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Quantification of aortic elasticity: development and experimental validation of a method using computed tomography

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Abstract Aortic distensibility depending on aortic cross-sectional area changes is an important parameter for the grading of vascular diseases. This study measured aortic area changes by multidetector computed tomography. An image reconstruction algorithm was developed to assess aorta diameter and area as a function of the cardiac cycle with sufficient time resolution along the entire length of the aorta by

four-detector row computed tomography. The algorithm was tested on porcine aortic specimens and compared with an optical reference method. The error of the relative vessel area change comparing the two methods was found to be about 3%. Initial tests on patient datasets indicate that clinical application is feasible. The proposed method has the advantage that it can easily be integrated into a modified routine CT angiography study and allows the measurement of aortic cross-sectional area changes.

Keywords Aortic elasticity · Aortic distensibility · Multidetector-row computed tomography · Functional imaging of vessel wall

Introduction

Multidetector-row computed tomography (MDCT) as used for vessel imaging [1, 2] allows very accurate depiction of anatomy; however, functional information is not provided. Vessel elasticity quantified as distensibility is an interesting functional parameter of the vessel wall [3–6]. Several methods have been proposed to achieve this including pulse-wave velocity measurement employing either magnetic resonance velocity mapping [7–11] or Doppler ultrasound [11–14]. Ultrasound methods suffer from inconstant applicability. Magnetic resonance (MR) pulse wave velocity measurements are unreliable in situations with complex flow patterns [9]. It has been shown that MDCT with retrospective electrocardiographic (ECG)-gating provides car-

diac images with high temporal resolution [15–17]. Thus the potential for a combined morphology and functional image protocol makes the CT method attractive. In addition, MDCT is readily available and applied in aneurysm follow-up studies [18, 19]. Therefore CT could potentially provide further preventative information in the treatment of a frequent disease in industrial countries.

In this study we demonstrate that aortic wall movements can be visualized with MDCT. The method is based on ECG-gating and a special image reconstruction algorithm to obtain time-resolved images from CT angiography data. We provide experimental validation of this method in a phantom setup and show preliminary results of its application to patient data.

Materials and methods

Our method for measuring aortic area changes was validated using a phantom setup with porcine aortic specimens. In addition, it was tested on angiography datasets from patients undergoing routine MDCT coronary angiography.

Vascular elasticity is quantified as distensibility D [20] which is defined as the relative change in vessel cross-sectional area A that occurs during the cardiac cycle, divided by the corresponding change in blood pressure Δp : $D = \Delta A / (A_0 \cdot \Delta p)$. A_0 is the minimum vessel area, and ΔA is the difference between maximum and minimum cross-sectional area [21]. While Δp can be determined by sphygmomanometry, the relative change in vessel cross-section $\Delta A / A_0$ must be calculated from time-resolved images of the aorta. Below, this value is defined as relative vessel area change = $\Delta A / A_0$ 100%.

Image acquisition and reconstruction

All experiments were performed using a multidetector-row CT scanner (SOMATOM Volume Zoom, Siemens Medical Solutions, Erlangen, Germany). To reconstruct time resolved CT data retrospective ECG-gating was added to a slightly modified CT angiography protocol. The acquired raw dataset was used to obtain two image sets. First, standard angiography images without ECG synchronization were calculated with the conventional image reconstruction environment of the CT scanner. Second, time-resolved

images were calculated with the present ECG-gated algorithm. For this the raw projection data from the CT scanner were transferred to a standard PC via a local network. On this PC retrospective ECG-gating and image reconstruction was performed using programs developed using Matlab (MathWorks, Natick, Mass., USA) and Visual C++ (Microsoft, Redmond, Wash., USA). An algorithm was developed that uses data from several heart beats for image reconstruction [22]. For this scanner such a multiphasic image reconstruction algorithm with sufficient time resolution was commercially not available. The selection of data belonging to a certain heart phase allows the improvement in temporal resolution at the expense of spatial resolution (Fig. 1). Temporal resolution depends on the number of rotations used for interpolation, heart rate, and scanner rotation time [15]. For an interpolation range of four rotations, which was used in this study, temporal resolution ranged between 90 and 250 ms. With a heart rate of 70 bpm, as was used in the phantom experiments (see below), a temporal resolution of 140 ms was obtained. To provide some oversampling 20 time frames per heart cycle are calculated. Images were reconstructed at 0%, 5%, 15%... 95% of the RR interval of the ECG. From this image series vessel area was calculated by simple thresholding by two experienced readers. The threshold value S_t , which is a critical value for the determination of the vessel area, was calculated from the mean signal intensity S_v in the vessel and the signal intensity in the background S_b to $S_t = (S_v + S_b) / 2$.

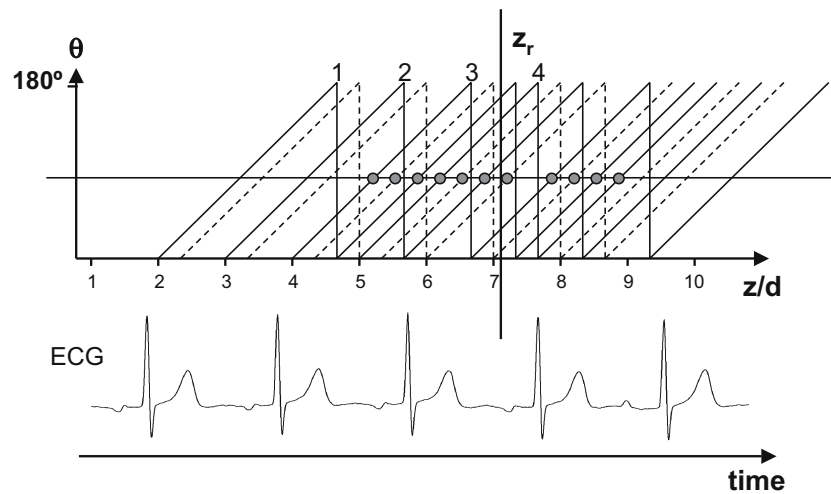


Fig. 1 Principle of retrospective cardiac gating. *Upper row* Plot of detector angle for each of four detectors as a function of table position z over slice collimation d for a pitch value of 0.66. The first step is to make use of opposite projections, i.e., projections where X-ray tube and detector are interchanged (*dashed lines*). The same projection angle is available at different heart phases, and each measured projection can be assigned a time within the cardiac cycle

where it was acquired. A number of possible data values for each angle are available (*circular dots*), which differ in spatial distance to the desired reconstruction position z_r . Considering the ECG signal, these values also differ with respect to the desired temporal position. These values are filtered so that projections which fit best contribute most to the image

Experimental setup

To test the accuracy of the method a phantom setup was constructed. The phantom provided an artificial pulsatile circulation through ex-vivo porcine aortic specimens (Fig. 2). Water from a reservoir enters a self-constructed pulsatile pump, which consists of a cylinder with two valves and a pneumatically driven piston. The pump system allowed the programming of arbitrary pressure waveforms. An idealized physiological pressure profile with minimum pressure of 80 mmHg and maximum pressure 120 mmHg was used. Flow rate was not measured. The pulsatile flow enters a porcine aortic specimen, which is located inside a water-filled chamber. After passing the specimen the flow passes a hydraulic resistance, which can be changed to set systolic pressure. Before returning to the reservoir it reaches an overflow chamber, which can be adjusted in height to select diastolic pressure.

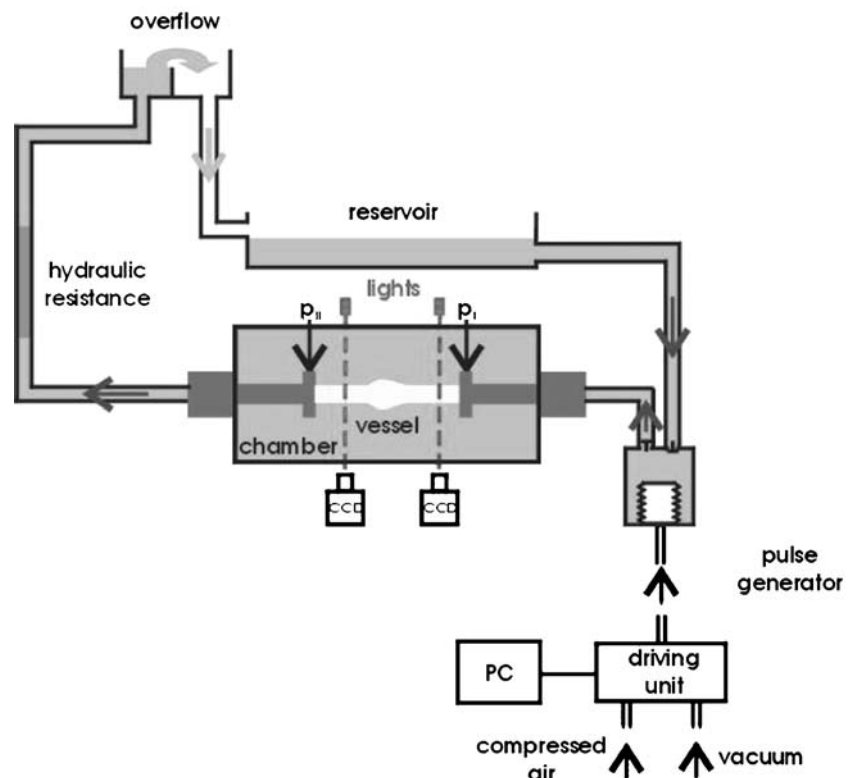
The cross-sectional measurements were performed at two locations (distance 90 mm) using two line charge-coupled-device (CCD) cameras (DALSA, Waterloo, Ont., Canada) illuminated by a 500-W halogen floodlight. The CCD camera has a 0.1 mm pixel spacing and is read out at a temporal resolution of 0.1 ms. As change in area varies along the length of the specimen, measurement at two locations gives two different change in area values for each specimen. Thus 14 relative change in area values were calculated from the 7 specimens.

To simulate the human aorta specimens of porcine aorta were used. Seven porcine aortas were obtained from a local slaughterhouse 12 h before the experiment. Specimens were cut to a length of 20 cm, and branching vessels were cut and tightly sutured. Pump frequency was set to 70 bpm and pulse pressure to 40 mmHg. The horizontal projections of the line-scan CCD camera underwent a simple threshold algorithm to detect the vessel boundary. Vessel cross-sectional area A was calculated assuming a circular vessel cross-section.

The entire phantom set-up was placed on the patient table of the CT scanner. The specimens were scanned at 120 kVp, 150 mAs, with 2.5 mm collimation, a pitch of 0.375, and a scan length of 25 cm. The collimation of 2.5 mm was used to achieve a reasonable image acquisition time for the length of aorta. The control signal from the driving unit was recorded during the measurement as a substitute for the ECG signal using a separate PC. For each of the seven specimens two positions were analyzed corresponding to the CCD camera locations, resulting in 14 change in area values.

Vessel area was then plotted as a function of time within the cardiac cycle for each method. Furthermore, the relative changes in vessel area as a function of minimum vessel area detected by the CCD camera were plotted against the CT result for all 14 measurements and correlation was calculated. The Bland-Altman [23] test was performed to

Fig. 2 Schematic representation of the phantom setup, consisting of a computer-controlled pulsatile pump and an aortic specimen, which is located inside a water-filled chamber. The cross-section of the specimen is measured at two locations using two line-CCD cameras. The setup fits onto the patient table of the CT scanner



assess the statistical significance of the degree of concordance of the two methods.

Study on patient CT angiography datasets

The method was also tested on scans of two patients who had been enrolled in a previous heart study with cardiac CT for coronary angiography (protocol: 120 kVp, 150 mAs, 1 mm collimation, pitch 0.375) for which ethics approval and informed consent had been properly obtained [24]. We selected a dataset from one 64 year-old patient who had obvious atherosclerotic changes (i.e., vessel wall calcification and clinical symptoms of angina pectoris) and from a 17 year old patient requiring a CT for a pulmonary vein abnormality who otherwise was not known to have any cardiovascular disease.

While the standard angiography images were reconstructed on the scanner console, the CT raw data were used to obtain a second, time-resolved image set. This allowed analyzing vessel area changes in the upper part of the descending thoracic aorta covered by the cardiac scan. Images were reconstructed and processed as described above. The patient datasets were reconstructed using the same protocol as for the phantom study. Blood pressure was not measured.

Results

The ECG-gated CT images from the phantom measurement showed good contrast between the contrast-medium inside the vessel and the surrounding water (Fig. 3a). Data from four rotations were used for ECG gating. With a table feed of $0.375 \times 10 \text{ mm} = 3.75 \text{ mm}$ per rotation, this gives a range of 15 mm in z , from which the data are taken. Additionally, the collimation of 2.5 mm broadens the slice profile so that the effective z -axis resolution is approx. 17.5 mm. Vessel area was determined in all samples using a threshold segmentation. The threshold was set to the mean value between vessel and background levels. From these values the relative area as a function of minimum area was calculated (Fig. 3b). The corresponding data from the CCD camera (Fig. 3c) allowed reliable detection of the edge of the vessel. A plot of vessel area as a function of time within the cardiac cycle indicates that there is a good agreement between the methods for this measurement (Fig. 3d). Considering the pulse pressure of 40 mmHg a mean distensibility of $(2.7 \pm 0.9) \times 10^{-5} \text{ Pa}^{-1}$ was calculated from the CT data over all 14 measurements, while the distensibility was $(2.8 \pm 1.0) \times 10^{-5} \text{ Pa}^{-1}$ with the optical method. The standard deviations are indicated as error bounds with the mean values.

To assess the degree of agreement between the two methods the relative changes in vessel area detected by the

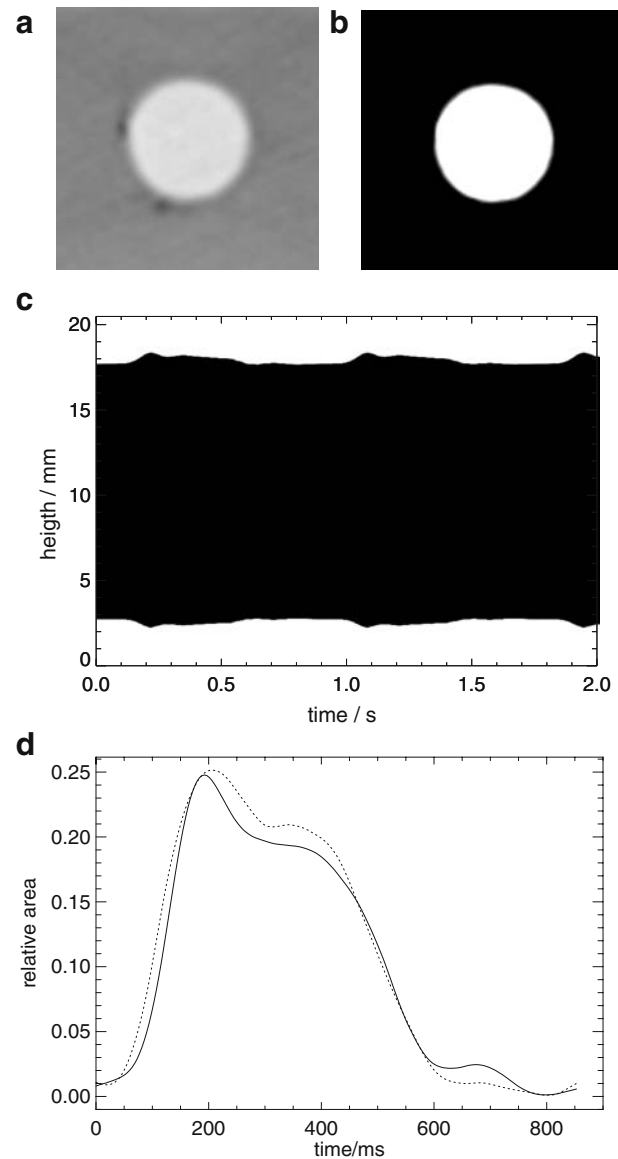


Fig. 3 Processing steps required to calculate vessel area, shown for one example measurement. The reconstructed CT images (a) are segmented using a simple gray-scale threshold (b). From the data of the line-scan CCD camera (c), vessel area is calculated from horizontal projection of the vessel assuming a circular cross-section. The resulting area vs. time curves for both methods are shown (d); *solid line* CCD data; *dashed line* CT data. Relative area is defined as area relative to the minimum cross-sectional area

CCD camera were plotted against the CT result for all 14 measurements in Fig. 4a. The line that represents perfect correlation ($y=x$) is included for reference. An excellent correlation between the two methods was found, as is described by the linear correlation coefficient $R^2=0.96$.

Furthermore, the Bland-Altman analysis was performed where the difference between the two methods was plotted

as a function of the mean (Fig. 4b). The mean of the differences (shown as a solid line) is approx. 0, indicating that there is no substantial bias between the two methods. The lines corresponding to the mean plus and minus two standard deviations are shown as dashed lines. These values of the relative vessel cross-sectional area change lie at approx. 0.03 above and below the mean difference. Since 95% of the differences are expected to fall between these limits, the CT measurement does not deviate by more than $\pm 3\%$ from the CCD value.

The CT method was applied to two patient datasets (Fig. 5). CT cross-sections are shown through the thoracic aorta during both diastole and systole for a young patient without aortic disease and a 64-year-old patient with coronary heart disease. The corresponding plot of the relative vessel area vs. time within the cardiac cycle shows reduced vessel cross-sectional area change in the patient with coronary heart disease compared to the young patient.

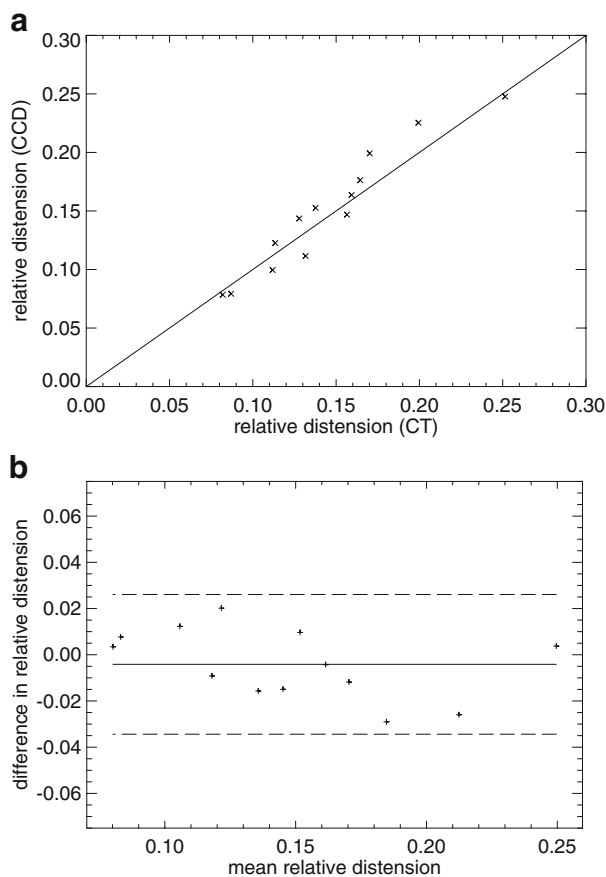


Fig. 4 **a** Plot of the relative cross-sectional area change detected by the CCD camera vs. the relative area change measured by CT $y=1.0848x$, $R^2=0.96$ The line that represents perfect correlation ($y=x$) is included. **b** Bland-Altman plot of the difference between the two methods vs. their mean

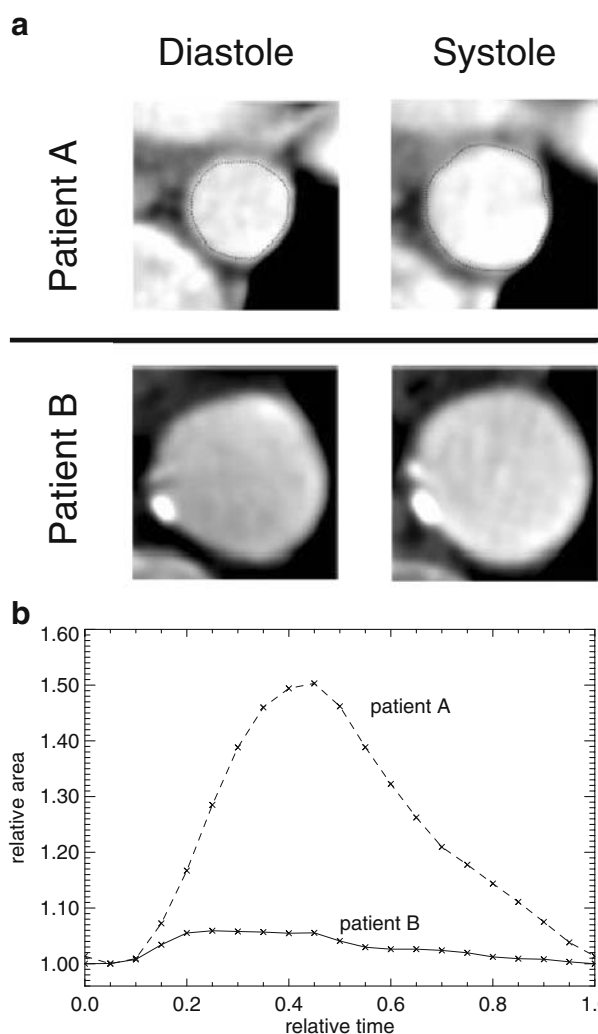


Fig. 5 **a** Images of the thoracic aorta of a 17-year-old patient (*A*, upper row) without cardiac disease are shown. Only the two time frames with minimum (diastole) and maximum (systole) distension were selected for display. Taking into account that the 50% change in area corresponds to only a 22% change in diameter, it can be seen that there is a significant difference in vessel cross-sectional area between diastole and systole. Dotted line Contours. Lower row (*patient B*) A dataset from the thoracic aorta of a patient with known cardiovascular disease. There is hardly a vessel area change visible between the two images. **b** Relative vessel area change is plotted vs. time within the cardiac cycle using data from all time frames of patient A (dashed line) and patient B (solid line) The time profile showed normal pulsatile vessel area change for patient A and greatly reduced pulsatile change in vessel area in patient B. Relative area is defined as area relative to the minimum cross-sectional area

Discussion

This study demonstrates that it is possible to calculate change in area from a dataset that is originally acquired for CT angiography using a special ECG-gated image reconstruction algorithm. The development of a dedicated off-

line algorithm for this CT scanner was necessary to obtain sufficient time resolution. Such algorithms are now implemented in newer scanners. We tested the accuracy of this method using an experimental setup with porcine aortic specimens and measured change in area with an optical reference method. In 14 measurements a mean distensibility value of $2.7 \times 10^{-5} \text{ Pa}^{-1}$ was found, applying an idealized physiological pressure profile (80–120 mmHg). The values correspond to those reported in the literature for elderly human subjects. For example, Mohiaddin et al. [11] using pulse wave velocity measurements found flow velocity increasing linearly with age, from 4.3 m/s (age 10–19 years) to 7.2 m/s (age 50–59 years), which corresponds to a distensibility from $5.2 \times 10^{-5} \text{ Pa}^{-1}$ in young subjects up to $1.8 \times 10^{-5} \text{ Pa}^{-1}$ in the elderly.

There is a good agreement between the CT method and the reference method, and Bland-Altman analysis shows that the error in relative vessel area change can be expected to be about 3%. The results are comparable to distensibility values of the abdominal aorta found in healthy elderly human subjects [11], which indicates that the porcine aorta is a reasonable model especially for the age group of patients with aortic diseases.

Relative aortic cross-sectional area changes found in young human subjects can be as high as 50%; however, they can be as low as a few percent in older subjects and in those with diseased vessels [14]. This somewhat limits the sensitivity of distensibility measurements: a relative area change of 5% is hardly detectable by this method. The relative error of the area measurement was found to be 3%. This sets a lower limit for the vessel cross-sectional area changes that can be detected by this method. Even with this limitation this method may be useful in detecting substantial distensibility changes related to aortic disease.

There are some limitations of our phantom study. The optical setup that we used was only able to measure a horizontal projection of the aortic diameter, thus a circular cross-section had to be assumed, which may have introduced some systematic error. Furthermore, it was not tested how accuracy depends on heart rate. As temporal resolution of ECG-gated CT depends on heart rate [15], it is expected that accuracy of change in area measurement also changes with heart rate. However, the temporal resolution of 140 ms used in our study is a typical value for a retrospective multiphase ECG-gating algorithm.

In the phantom study it was possible to determine vessel cross-sectional area by a simple threshold segmentation. In patient images this process is more difficult, and manual segmentation may be an obstacle in using this method in larger patient studies. Algorithms for fully automated vessel segmentation will help to make clinical application practicable. In this pilot study only a few variables were explored in the experimental setup. The leverage of other variables was not examined, such as different degrees of atherosclerosis (there is no atherosclerosis in pigs), different heart rates, and various pulse pressures.

In our study we used a 2.5 mm collimation to cover the entire length of aorta. Recent developed scanners (16- to 64-row detector CTs) allow smaller collimation. In patient examination online ECG-related tube current modulation (ECG pulsing) maintains radiation exposure acceptably [25]. Secondly, improved rotation speed will increase temporal resolution, which is expected to result in more accurate determination of aortic change in area [26]. Application of the proposed method to two patient datasets demonstrates that changes due to age and vascular disease can be detected using CT. This indicates that CT measurements in cross-sectional area change are feasible in patients.

Compared to the established noninvasive distensibility measurements methods that employ MR and ultrasound imaging, the proposed CT method has several advantages. The method requires a modified routine CT angiography examination with additional recording of an ECG signal during the scan and the subsequent reconstruction and postprocessing. Meanwhile such algorithms with adequate time resolution are commercially available for newer scanners so there will be no need of a dedicated offline reconstruction algorithm as for our experiment. Thus the relative change in area value is obtained from the same CT scan which typically lasts less than 1 min, and there is no need for an additional examination or additional X-ray dose. As CT angiography is routinely performed for many aortic diseases [27], the presented method fits well into a clinical examination protocol. We are convinced that this will make it possible to study cross-sectional area change in larger groups of patients with an indication for CT angiography with little additional effort. Aortic distensibility can then be calculated from estimated aortic pressure using brachial arterial pressure; however, the measurement of blood pressure may lead to further inaccuracy of distensibility determination. We suggest the estimation of aortic pressure using brachial arterial pressure obtained by the auscultatory method and believe it to be equal to systemic blood pressure in the abdominal aorta.

It is well known that the arterial pressure waves undergo transformation with more prominent peaks the further the waves have traveled from the heart. Thus the peak pressure in the brachial artery is higher than in the aorta. However, there are indications that these differences in aortic and brachial pressures are reduced at older ages [28]. Comparing intra-arterial pressure in the abdominal aorta and brachial blood pressure by the auscultatory method, Imura et al. [29] found that the pulse pressure is approx. 10% less by the auscultatory method. Recalculation of their data shows a slight underestimation of stiffness by the auscultatory method. Although a small systematic error of obtained pressure values exist in patient studies, the error is consistent, and therefore the distensibility measurements are valid, and comparisons between individuals are possible. One example could be the investigation of patients with aortic aneurysms, where distensibility might be a relevant factor for the predication of the risk for rupture [30].

The proposed method will benefit from the ongoing improvements in CT technology [31]. Firstly, with an increased number of simultaneously measured slices it will be easier to combine ECG-gating with sufficient volume coverage [26]. Secondly, improved rotation speed will increase temporal resolution, which is expected to result in more accurate determination of aortic change in area.

In summary, measurement of aortic cross-sectional area change using CT with ECG-gating is feasible. It can simply be integrated into modified clinical routine scanning protocols so that the value of pulsatile change in cross-sectional area can be analyzed in future patient studies.

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