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A left ventricular phantom for 3D echocardiographic twist measurements

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Abstract: Traditional two-dimensional (2D) ultrasound speckle tracking echocardiography (STE) studies have shown a wide range of twist values, also for normal hearts, which is due to the limitations of short-axis 2D ultrasound. The same limitations do not apply to three-dimensional (3D) ultrasound, and several studies have shown 3D ultrasound to be superior to 2D ultrasound, which is unreliable for measuring twist. The aim of this study was to develop a left ventricular twisting phantom and to evaluate the accuracy of 3D STE twist measurements using different acquisition methods and volume rates (VR). This phantom was not intended to simulate a heart, but to function as a medium for ultrasound deformation measurement. The phantom was made of polyvinyl alcohol (PVA) and casted using 3D printed molds. Twist was obtained by making the phantom consist of two PVA layers with different elastic properties in a spiral pattern. This gave increased apical rotation with increased stroke volume in a mock circulation. To test the accuracy of 3D STE twist, both single-beat, as well as two, four and six multi-beat acquisitions, were recorded and compared against twist from implanted sonomicrometry crystals. A custom-made software was developed to calculate twist from sonomicrometry. The phantom gave sonomicrometer twist values from 2.0° to 13.8° depending on the stroke volume. STE software tracked the phantom wall well at several combinations of temporal and spatial resolution. Agreement between the two twist methods was best for multi-beat acquisitions in the range of 14.4–30.4 volumes per second (VPS), while poorer for single-beat and higher multi-beat VRs. Smallest offset was obtained at six-beat multi-beat at 17.1 VPS and 30.4 VPS. The phantom proved to be a useful tool for simulating cardiac twist and gave different twist at different stroke volumes. Best agreement with the sonomicrometer reference method was obtained at good spatial resolution (high beam density) and a relatively low VR. 3D STE twist values showed better agreement with sonomicrometry for most multi-beat recordings compared with single-beat recordings.

Keywords: *in vitro*; myocardial twist; rotation; sonomicrometer; speckle tracking; three-dimensional echocardiography; volume rate.

List of abbreviations: 2D, two-dimensional; 3D, three-dimensional; ABS, acrylonitrile butadiene styrene; CAD, computer-aided design; CMR, cardiac magnetic resonance; ECG, electrocardiogram; FR, frame rate; HR, heart rate; PVA, polyvinyl alcohol; ROI, region of interest; STE, speckle tracking echocardiography; VPS, volumes per second; VR, volume rate.

Introduction

Left ventricular rotation and twist are important features of the normal left ventricular contraction and have shown to be modified by ischemia and hypertrophy [1–4]. Torsion, which in cardiology is calculated as twist divided by the end-diastolic left ventricular length, gives the possibility to compare the twisting action of hearts of different sizes. Peak systolic twist and torsion measurements by two-dimensional (2D) speckle tracking echocardiography (STE) have been published with a range of different values, also for normal hearts. As early as 2007, Weyman showed a span from 6.7° to 14.5° for twist in normal cohorts [5]. Newer publications also show large variation in twist values in normal individuals, where mean values of 7.9°–20° have been reported [6, 7]. The different result is believed to be caused by, in addition to possible variation between cohorts, limitations in the applied method. For 2D STE twist measurements, this includes variable image quality, the selection of the basal and apical planes, in- and out-of-plane motion, low frame rate (FR) as well as vendor differences in available acquisition methods and software algorithms [8]. For 2D STE torsion measurement, uncertainty in determining the end-diastolic distance between the selected planes can lead to inaccurate estimates. For three-dimensional (3D) STE methods, limitations in beam density and low volume rate (VR) could lead

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to inaccurate strain measurements [9]. When comparing 2D with 3D STE measurements of torsion, studies have shown that 2D STE is not a reliable method to measure left ventricular torsion because of these limitations [10–12]. Measurements of twist and torsion are to be used with caution according to the current guidelines [13, 14]. Some studies have compared rotation and twist from STE to cardiac magnetic resonance (CMR) tagging. Generally it seems that CMR gives higher values for twist than 2D STE [15, 16]. However, CMR has its shortcoming with regard to especially temporal resolution.

To be able to assess the accuracy of rotation and twist measurements by STE, experimental studies have been performed comparing 2D STE with implanted crystals in dogs [15]. Other studies have used a rotating actuator for *ex vivo* hearts with a stepping motor for the control of basal rotation with a fixed apex [17, 18].

A synthetic twist phantom has been commercially available and has been used for *in vitro* evaluation of echocardiographic measurements [19], but is not suitable for apical views due to the apical attachment. Most 3D deformation algorithms are based on apical 3D views of the left ventricle, a twisting phantom should therefore not include an apical attachment. There is a need for a simplified synthetic phantom setup compared to the published animal and *ex vivo* setups. A twisting synthetic phantom with implantable sonomicrometry crystals for apical views is thus ideal to investigate and optimize 3D STE measurement of rotation and twist and has the advantage of enabling repetitive measurements over time with the same phantom in comparison to *ex vivo* setups. In previous studies, we used a pump rig with a phantom made of polyvinyl alcohol (PVA) to evaluate the accuracy of 2D and 3D strain measurements [9, 20]; however, these phantoms had no twist properties.

The aim of this study was to develop a twisting phantom which enabled different levels of twist to be simulated and further to quantify the effect of different acquisition methods. This includes both single-beat and multi-beat, as well as the accuracy of STE twist measurements against a reference method at different VRs.

It is important to emphasize that this phantom's single purpose was to generate twist for ultrasound measurements, not to mimic the physiology of the human heart.

Materials and methods

Left ventricular phantom construction

A phantom was designed to mimic a contracting and twisting left ventricle (Figure 1), using a similar technique as has been recently published for other cardiac simulation studies [21]. This phantom was entirely made from PVA with wall properties to introduce twist, thereby avoiding any apical deformation attachment. It has a truncated prolate spheroid shape and consists of two layers with different thickness and elastic properties in a spiral layout which forces it to twist when the phantom is inflated or deflated. This spiral structure is divided into eight continuous bands, with the inner layer differing in thickness from 0.1 to 8 mm at the base and from 0.1 to 4 mm at the apex. The internal diameter is 42 mm and the total length of the phantom is 92 mm (Figure 1A and B). These dimensions were based on our previous study [9]. The spiral structure is angled 45° to the longitudinal direction of the phantom, but narrows to 0° at the apex, which is necessary for the bands to meet. The outer layer gives the phantom a smooth surface and results in a total thickness of 12 mm at the base and 8 mm at the apex in the relaxed state (end systole). The thinner wall at the apex was found necessary to avoid spherical ballooning during water inflation (diastole). The phantom was casted using 3D printed molds in acrylonitrile butadiene styrene (ABS) plastic, with a one-part internal mold, a four-part external mold for the inner layer and a one-part external mold for the outer layer. The basal part of the phantom was anchored in a threaded mounting base, made of ABS plastic (Figure 1B). The molds were designed using computer-aided design (CAD) software (Rhino 5, Robert McNeel & Associates, Seattle, WA, USA). Both PVA layers were made of a material solution consisting of 10% by weight PVA (M_w 89K–98K, 99+% hydrolyzed, Sigma-Aldrich, Saint Louis, MO, USA) and 90% water. During casting, the solution was frozen for 12 h in –18°C, and then thawed at room temperature for 12 h. The inner layer first underwent five freezing cycles before it was taken out of the inner layer mold, which was replaced by the outer layer mold. Additional PVA material was then added to the mold, and it went through one more freezing cycle, which gave the inner layer a total of six cycles and the outer layer one. This made the inner layer rigid, which was necessary to make the phantom twist, ending up with a phantom with smooth inner and outer surfaces (Figure 1C).

Pump rig

The phantom was installed in a custom-made pump-rig similar to a previously published *in vitro* setup [22, 23]. The phantom itself was submerged in a water container with the apex pointing toward the surface, connected via rigid pipes to a dual-cylinder pump. Absorbing sheets covered the wall of the reservoir to reduce ultrasound reflections. The pump inflates and deflates the phantom using water, thus simulating the deformation of the left ventricle. The pump was driven by a stepper motor controlled by custom-made software, simulating heart cycles at different stroke volumes and pump rates, hereinafter referred to as heart rate (HR). More details about the pump rig can be found elsewhere [9, 20]. A 3D ultrasound probe (4V, GE Vingmed Ultrasound, Horten, Norway) was partially submerged 4 cm above the phantom apex, and connected to an ultrasound scanner (Vivid E9, GE Vingmed Ultrasound).

Sonomicrometry as the gold standard

Sonomicrometry has proven to be an accurate reference method for measuring dimensional changes for both *in vitro* and animal studies

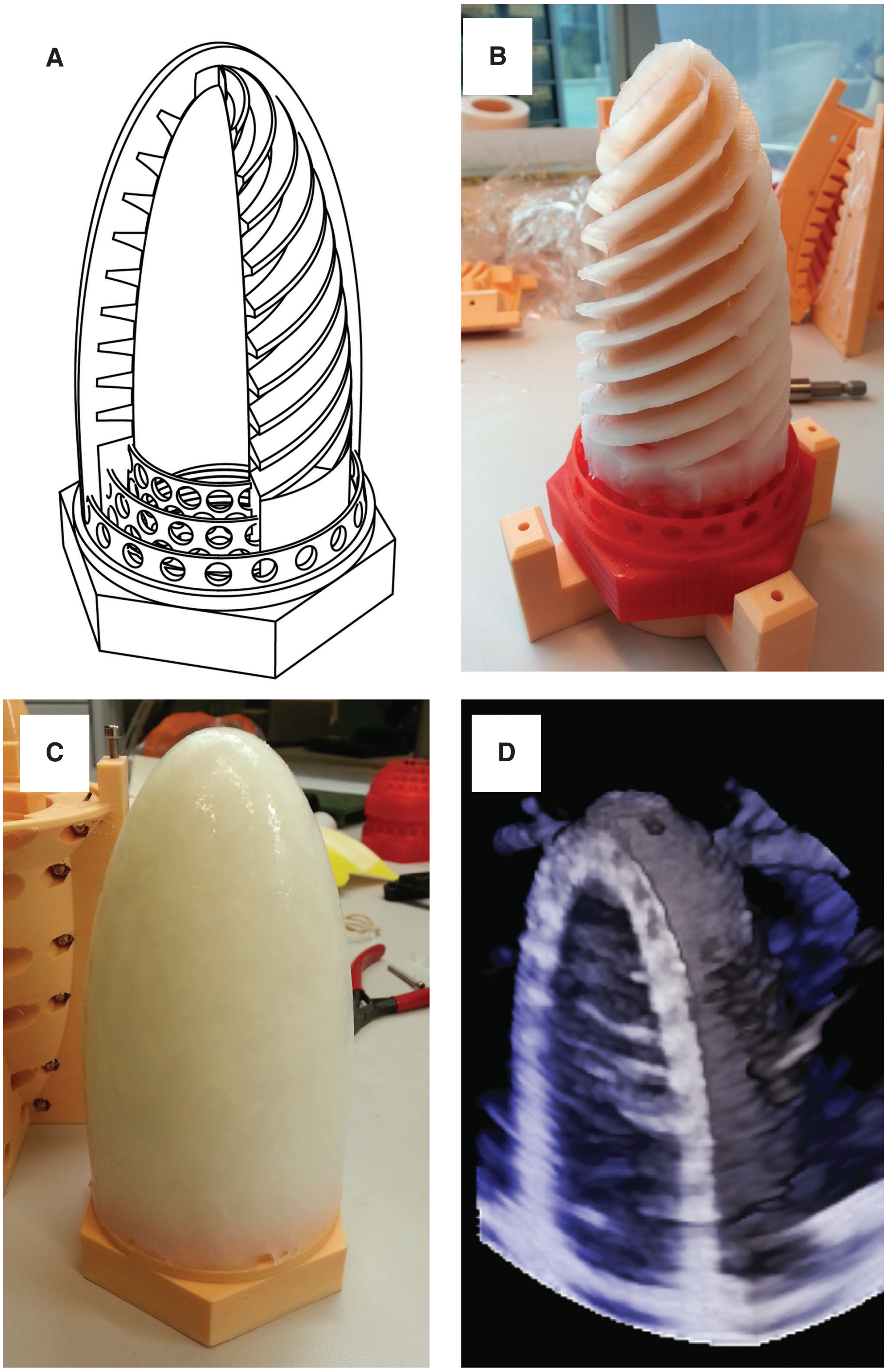

Figure 1: Design of the twisting ultrasound phantom.
(A) Schematic view of the phantom components. (B) Spiral layer and (C) final phantom including a smooth outer layer. (D) Appearance in 3D B-mode imaging.

[15, 23–25]. In this study, a total of six crystals were used. Three crystals were placed in an equilateral triangle at the base of the phantom, and three other crystals were placed in an opposite triangle at the apex, giving the crystal placement the shape of a triangular antiprism (Figure 2A). The crystals were placed at mid wall in the same planes as the ultrasound software would calculate twist, for direct comparison. A small drop of cyanoacrylate glue was used to fix each crystal in place during the complete protocol. The sonomicrometer method with six crystals defined two planes. A direct measurement of the distances between all crystals will correlate directly to strain, depending on the direction. The distances between all sonomicrometer crystals were logged at 192 samples/s using a commercial

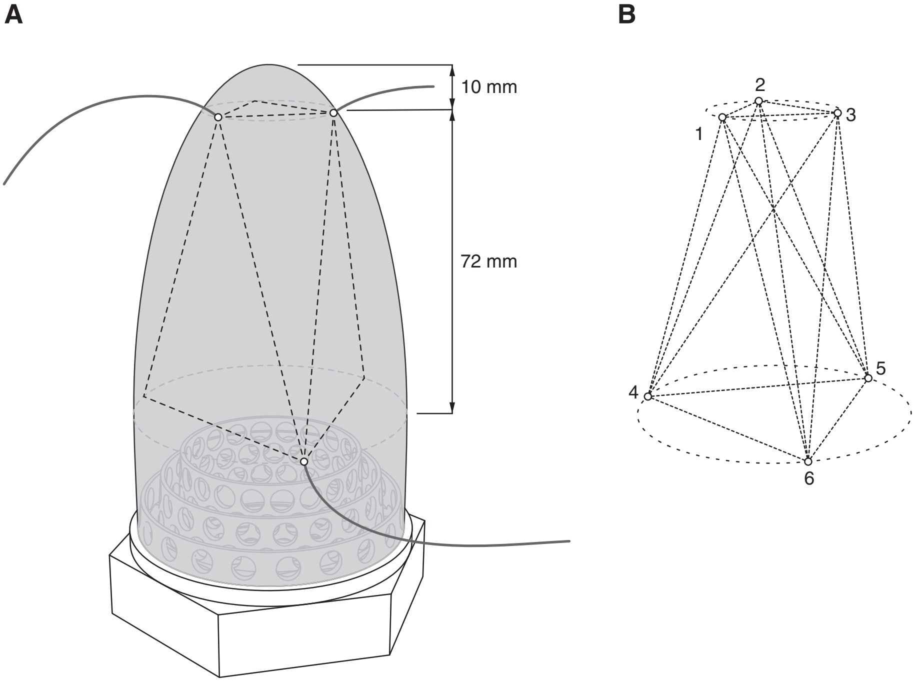

Figure 2: Sonomicrometer reference method.
(A) The two planes with three crystals in each plane. (B) Measured distances between all crystals make it possible to calculate the Cartesian coordinates by use of trilateration, which form the basis for twist estimation (see text for details).

sonomicrometer system (DS3-8 and LabChart Pro v7, Sonometrics Corporation, Ontario, Canada). Measurement resolution is specified by the manufacturer to be within 0.0124 mm given ideal conditions. In this study, our interest was to measure twist between the two planes of crystals. Measuring the angle rotation requires an external fixed reference for observation of the crystal movements and was not carried out. Torsion was not calculated in this one-size phantom study. A custom-made software application was written using MATLAB (MATLAB 2014b, MathWorks Inc., Natick, MA, USA) to calculate twist based on the distances measured by sonomicrometry (Figure 2B). This software used the method of trilateration to calculate the spatial coordinates of the crystals by knowing all the distances between them. Knowing the coordinates of the crystals, it then calculated the relative angles of the two planes using trigonometric functions. This was done for each sample from the sonomicrometer and a twist curve was produced where the peak twist value was selected for comparison with STE peak twist.

Acquisition protocol

The amount of twist was controlled by the stroke volume of the pump, which determined the amount of deformation of the phantom. A series of 21 different stroke volumes (5–105 ml with 5-ml intervals) were recorded using 11 recordings with different acquisition settings for each volume, 231 recordings in all. Recordings were obtained for single-beat using 25.5 volumes per second (VPS); for two-beat multi-beat using 14.4, 21.2 and 47.9 VPS; for four-beat multi-beat using 20.3, 27.0 and 42.4 VPS; and for six-beat multi-beat using 17.1, 30.4, 43.2 and 63.6 VPS. These acquisition settings were chosen because of hardware limitations and software requirements as well as for optimizing image quality. All recordings were done at HR 60 beats/min and with a systolic/diastolic time ratio of 30:70. Multi-beat recordings require an electrocardiography (ECG) signal to detect each heartbeat. This was achieved by sending the start/stop trigger pulse from the pump to a digital logger, corresponding to the start and end of injection (diastole). The signal was then modified and scaled to mimic the QRS of an ECG. This signal was connected to the ECG input of the scanner (Figure 3, lower left). To keep the same starting point of the deformation cycle (relaxed phantom or systole), a small positive starting pressure was given, keeping the same symmetric and slightly stretched phantom as the starting point for all 231 recordings.

All recordings were carried out with harmonic imaging at 1.7/3.3 MHz, and the quality of the B-mode recordings was optimized for a large stroke volume, resulting in settings for depth 0–14 cm and sector angle 75°. All acquisition settings were kept constant throughout all recordings.

Speckle tracking analysis of twist

Recorded ultrasound 3D images were analyzed using the 4D Auto LVQ tool of EchoPAC workstation software (EchoPAC BT201, GE Vingmed Ultrasound). The lumen of the phantom as well as the region of interest (ROI) were defined in end systole (relaxed phantom) and end diastole (expanded phantom). The software then calculated the rotational data in four different levels using STE, as shown in Figure 3. The rotational values of the basal segments were subtracted from the values of the apex segments, thus corresponding to the twist values from the same planes as measured by the sonomicrometer method.

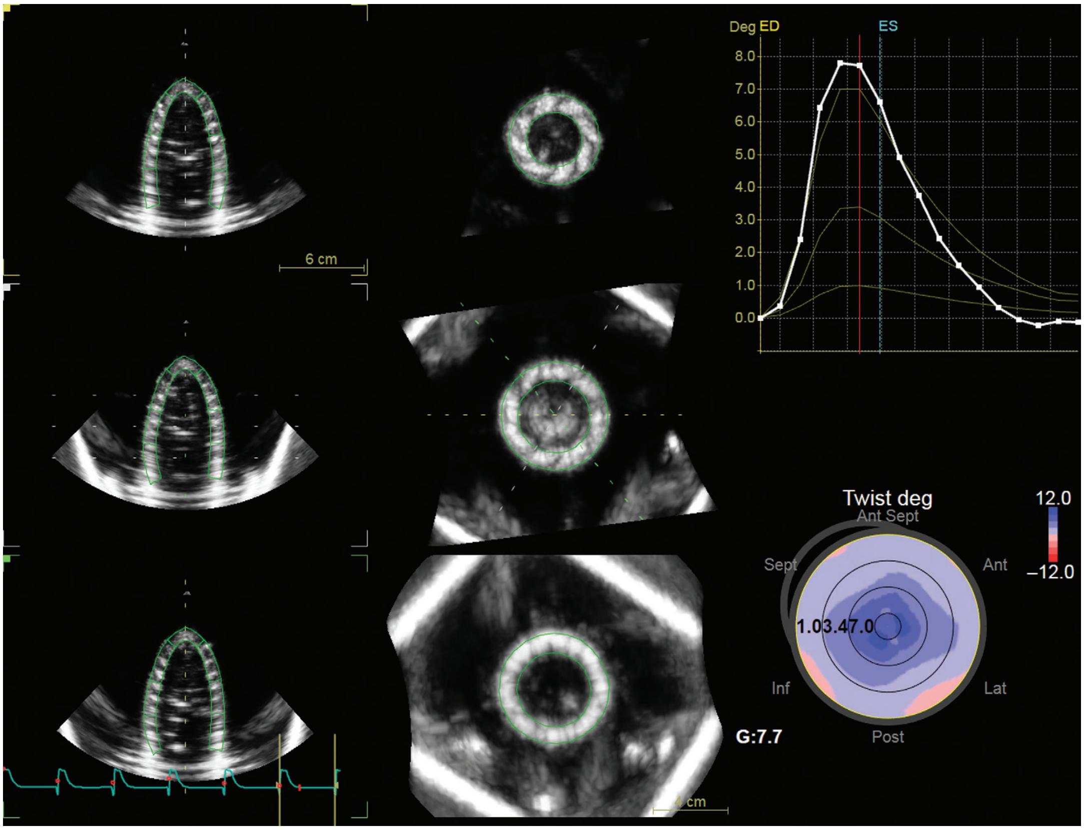

Figure 3: Speckle tracking of the twisting phantom.
From left, three long-axis views, three short-axis views, time-curve (upper, right) and the rotation at three levels, base, mid and apical. The values of the fourth level, apex, are not presented with a curve, but are provided with the software. The twist curve, which was used in this study, is calculated by subtracting base rotation from apex rotation, which gives 7.7° in this example.

Statistics

Linear correlation coefficient, giving the association between the two twist methods, and Bland-Altman analysis [26], giving the mean difference and limits of agreement [±1.96 standard deviation (SD)] as absolute differences between the methods, were calculated for each VR setting.

Results

The ultrasound appearance of the constructed phantom in B-mode is shown in Figures 1D and 3 and is close to a clinical recording but with somewhat more “spotty” echo appearance with less distinct speckles than myocardium. The current setup gave a range of sonomicrometer twist values from 2.0° to 13.8° (Figure 4). The EchoPAC software was able to track the movement of the phantom wall at low and medium VR (as in Figure 3), but had difficulties at the highest recorded VR, probably due to the reduced beam density with corresponding low spatial resolution,

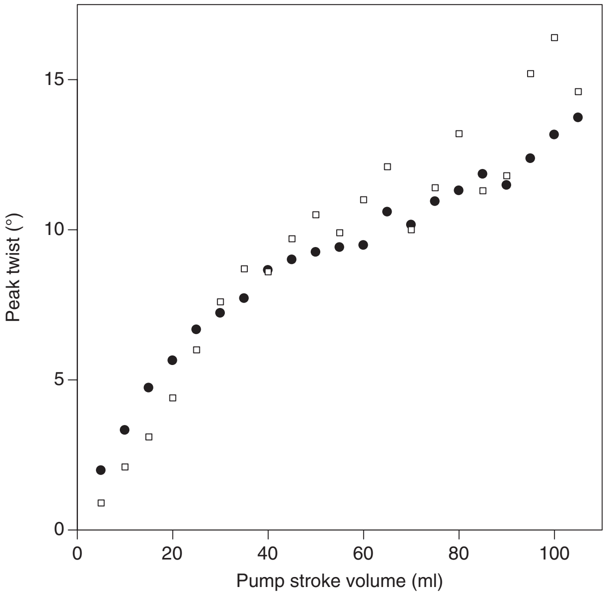

Figure 4: Peak twist vs. pump stroke volume measured with sonomicrometry (filled circles) and 3D STE using six-beat multi-beat acquisition at 17.1 VPS (open squares).
n = 21.

Table 1: Comparison of 3D STE twist with sonomicrometry.

Mode	Volume rate (VPS)	R	Bland-Altman	
			Mean diff (°)	±1.96 SD (°)
One beat	25.5	0.630	−4.62	2.46
Two beat	14.4	0.960	−1.19	1.00
	21.2	0.906	−3.94	1.38
	47.9	0.740	−5.52	2.23
Four beat	20.3	0.973	−0.17	1.91
	27.0	0.942	−1.21	1.18
	42.4	0.849	−5.03	1.67
Six beat	17.1	0.977	0.45	1.31
	30.4	0.944	−0.99	1.65
	43.2	0.941	−2.01	1.28
	63.6	0.603	−6.32	3.05

Mean diff, mean of the differences between 3D twist and sonomicrometer twist; R, linear correlation coefficient; ±1.96 SD, limits of agreement according to Bland-Altman analysis.

and also the appearance of the phantom wall at high VR. More details on this are provided in the Limitations section.

A total of 231 3D ultrasound recordings were analyzed for 21 different volumes at 11 different acquisition settings. A summary of the results from the correlation and Bland-Altman analysis is shown in Table 1. The best association between twist by 3D STE and sonomicrometry measured by correlation was achieved for six-beat multi-beat at 17.1 VPS with a correlation coefficient of 0.977. Best agreement between measurements based on mean difference was achieved for four-beat multi-beat at 20.3 VPS with a correlation coefficient of 0.973 and an agreement of −0.17° ± 1.91° (mean difference ± 1.96 SD), followed by six-beat multi-beat 17.1 VPS with an agreement of 0.45° ± 1.31°. Figures 5 and 6 show examples of scatter plots and corresponding Bland-Altman plots of the best results obtained

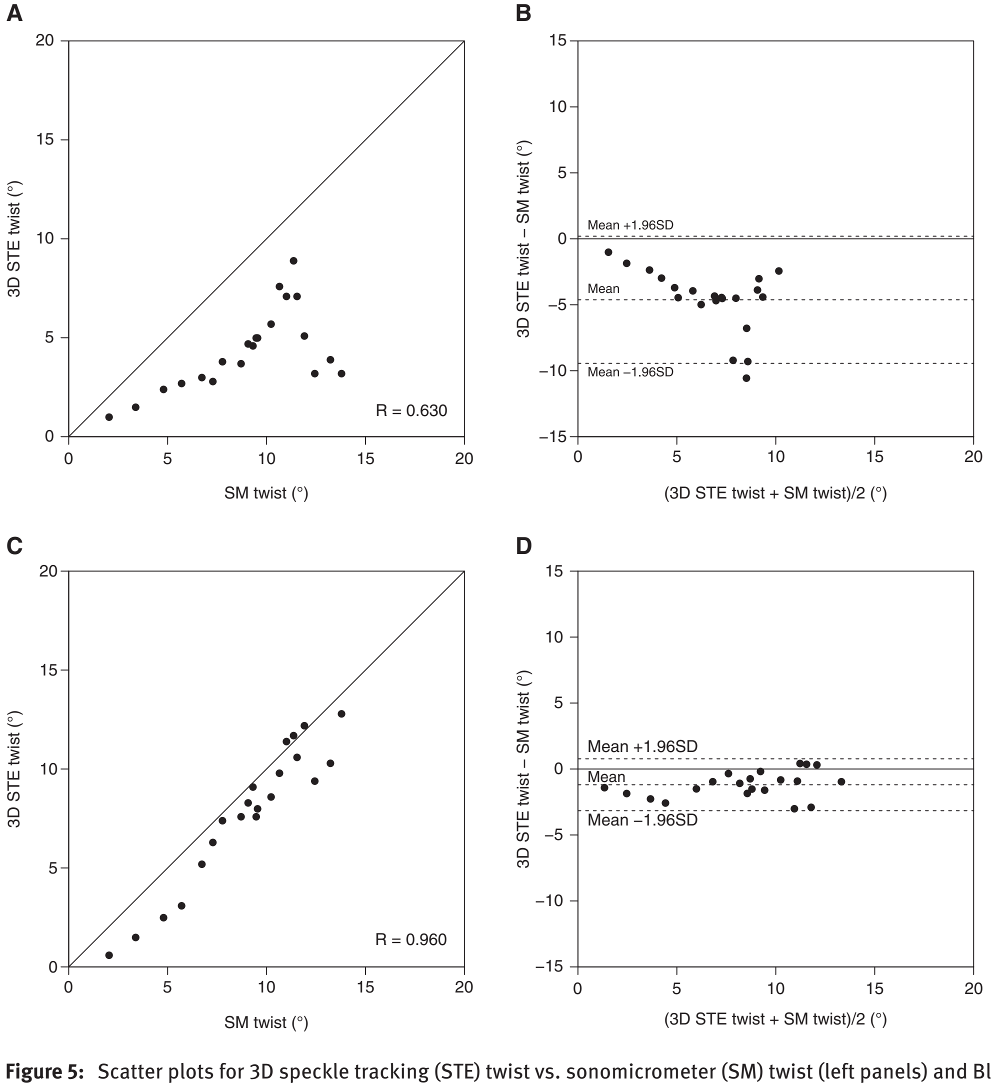

Figure 5: Scatter plots for 3D speckle tracking (STE) twist vs. sonomicrometer (SM) twist (left panels) and Bland-Altman plots (right panels). (A) and (B) show results for single-beat acquisition at 25.5 VPS, and (C) and (D) show results for two-beat multi-beat at 14.4 VPS. n = 21 for all scatter plots.

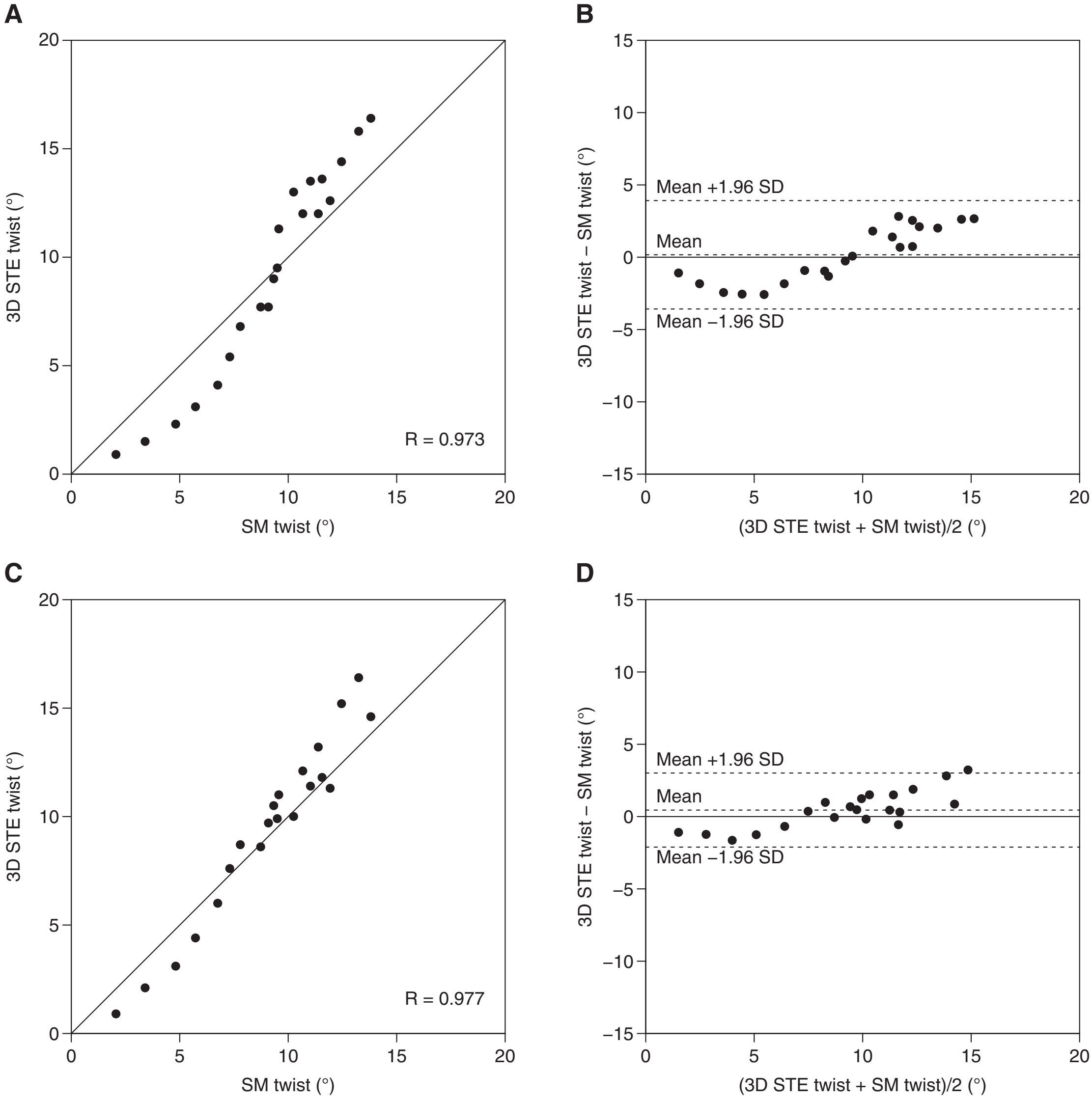

Figure 6: Scatter plots for 3D speckle tracking (STE) twist vs. sonomicrometer (SM) twist (left panels) and Bland-Altman plots (right panels). (A) and (B) show results for four-beat multi-beat acquisition at 20.3 VPS and (C) and (D) for six-beat multi-beat at 17.1 FPS. n = 21 for all scatter plots.

for each acquisition method, single-beat, two-, four- and six-beat multi-beat.

Discussion

The phantom developed in this study proved to be a useful tool for investigating the accuracy of twist measurement and gave a B-mode appearance similar to normal myocardium (Figures 1 and 3). Good speckle tracking as well as the ability to support large stroke volumes up to 120 ml were demonstrated. It had, however, some limitations in tracking at high scanner VR and some limitations in the achieved range of twist values. The measurement of 2D STE twist has been used for some years, but the accuracy of 2D derived twist measurements is debated [10, 11]. Using 3D STE for twist measurements is a relatively new method, and few studies have evaluated the accuracy of different 3D acquisition methods in animals and *ex vivo* investigations. The phantom developed in this study is an improvement compared to previous phantoms and *ex vivo* preparations because of the synthetic nature of the phantom. It has the ability to repeat and reproduce tests of acquisition methods and software over time, and eliminates the need for any external apical attachment [18, 19, 27].

Volume rate dependency

This study shows that high spatial resolution is as important as high temporal resolution for accurate 3D STE twist measurements (Table 1). The reason for this is two-fold. First, low spatial resolution for a cardiac sector probe, especially the lateral resolution at sector depths, gives large presentation of individual speckles, thus reducing the tracking accuracy. Second, for 3D acquisition, the speckles can be followed through an increased number of frames compared to 2D short-axis recordings, where speckles disappear out of the 2D plane due to the in- and out-of-plane motion. This is a limitation for any 2D left ventricular short-axis recording and will influence the measurement of circumferential strain as well as rotation, twist and torsion. This effect is reduced for 3D acquisitions [10, 11]. As seen from Table 1, good agreement was found for several multi-beat settings at relatively low VR compared to the FR of typical 2D recordings. Single-beat STE recordings (VR = 25.5 VPS) gave relatively poor agreement with sonomicrometry due to poor spatial resolution compared to any multi-beat recording. The best agreement between 3D STE and the reference method was achieved using four-beat multi-beat at 20.3 VPS and six-beat multi-beat at 17.1 VPS (Table 1). Sufficient VR for a 3D recording in a clinical setting must be seen relatively to the HR of the patient, and a better measure of sufficient VR is the VR/HR ratio corresponding to the FR/HR ratio for 2D acquisitions. In this study, all recordings were carried out at 60 strokes/min and thus the VR/HR ratio for VR = 20.3 VPS equals 0.34 which is lower than that recommended for 2D deformation measurements [28].

Being able to track speckles through more B-mode frames in a 3D dataset compared to a 2D dataset opens for less requirement for high temporal resolution, enabling an increased beam density and thus a better lateral resolution to be used. This is similar to the findings in our previous 3D phantom study on strain, where the best agreement with the same reference method was 36.6 VPS for longitudinal strain and 30.2 for circumferential strain [9].

The phantom and pump setup shown in this study is a useful utility for evaluating twist measurements. Rotation and torsion measurements are also possible to evaluate depending on the setup. The sonomicrometry system showed a reduced increment of peak twist at stroke volumes above 60 ml (Figure 4). This is probably caused by a reduced twist deformation when the phantom shape becomes more spherical.

Tracking limitations

Tracking was difficult especially at high VR and high stroke volumes. The results for high VR are thus not necessarily only a result of limitations of the STE algorithm but also a result of the changing properties of the PVA phantom. It was noted that at the highest stroke volumes the echo appearance of the phantom changed and included a stronger echo from the transition between the spiral layer and the smoothing layer of the phantom wall (Figure 3). This artificially strong echo was detected and followed by the tracking algorithm and could be the cause of the underestimation at high VR and large stroke volume.

The phantom appears with less defined speckles in the B-mode recording than myocardium in a good quality clinical recording. Adding particles to the PVA would increase the speckle appearance [23, 29, 30]. Based on several previous studies, sufficient backscatter from the PVA is present without additives [9, 20, 22], and too strong speckle appearance would make the phantom less relevant as a test object for clinical measurements where image quality varies between patients.

Other limitations

Clinical 2D twist studies have shown a great variation in twist, and a test phantom should produce all published twist values. As twist is load-dependent, this will result in twist variation in addition to vendor differences and the effect of different definition of selected planes [31]. It has been shown that ischemia reduces ventricular twist [2]; another study showed increased twist in the hypertrophic left ventricle with a mean value of twist angle for concentric hypertrophy measured to 19.4° [1]. In this study, we obtained 13.8° as our maximum twist value at 105 ml (Figure 4), covering the range of normal and ischemic values, but not for all peak values reported for hypertrophy. One possible solution for obtaining higher twist values would be to decrease the pressure in the phantom at the end of systole (relaxed phantom). We found this hard to reproduce because at this point in the pump cycle it was necessary to start injection of fluid with a symmetric phantom and slightly stretched phantom. A clinically measured peak systolic twist value is derived from the clockwise rotation of the base (as seen from the apex during systole), and the counter-clockwise rotation of the apex. This deformation is challenging to mimic in a physical phantom and it is easier to cover a larger range of twist values with an *ex vivo* preparation, as published by Ashraf and coworkers [27]. Design improvements should be considered in the future, including increasing the number of spirals and the spiral angle.

Accuracy of the reference system

Sonomicrometry is considered the gold standard for experimental and laboratory measurement of dimensional changes. Applications include positioning the crystals at different levels of the left ventricle to measure twist and torsion in large animals [15]. Sonomicrometry relies on the receiving crystal being in the beam of the transmitted crystal and also on sufficient amplitude of the received RF pulse throughout the heart cycle to avoid triggering errors. In this study, the received crystal amplitude was carefully checked for all crystal combinations throughout the experiment. Any sonomicrometry triggering error was identified and corrected if needed. All crystals were implanted at mid-wall, as the EchoPAC software gives a mid-wall weighted measure of deformation.

Clinical implications

This study recommends a lower VR for twist measurement using 3D echocardiography than recommendations for 2D strain and twist measurements. The balance between temporal and spatial resolution is different for 3D STE because the speckles can be followed through more frames than for short-axis 2D recordings, where in- and out-of-plane motion is a major limitation. The setup in this study is not directly transferrable to a clinical situation, where the apex of the heart is almost stationary, and the atrioventricular plane is moving in the longitudinal chamber direction. In this setup, however, the base of the phantom is stationary, and the apex is moving and the purpose of this study is to evaluate twist measurements, not to simulate the heart contraction.

This study was carried out using equipment from one vendor only and is not directly transferrable to other vendors. However, the main conclusion should be relevant because the temporal and spatial resolution are limitations in all 3D echocardiography regardless of the vendor. A standardization of measurement of rotation, twist and torsion is strongly needed, such as the recent standardization of longitudinal strain measurements [13, 32]. These studies were carried out in collaboration with the industry, where newer versions of different software gave less variation in strain between vendors. Few, if any, similar studies exist on twist and torsion and this study shows a useful tool for testing different algorithms and for vendor comparison for the improvement of the accuracy of twist measurements.

Conclusion

The twisting left ventricular phantom developed in this study was a practical tool to study the accuracy of 3D echocardiographic measurements of twist. It gave a useful range of twist values at different stroke volumes and has the advantage of enabling measurements to be carried out over time due to synthetic material design. Best agreement between STE and sonomicrometer values using correlation coefficients was obtained for multi-beat acquisition using a VR between 17.1 and 30.4 VPS, while accuracy was reduced for single-beat at 25.5 VPS and multi-beat at a higher VR. Smallest offset and limits of agreement using a Bland-Altman analysis were obtained at 17.1 VPS using six-beat multi-beat acquisitions. Twist values showed good agreement with sonomicrometry with multi-beat giving better accuracy than single-beat.

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