Inspire

Your latest news on RESILIA tissue

Newsletter #1 – April 2022

Life^{R}

Life to the power of RESILIA

A promise of freedom. That's the power of RESILIA tissue.

Edwards

In this issue

We hope you enjoy this first issue of *Inspire*. Want to learn more about RESILIA tissue? Visit **edwards.com/inspiring**

ON THE CIRCUIT

Exciting data on RESILIA tissue were presented at three recent congresses

Firstly, Mubashir Mumtaz (UMPC Central Pennsylvania, Harrisburg, PA, US) revealed the results of a sub-analysis of 5-year data from the COMMENCE trial at the Society of Thoracic Surgeons (STS) 58th Annual Meeting in January 2022. Dr Mumtaz and colleagues evaluated patient and valve factors that impact the haemodynamic performance of a bioprosthesis with RESILIA tissue. The results were encouraging for the durability of RESILIA tissue – find out more on page 2.

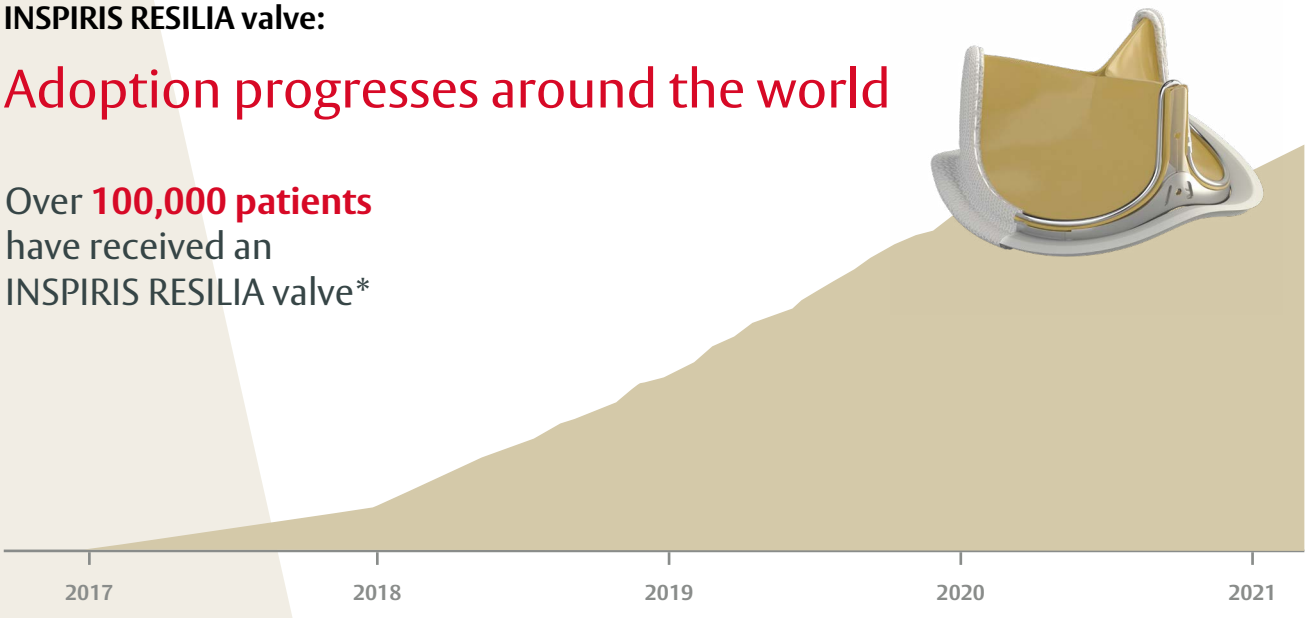
Next, in February 2022, Ruggero De Paulis (European Hospital, Rome, Italy) presented 1-year data from the INDURE registry at the 51st German Society for Thoracic, Cardiovascular and Vascular Surgery (DGTHG) Annual Meeting. This European registry is the first to study the long-term performance of INSPIRIS RESILIA valve in patients aged 60 years and younger. Turn to page 3 to read his views on the preliminary results.

Young patients were also central to Alessandra Francica's presentation at the Heart Valve Society (HVS) meeting in Miami in March 2022. The team at the University of Verona Medical School, Italy, assessed the short- and mid-term outcomes of INSPIRIS RESILIA valve in patients with an average age of 57 years. How did the valve fare? Turn to page 4 to see.

INSPIRIS RESILIA valve:

Adoption progresses around the world

Over **100,000 patients** have received an INSPIRIS RESILIA valve*



*Data to September 2021

Haemodynamic change over 5 years following aortic valve replacement with a RESILIA tissue valve

Mumtaz M *et al*. Presented at the Society of Thoracic Surgeons Annual Meeting, 2022.

The COMMENCE aortic trial is an FDA pivotal trial designed to evaluate the safety and effectiveness of a bioprosthetic valve with RESILIA tissue. At the STS Annual Meeting in January 2022, Dr Mubashir Mumtaz (UMPC Central Pennsylvania, Harrisburg, PA, US) presented the results of a sub-analysis of the 5-year COMMENCE data, investigating patient and valve factors that impact haemodynamic performance.[1] Using longitudinal models, changes in mean gradient and effective orifice area (EOA) were estimated over 5 years post-operatively.

Among various variables examined, only **patient age at implant and valve size** were statistically significantly associated with mean gradient change over 5 years. Only **valve size** was found to be independently associated with a decrease in EOA.

Key patient demographics at baseline

- N=663
- Mean age: 66.7 ± 11.6 years
- Male: 71.6%
- Average STS score: 1.9 ± 1.7%
- Average euroSCORE II: 2.5 ± 2.8%
- NYHA Class: I (23%); II (51%); III (24%); IV (2%)

How did patient age affect mean gradient and EOA?

Mean gradient change over 5 years:

+3.6 mmHg	+2.4 mmHg	+1.6 mmHg
for 55-year-olds	for 65-year-olds	for 75-year-olds

Average EOA change over 5 years for 21–27 mm valves for these ages:*

−0.27 to −0.29 cm^2

How did valve size affect mean gradient and EOA?

Mean gradient change over 5 years by valve size:*

+2.7 mmHg	+1.8 mmHg	+0.9 mmHg	+0.9 mmHg
21 mm	23 mm	25 mm	27 mm

Average EOA change over 5 years for 21–27 mm valves:*

−0.19 to −0.30 cm^2

In summary, the increase in mean gradient and the decrease in EOA across all ages and valve sizes were minimal. These results are encouraging for the potential durability of RESILIA tissue.†

*19 and 29 mm not reported (because sample size less than the recommended minimum of 30 patients[2]).

†No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients.

'The average increase in mean gradient over 5 years was mild, and the decrease in EOA was minimal.'

Mubashir Mumtaz

CONGRESS DEEP DIVE

Professor Ruggero De Paulis on INDURE registry

De Paulis R *et al*. Presented at 51st Annual Meeting of the German Society for Thoracic and Cardiovascular Surgery (DGTHG), 2022.

Ruggero De Paulis (European Hospital, Rome, Italy) presented 1-year data from the INDURE registry at the DGTHG Annual Meeting.[3] We caught up with him to find out the background to the registry and the latest results.

Q. What is INDURE registry?

A. INDURE is a prospective registry in 21 centres across Europe, following more than 400 patients for at least 5 years [after aortic valve replacement with INSPIRIS RESILIA valve]. This is the first time that the function of a biological valve has been explored in a large group of patients below the age of 60. A good number of patients are below the age of 50 because more of them are asking for a biological valve to avoid life with anticoagulation.

Q. Can you describe a typical patient in the registry?

A. Most patients had a bicuspid valve – more than 80% in patients aged 50 and younger. Most of the time their valve was stenotic, but around 20% had severe aortic regurgitation. Where possible, we tried to use large valve sizes, which last longer and have greater potential for future valve-in-valve.

Q. What were the key 1-year outcomes?

A. We saw no structural valve deterioration (SVD). Mortality was around 3% and the incidence of pacemaker implantation was similar. In the first year, we are testing the safety of the prosthesis. The most important data will follow in the years to come.

'At 1 year, we saw no structural valve deterioration.'

Ruggero De Paulis

Key takeaway:
More young patients are asking for a bioprosthesis. Early real-world results for INSPIRIS RESILIA valve in this population are promising, and follow-up is ongoing.

Positive 3-year results for INSPIRIS RESILIA valve

Francica A *et al*. Presented at the Heart Valve Society Annual Meeting, 2022.

A team led by Prof. Francesco Onorati under the supervision of Prof. Giuseppe Faggian, Chief of Cardiac Surgery at the University of Verona Medical School, Italy, recently assessed the short- and mid-term outcomes of INSPIRIS RESILIA valve in 161 patients (mean age 56.8 ± 10.0 years). They used Kaplan–Meier curves to assess survival and freedom from reoperation, SVD, endocarditis and rehospitalisation. Short- and mid-term echocardiographic data were also assessed. Alessandra Francica presented their results at HVS 2022 in March.[4]

100% freedom from SVD at 3 years

Overall survival was **99.4%** at 30 days and **93.8%** at 3 years. Freedom from cardiovascular death and from SVD was **100%**. One patient underwent reoperation for endocarditis, while two patients required pacemaker implantation. Patients who had surgical aortic valve replacement for aortic regurgitation showed stable left ventricular (LV) reverse remodelling (LV end-diastolic volume: 123.8 ± 32.5 mL at 3 years *vs* 238.5 ± 131.04 mL pre-operatively, p<0.01).

Mean gradient change over time in patients with aortic stenosis:

Pre-operative		**42 mmHg**
30 days		**12 mmHg**
3 years		**13 mmHg**

The team concluded that INSPIRIS RESILIA valve is effective in young patients, with good safety outcomes and excellent short- and mid-term haemodynamic performance.

'INSPIRIS RESILIA valve is my gold standard biological valve.'

Francesco Onorati

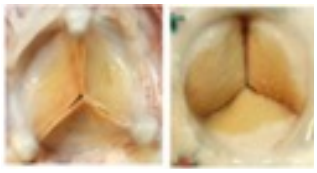
Influence of tissue technology on pannus formation on bioprosthetic heart valves

Tod TJ *et al. Cardiovasc Eng Technol*. 2021; **12**: 418–25.

Bioprosthetic heart valves have various modes of failure. Tissue degeneration and calcification are the major modes; however, pannus formation – growth of abnormal tissue around the valve[5] – can also be an issue. Tara Tod (Edwards Lifesciences, Irvine, CA, US) teamed up with researchers at Tanta University, Egypt, and University Hospitals Leuven, Belgium, to examine the effect of RESILIA tissue on pannus formation. They recently reported their results in *Cardiovascular Engineering and Technology*.[6]

The publication reports the outcomes of two independent studies using a juvenile sheep model of mitral valve replacement with bovine pericardial tissue (Table 1).

Table 1. Study descriptions

Study duration	5 months	8 months
Purpose	To evaluate safety and efficacy of RESILIA tissue in a sheep model	To evaluate calcification and haemodynamics in a long-term sheep model
Control valves*	N=7  Treated with ThermaFix process	N=14  Treated with XenoLogiX treatment
RESILIA tissue valves*	N=10 	N=16 

*Control valves were commercially available Carpentier-Edwards PERIMOUNT mitral valves, models 6900P and 7000TFX. Test valves were the same models configured with RESILIA tissue.

In the 5-month study, the pannus area measured over the whole RESILIA tissue valves was significantly lower than that of the control valves (Table 2). A two-sample t-test showed that the pannus on the atrial and ventricular side of each leaflet was significantly lower in test tissue samples (1.44 ± 1.52 mm^2) compared with the controls (2.61 ± 2.15 mm^2; p=0.027).

Table 2. Summary data for the whole valve from the 5-month study

Treatment group	Pannus area over the whole valve area (thousands of pixels)	T-test comparison: p value
Control tissue	656.2 ± 385.43	0.01
RESILIA tissue	234.4 ± 265.4	

Similarly, in the 8-month study, pannus measured in RESILIA tissue (0.095 ± 0.049 mm^2) was significantly lower than in control tissue (0.134 ± 0.066 mm^2; p=0.002).

The authors conclude that RESILIA tissue valves were associated with reduced pannus formation when compared with control valves. RESILIA tissue may beneficially influence both short- and long-term† valve behaviour of bioprosthetic valves‡ and improve long-term outcomes for patients.

RESILIA tissue valves led to less pannus formation compared with control valves

†No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients.

‡RESILIA tissue tested against tissue from commercially available bovine pericardial mitral valves from Edwards in a juvenile sheep model.

A surgeon's review of INSPIRIS RESILIA valve

Mr Alan Soo is a consultant cardiothoracic surgeon and clinical lead at University Hospital Galway, Ireland. He has a special interest in innovative medical device development and uses INSPIRIS RESILIA valve regularly in his practice. We spoke with him to find out how the valve has performed in his patients.

Q. Could you tell us about the use of INSPIRIS RESILIA valve in your practice?

A. I started using INSPIRIS RESILIA valve approximately one year after launch, as I was keen to use a new generation valve. I discovered the sewing cuff was very surgeon-friendly, unlike other new generation valves I had tried, and was impressed by its haemodynamic performance. I've since completely converted to INSPIRIS RESILIA valve unless otherwise contraindicated. In my practice, I recommend it for anyone 65 years and above, as well as younger patients with a shorter life expectancy. For those under 65 years old, it is really down to patient choice.

Q. Do your patients ask for a bioprosthesis over a mechanical valve?

A. In Ireland, patients are concerned about the impact of long-term anticoagulation on their way of life, so bioprosthetic valves are definitely more popular than mechanical valves. I have patients in their thirties who ask for a bioprosthetic valve, knowing that the prospect of reintervention is very high.

Q. How has INSPIRIS RESILIA valve improved outcomes for your patients?

A. We did an audit on a small number of our patients and found that the immediate postoperative gradients for INSPIRIS RESILIA valve were much better than previous generation valves.

Q. Have you experienced any other improvements or benefits since using INSPIRIS RESILIA valve and would you recommend it to other surgeons?

A. The sewing cuff is probably one of the best I've used. Valve replacement using a semi-continuous suturing technique can be quite challenging if the sewing cuff is stiff, but I have encountered no problems with INSPIRIS RESILIA valve. I would recommend it to other surgeons for two reasons: the ease of use compared with other valves and the good haemodynamic gradients.

References:

1. Mumtaz M, Bavaria J, Griffith B *et al.* Association of patient factors and bioprosthesis size with hemodynamic change over 5 years following RESILIA tissue-based aortic valve replacement. Society of Thoracic Surgeons Annual Meeting, 29–30 January 2022.
2. Durko AP, Pibarot P, Atluri P *et al.* Essential information on surgical heart valve characteristics for optimal valve prosthesis selection: Expert consensus document from the European Association for Cardio-Thoracic Surgery (EACTS)-The Society of Thoracic Surgeons (STS)-American Association for Thoracic Surgery (AATS) Valve Labelling Task Force. *Eur J Cardiothorac Surg.* 2021; **59**: 54–64.
3. De Paulis R, Senage T, Borger M *et al.* Surgical aortic valve replacement in patients under 60 years old: A prospective, multicentre real-world registry in Europe and Canada. 51st Annual Meeting of the German Society for Thoracic and Cardiovascular Surgery, 19–22 February 2022, Hamburg, Germany.
4. Francica A, Tonelli F, Rossetti C *et al.* Edwards INSPIRIS RESILIA® prosthesis for aortic valve replacement in young adults: Short-term and mid-term clinical outcome and haemodynamic performances. Heart Valve Society Annual Meeting, 2–5 March 2022, Miami, FL, US.
5. Ha H, Koo HJ, Huh HK *et al.* Effect of pannus formation on the prosthetic heart valve: In vitro demonstration using particle image velocimetry. *PLoS One.* 2018; **13**: e0199792.
6. Tod TJ, Gohres RA, Torky M *et al.* Influence of tissue technology on pannus formation on bioprosthetic heart valves. *Cardiovasc Eng Technol.* 2021; **12**: 418–25.

No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients.

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