## Supplementary material

### Inclusion and exclusion criteria

The population consisted of vEDS patients from our institution and healthy subjects of Caucasian origin with no tobacco history, a weight between 60 and 100 kg, and a body mass index between 18 and 30 kg/m2. Brachial blood pressure was checked as normal (below 140 mm Hg for the systolic and 90 mm Hg for the diastolic blood pressure after 10 min of recumbent rest), electrocardiogram did not present any abnormalities, and laboratory tests (blood tests, urine analysis and toxins research) were within normal range.

Subjects were excluded: if pregnant; having allergy to ultrasound gel or skin lesions (severe eczema, wounds, etc. …), which prevents the application of the ultrasound probe on the region of interest; subjects not affiliated with French social security health benefits; refusal, lack of language skills or mental inability to sign consent; acute or chronic systemic disease; alcohol abuse; medication; current smoking; ingestion of excessive amounts of common tea, licorice, coffee, chocolate and/or beverages containing caffeine (>5 cups/day, about 500 mg of caffeine/day); and subjects in the exclusion period on the national register of persons undergoing biomedical research.

### Protocol procedure

Ultrafast ultrasound imaging (UF) and SphygmoCor were performed successively on the same day and in the same examination room to measure two different types of PWV:

- a local carotid PWV (ufPWV) using the UF device

- a regional carotid to femoral PWV (cfPWV) using the SphygmoCor device.

**Ultrafast ultrasound imaging of local carotid PWV (ufPWV)**

**Ultrasound data recording**

The ultrafast ultrasound imaging system Aixplorer used in this study is developed by the SuperSonic Imagine company (Aix-en-Provence, France). It is equipped with a linear array probe (128 elements, 8 MHz central frequency, pitch 0.2 mm, 28 mm elevation focus). It is well-known that frame rate limitation of conventional ultrasound imaging scanner is due to the trade-off between frame rate and the number of scan-lines (focused beams). In order to obtain both a very high frame rate and a large field of view, the Aixplorer prototype used the concept of ultrafast plane wave imaging (Figure S1) [1,2]. In its original form, it added coherently sub-images obtained by beam forming of the backscattered echo from plane waves transmitted with different inclinations. This system is programmable per channel both to receive (128 channels) and to transmit (256 channels). It allows switching between the following sequences: conventional B-mode imaging and Ultrafast imaging sequence. Plane wave transmit enables the reconstruction of a complete frame from a single transmit/receive event. Beam forming is performed in our study using receive-only dynamic focusing. It enables an imaging frame rate equal to the pulse repetition frequency (transmit rate). This concept has been used to reach frame rates of up to 20 kHz in order to enable the imaging of shear wave propagation in the body. The precision of the PWV measurement is determined by the frame rate of the system [3]. In this study, this sequence was used to image the arterial pulse wave in arteries with a frame rate of 1,000 images/s (Figure S2). The acquisition of 2D ultrasound images was triggered on the R wave through the ECG-coupled imaging system, and the total acquisition duration was one second and half. Acquisitions required no apnea from the patient. Quality acquisitions were validated with instant viewing of the movie of the pulse wave propagation on the computer connected to the ultrasonic device (Movie S3). For each site (right and left CCA), measurements were repeated three times. The median value of the three measurements was used for ufPWV calculation of one subject, whereas the three measurements for each subject were taken into account for repeatability evaluation.

**Calculation of carotid PWV**

Tissue particle velocities are typically on the order of few mm/s (Figure S2 B), whereas the propagation speed of the arterial pulse wave is typically m/s. For all plane transmit insonifications, radiofrequency (RF) ultrasonic backscattered echoes are beam formed to obtain a stack of two-dimensional images in the IQ space, with a demodulation frequency equal to the transmit frequency (8 MHz). A frame-to-frame conventional axial velocity estimation is performed using an IQ cross-correlation algorithm [4]. Finally, a movie of the axial velocity is obtained with a frame rate of 1,000 Hz (Movie S3). Automatic segmentations of the anterior and posterior arterial walls were performed for each frame (Figure S2 A). Anterior and posterior wall velocities were subtracted in order to remove the global motion of the artery. A space-time representation of the arterial wall velocity is presented in Figure S2 B. In a single cardiac cycle, it was found that estimation of radial velocity exhibits two acceleration peaks (Figure S2 B lower frame) corresponding to two propagating waves: the first wave corresponds to the beginning of the systole (after aortic valve opening), the second wave corresponds to the end of the systole (after aortic valve closure). These two waves propagate in the same direction (from the aortic arch toward the brain). Between these two incident waves, early reflection waves can also be detected propagating backward (Figure S2 D). Khir et al. reported the same three characteristics using the wave intensity waveform [5]: ‘the first positive peak occurring at the start of systole represents the initial, forward compression (dP > 0) wave generated by the contraction of the ventricle. The second positive peak occurring at the end of systole indicates a forward expansion (dP < 0) wave dominating the flow at this time of the cardiac cycle. This indicates that it is a forward wave generated by the inability of the ventricle to contract quickly enough to keep up with the momentum of the blood in the arteries generated by the earlier part of systole, which is the predominant cause of the halt of blood flow at the end of systole [6]. In mid-systole there is a period when the wave intensity is negative, indicating that backward, reflected waves are dominating the forward waves.’ Conventionally [7] a linear regression of the first and the second acceleration peaks was performed successively to compute the wave velocities based on the space-time representation (Figure S2 C). Therefore two PWV were provided: one in early-systole and one in end-systole.

**Measurement of aortic PWV (cfPWV) by SphygmoCor**

**Device**

cfPWV was measured by a conventional method using SphygmoCor and more particularly its application pulse wave velocity SphygmoCorVx system dedicated to the calculation of aortic PWV.

**Measurement protocol**

Pressure sensors (high fidelity applanation tonometers) were placed successively on two arterial sites distant (carotid and ipsilateral femoral sites) and recorded the passage of the pulse wave on each site. Measurements were performed according to the recent guidelines [8-10]. For the purpose of the study, three measurements of cfPWV for each subject were performed. Each measurement was displayed by the device as a mean ± standard deviation of 10 PWV recordings after obtaining a well-shaped arterial pulse wave. One of three measurements with the lowest coefficient of variation was allocated as the subject’s cfPWV, whereas the three measurements for each subject were taken into account for repeatability evaluation.

**Calculation of aortic PWV (cfPWV)**

cfPWV calculation was derived from the ratio of the transit time over the distance between the two sites (carotid and femoral, relative to ECG R wave). The transit time was assessed as the time difference between two characteristic points on carotid and femoral waveforms detected by the “intersecting tangent algorithm”. This type of algorithm presents the advantage of not underestimating PWV in case of low-rise time of the waveform, as does the Complior system by using the point of maximal upstroke during systole in its algorithm [11]. The carotid to femoral (cf) distance calculation was the direct distance measurement between the carotid and femoral sites corrected by a scaling factor of 0.8 [10].

**References**

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## Supplementary figure legend

**Figure S1.** **Ultrafast Ultrasound Imaging Principle**

**(Left panel**) Conventional imaging with 128 focusing lines in emission and reception

**(Right panel**) Ultrafast ultrasound imaging acquisition with one plane wave emission and focusing only on reception

**Figure S2. Carotid Arterial Pulse Wave Velocity Computing Using Ultrafast Ultrasound Imaging**

**(A)** Automatic segmentations of the anterior and posterior arterial walls were performed for each frame. **(B)** Tissue velocity along the arterial wall as a function of time. The three plots show at one location of the wall (from top to bottom): displacement, velocity and acceleration of the arterial wall. The latter displays the two acceleration peaks corresponding to the two propagating waves. **(C)** Calculation of the PWV derived from the slope of the acceleration peak. **(D)** Magnification of the dotted outline square in B showing the visualization of the early reflection waves, propagating backward between the 2 incident waves.

**Movie S3.** **Movie of The Propagation of The Arterial Pulse Wave Through The Carotid Arterial Wall**

## FIGURE S1

## Figure 1_Pernot_EHJ FIGURE S2

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