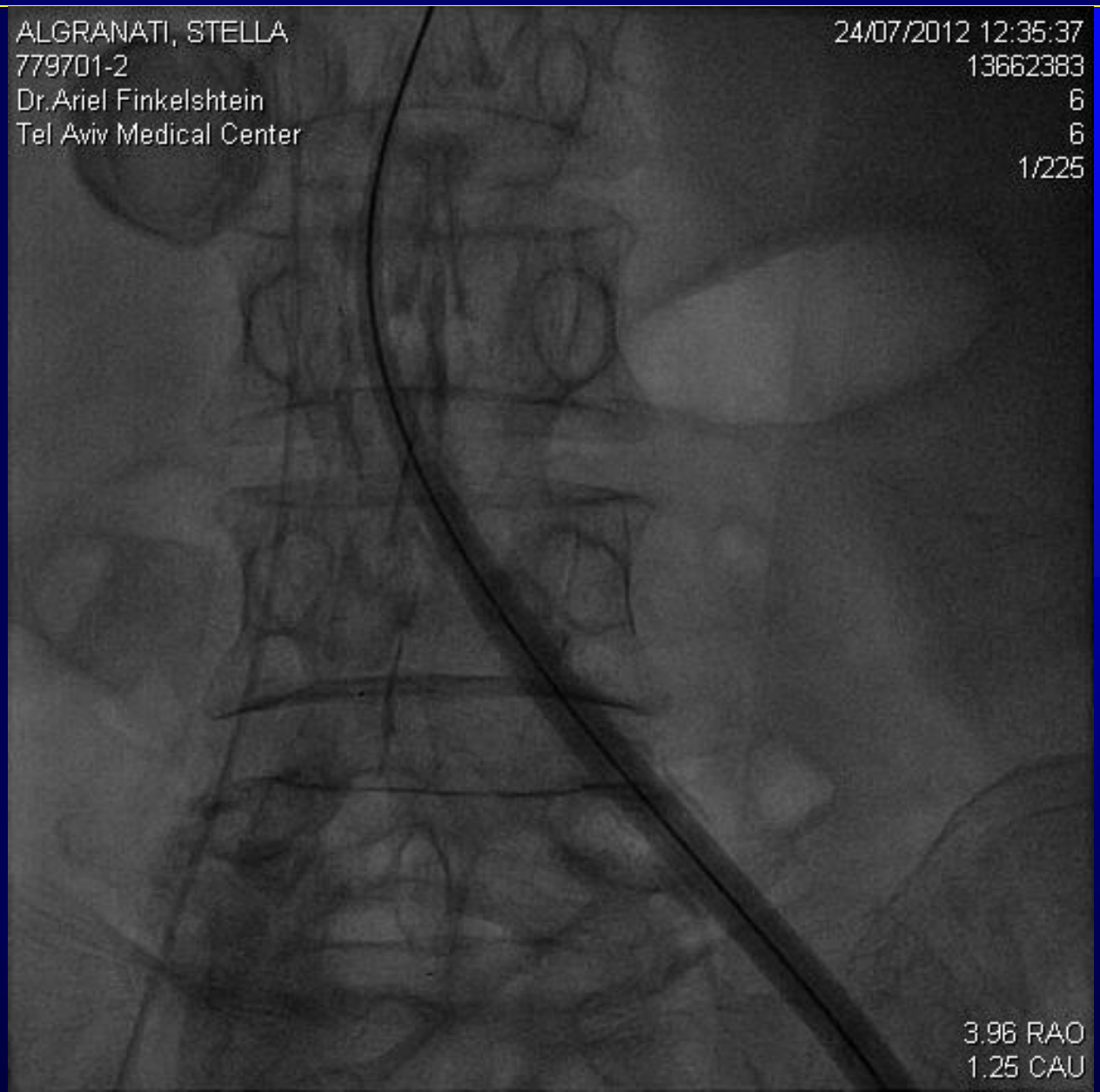
- ***Vascular complications***
- ***Calcium***
- ***Positioning-three dimention***

I have a dream…

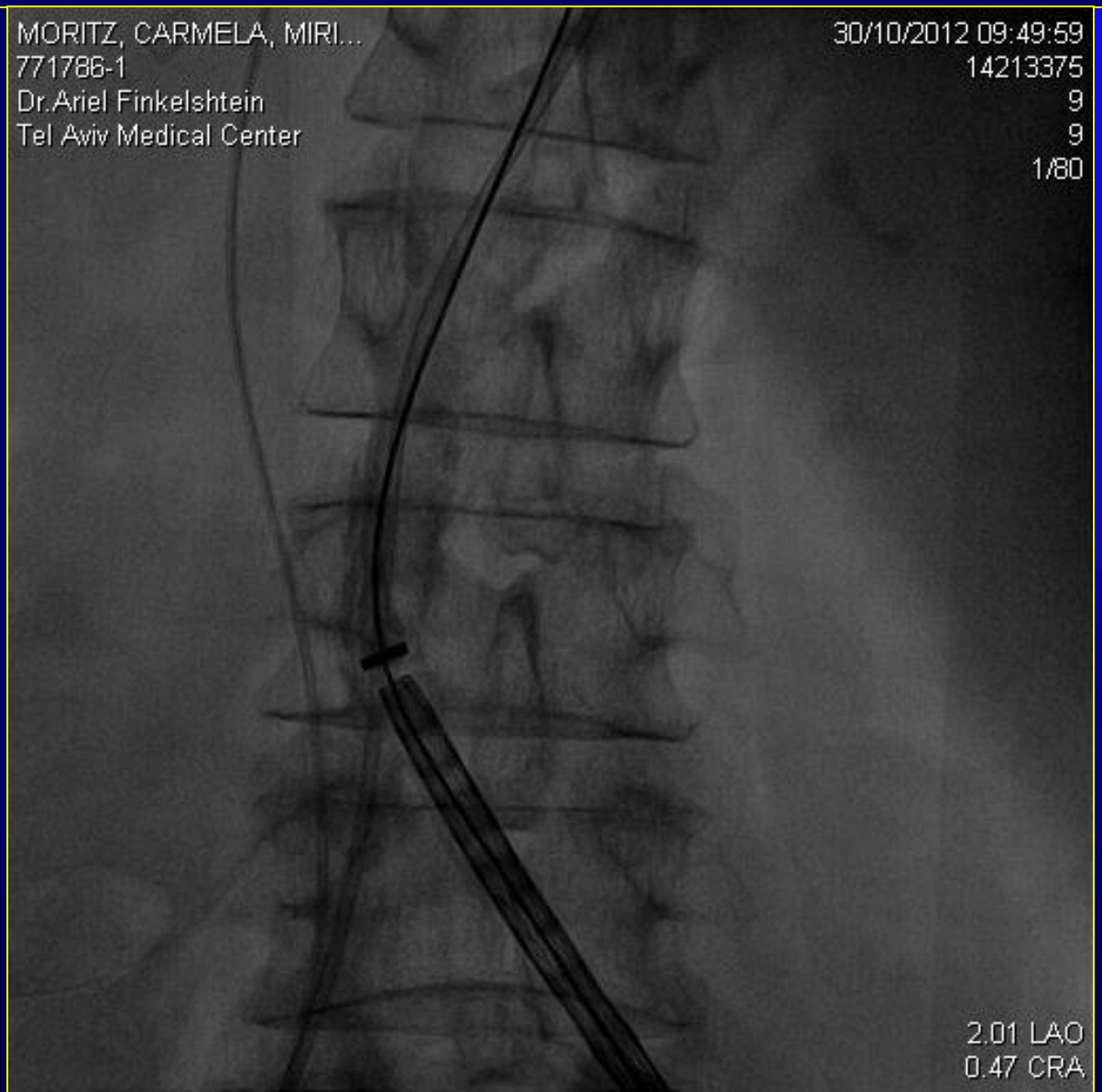
My TAVI dream

- Vascular complications→Lower profile
- Calcium→Anti calcium technology
- Better positioning→On line imaging

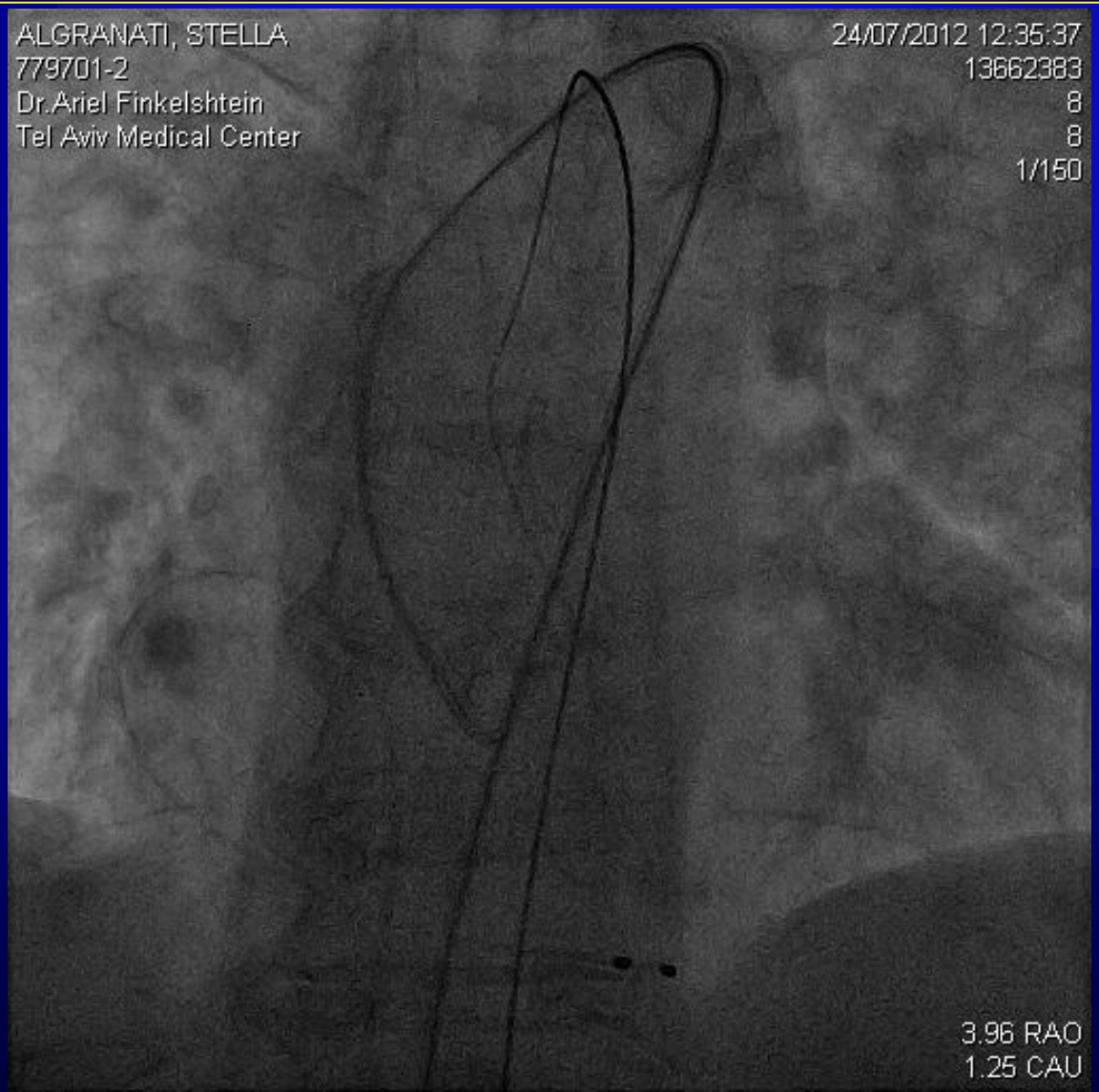
What doesn’t go with force…



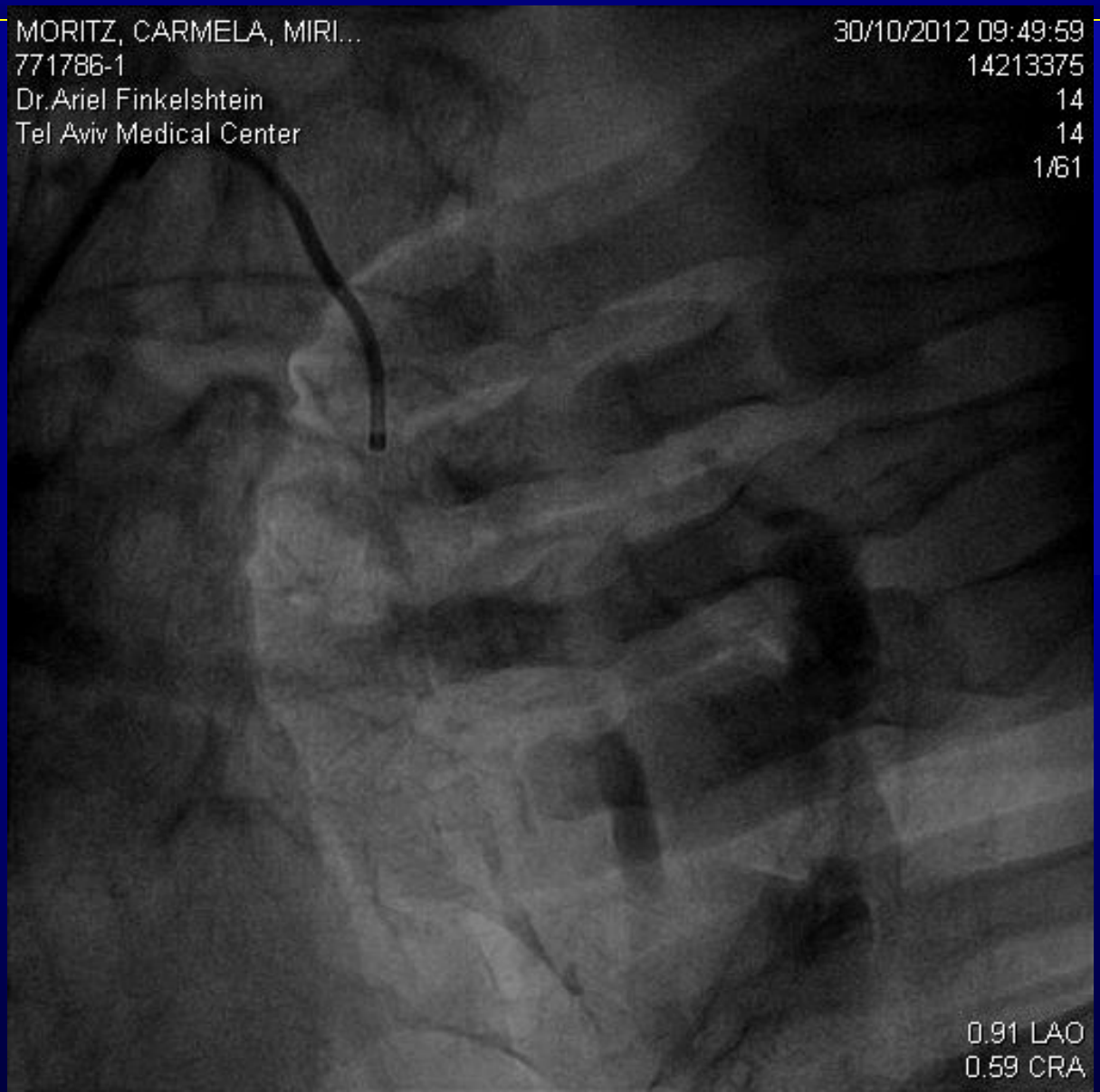
This is not enough…



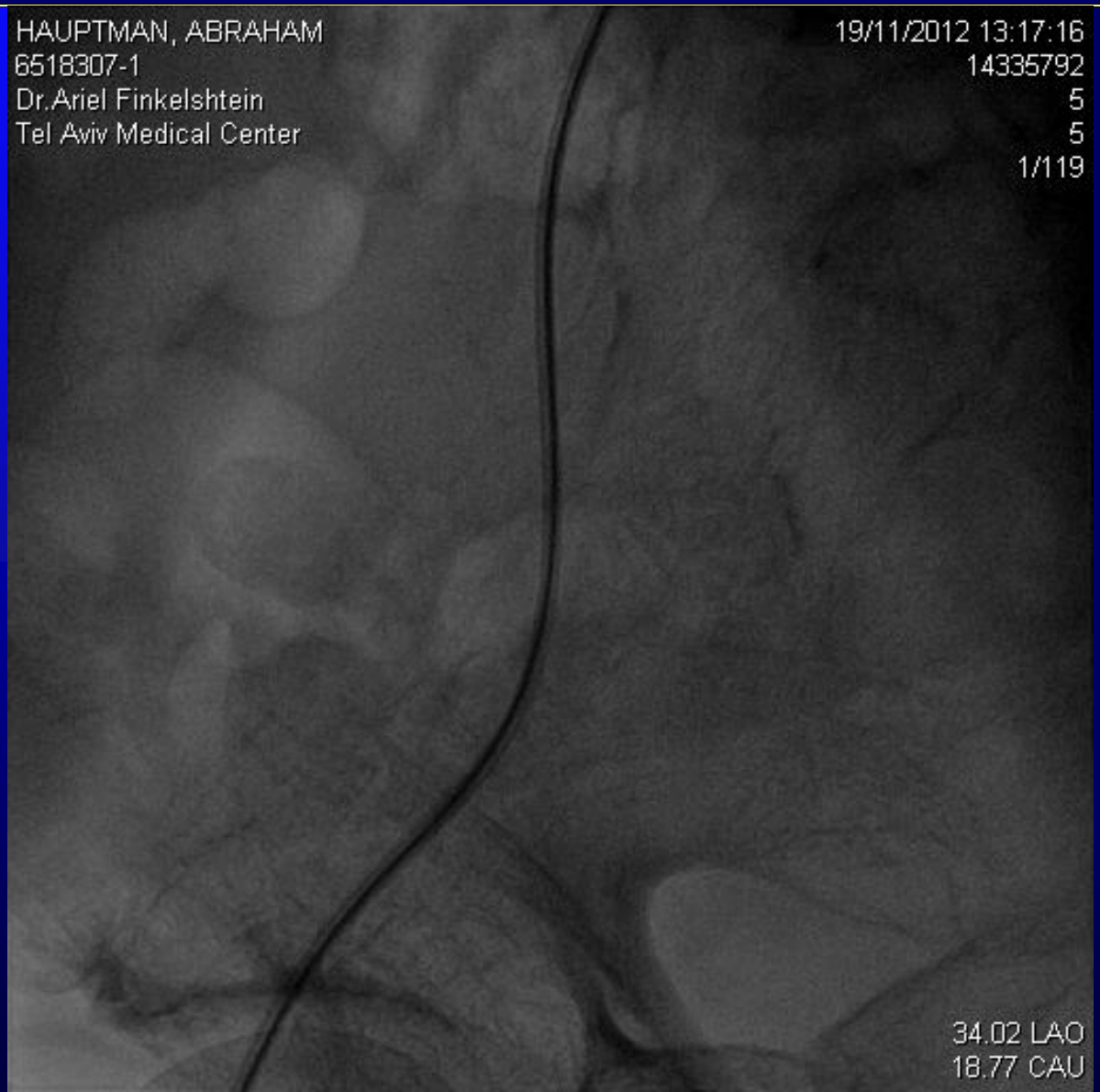
This is a buddy pigtail



This time we were not that lucky



Long, long torturouse road

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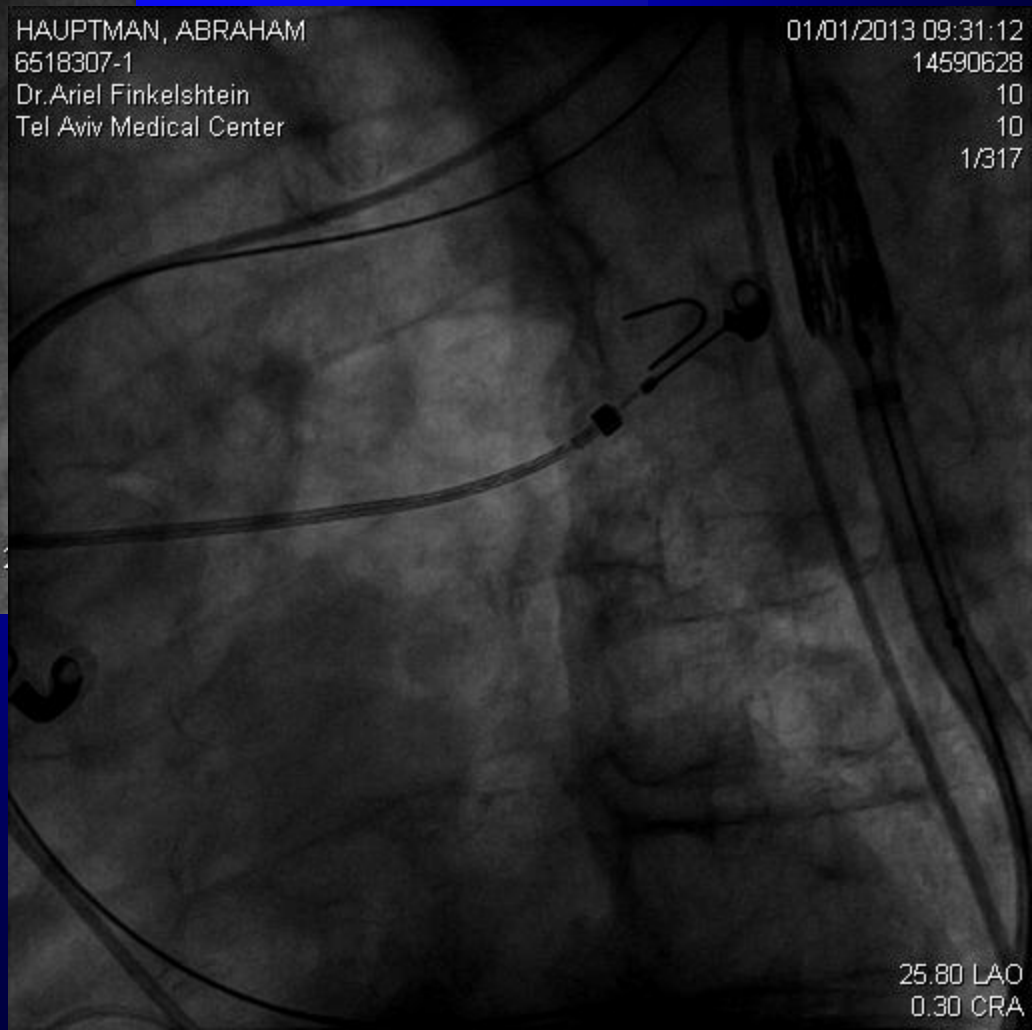
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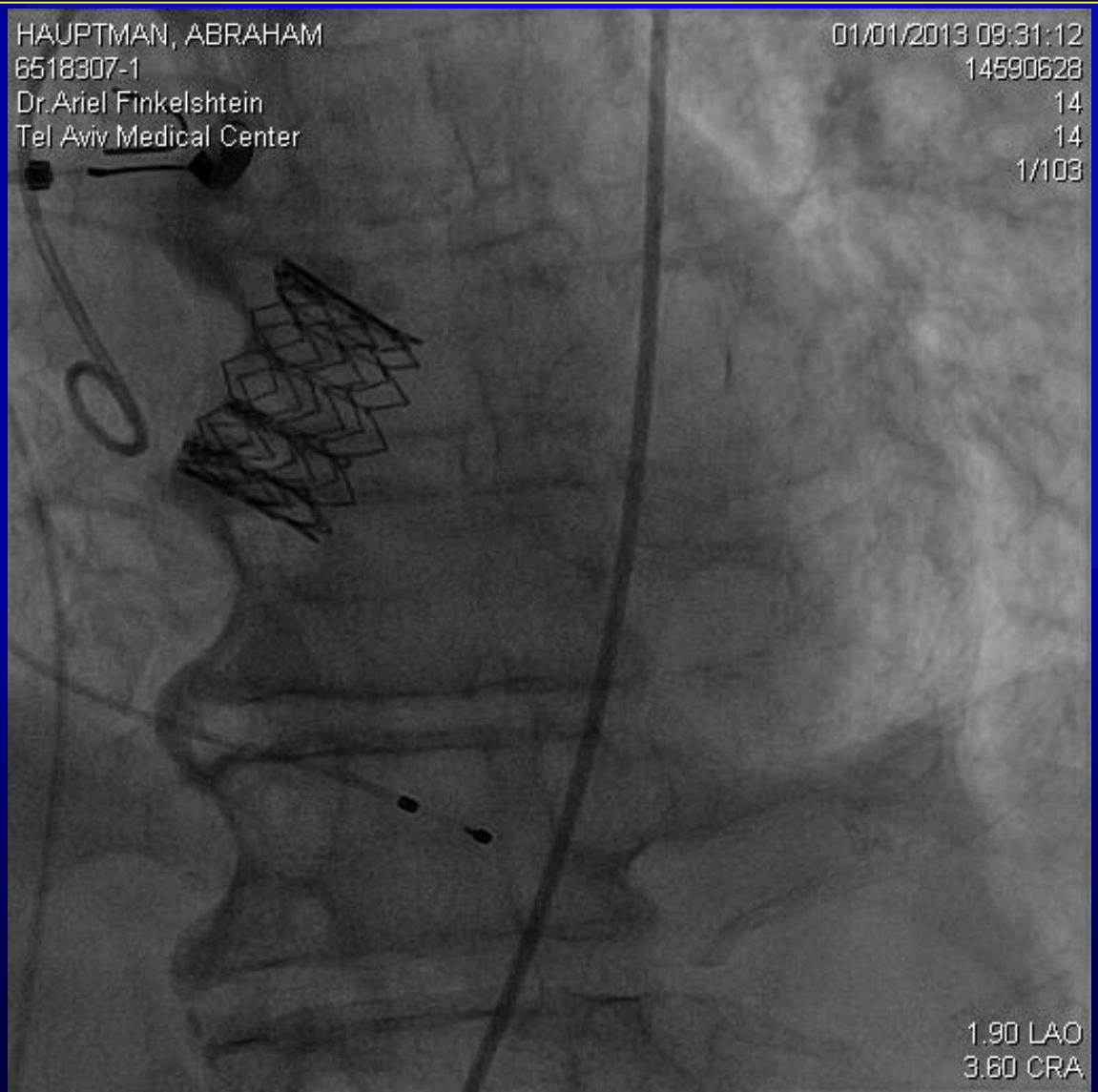
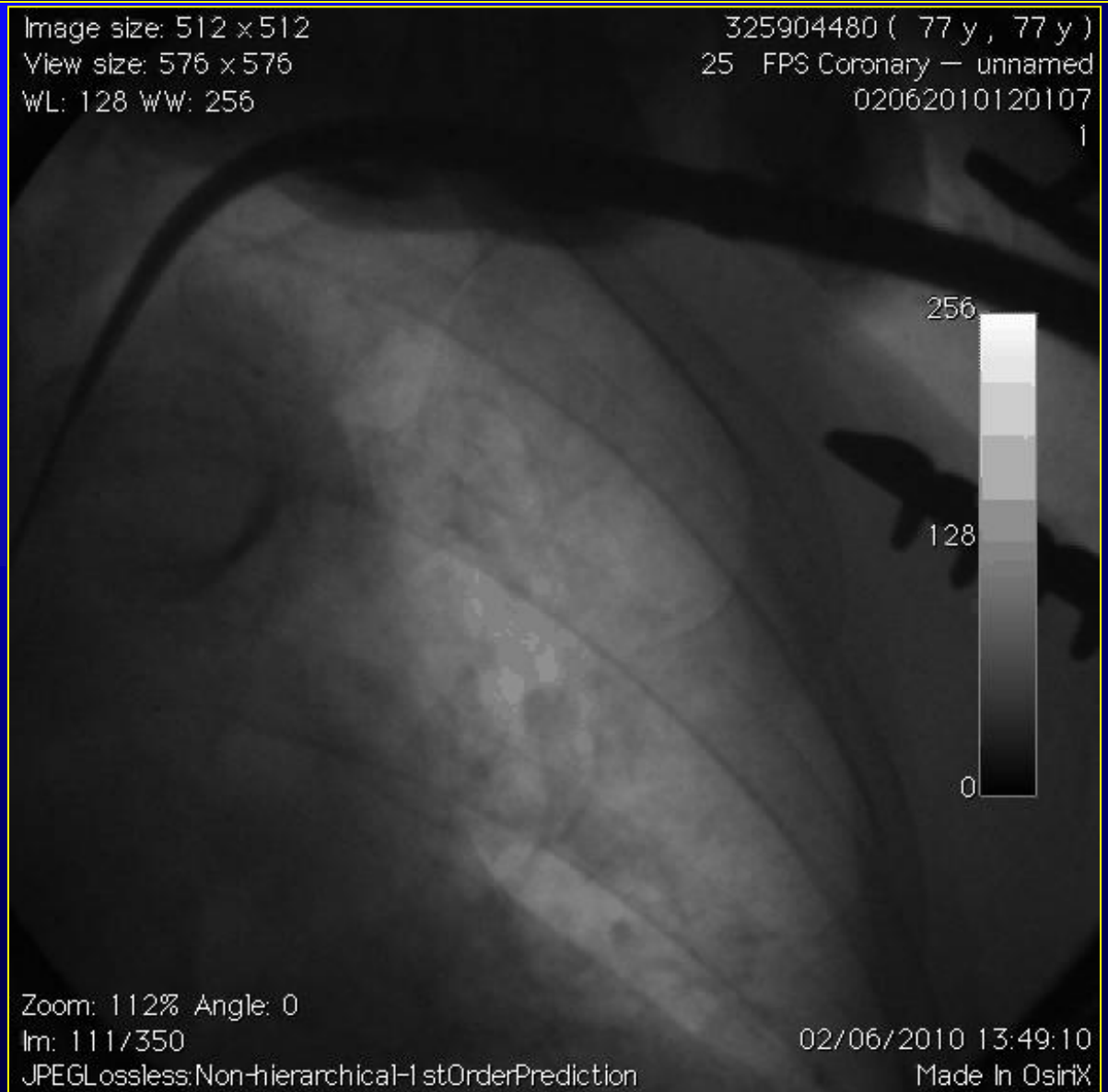
Don’t let it mislead you…



Don’t you ever forget: there are some other access site alternatives. Like this…



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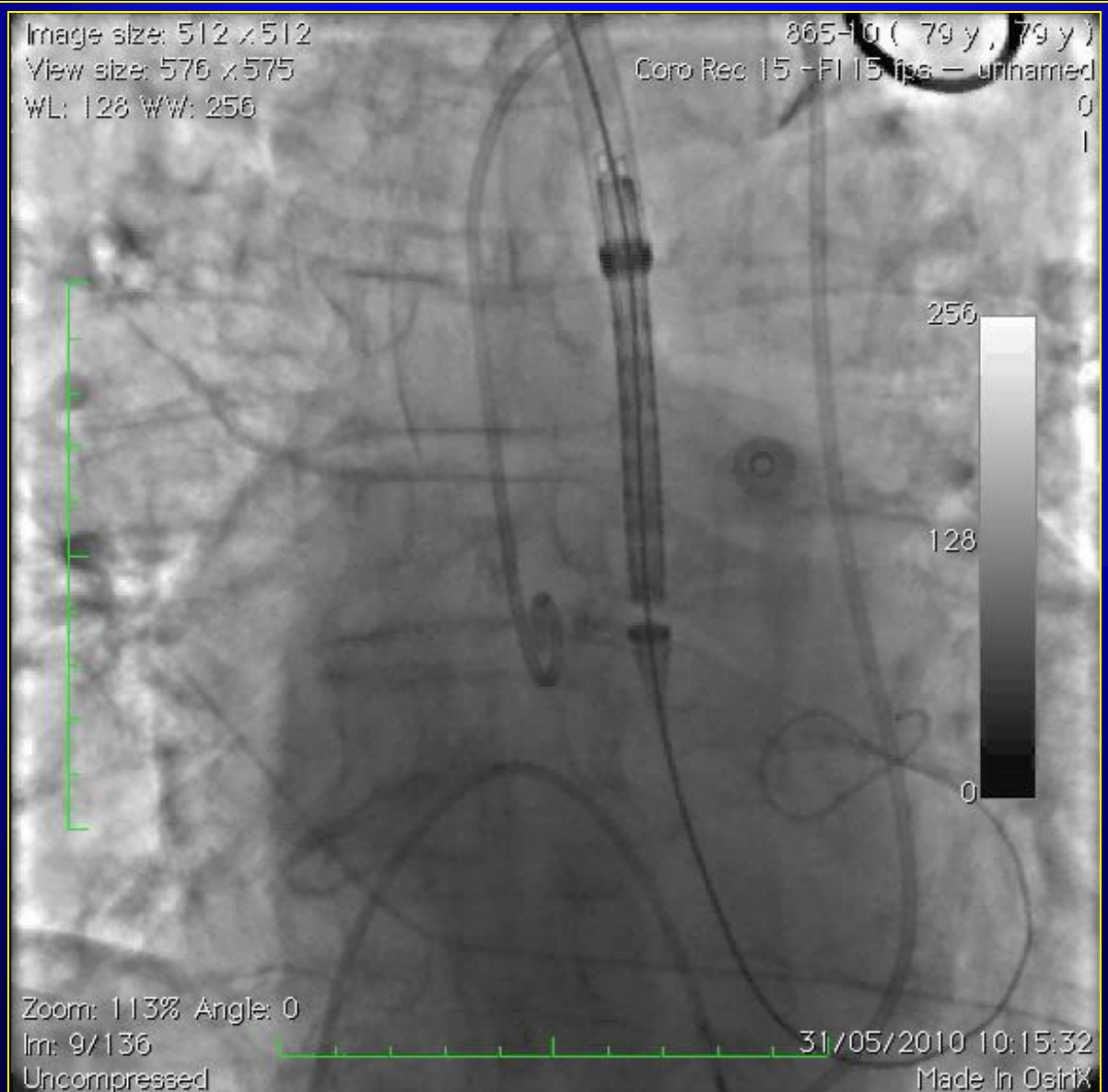
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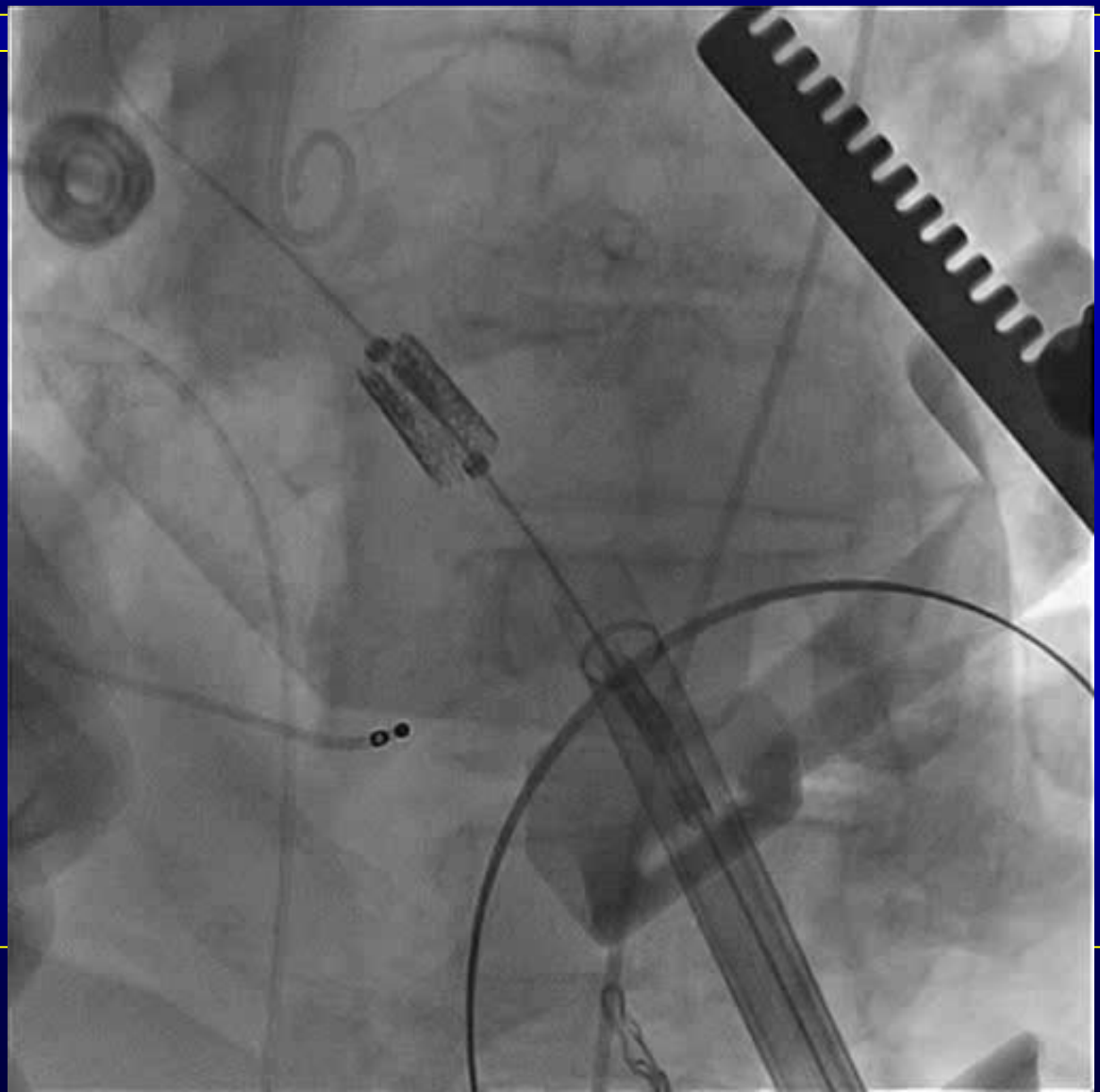
And this



Houston, we have a problem

- Vascular complications is a major threat during or following the course of TAVI.
- The problem includes perforation of the iliac-femoral arteries, critical stenosis and occlusion of the arteries, bleading and pseudoaneurysm formation.
- TAVI related vascular complications rate are in the range of ~10%-15%.
- Major vasclar complications→increased mortality.

Where does the evidence come from?

Randomized controlled trials

Registries

Small observational studies & reports

Randomized trials

PARTNER US completed

PARTNER US Cohort B

PARTNER US Cohort A

REGISTRIES

FRANCE registry

German TAVI registry

U.K. TAVI registry

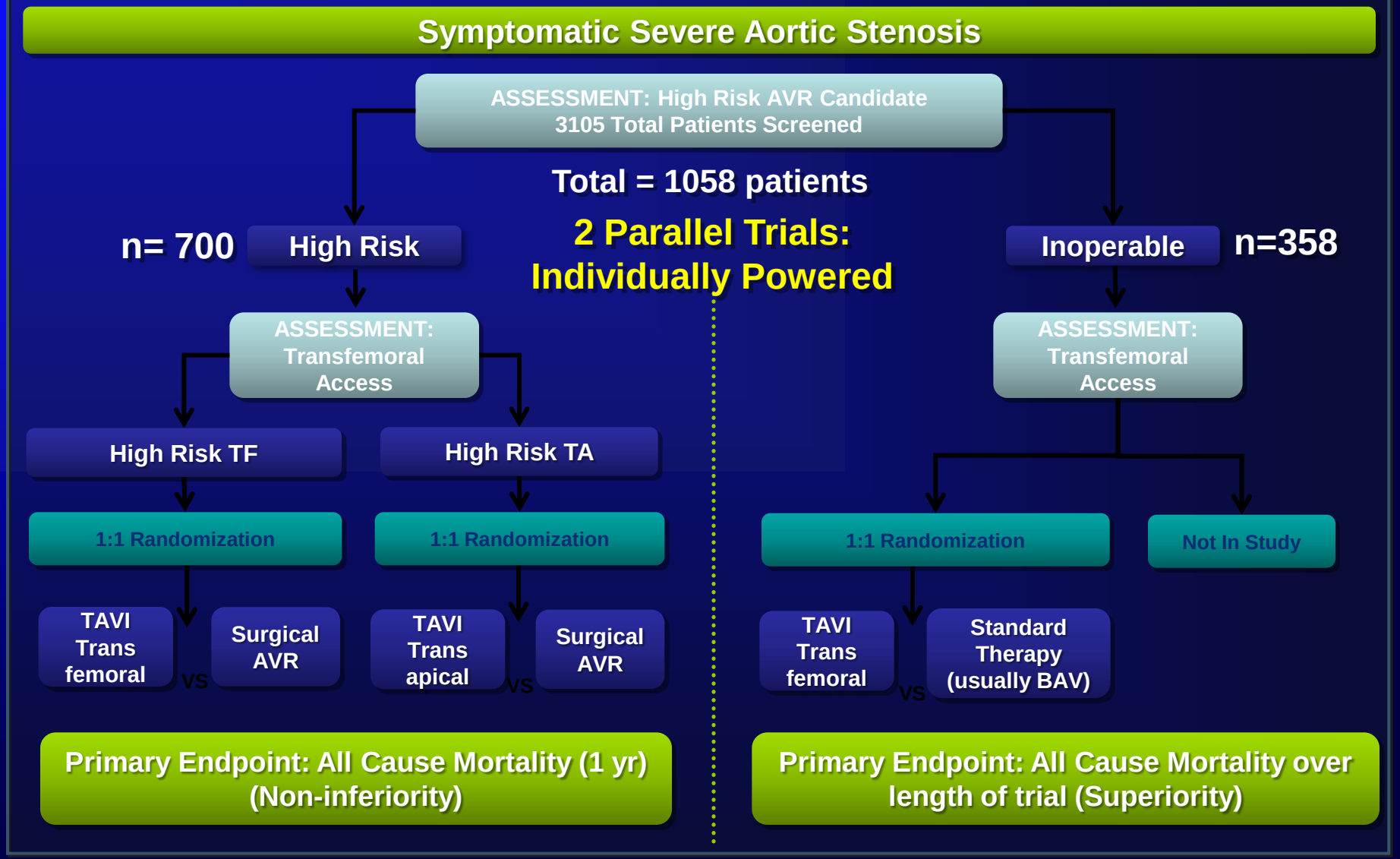
SOURCE registry

CoreValve Italian registry

ADVANCE registry

PARTNER EU registry

PARTNER Study Design



Vascular complications in PARTNER

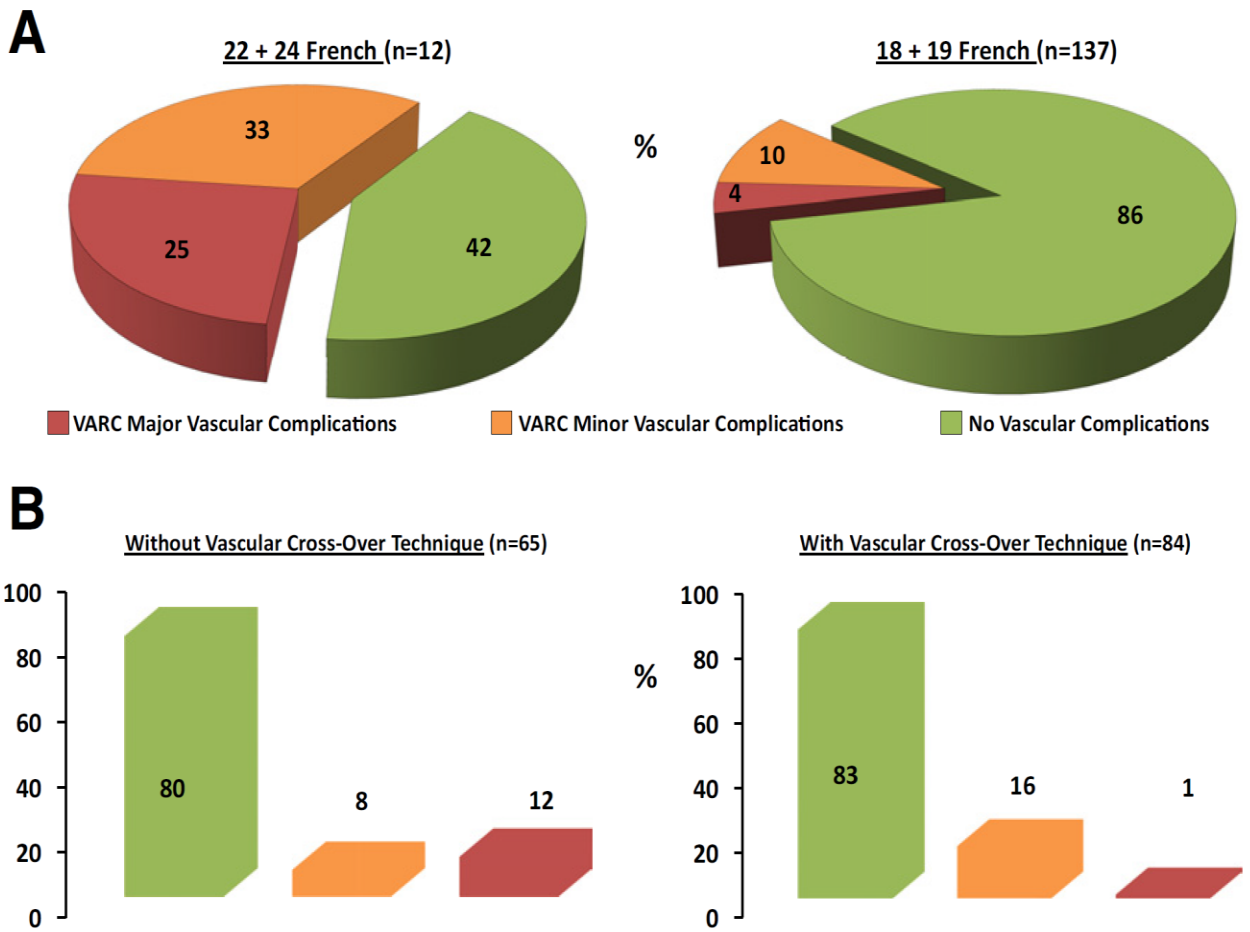
- **Partner 1 trial**
  - **–TAVI v's standard TX (including balloon valvuloplasty) in non-operable patients**
  - **–179 patients in TAVI group**
  - **–22 or 24 Fr sheath**
  - **– In one year**
    - **Overall 32%**
    - **Major 17%**

Table 2. Clinical Outcomes at 30 Days and 1 Year.*

Outcome	30 Days			1 Year		
	TAVI (N=179)	Standard Therapy (N=179)	P Value†	TAVI (N=179)	Standard Therapy (N=179)	P Value†
	no. of patients (%)			*no. of patients (%)*		
Vascular complications						
All	55 (30.7)	9 (5.0)	<0.001	58 (32.4)	13 (7.3)	<0.001
Major	29 (16.2)	2 (1.1)	<0.001	30 (16.8)	4 (2.2)	<0.001

Leon M et al. Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery. N Engl J Med 2010;363:1597-1607.

Vascular complications in PARTNER

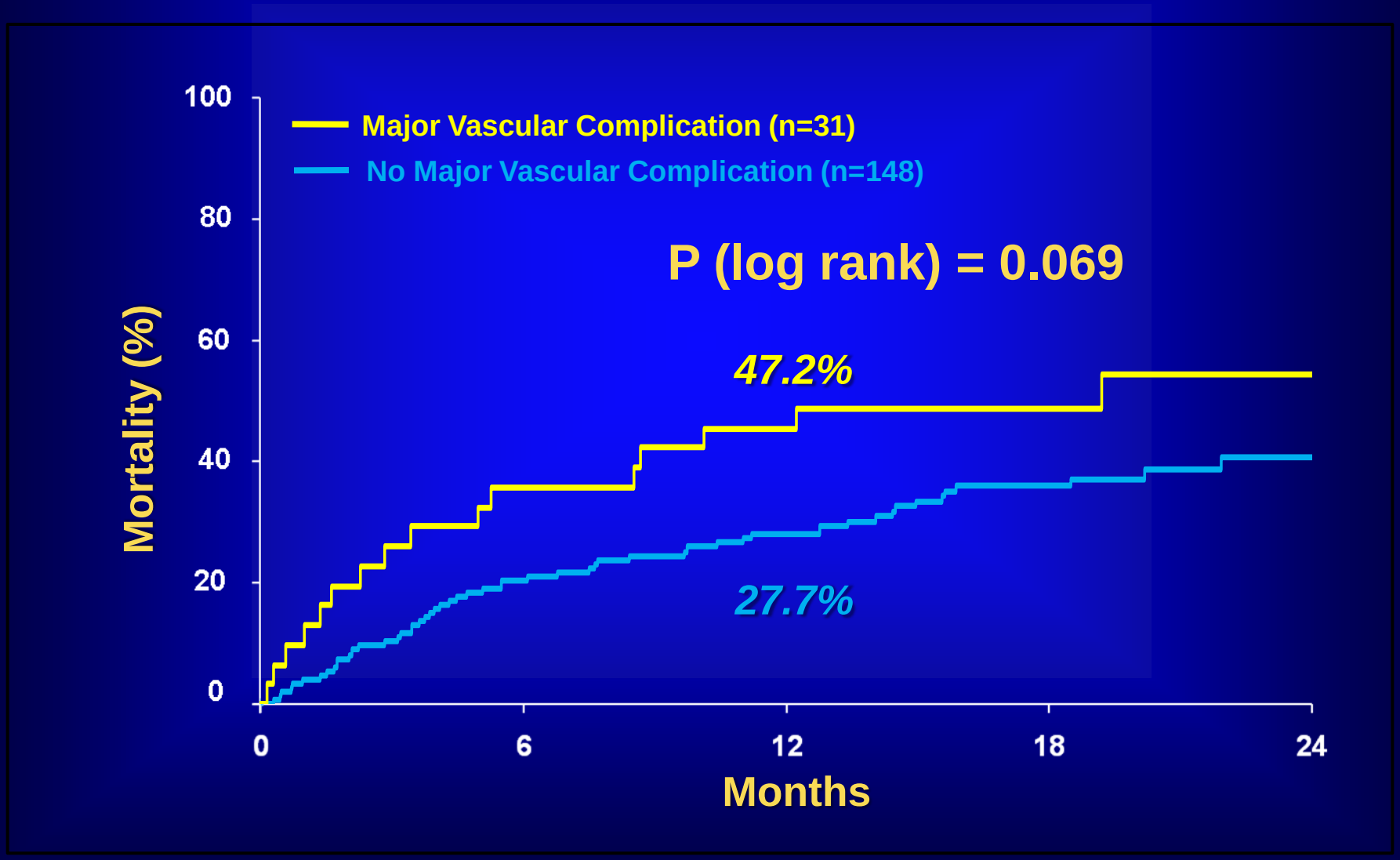


Occurrence of vascular complications according to vascular access sheath size (A) and by vascular closure crossover technique (B).

Stortecky et al. Percutaneous Management of Vascular Complications in Patients Undergoing Transcatheter Aortic Valve Implantation. J Am Coll Cardiol int 2012;5

Mortality vs. Major Vasc Complics

TAVI patients



European Heart Journal (2011) **32**, 191–197
doi:10.1093/eurheartj/ehq261

CLINICAL RESEARCH
Valvular medicine

Transcatheter aortic valve implantation: early results of the FRANCE (FRench Aortic National CoreValve and Edwards) registry

Hélène Eltchaninoff[1]*, Alain Prat[2], Martine Gilard[3], Alain Leguerrier[4], Didier Blanchard[5], Gérard Fournial[6], Bernard Iung[7], Patrick Donzeau-Gouge[8], Christophe Tribouilloy[9], Jean-Louis Debrux[10], Alain Pavie[11], and Pascal Gueret[12], on behalf of the FRANCE Registry Investigators

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Received 12 February 2010; revised 13 June 2010; accepted 15 July 2010; online publish-ahead-of-print 15 September 2010

FRANCE registry – early results

Table 3 Early complications (one patient could have more than one event)

Approach and type of valve	Total ($n = 244$)	TF Edwards[a] ($n = 95$)	TF CoreValve ($n = 66$)	TA Edwards ($n = 71$)	SC CoreValve ($n = 12$)
Thirty-day mortality	31 (12.7)	8 (8.4)	10 (15.1)	12 (16.9)	1 (8.3)
Tamponade	5 (2.0)	2 (2.1)	2 (3.0)	0	1 (8.3)
Stroke	9 (3.6)	4 (4.2)	3 (4.5)	2 (2.8)	0
Coronary occlusion	3 (1.2)	2 (2.0)	1 (1.5)	0	0
New pacemaker	29 (11.8)	5 (5.3)	17 (25.7)	4 (5.6)	3 (25.0)
Vascular complications: Total	16 (7.3)	6 (6.3)	5 (7.5)	4 (5.6)	1 (8.3)
Aortic rupture	2 (0.8)	2 (2)	0	0	0
Iliofemoral dissection	8 (3.2)	4 (4.2)	3 (4.5)	1 (1.4)	0
Thrombosis/distal embolization	3 (1.2)	0	0	2 (2.8)	1 (8.3)
Retroperitoneal haematoma	2 (0.8)	0	2 (3.0)	0	0
LV apex bleeding (re-surgery)	1 (0.4)	NA	NA	1 (1.4)	NA
Renal failure requiring dialysis	4 (1.6)	1 (1.0)	1 (1.5)	2 (2.8)	0
Infection[b]	7 (2.8)	1 (1.0)	1 (1.5)	5 (7.0)	0
Transfusion (≥1 blood units)	52 (21.3)	8 (8.4)	9 (13.6)	25 (27.4)	10 (83.3)

Values are given in *n* (%).
NA, not applicable.
[a]Including one retroperitoneal implantation.
[b]Pulmonary in five; erisypele in one, unknown in one.

The German Registry

European Heart Journal (2011) **32**, 198–204
doi:10.1093/eurheartj/ehq339

CLINICAL RESEARCH
Valvular medicine

Transcatheter aortic valve implantation: first results from a multi-centre real-world registry

Ralf Zahn[1]*, Ulrich Gerckens[2], Eberhard Grube[2], Axel Linke[3], Horst Sievert[4], Holger Eggebrecht[5], Rainer Hambrecht[6], Stefan Sack[7], Karl Eugen Hauptmann[8], Gert Richardt[9], Hans-Reiner Figulla[10], and Jochen Senges[11], on behalf of the German Transcatheter Aortic Valve Interventions—Registry Investigators

[1]Abteilung für Kardiologie, Herzzentrum, Ludwigshafen, Germany; [2]Klinik für Kardiologie, Helios Klinikum, Siegburg, Germany; [3]Klinik für Kardiologie, Herzzentrum, Leipzig, Germany; [4]CardioVasculäres Centrum Frankfurt, Katharinen-krankenhaus, Frankfurt, Germany; [5]Klinik für Kardiologie, Universitätsklinikum, Essen, Germany; [6]Abteilung für Kardiologie, Herzzentrum, Bremen, Germany; [7]Abteilung für Kardiologie, Klinikum München Schwabing, München, Germany; [8]Abteilung für Kardiologie, Krankenhaus der Barmherzigen Brüder Trier, Germany; [9]Abteilung für Kardiologie, Segeberger Kliniken, Bad Segeberg, Germany; [10]Abteilung für Kardiologie, Universitätsklinikum Jena, Jena, Germany; and [11]Institut für Herzinfarktforschung, Ludwigshafen, Germany

Received 30 May 2010; revised 16 August 2010; accepted 23 August 2010; online publish-ahead-of-print 23 September 2010

German registry – early results

Clinical course	
Time at intensive care unit (days)[a]	2 (1–3)
Groin problems	19.5% (130/668)
With need of transfusion	17.1% (115/671)
Severe	4.0% (27/668)
Need for haemodynamic support (IABP or ECLS[b])	1.8% (12/656)
Pericardial tamponade	1.8% (12/670)
Aortic dissection	0.4% (3/670)
Coronary ischaemia	0.1% (1/670)
Myocardial infarction	0.3% (2/673)
Stroke	2.8% (19/670)
Pulmonary embolism	1.3% (9/670)
In-hospital death	8.2% (57/697)
30 day death	12.4%

The British (U.K.) Registry

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EXPEDITED PUBLICATIONS

Long-Term Outcomes After Transcatheter Aortic Valve Implantation in High-Risk Patients With Severe Aortic Stenosis

The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry

Neil E. Moat, MBBS, MS,* Peter Ludman, MA, MD,† Mark A. de Belder, MA, MD,‡ Ben Bridgewater, PHD,§ Andrew D. Cunningham, PHD,‖ Christopher P. Young, MD,¶ Martyn Thomas, MD,¶ Jan Kovac, MD,# Tom Spyt, MD,# Philip A. MacCarthy, BS, PHD,** Olaf Wendler, MD, PHD,** David Hildick-Smith, MD,†† Simon W. Davies, MBBS, MD,* Uday Trivedi, MBBS,†† Daniel J. Blackman, MD,‡‡ Richard D. Levy, MD,§ Stephen J. D. Brecker, MD,§§ Andreas Baumbach, MD,‖ Tim Daniel, MB, CHB,¶¶ Huon Gray, MD,## Michael J. Mullen, MBBS, MD***

London, Birmingham, Bristol, Middlesbrough, Manchester, Leicester, Brighton, Leeds, and Southampton, United Kingdom

U.K TAVI registry 30-d, 1y & 2y results

Table 2 Outcomes

Variables	All Patients (n = 870)	Transfemoral Route (n = 599)	Other Routes (n = 271)	p Value	Medtronic CoreValve (n = 452)	Edwards (n = 410)	p Value
Procedural success	846/870 (97.2)	583/599 (97.3)	263/271 (97.1)	0.82	444/452 (98.2)	402/410 (98.1)	0.84
All-cause mortality at end of follow-up	249/870 (28.6)	153/599 (25.5)	96/271 (35.4)	0.003	122/452 (27.0)	122/410 (29.8)	0.37
30-day survival, % dead	62/870 (7.1)	33/599 (5.5)	29/271 (10.7)	0.006	26/452 (5.8)	35/410 (8.5)	0.11
1-yr survival, % dead	186/870 (21.4)	111/599 (18.5)	75/271 (27.7)	0.002	93/452 (21.7)	89/410 (20.6)	0.68
2-yr survival, % dead	229/870 (26.3)	135/599 (22.5)	94/271 (36.7)	<0.001	108/452 (23.9)	116/410 (28.3)	0.14
MACCE, in hospital	90/870 (10.3)	56/599 (9.4)	34/271 (12.6)	0.15	42/452 (9.3)	48/410 (11.7)	0.25
Stroke, in hospital	35/864 (4.1)	24/594 (4.0)	11/270 (4.1)	0.98	18/448 (4.0)	17/408 (4.2)	0.91
MI	11/864 (1.3)	6/594 (1.0)	5/270 (1.9)	0.31	5/447 (1.1)	6/409 (1.5)	0.65
AR moderate/severe	115/849 (13.6)	91/585 (15.6)	24/264 (9.1)	0.01	76/439 (17.3)	39/405 (9.6)	0.001
Surgical conversion	6/850 (0.7)	0/592 (0)	6/268 (2.2)	0.001*	0/450 (0)	6/402 (1.5)	0.01*
Major vascular complication	55/869 (6.3)	50/598 (8.4)	5/271 (1.9)	<0.001	28/451 (6.2)	26/410 (6.3)	0.94
Repeat procedure	7/870 (0.8)	7/599 (1.2)	0/271 (0)	0.11*	7/452 (1.6)	0/410 (0)	0.02*
Pacemaker	141/867 (16.3)				110/451 (24.4)	30/408 (7.4)	<0.001

The Italian Registry

EUROPEAN SOCIETY OF CARDIOLOGY®

European Heart Journal (2012) **33**, 969–976
doi:10.1093/eurheartj/ehr491

FASTTRACK CLINICAL

Transcatheter aortic valve implantation: 3-year outcomes of self-expanding CoreValve prosthesis

Gian Paolo Ussia[1,2]*, Marco Barbanti[1], Anna Sonia Petronio[3], Giuseppe Tarantini[4], Federica Ettori[5], Antonio Colombo[6], Roberto Violini[7], Angelo Ramondo[8], Gennaro Santoro[9], Silvio Klugmann[10], Francesco Bedogni[11], Francesco Maisano[6], Antonio Marzocchi[12], Arnaldo Poli[13], Marco De Carlo[3], Massimo Napodano[4], Claudia Fiorina[5], Federico De Marco[10], David Antoniucci[9], Emanuela de Cillis[14], Davide Capodanno[1,2], and Corrado Tamburino[1,2], on behalf of the CoreValve Italian Registry Investigators

[1]Interventional Structural and Congenital Heart Disease Programme, Invasive Cardiology Division of Cardiology, Ferrarotto Hospital, University of Catania, Catania, Italy; [2]ETNA Foundation, Catania, Italy; [3]AOU Pisana, Pisa, Italy; [4]University of Padova, Padua, Italy; [5]Spedali Civili, Brescia, Italy; [6]Scientific Institute S. Raffaele, Milan, Italy; [7]Division of Interventional Cardiology, A.O. San Camillo Forlanini Hospital, Rome, Italy; [8]Division of Cardiology, Bassano del Grappa, Padua, Italy; [9]Careggi Hospital, Florence, Italy; [10]Niguarda Ca'Granda Hospital, Milan, Italy; [11]Clinical Institute S. Ambrogio, Milan, Italy; [12]Policlinico S. Orsola-Malpighi, University of Bologna, Bologna, Italy; [13]Ospedale Civile, Legnano, Italy; and [14]Division of Cardiovascular Surgery, Ospedale Policlinico, Bari, Italy

Received 22 October 2011; revised 1 December 2011; accepted 14 December 2011; online publish-ahead-of-print 12 January 2012

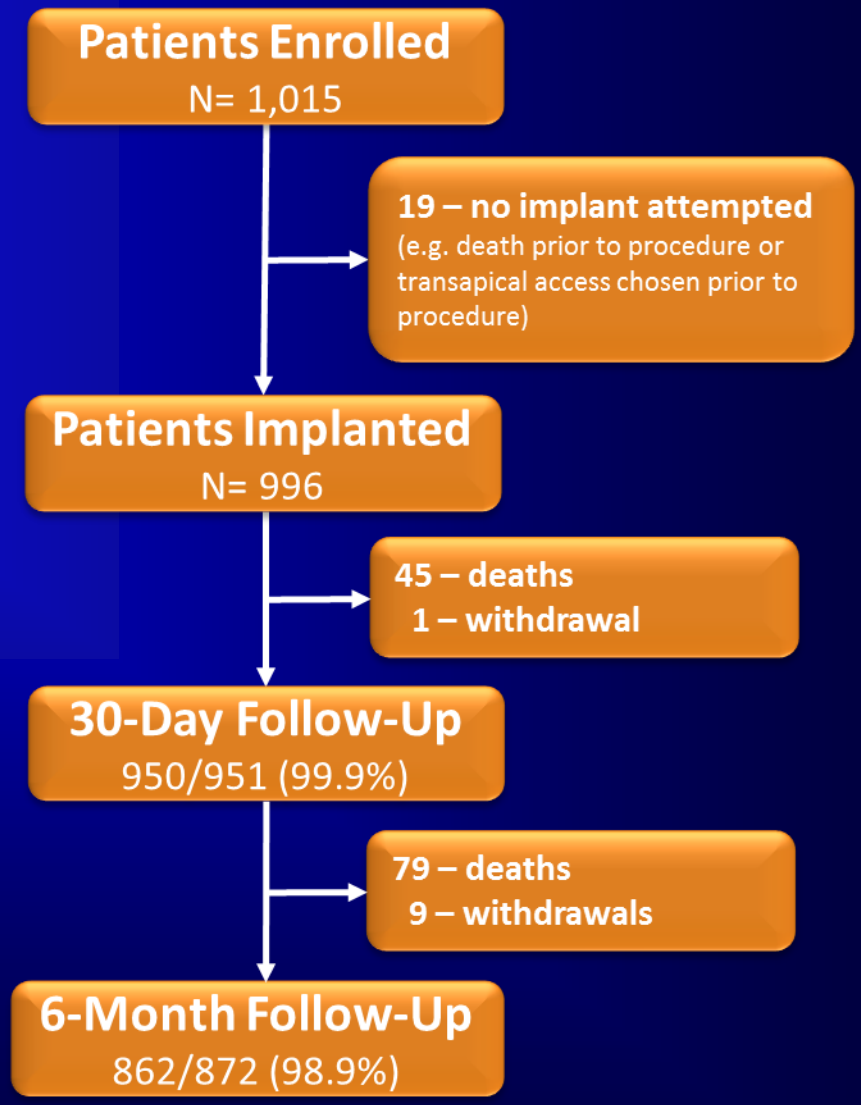
CoreValve Italian registry [n=181]
Procedural variables

	Overall population (*n* = 181)
Procedural variables	
Procedure time, min ± SD	68.6 ± 28.4
Fluoroscopy time, min ± SD	17.9 ± 8.7
Approach	
Trans-femoral, *n* (%)[a]	172 (95.0)
Trans-subclavian, *n* (%)	9 (5.0)
Anaesthesia	
Local, *n* (%)	103 (56.9)
General, *n* (%)	78 (43.1)
Device[b]	
CRS 26 mm, *n* (%)	107 (59.1)
CRS 29 mm, *n* (%)	74 (40.9)
Device success, *n* (%)[c]	166 (91.7)
Post-dilatation, *n* (%)	18 (9.9)
Reposition with snaring, *n* (%)	1 (0.5)
Valve-in-valve, *n* (%)	8 (4.4)
Higher implantation, *n* (%)	1 (0.5)
Lower implantation, *n* (%)	7 (3.9)
Valve-on-valve, *n* (%)	0 (0.0)
Procedural complications	
Major vascular complications, *n* (%)[c]	6 (3.3)
Percutaneous treatment, *n* (%)	3 (1.7)
Covered stent, *n* (%)	2 (1.1)
Not-covered stent, (%)	1 (0.5)
Surgical treatment, *n* (%)	2 (1.1)
Conservative treatment, *n* (%)	1 (0.5)
Procedural MI, *n* (%)[c]	8 (4.4)
RBC Units transfusions ≥4, *n* (%)	11 (6.1)
RBC Units transfusions ≥2 and <4, *n* (%)	40 (22.1)

CRS, CoreValve Revalving System; MI, myocardial infarction; RBC, red blood cells.
[a]All cases with totally percutaneous access.
[b]Refers to the first prosthesis implanted.
[c]According to VARC definitions.

CoreValve ADVANCE Study

- 1,015 patients enrolled from March 2010 to July 2011
  - 5 year follow-up
- 44 centers - 12 countries in Western Europe, Asia and South America
- All centers had conducted at least 40 TAVI procedures prior to the study and had Heart Team in place



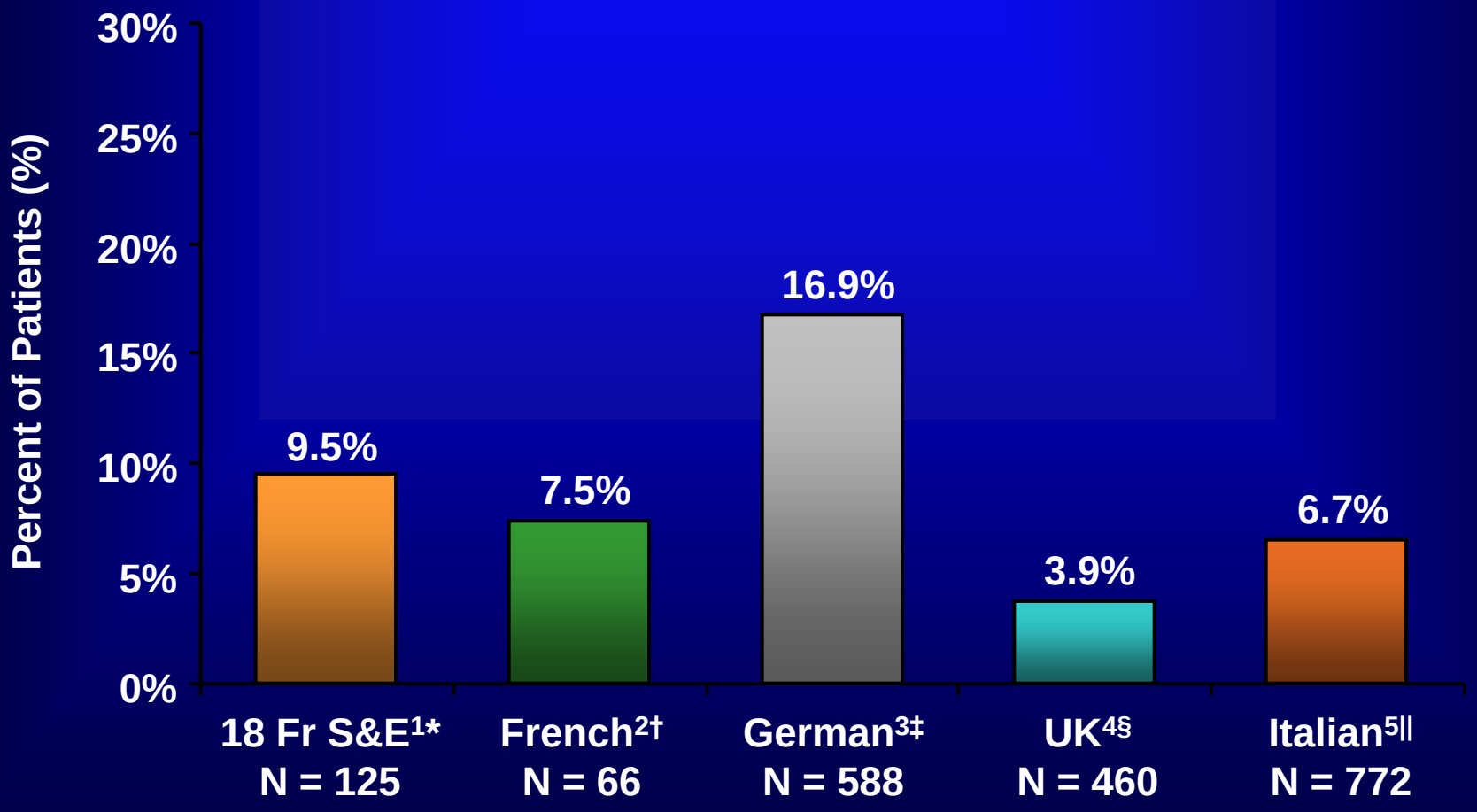
30-day Outcomes

Primary Endpoint N=996	Kaplan-Meier Estimates, %
MACCE	8.3
All-cause Mortality	4.5
Myocardial Infarctions	0.2
Emergent cardiac surgery or percutaneous re-intervention	1.7
Stroke	2.9

Additional VARC Endpoints N=996	Kaplan-Meier Estimates, %
Cardiovascular Mortality	3.4
Major Bleeding	9.7
Life Threatening Bleeding	4.0
Major Vascular Complications	10.7
Acute Kidney Injury - Stage III	0.4

Additional Endpoint N=996	Kaplan-Meier Estimates, %
New Pacemaker Implantation	26.3

Vascular Complications



Vascular complications in TAVI

- **Meta-analysis:**
  - **16 studies describing vascular complications in accordance to first VARC definitions**
  - **3519 patients (64-504 patients per study)**
  - **Different TAVI approaches including trans-apical and subclavian approaches**
  - **Different vascular access and closure approaches**
  - **Only 4 studies included solely trans-femoral (120-186 patients)**

Table 3 30-Day and 1-Year VARC Outcomes After TAVR

Outcome	Reported Rate Min, Max, %	Cumulative Rate	I^2, %	Cochran's Q	p Value Heterogeneity	Pooled Estimate Rate, %	95% CI
Vascular complications							
Major	5.0, 23.3	282/2,417	81.3	64.1	<0.0001	11.9	8.6–16.4
Minor	5.6, 28.3	203/2,142	88.8	88.9	<0.0001	9.7	6.7–14.0
All	9.5, 51.6	511/2,740	92.6	176.6	<0.0001	18.8	14.5–24.3

Généreux P et al. Clinical Outcomes After Transcatheter Aortic Valve Replacement Using Valve Academic Research Consortium Definitions A Weighted Meta-Analysis of 3,519 Patients From 16 Studies. J Am Coll Cardiol 2012;59:2317–26

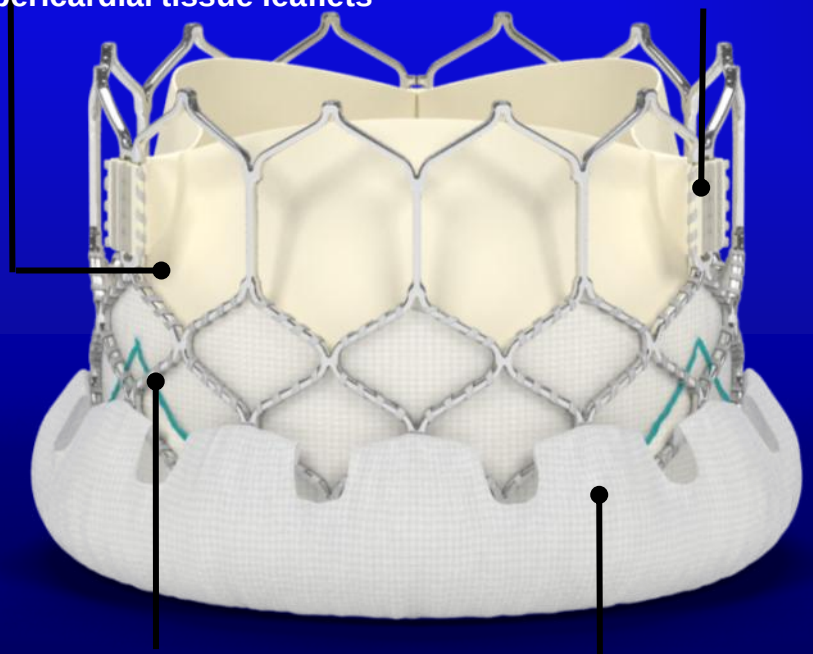
The problem- the culprit

- Large catheters, potentially traumatic.
- Closure devices designed for smaller ports.
- Very sick and “vulnerable” patients.
- “hostile” peripheral vessels (calcified, tortuous and thin vessels).

I have a dream…

Edwards SAPIEN 3 Transcatheter Heart Valve System

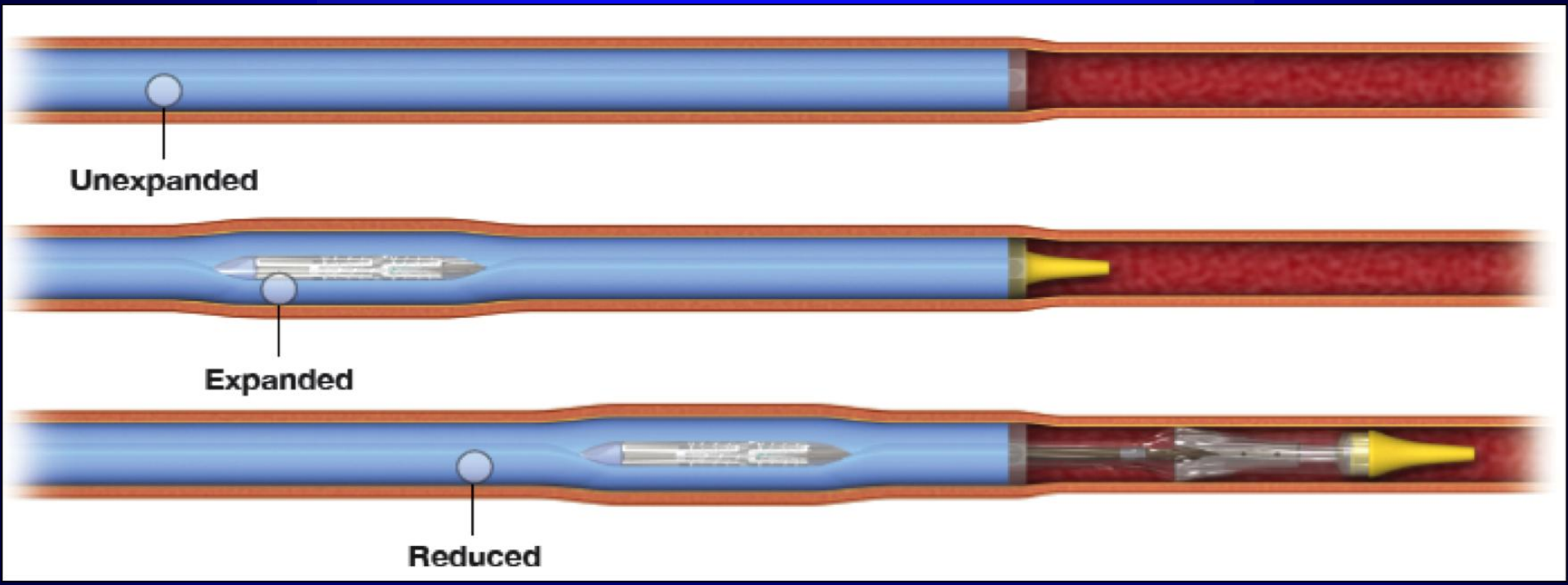
Bench top Testing * Proof of Concept * Feasibility * OUS Study * Randomized Trial



Valve	TF	TA/TAo
20-26mm	14Fr	18Fr
29mm	16Fr	21Fr

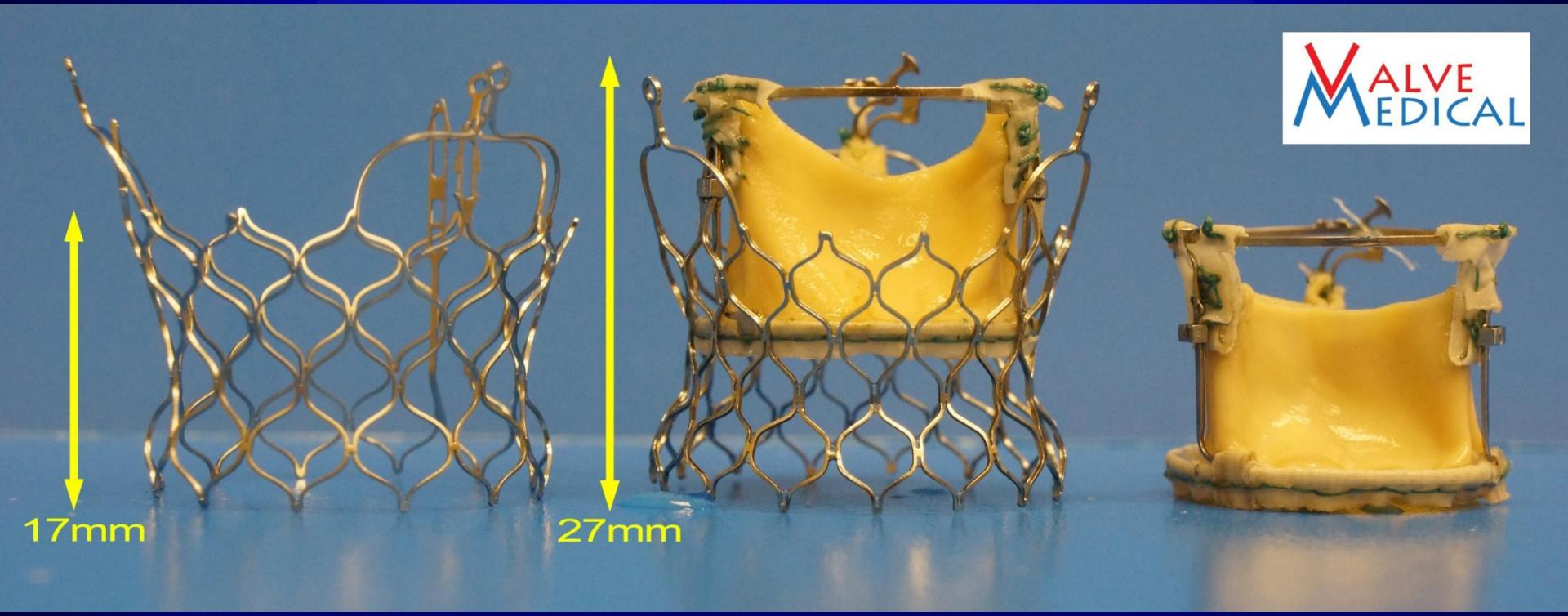
Not approved for sale

Edwards eSheath Introducer Sheath Mechanism

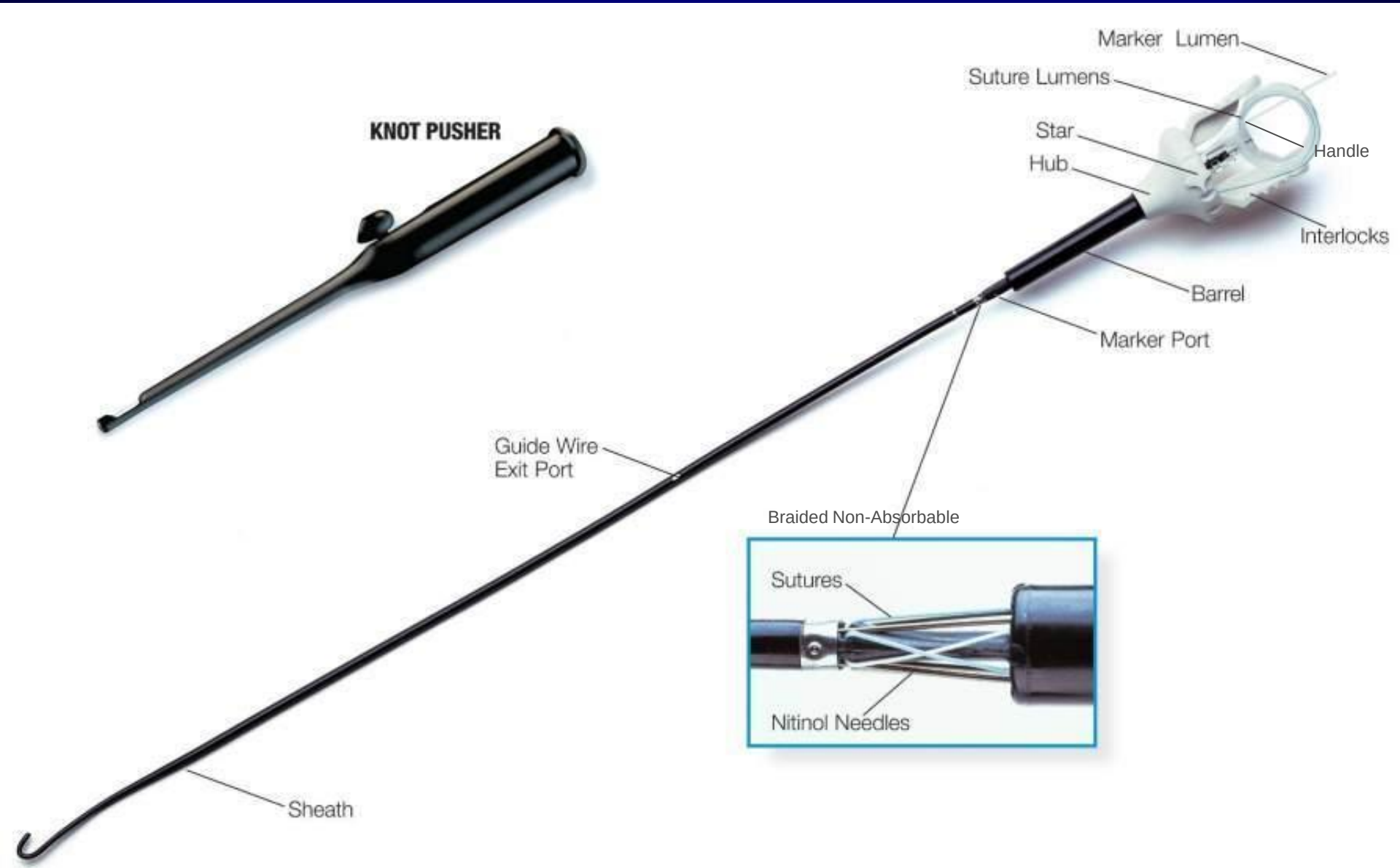


- **14 Fr, 16 Fr, 17 Fr, & 18 Fr sheath sizes**

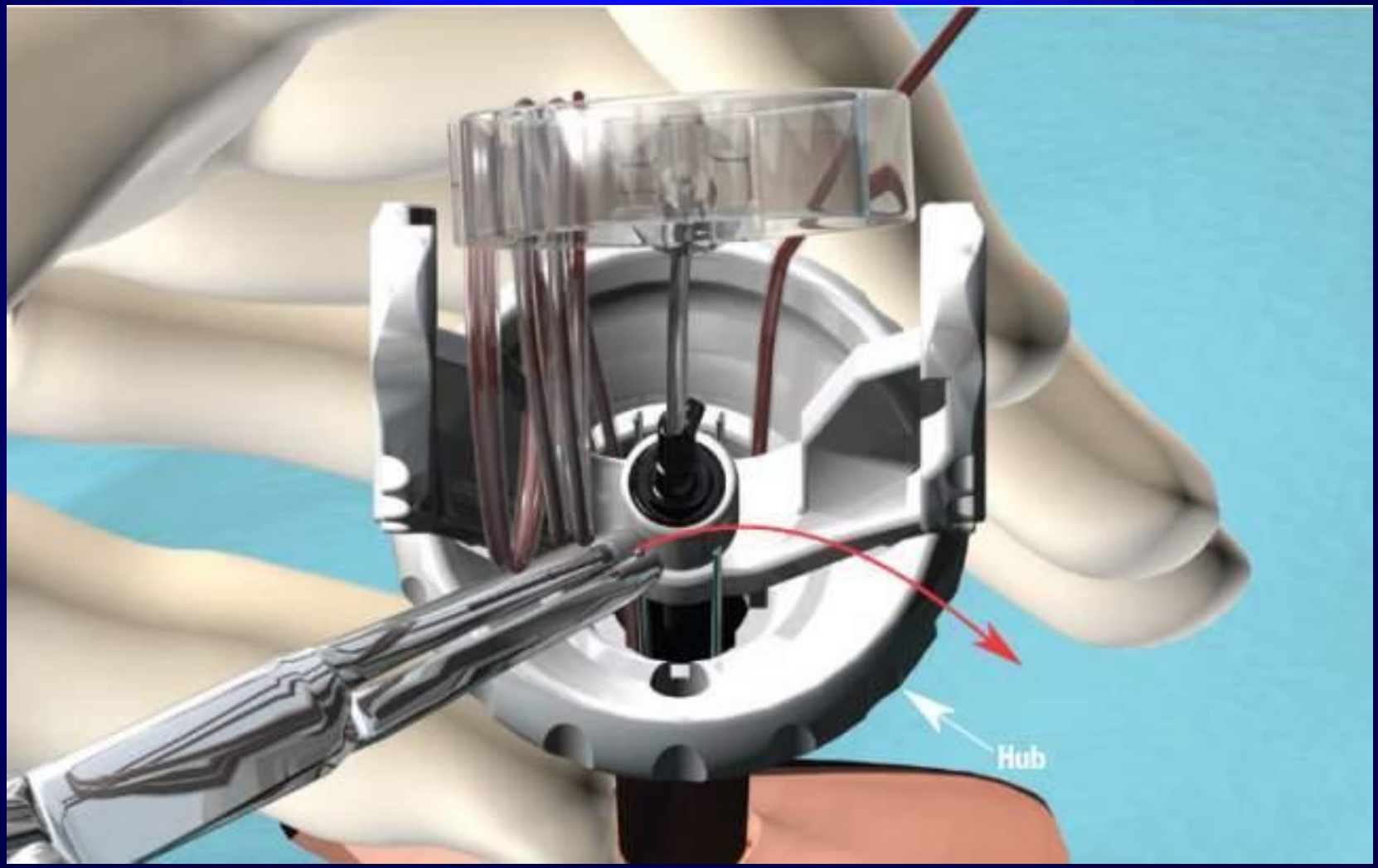
Medinol Valve



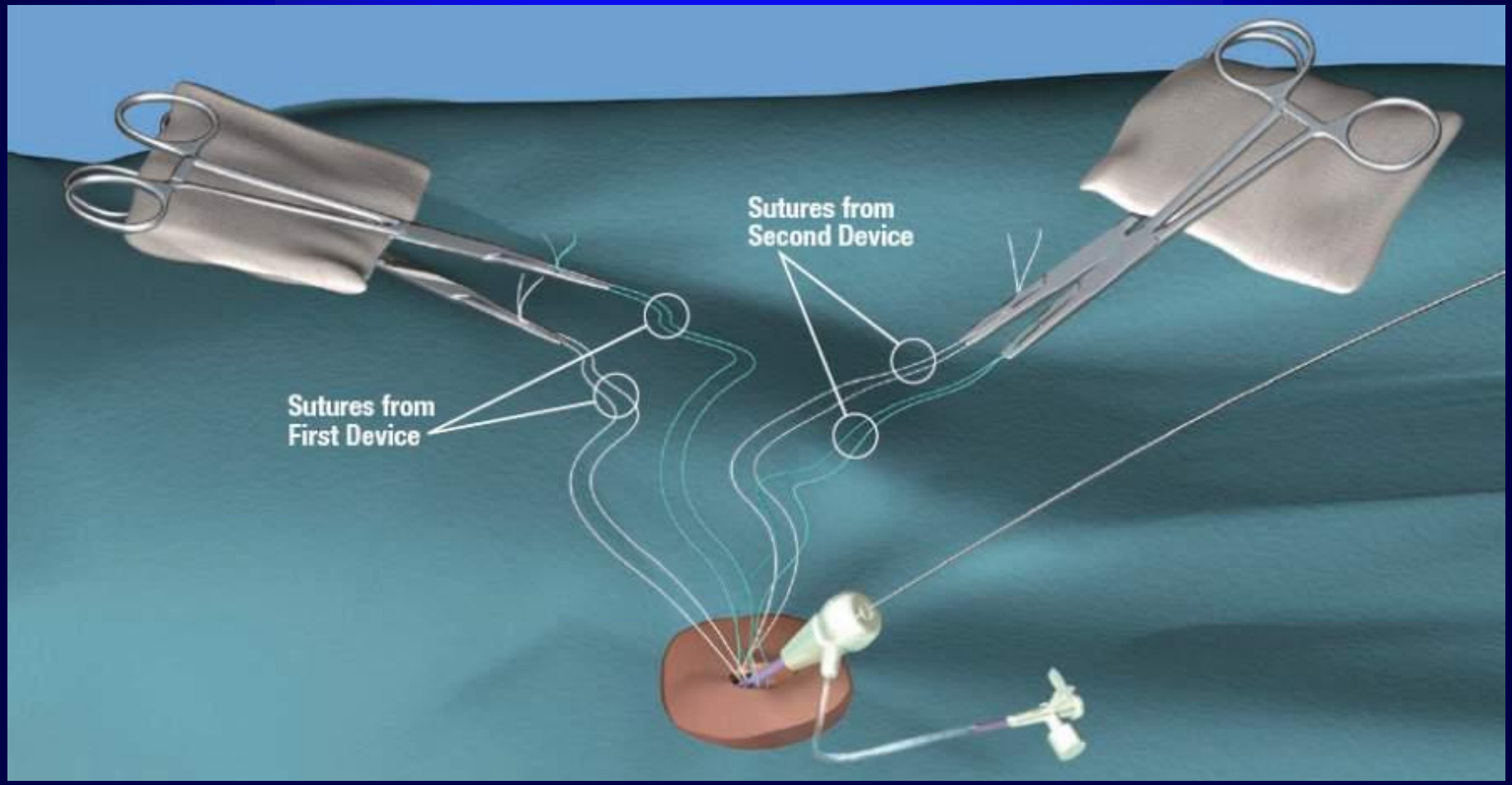
My best friend in the TAVI miliieu…



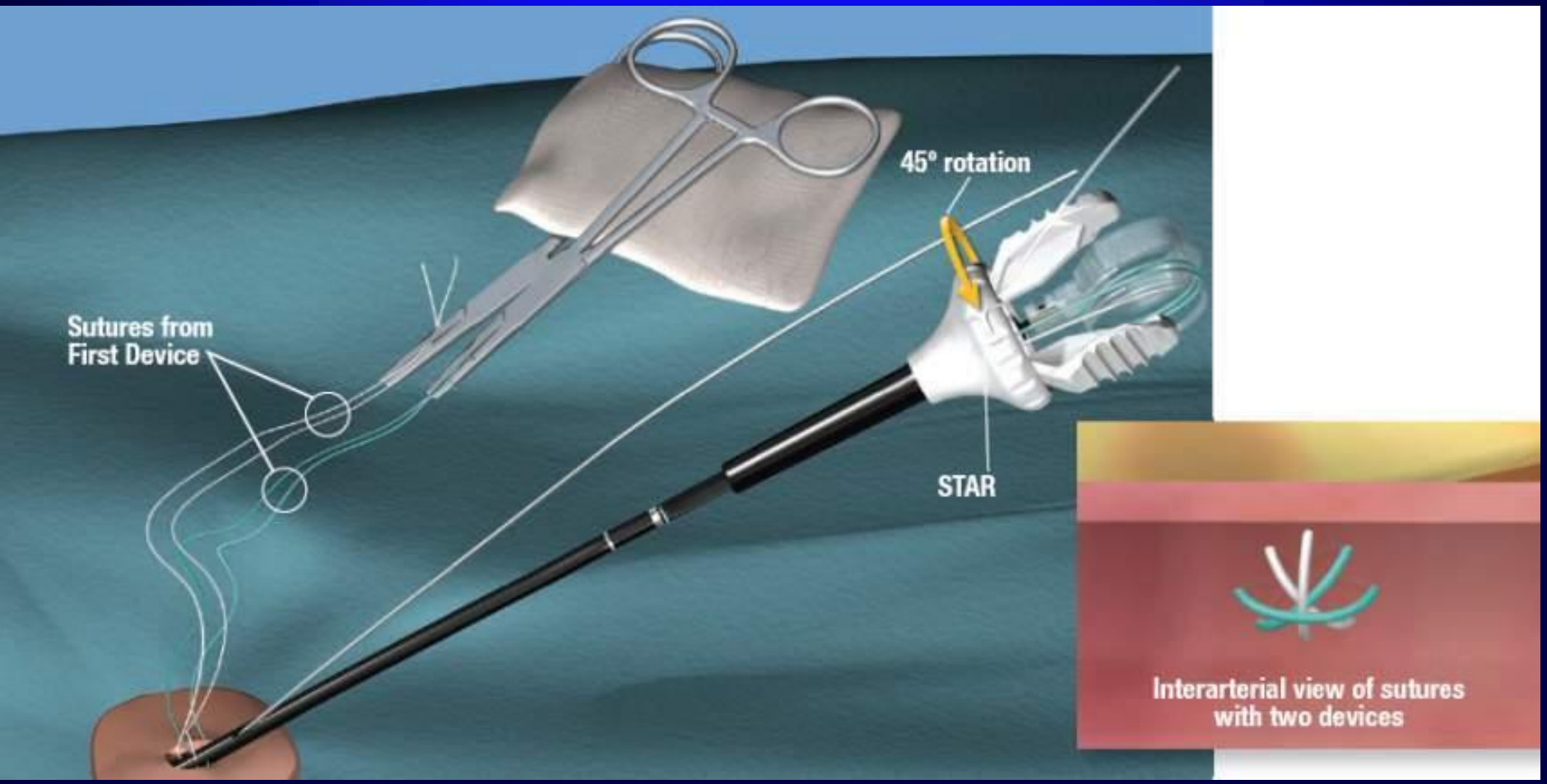
He is pretty ugly…



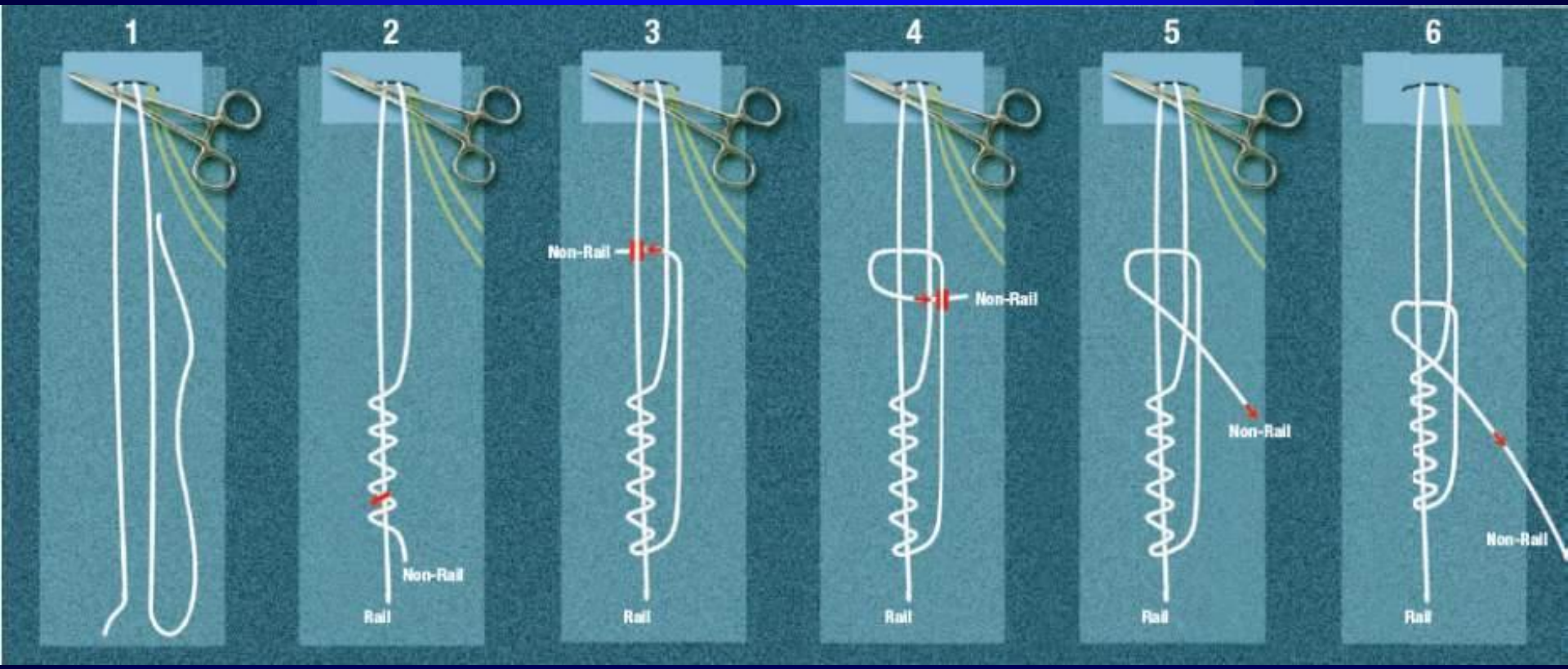
He is quite complicated to use…



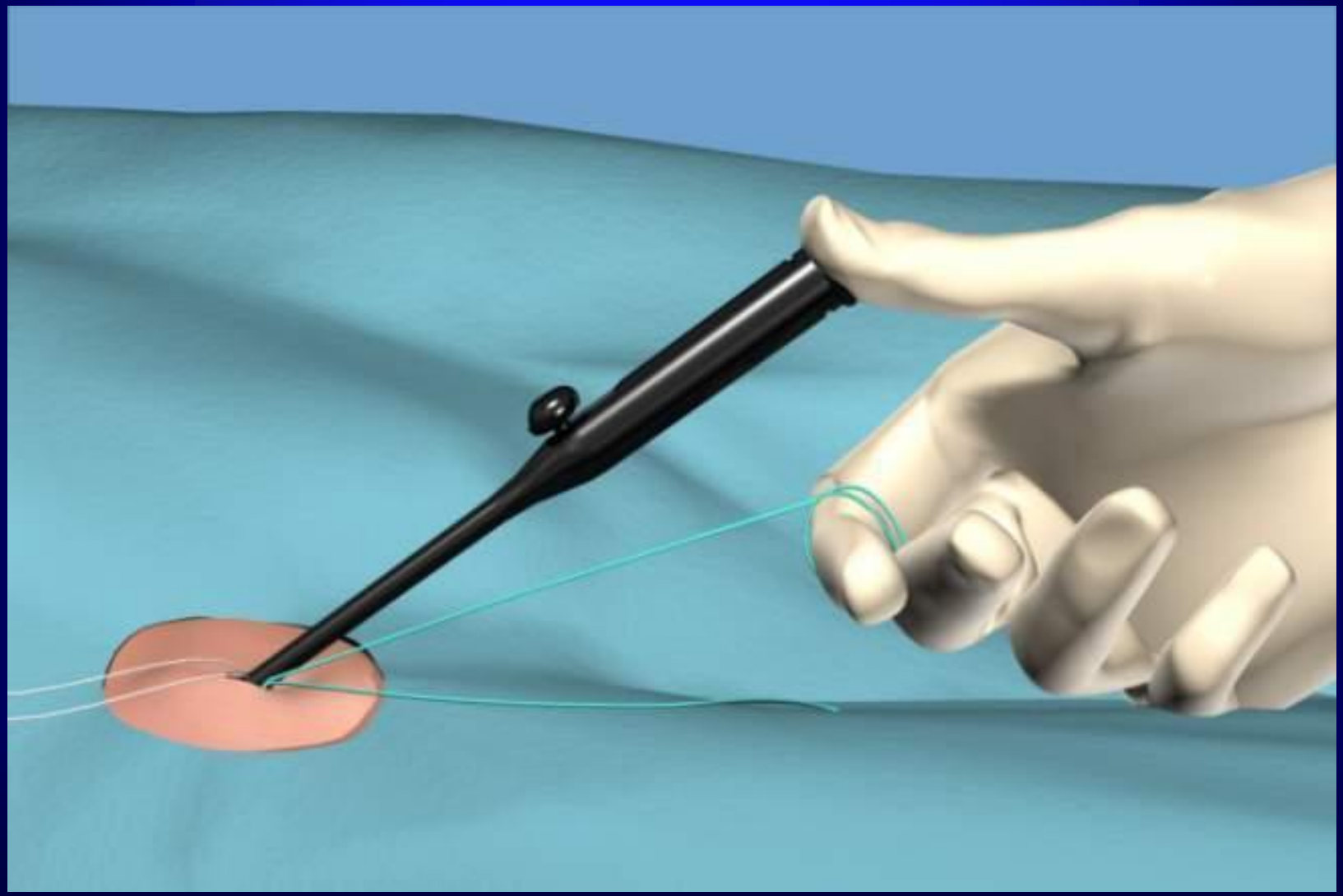
Its learning curve is long…



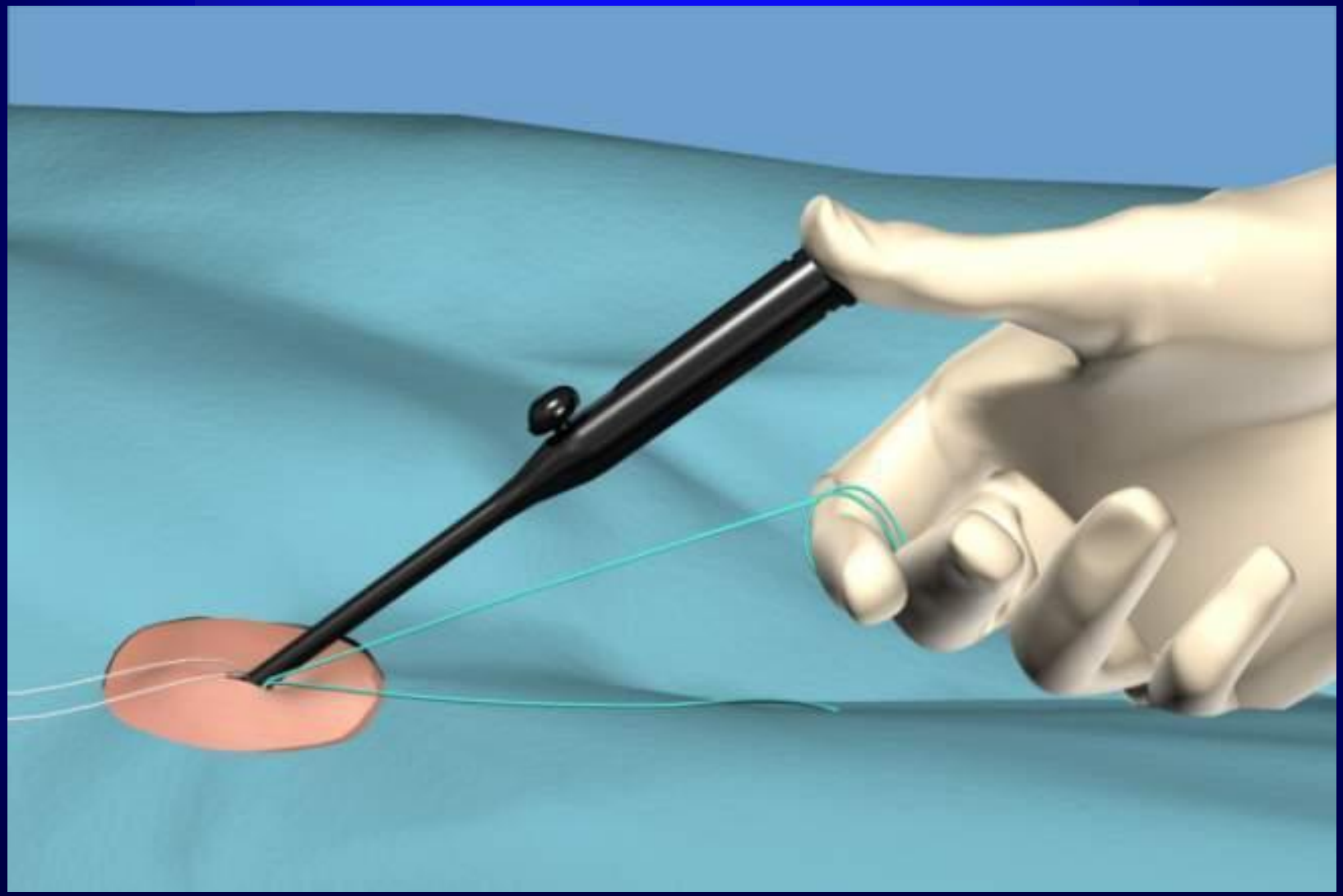
And… one need to be a scoute in order to manipulate the ties…



But it is my only friend….



…It is still my only friend….



The unmet needs

- Smaller, less traumatic vascular entry ports.
- Lower profile, more flexible delivery systems.
- Designated “big holes” closure devices:
- surute based
- sealant (external plugs, hemostatic pads)
- combinations of the above

My TAVI dream

- Lower profile
- Anti calcium technology
- Better on line imaging

Yes, there is a problem. We call it Calcium…


ADANI, YONA
64389-0
Dr.Ariel Finkelshtein
Tel Aviv Medical Center
26/03/2012 12:37:51
12947762
6
6
1/241
And if it looks like a Ca, it is a Ca...
ADANI, YONA
64389-0
Dr.Ariel Finkelshtein
Tel Aviv Medical Center
26/03/2012 12:37:51
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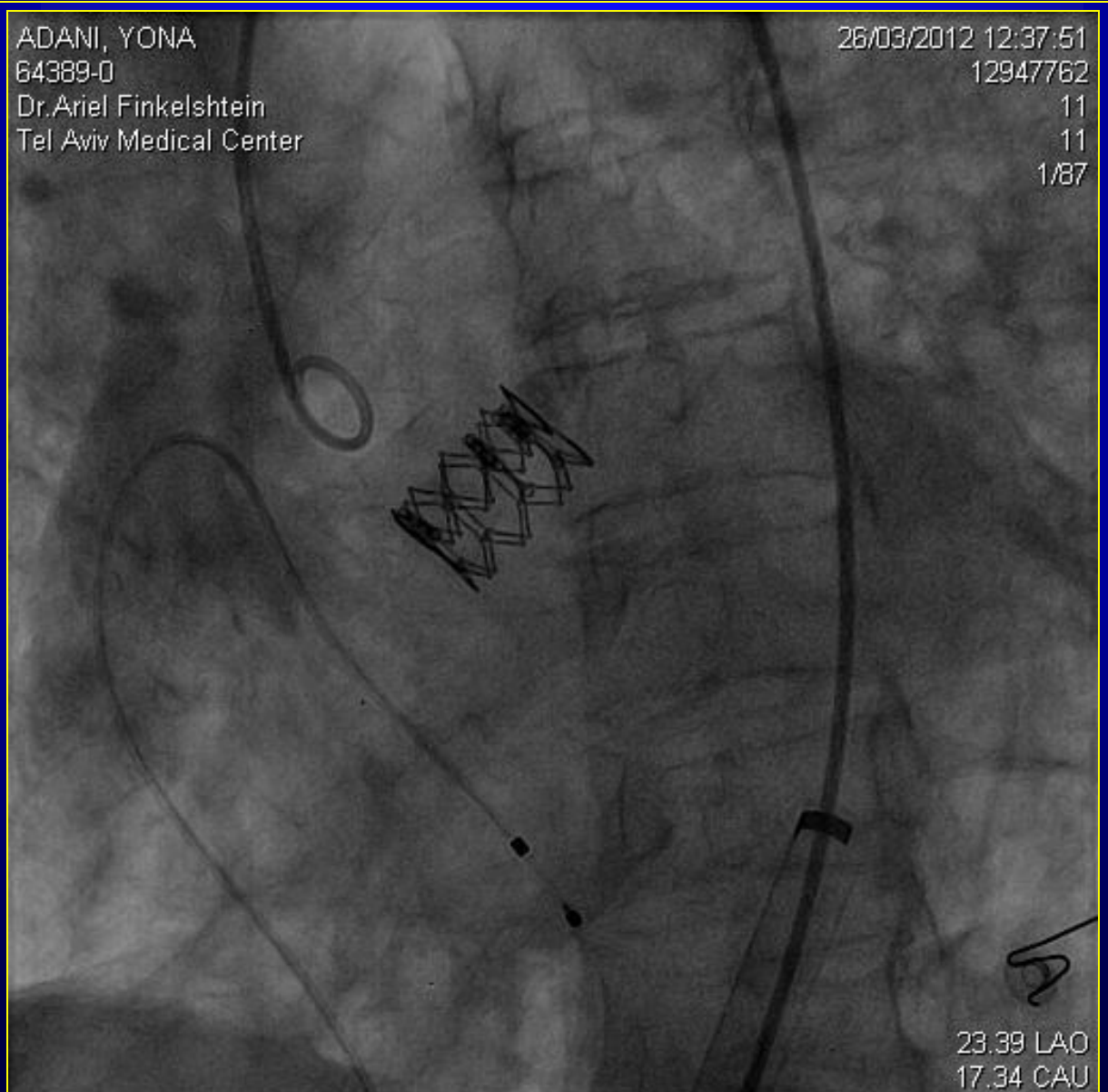
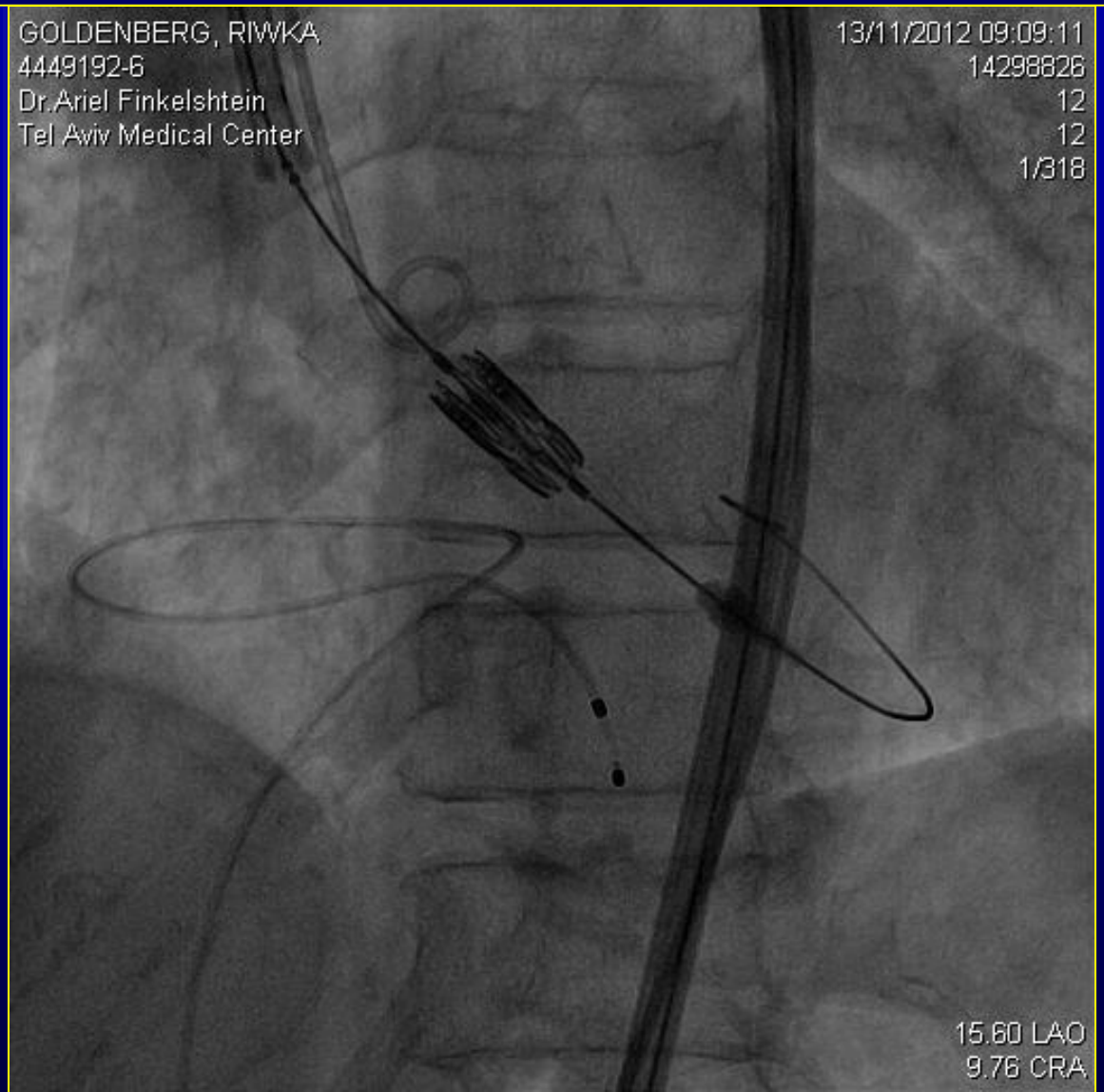
1/354
23.85 LAO
8.46 CRA

You got to be lucky sometimes



Lucky again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Dr.Ariel Finkelshtein
Tel Aviv Medical Center
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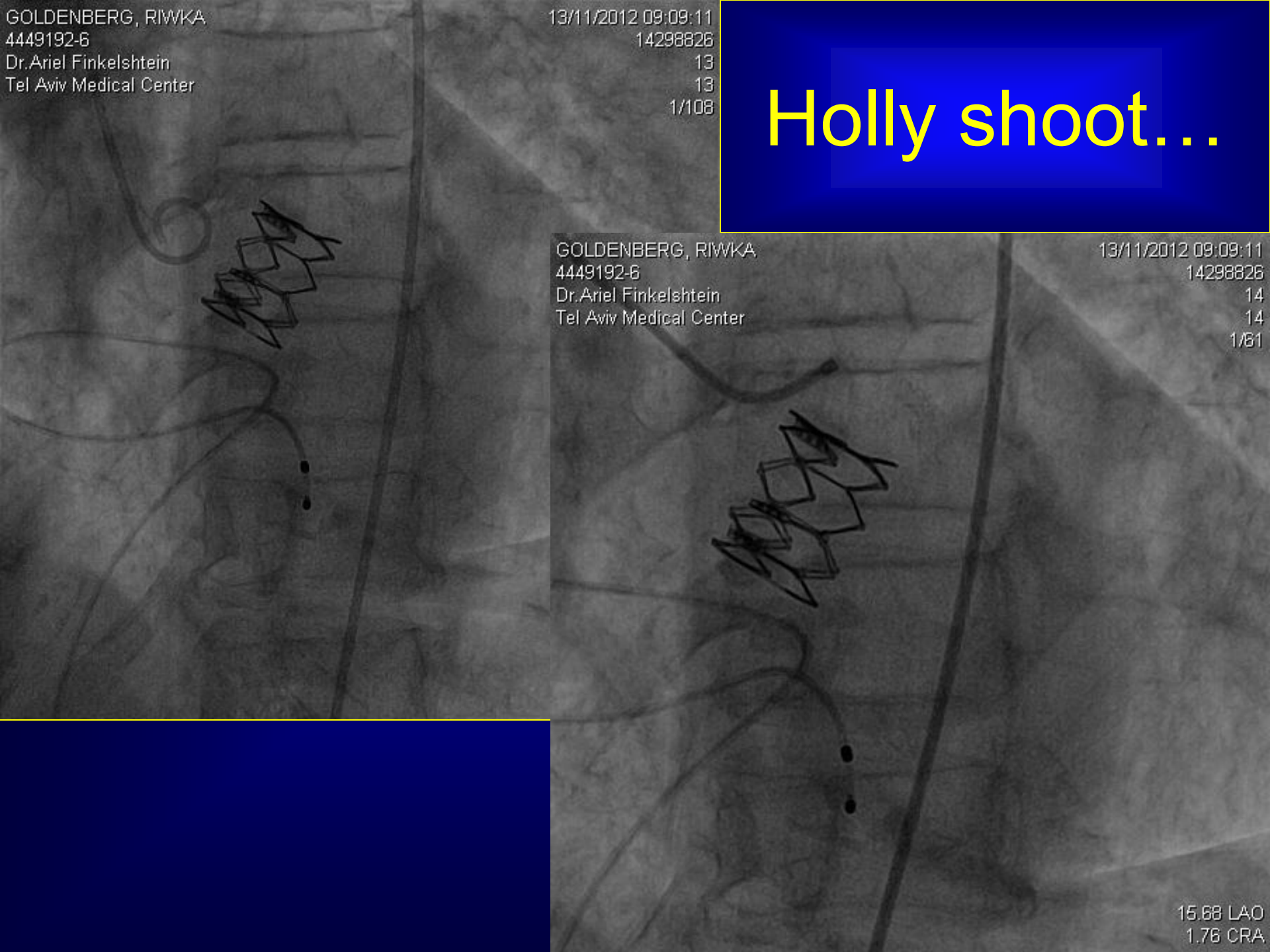
9.76 CRA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Tel Aviv Medical Center
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Holly shoot…
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Dr.Ariel Finkelshtein
Tel Aviv Medical Center
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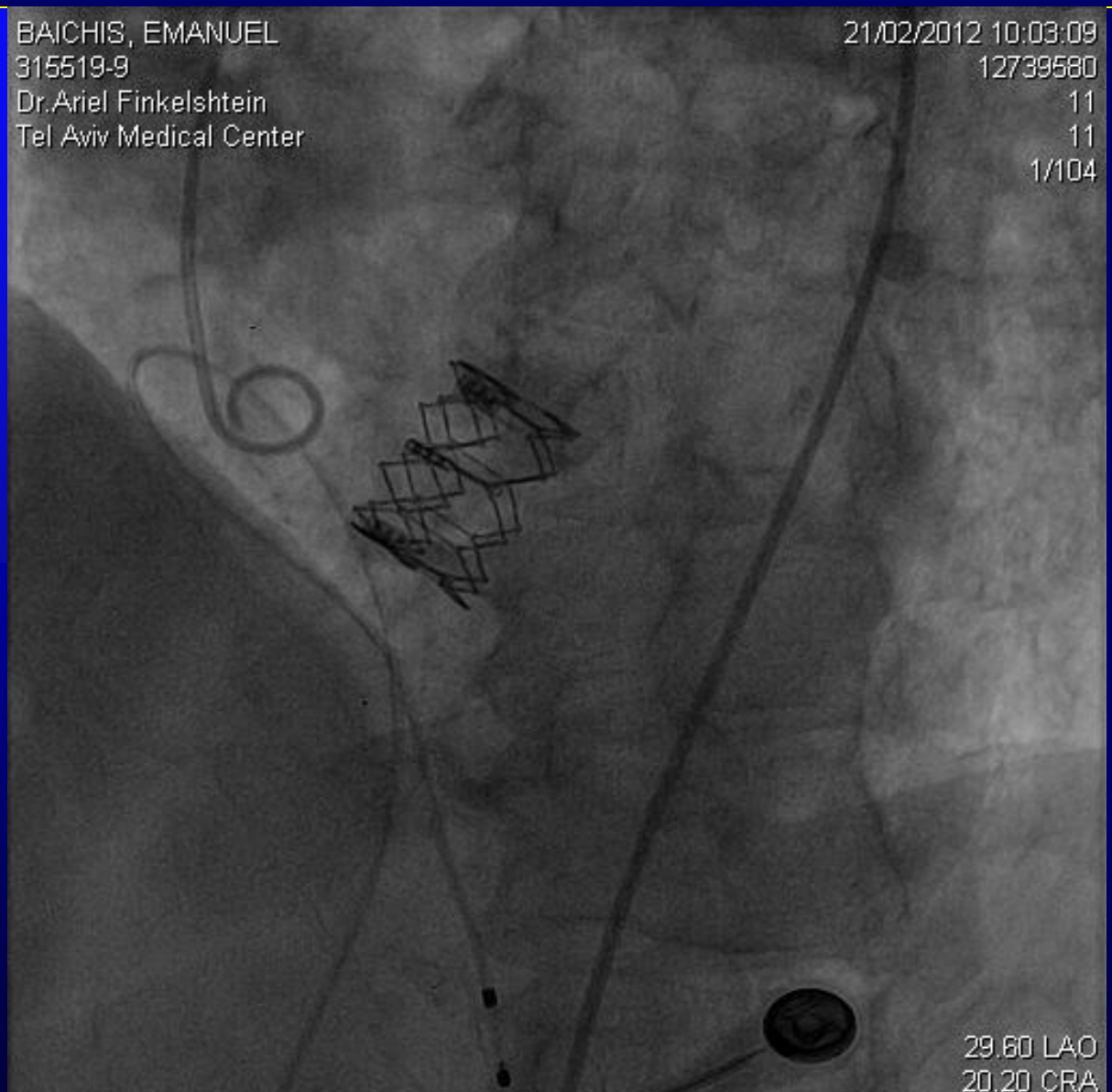
1.76 CRA

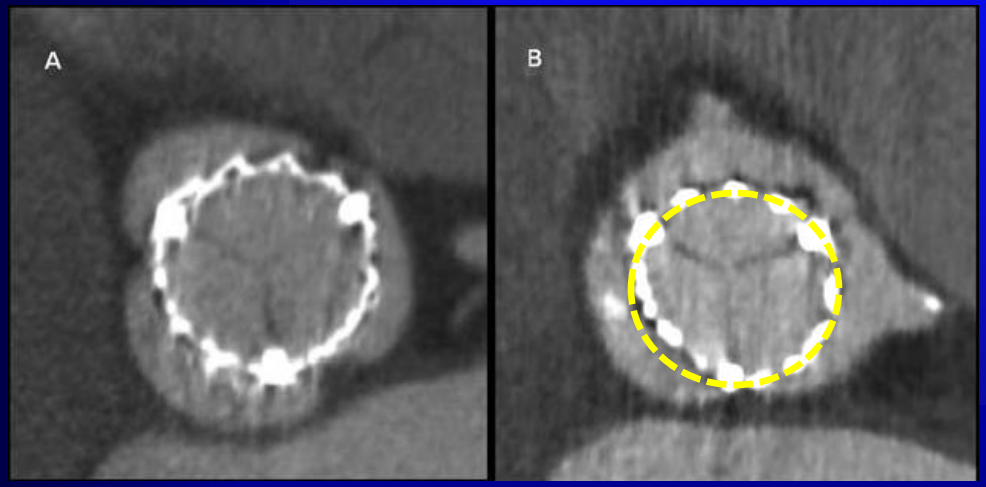
I am tired of being lucky…

And what about the PVL?

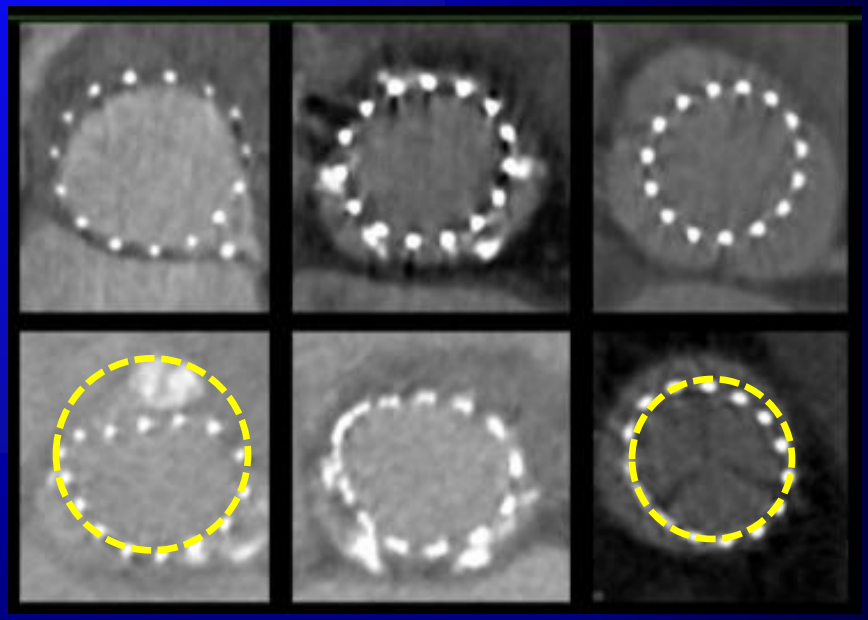


This is the Achilles Heel of TAVI

Geometry and Apposition of based on MSCT



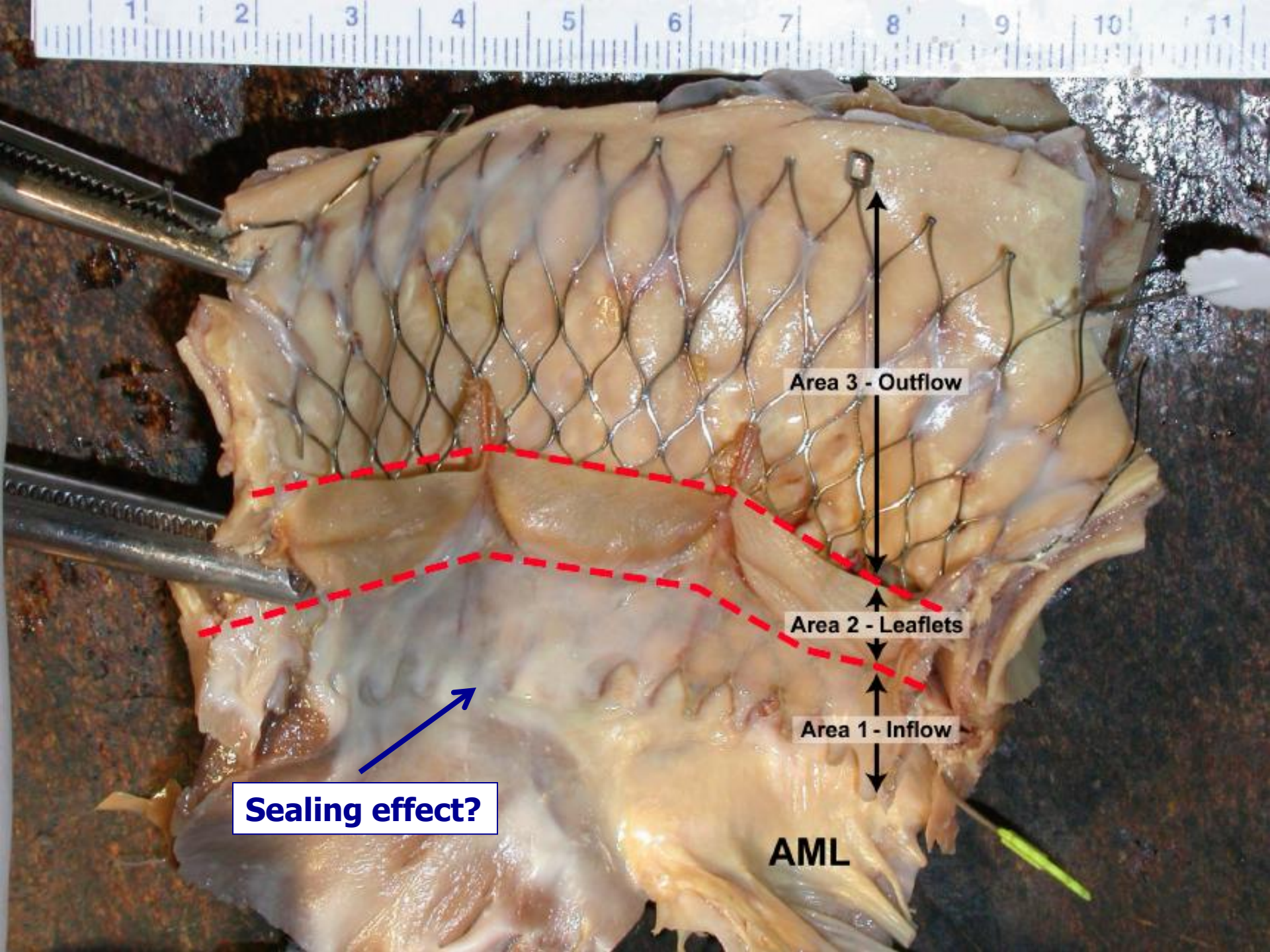
Delgado et al. Euro Heart J 2010;31:1114-1123



Schultz C et al. JACC 2009; 54:911-8

86% circular (eccentricity index <0.1)

50% circular (D1/D2 <0.1)


Area 3 - Outflow
Area 2 - Leaflets
Area 1 - Inflow
Sealing effect?
AML

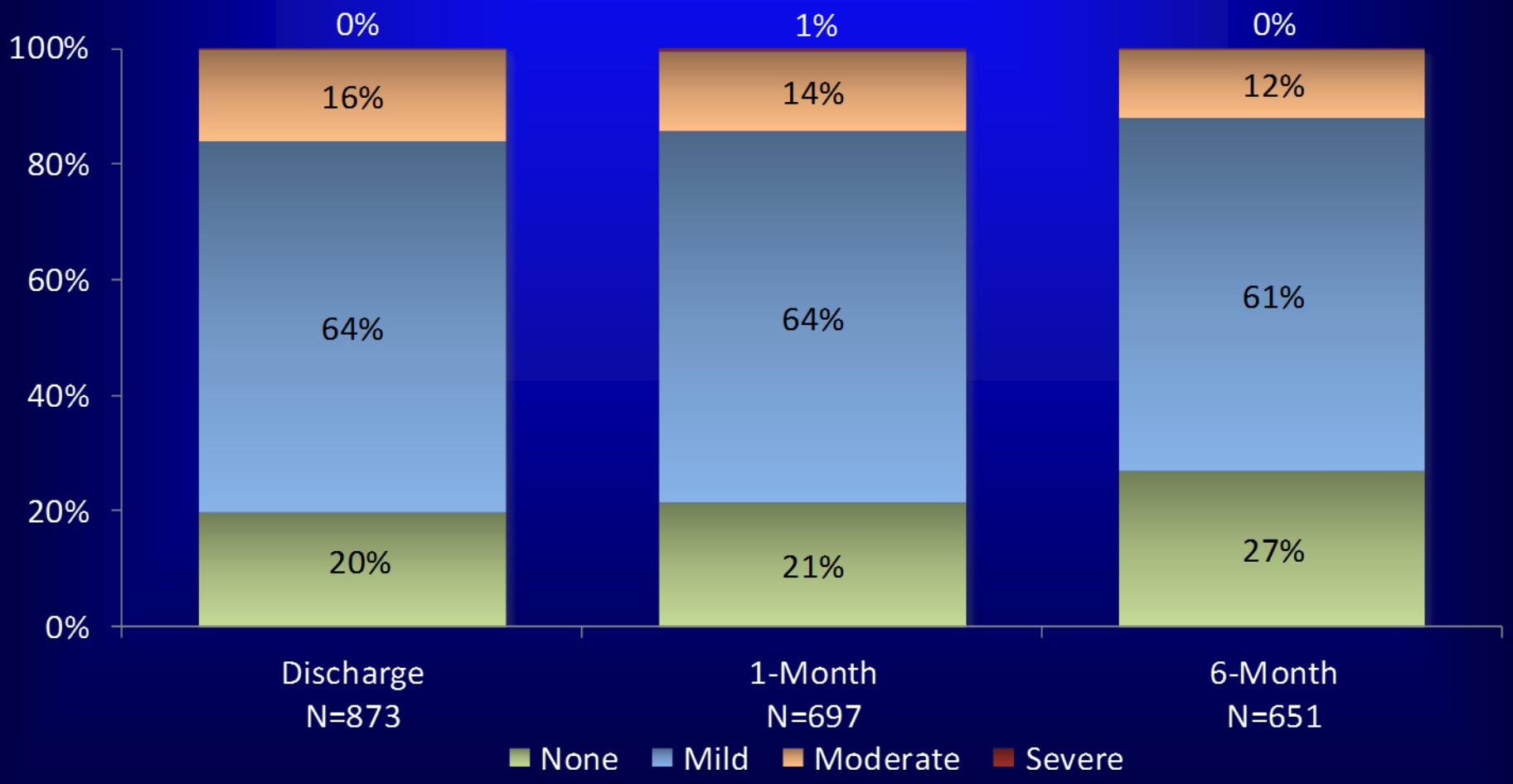
U.K TAVI registry 30-d, 1y & 2y results

Table 2 Outcomes

Variables	All Patients (n = 870)	Transfemoral Route (n = 599)	Other Routes (n = 271)	p Value	Medtronic CoreValve (n = 452)	Edwards (n = 410)	p Value
Procedural success	846/870 (97.2)	583/599 (97.3)	263/271 (97.1)	0.82	444/452 (98.2)	402/410 (98.1)	0.84
All-cause mortality at end of follow-up	249/870 (28.6)	153/599 (25.5)	96/271 (35.4)	0.003	122/452 (27.0)	122/410 (29.8)	0.37
30-day survival, % dead	62/870 (7.1)	33/599 (5.5)	29/271 (10.7)	0.006	26/452 (5.8)	35/410 (8.5)	0.11
1-yr survival, % dead	186/870 (21.4)	111/599 (18.5)	75/271 (27.7)	0.002	93/452 (21.7)	89/410 (20.6)	0.68
2-yr survival, % dead	229/870 (26.3)	135/599 (22.5)	94/271 (36.7)	<0.001	108/452 (23.9)	116/410 (28.3)	0.14
MACCE, in hospital	90/870 (10.3)	56/599 (9.4)	34/271 (12.6)	0.15	42/452 (9.3)	48/410 (11.7)	0.25
Stroke, in hospital	35/864 (4.1)	24/594 (4.0)	11/270 (4.1)	0.98	18/448 (4.0)	17/408 (4.2)	0.91
MI	11/864 (1.3)	6/594 (1.0)	5/270 (1.9)	0.31	5/447 (1.1)	6/409 (1.5)	0.65
AR moderate/severe	115/849 (13.6)	91/585 (15.6)	24/264 (9.1)	0.01	76/439 (17.3)	39/405 (9.6)	0.001
Surgical conversion	6/850 (0.7)	0/592 (0)	6/268 (2.2)	0.001*	0/450 (0)	6/402 (1.5)	0.01*
Major vascular complication	55/869 (6.3)	50/598 (8.4)	5/271 (1.9)	<0.001	28/451 (6.2)	26/410 (6.3)	0.94
Repeat procedure	7/870 (0.8)	7/599 (1.2)	0/271 (0)	0.11*	7/452 (1.6)	0/410 (0)	0.02*
Pacemaker	141/867 (16.3)				110/451 (24.4)	30/408 (7.4)	<0.001

CoreValve ADVANCE Study

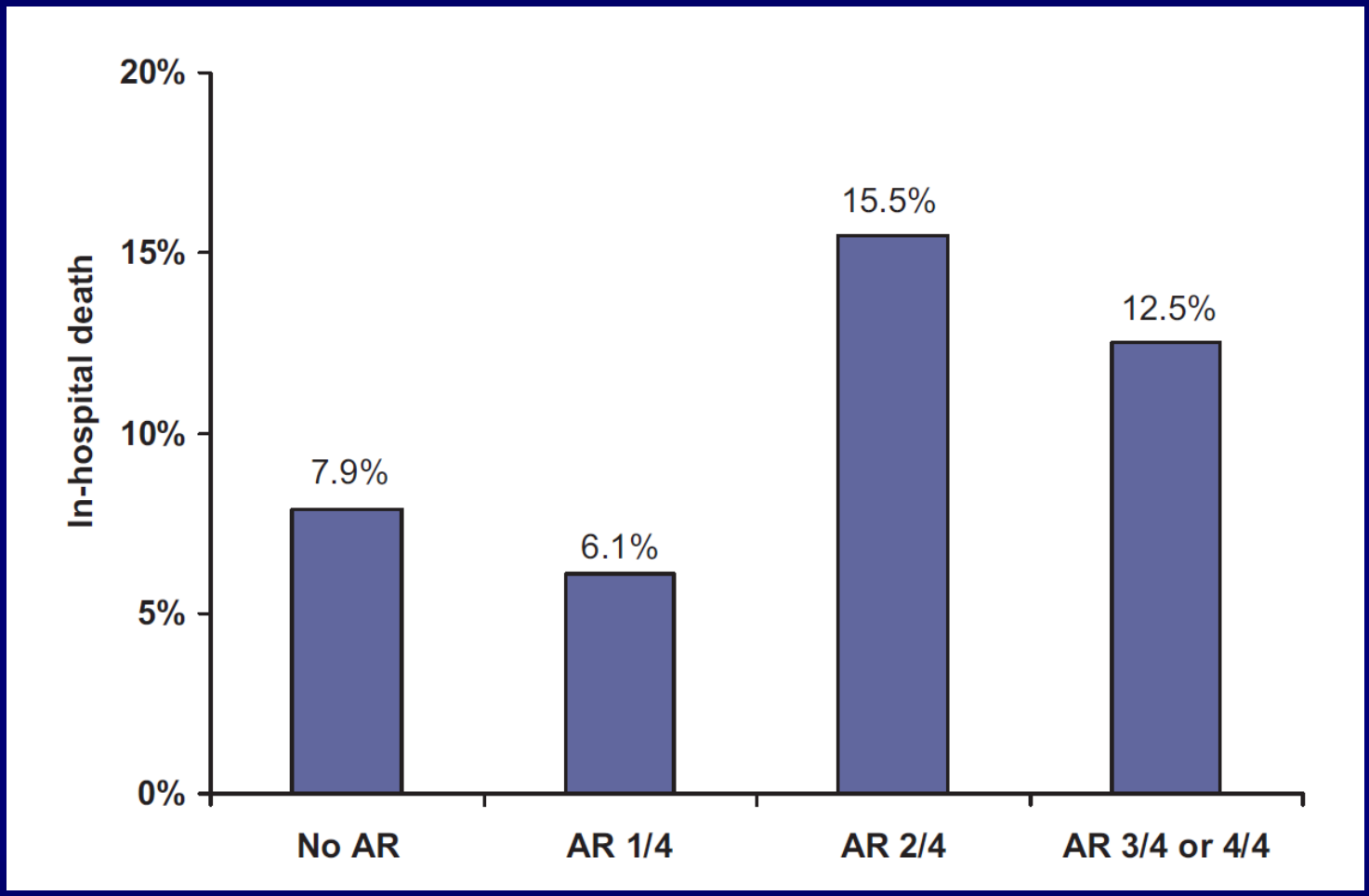
echo assessment



German registry – early results

Procedural results	
Technical successful	98.4% (684/695)
Conversion to open heart surgery	0.7% (5/695)
Unsuccessful termination of the procedure	0.9% (6/695)
Gradient after the procedure (mmHg)[a]	5 (0–8)
Residual aortic insufficiency	72.4% (499/689)
none	27.6% (190/689)
Grade 1	54.9% (378/689)
Grade 2	15.2% (105/689)
Grade 3	2.0% (14/689)
Grade 4	0.3% (2/689)
Implantation of a pacemaker	39.3% (262/667)

AR following TAVI-German TAVI registry



Abdel-Wahab et al. Aortic regurgitation after transcatheter aortic valve implantation: incidence and early outcome. Results from the German transcatheter aortic valve interventions registry. *Heart 2011;97:899e906*

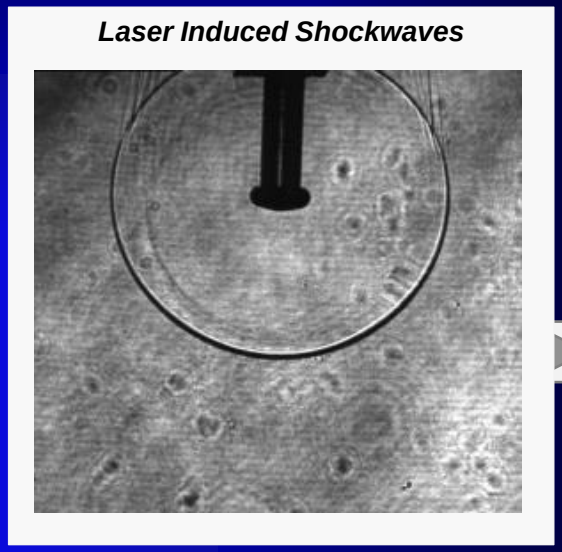
I have a dream…

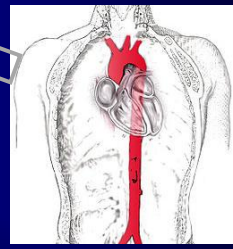
Stone baster…

ReLeaf's Therapy – Valve Restoration

Technology

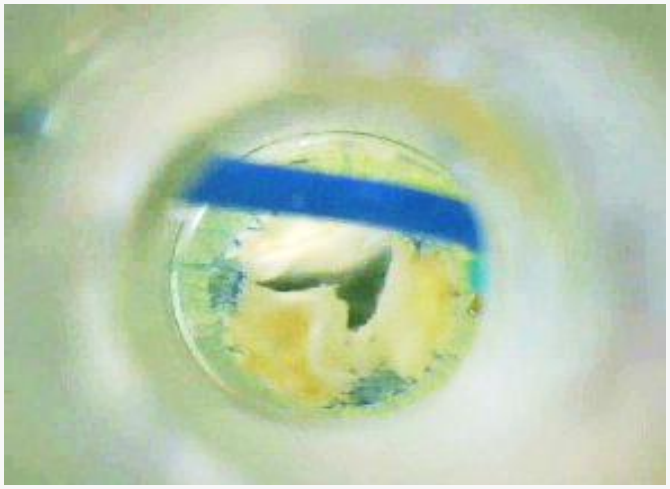
- Laser Induced Shockwaves
- Intense light pulse is converted into pressure wave that pulverizes hard tissue

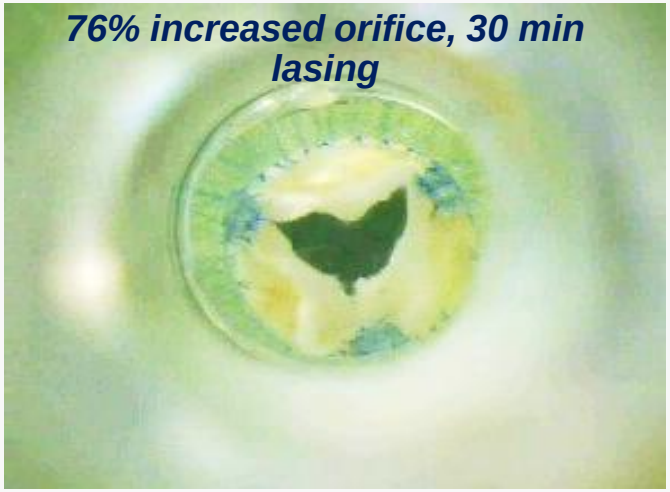




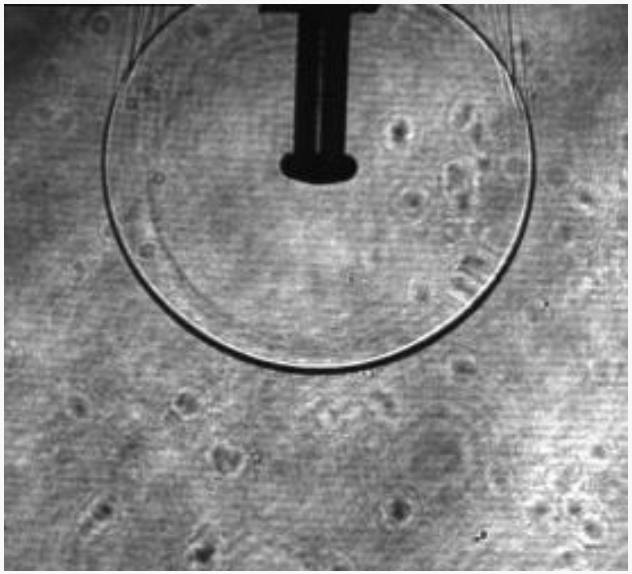
Releaf Medical- decalcification technology

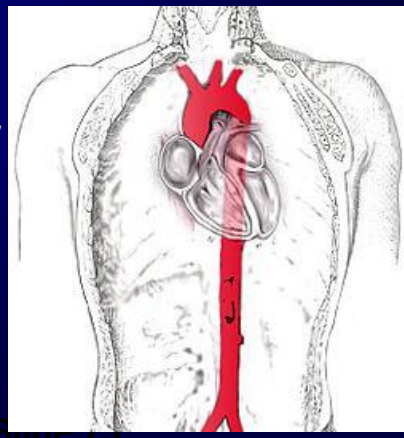
Treated human calcific AV





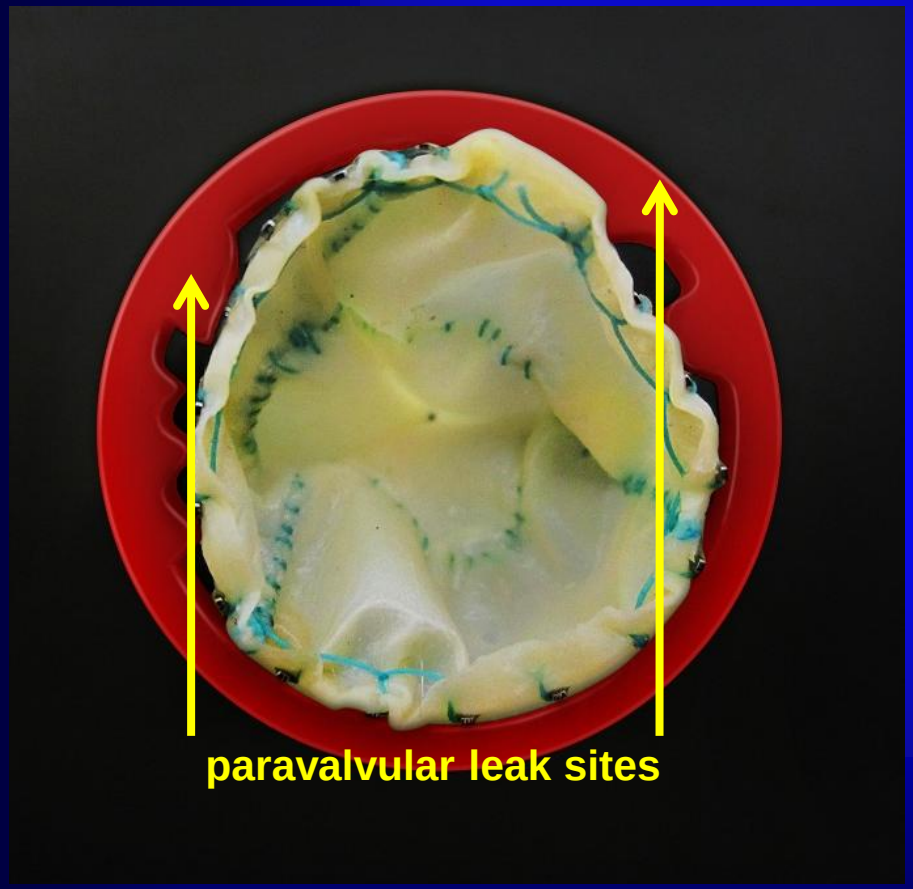
Laser Induced Shockwaves



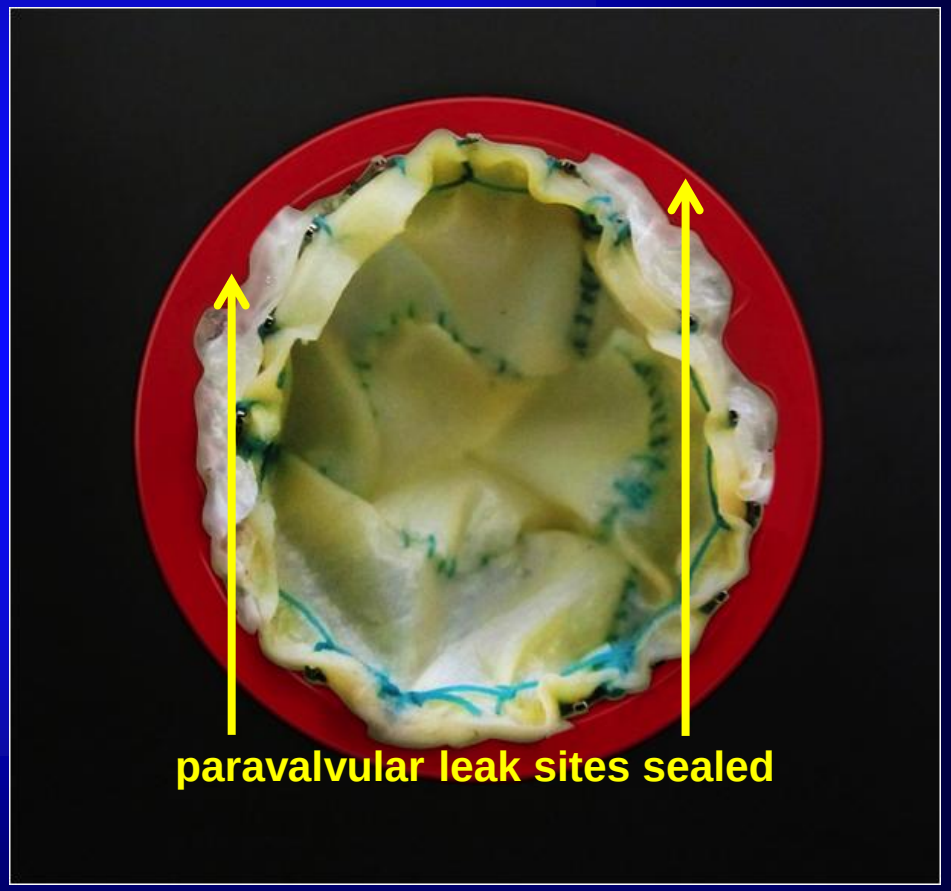


endoluminal sciences expandable skirt technology

current gen tissue skirts

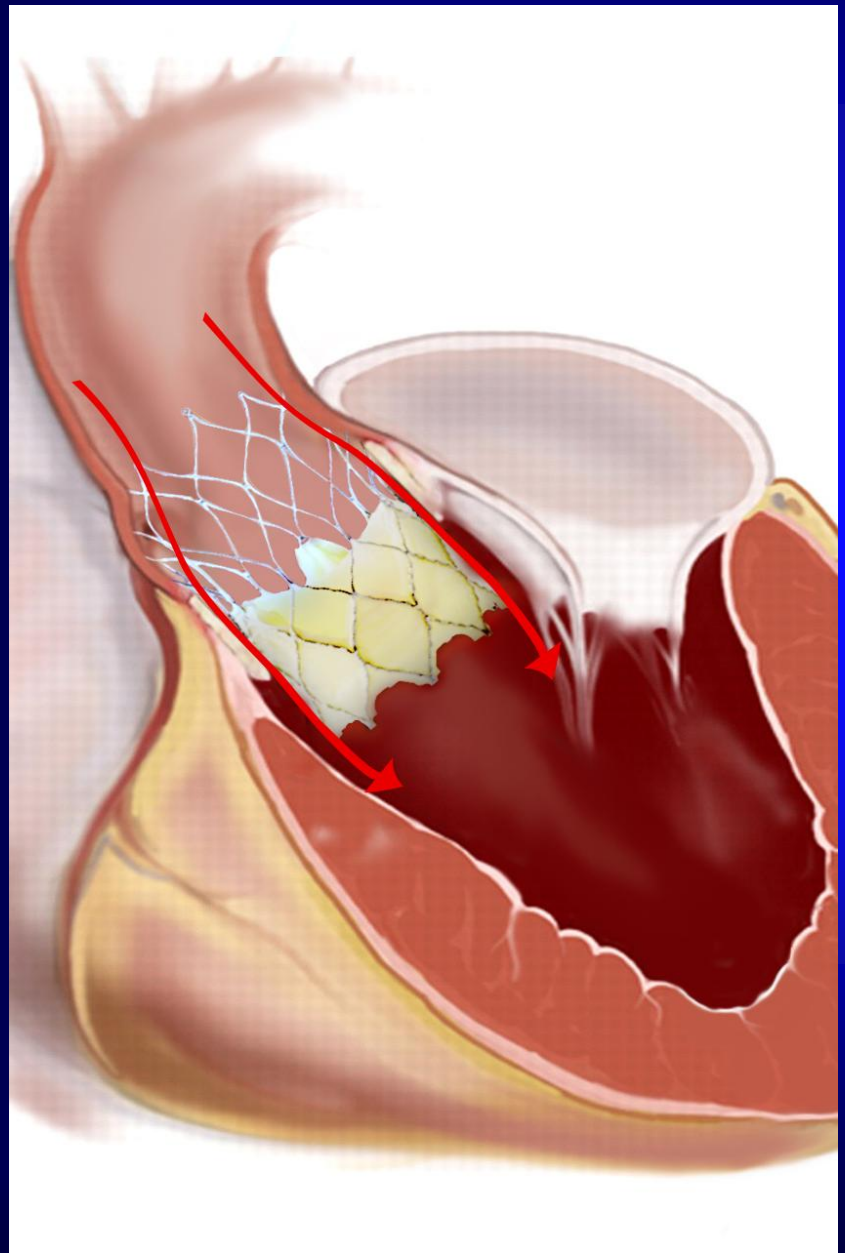


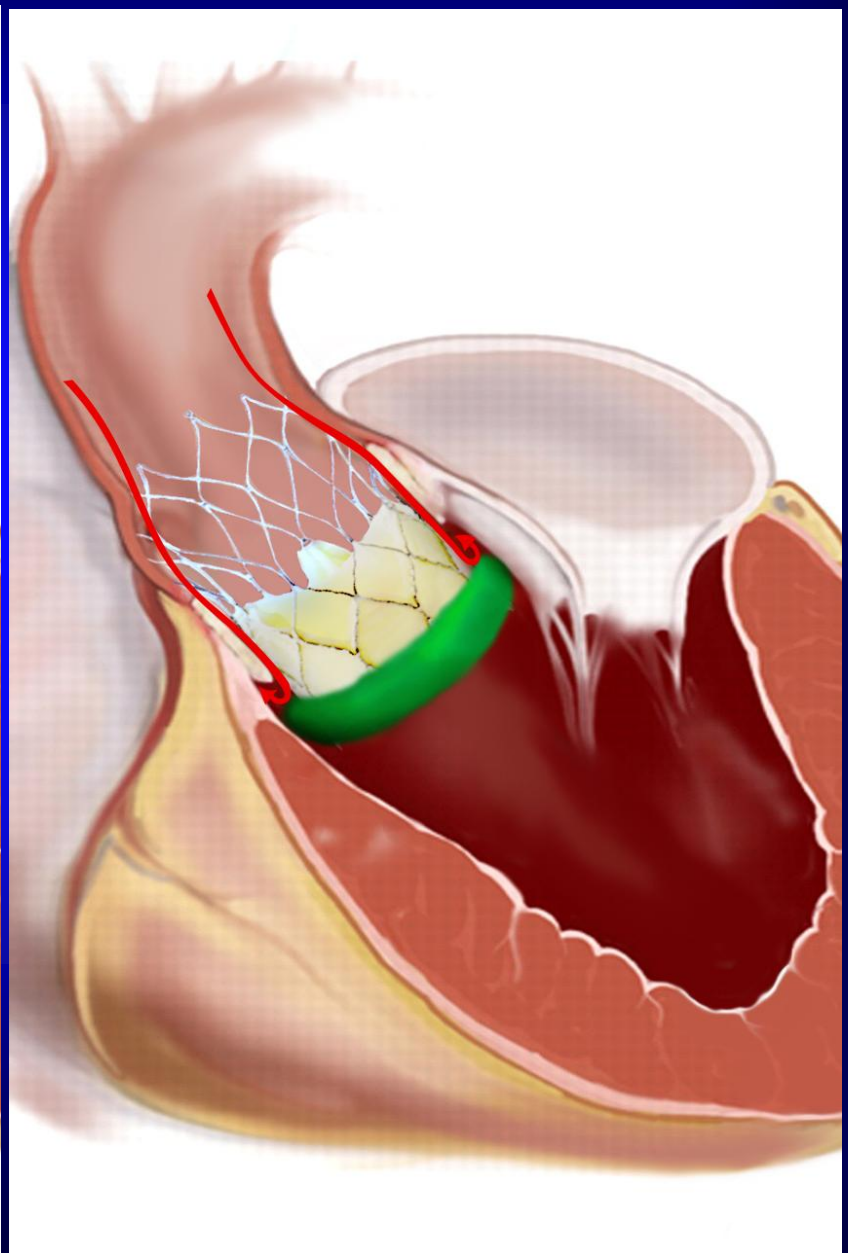
next gen “expandable” skirts



Curtesy to Raj Makkar

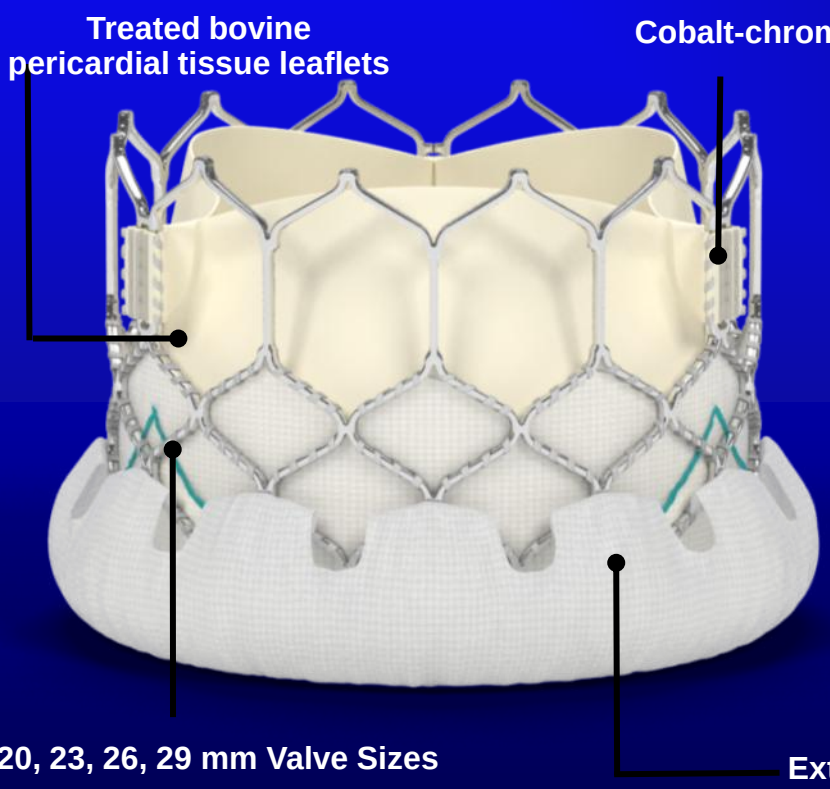
Endoluminal expandable skirt technology

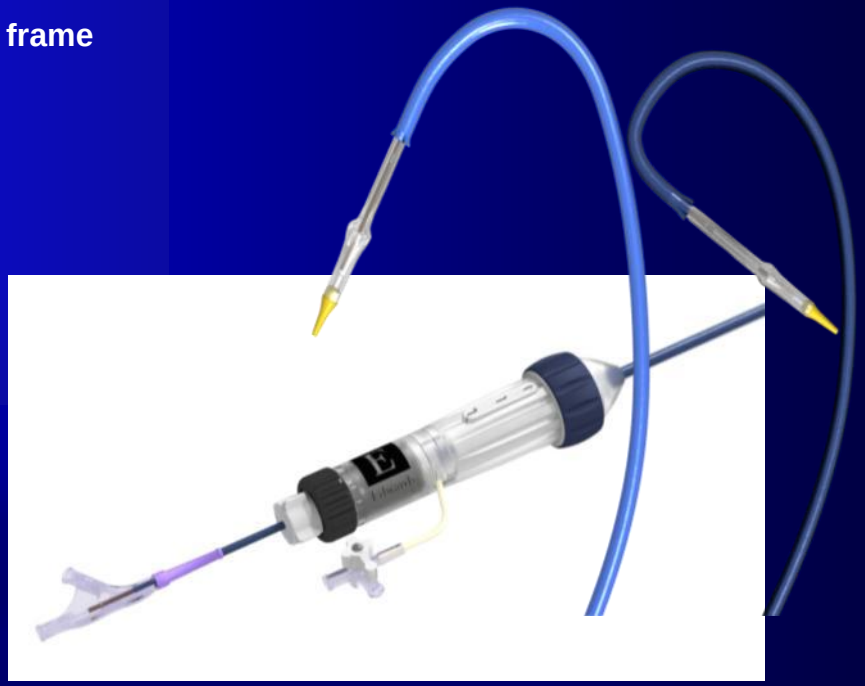




Edwards SAPIEN 3 Transcatheter Heart Valve System

Bench top Testing * Proof of Concept * Feasibility * OUS Study * Randomized Trial





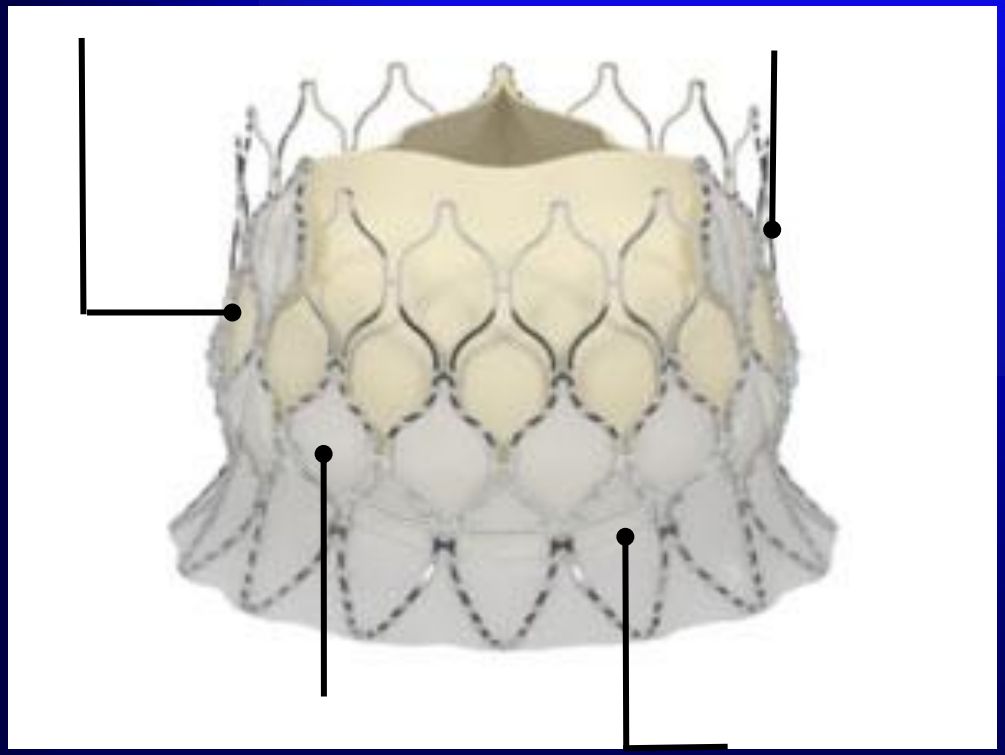
Valve	TF	TA/TAo
20-26mm	14Fr	18Fr
29mm	16Fr	21Fr

Edwards CENTERA Self-Expanding Transcatheter Heart Valve System

Bench top Testing * Proof of Concept * Feasibility * OUS Study * Randomized Trial

Treated bovine pericardial tissue leaflets

Self-expanding nitinol frame



- **Motorized delivery**
- **14 Fr system**

23, 26, 29 mm valve sizes

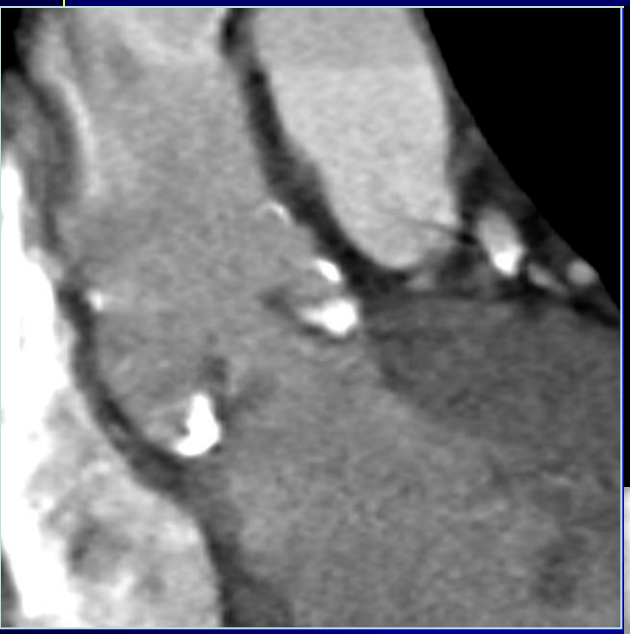
Discrete valve design

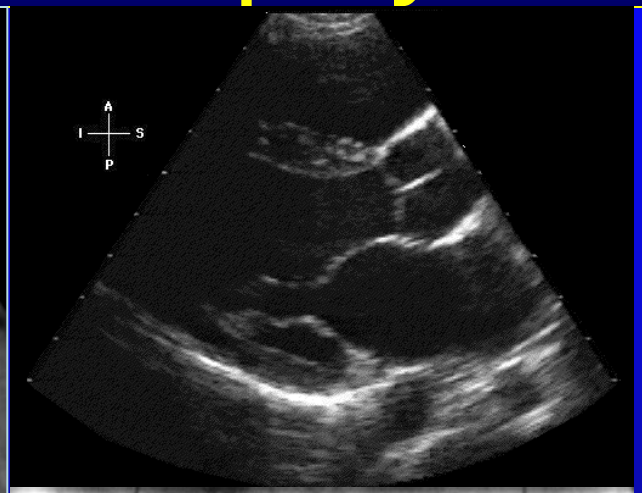
Not approved for sale

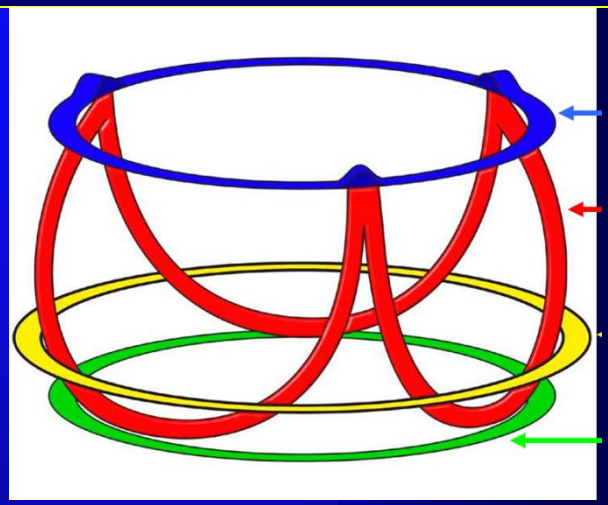
My TAVI dream

- Lower profile
- Anti Calcium technology
- Better on line imaging

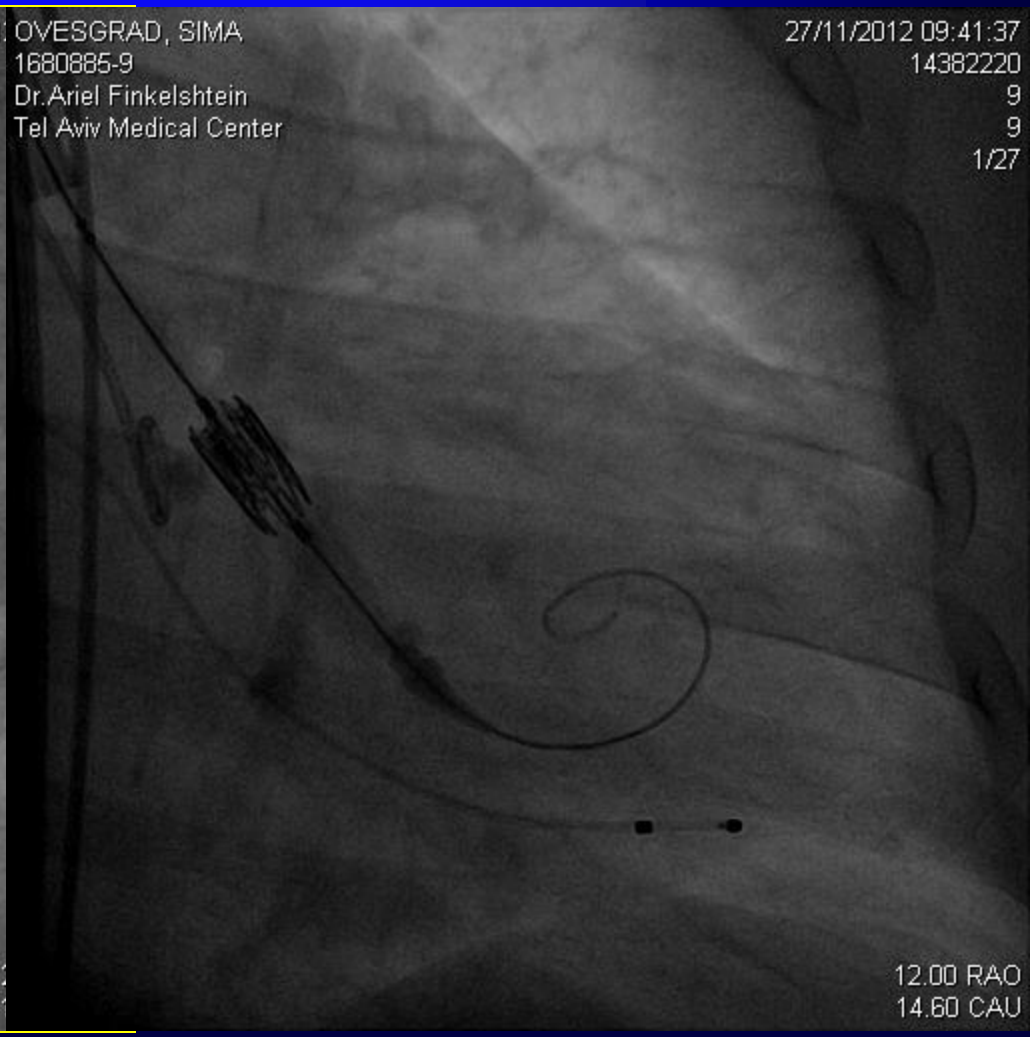
How exactly am I suppose to deploy it?





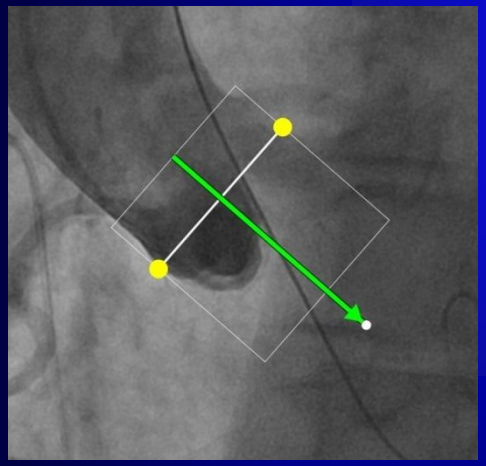


How exactly am I suppose to deploy it?

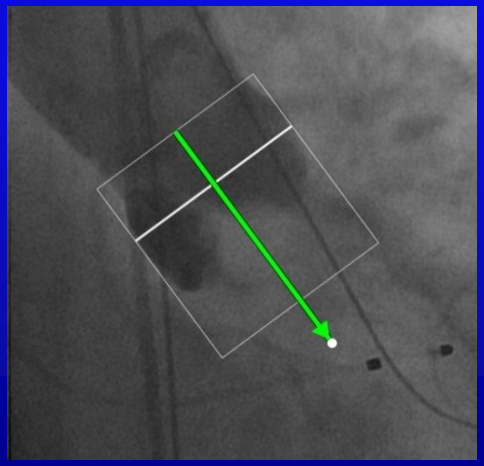


Paeion- Optimal Projection

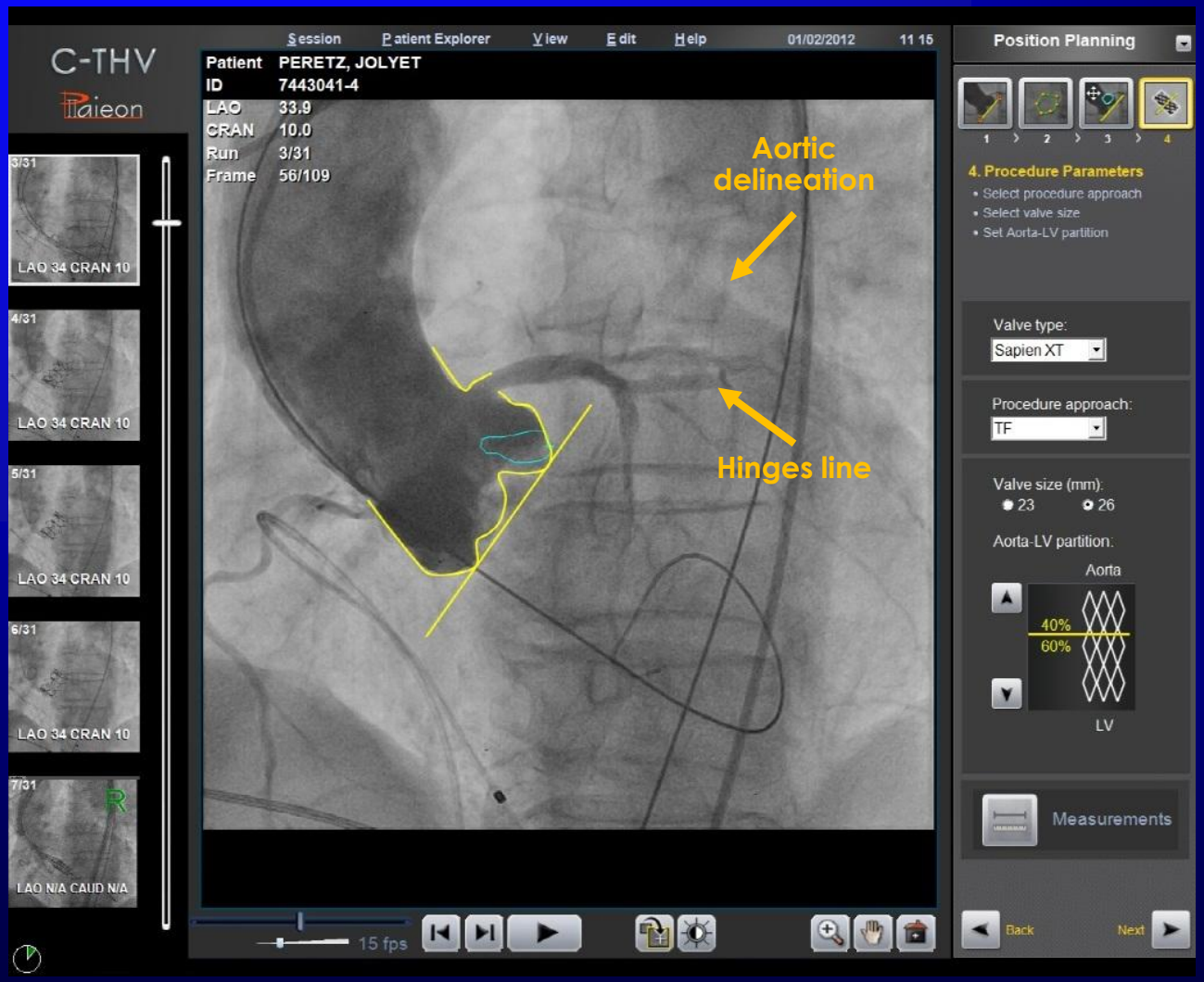
Marking 1st projection

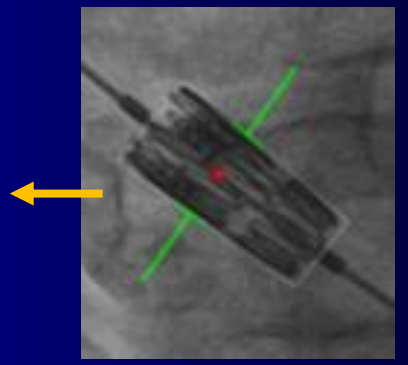


Marking 2nd projection



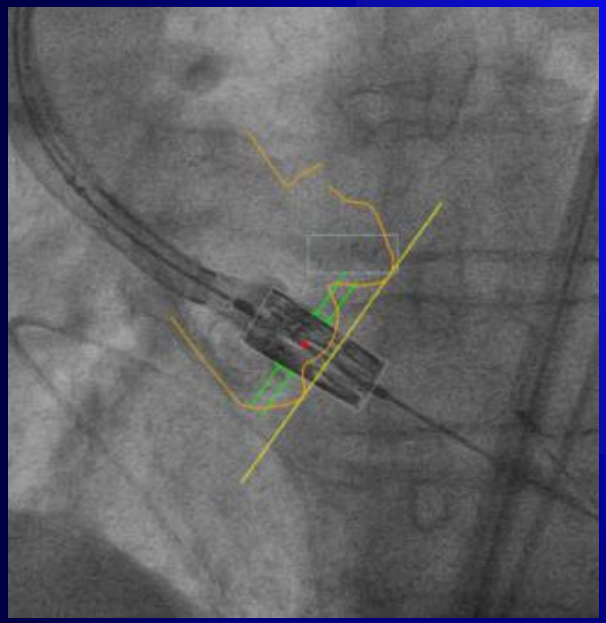
C-THV Position Planning – Sapien XT



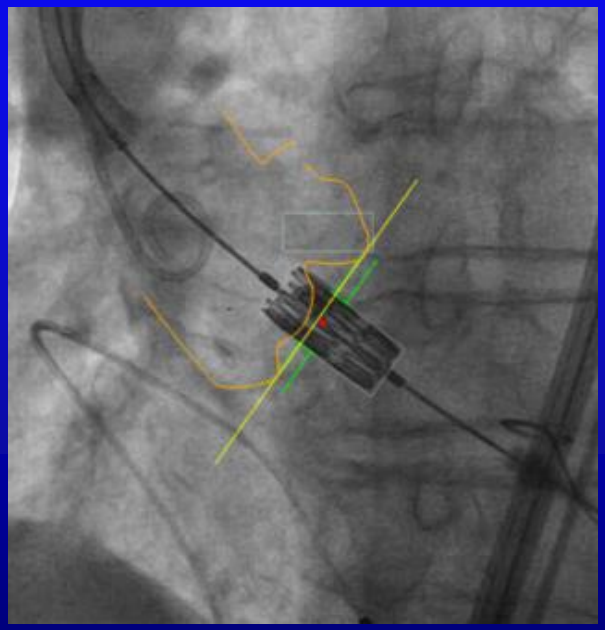


C-THV Real-Time Positioning Sapien XT

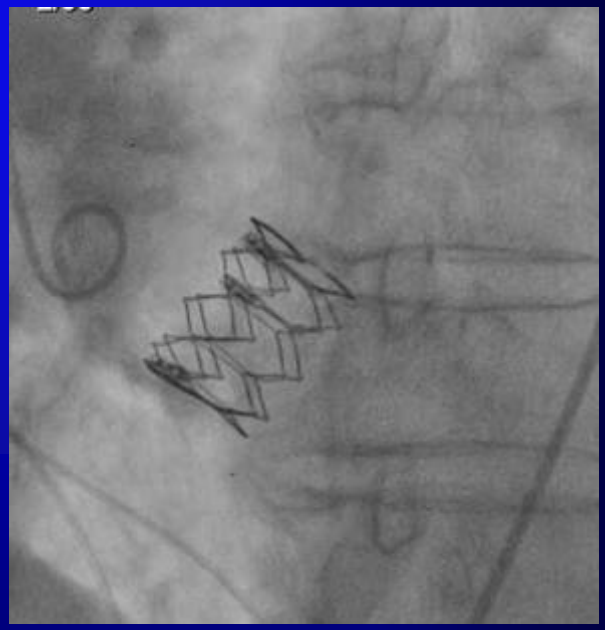
Real-Time Positioning



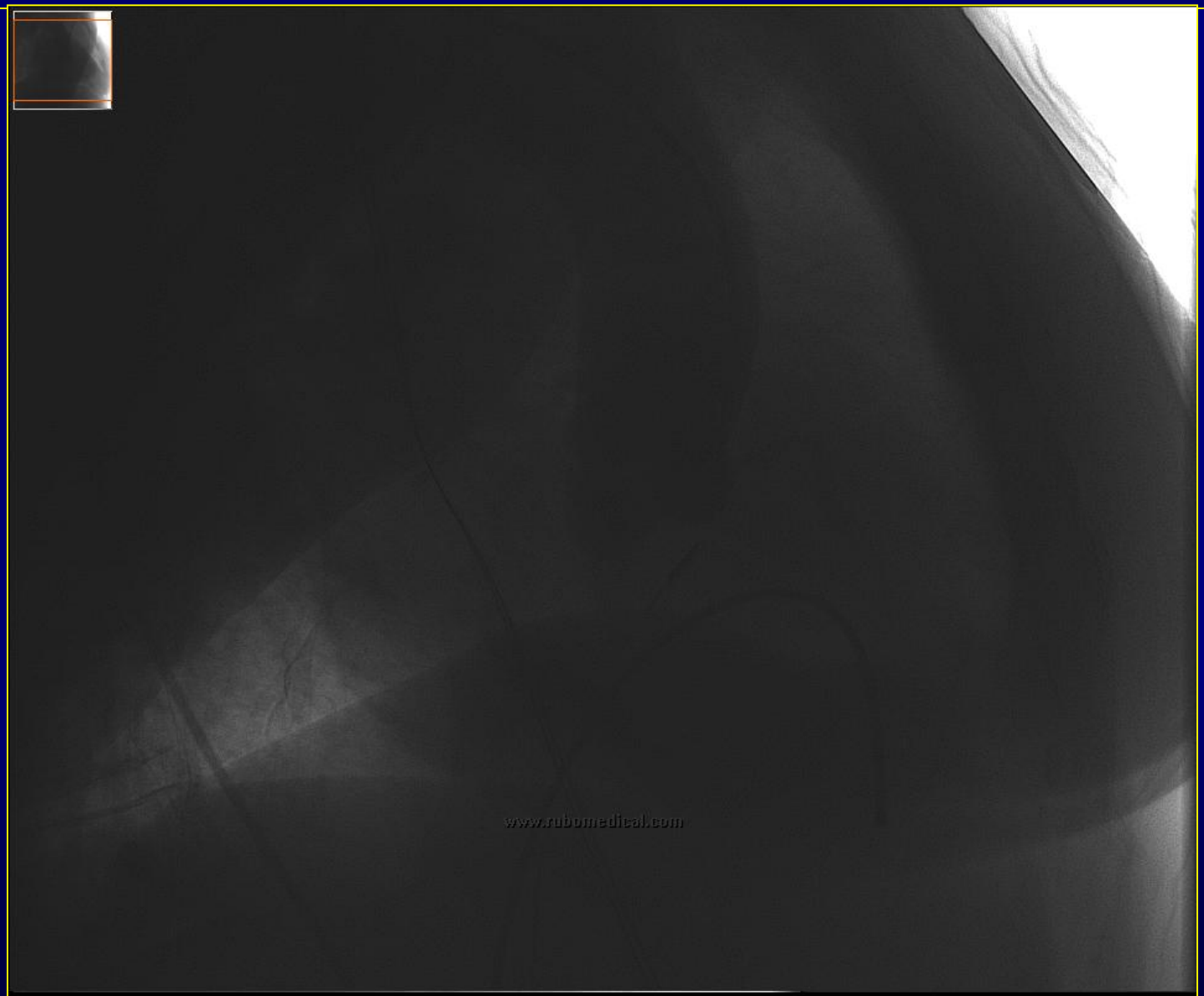
Deployment



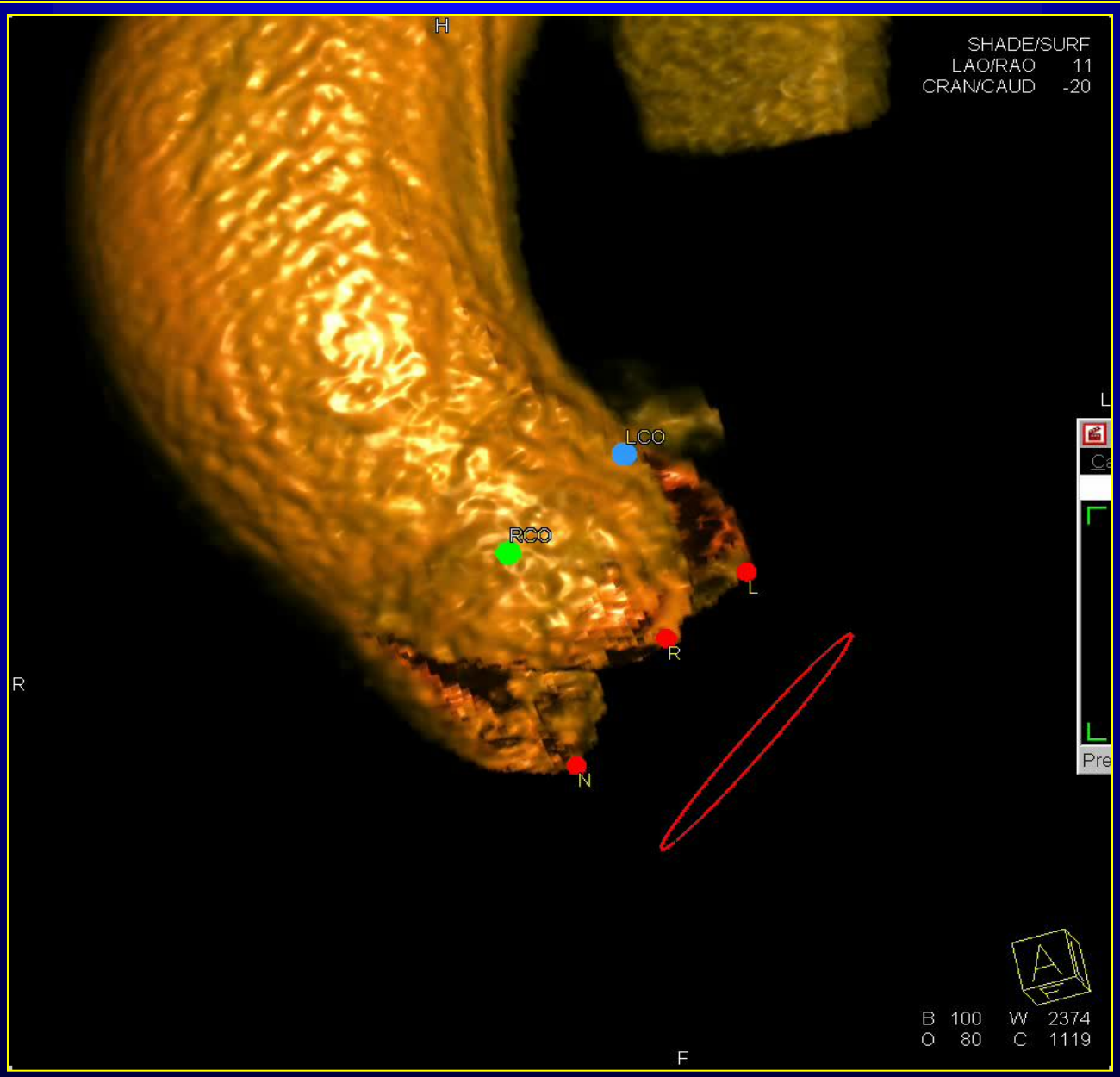
Post-Deployment Injection



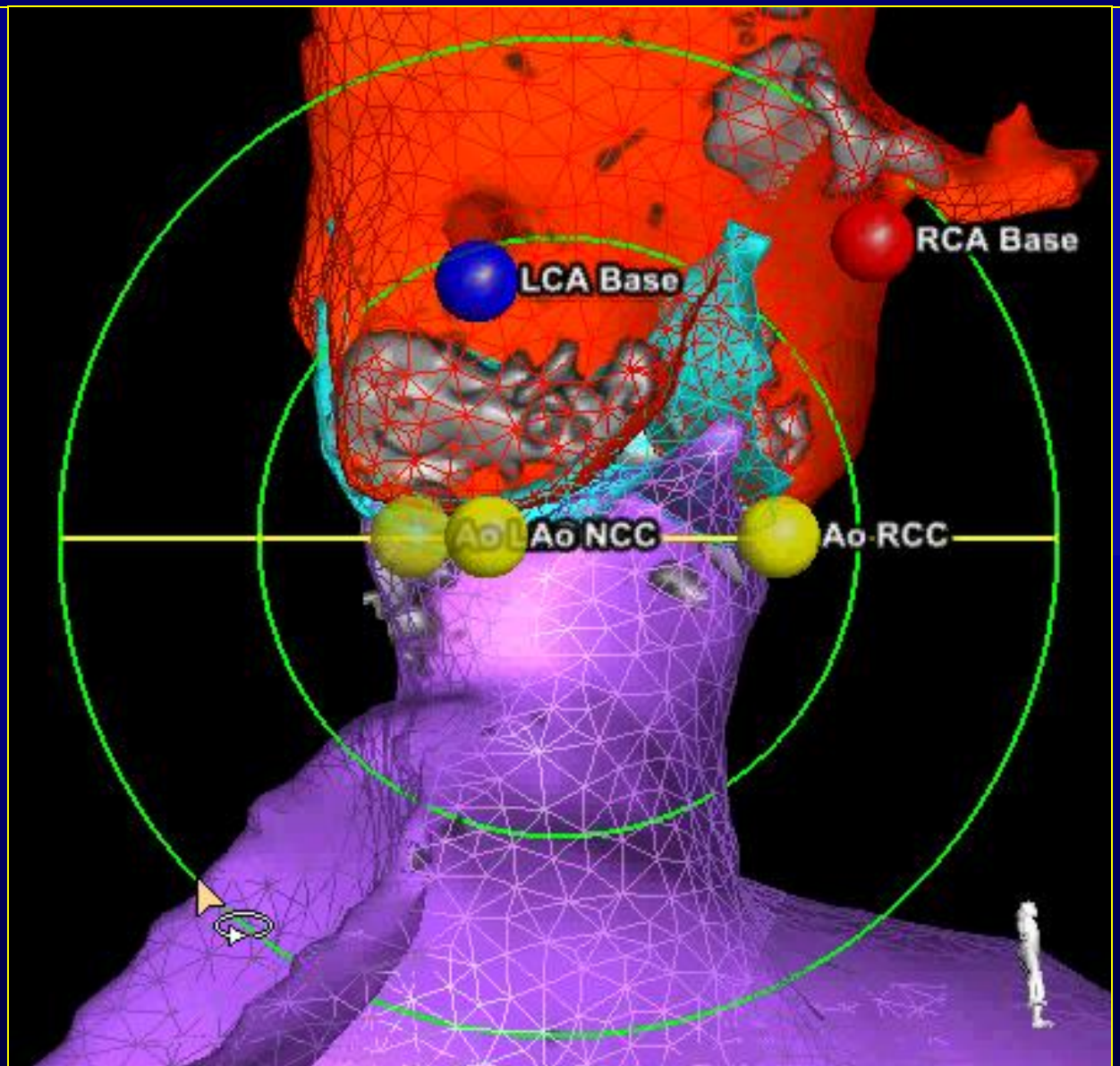
I love to have this



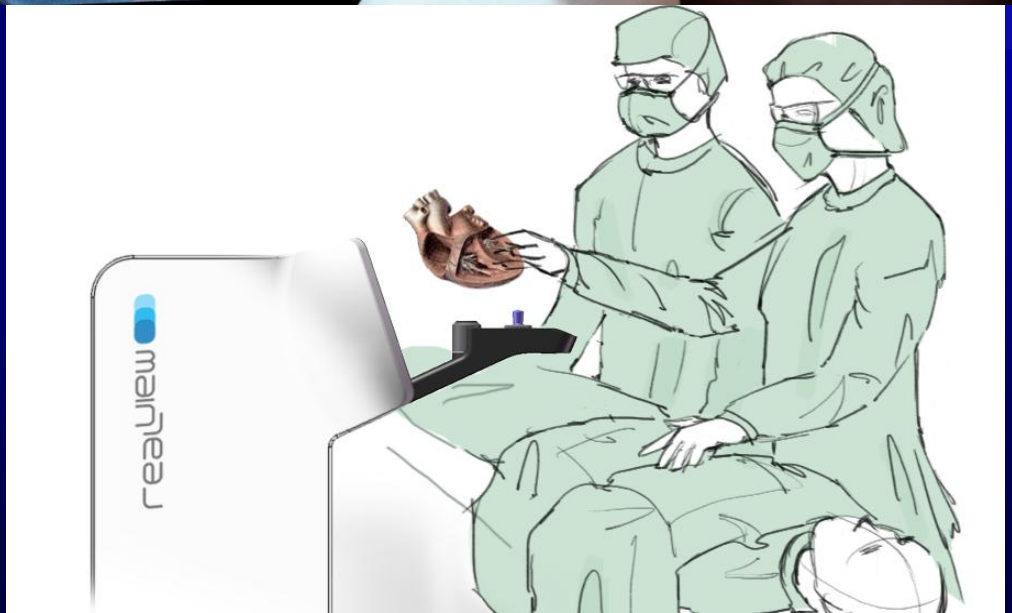
And this


H
SHADE/SURF
LAO/RAO 11
CRAN/CAUD -20
LCO
RCO
L
R
N
R
F
B 100 W 2374
O 80 C 1119

And mainly this…



RealView Imaging - Medical Holography in the Cath Lab



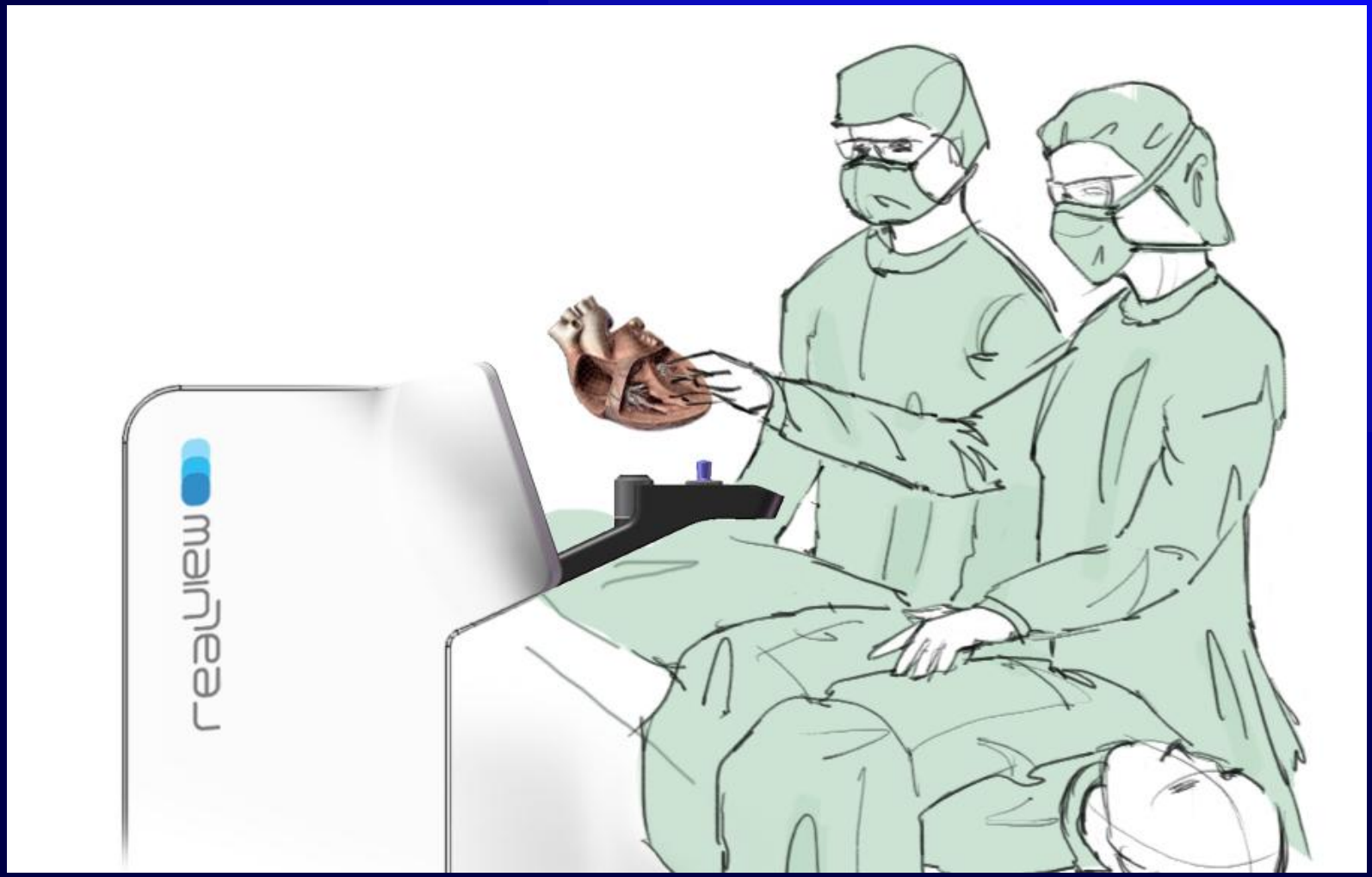
RealView Imaging's

"In-Air" Holographic Display and Interface System for Medical Imaging Applications

Key differentiators:

- **True visualization: true volume in true space**
- **Direct and precise interaction within the image**

RealView Imaging - Holographic Concept for the Cath Lab



TAVI Technologies-what is needed

- ***Lower profile devices*** **~ 16-14 Fr or smaller**
- ***Dedicated delivery systems***
- ***Better big holes closure devices***
- ***Anti Ca technology***
- ***Improved circumferential annulus fixation***

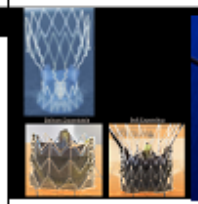
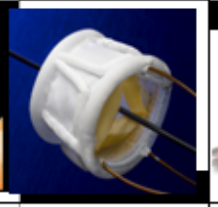
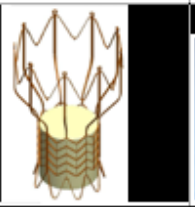
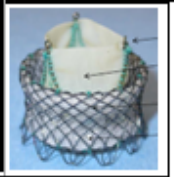
  To reduced para-valvular AR
- ***Optimal positioning before/during deployment (improved placement position)***

  Advanced imaging

  Localization and stabilizing features

  Retrievable and repositionable

Valve Prosthesis

COMPANY	Edwards	CoreValve	St. Jude Medical	Direct Flow Medical, Inc.	Sadra Medical	JenaValve	Ventor	MDT Internal Program	HEART LEAFLET TECH (HLT)
PRODUCT NAME	Edwards SAPIEN™ THV	CoreValve ReValving™	TBD	Direct Flow™	Sadra Lotus™ Valve System	JenaValve JenaClip™	Ventor Embracer™	TBD	Heart Leaflet
VALVE PHOTO									
TISSUE	Bovine Pericardium	Porcine Pericardium	Bovine Pericardium	Bovine Pericardium	Bovine Pericardium	Porcine	Bovine Pericardium	Porcine Pericardium	Porcine Pericardium
STENT	Stainless steel	Nitinol	Nitinol & Stainless Steel	Polyester fabric	Nitinol	Nitinol	Nitinol	Nitinol	Nitinol
RETRIEVABLE	—	—	TBD	X	X	X	—	X	X
REPOSITIONABLE	—	—	Nitinol	X	X	X	X	X	X
ACCESS & FRENCH SIZE	TA → 26F	—	TBD	—	—	TA → 25F	TA → 24F		—
	TF → 22F	TF → 18F	TBD	TF → 22F	TF → 21F	TF → 21F	TF → 16F	TF → 16F	TF → 16F
# OF IMPLANTS	All = 2000+	All = 2000+	Preclinical	FIM = 8 Paraguay FIM = 31 Germany	FIM = 3 Feasibility = 8	Temporary implants = 7 of 15 planned	TA FIM = 18	Preclinical	Temporary implants = 4

PARTNER Final Thoughts

Rarely, in Medical Research,

has so dramatic an improvement in Survival,

been achieved in such a Short Time,

with so few Iterations;

And it is only the Beginning of a Flooding Tide,
that Floats All Boats!!!

Martin B. Leon

Those are my TAVI dreams…

My TAVI dream…

Now, let's talk about my true small tiny TAVI dream…

THANK YOU FOR YOUR ATTENTION

Transcatheter Aortic Valve Implantation in High Risk Patients with Severe Aortic Stenosis:

TASMC Experience - First 300 Patients

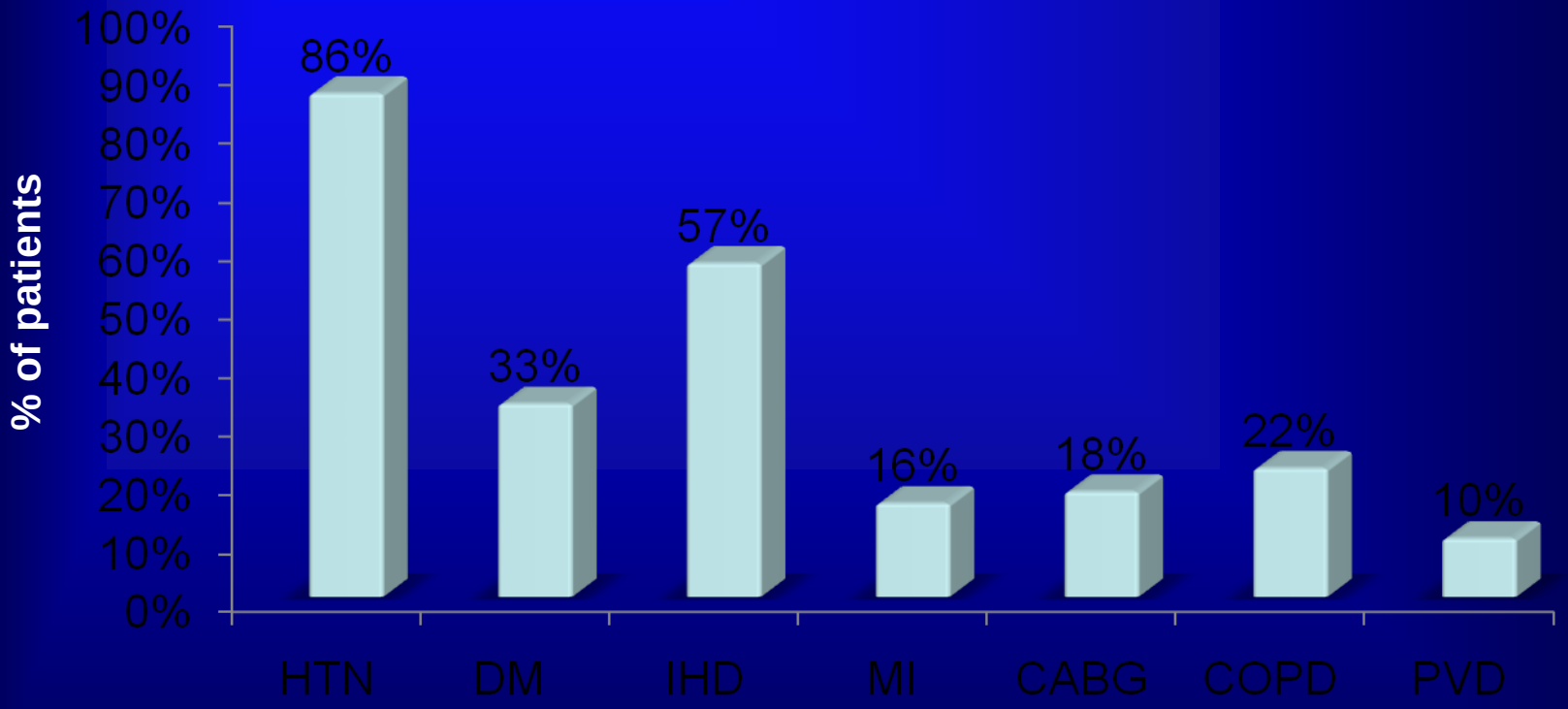
Finkelstein et al, submitted

PAVI - TASMC

- 300 patients between March 2009 to Sept. 2012
- Age: 83.3 ± 5.4, range 63-98
- 115 Males (38%), 185 Female (62%)
- Logistic EuroScore (%): **26 ± 13.1**
- Approach: 293 - Transfemoral, 7 – subclavian
- 250 – CoreValve, 50 - Edwards

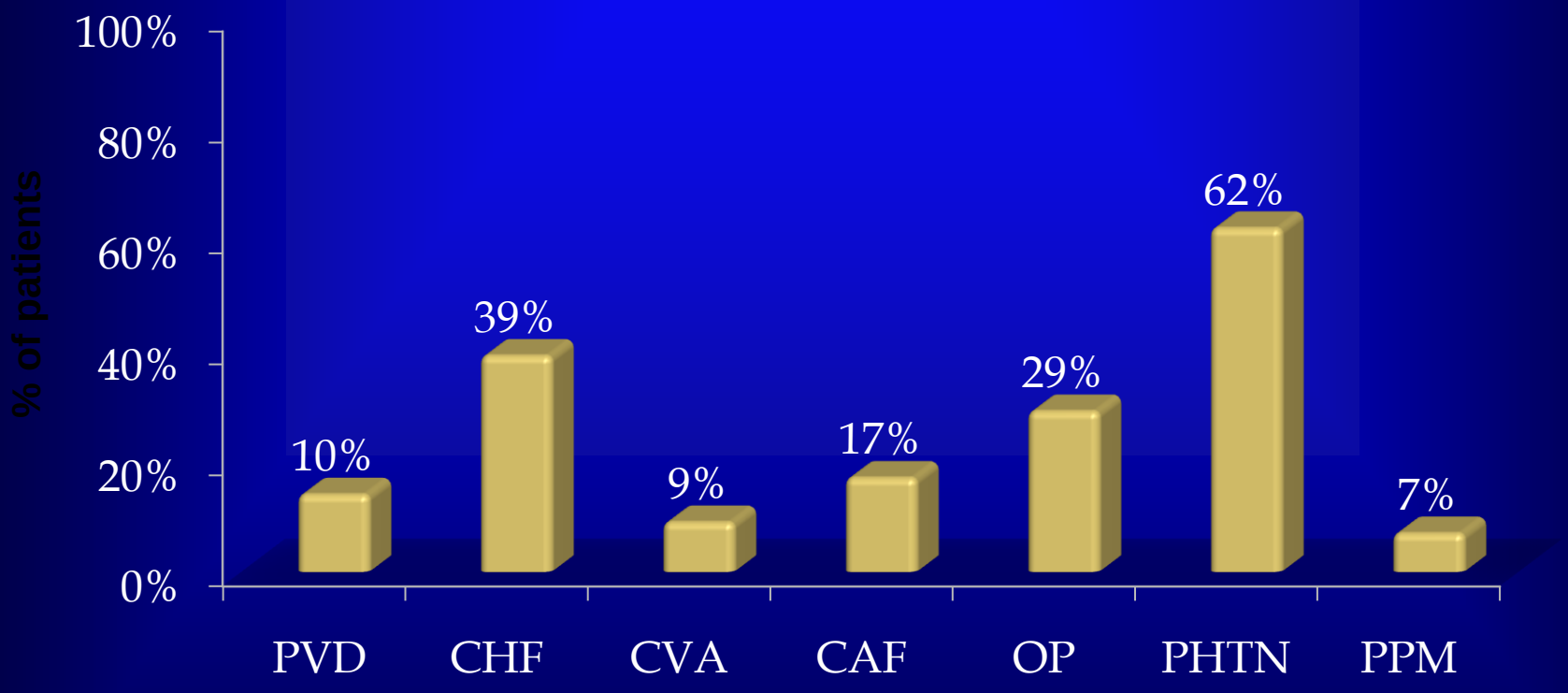
Finkelstein et al, submitted

Co-Morbidities



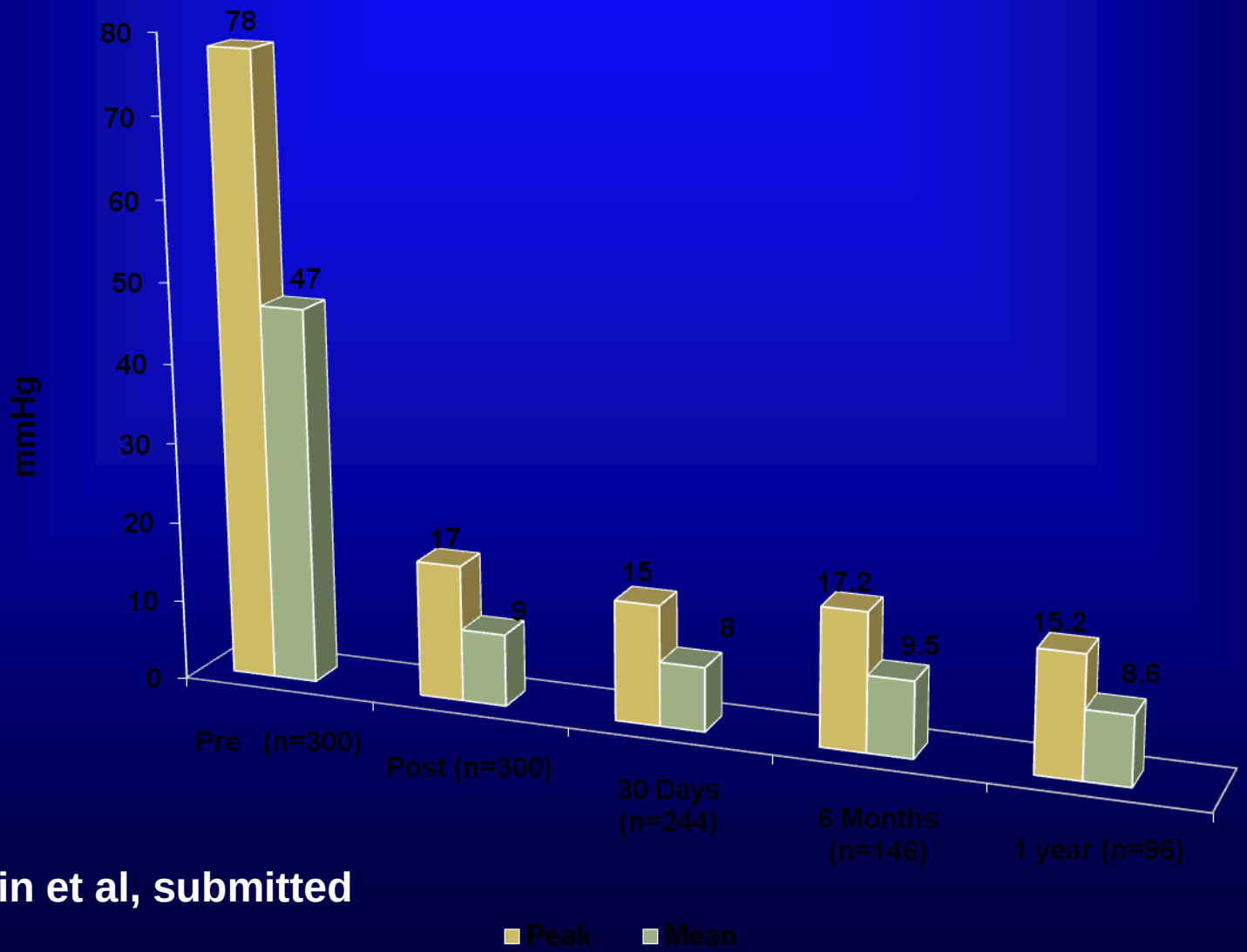
Finkelstein et al, submitted

Co-Morbidities



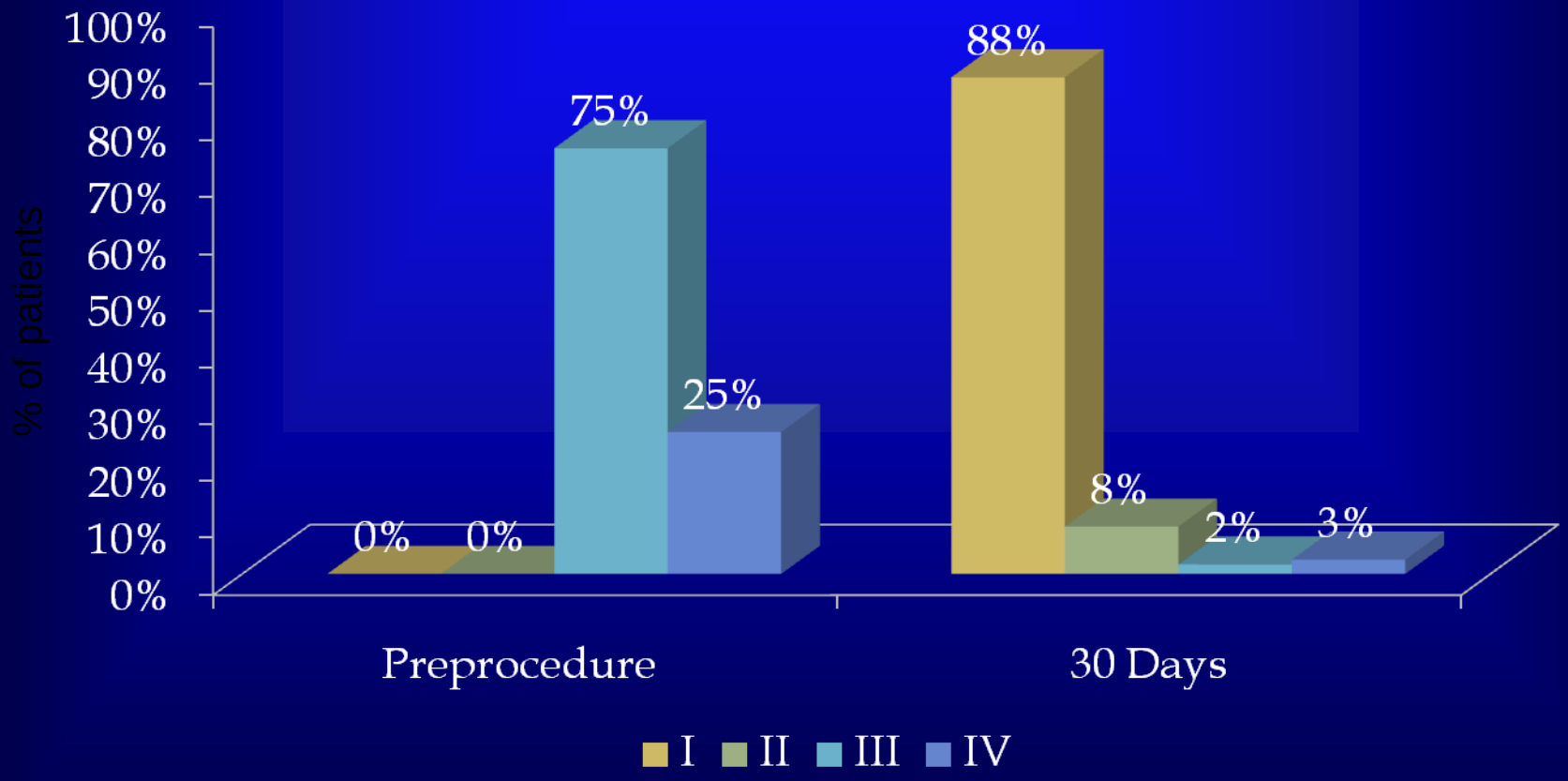
- OP=Osteoporosis;
  PHTN=Pulmonary Hypertension;
  PPM=Permanent Pacemaker

Peak & Mean Echo Pressure Gradients



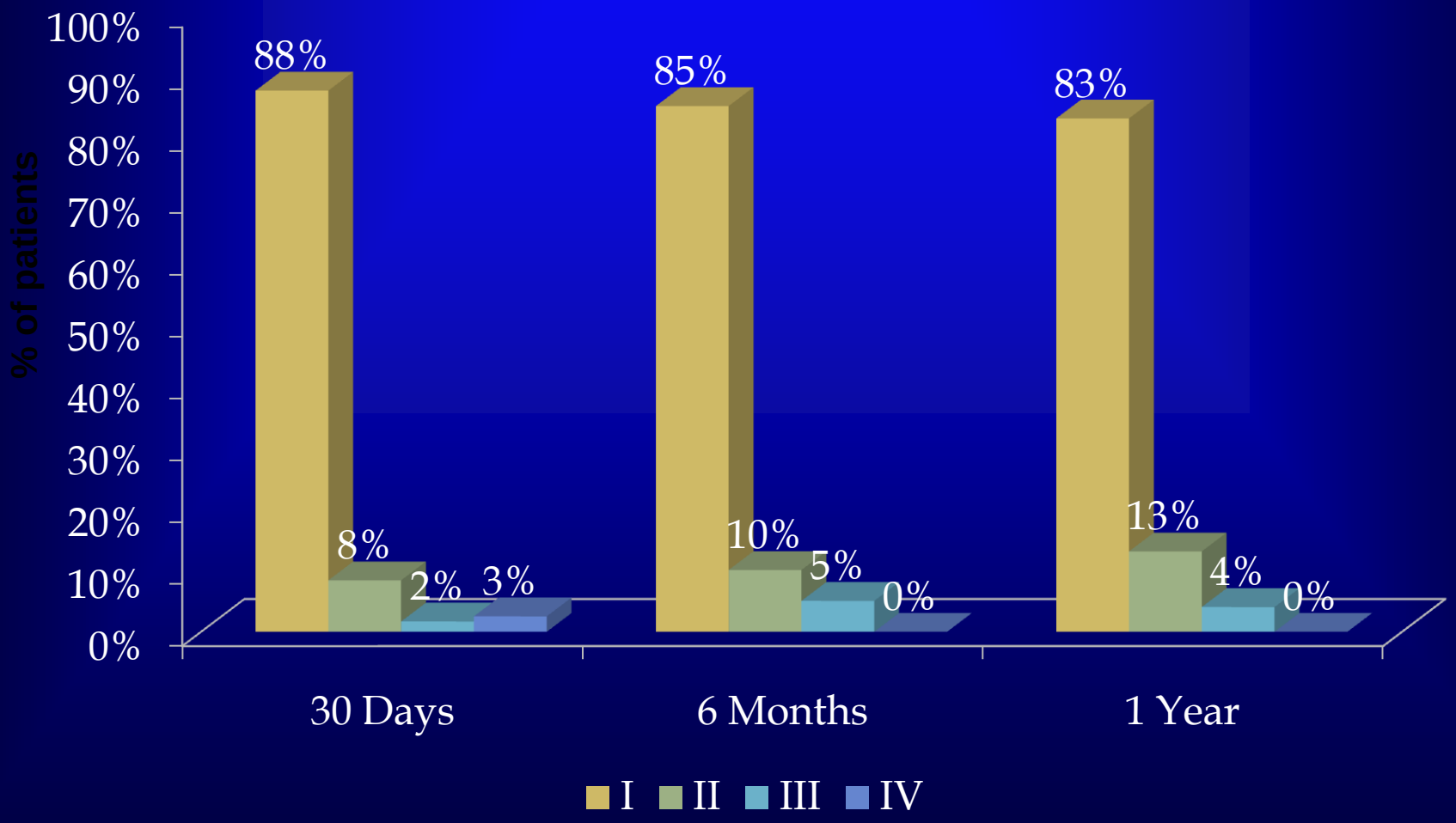
Finkelstein et al, submitted

NYHA Class

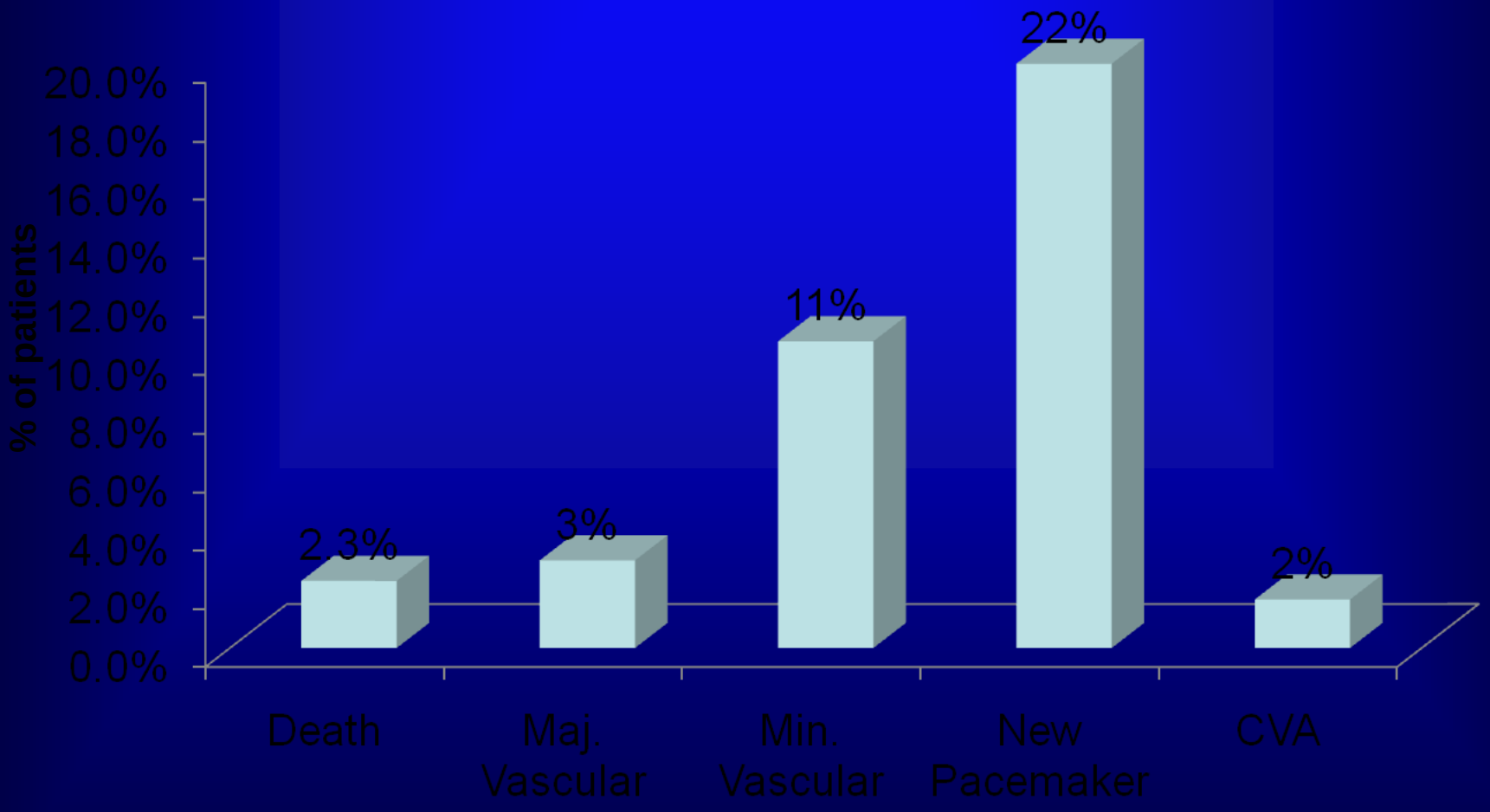


Finkelstein et al, submitted

NYHA Class

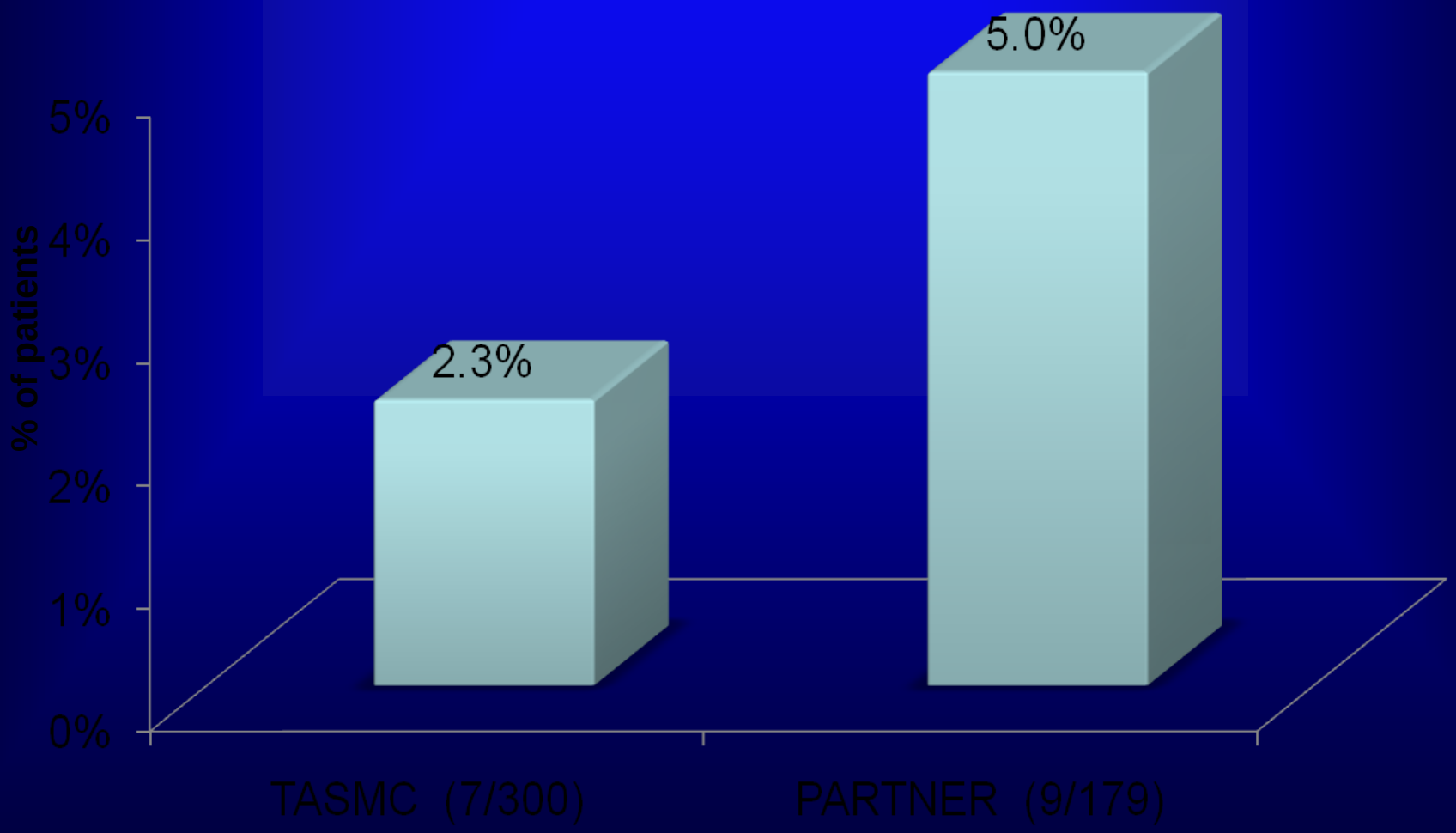

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
% of patients
88%
8%
2%
3%
85%
10%
5%
0%
83%
13%
4%
0%
30 Days
6 Months
1 Year
I
II
III
IV

Complications (30 Days)

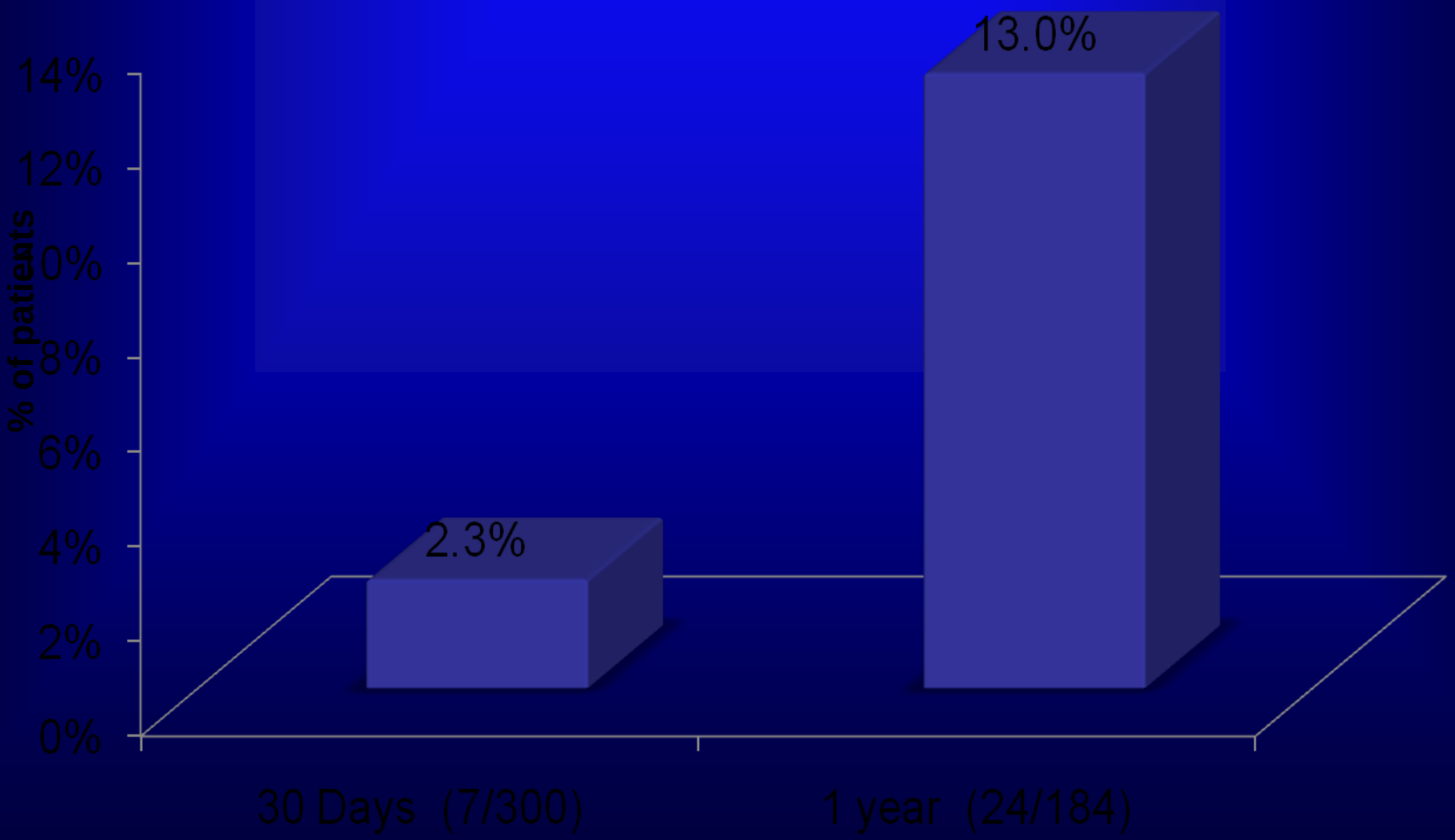


1% cardiogenic shock; 2% sepsis, 2% mod.-sev. AR

30 Days Mortality

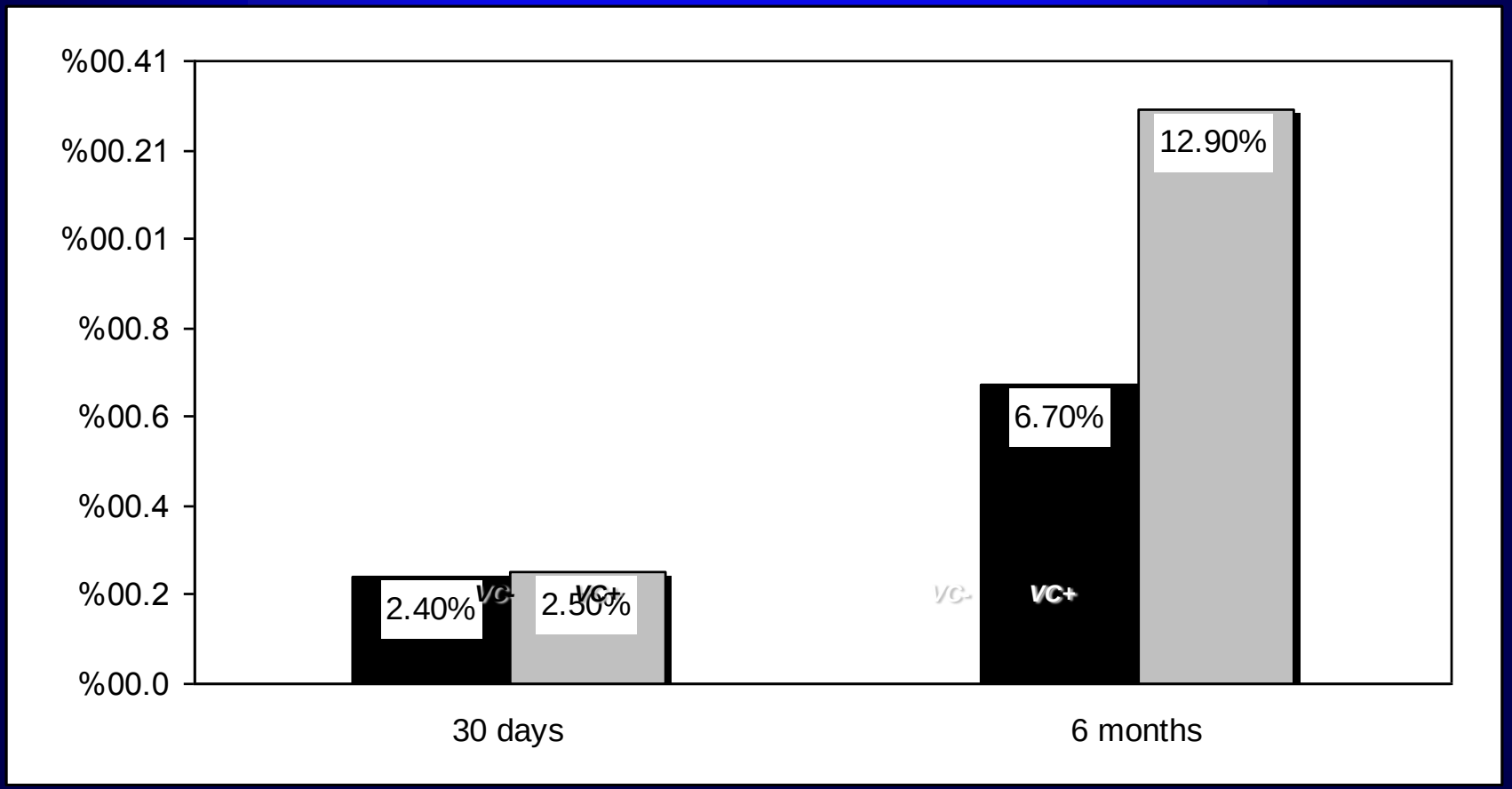


Mortality

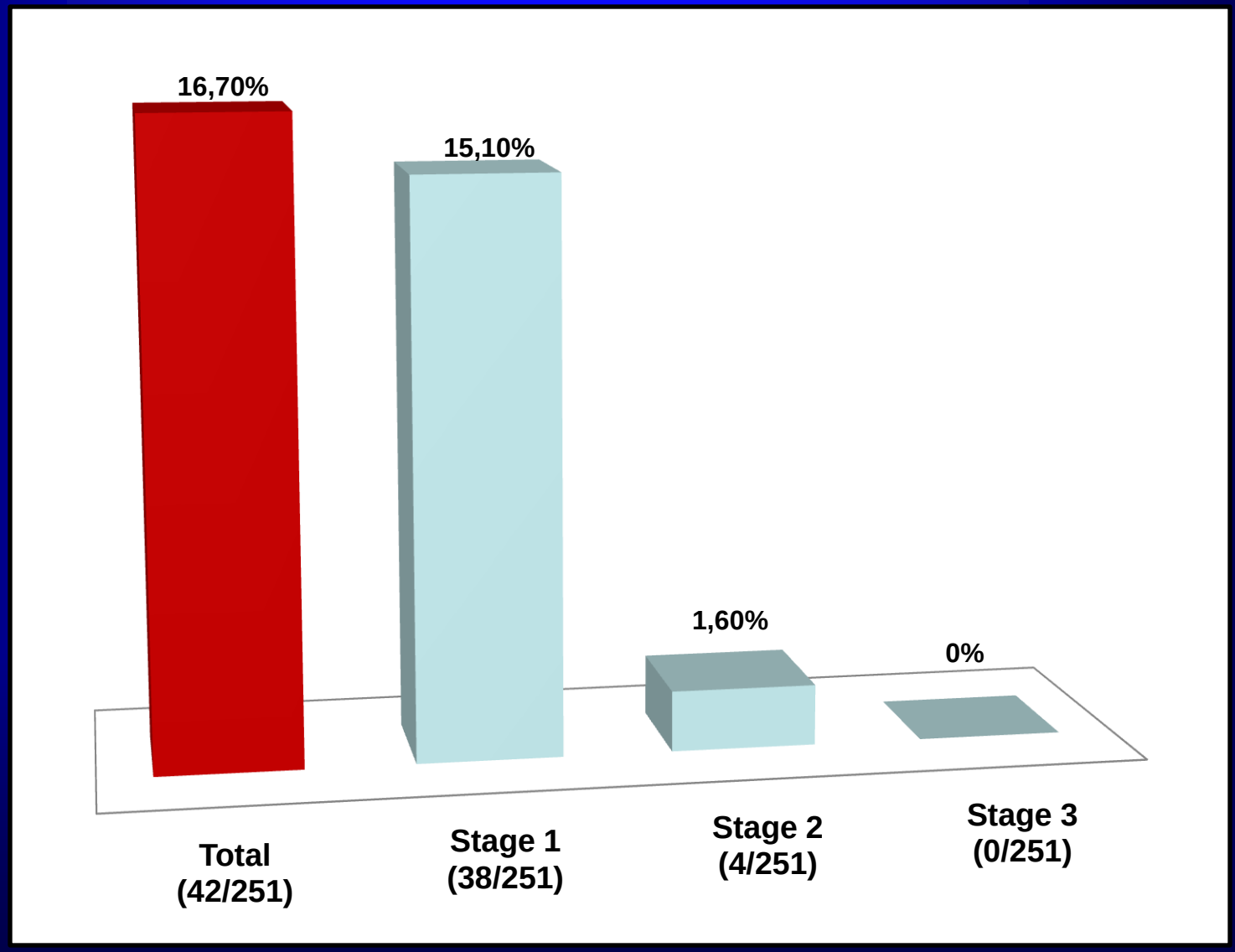


Vascular complications in TAVI

- **No relation to mortality observed between with and without VC**
  - **–30 days ➔ 1/39 [2.5%] vs 6/254 [2.4%]; p=0.939**
  - **–6 months ➔ non significant trend. 4/31 [12.9%] vs 14/208 [6.7%]; p=0.224**

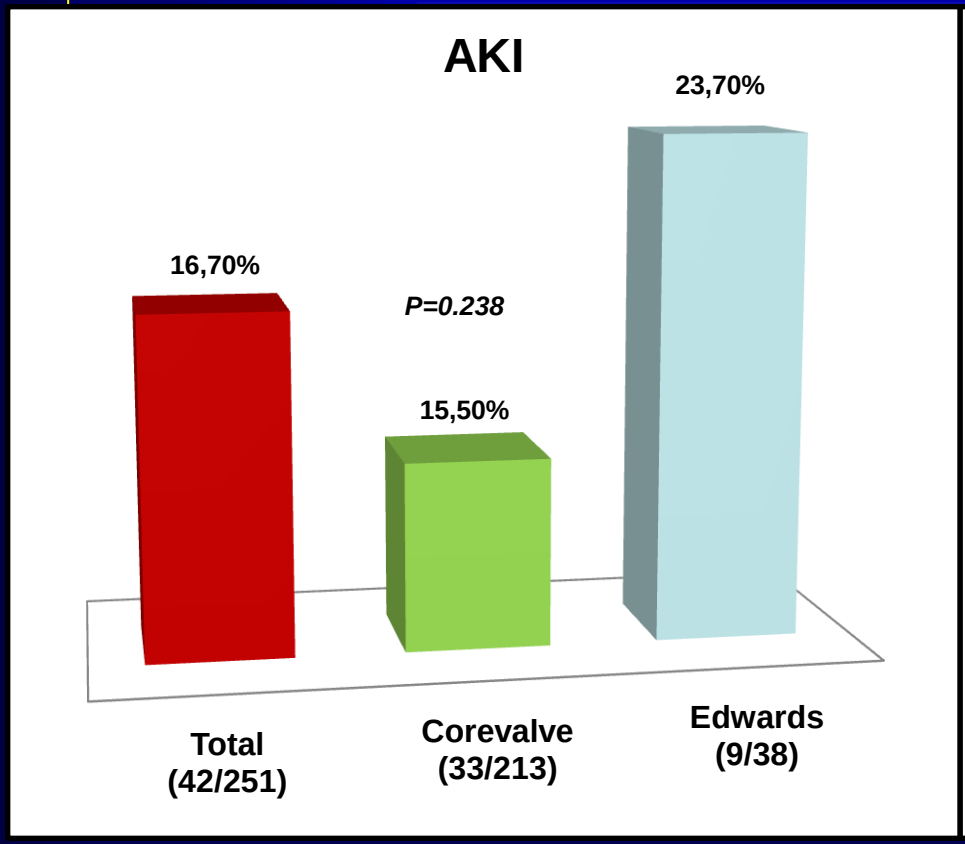


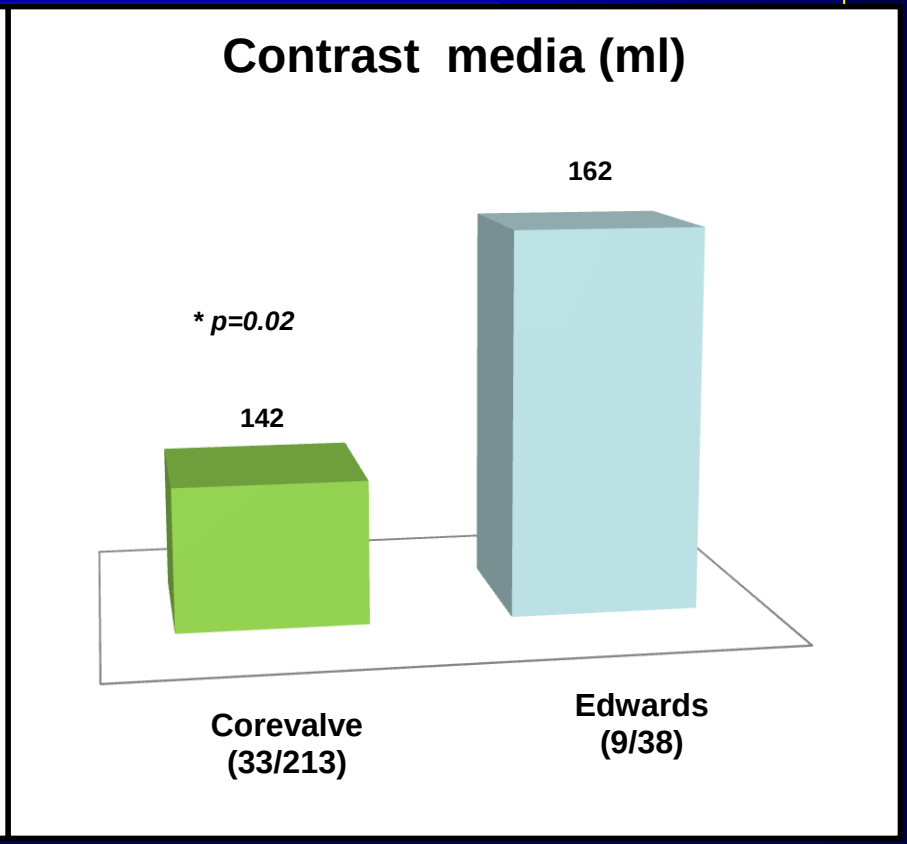
Acute Kidney Injury following TAVI



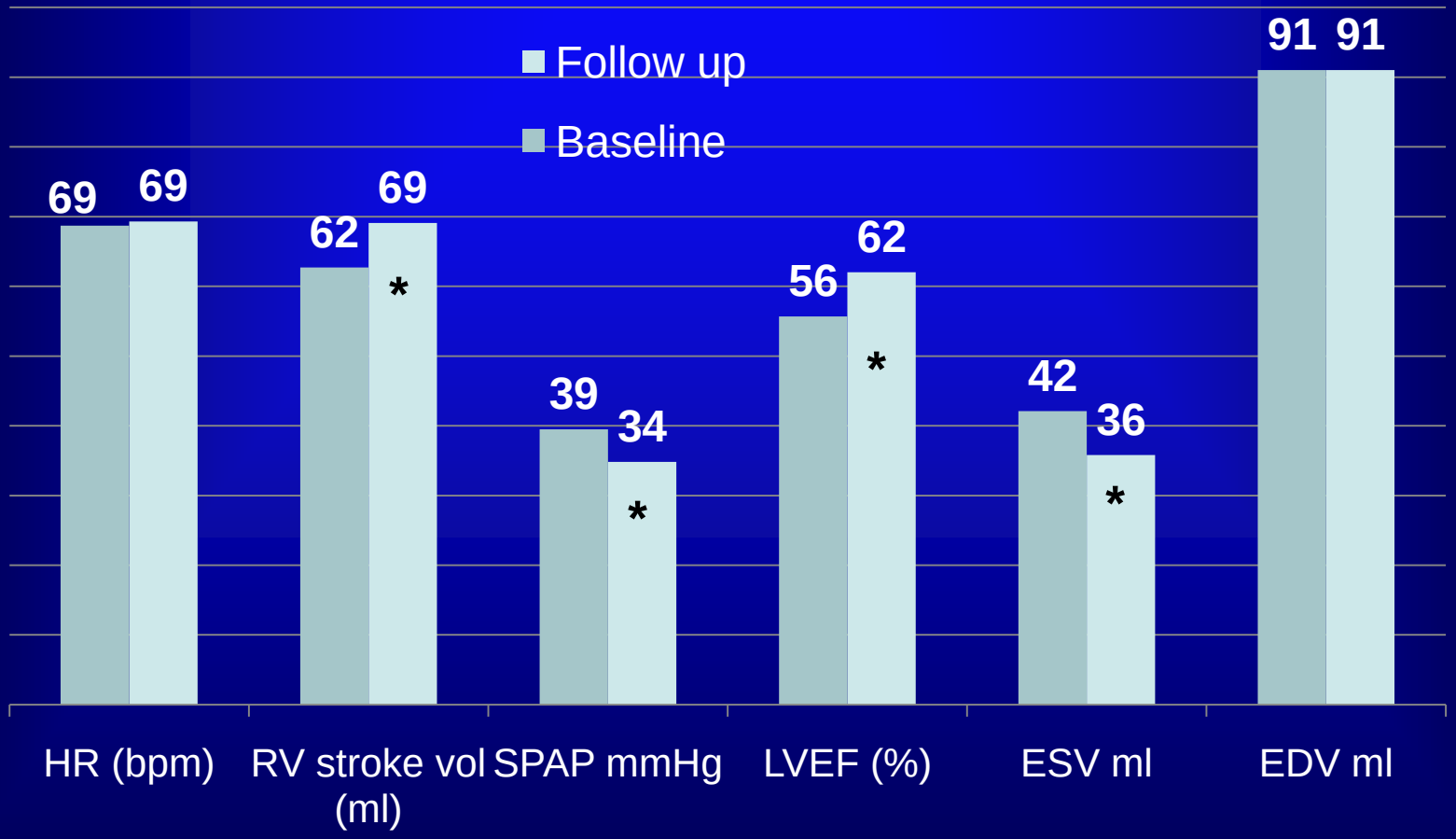
Acute Kidney Injury following TAVI

Edwards vs. CoreValve:





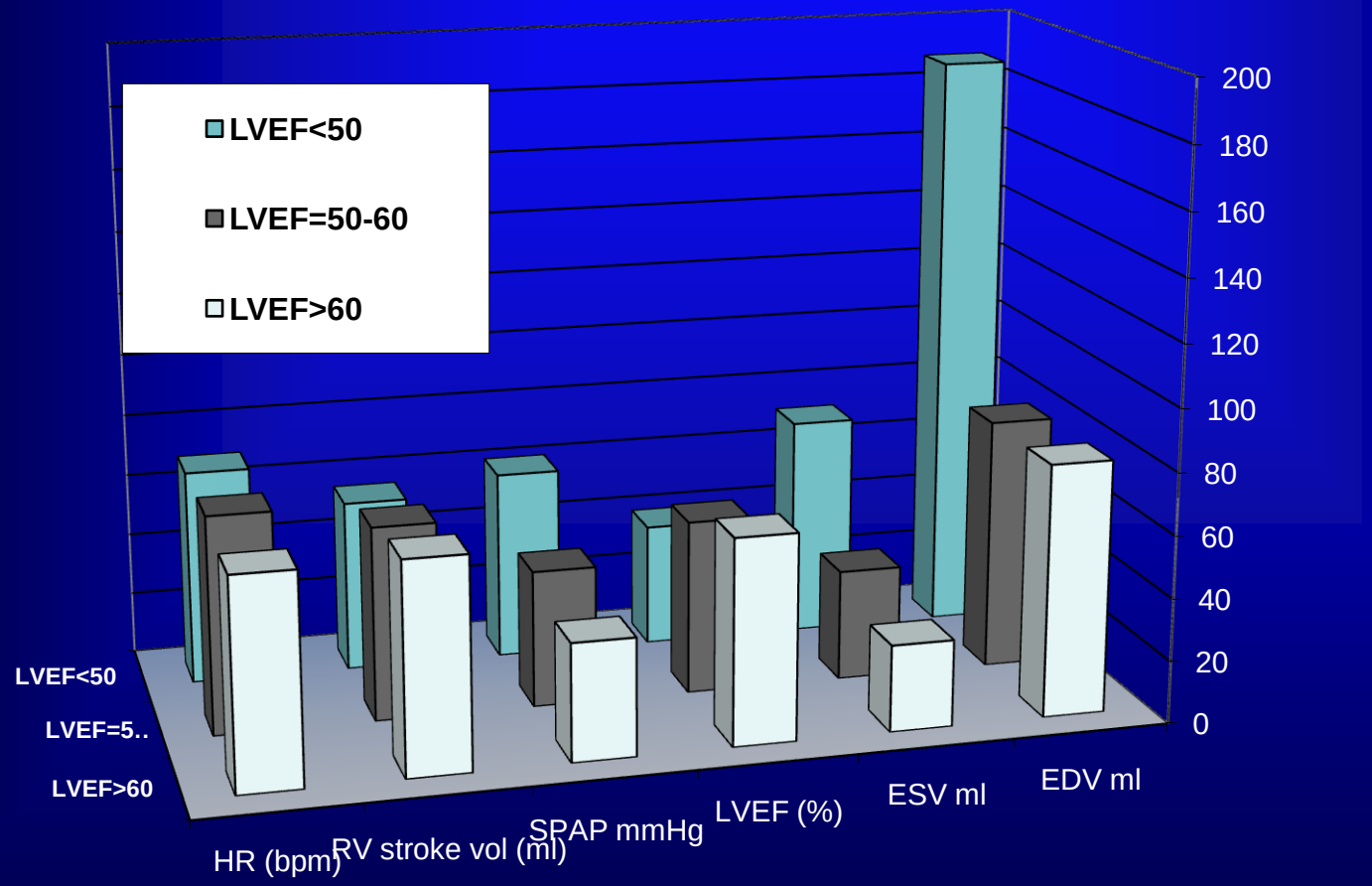
Hemodynamic effect of TAVI (entire cohort)



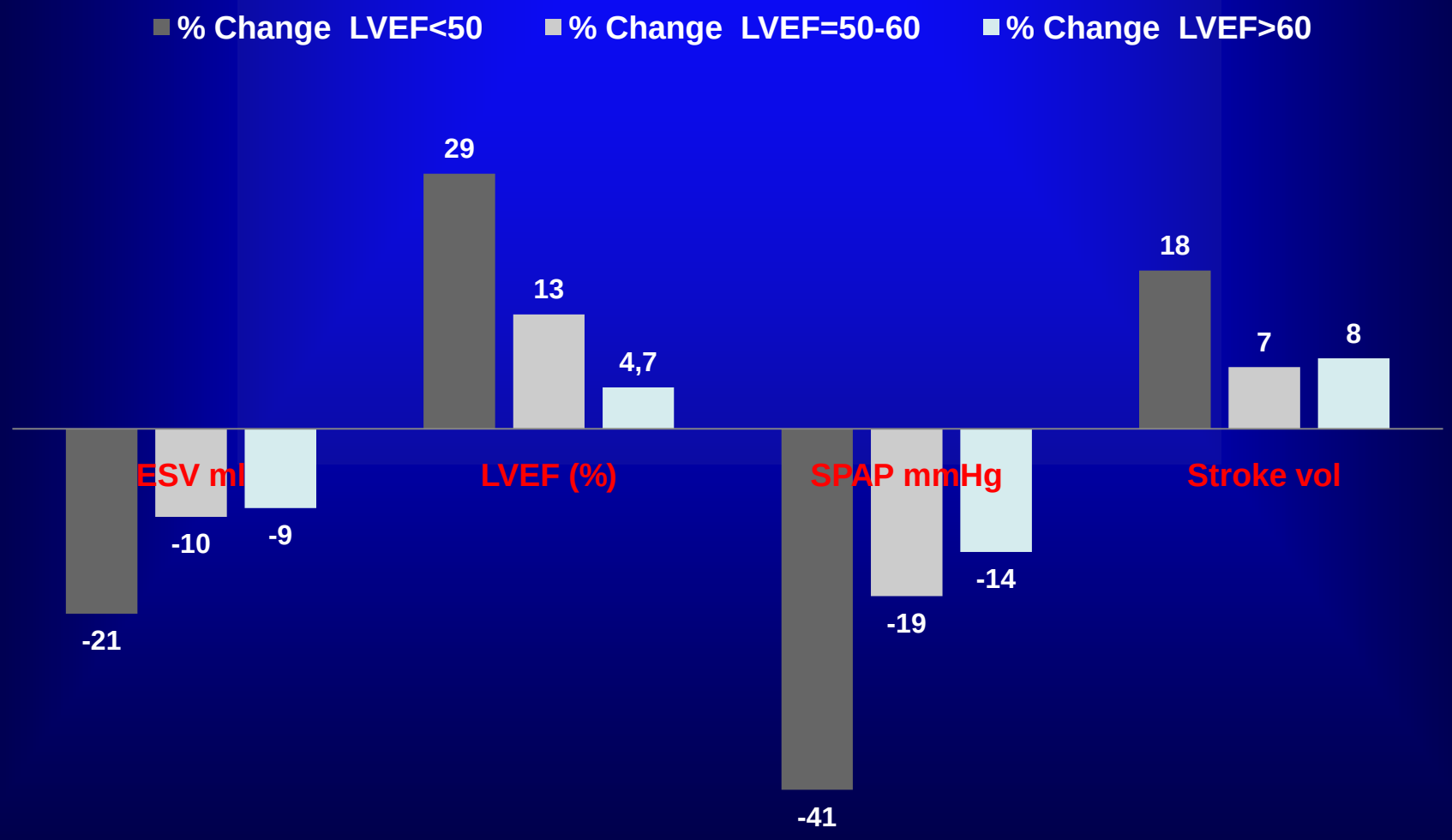
* P<0.001

HR-heart rate, RV –right ventricle, SPAP-systolic pulmonary artery pressure, ESV-end systolic volume.

Baseline hemodynamic profile of TAVI patients with normal (EF≥60%, n=56), near normal (EF=50-60%, n=66), and abnormal (EF<50%, n=44) LV systolic function



Hemodynamic effect of TAVI in subgroups of abnormal, near normal and normal LV systolic function



ReLeaf's Therapy – Highlights

Safe

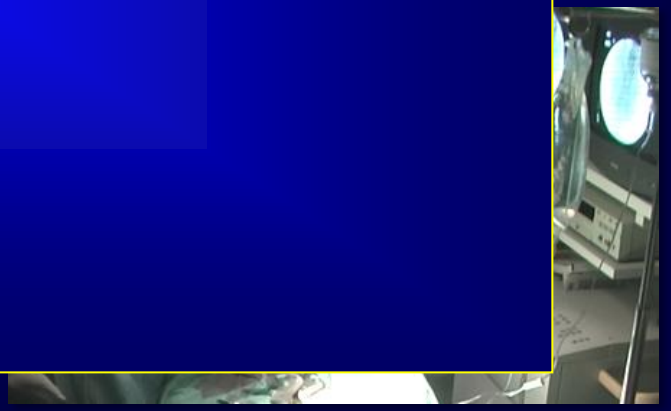
- No implant
- Safe femoral access (low profile catheter)
- Preserves native valve tissue
- Short hospital stay

Simple

- 45 min. intuitive procedure
- Of the shelf complementary devices, standard imaging

Cost - effective

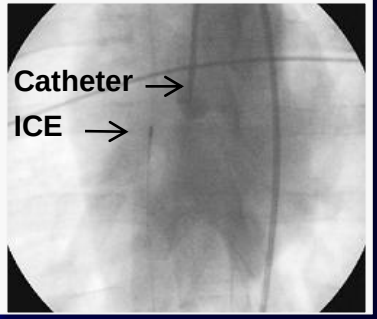
- Significant relief in symptoms
- 2-3 years effect
- Low Cost



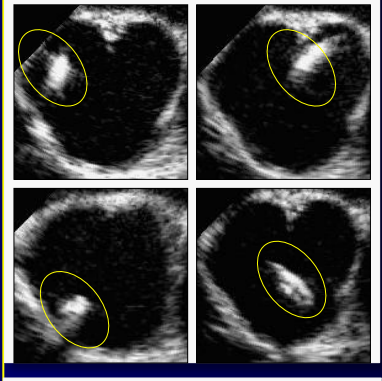
In-Vivo Study

- **Animal model**
  - Porcine native aortic valve
- **Procedures**
  - Open heart surgery (n=2), Catheterization (n=4)
  - Navigation, energy delivery, emboli capture
  - 1-2 month FU (echo), histology
- **Results**
  - Short and simple minimally invasive procedure
  - Easy navigation & energy delivery to the AV
  - No aortic regurgitation, no tissue scarring
  - Further testing with improved emboli release method needed

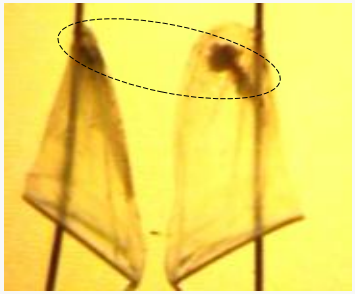
Fluoroscopy



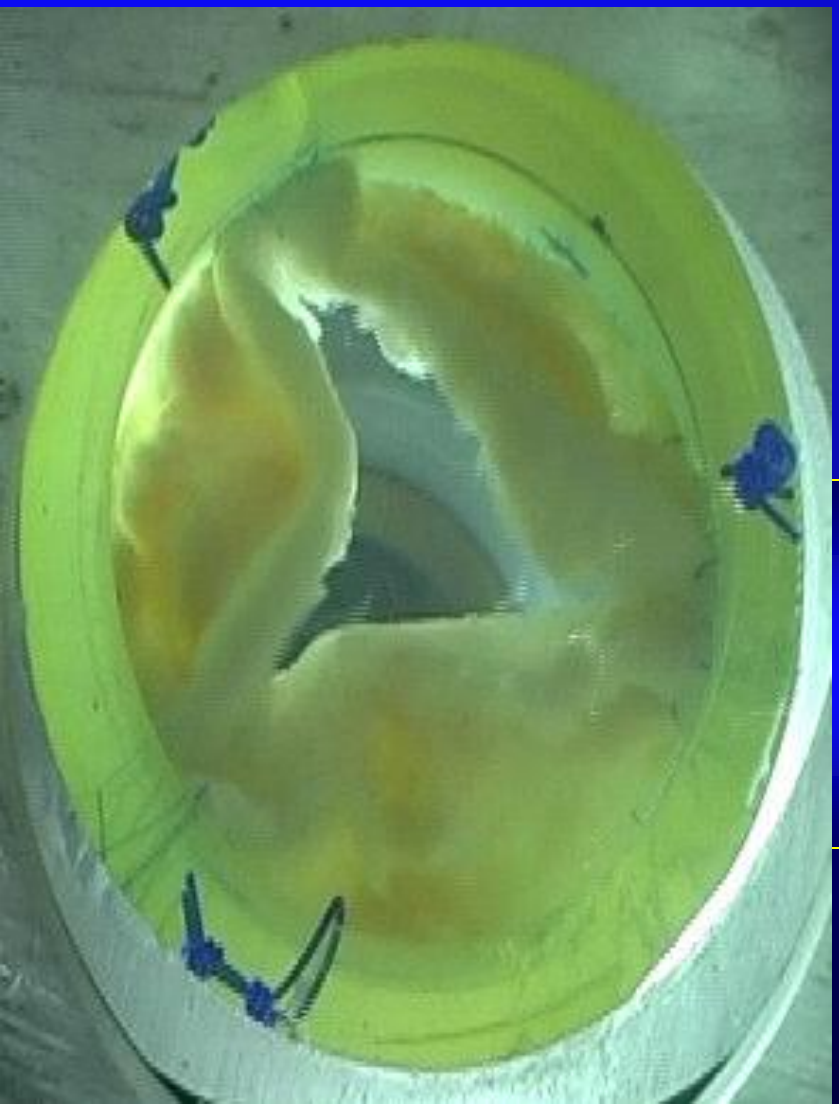
Intracardiac Echo

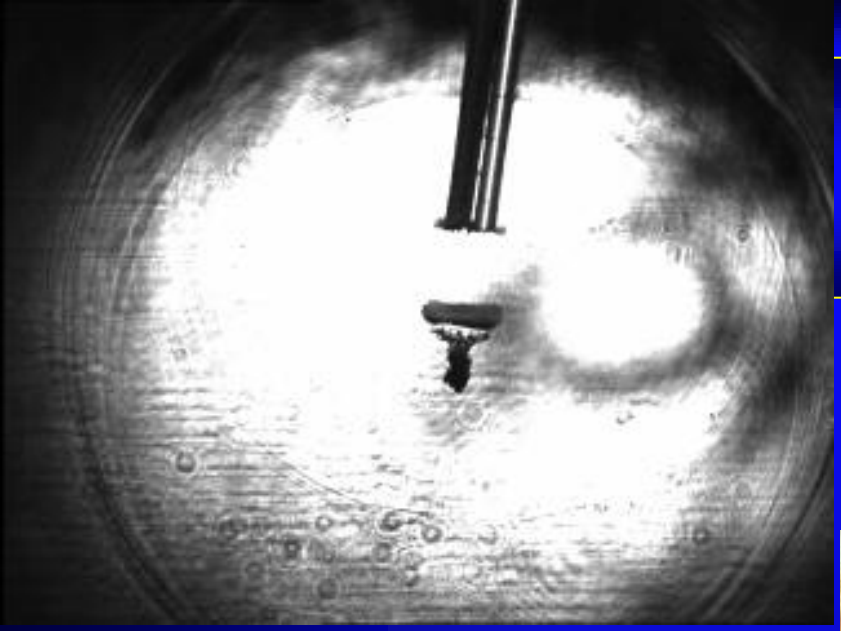


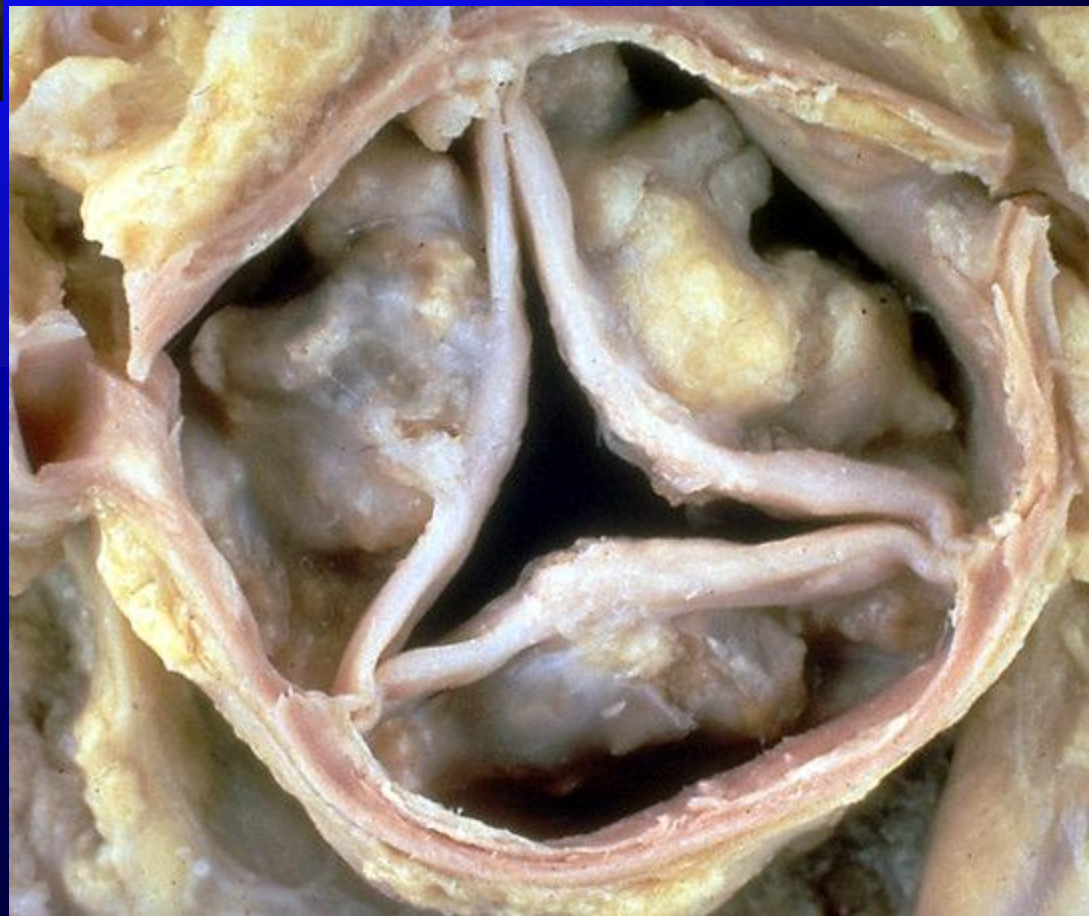
Filters after trial



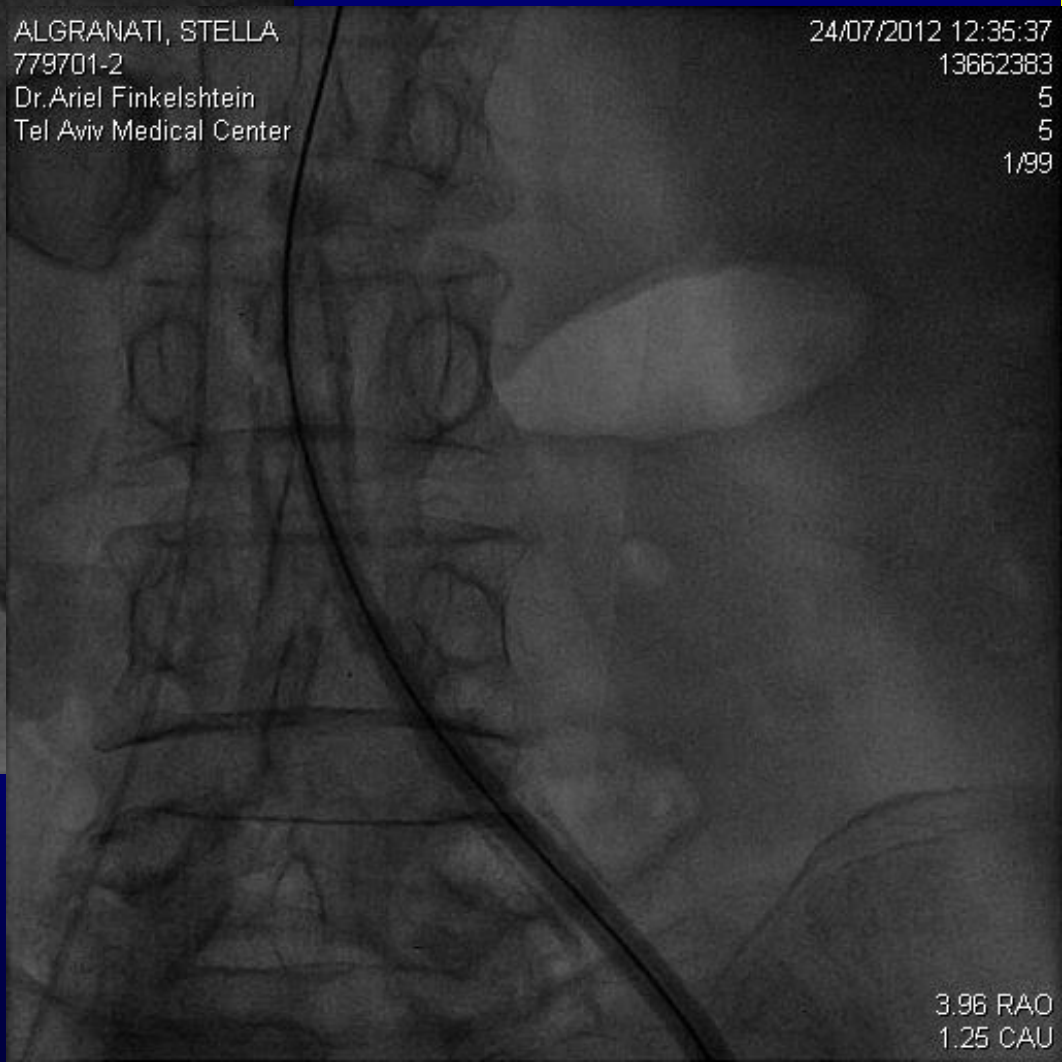
Releaf Medical- decalcification technology







You start with that…



Vascular complications in TAVI

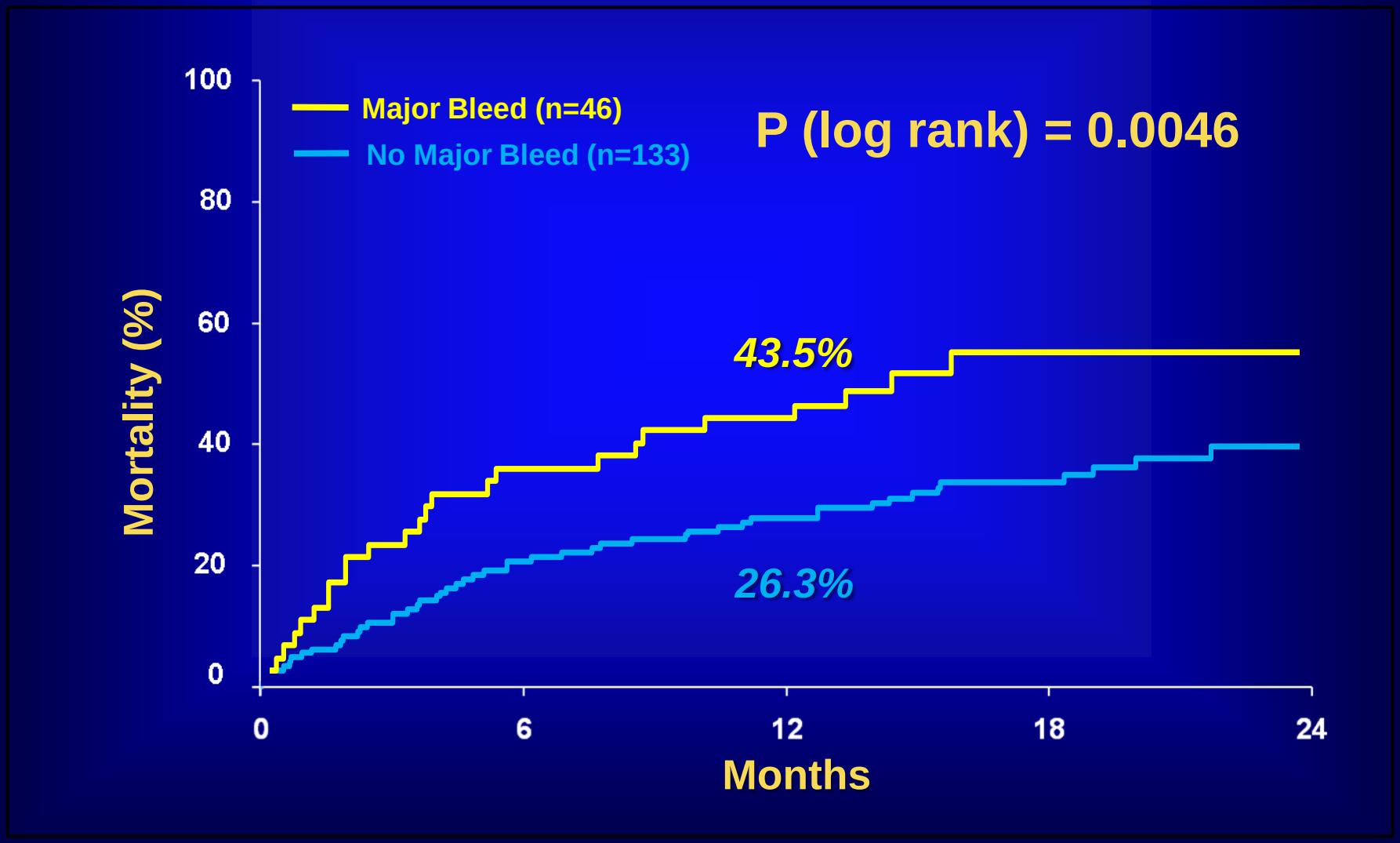
- **Partner 2 trial:**
  - **TAVI v's AVR high-risk patients candidates for surgery**
  - **348 patients in TAVI group**
  - **22 or 24 Fr sheath**
  - **In one year**
    - **Overall 18%**
    - **Major 11%**

Table 2. Clinical Outcomes at 30 Days and 1 Year in the Intention-to-Treat Population.*

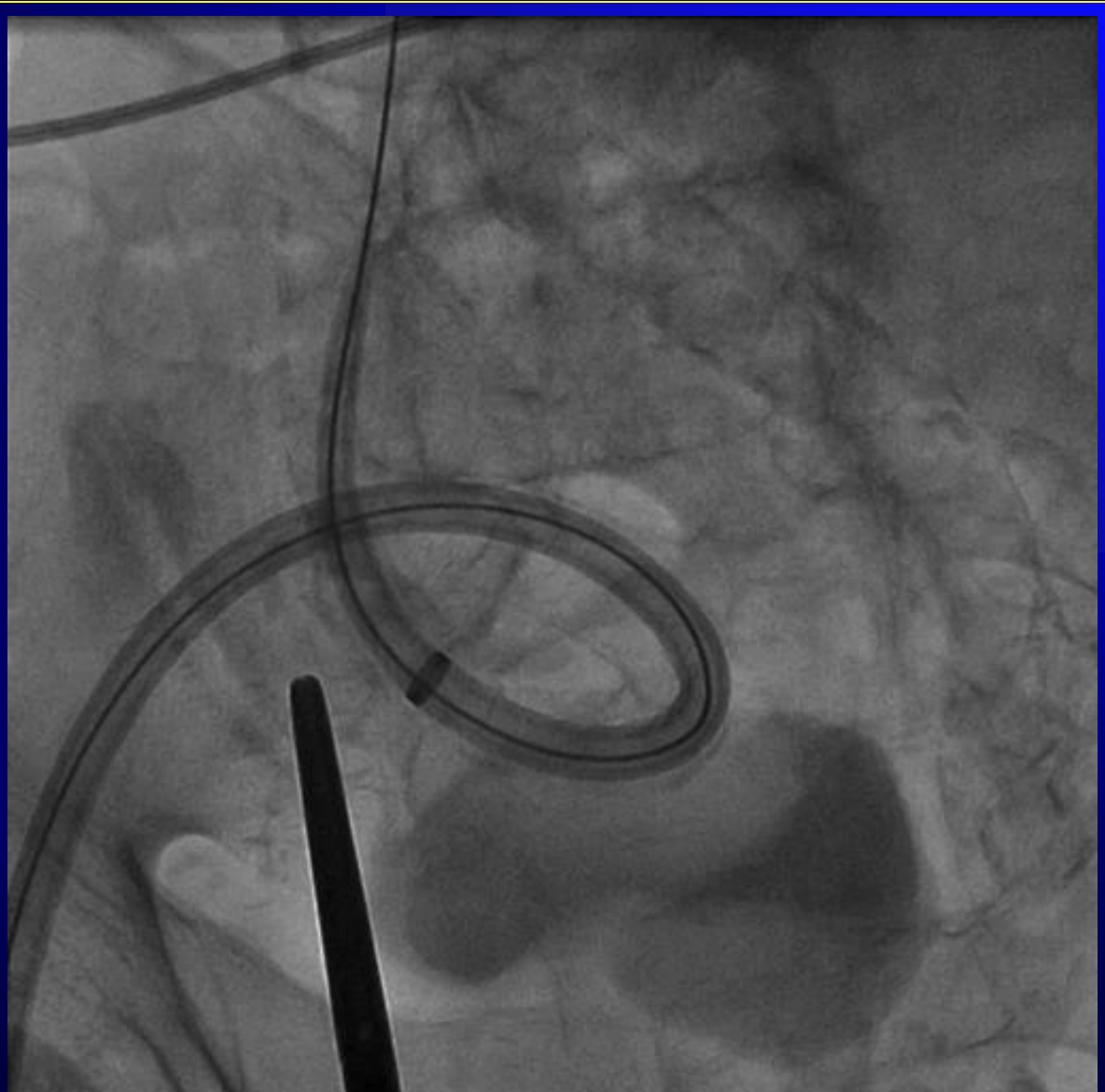
Outcome	30 Days			1 Year		
	Transcatheter Replacement (N=348)	Surgical Replacement (N=351)	P Value	Transcatheter Replacement (N=348)	Surgical Replacement (N=351)	P Value
Vascular complication						
Any	59 (17.0)	13 (3.8)	<0.001	62 (18.0)	16 (4.8)	<0.001
Major	38 (11.0)	11 (3.2)	<0.001	39 (11.3)	12 (3.5)	<0.001

Smith C et al. Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients. N Engl J Med 2011;364:2187-98.

Mortality vs. Major Bleeding
TAVI patients



Sometimes we just go one step further…



AR following TAVI

- Edwards Sapien prosthesis
  - 84 patients with serial echocardiography
  - 75% had AR following implant
  - Mostly paravalvular
  - At one year:
    - The mean AR grade increased (not significantly)
    - Not resulting in LV function impairment

Yared k et al. Impact of Aortic Regurgitation After Transcatheter Aortic Valve Implantation: Results From the REVIVAL Trial . *J Am Coll Cardiol Img*. 2012;5(5):469-477

AR following TAVI

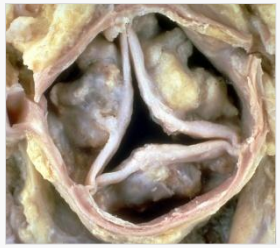
- AR index
  - 146 patients, 71 mild AR, 22 mod to sev AR
  - AR index independently predicted 1-year mortality hazard ratio: 2.9, 95% confidence interval: 1.3 to 6.4; p = 0.009.

Sinning et al. Aortic Regurgitation Index Defines Severity of Peri-Prosthetic Regurgitation and Predicts Outcome in Patients After Transcatheter Aortic Valve Implantation . *J Am Coll Cardiol Img*. 2012;59(13):1134-1141

Calcific Aortic Stenosis

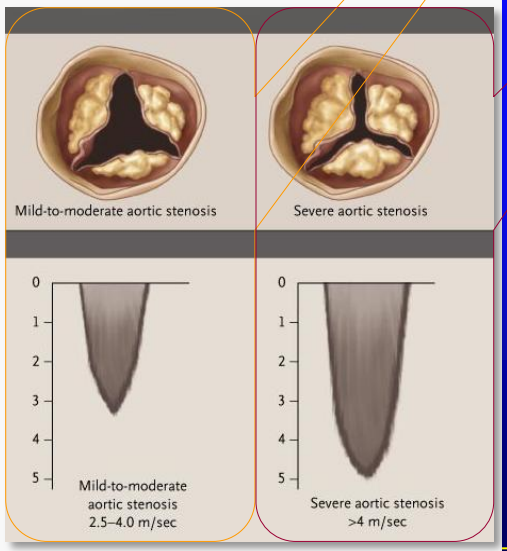
Normal

Stenotic

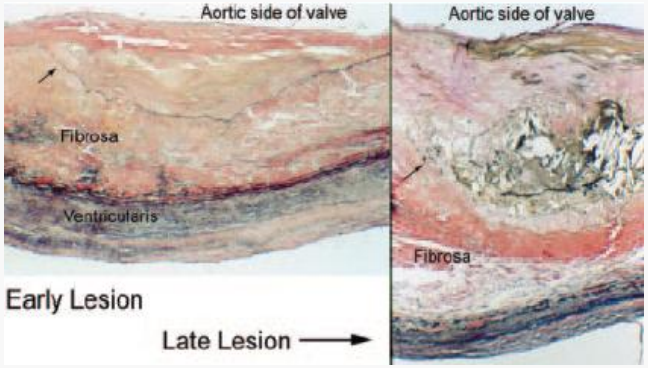


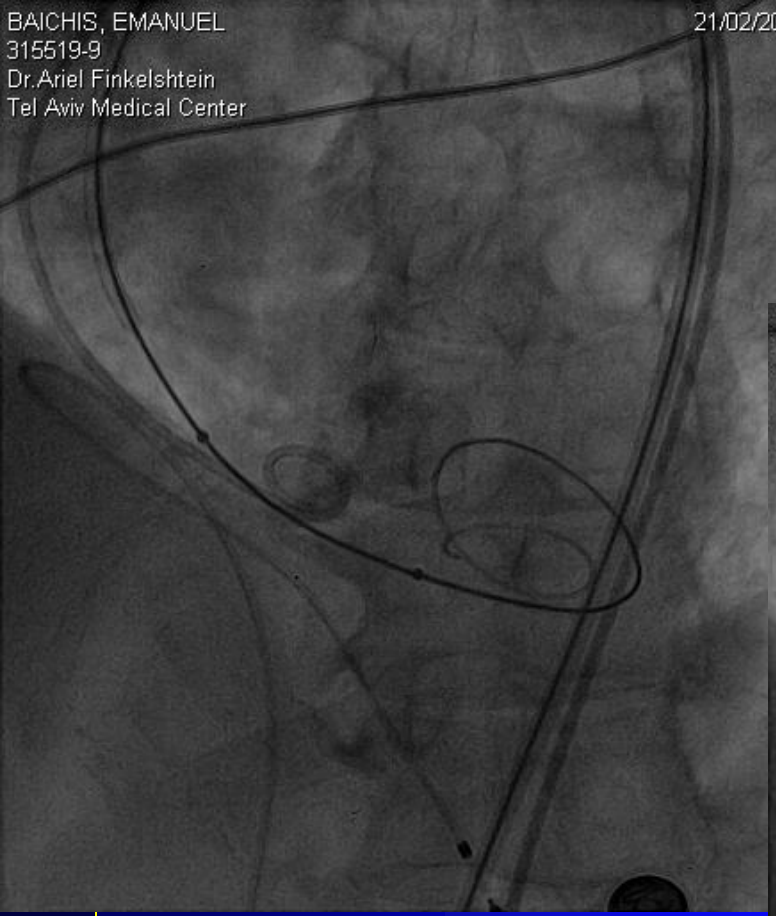
- **Patients with mild to moderate aortic stenosis**
  - **Mostly Asymptomatic**
  - **No therapy required**

Disease Progression

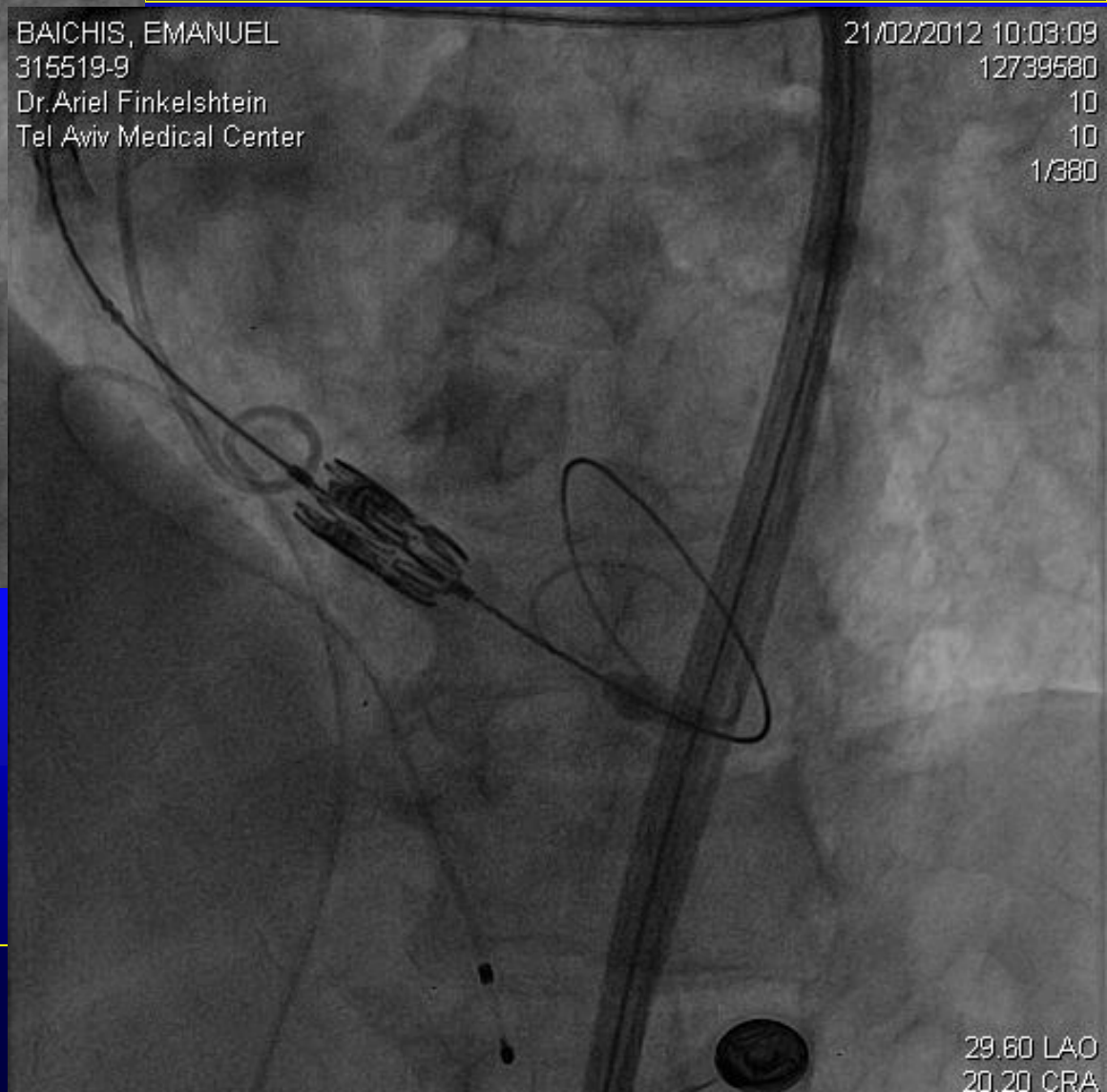


Calcium accumulation

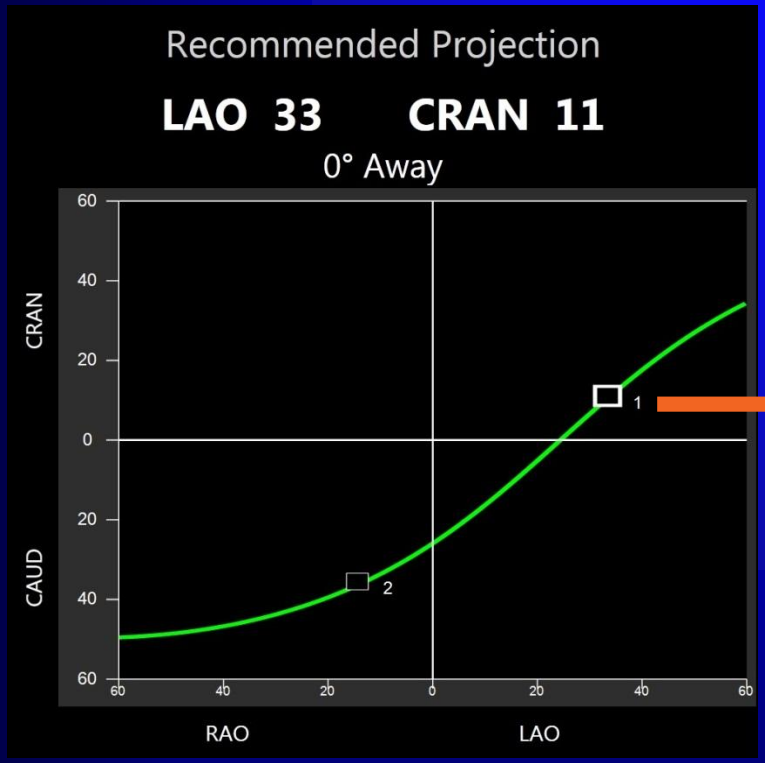


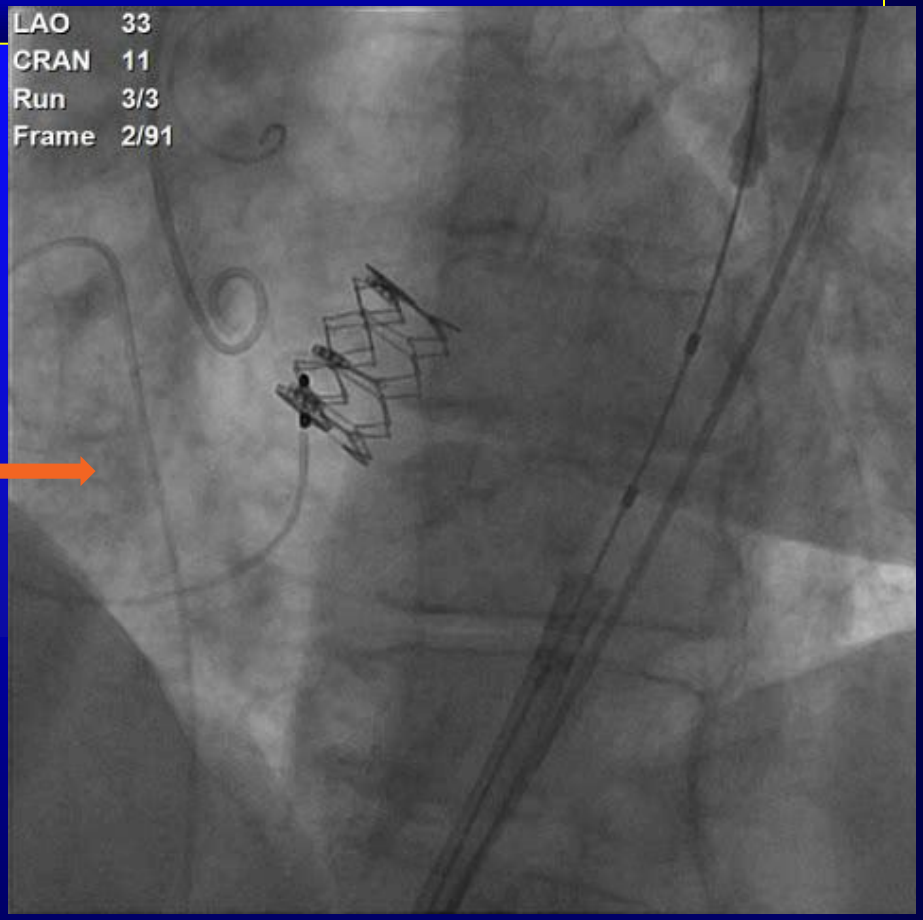


Sometimes you are not that lucky…



C-THV Optimal Projection





PARTNER US cohort B

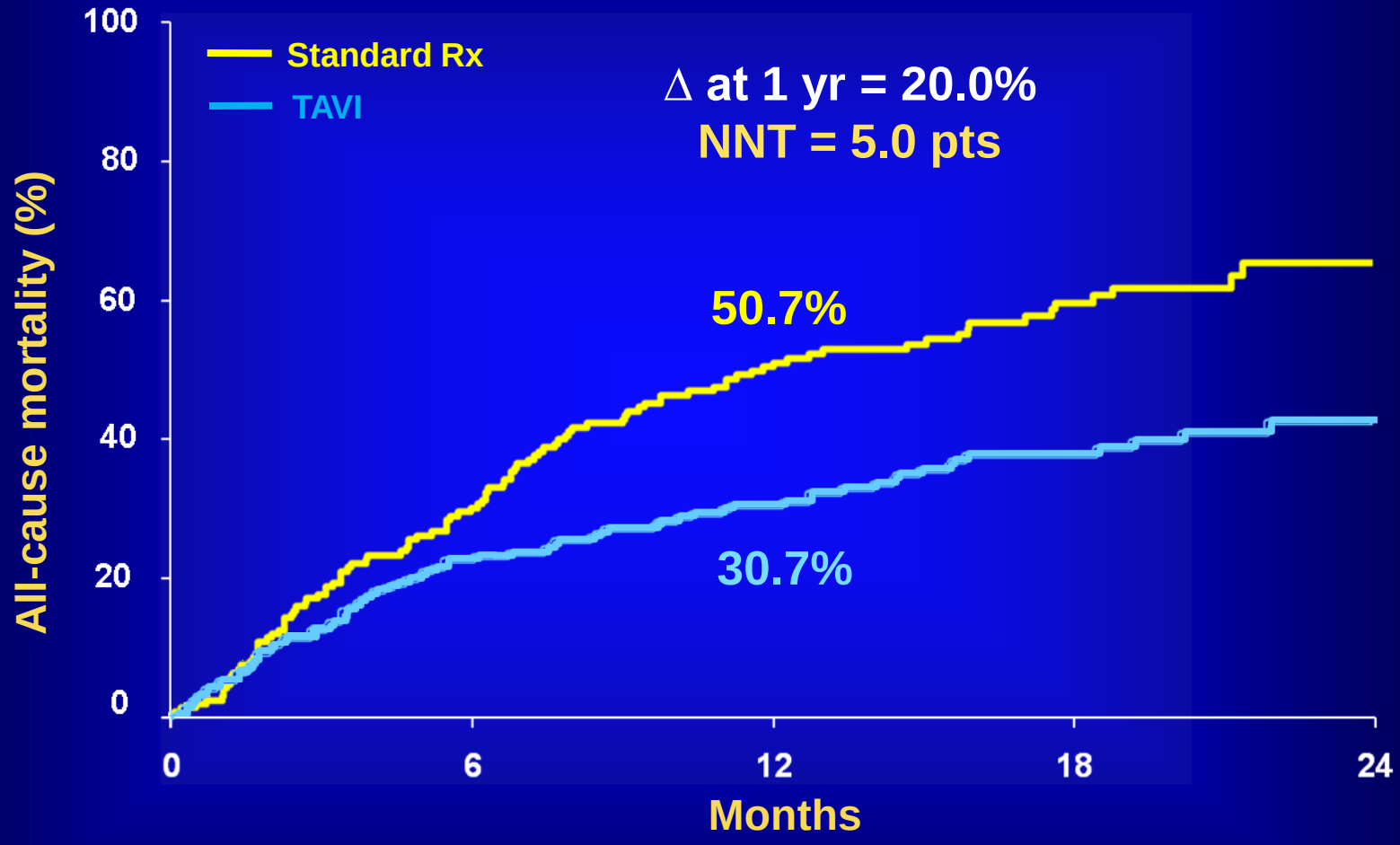
23mm and 26mm
valve sizes

22F and 24F
sheath sizes

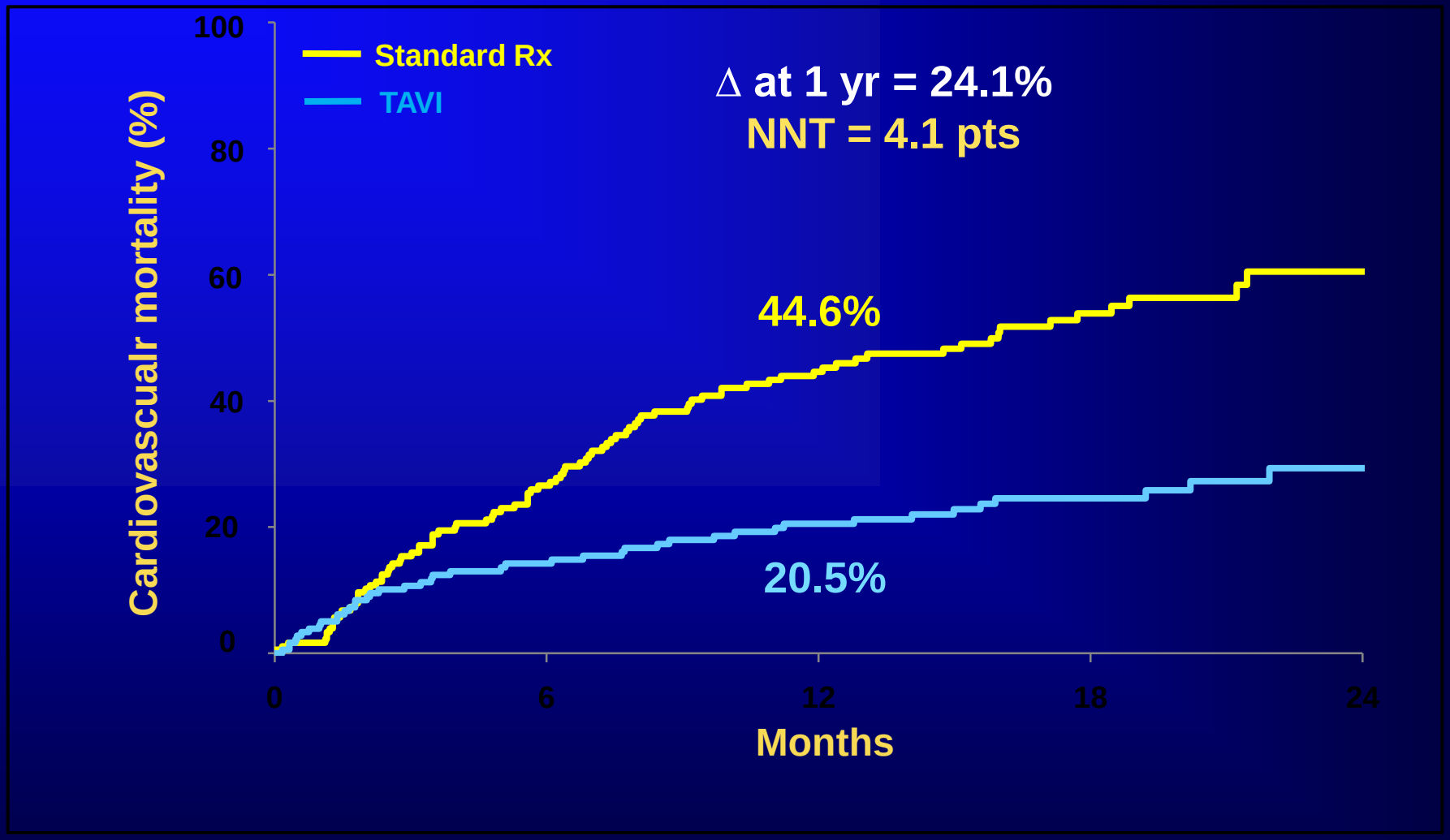
Patient Characteristics -

Characteristic	TAVI n=179	Standard Rx n=179	P value
Age - yr	83.1 ± 8.6	83.2 ± 8.3	0.95
Male sex (%)	45.8	46.9	0.92
STS Score	11.2 ± 5.8	12.1 ± 6.1	0.14
Logistic EuroSCORE	26.4 ± 17.2	30.4 ± 19.1	0.04
NYHA			
I or II (%)	7.8	6.1	0.68
III or IV (%)	92.2	93.9	0.68
CAD (%)	67.6	74.3	0.20
Prior MI (%)	18.6	26.4	0.10
Prior CABG (%)	37.4	45.6	0.17
Prior PCI (%)	30.5	24.8	0.31
Prior BAV (%)	16.2	24.4	0.09
CVD (%)	27.4	27.5	1.00

1ry Endpt - All Cause Mortality



Cardiovascular Mortality

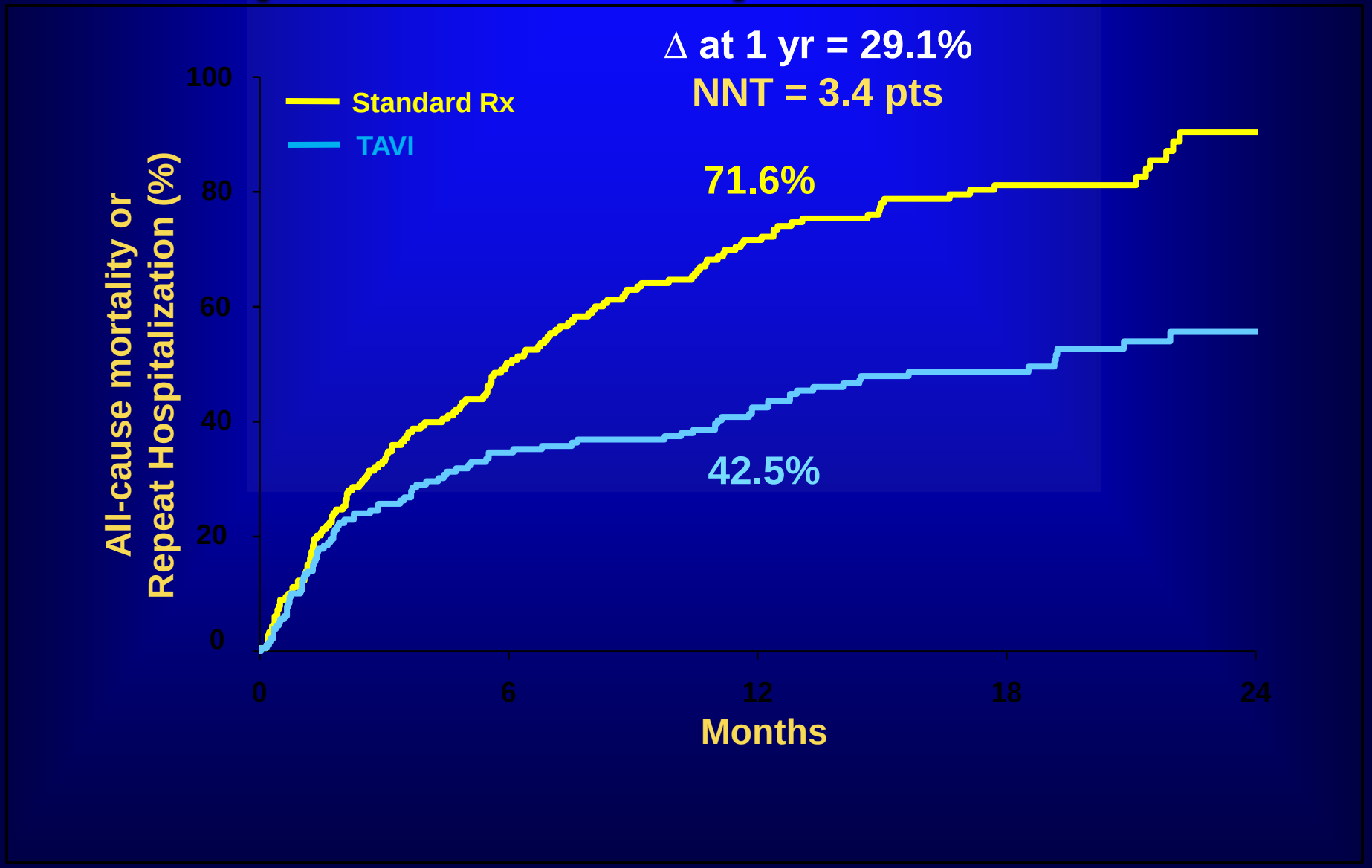


5 Medical Therapies Proven to Reduce Death

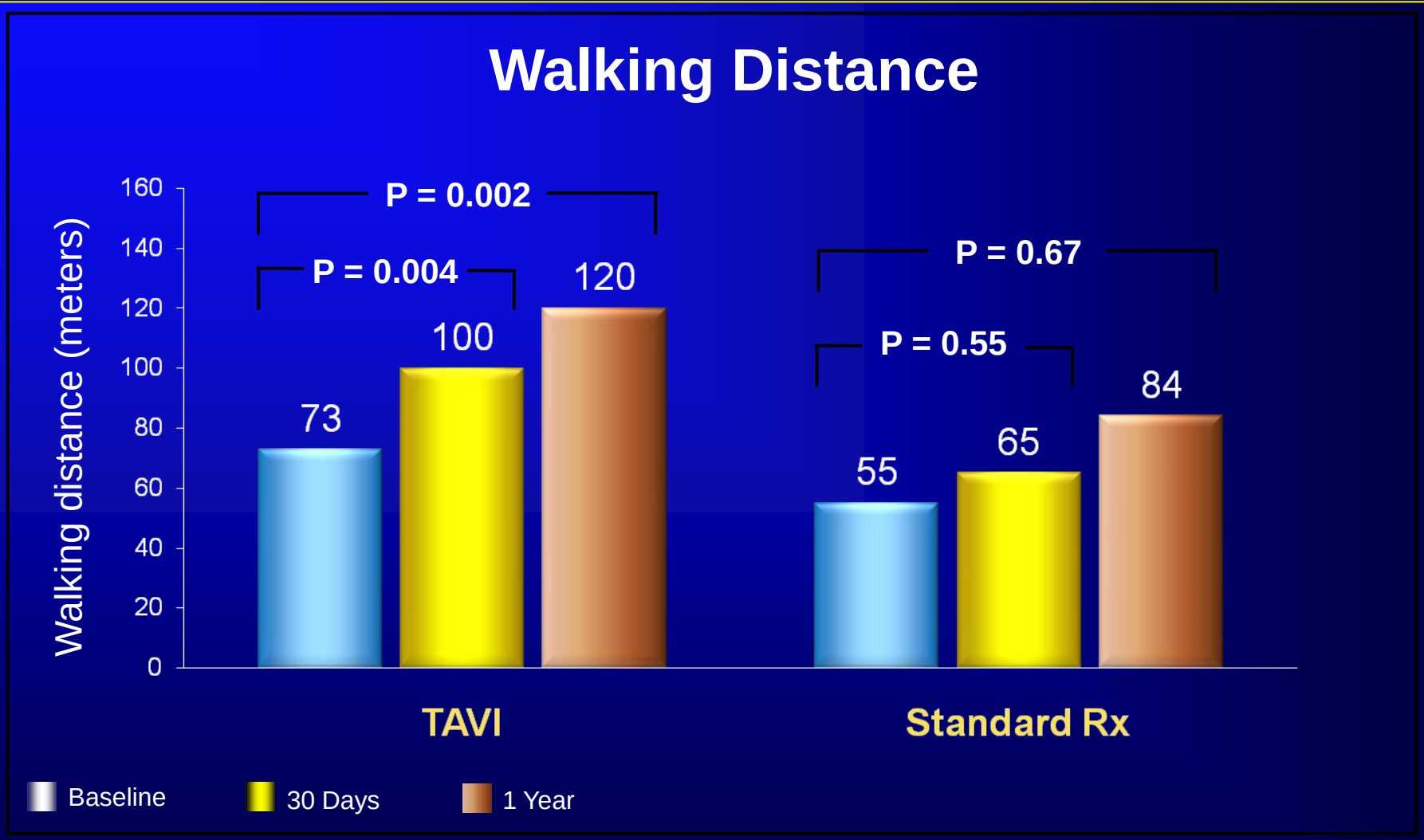
Therapy	Indication	# pts	Reduction in deaths	
			Relative	Absolute
Aspirin	MI	18,773	23%	2.4%
Fibrinolytics	MI	58,000	18%	1.8%
Beta blocker	MI	28,970	13%	1.3%
ACE inhibitor	MI	101,000	6.5%	0.6%
Aspirin	**2nd prev**	**54,360**	**15%**	**1.2%**
Beta blocker	**2nd prev**	**20,312**	**21%**	**2.1%**
Statins	**2nd prev**	**17,617**	**23%**	**2.7%**
ACE inhibitor	**2nd prev**	**9,297**	**17%**	**1.9%**

Adapted from Granger CB and McMurray JJV *JACC* 2006; 48:434

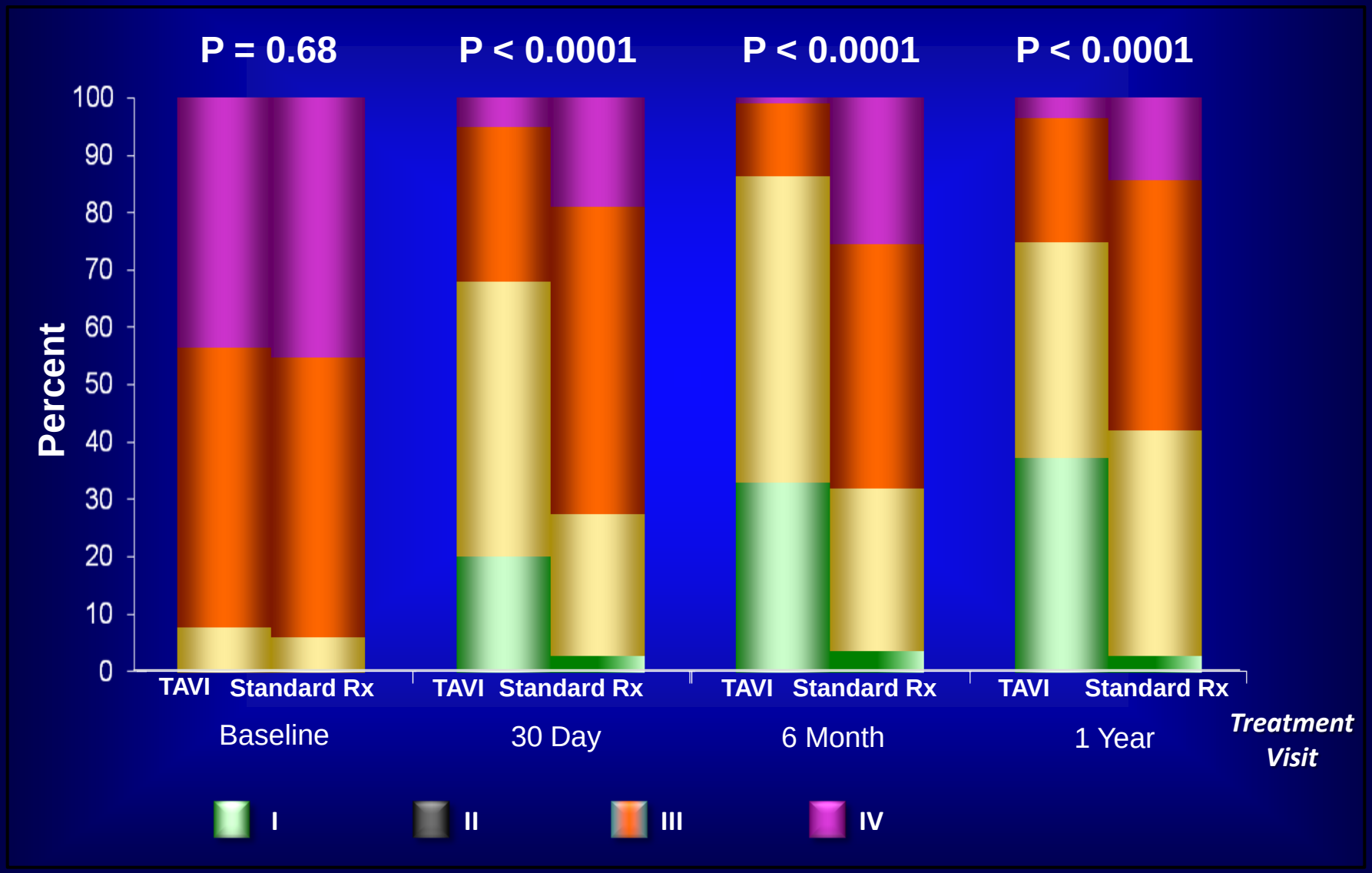
Repeat Hospitalizaion



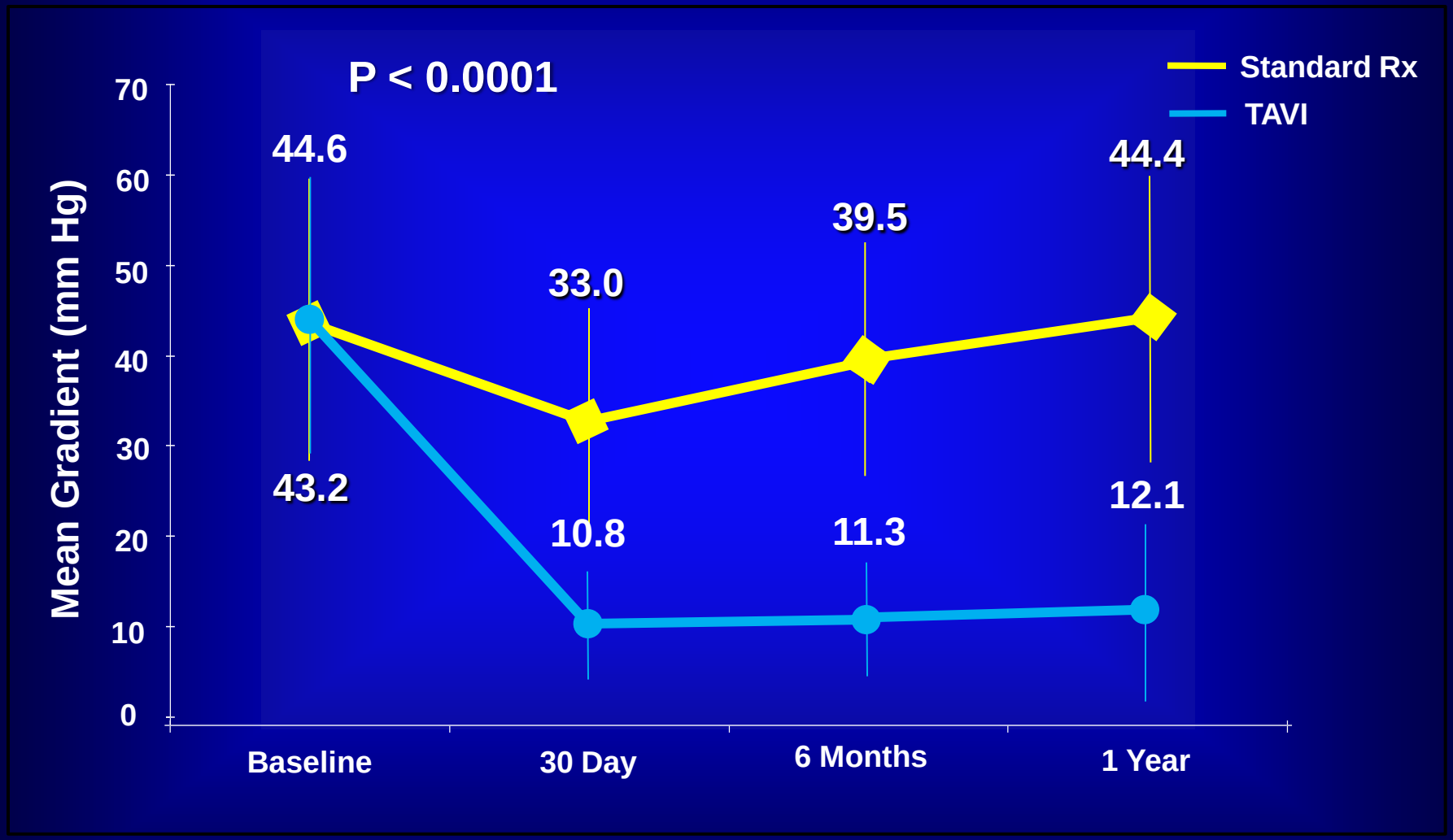
Six-Minute Walk Tests



NYHA Class Over Time

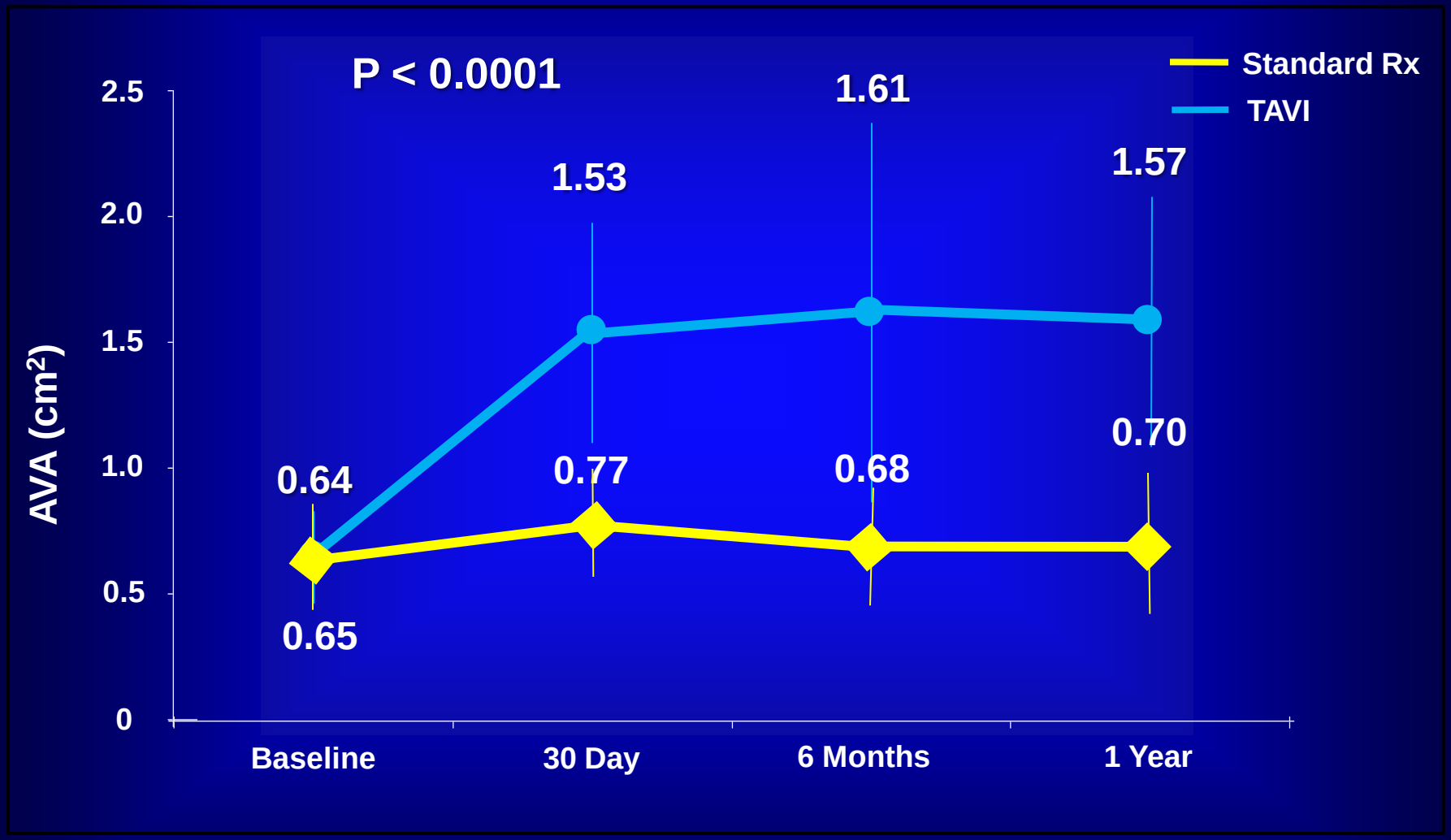


Mean Gradients Over Time



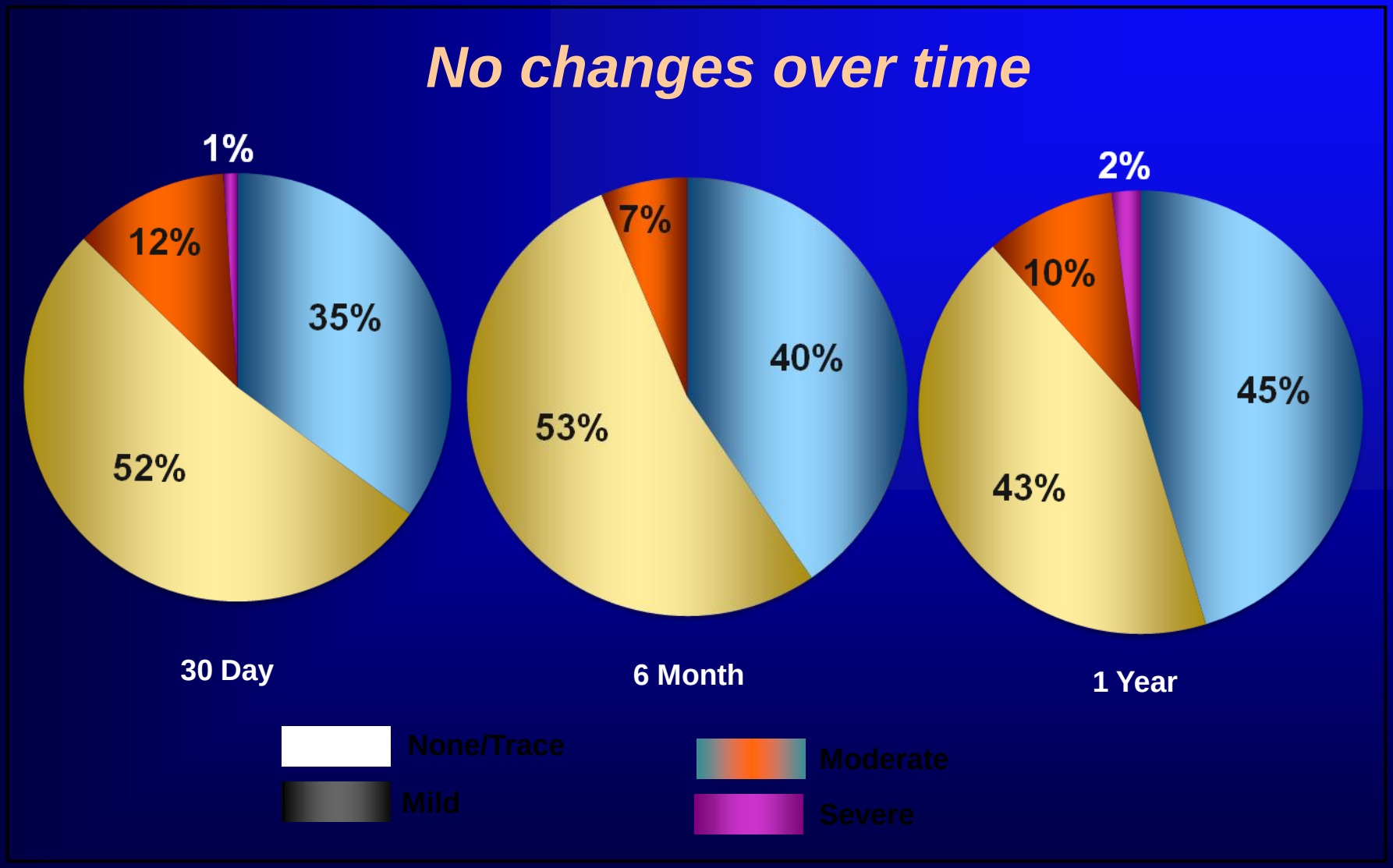
Error bars = ± 1 Std Dev

Aortic Valve Areas Over Time



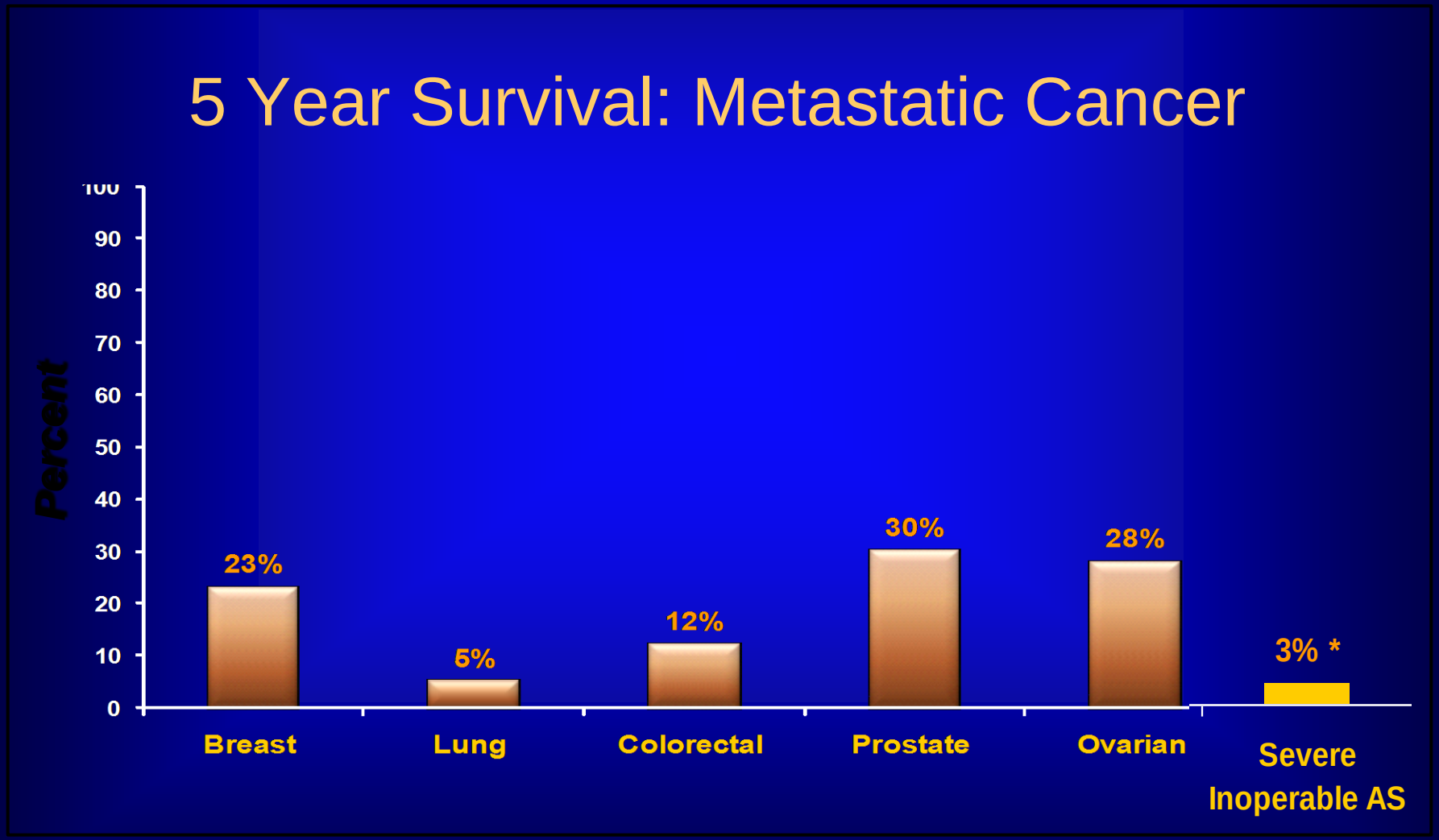
Error bars = ± 1 Std Dev

Paravalvular Regurgitation: TAVI



Mortality in Standard Rx

Perspectives



Courtesy of Murat Tuzcu, Interventional PI, CCF

**** Constant Hazard Model***

PARTNER US cohort A

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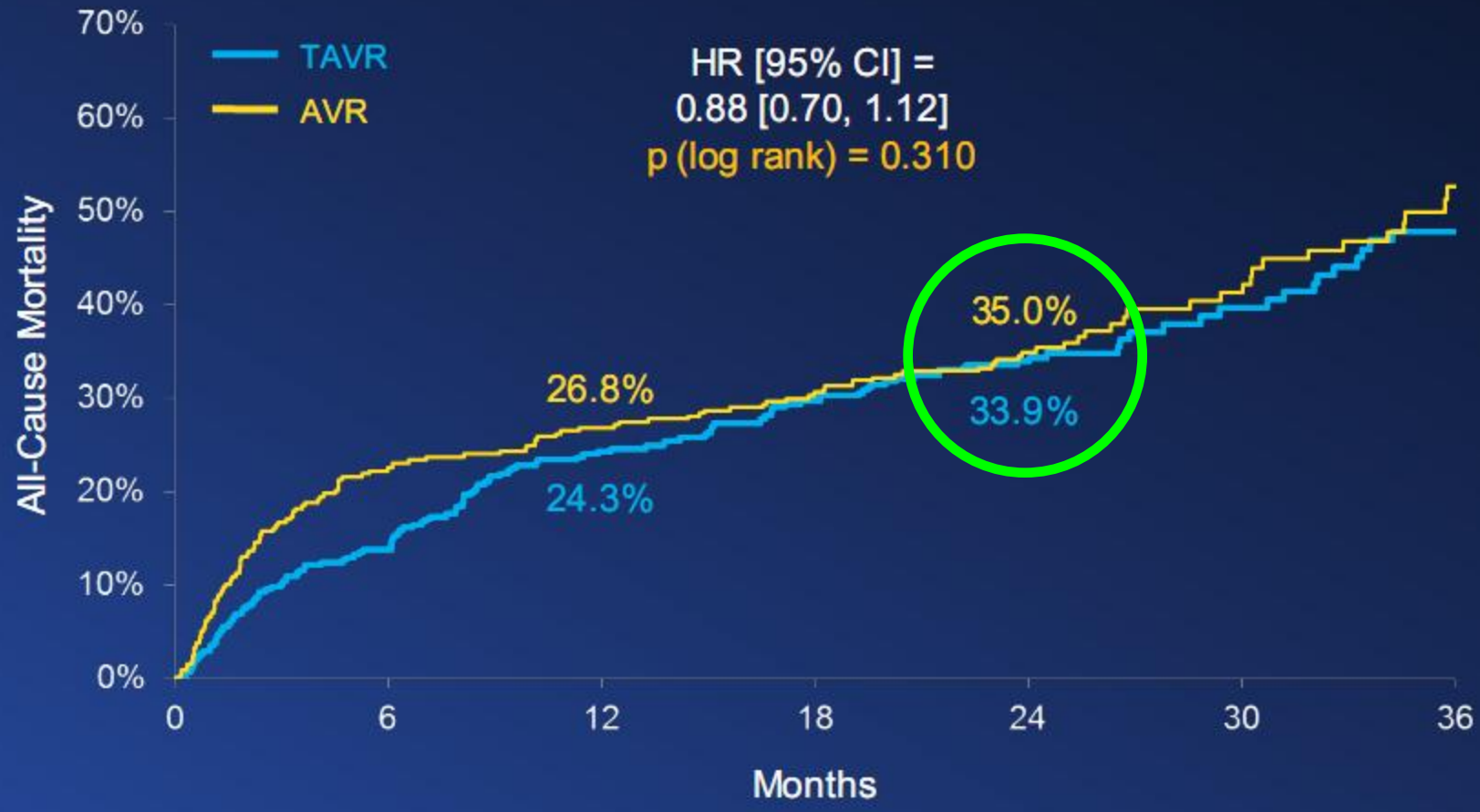
Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

All-Cause Mortality (ITT)

ACC 2012 | Chicago | March 26, 2012

THE PARTNER TRIAL



Numbers at Risk

TAVR	348	298	280	234	172	70	31
AVR	351	252	236	217	165	65	32

CoreValve Italian registry 30-d outcomes

Table 4 **Overall outcomes of patient population according to VARC definition**

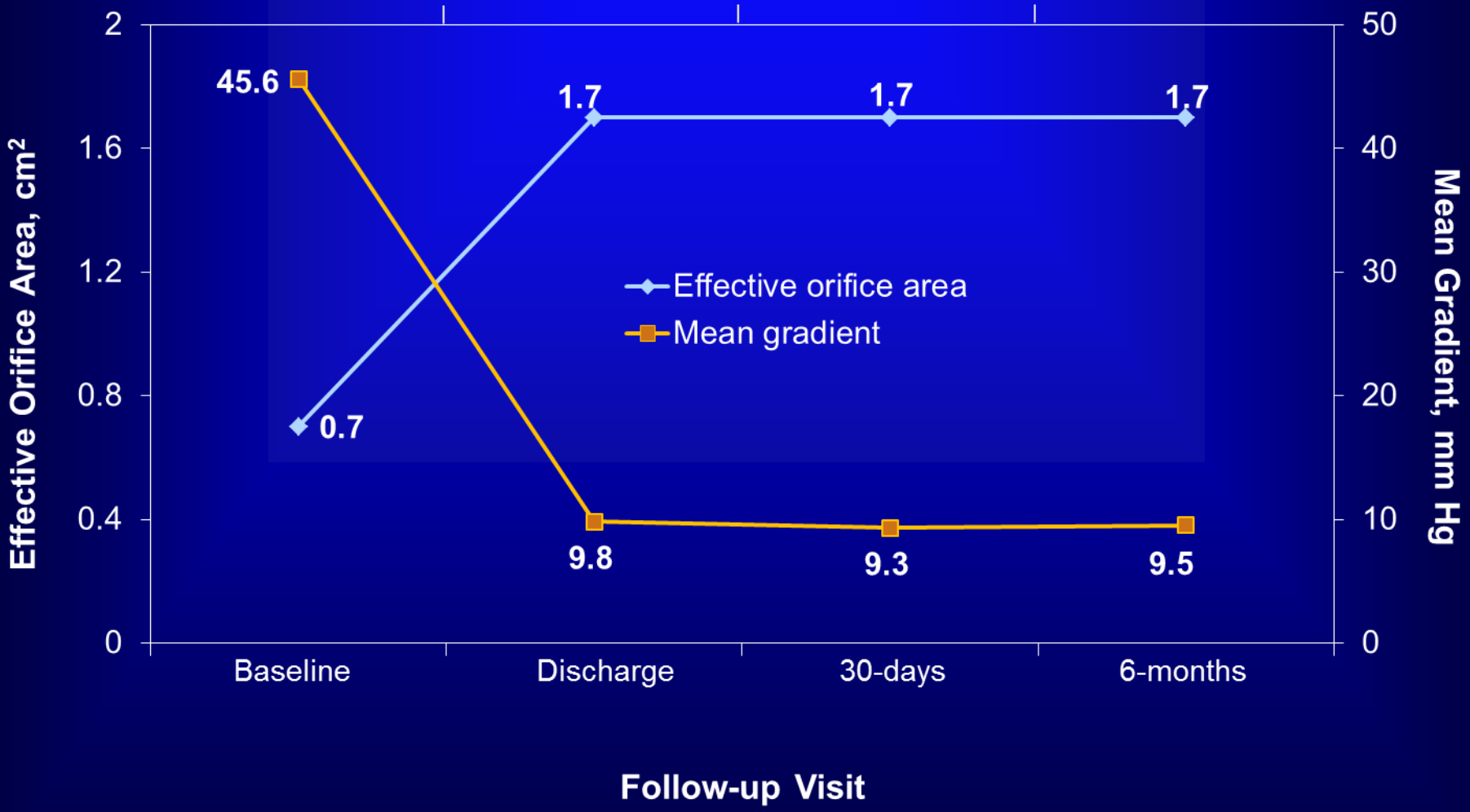
30-day outcomes	
All cause death, *n* (%)	20 (11.2)
Cardiovascular death, *n* (%)	12 (6.7)
Procedural MI, *n* (%)	8 (4.5)
Spontaneous MI, *n* (%)	1 (0.6)
Major stroke, *n* (%)	5 (2.8)
Life-threatening bleeding, *n* (%)	15 (8.4)
Major bleeding, *n* (%)	19 (10.7)
AKI stage 1, *n* (%)	10 (5.6)
AKI stage 2, *n* (%)	11 (6.2)
AKI stage 3, *n* (%)	12 (6.7)
AKI requiring renal replacement therapy, *n* (%)	4 (2.2)
PM implantation, *n* (%)	22 (12.1)
Combined safety endpoint, *n* (%)	46 (25.8)

Procedural Results

Procedural Parameters N=996	%
Successful vascular access, delivery & deployment of device & successful retrieval of the delivery system	97.8
Correct position of the device in the proper anatomical location	98.7
Mean aortic valve gradient < 20 mmHg	96.2
No severe AR requiring intervention	97.9
Only one valve implanted in the proper anatomical location	96.0

Major Complications; Valve Related N=996	%
Annulus Rupture	0.0
Valve Embolization	0.3
Conversion to open AVR	0.1
Coronary Compromised	0.1

Valve Performance



Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Company	Financial Relationship
Edwards Lifesciences	consultant and proctor
Medtronic	consultant and proctor


MEMBER