Strain Measurement of Abdominal Aortic Aneurysm with Real-time 3D Ultrasound Speckle Tracking

P. Bihari a, A. Shelke b, T.H. Nwe c,d, M. Mularczyk e,f, K. Nelson a, T. Schmandra a, P. Knez a, T. Schmitz-Rixena

a Department of Vascular and Endovascular Surgery, J.W. Goethe University, Theodor-Stern-Kai 7, 60590 Frankfurt am Main, Germany
b Institute for Cell Biology and Neurosciences, J.W. Goethe University, Frankfurt am Main, Germany
c Department of Cardiology, University Medical Center, Philippus-University of Marburg/Lahn, Marburg, Germany
d Department of Cardiac and Thoracic Vascular Surgery, University Medical Center, Philippus-University of Marburg/Lahn, Marburg, Germany
e State Materials Testing Institute, Technical University Darmstadt, Darmstadt, Germany
f Institute for Materials Science, Technical University Darmstadt, Darmstadt, Germany

WHAT THIS PAPER ADDS

Three-dimensional ultrasound speckle tracking technique has been validated for detection of local displacement and strain parameters of abdominal aortic aneurysm. The technique offers the prospect of individual, non-invasive rupture risk analysis of aortic aneurysms.

Objectives: Abdominal aortic aneurysm rupture is caused by mechanical vascular tissue failure. Although mechanical properties within the aneurysm vary, currently available ultrasound methods assess only one cross-sectional segment of the aorta. This study aims to establish real-time 3-dimensional (3D) speckle tracking ultrasound to explore local displacement and strain parameters of the whole abdominal aortic aneurysm.

Materials and methods: Validation was performed on a silicone aneurysm model, perfused in a pulsatile artificial circulatory system. Wall motion of the silicone model was measured simultaneously with a commercial real-time 3D speckle tracking ultrasound system and either with laser-scan micrometry or with video photogrammetry. After validation, 3D ultrasound data were collected from abdominal aortic aneurysms of five patients and displacement and strain parameters were analysed.

Results: Displacement parameters measured in vitro by 3D ultrasound and laser scan micrometer or video analysis were significantly correlated at pulse pressures between 40 and 80 mmHg. Strong local differences in displacement and strain were identified within the aortic aneurysms of patients.

Conclusion: Local wall strain of the whole abdominal aortic aneurysm can be analysed in vivo with real-time 3D ultrasound speckle tracking imaging, offering the prospect of individual non-invasive rupture risk analysis of abdominal aortic aneurysms.

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Abdominal aortic aneurysm formation results from a degenerative disease process characterised by dilatation in the wall of the abdominal aorta. The disease affects about 2% of the elderly population1 and the main risk is rupture, associated with an overall mortality rate of 65–85%. Inflammatory processes including increased local production of matrix-degrading enzymes associated with an abnormally shortened half-life of elastin,2 apoptosis of smooth muscle cells and adherent mural thrombus play important roles in aneurysm pathogenesis. Degradation of elastic fibre and collagen results in weakening, dilatation and finally rupture of the aortic wall.3

Rupture can be electively prevented by open or endovascular repair of the aneurysm. The prevailing opinion is that aneurysms with a diameter larger than 5.5 cm are at increased risk of rupture and require operation.4 Although this statistical criterion applies to most patients, smaller aneurysms also rupture at a rate of 1.0% per year and larger aneurysms may remain unruptured.5 Therefore, there is a need for other predictive parameters, allowing a more accurate rupture risk analysis. Since rupture results from mechanical failure of the aortic wall, direct measurement of biomechanical properties of the vessel wall has been proposed as a predictive factor for rupture risk.1 Currently available in vivo methods for calculating biomechanical properties of the aorta are all based on visualising aortic wall pulsation with ultrasound,6 magnetic resonance imaging7 or computed tomography.8 The first in vivo methods described aortic wall motion as a change in
diameter (or cross-sectional area) during pulsation. From change in diameter (or cross-sectional area) and pulse pressure, stiffness of the aorta can be calculated.\textsuperscript{9} Development of new ultrasound techniques, such as tissue Doppler imaging or 2D speckle tracking, has enabled more detailed study of arterial wall motion. With these techniques, not only diameter change but also strain parameters along an arterial segment can be evaluated. However, these methods are limited in that data are collected from only one cross-sectional segment of the aorta. Such measurements might be sufficient to analyse healthy aorta, but aneurysms are complex 3D structures and their biomechanical properties vary spatially.\textsuperscript{1,10}

Through advances in medical sonography, real-time 3D ultrasound speckle tracking imaging has recently been introduced,\textsuperscript{11–13} enabling radial, longitudinal and circumferential strain measurement. The technique is not limited to detection in just one cross-sectional segment, but detects the whole 3D structure. This method has already been applied in echocardiography,\textsuperscript{11,12} but not to abdominal aneurysms.

The aim of this study was to establish and validate 3D ultrasound speckle tracking imaging for abdominal aortic aneurysms, to gain \textit{in vivo} biomechanical parameters relevant to rupture risk. The method was validated employing a silicone vascular model \textit{in vitro}, and displacement and strain parameters of aneurysmal abdominal aorta in patients were measured \textit{in vivo}.

**MATERIALS AND METHODS**

**3D ultrasound speckle tracking imaging**

Ultrasound measurements (Fig. 1) were carried out with a commercial real-time 3D-echocardiography Artida system (Toshiba Medical Systems Co, Tochigi, Japan). Full-volume electrocardiogram (ECG)-gated 3D data sets were acquired at 2.5 MHz using a PST-25SX, 1–4 MHz phased array matrix transducer (Toshiba Medical Systems Co, Tochigi, Japan). For ECG-gating during \textit{in vitro} experiments, an external trigger signal synchronised with the work cycle of the pump was employed. To obtain data sets, 2–6 sectors were scanned and automatically integrated into a pyramidal data image with a frame rate of approximately 24 fps.

Ultrasound data were stored and transferred to a computer (HP Z400 workstation, Hewlett-Packard Company, Palo Alto, CA, USA) for off-line analysis. The images were analysed with commercial software (3D Wall Motion Tracking, Toshiba Medical Systems Co, Tochigi, Japan), specifically developed for the analysis of data acquired by the Artida (Fig. 2). Speckle tracking imaging is a post-processing method to analyse the ultrasound data. The image-processing algorithm automatically subdivides the region of interest into numerous small overlapping cubes with a volume of approximately 1 cm\(^3\).\textsuperscript{13} Every cube incorporates specific 3D grey-scale image data and cube displacement is tracked during the heart cycle. Thus, \textit{real-time} speckle tracking imaging is used to analyse volume displacement of all units composing a 3D structure.\textsuperscript{11}

Displacement is calculated from the change of the \(x,y,z\) coordinates of the point of interest. Strain is calculated as: 
\[
\text{Strain} = \frac{L(t) - L_0/L_0}{\text{Pulse frequency}}
\]

Displacement is calculated from the change of the \(z\) coordinate, local displacement and strain values for each matrix point and each frame. To obtain data relevant to the aorta, and not for the heart, the apex region was removed and raw output data were further processed and visualised by MatLab Software (MathWorks, Natick, MA, USA).

**In vitro experiments**

**Experimental set-up.** A silicone aneurysm model with compliance, similar to that found in abdominal aortic aneurysms, was fabricated using a silicone rubber elastomer Med 4210 (Silicone Technology, Carpenteria, CA, USA).\textsuperscript{14} The size of the silicone aneurysm model (length 220 mm, diameter at the sides 15 mm, diameter at the middle 32 mm, length of the aneurysmal portion 70 mm and thickness 1 mm) was chosen to fit into the measurement field of the laser scan micrometer (see below). A pulsatile flow system\textsuperscript{15} with minor modifications was employed. A piston pump generated pulse pressure with a pump volume of 33.6 ml and a pulse frequency of 60 min\(^{-1}\). Mean systemic pressure was variably set with a height-adjustable reservoir. Amplitude between systolic and diastolic pressure (pulse pressure) could be modified with the size of an elastic reservoir. The vascular model was mounted horizontally in a water bath and connected through elastic tubing to the pump system (Fig. 3). Distilled water was used in the water bath and as perfusion fluid in the pulsatile flow system.

Pressure changes in the vascular model were measured with a pressure transducer (Statham P-23 ID, Gould, Cleveland, OH, USA) linked to a pressure monitor (Siemens, Erlangen, Germany). A mean systemic pressure of 90 mmHg...
and pressure amplitudes of 40, 60 and 80 mmHg were used (systolic/diastolic pressures of 117/77, 130/70, and 143/63 mmHg, respectively). To compare the laser versus 3D ultrasound techniques, two additional pressure set-ups with a pressure amplitude of 60 mmHg and mean arterial pressure of 60 and 120 mmHg were used (systolic/diastolic pressures of 100/40 and 160/100 mmHg, respectively).

Since strain is derived from displacement, validation was carried out by comparing displacement data gained by 3D ultrasound speckle tracking and by high-speed laser scan micrometer and video photogrammetry, both of which served as reference methods.

**Validation with high-speed laser scan micrometer.** The external vertical diameter of the vascular model was measured with a high-speed laser scan micrometer, type LS-5001 (Keyence, Osaka, Japan) with ±0.2 μm accuracy, ±0.03 μm reproducibility and a 4-cm maximum measurement field. The laser scan beam transversely crosses the vessel model in a vertical plane. The external vertical radial diameter is determined by measuring the laser plane interruption by the vessel model (Fig. 3). The internal vertical radial diameter was calculated by using the wall thickness of the silicone aneurysm model. The diameter measurement was an average of four pump cycles, whereby the maximum and minimum diameters were automatically detected and determined. All values were digitised using a data acquisition card (Advantech PCL-818HG) and the data acquisition software DASYLab 4.0 (National Instruments Services GmbH & Co. KG, Moenchengladbach). The vertical diameter of the vessel was measured simultaneously with 3D ultrasound from the top and with the laser scan micrometer from the side, at different points along the vessel. To identify selected points of the silicone vessel on the 3D ultrasound image, 2-mm metal screw nuts were used. In the aneurysmal middle section of the silicone vascular model, systolic ($D_{\text{syst}}$) and diastolic internal diameter ($D_{\text{diast}}$) and diameter difference ($D_{\text{diff}}$) were measured from the $x$, $y$ and $z$ coordinates from the 3D data sets and compared with the corresponding laser measurements. Each measurement was repeated five times.

**Validation with video photogrammetry.** Besides radial diameter change, 3D ultrasound detects wall motion in the

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**Figure 2.** Image processing shown by analysing the middle section of the silicone aneurysm model. A. Speckle tracking software of Artida 3D ultrasound machine displays multiplanar reconstruction images corresponding to three short-axes, and horizontal and sagittal long-axes views, B. 3D ultrasound image, and C. 3D reconstruction of the silicone vascular model.

**Figure 3.** Experimental set-up: the aneurysm-shaped silicone model is mounted horizontally in a water bath and connected through elastic tubing to the piston pump. The mean systemic and pulse pressures were set by a height-adjustable reservoir and an elastic reservoir, respectively. The vertical diameter (blue line) of the vessel was measured simultaneously with 3D ultrasound and laser scan micrometer. The laser plane is shown in cross section, the interruption is marked with incomplete red lines. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Validation with high-speed laser scan micrometer. Vertical diameter change in the middle of the silicone aneurysm model was calculated from 3D ultrasound data and compared to laser scan micrometer measurements. Diameters measured by laser and ultrasound (Fig. 4A) correlated significantly (R = 0.998, y = 0.7758x + 7.3396). To obtain more detailed information about the accuracy of 3D ultrasound, the differences between values of the two methods were analysed at the same mean arterial pressure, but at different pulse pressures. Increasing the pulse pressure caused a slight decrease in the diastolic and a stronger increase in the systolic diameter of the pulsating silicone model (Fig. 4B). The mean difference between diameters measured with laser and ultrasound was 0.45 ± 0.33 mm. 3D ultrasound measurements showed higher accuracy when used to evaluate diastolic (mean difference 0.36 ± 0.25 mm) than systolic (mean difference = 0.55 ± 0.38 mm) diameters. The calculated diameter change during the pulse cycle is shown in Fig. 4C. The mean difference in systolic–diastolic diameter change between measurements by laser and ultrasound was 0.48 ± 0.34 mm.

To investigate the capability of 3D ultrasound to detect local differences, the vertical diameter was analysed at the same pressure setting but at different positions along the aneurysm-shaped silicone model. 3D ultrasound detected local differences in diastolic and systolic diameter in the aneurysmal part of the silicone vascular model (Fig. 5A and B), almost identical to the values attained by laser. The mean difference in systolic–diastolic diameter change between measurements by laser and ultrasound measured in the middle section of the silicone aneurysm model was 0.76 ± 0.2 mm. The change in vertical diameter is a result of local radial displacement at the top and bottom of the silicone model. The local radial displacement data are visualised as colour coding on the surface of the 3D reconstruction (Fig. 5C).

Validation with video photogrammetry. Displacement in the x (longitudinal), y (transversal) and z (vertical) directions calculated from 3D ultrasound tracking data was compared with displacement analysed from video photogrammetry (Fig. 6). The displacement in the y and z directions was increased with increasing pulse pressure, but displacement in the x direction did not change. 3D ultrasound measurement correlated significantly with video analysis (data not shown) with R = 0.872, 0.969 and 0.769 in the x, y and z directions, respectively. The analysis carried out with 3D ultrasound or video photogrammetry resulted in similar displacement values in all three directions. The maximum difference between 3D ultrasound and video analysis was 0.24 mm, 0.54 mm and 0.76 mm in the x, y and z directions, respectively.

Investigation of aortic aneurysm in vivo

Data from patients with abdominal aortic aneurysm, using 3D ultrasound and wall motion analysis, were collected and analysed. Peak displacement and strain continuously changed during the pulse cycle and, from these parameters, local peak radial, longitudinal and 3D displacement and longitudinal and circumferential strain were determined.

RESULTS

In vitro experiments

Validation with high-speed laser scan micrometer. Vertical diameter change in the middle of the silicone aneurysm

Investigation of aortic aneurysm in vivo

Five male patients (age 74.6 ± 5.7 years) with fusiform, infrarenal abdominal aortic aneurysms with low calcification and medium-size thrombus burden were investigated with the Artida real-time 3D ultrasound system. Image sequences were generated from the infrarenal aorta from the ventral sagittal position, during two cardiac cycles, while patients held their breath. Blood pressure was gained from brachial arteries on both sides using a conventional sphygmomanometer before and after ultrasound measurements. Patients gave informed consent and use of data concerning patients was approved by the local Ethics Committee. Peak local displacement and strain parameters (P) of a pulse cycle for each of 36 by 36 matrix points designated on the aneurysm and visualised by colour coding on the surface of the 3D aneurysm reconstructions were calculated by the following equation: \( P_{\text{peak}} = P_{\text{max}} - P_{\text{min}} \), where \( P_{\text{max}} \) and \( P_{\text{min}} \) are the maximum and minimum values, respectively, of a given parameter at a given matrix point during the pulse cycle. Mean (over the whole aneurysm), minimum and maximum peak data within an aneurysm were then calculated.

Statistics

Data analysis was performed with a statistical software package (SigmaStat for Windows, Jandel Scientific, Erkrath, Germany). Pearson product moment correlation was used to analyse the linear relationship between two variables. Mean values and standard deviation are given. P values <0.05 were considered significant.
Areas with higher and lower peak displacement values and areas with different strain values could be identified. Table 1 shows the mean, maximum and minimum local peak values over the whole aneurysm. Marked differences between mean and maximum values indicate strong local differences in the biomechanical properties of the abdominal aortic aneurysm. Although patients had similar blood pressures, the difference between mean and maximum values varied strongly between patients (Fig. 9). This suggests that there are aneurysms with strongly heterogeneous local biomechanical parameters and those with even distribution. Mean and maximum values for longitudinal (cranio-caudal) displacement are, except for patient 4, higher than radial (in transversal plane) displacement.

**DISCUSSION**

Aneurysm rupture is mechanical failure of the vascular wall. Irregular geometry leads to differences in wall stress distribution, and disproportional degradation of structural elements results in local differences of tensile strength.
Thus, the relation of wall strength to wall stress can be quite heterogeneous. An aneurysm ruptures if, at one location, wall stress becomes higher than the tensile strength of the vascular tissue. Knowledge of local mechanical aortic wall parameters is, therefore, necessary to correctly analyse rupture risk.

To non-invasively estimate rupture risk, measurement of various biomechanical properties of the aortic wall, such as compliance, stiffness or strain, has been proposed. These parameters are all derived from quantifying blood pressure change-induced deformation of the vascular wall. Aortic wall deformation can be analysed in vivo using sonography. However, all currently available methods are limited to conveying information about wall motion in only one cross section. The recently developed real-time 3D ultrasound speckle tracking imaging can be used to analyse local wall motion change in every direction.

In the in vitro validation studies, 3D ultrasound speckle tracking imaging was compared with reference methods. The use of an in vitro pulsatile perfusion system and a silicone vascular model ensured standardised conditions. Since every parameter of the speckle tracking analysis is derived from displacement data, comparison with other highly accurate methods, which also detect displacement, was used for validation. Radial displacement was determined with a high-speed laser scan micrometer and longitudinal and circumferential displacements were validated with video photogrammetry. The methodological comparisons show that 3D ultrasound speckle tracking data significantly correlate with data obtained through laser scan micrometry or video photogrammetry, though the displacement values were underestimated by 3D speckle tracking ultrasound. The measured mean differences between 3D ultrasound speckle tracking and the reference methods were under 0.76 mm, comparable with the spatial ultrasound resolution, which is around 0.6 mm at a frequency of 2.5 MHz. The 3D ultrasound method was also able to detect differences in displacement between different regions of the silicone aneurysm model.

After in vitro validation, abdominal aortic aneurysms of patients were investigated with 3D ultrasound speckle tracking. The most interesting finding uncovered by 3D ultrasound speckle tracking of aortic aneurysms is that there are marked differences in local displacement and strain values within the aneurysm (Table 1). The varying consistency of the aortic wall, well known by vascular surgeons performing open aortic surgery, is therefore reflected by this non-invasive measurement method. Furthermore, in spite of similar mean displacement and strain data, maximum local peak values showed strong individual differences. In some aneurysms, displacement and strain were evenly distributed and in others movement of the aortic wall showed large local differences. This corresponds to recent reports on ex vivo tensile testing, showing differences in yield stress and strain of different abdominal aortic aneurysmal regions. Ex vivo and in vivo tests are important for understanding the mechanical properties of the aortic wall and for predicting the risk of aneurysm rupture.

Figure 6. Comparison of 3D ultrasound with video analysis. Displacement in A. x (longitudinal), B. y (transversal) and C. z (vertical) directions of a selected point of the silicone model with different pulse pressures. Measurements were carried out simultaneously with video analysis (○) and with the Artida 3D ultrasound machine (●) (n = 3).

Figure 7. 3D reconstruction of an infrarenal aortic aneurysm (patient 2) with colour coding of peak A. radial, B. longitudinal and C. 3D displacement (mm). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
vivo investigations have also reported differing regional inflammatory activities, which may result in differing local mechanical properties. Aneurysm enlargement, intraluminal thrombus and calcification are also localised differential processes. Such local differences might explain controversial rupture risk estimation. Rupture risk, determined from mechanical parameters of the aorta, diastolic blood pressure and diameter, has been suggested to provide a more accurate assessment of rupture risk than diameter alone. However, other investigators have failed to find a correlation between biomechanical parameters and rupture risk. Possibly, this controversy is due to techniques registering only one aortic section, and the area responsible for rupture may not have been in the investigated section.

In practice, investigation with 3D ultrasound is the same as conventional sonography of the abdominal aorta with additional ECG detection. Data acquisition requires about 15 min and off-line data processing about 30 min. Limitations are similar to conventional 2D ultrasound with data loss occurring when ultrasound propagation is impeded. Likewise, aspect ratio and depth are limited by the scanning area of the ultrasound probe.

The currently available, most accurate method for predicting rupture risk is to compare peak wall stress determined by computer tomography-based finite element analysis with an assumed, constant tissue wall strength. However, accurate stress calculation requires knowledge of local elasticity, which can be calculated from stress—strain relations. The 3D ultrasound speckle tracking presented here determines local strain parameters, facilitating calculation of local elastic moduli, enabling a more exact calculation of local peak wall stress.

In conclusion, the data from this small patient collective indicate that local displacement and strain parameters of the abdominal aortic aneurysm are heterogeneous, with the heterogeneity being more or less pronounced in individual aneurysms. 3D ultrasound speckle tracking has proven to be capable of detecting heterogeneity of local biomechanical parameters over the whole aneurysm. The method offers the prospect of individual non-invasive rupture risk analysis and screening of all abdominal aortic aneurysms, including larger aneurysms which may remain stable and for smaller aneurysms, which may be below the size conventionally requiring revision, but still at rupture risk.

| Table 1. Mean, maximum and minimum peak displacement and strain values over whole aneurysm with blood pressure and aneurysm diameter from 5 patients. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Aneurysm diameter (mm) | Blood pressure (mmHg) | Displacement (mm) | Strain (%) |
| | | Radial | Longitudinal | 3D | Circumferential | Longitudinal |
| Patient 1 | 41.7 | 120/75 | Mean 0.25 | 0.46 | 0.63 | 2.69 | 2.05 |
| | | | Max 0.98 | 1.27 | 2.26 | 8.10 | 7.65 |
| | | | Min 0.02 | 0.05 | 0.08 | 0.30 | 0.11 |
| Patient 2 | 76.3 | 135/75 | Mean 0.76 | 1.18 | 1.80 | 4.71 | 3.61 |
| | | | Max 2.90 | 3.13 | 6.57 | 19.80 | 14.28 |
| | | | Min 0.00 | 0.00 | 0.00 | 0.19 | 0.09 |
| Patient 3 | 26.7 | 110/45 | Mean 0.38 | 0.46 | 0.75 | 4.20 | 2.42 |
| | | | Max 0.80 | 0.92 | 2.30 | 17.64 | 6.10 |
| | | | Min 0.06 | 0.06 | 0.33 | 0.57 | 0.33 |
| Patient 4 | 71.2 | 140/95 | Mean 0.67 | 0.62 | 1.08 | 3.74 | 2.94 |
| | | | Max 3.36 | 2.20 | 3.54 | 15.61 | 11.61 |
| | | | Min 0.01 | 0.00 | 0.02 | 0.09 | 0.10 |
| Patient 5 | 66.7 | 130/60 | Mean 0.58 | 1.14 | 1.73 | 5.83 | 3.64 |
| | | | Max 1.50 | 3.48 | 6.54 | 24.57 | 13.03 |
| | | | Min 0.01 | 0.00 | 0.06 | 0.37 | 0.05 |

*Values may be below the limit of detection generally encountered for ultrasound (0.6 mm).*
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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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