



# Non-Invasive Ultrasound Treatment of Calcific Aortic Stenosis First-in-Man

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By and For you

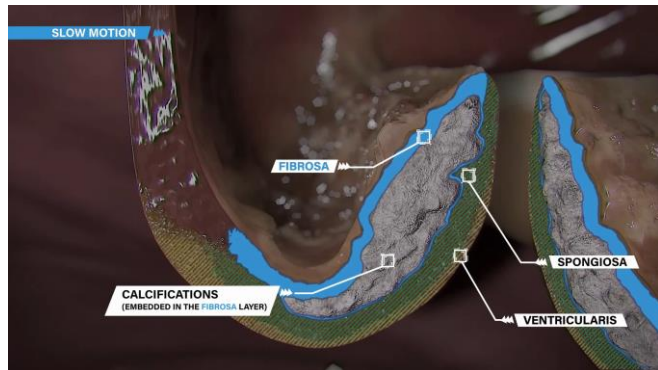
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# Non-Invasive Ultrasound Therapy (NIUT)



Focused, very high frequency and short ultrasound pulses create microscopic cavitation bubbles

When cavitation bubbles burst, they produce shockwaves

Shockwaves cause microfragmentation in valve calcium without tissue damage

Therapeutic ultrasounds	NIUT	Lithotripsy	HIFU*
Ability to penetrate deep in tissue	+	-	-
Preservation of tissue through which ultrasounds pass	+	+	-
Energy	Mechanical	Mechanical	Heat
Therapeutic effect	Hard tissue softening	Break-up of stone	Tissue ablation by coagulation necrosis

\* HIFU: High Intensity Focused Ultrasound

# Bubble cavitation detection with Echo Imaging



# Study design

- **Design:** Prospective, multi-center clinical evaluation of the Valvsoft® NIUT (N=10) in severe symptomatic CAS patients not eligible for SAVR/TAVR (First-in-Man)
- **Objectives:** To evaluate the safety and feasibility of the Valvsoft® system in severe calcific aortic stenosis patients not eligible for valve replacement
  - Primary safety endpoint: procedure related mortality @ 30 days
  - Primary Performance endpoint: improvement in pressure gradients and aortic valve area post-procedure at one month measured by independent core lab
  - Secondary endpoints: safety and performance beyond one months
- **Centers:** Hospital Européen Georges-Pompidou, Paris, France and Amphia Hospital, Breda, The Netherlands

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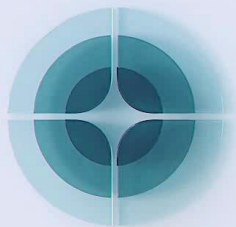
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**Monitoring:** MD-Clinicals,  
Lonay, Switzerland

**Core Lab:** Cardialysis,  
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# Film of the procedure



**CARDIAWAVE**

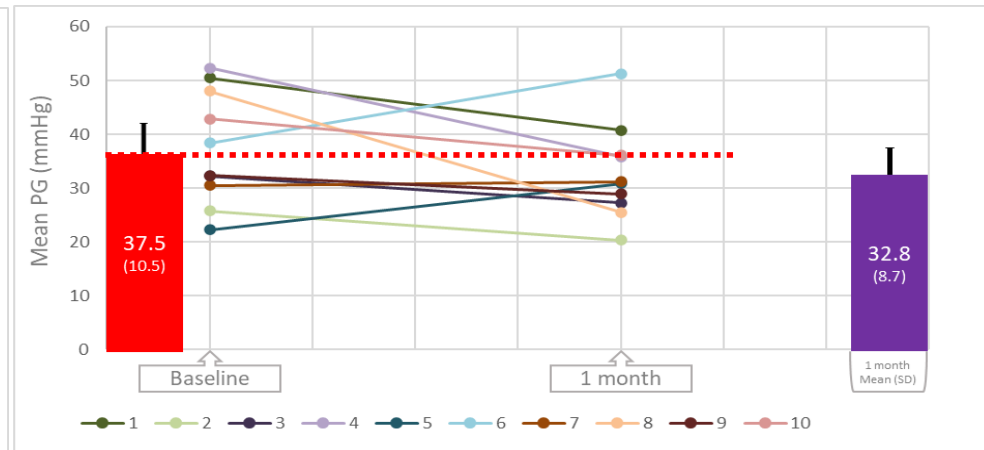
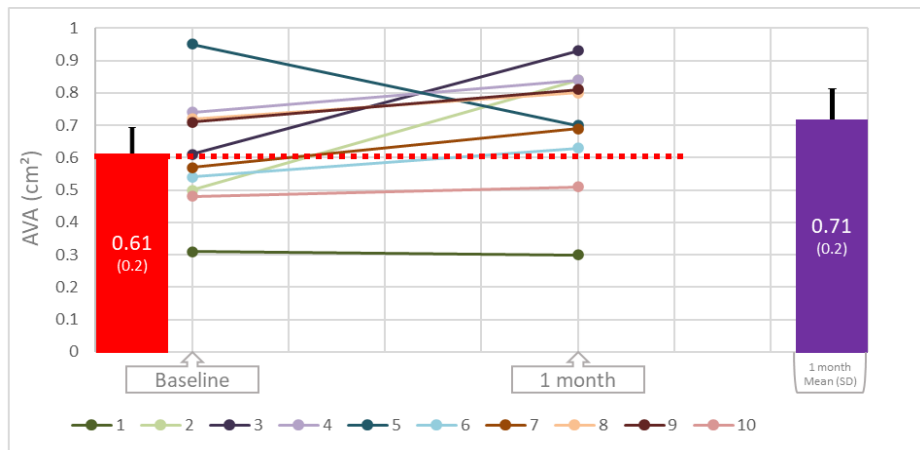
Non-invasive therapy to treat aortic stenosis

Valvosoft<sup>®</sup> Procedure

# Baseline Patient Characteristics

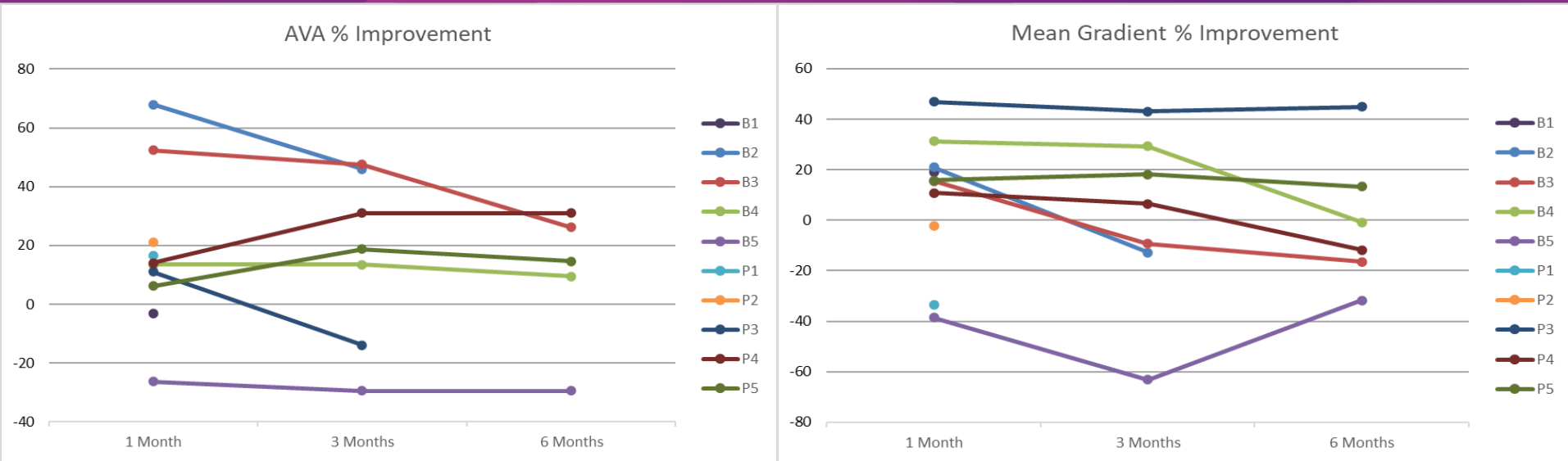
Patient	Age	Gender	NYHA	Calcification	CAD	CHF	DM	Kidney disease
B1	80	Female	4	Severe	-	+	-	+
B2	77	Male	4	Severe	+	+	-	-
B3	79	Male	4	Severe	+	+	-	-
B4	79	Female	3	Severe	-	+	-	-
B5	77	Female	4	Severe	+	-	+	+
P1	91	Female	4	Severe	-	-	-	-
P2	86	Male	4	Severe	+	+	-	+
P3	93	Female	4	Severe	-	+	-	+
P4	93	Male	3	Severe	-	+	-	+
P5	86	Male	2	Severe	+	+	-	-

# Safety & Performance at one month



- No deterioration of cognitive function
- Seven patients improved the NYHA class
- Some isolated extrasystoles during procedure that ceased when dose was lowered
- One hospitalization for right heart failure (resolved)
- No procedure or device related major adverse events at 6 months

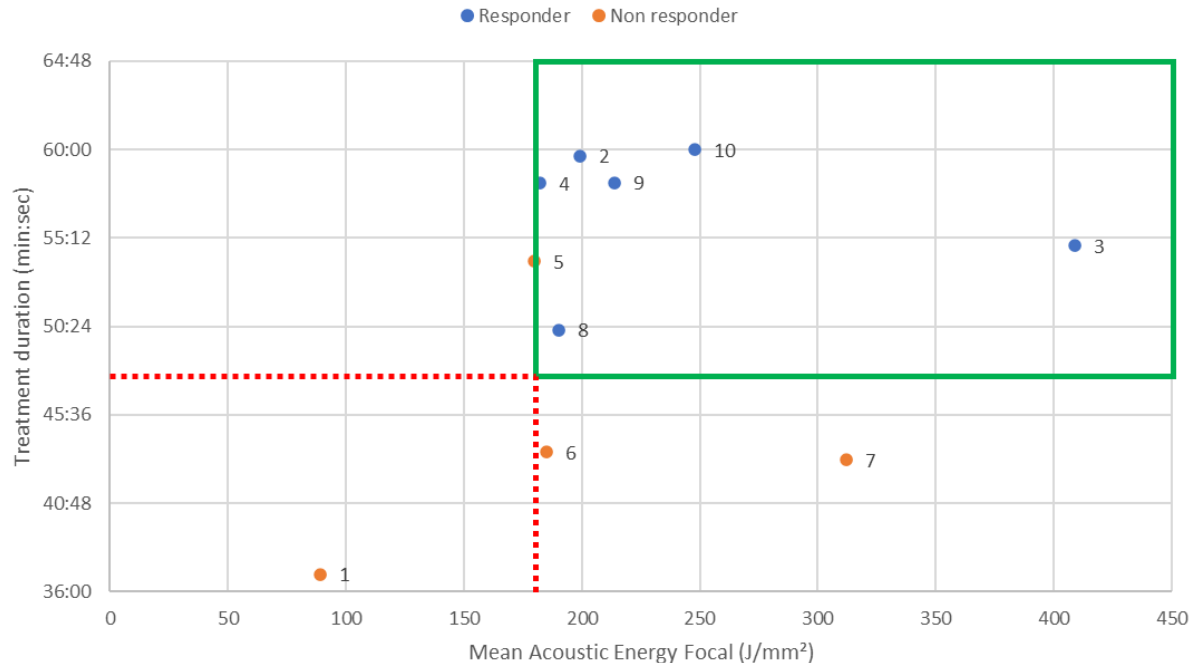
# Performance at 6 months



**Treatment effect largely maintained at 6 months**



# What was different in patients who responded?



- All six responders received  $>180\text{J/mm}^2$  for at least 45 minutes
- Out of the 4 non-responders, 3 received less focal energy and/or for a duration shorter than 45 minutes
- A minimum of treatment duration and focal energy may be needed to obtain a clinically significant effect

- **Patients non-eligible for valve replacement**
- **Patients needing emergent non-cardiac surgery**
- **Bridge to TAVR**
- **Facilitate TAVR procedure**
- **Young patients to delay valve replacement**
- **Moderately severe patients to delay disease progression**

# From safety to efficacy

- Higher energy dose to be applied
- Full 60 minutes duration of ultrasound application
- Repeated treatment sessions
- Improved device imaging guidance

# Conclusions

- Non-Invasive Ultrasound Therapy (NIUT) is a new transthoracic therapy to treat Calcific Aortic Stenosis
- NIUT is feasible and safe in a FIM study involving 10 patients with severe symptomatic aortic stenosis not eligible for valve replacement
  - No procedure or device related major adverse events at 6 months
  - Improvement of AVA and Pressure Gradient in the majority of patients
  - Treatment result largely maintained at 6 months follow-up
- Performance increases with longer treatment time and higher energy dose
- NIUT is complimentary to TAVR and can widen treatment possibilities for patients not eligible for valve replacement and could be applied in the near future, to slow down progression of the disease and thus delay valve replacement

**I, Sander IJsselmuiden, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.**