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# 4D FLOW MRI STUDY OF LARGE-SCALE HEMODYNAMICS CORRELATION PERSISTENCE IN THE HEALTHY HUMAN AORTA USING NETWORK SCIENCE

**Karol Calò (1), Andrea Guala (2), Diego Gallo (1), Jose Rodriguez Palomares (2), Stefania Scarsoglio (1), Luca Ridolfi (1), Umberto Morbiducci (1)**

(1) PolitoBIOMed Lab, Department of Mechanical and Aerospace Engineering, Politecnico di Torino, Turin, Italy

(2) Hospital Universitari Vall d'Hebron, Department of Cardiology, CIBER-CV, Vall d'Hebron Institut de recerca (VHIR), Universitat Autonoma de Barcelona, Barcelona, Spain

## INTRODUCTION

The quantitative characterization of the large-scale features of the aortic hemodynamics is currently based on spatially and/or temporally-averaged quantities which do not fully capture the four-dimensional complexity of real cardiovascular flows. Aiming at extracting as much information as possible from *in vivo* hemodynamic data, this study proposes a network-based approach [1] to analyze the spatiotemporal correlation of large-scale flows in a 4D flow MRI dataset of 42 healthy thoracic aortas [2]. In detail, the correlation between the flow rate waveform at the inflow of the ascending aorta (AAo) and the axial velocity waveforms obtained from measured phase velocities at each voxel of the aortic domain was used to build a subject-specific *"one-to-all"* network [3]. An ad-hoc network metric was introduced to quantify the anatomical length of persistence of the correlation between the inflow rate and the large-scale fluid structures along the main flow direction. The analysis was then completed with a geometric characterization of the investigated subjects, exploring possible links between aortic geometric attributes and the dynamic similarity between inflow rate and axial flow.

## METHODS

The adopted methods are summarized in **Fig. 1**. The study population comprises 42 healthy volunteers with a tricuspid aortic valve. All details on 4D flow MRI acquisition protocol and data processing are reported elsewhere [2,4]. The study was approved by the ethics committee of the Vall d'Hebron Hospital and written informed consent was obtained from all participants. Subject-specific 3D geometry of the thoracic aorta was semi-automatically reconstructed from an angiography derived from 4D flow MRI data using ITK-Snap and its centerline was computed using VMTK (www.vmtk.org). Anatomical landmarks of the sinotubular junction (STJ), first and last supra-aortic vessels and location of the pulmonary artery (PA) bifurcation were identified from co-registered 2D cine images. For each subject the time-resolved waveforms along the cardiac cycle of the three velocity components in each voxel were obtained as reported elsewhere [2], and 3D velocity data were exported using in-house Matlab code (MathWorks Inc, USA).

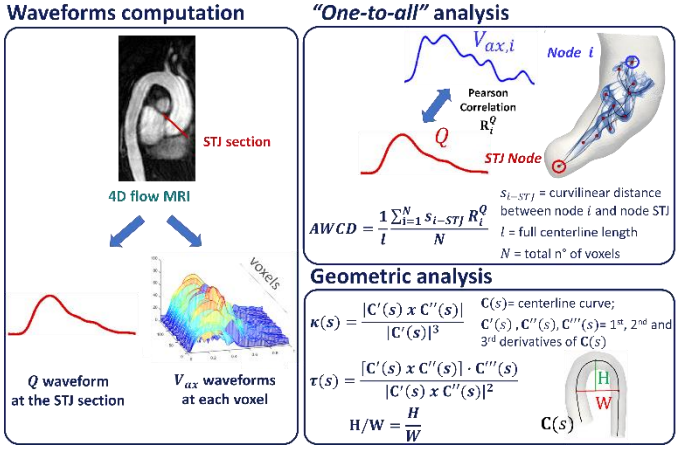


**Figure 1: Overview of study methods.**

The inflow rate $Q$ waveform was computed at the STJ cross-section and the (through-plane) axial velocity component $V_{ax}$ waveform in each voxel of the investigated aortic domain was obtained as proposed in [5]. Inspired by a previous *in silico* study on carotid bifurcation hemodynamics [3], here an *in vivo "one-to-all"* network approach was adopted to characterize the aortic large-scale intravascular hemodynamics by investigating the relationship between the shape of the subject-specific inflow rate waveform and that of the $V_{ax}$ component in each voxel. In this study, the nodes of the *"one-to-all"* network are represented by the center of the STJ section and by all the voxels of the

aortic domain. The link between the STJ node and each voxel was weighted by the Pearson correlation coefficient $R_i^Q$ between $Q$ and $V_{ax}$ waveform at the *i-th* voxel, which measures the dynamic similarity between the inflow rate and the axial velocity waveforms in the aorta. To quantitatively characterize the *"one-to-all"* network structure, the curvilinear distance $s_{i-STJ}$ between the STJ node and voxel $i$ was calculated along the centerline, weighted by the value of $R_i^Q$ and averaged over all the $N$ voxels, obtaining the ad-hoc network metric *Averaged Weighted Curvilinear Distance AWCD* [3] that quantifies the anatomical length of persistence of the $Q$ *vs.* $V_{ax}$ waveforms correlation *in vivo*:

$$AWCD = \frac{1}{l}\frac{\sum_{i=1}^{N} s_{i-STJ} R_i^Q}{N}. \qquad (1)$$

To account for the geometric variability of the investigated dataset, *AWCD* was normalized with respect to the full thoracic aorta centerline's length $l$. To complete the analysis, the aortic geometry was characterized in terms of average curvature $\bar{\kappa}$ and torsion $\bar{\tau}$ [6], width W of the aortic arch (3D distance between the points of the AAo and descending aorta (DAo) at the level of the right PA), height H of the aortic arch (maximal vertical distance between W and the highest point of the aortic arch) and height over width ratio (H/W).

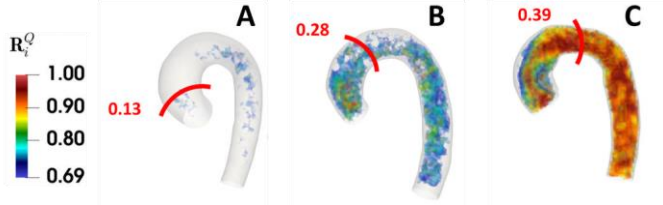


**Figure 2: $R_i^Q$ volumetric maps and *AWCD* (red line) for three representative subjects (presenting, respectively, the minimum, around the mean and the maximum $R_i^Q$ value). Only $R_i^Q$ values above the full dataset median value ($\widehat{R^Q} = 0.69$) are shown.**

## RESULTS

The influence of the subject-specific inflow rate on the aortic axial flow structures is presented in **Fig. 2**, where the volumetric maps of $R_i^Q$ values above the median ($\widehat{R^Q} = 0.69$) of the distribution pooled over the entire dataset is displayed. In detail, the three subjects presenting the minimum, around the mean and the maximum value of $Q$ *vs.* $V_{ax}$ correlation are presented here. Notably, it emerged that, in those subject with $R_i^Q$ mostly below the median, $Q$ and $V_{ax}$ waveforms are weakly correlated ($R_i^Q$ = 0.30 on average for case A), with a non-negligible amount of negative $R_i^Q$ values (i.e., indicative of retrograde axial flow [3]). In subject C, on the other hand, axial structures waveforms are strongly correlated with the inflow rate ($R_i^Q$ = 0.84 on average) and the negative correlations are mostly confined to the AAo inner wall. To quantify the anatomical persistence length of the $Q$ *vs.* $V_{ax}$ correlation, *AWCD* is reported in **Fig.2** and represented with a red line. Consistently with the $R_i^Q$ distribution, subject A presents the lowest *AWCD* with the correlation between $Q$ and $V_{ax}$ only persisting for 13% of the full thoracic aortic length, whereas in subject B the dynamical similarity between axial flow and inflow rate vanishes, on average, at the distal end of the AAo. In subject C, *AWCD* is among the highest in the dataset, with the $Q$ *vs.* $V_{ax}$ correlation propagating almost for the 40% of the full aortic length. Regarding the geometric analysis, as an example **Fig.3** displays *AWCD* box plots obtained after stratifying the 42 subjects in three groups based on H/W tertiles. In the range of H/W values ([0.31,0.64], median = 0.43) characterizing the healthy aortas, an increasing trend for *AWCD* emerged, even if not significant ($p$ = 0.62). Similarly, no significant links emerged between the *"one-to-all" AWCD* metric and all the other investigated geometric attributes.

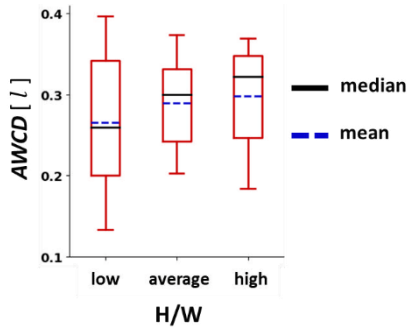


**Figure 3: Box plots of *AWCD* distributions obtained by dividing H/W in three groups based on tertile values.**

## DISCUSSION

In this study, a *"one-to-all"* network approach is adopted to quantitatively investigate the anatomical length of persistence of the similarity between the inflow rate at the STJ and the large-scale fluid structures along the main flow direction *in vivo* on a 4D flow MRI dataset of healthy human aortas. To do that, an ad-hoc network metric, the *AWCD*, was introduced to measure the anatomical persistence length of the correlation. The findings of the study suggest that in those healthy subjects where $R_i^Q$ values are low, the $Q$ *vs.* $V_{ax}$ correlation generally persists up to the mid AAo, whereas in cases where the correlations are higher their anatomical persistence length extend distally up to one third of the full thoracic aortic length (i.e., *AWCD* > 0.33) to include large portions of the aortic arch. No significant association emerged between the anatomical persistence length of the correlation and the geometric attributes, although a clear trend was observed between *AWCD* and H/W suggesting that the role of geometric features in transporting large-scale fluid structures dynamically similar to the inflow rate waveform downstream in the healthy aorta deserves further investigation. In conclusion, the here-proposed approach allows for the first time to evaluate the anatomical length of healthy aorta over which the subject-specific inflow rate waveform markedly shapes the large-scale fluid structures, thus providing a measure of the spatiotemporal aortic flow coherence *in vivo*. Besides investigating more in detail the role of geometric attributes on aortic flow heterogeneity, future studies should also adopt the here presented approach to analyze the impact that aortic stiffness and distensibility might have on large-scale hemodynamics.


## ACKNOWLEDGEMENTS

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