Intrepid Transcatheter Mitral Valve

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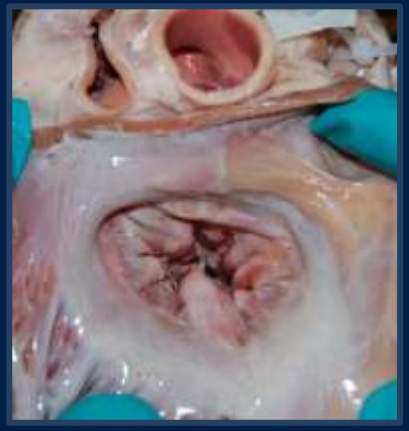
Medtronic, CoreValve: C, SB, AB, OF
Direct Flow: C, SB, AB
Mitralign: AB, SB, E
Boston Scientific: C, SB, AB
Biosensors: E, SB, C, AB
Kona: AB, E
Abbott Vascular: AB
InSeal Medical: AB, E,
Valtech: E, SB,
Claret: SB
Keystone: AB
Shockwave: E, AB

Key

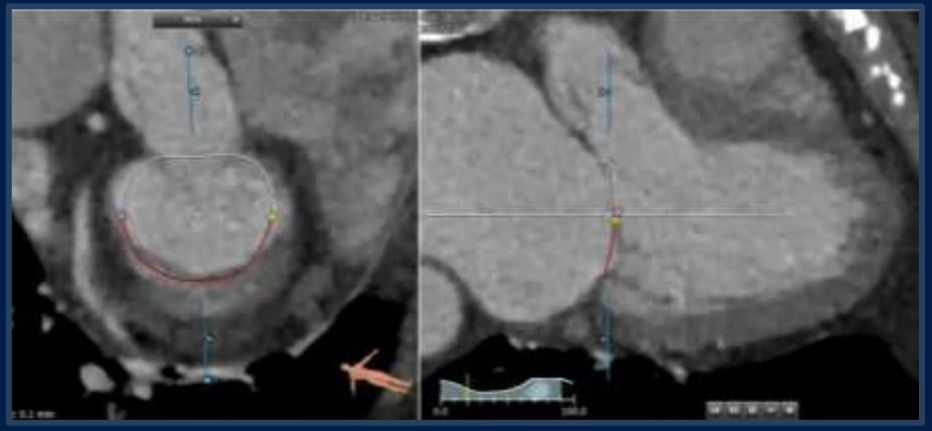
G – Grant and or Research Support E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria R – Royalty Income I – Intellectual Property Rights
SB – Speaker's Bureau O – Ownership OF – Other Financial Benefits'

Mitral Valve Anatomy

Anatomically & Physiologically Challenging



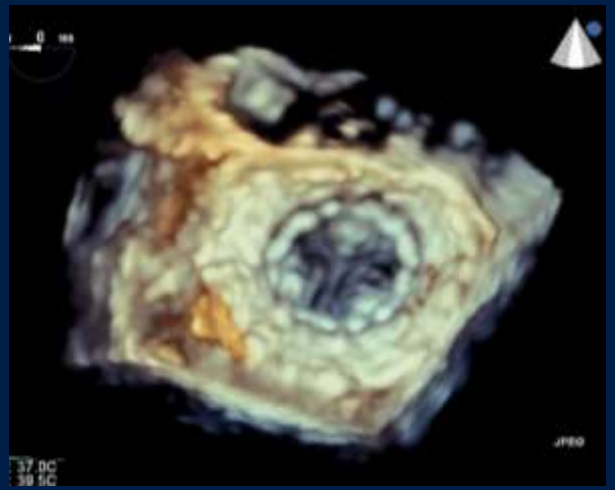
Native mitral annulus
is large &
asymmetric



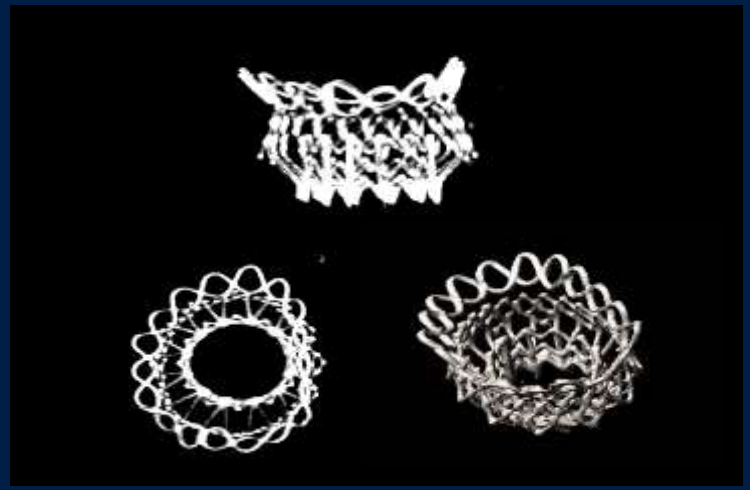
Highly mobile over cardiac
cycle
Very little to “hold on to”
LVOT is sensitive to obstruction

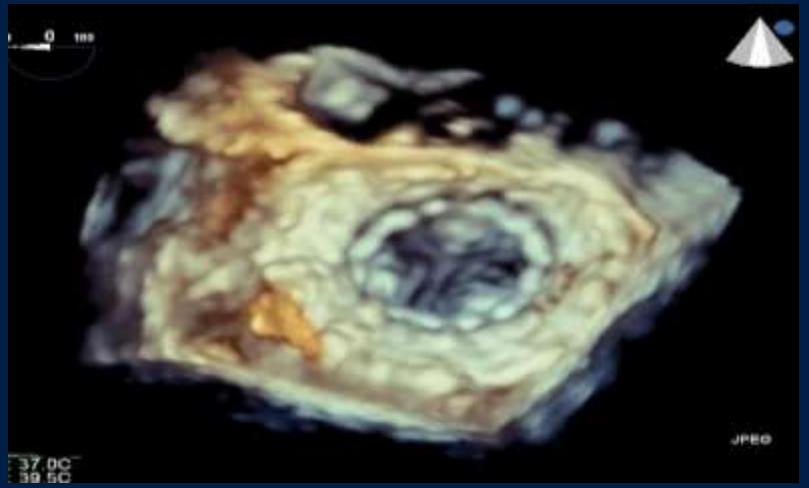
Dual Stent Design

- Conformable Outer Stent engages the annulu
  providing fixation & sealing while isolating the
  inner stent from the dynamic anatomy
- Circular Inner Stent houses a 27 mm tricuspic
  bovine pericardium valve
  - Flexible Brim aids imaging during delivery
  - One valve size significantly reduces development & manufacturing complexity
  - One implant platform regardless of delivery approach: trans-apical or trans-septal



Medtronic Intrepid^{tm} TMVR
Fixation and Sealing





- Cork effect produced by variable stiffness along the height of the Outer Stent
- Outer stent engaging with, and conforming dynamically to the annulus
- Circular inner stent isolated from the fixation and sealing
- Leveraging but not relying upon the native leaflets

Transapical Delivery System

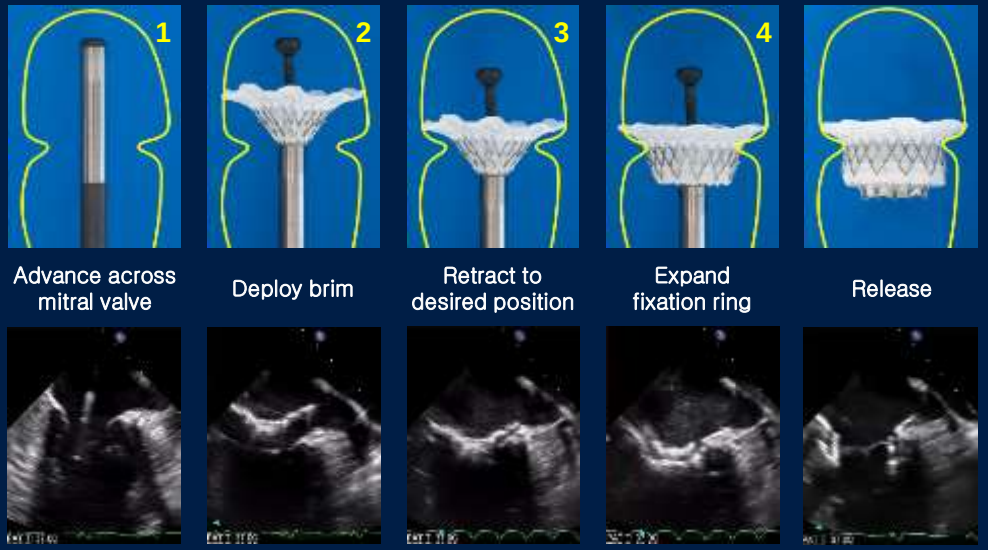
Controlled Deployment Of Self-expanding Implant

Hydraulic mechanism provides for controlled, precise deployment

No need for rotational alignment

No need to search for leaflets

Accommodates tilt & lateral misalignment

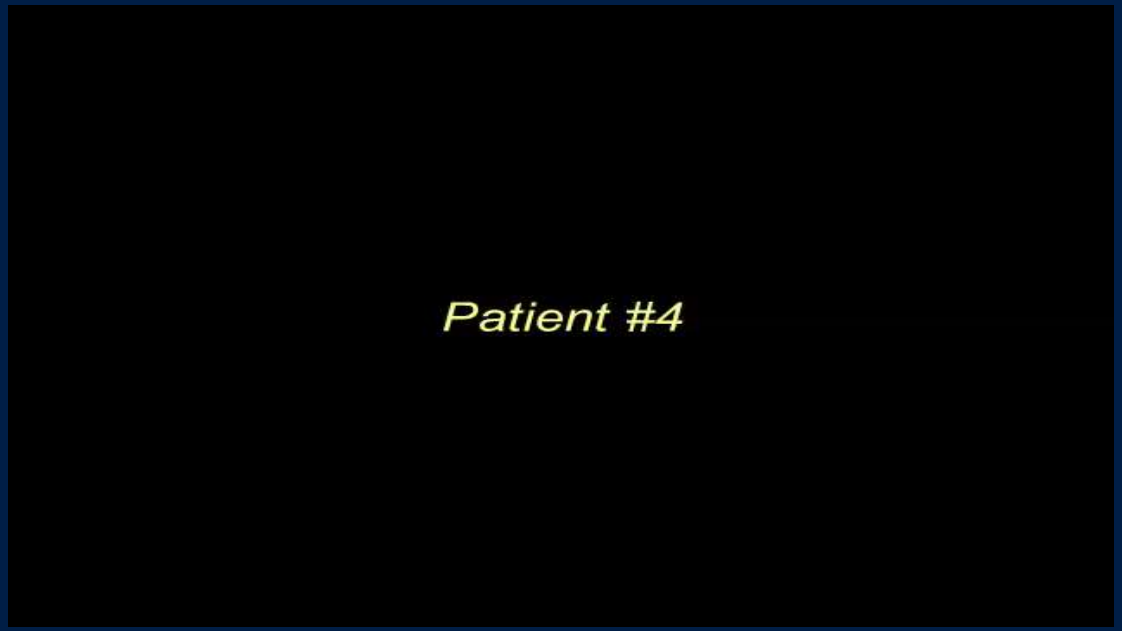


Medtronic Intrepid^{tm} TMVR

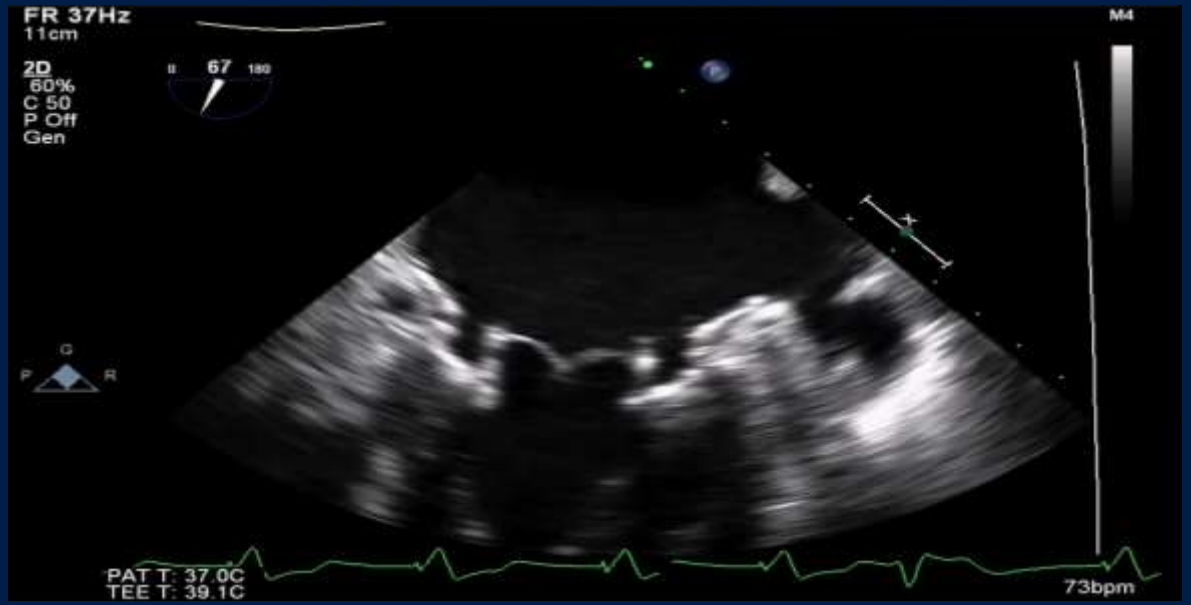
Case Presentation – Monash Heart Melbourne

- 88 y.o. Female, 154 cm, 60 kg
- MR Grade 4+ (DMR with P2 flail)
- NYHA Class II/III (2 recent CHF hospitalizations)
- LVEF: 55%
- Cardiac history
  - Aortic valve surgical replacement, 23 mm Mosaic (2001)
  - Minor coronary artery disease (2001)
  - Chronic AF on warfarin
  - Pacemaker (2003)
  - Mild Ao stenosis; moderate-severe tricuspid regurgitation
- Medical history
  - Mild-to-moderate renal impairment
  - Pulmonary hypertension (PAP = 67mmHg)
  - HTN; epilepsy; GERD all stable on Rx
  - STS = 10.6%; Euroscore II = 14.0%

Medtronic Intrepid^{tm} TMVR
Case Presentation – Monash Heart Melbourne

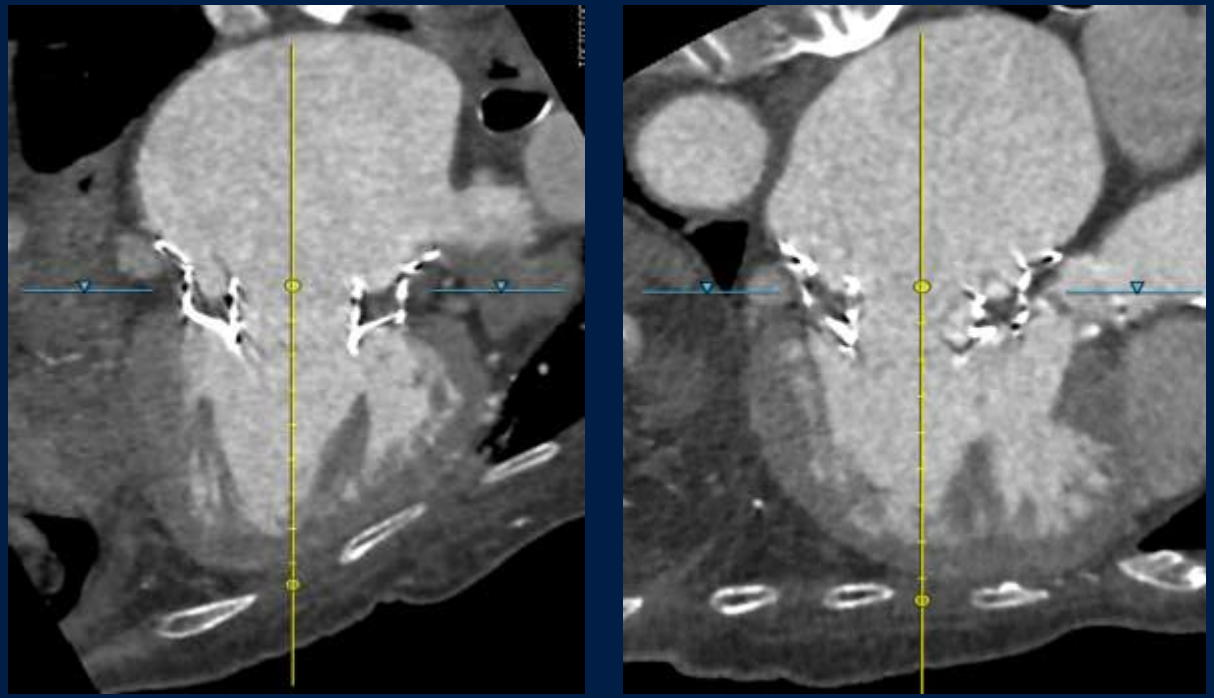


Medtronic Intrepid^{tm} TMVR
Results



Post Procedure: Good Valve Function – No PVL or TVL

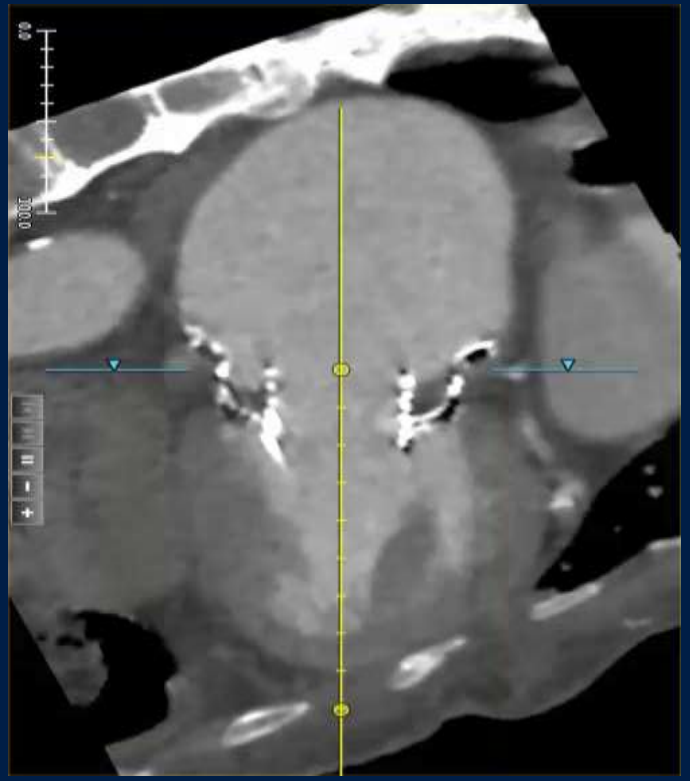
Medtronic Intrepid^{tm} TMVR
Results



12–Month Follow–up: Stable position & excellent ingrowth

Medtronic Intrepid^{tm} TMVR

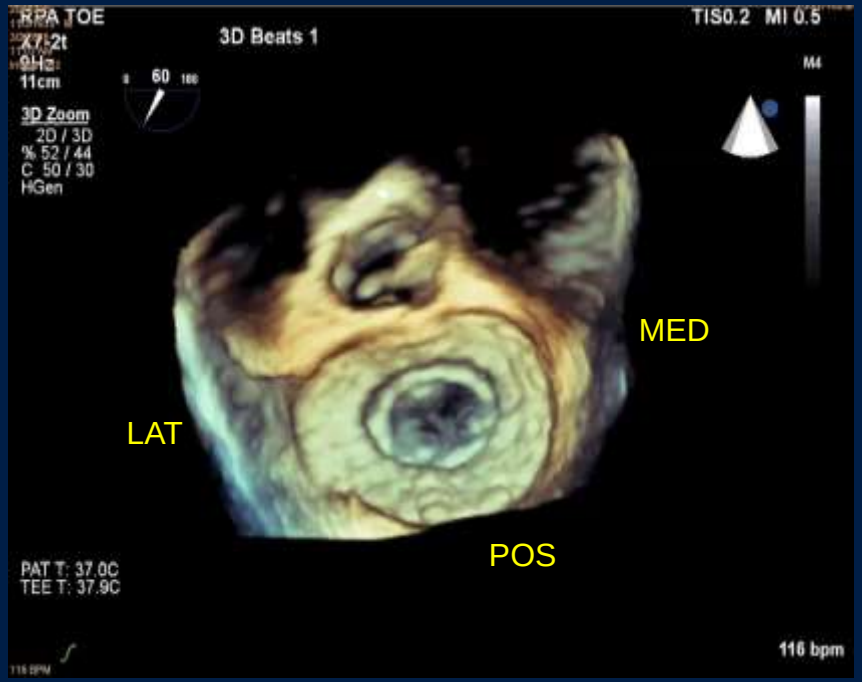
Results

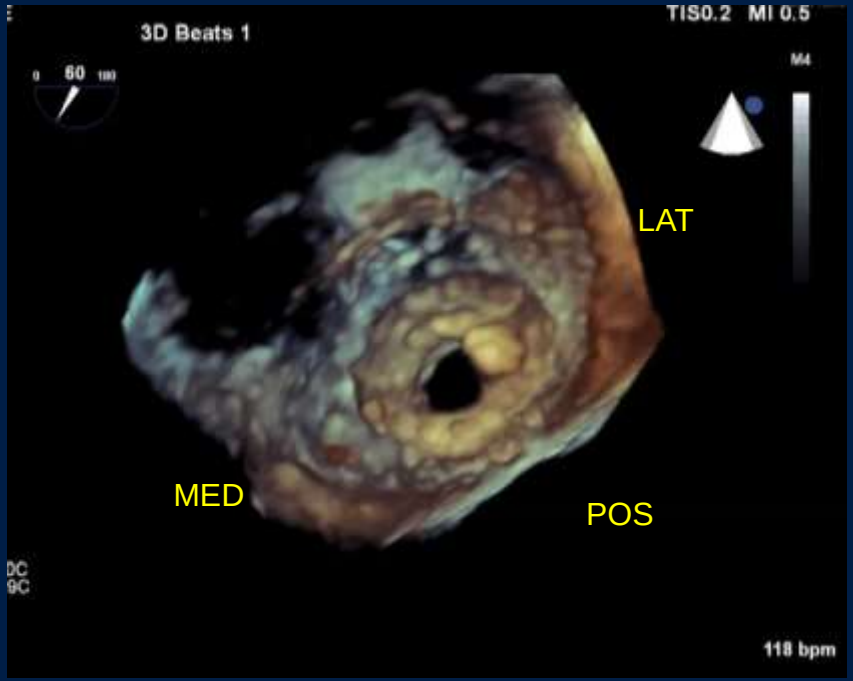


12-Month Follow-up: Stable position & excellent ingrowth

Clinical Experience

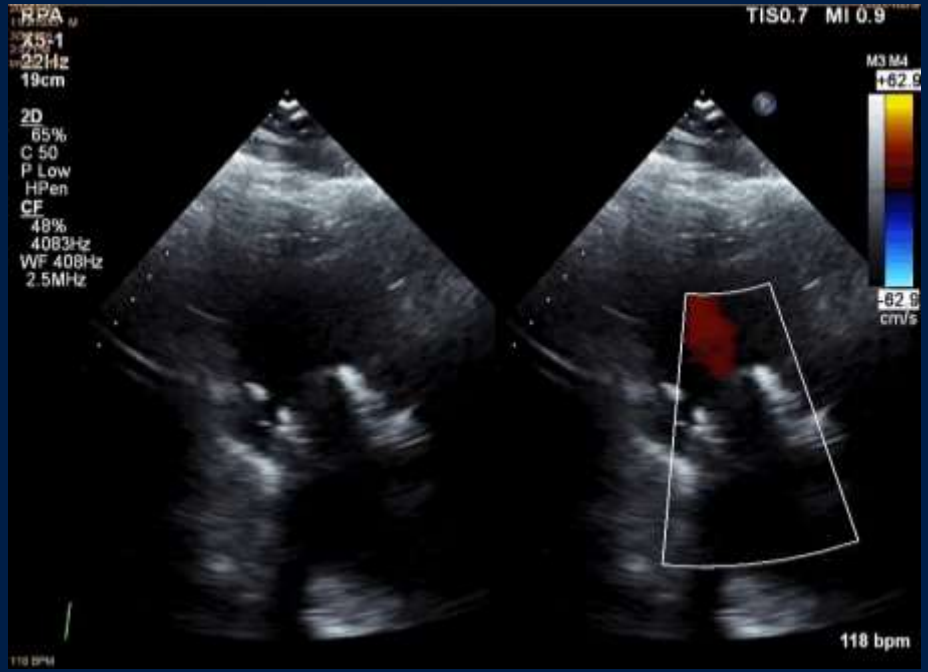
Results





Clinical Experience

Results



Clinical Experience

FIM & Pilot Studies

Design	Multi-Center, prospective, non-randomized, single-arm
Population	Patients with severe, symptomatic MR ineligible for standard surgery
Sites	John Paul II Hospital, Krakow, PL, Monash Heart, Melbourne, AU, St. Thomas' Hospital, London, UK, The Alfred Hospital, Melbourne, AU, Royal Prince Alfred Hospital, Sydney, AU
Objectives	Primary Objective: To evaluate the safety of the Intrepid TMVR • The nature, severity and frequency of any complications associated with the delivery and/or implantation of the device Secondary Objective: To evaluate the performance of the Intrepid TMVR • The degree of improvement of MR grade, symptoms and the durability of TMVR function • The ability to accurately deliver & place the implant within the native anatomy • The fit of the implant within the native anatomy, including fixation, sealing and compatibility with native structures (e.g., the LVOT/aortic valve)

Clinical Experience

Fim & Pilot Studies

Inclusion criteria	• Severe MR (MR Grade 3–4+) • Symptomatic MR (NYHA Class II–IV) • Trans-apical access deemed feasible by the treating physicians • Native mitral valve geometry / size compatible with the Twelve TMVR • No or minimal mitral valve calcification
Exclusion criteria	• LVEF < 20 • Pulmonary HTN (> 70 mmHg systolic) • Any interventional or surgical procedure performed within 30 days • Prior stroke within 4 weeks • Need for coronary revascularization • History of, or active, endocarditis • Renal insufficiency (Cr > 2.5 mg/dL) • Evidence of intracardiac mass, thrombus, or vegetation

Clinical Experience

March 28, 2016

Patient	1	2	3	4	5	6	7	8*	9	10	11	12	13
Age	64	63	81	88	83	75	77	85	61	74	73	80	63
Sex	M	M	M	F	M	F	F	M	F	M	M	M	F
BMI	22.8	39.8	29.1	25.3	28.7	45.7	35.0	21.3	23.9	31.1	32.0	32.7	32
NYHA	III	III	III	II-III	III-IV	III	III	III	III	II	III	III	III
STS Mortality	5.9%	2.2%	5.9%	10.6%	10.0%	4.8%	3.2%	10.8%	1.6%	2.6%	4.2%	6.6&	2.6%
Euroscore Mortality	17.3%	1.9%	6.5%	14.0%	19.3%	2.1%	3.0%	8.6%	5.1%	2.3%	7.8%	4.3%	9.1%
Co-morbidities	Prior CABG Prior MI HTN Diabetes Afib	Prior MI HTN Diabetes Renal Insuf	Prior CABG Prior MI HTN Diabetes Afib	Prior AVR Renal Insuf Afib	Prior MI HTN Diabetes Renal Ins	HTN Renal Ins AFib	HTN Renal Insuf Afib	Prior CABG BAV/TAVI HTN Diabetes AFib	CAD AFib Lung Dis	CAD, HTN Diabetes Renal Insuf Lung Dis Afib	Prior CABG Diabetes HTN Afib	HTN Diabetes Renal Insuf Afib	Prior CABG AVR HTN PHTN
Valve Etiology	FMR	FMR	FMR	DMR	FMR	FMR	FMR	FMR	FMR	DMR	Mix	FMR	FMR
MR Grade Pre	3+	4+	3+	4+	4+	3+	4+	3+	3+	4+	4+	3+	4+
Pre-Op LVEF	28%	27%	49%	55%	30%	55%	35%	35%	35%	45%	76%	43%	25%
PAP	50	40	47	67	63	33	41	50	58	46	59	ND	63

*: Compassionate Use case

Clinical Experience

March 28, 2016

Patient	1	2	3	4	5	6	7	8*	9	10	11	12	13	Summary
Successful Deployment	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12/13
Apical Access Time (min)	NA	29	25	25	19	25	53	22	36	19	31	32	23	28
Deployment Time (min)	NA	12	4	10	9	16	12	9	29	11	12	26	12	14
MR Grade Post	0	0	0	0	0	0	1	0	0	0	0	0	0	0
NYHA Post	NA	NA	II	II	II	II	III	I	I	II	II	III	III	8/11
Mean LVOT Grad. (mmHg)	NA	4	1	2	2	2	3	3	4	7	9	1	1	3
Mean MV Grad. (mmHg)	NA	2	3	4	6	5	5	2	4	4	2	4	3	4
Survival (days)	1	28	411+	327+	250+	250+	54	172+	150+	150+	138+	26+	13+	1931+

Medtronic Intrepid^{tm} TMVR
Clinical Results

- 21 implants to date
- Following data presentation on first 15 patients as presented by Dr. Ian Meredith at EuroPCR 2016

Clinical Results
Early Clinical Experience

Sites	
John Paul II, Krakow, Poland	3
Monash Heart, Melbourne, Australia	4
Alfred, Melbourne, Australia	3
St. Thomas', London, United Kingdom	2
Royal Prince Alfred, Sydney, Australia	3
	15

Patient Demographics

Baseline Characteristics (n=15)		
Age (years)	75	(range: 61–88)
Sex (male)	10	
NYHA Functional Class		
II	1	
III	13	
IV	1	
Prior MI / Coronary Artery Disease	8	
Previous CABG	5	
Atrial Fibrillation	11	
Pacemaker/BiV/ICD	6	
STS Score mean (%)	5.3	(range: 1.6–10.8)

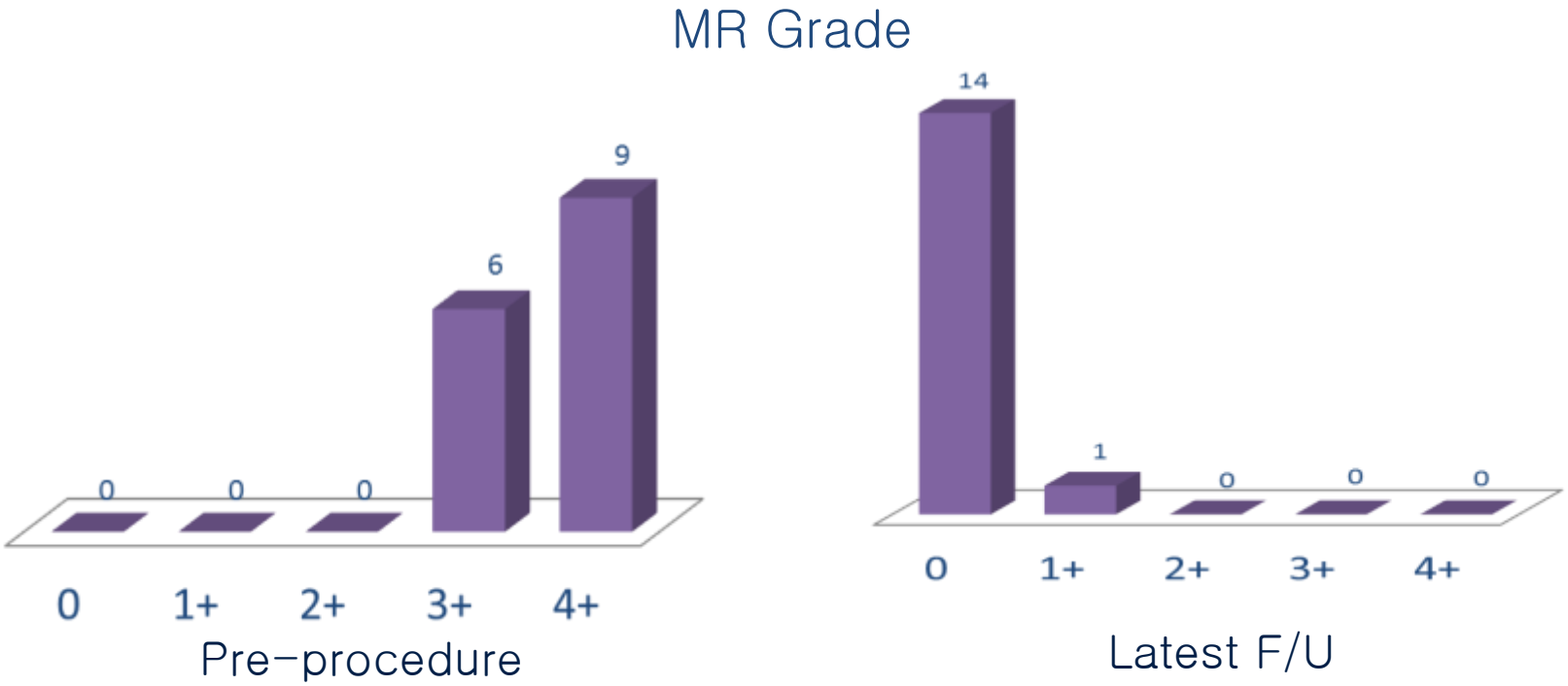
Patient Demographics

Baseline Echocardiogram (n=15)		
	Secondary MR	Primary MR
MR Etiology	11	4
LVEF mean (%)	35	57
≤ 30	5	0
31 – 50	5	1
> 50	1	3
LVEDD (mm)	66	55
LVESD (mm)	53	35
MR grade ≥ 3+ (%)	100	

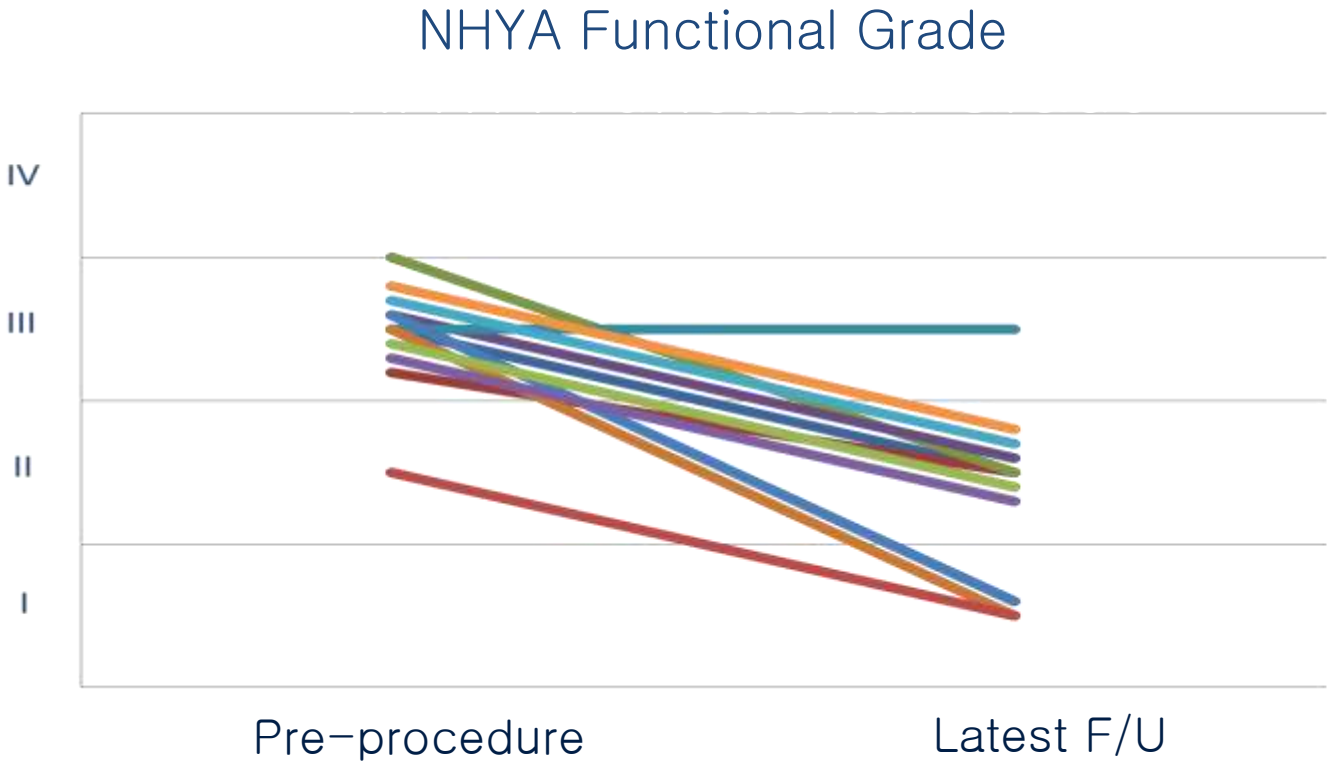
Clinical Results

Procedural Outcomes (n=15)		
Successful Deployment	14	
Apical Access Time (minutes)	31	range: 19–54
Deployment Time (minutes)	14	range: 4–29
Mean LVOT Gradient (mmHg)	3	range: 1–9
Mean MV Gradient (mmHg)	4	range: 2–6

Clinical Results



Clinical Results



Clinical Results

30-day Survival (n=14)*	
Survival	12

30-day SAEs (n=14)	
Death	2
CV	2
Non CV	0
MI	0
Major/Disabling CVA	0
Re-Hosp	1**

*- one subject not yet at 30 days
**- fluid overload

Thank You For Your kind Attention