

# In vitro hydrodynamic and acute clinical performance of a novel self-expanding transcatheter heart valve in various surgical bioprostheses



Alexander Sedaghat<sup>1\*</sup>, MD; Jan-Malte Sinning<sup>1</sup>, MD; Nikos Werner<sup>1</sup>, MD; Georg Nickenig<sup>1</sup>, MD; Lenard Conradi<sup>2</sup>, MD; Stefan Toggweiler<sup>3</sup>, MD; Ulrich Schäfer<sup>4</sup>, MD

1. Med. Klinik und Poliklinik II, Herzzentrum, Universitätsklinikum Bonn, Bonn, Germany; 2. Klinik und Poliklinik für Herz- und Gefäßchirurgie, Universitäres Herzzentrum Hamburg, Hamburg, Germany; 3. Herzzentrum, Luzerner Kantonsspital, Lucerne, Switzerland; 4. Klinik und Poliklinik für Allgemeine und Interventionelle Kardiologie, Universitäres Herzzentrum Hamburg, Hamburg, Germany

## Introduction

Transcatheter aortic valve-in-valve (ViV) implantation has evolved as a valuable alternative to surgical redo operations for degenerated surgical bioprostheses<sup>1</sup>. The variety of surgical and transcatheter prostheses as well as patient-related and procedural factors in clinical routine make randomised trials in this context virtually impossible. To compensate for the lack of these data, *in vitro* measurements of ViV hydrodynamics have been increasingly implemented and have helped to understand the influence of prosthesis type, size and implantation height on the procedural result in ViV implantation<sup>2,3</sup>. In this study, we aimed to assess *in vitro* hydrodynamic performance of the novel NVT Allegra™ (NVT GmbH, Hechingen, Germany) in different surgical aortic valve bioprostheses. Additionally, we analysed the haemodynamic outcomes of the first four patients undergoing TAVI with this transcatheter heart valve (THV) for the treatment of degenerated surgical aortic valve bioprostheses.

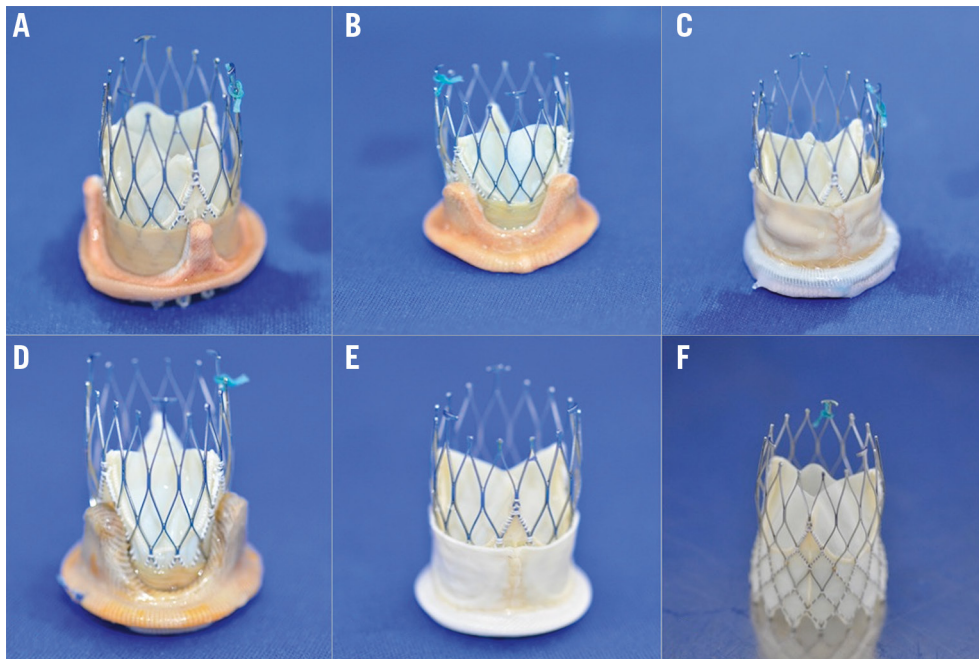
## Methods

### IN VITRO VALVE-IN-VALVE ANALYSIS

*In vitro* hydrodynamic performance was investigated using the self-expanding 23 mm NVT Allegra THV in five surgical heart valves (SHVs) with nominal sizes of 23 mm (**Figure 1**). The NVT Allegra is a self-expanding THV prosthesis, which has recently received CE-mark approval.

For *in vitro* assessment, all SHVs were positioned in Plexiglas aortic root compartments with three valvular sinuses. THV valve size and implantation height were based on recommendations provided by the manufacturer. The resulting ViV configurations were warmed up to a physiological temperature of 37°C to ensure proper stent expansion. Hydrodynamic measurements in this study were performed with saline solution using a pulse duplicator developed at the Department of Cardiovascular Engineering at the Helmholtz Institute, Aachen, Germany<sup>4</sup>. The following

\*Corresponding author: Med. Klinik und Poliklinik II - Herzzentrum, Universitätsklinikum Bonn, Sigmund-Freud-Str. 25, 53105 Bonn, Germany. E-mail: alexander.sedaghat@ukb.uni-bonn.de



**Figure 1.** Valve-in-valve pairings using the NVT Allegra with five different valves. A) PERIMOUNT. B) Mosaic. C) Mitroflow. D) aspire. E) Trifecta. F) NVT Allegra.

parameters were obtained: a) mean systolic pressure difference (mmHg), b) effective orifice area (cm<sup>2</sup>), c) leakage volume (% of stroke volume), and d) total regurgitation (% of stroke volume). Measurements were performed at a physiological cardiac output of 5 l/min, repeated twice, and data were collected as a mean with standard deviation across five cycles.

### FIRST CLINICAL EXPERIENCE

Four patients with degenerated bioprostheses were treated via a transfemoral approach with the 23 mm NVT Allegra as previously described<sup>5</sup>. All patients underwent preprocedural evaluation. Afterwards, all patients were discussed by the local multidisciplinary Heart Team at the University Heart Center in Hamburg, Germany.

## Results

### IN VITRO HYDRODYNAMICS

Mean systolic pressure gradients, effective orifice areas and regurgitation after ViV implantation with the 23 mm NVT Allegra are shown in **Figure 2**. Mean pressure gradients ranged between 5.0±0.1 and 8.4±0.1 mmHg; the lowest gradients were found in the Trifecta™ (St. Jude Medical, St. Paul, MN, USA). All ViV pairings resulted in effective orifice areas above 1.5 cm<sup>2</sup>. Both leakage volume and total regurgitation were found to be highest in the ViV configuration with the aspire™ prosthesis (Vascutek Ltd, Inchinnan, UK). The lowest degree of both leakage volume and total regurgitation was observed for the ViV pairing using the Trifecta with 2.3±1.1% and 5.1±1.3%, respectively (**Figure 3**).

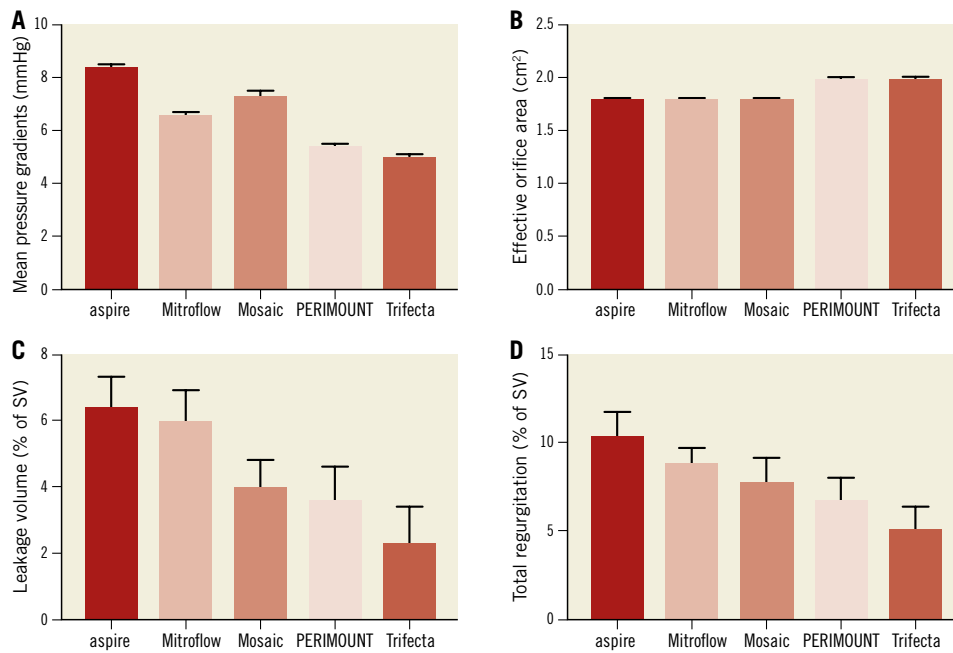
### FIRST IN HUMAN APPLICATION

In a small subset of high-risk surgical patients (n=4, log. EuroSCORE 35.8±15.5%; STS-PROM 7.4±6.1%, age 81.2±4.7 years, all female) with degenerated aortic bioprosthetic valves (PERIMOUNT 21 mm [Edwards Lifesciences, Irvine, CA, USA], Epic™ 23 mm [St. Jude Medical], Mosaic® 21 mm [Medtronic, Minneapolis, MN, USA] and Mitroflow 21 mm [Sorin, Milan, Italy]), NVT Allegra prostheses were implanted transfemorally (**Table 1**). All procedures were performed under local anaesthesia; mean procedural duration was 52±7 min. ViV-TAVI using the Allegra led to improved haemodynamic results. Post-procedural mean (invasive and) echocardiographic analysis showed mean transvalvular gradients below 20 mmHg. During ViV-TAVI, neither coronary obstruction nor significant (paravalvular) leakage occurred. All patients were discharged home without any complication after a median of seven days.

### Discussion

In this study, ViV function of a novel self-expanding THV with supra-annular leaflet position, namely the NVT Allegra, was evaluated in five different surgical prostheses with a label size of 23 mm. Comparable with other self-expanding THVs, the NVT Allegra showed good hydrodynamic properties with regard to mean systolic pressure gradients as well as effective orifice areas and regurgitation at a neutral position.

In addition, in a small series of ViV-TAVI (n=4), implantation of the 23 mm NVT Allegra in degenerated bioprostheses with different modes of failure resulted in favourable haemodynamics with low mean transprosthetic gradients, as determined by invasive

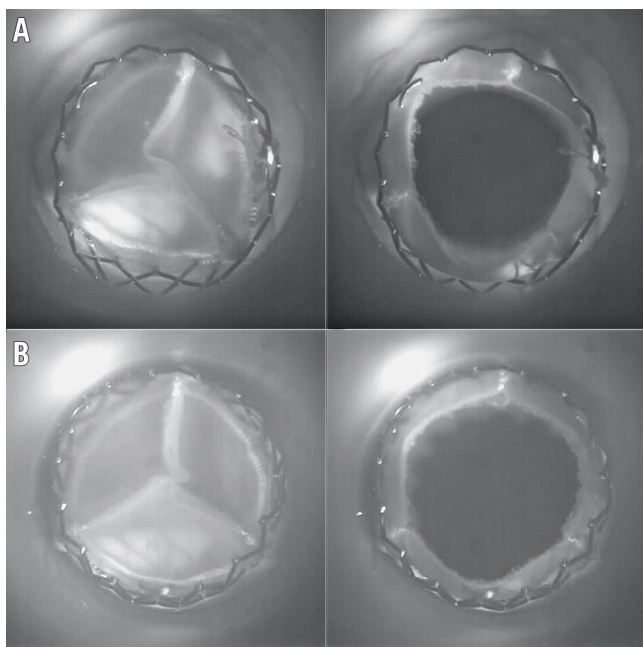


**Figure 2.** Hydrodynamic results. Mean systolic pressure gradients (A), effective orifice areas (B), leakage volumes (C) and total regurgitation (D) of the 23 mm NVT Allegra in the different surgical bioprostheses.

haemodynamic assessment and echocardiography, and no aortic regurgitation. VARC-2 criteria for device success were met with mean aortic valve gradients <20 mmHg in all cases. An ancillary hydrodynamic *in vitro* analysis of the 23 mm NVT Allegra

**Table 1.** Haemodynamic parameters of patients undergoing ViV-TAVI with the NVT Allegra.

Patient	Baseline	Post ViV-TAVI
<b>#1 (Edwards PERIMOUNT 21 mm)</b>		
Pmax/MPG (mmHg) (invasive)	95/111	1/11
Pmax/MPG (mmHg) (echo)	159/115	37/16
EOA (cm <sup>2</sup> ) echo	0.5	1.1
Failure mode (AS/AR/MIX)	AS	–
Aortic regurgitation (O-III+)	–	0
<b>#2 (St. Jude Epic 23 mm)</b>		
Pmax/MPG (mmHg) (invasive)	32/45	2/9
Pmax/MPG (mmHg) (echo)	55/45	18/10
EOA (cm <sup>2</sup> ) (echo)	0.8	1.7
Failure mode (AS/AR/MIX)	MIX	–
Aortic regurgitation (O-III+)	AR III+	0
<b>#3 (Medtronic Mosaic 21 mm)</b>		
Pmax/MPG (mmHg) (invasive)	7/20	2/9
Pmax/MPG (mmHg) (echo)	30/18	15/11
EOA (cm <sup>2</sup> ) (echo)	1.2	1.6
Failure mode (AS/AR/MIX)	AR	–
Aortic regurgitation (O-III+)	AR III+	0
<b>#4 (Sorin Mitroflow 21 mm)</b>		
Pmax/MPG (mmHg) (invasive)	16/18	6/15
Pmax/MPG (mmHg) (echo)	46/26	30/15
EOA (cm <sup>2</sup> ) (echo)	1.1	1.2
Failure mode (AS/AR/MIX)	AR	–
Aortic regurgitation (O-III+)	AR III+	0



**Figure 3.** High-speed camera images obtained during *in vitro* ViV testing during end systole and diastole. A) Mosaic. B) Trifecta. Minimal “pin-wheeling” and no leaflet/stent-frame contact are visible.

within a 21 mm Sorin Mitroflow SHV was performed to complement the clinical data: this showed that mean systolic pressure gradient ( $12.2 \pm 0.2$  mmHg) as well as effective orifice area (EOA  $1.4 \text{ cm}^2$ ) *in vitro* were well in line with the results in patient #4.

### Limitations

Several limitations in this study need to be acknowledged: the surgical bioprostheses used in the *in vitro* analysis were unimplanted and not degenerated, therefore lacking calcification and/or pannus, both of which may cause incomplete THV expansion and thus paravalvular leakage in ViV-TAVI. Second, the effects of THV position on hydrodynamic outcome or stability were not evaluated in this study. In this analysis, all THVs were implanted at the optimal position; however, in clinical routine this may not always be achievable. Finally, surgical heart valves in the *in vitro* analysis were not identical to those in the clinical ViV cohort, limiting the direct comparison of both.

### Conclusion

Both of the observed hydrodynamic properties of the NVT Allegra in our early clinical experience are encouraging and indicate a potential role for this novel THV in valve-in-valve TAVI. Given the small size of this analysis, it remains for prospective studies such as the recently initiated VIVALL trial (NCT03287856) to evaluate the clinical performance of the NVT Allegra for the valve-in-valve indication.

### Impact on daily practice

With the lack of randomised studies, *in vitro* valve-in-valve analyses have gained increasing importance, providing reliable information on optimal THV choice and THV position. The NVT Allegra, a novel supra-annular THV, displayed good performance with regard to mean pressure gradients and regurgitation in different surgical prostheses in benchmark tests. These results were confirmed in the clinical setting. The results of this analysis strengthen the role of *in vitro* valve-in-valve tests as a precursor to clinical use of novel THVs and indicate the safety and feasibility of ViV-TAVI with the NVT Allegra.

### Acknowledgements

*In vitro* measurements were performed with the support of the company ac.biomed GmbH (Aachen, Germany).

### Conflict of interest statement

A. Sedaghat has received travel grants from NVT. J.M. Sinning and N. Werner have received speaker honoraria as well as research support from Medtronic. U. Schäfer and S. Toggweiler are consultants for NVT. G. Nickenig has received speaker honoraria from Edwards Lifesciences as well as Medtronic. L. Conradi is a consultant for Edwards Lifesciences and has received speaker honoraria from Medtronic.

### References

1. Dvir D, Webb JG, Bleiziffer S, Pasic M, Waksman R, Kodali S, Barbanti M, Latib A, Schaefer U, Rodés-Cabau J, Treede H, Piazza N, Hildick-Smith D, Himbert D, Walther T, Hengstenberg C, Nissen H, Bekerredjian R, Presbitero P, Ferrari E, Segev A, de Weger A, Windecker S, Moat NE, Napodano M, Wilbring M, Cerillo AG, Brecker S, Tchetché D, Lefèvre T, De Marco F, Fiorina C, Petronio AS, Teles RC, Testa L, Laborde JC, Leon MB, Kornowski R; Valve-in-Valve International Data Registry Investigators. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. *JAMA*. 2014;312:162-70.
2. Azadani AN, Jaussaud N, Matthews PB, Ge L, Chuter TA, Tseng EE. Transcatheter aortic valves inadequately relieve stenosis in small degenerated bioprostheses. *Interact Cardiovasc Thorac Surg*. 2010;11:70-7.
3. Simonato M, Azadani AN, Webb J, Leipsic J, Kornowski R, Vahanian A, Wood D, Piazza N, Kodali S, Ye J, Whisenant B, Gaia D, Aziz M, Pasala T, Mehilli J, Wijeyesundera HC, Tchetché D, Moat N, Teles R, Petronio AS, Hildick-Smith D, Landes U, Windecker S, Arbel Y, Mendiz O, Makkar R, Tseng E, Dvir D. In vitro evaluation of implantation depth in valve-in-valve using different transcatheter heart valves. *EuroIntervention*. 2016;12:909-17.
4. Kuetting M, Sedaghat A, Utzenrath M, Sinning JM, Schmitz C, Roggenkamp J, Werner N, Schmitz-Rode T, Steinseifer U. In vitro assessment of the influence of aortic annulus ovality on the hydrodynamic performance of self-expanding transcatheter heart valve prostheses. *J Biomech*. 2014;47:957-65.
5. Wenaweser P, Stortecky S, Schütz T, Praz F, Gloekler S, Windecker S, Elsässer A. Transcatheter aortic valve implantation with the NVT Allegra transcatheter heart valve system: first-in-human experience with a novel self-expanding transcatheter heart valve. *EuroIntervention*. 2016;12:71-7.