# The role of ECG-synchronization in the planning of endovascular aortic repair

Ph.D. Thesis

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# Introduction

Cardiovascular disease is the leading cause of death in developed countries, with a yearly mortality rate of 60 000 in Hungary, twice as much as the mortality of malignant neoplasms. Besides coronary artery disease and stroke, a large proportion of the cases is related to aortic disease. Aortic disease involves aortic aneurysms, acute aortic syndrome (aortic dissection, intramural hematoma, penetrating aortic ulcer, blunt thoracic aortic injury), connective tissue disorders (e.g. Marfan syndrome) and other congenital abnormalities (e.g. coarctation of the aorta).

An Egyptian papyrus was the first to mention an arterial aneurysm. The Ebers Papyrus is dated to circa 1550 BC, and describes a traumatic arterial pseudoaneurysm, which should be treated with „knife and fire". After 3500 years of this open surgical dominance, Volodos, a Ukrainian vascular surgeon performed the first thoracic endovascular aortic repair in 1986, followed by the first abdominal endovascular aortic repair in 1989.

The endovascular technique became widespread in the following years. Besides the advancements in interventional radiology, rapid progressions in diagnostic radiology was also mandatory to cover the needs of this new technique. Given its unprecedented diagnostic accuracy, computed tomography (CT) gained wider and wider availability, becoming the first choice imaging modality in aortic disease already in the early years of its evolution. Since then, spatial and temporal resolution vastly improved due to the technical developments. With a first generation CT scanner, imaging of a slice took several minutes, whereas nowadays' state-of-the-art equipments using wide detectors enables us to use ECG-synchonization: one can create multiphasic images within one heart cycle.

# Objectives

Our objective was to tell whether or not the use of the diastolic phase images of the ECG-synchronized CT datasets leads to undersizing in endovascular aortic repair planning. In order to precisely quantify the rate of the aortic strain, we performed the following studies:

1. Elderly patients
    a. Is aortic strain measurable on retrospectively gated CT images?
    b. What phases of the R-R cycle can be used to measure the largest and smallest diameters of the aorta?
    c. What is the rate of aortic strain in our elderly, atherosclerotic study population?
2. Young adults
    a. Is aortic strain measurable on prospectively triggered CT images?
    b. What is the rate of aortic strain in our study population of adults younger than 50 years?

# Methods

Our studies were performed using the 256-slices CT scanner (Brilliance iCT, Philips Healthcare, Best, The Netherlands) of the Imaging Department of the Heart and Vascular Center of Semmelweis University. Patients gave informed consent to participate in our study. Study protocol and consent form was approved by the Regional Ethical Committee (TUKEB 133/2011).

## First study: elderly population

### CT imaging

Imaging of the aorta was performed in 28 patients (14 men, mean age 72.9 ± 12.0 years) using an ECG-gated protocol tailored for the imaging of the aorta. The study was performed on images readily available from patients being evaluated for transcatheter aortic valve repair or from patients with suspected acute aortic syndrome. Hemodynamic parameters were measured with an electronic sphygmomanometer before contrast administration. Low-dose (tube voltage: 100 kV) native scan was followed by a retrospective ECG-gated CT angiography of the whole aorta (100 kV) with a reduced field of view to maximize spatial resolution. Nonionic contrast agent was injected into an antecubital vein at a flow rate of 4-5 ml/s using a power injector. Images were reconstructed using a sharp convolution kernel and iterative reconstruction algorithm (iDose4, Philips Healthcare, Best, The Netherlands) with a slice thickness of 1 mm and an increment of 1 mm. Multiphase images were reconstructed corresponding every 10% of the R-R cycle resulting in ten series of images for each patient. Datasets were transferred to standalone workstations for further analysis.

### Image analysis

Image analysis, vessel segmentation and cross-section measurements were performed by two independent radiologists experienced in cardiovascular imaging. Aortic calcifications were calculated using the dedicated coronary calcium scoring software of an Extended Brilliance Workspace (HeartBeat CS, Philips Healthcare, Best, The Netherlands).

Computed tomography angiography images were analyzed using an Advantage Workstation (GE Healthcare Europe GmbH, Freiburg, Germany). After automatic vessel segmentation and centerline detection, cross section area of the lumen was measured in a semiautomatic fashion at the following nine locations: ascending aorta proximal to the brachiocephalic trunk (Ishimaru Z0), between left common carotid artery and left subclavian artery (Ishimaru Z2), immediately distal to the left subclavian artery (Ishimaru Z3), 5 cm distal to the left subclavian artery (Ishimaru Z4), 5 cm above celiac trunk ostium (ACT), below renal ostia (REN), middle infrarenal aorta (MIR), right and left common iliac artery (RCIA and LCIA). Position was matched in 3D between series of different phases by recording the slice number which involved the segment of the centerline at the exact point of the measurements taken. Cross section areas were recorded in $mm^2$. Diameter was calculated as the diameter of a virtual circle with the same cross-sectional area (area derived effective diameter). To minimize measurement errors and increase interreader agreement, direct diameter measurements were avoided. Pulsatility was defined as the largest difference between systolic maximum and diastolic minimum diameter or area. Vessel strain was calculated as a ratio of pulsatility and minimum area $[(A_{max}-A_{min})/A_{min}]$.

### Statistical analysis

Data processing and analysis were performed using IBM SPSS Statistics 22.0 (IBM Corporation, Armonk, NY, USA) and R (R Foundation for Statistical Computing, Vienna Austria) software. Shapiro-Wilk test was used to assess the normality of the data. Wilcoxon's signed-rank test was used to compare diastolic and systolic measurements. Correlations were analyzed with Spearman's rho test. Lin's correlation was utilized to evaluate inter- and intrareader agreement. Statistically significant difference was established at $P < .05$. Continuous variables are presented as median (interquartile range).

## Second population: young adults

All adult patients under the age of 50 were included in this study who underwent coronary CT angiography (CCTA) between August 2015 and October 2015. Exclusion criteria were extreme tortuosity or incomplete visualization of the descending aorta within the field of view of the CCTA scan. Analysis of the descending aorta was performed in 52 patients (35 men, mean age 41.1 ± 7.3 years). We have performed all measurements on CCTA images readily available from patients with suspected coronary artery disease.

## CT imaging

Oral and/or intravenous β-blocker medication before and during the CCTA examination was administered using metoprolol (Betaloc; 1 mg/mL; AstraZeneca, Luton, United Kingdom; 5-mg ampoule) in order to achieve a heart rate less than 65 bpm. Blood pressure was measured with an electronic sphygmomanometer after contrast administration. Heart rate was continuously recorded during the scan.

We have modified the routine CCTA scan protocol in order to enable the analysis of the diameter changes of the descending aorta during the cardiac cycle: native calcium score scans were acquired in late systole. These low dose, non-contrast scans were acquired using the following image parameters: slice collimation of 128 x 0.625 mm, rotation time of 270 ms, tube voltage of 120 kV and tube current of 30 mAs, triggered on late systole (35%). Contrast-enhanced scans were acquired in late diastole using prospective ECG triggering at 78% ± 3% padding with the following parameters: slice collimation of 128 x 0.625 mm, rotation time of 270 ms, tube voltage of 80-120 kV and tube current of 150-300 mAs depending on the patients' body habitus. The FOV of both scans were reduced to increase spatial resolution. Nonionic contrast agent (Iomeron 400; Bracco Ltd, Milan, Italy) was injected into an antecubital vein via an 18-ga cannula using a dual-syringe power injector at a flow rate of 4.5-5.5 ml/s depending on the patients' body habitus and tube voltage, followed by a saline chaser. Images were reconstructed using model-based iterative reconstruction algorithm (IMR; Philips Healthcare, Best, The Netherlands). Datasets were transferred to a workstation for further analysis.

## Image analysis

CT images were analyzed using an IntelliSpace Portal (Intellispace Portal; Philips Healthcare, Best, the Netherlands) client workstation. Systolic native and diastolic contrast-enhanced images matched by table position were synchronously analyzed using the same window level and width. Effective diameter (representing the diameter of a virtual circle with the same cross-section area) was measured by placing an ellipsoid region of interest at three positions along the descending aorta, one measurement in each third of the visible segment (P1, P2 and P3). Locations of the measurements were chosen to have a good delineation between the aorta and the surrounding tissues on both the native and the contrast-enhanced image. Each measurement was performed three times by two independent readers experienced in cardiovascular radiology and the measurements were averaged. Pulsatility [mm] was defined as the difference between systolic and diastolic diameter ($d_{systolic}$-$d_{diastolic}$). Aortic strain [%] was calculated as a ratio of pulsatility and diastolic diameter [($d_{systolic}$-$d_{diastolic}$)/$d_{diastolic}$].

## Statistical analysis

Shapiro-Wilk test was used to assess normality. Since all parameters showed normal distribution, continuous variables are expressed as mean ± standard deviation (SD), while categorical variables are expressed as frequencies and percentages. Paired t test was used to compare diastolic and systolic measurements, while ANOVA and Tukey's post-hoc test were used to analyze the parameters at different locations. Correlations of continuous variables were calculated using Pearson's correlation coefficient. Intraclass correlation coefficient was used to evaluate inter- and intrareader agreement. A P value less than 0.05 was considered significant. Data processing and analysis were performed using IBM SPSS Statistics 23.0 (IBM Corporation, Armonk, NY, USA) software.

# Results

## First study: elderly population

A total of 4320 measurements on 28 patients were performed, involving 1800 repeated measurements on 20 patients to evaluate inter- and intrareader reproducibility.

Wilcoxon's signed-rank test showed significant difference between the cross-section areas of the diastolic and systolic phases ($P<.001$) at every anatomic location measured.

Area pulsatility is reducing along the course of the aorta: the highest level was measured at the Z0 position (42.9 $mm^2$ [28.8-74.0 $mm^2$]) with a continuous decrease along the aorta to an almost negligible value at the level of the iliac arteries (8.5 $mm^2$ [6-12 $mm^2$]. This equals to a diameter pulsatiliy of 1.0 mm (0.6-1.6 mm) at the thoracic aorta (Z0), 0.7 mm (0.6-1.0 mm) at the abdominal aorta (REN), and 0.5 mm (0.4-0.8 mm) at the common iliac arteries. As vessel diameter is decreasing more rapidly than pulsatility, vessel strain is somewhat higher in the infradiaphragmatic segments but does not reach the level of significance – 3-5% was found throughout the aorta with wide interquartile ranges.

To identify the positive and negative extremes in the R-R cycle of aortic pulsatility, we derived a parameter representing the precession of the actual diameter relative to the mean diameter $[(d_{actual}-d_{mean})/d_{mean}]$. This resulted in a graph resembling an arterial pressure curve, with a systolic extreme at 30% and a diastolic extreme at 90% of the R-R cycle.

Lin's concordance coefficients were 0.987 for interreader (range: 0.985-0.991; strength of agreement: substantial) and 0.994 for intrareader (range: 0.993-0.995; strength of agreement: almost perfect) correlations.15 A higher interreader variability was found between iliac artery measurements (concordance coefficients were 0.831 for RCIA and 0.267 for LCIA; strength of agreement: poor). Therefore, iliac artery measurements were excluded from correlation analysis.

Negative correlations were found between aortic strain and age ($r=-0.498$, $P=.007$ at Z3; $r=-0.586$, $P=.001$ at Z4; $r=-0.539$, $P=.003$ at ACT), aortic strain and plaque area ($r=-0.429$, $P=.026$ at Z4; $r=-0.436$, $P=.023$ at ACT), and age and BMI ($r=-0.412$, $P=.029$). Positive correlation between age and plaque area ($r=0.594$, $P=.001$) was found. Pulse pressure did not show any significant correlation with the other parameters.

## Second study: young adults

A total number of 936 measurements on 52 patients were performed.

Significant difference was found between systolic and diastolic diameters at every location (all P<.001). Average aortic pulsatility was 1.5 ± 0.6 mm at P1, 1.6 ± 0.7 mm at P2 and 1.7 ± 0.7 mm at P3, with a corresponding aortic strain of 6.7 ± 3.1% at P1, 7.4 ± 3.5% at P2 and 8.1 ± 3.6% at P3. The differences between the pulsatility and strain of the measurement points were not significant (P=.739 and P=.344, respectively). Average descending aortic pulsatility was 1.6 ± 0.6 mm (range 0.3-3.4 mm) with a corresponding aortic strain of 7.4 ± 3.2% (range 1.5-16.2)

Aortic strain and pulsatility did not show any significant correlation with pulse pressure (P=.693), patient age (P=.649) or other anamnestic data.

Intraclass correlation coefficient was in the range of 0.95-0.96 for interobserver and in the range of 0.95-0.97 for intraobserver analysis, both representing excellent agreement.

Average effective dose was 3.6 mSv per patient.

# Conclusions

Based on our two studies the following conclusions can be made:

1. Elderly patients
   a. Aortic strain can be measured on restrospective ECG-gated CTA images with high reliability and reproducibility, low intra- and interobserver variability.
   b. Maximal aortic diameter can be measured at 30%, whereas minimal diameter can be measured at 90% of the R-R cycle.
   c. Thoracic aortic strain is around 3-4%, which is somewhat larger in the abdominal segment. This equals to a systolodiastolic diameter change of circa 1.1 mm in the thoracic aorta, and a <1 mm change in the abdominal segment.
2. Young adults
   a. Aortic strain can also be measured on prospective ECG-triggered CT angiography images with high reliability and reproducibility, at a much lower radiation dose.
   b. Thoracic aortic strain is around 7-8% in young adults (<50 years), which equals to a 1.6 mm systolodiastolic diameter change.

In conclusion, the pulsatility of less than 10% measured in our study population provides evidence that diastolic image use in endovascular aortic repair planning does not lead to undersizing.

# Publications

## Publications related to this work

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