September 12-14
2018
Les Comtes de Méan
Liège, Belgium

6th International Meeting on Aortic Diseases

New insights into an old problem CHU Liège, APF

www.chuliege-imaa.be

Searching for early biomechanically-driven indexes of aortic remodeling: where are we at?

Emiliano Votta

Politecnico di Milano

Department of Electronics, Information and Bioengineering

Biomechanics Research Group

www.biomech.polimi.it

CHU de Liège

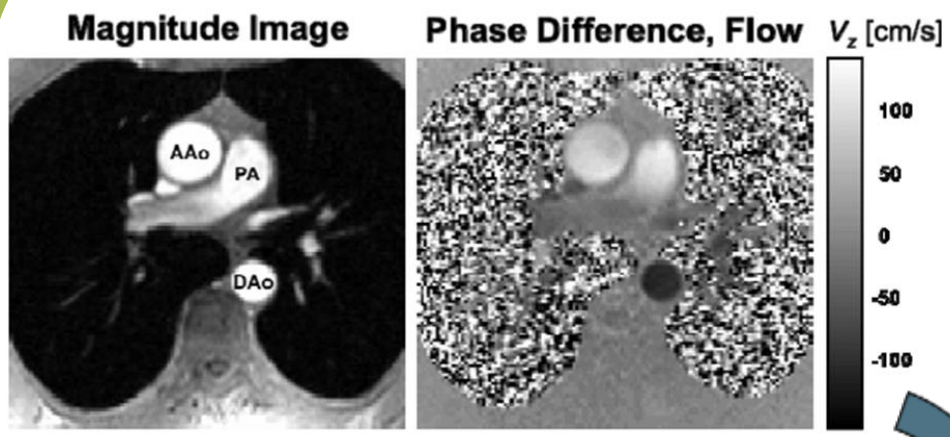
Disclosure of Interest

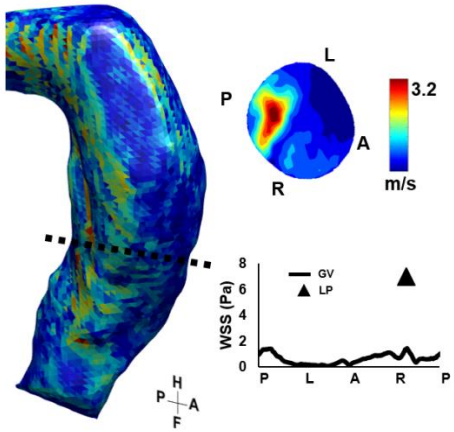
Speaker name: Emiliano Votta

- I do not have any potential conflict of interest

BAV: Aortopathy & Biomechanics

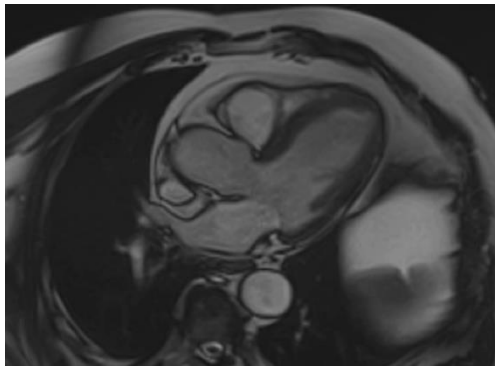
Fluid-dynamics

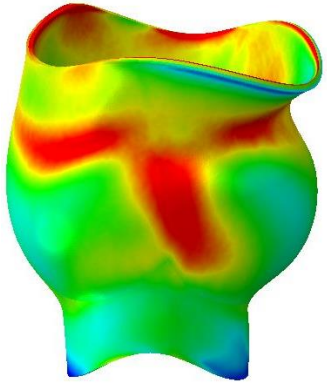




Structural response

cine- sequence





BAV: Aortopathy & Fluid dynamics

High prevalence (20-84%) of aortic dilation in BAV-affected population.

[Evangelista et al., Heart, 2018]

Colocalization of high **wall shear stress (WSS)** and increased concentration of transforming growth factor TGF-β1 and activation of aortic wall matrix metalloproteinase (MMP)

[Guzzardi et al., JACC, 2015]

In vitro stimulation (48 hours) of healthy porcine aortic tissue with BAV-related WSS histories caused an increase in the expression of MMPs involved in the degradation of the aortic wall tunica media

[Atkins et al., Biomech in Mechan, 2014]

BAV: Aortopathy & Fluid dynamics

ADULT: AORTA: AATS CONSENSUS GUIDELINES

ADULT

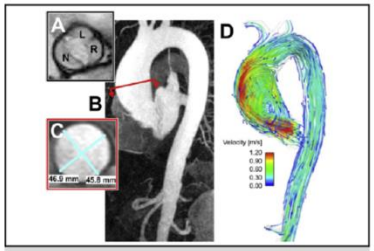
The American Association for Thoracic Surgery consensus guidelines on bicuspid aortic valve–related aortopathy: Executive summary

Check for updates

Michael A. Borger, MD, PhD,[a] Paul W. M. Fedak, MD, PhD,[b] Elizabeth H. Stephens, MD, PhD,[c] Thomas G. Gleason, MD,[d] Evaldas Girdauskas, MD, PhD,[e] John S. Ikonomidis, MD, PhD,[f] Ali Khoynezhad, MD, PhD,[g] Samuel C. Siu, MD,[h] Subodh Verma, MD, PhD,[i] Michael D. Hope, MD,[j] Duke E. Cameron, MD,[k] Donald F. Hammer, MD,[l] Joseph S. Coselli, MD,[m] Marc R. Moon, MD,[n] Thoralf M. Sundt, MD,[o] Alex J. Barker, PhD,[p] Michael Markl, PhD,[q] Alessandro Della Corte, MD, PhD,[r] Hector I. Michelena, MD,[s] and John A. Elefteriades, MD[t]

ABSTRACT

Bicuspid aortic valve disease is a common congenital cardiac disorder, being present in 1% to 2% of the general population. Associated aortopathy is a common finding in patients with bicuspid aortic valve disease, with thoracic aortic dilation noted in approximately 40% of patients in referral centers. Several previous consensus statements and guidelines have addressed the management of bicuspid aortic valve–associated aortopathy, but none focused entirely on this disease process. The current document is an executive summary of "The American Association for Thoracic Surgery Guidelines on Bicuspid Aortic Valve–Related Aortopathy." All major aspects of bicuspid aortic valve aortopathy, including natural history, phenotypic expression, histology and molecular pathomechanisms, imaging, indications for surgery, surveillance, and follow-up, and recommendations for future research are contained within these guidelines. The current executive summary serves as a condensed version of the guidelines to provide clinicians with a current and comprehensive review of bicuspid aortic valve aortopathy and to guide the daily management of these complex patients. (J Thorac Cardiovasc Surg 2018;156:473-80)



Typical patient with BAV with associated aortopathy.

Central Message

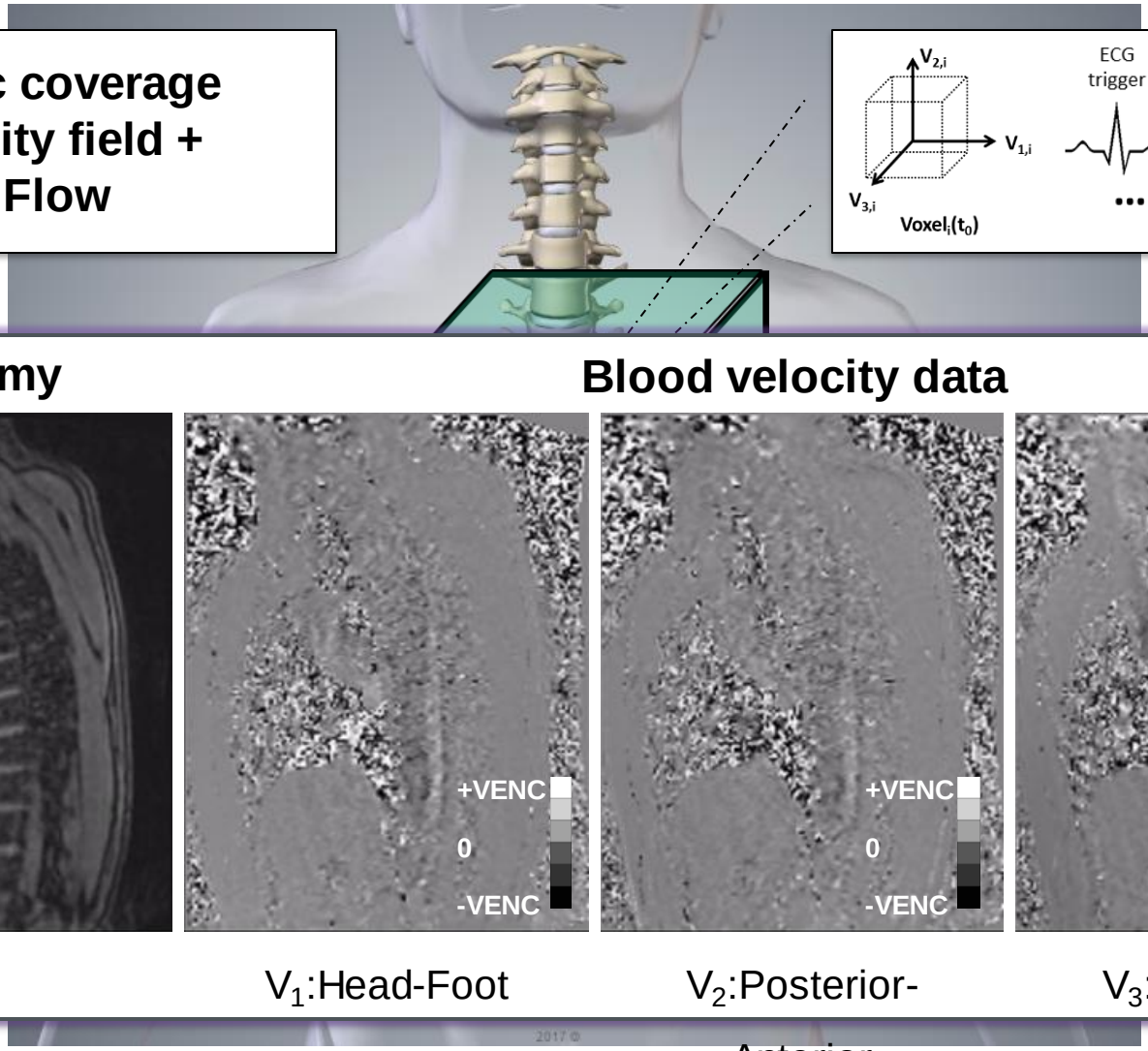
The current document is an executive summary of "The American Association for Thoracic Surgery Guidelines on Bicuspid Aortic Valve–Related Aortopathy."

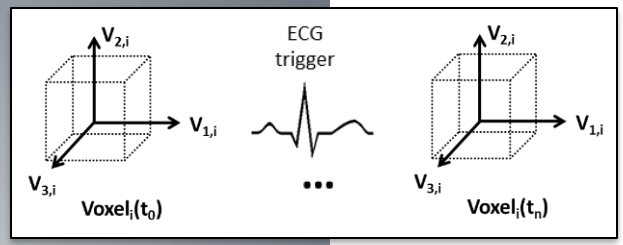
Perspective

BAV-related aortopathy is a common clinical entity. An increasing amount of literature has recently shown that BAV aortopathy is less dangerous than previously described. The current Executive Summary is a condensed version of the "American Association for Thoracic Surgery Guidelines on Bicuspid Aortic Valve–Related Aortopathy," providing clinicians with a current and comprehensive review of BAV aortopathy and its management.

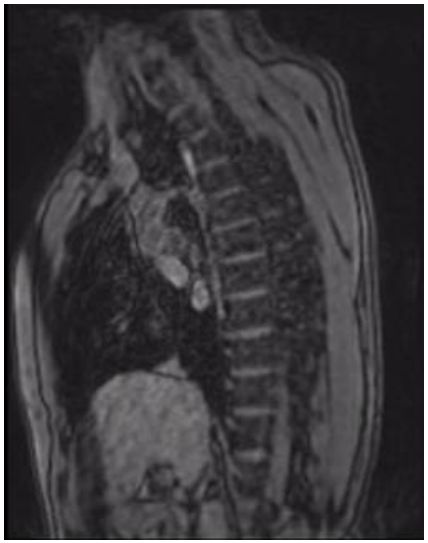
4D flow MRI

Volumetric coverage + 3D velocity field + Time = 4D Flow





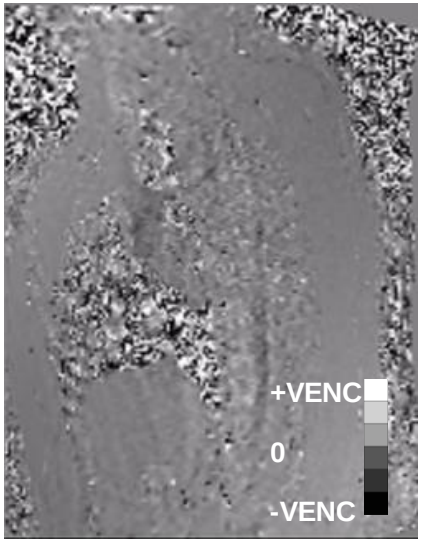
Anatomy



Blood velocity data

V_1:Head-Foot

V_2:Posterior-Anterior

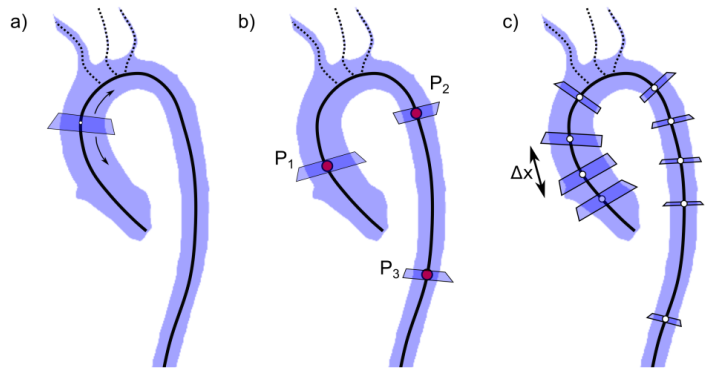


V_3:Right-Left

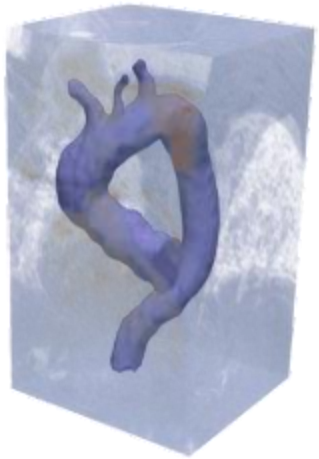
[Dyverfeldt et al., 2015, JCMR]

Assessing *in vivo* fluidynamic stimuli

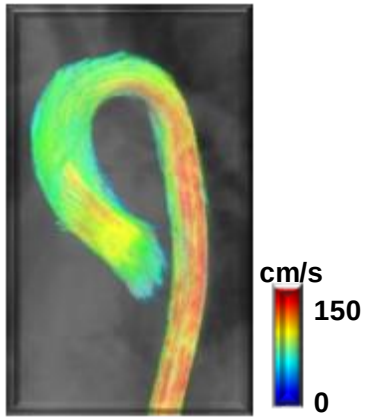
Repeatible analysis protocol



3D anatomy



3D Velocity field



Fluidynamic indexes

Wall shear stress ($\overrightarrow{WSS}$) and related indexes (the most commonly assessed ones)

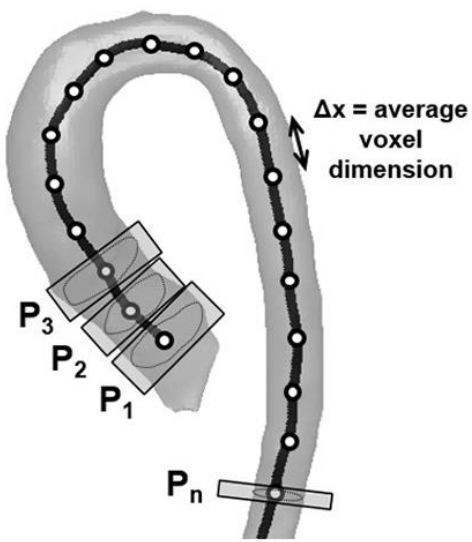
$$\tau_{ij} = \frac{1}{2}\left(\frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i}\right)$$

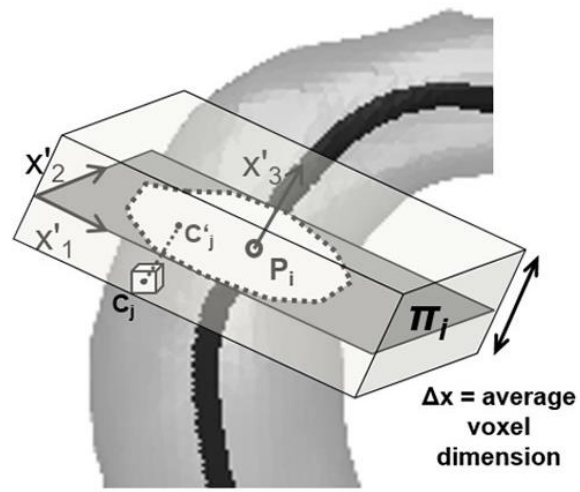
$$\mathbf{T} = \boldsymbol{\tau} \cdot \mathbf{n}$$

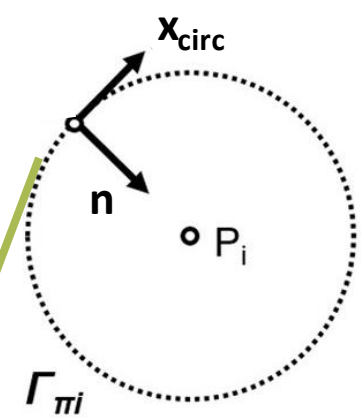
$$\overrightarrow{WSS} = \mathbf{n} \times (\mathbf{T} \times \mathbf{n})$$

Numerically (hence, non exactly) computed
Sensitive to noise

At best, errors by a factor of two affect results
[Piatti et al., J Biomech, 2017]







Uncertainty on wall position and inward normal

WSS-related indexes

How strong is the drag force on the endothelium?

- Maximum wall shear stress ($\left|\overrightarrow{WSS}\right|_{\max}$)

WSS-related indexes

How strong is the drag force on the endothelium?

- Maximum wall shear stress ($\left|\overrightarrow{WSS}\right|_{\max}$)

How is this drag force aligned in space?

- Components along mutually orthogonal directions (axial and circumferential)
- Transverse WSS, i.e., WSS component orthogonal to the main flow direction

WSS-related indexes

How strong is the drag force on the endothelium?

• Maximum wall shear stress ($\left|\overrightarrow{WSS}\right|_{\max}$)

How is this drag force aligned in space?

•Components along mutually orthogonal directions (axial and circumferential)
• Transverse WSS, i.e., WSS component orthogonal to the main flow direction

How much do magnitude and direction of the drag force change in time?

• Oscillatory shear index (OSI) - measures the tendency of the WSS to change direction throughout the cardiac cycle
• Relative residence time, similar to OSI

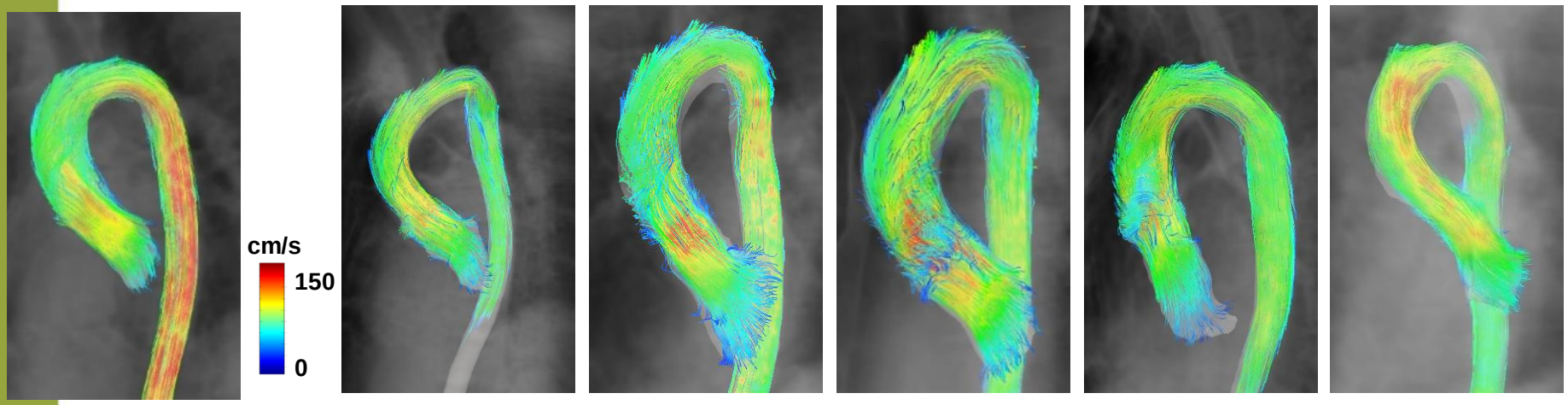
WSS-related indexes

Preliminary study on real subjects

[Piatti et al., Frontiers in Physiol, 2017]

- **Population**:
  - 10 Healthy volunteers (age= 23±7)
  - 5 BAV patients (age=25±10; fusion RL:RN:LN=4:1:0; Aortic diameter = 24.2±2.7 mm Cardiac Output = 5.2 ± 1.0)

HV **BAVs population**



WSS-related indexes

Preliminary study on real subjects

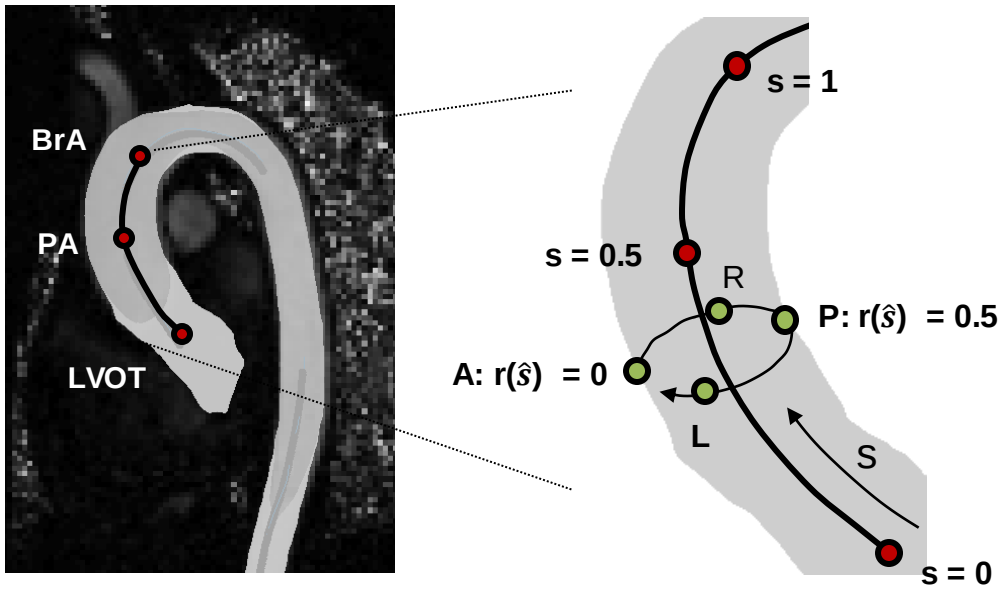
- **Population**:
  - 10 Healthy volunteers (age= 23±7)
  - 5 BAV patients (age=25±10; fusion RL:RN:LN=4:1:0; Aortic diameter = 24.2±2.7 mm Cardiac Output = 5.2 ± 1.0)

- **Tested hypotheses**:
  - some of the WSS-related indexes reveal derangements in absence of aortic dilation (tested based on 4D flow data analysis)
  - derangements, if any, may cause adverse aortic remodeling (tested by 3-year follow-up diameter measurements)

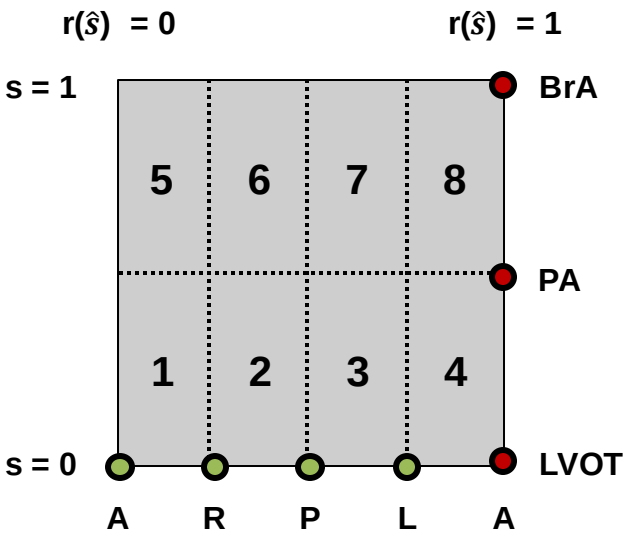
WSS-related indexes

Preliminary study on real subjects

Aortic wall reference system for 2D mapping



2D template definition

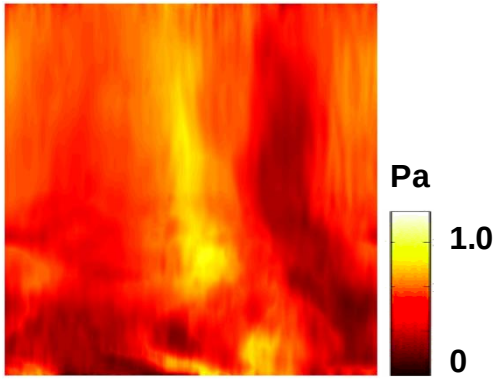


WSS-related indexes

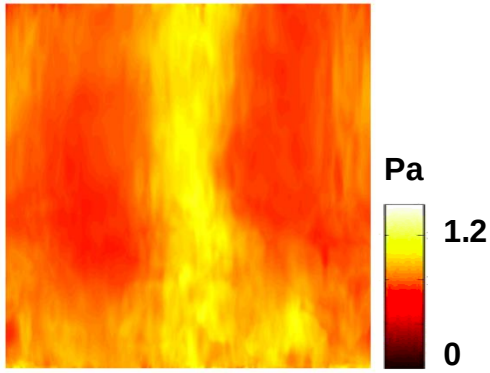
Preliminary study on real subjects: space distribution of indexes

Statistical heat maps for the Healthy Volunteers (HVs) group

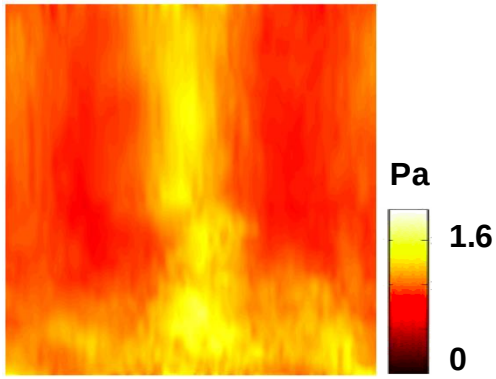
10th percentile



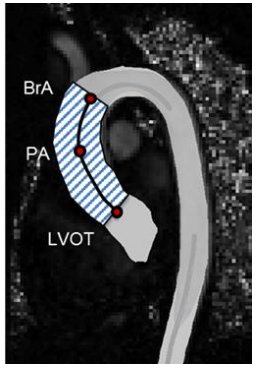
50th percentile

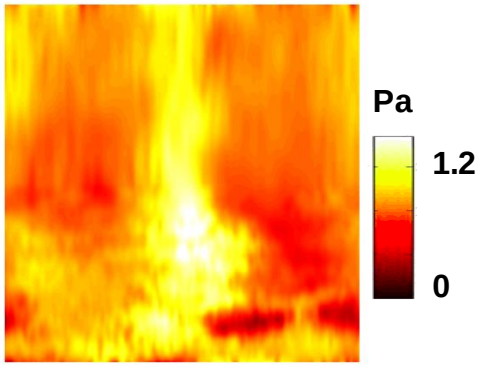


90th percentile



BAV01

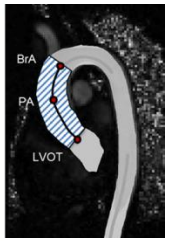


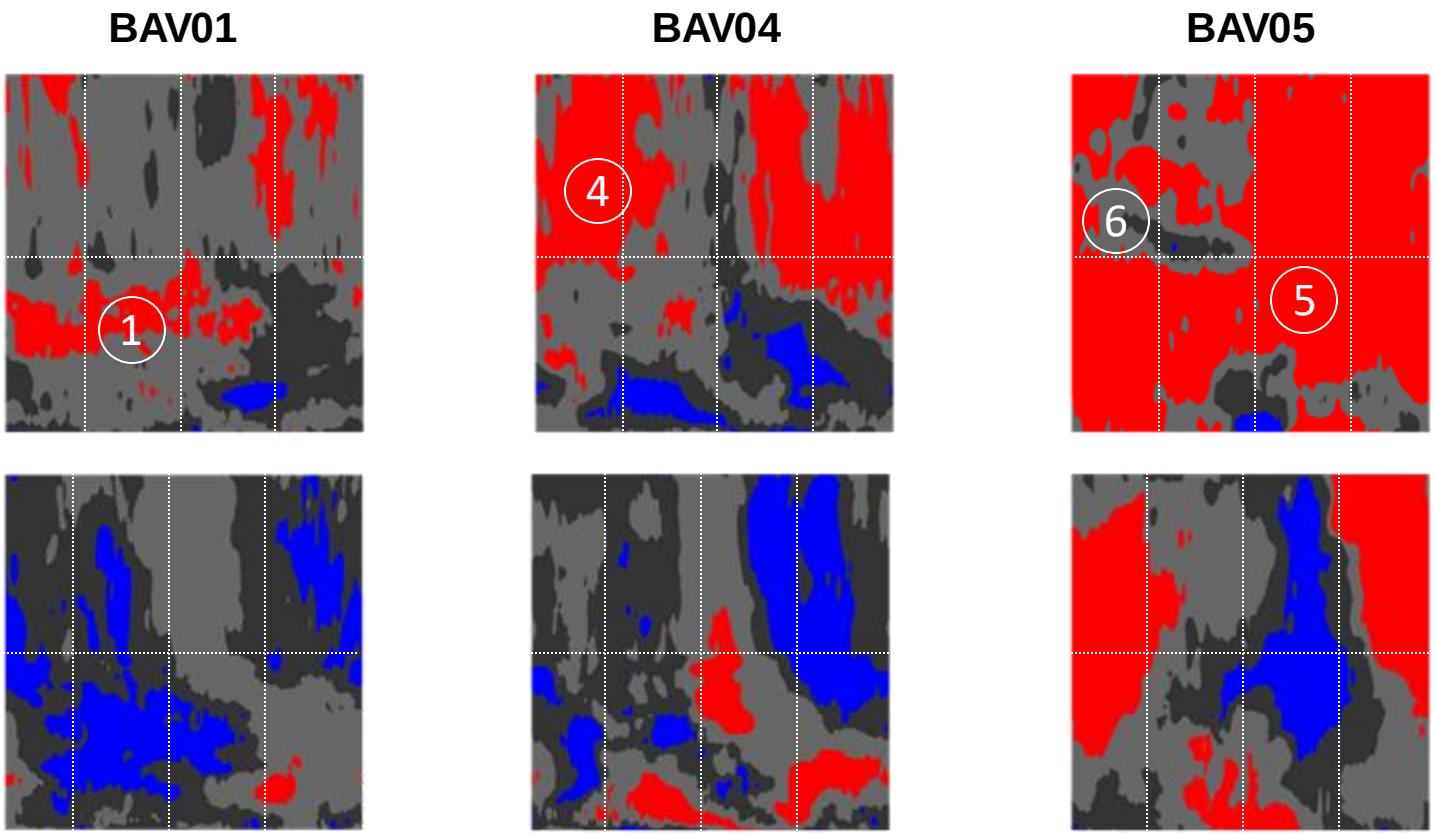


BAV-specific heat maps

WSS-related indexes

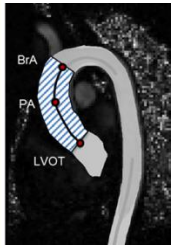
Preliminary study on real subjects: patient specific areas of derangements



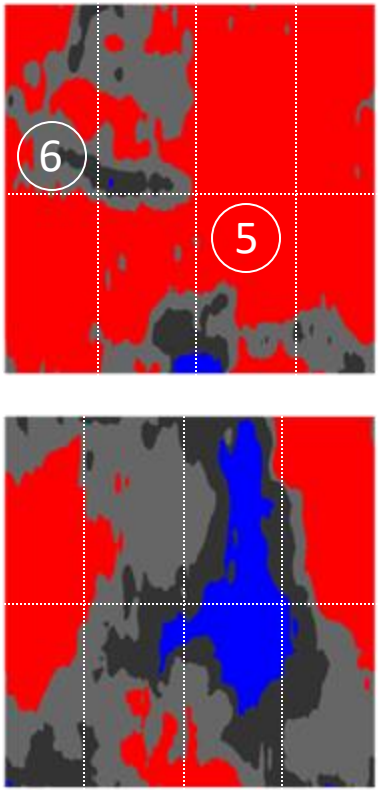


WSS-related indexes

Preliminary study on real subjects: time course of indexes at hot spots



BAV05

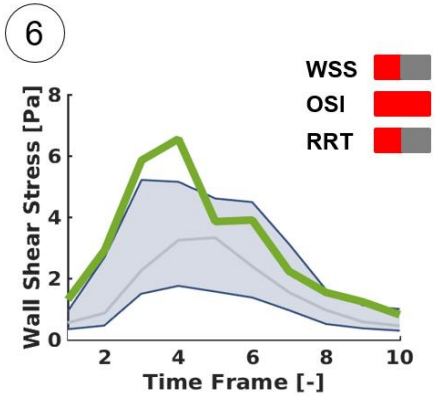


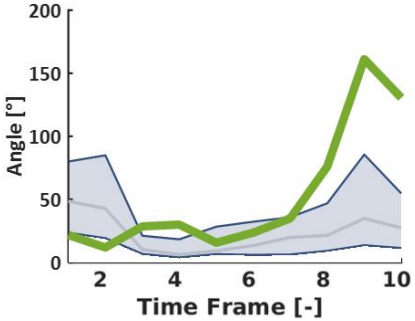
WSS

OSI

HVs distribution

BAV





Higher than HV 90th percentile

Lower than HV 10th percentile

Between HV 90th and 50th percentiles

Between HV 50th and 10th percentiles

WSS-related indexes

Preliminary study on real subjects: key findings

- Some indexes highlight greater (and notable!) derangements in BAV vs. HVs
  - Transverse WSS
  - Circumferential component of the WSS
  - OSI computed for the circumferential component of the WSS
  - Time course of WSS magnitude and orientation together is relevant

- These major derangements are observed prior to anatomical remodeling

  <u>Possible causative relationship with remodeling</u>

- No anatomical remodeling at 3-year follow up in these patients

High risk for of complications: 20 years after diagnosis, valve or cardiovascular surgery is required in 25% of patients. [Michelena et al., Circulation, 2008; Tzemos et al., JAMA, 2008]

WSS-related indexes

Our findings on WSS-related indexes were recently confirmed

- **4Dflow-based study on a large cohort of patients** (101 BAV patients, aortic diameter ≤ 45 mm, no severe valvular disease vs. 20 healthy subjects)

  - WSS magnitude lacks significance since its value is similar in controls and BAV
  - helical flow in BAV increases circumferential WSS
  - variation in WSS components may also influence the aortic morphotype

[Rodríguez-Palomares et al., J Magn Res Imag, 2018]

- CFD study with 4Dflow-based boundary conditions

  - stronger impact of the BAV anatomy on circumferential WSS than on axial WSS
  - OSI reveals differences between BAV and healthy conditions only if computed for the single components and not for the WSS as a vector
  - a new potential marker is proposed: the Shear Magnitude and Directionality Index (SMDI)

[Liu et al., Frontiers in Physiol, 2018]

WSS-related indexes

Final Remarks

- **Large cohorts of patients** undergoing 4Dflow acquisitions are needed and longitudinal follow-up studies are required

  - multi-center studies would be beneficial

- **The devil is in the detail**: small differences in the algorithms that compute WSS can lead to huge differences in WSS quantification

  - for different studies to be really comparable and for tresholds to be identified for risk assessment/stratification, these algorithms should be standardized

- **Need for consensus guidelines also for engineers and radiologists?**

My Partners in Crime

Francesco Sturla

Filippo PIatti

Alberto Redaelli

Selene Pirola

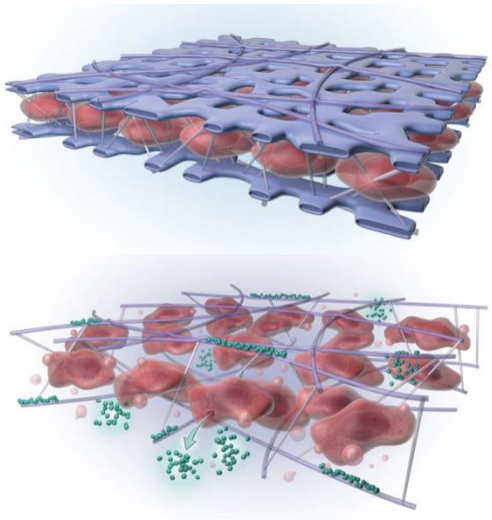
Giovanni Rossini

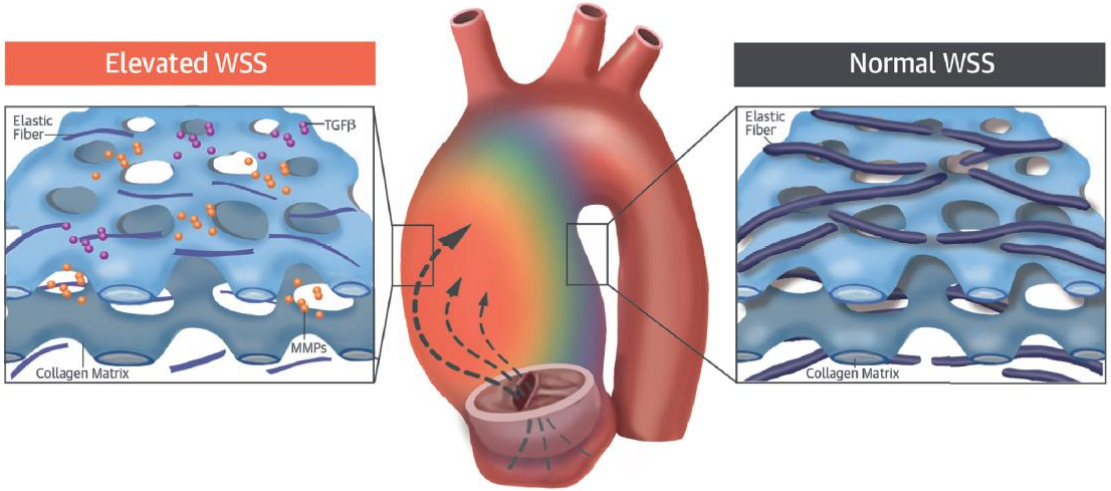
Malenka Bissell

Alessandro Della Corte

……

BAV: Aortopathy & Fluid dynamics





- Inherent fibrillin 1 deficiency
- ECM matrix distruption
- Smooth muscle cells detachment

[Verma, *N Engl J Med*, 2014]

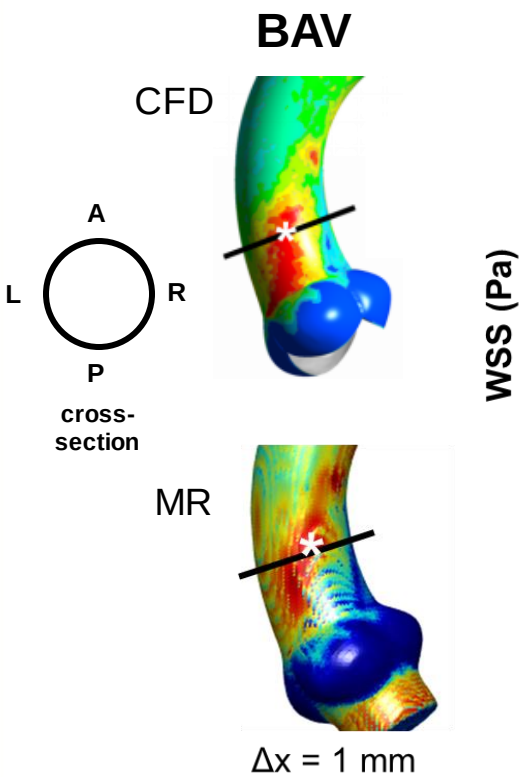
- Elevated aortic WSS generated by aberrant flow
- more severe ECM dysregulation

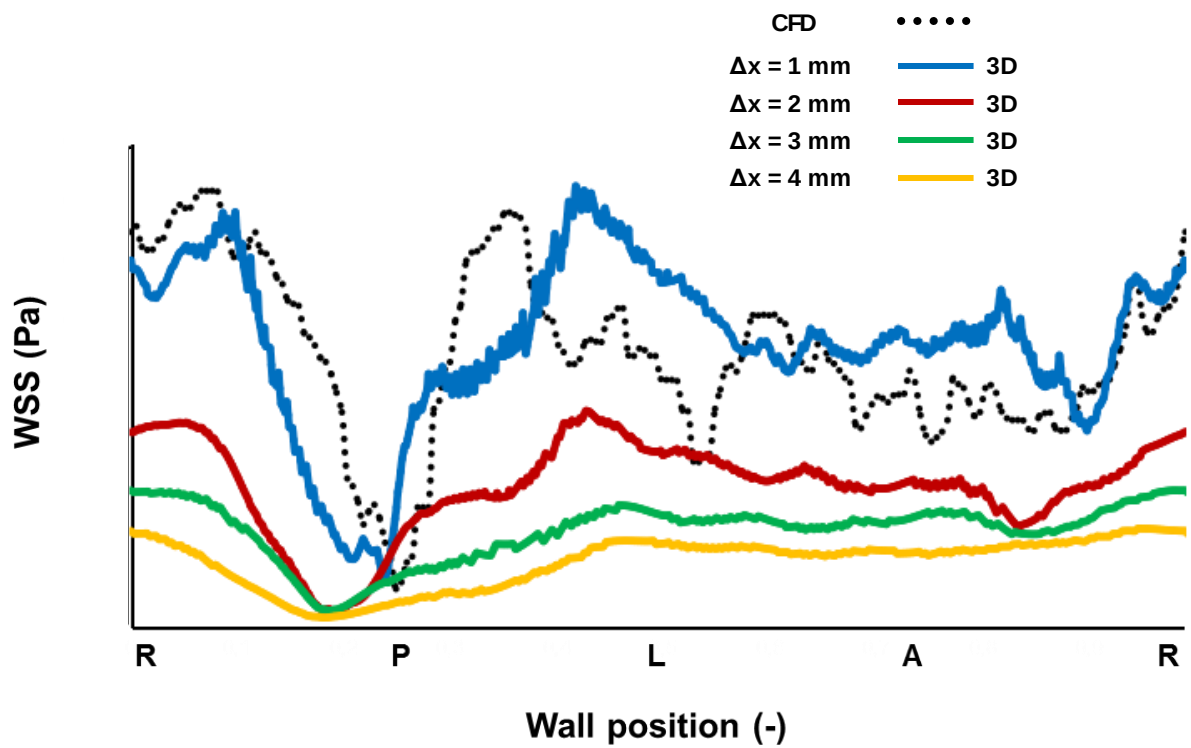
[Guzzardi, *J Am Coll Cardiol*, 2015]

Fluidynamic indexes

Wall shear stress computation: a general and benchmarked method

- Volumetric WSS: properly computes trends over space, but not local values



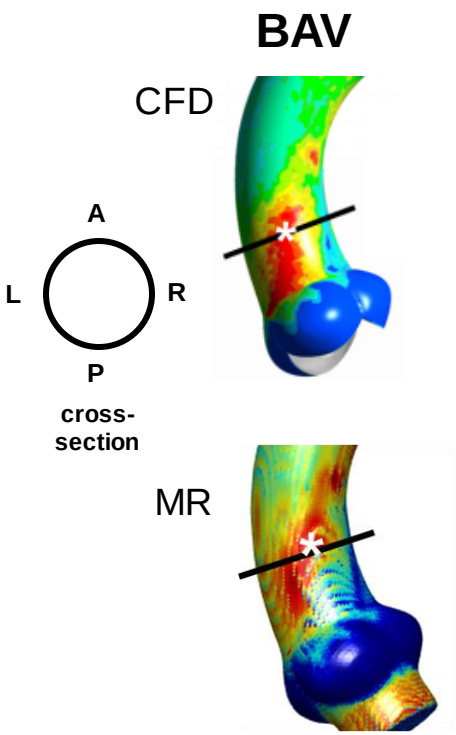


[Piatti et al., J Biomech, 2017]

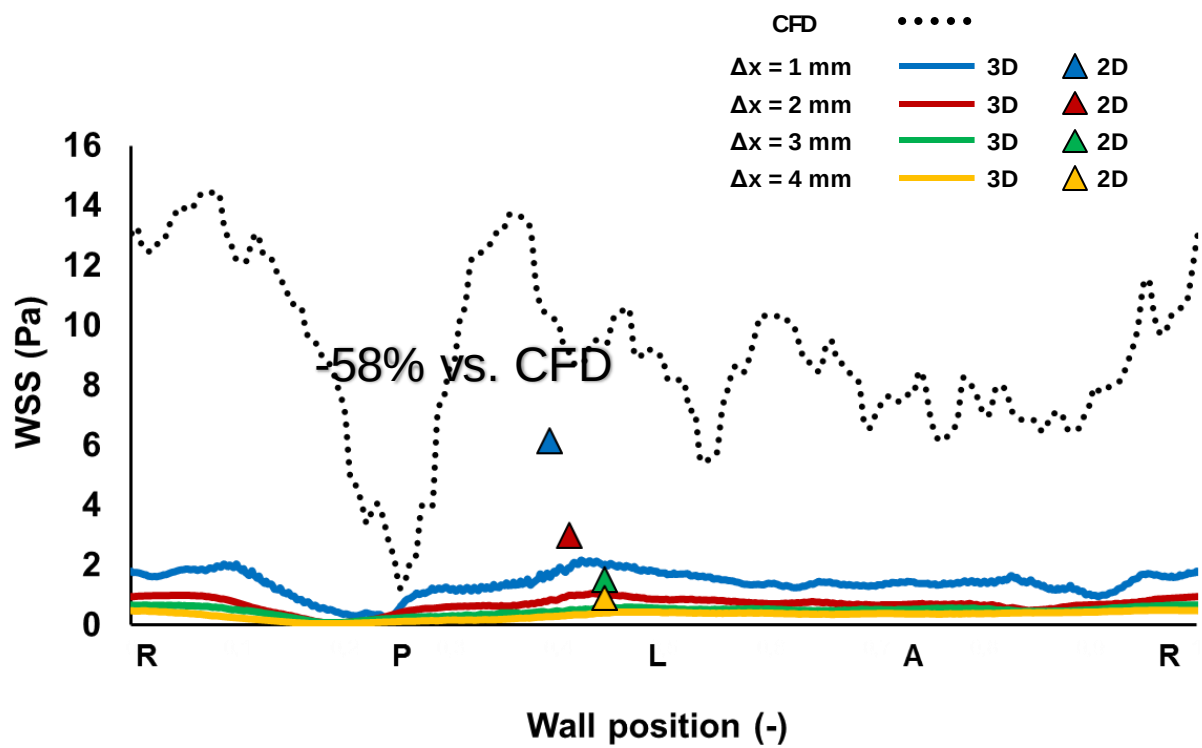
Fluidynamic indexes

Wall shear stress computation: a general and benchmarked method

- Volumetric WSS: properly computes trends over space, but not local values
- Local 2D WSS computation: improves local assesment



Δx = 1 mm



[Piatti et al., J Biomech, 2017]