Accuracy of Phase Contrast, Black-Blood, and Bright-Blood Pulse Sequences for Measuring Compliance and Distensibility Coefficients in a Human-Tissue Mimicking Phantom

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Purpose: To assess the accuracy of MR-derived luminal diameter variations and its implications for compliance (CC) and distensibility coefficients (DC) by comparison with high-resolution digital photography (HRDP) in a tissue-mimicking phantom with pulsatile flow.

Materials and Methods: Diameters, CC, and DC extracted using cine phase-contrast (CPC), cine bright-blood (CBrB), and a cine black-blood (CBB) sequence were compared. The diameter in the left–right direction was compared against HRDP, as the gold-standard. The experiments were performed using 2562 and 5122 matrix sizes. Bland-Altman analysis was performed to compare each sequence with the gold-standard in terms of diameter changes over the simulated cardiac cycle.

Results: The bias and 95% limits of agreement (LOA) for CBB and CBrB were comparable. The bias for CPC was larger, however, the LOA were comparable. Increasing spatial resolution improved agreement with HRDP for all sequences. CBrB-derived CC and DC were within 3% of the high resolution CBB values while CPC CC and DC were underestimated but still within 11%.

Conclusion: CPC images were found to underestimate the luminal area over the cardiac cycle. CBrB-derived diameters were more accurate in diastole while CBB-derived diameters gave the best results in systole. CC and DC varied depending on the pulse sequence.

Key Words: luminal area change; arterial stiffness; phase contrast; cine black blood; cine bright blood

INCREASED ARTERIAL STIFFNESS is an established independent risk factor for cardiovascular disease (1). Previous studies have linked increased arterial stiffness with genetic background (2) and the natural process of aging (3). Arterial stiffness has also been linked to traditional cardiovascular risk factors such as diabetes (4), hypertension, and a history of smoking (5). In recent years, several longitudinal studies have showed that aortic stiffness has a higher predictive value than traditional cardiovascular risk factors for determining the outcome of future fatal and nonfatal cardiovascular events (6,7).

Local arterial stiffness is often quantified using the distensibility or compliance coefficients. The distensibility coefficient (DC) is defined as $DC = \frac{DA}{D^P}$ where $A_{diast}$ is the minimum diastolic area, $A_{sys}$ is the maximum systolic area and $D^P$ is the local pulse pressure. The compliance coefficient (CC) is defined as $CC = \frac{DA}{\Delta A}$.

To measure CC and DC, both area and pressure changes should be measured at the same location along the arterial tree. For pressure measurements, applanation tonometry with waveform calibration to the brachial mean and diastolic pressures can be used for superficial vessels (8). For deep vessels like the aorta, local pressure cannot be measured directly and is estimated using transfer functions applied to peripheral waveforms. For practical reasons, the local pulse pressure $\Delta P$ is often replaced by the brachial pulse pressure measured using conventional sphygmomanometer cuffs. High definition echo-tracking devices can be used to monitor arterial distension, but their use is again limited to superficial arteries.

Several publications have used MR to measure luminal area variation over the cardiac cycle (9). The
accuracy of a pulse sequence in tracking vessel area changes is limited by temporal and spatial resolution, and will also vary depending on the contrast at the blood/wall interface. Although cine phase contrast was originally developed to quantify velocity and flow over the cardiac cycle, the magnitude images have previously been used to measure area variations (10–12). Cine bright-blood imaging has also been applied to measure area changes over the cardiac cycle (13,14). Intuitively, black-blood imaging is likely to produce a better contrast between the lumen and vessel wall. Buonocore and Bogren have previously presented a cine black-blood sequence where flow suppression is achieved using spatial presaturation bands (15). Separately, Berr et al developed a cine black-blood pulse sequence for cardiac MRI of the mouse heart using a double inversion recovery preparation to suppress signal from the lumen (16).

The aim of this work was to assess the accuracy of different MR pulse sequences for the measurement of DC and CC by means of experiments conducted on a human-tissue-mimicking phantom in comparison to high resolution digital photography (HRDP) as the gold standard. The pulse sequences considered in this study were two-dimensional (2D) cine phase-contrast and cine gradient echo, and a cine black-blood sequence with flow suppression achieved using spatial saturation bands.

MATERIALS AND METHODS

Experimental Setup

A polyvinyl alcohol cryogel (PVA-C) tube (inner diameter = 7.94 mm, outer diameter = 11.06 mm, length = 30 cm, $T_1 = 1600$ ms, $T_2 = 65$ ms, elastic modulus = 340 kPa) was used to simulate a human artery. The tube was manufactured following the protocol outlined in Surry et al (17) with additional modifications taken from Orr et al (18) and Chu and Rutt (19). PVA powder (99–100% hydrolyzed, Fisher Scientific, Loughborough, UK) was dissolved in de-ionized water to give a solution of 10 wt% PVA, 0.2 wt% germal plus biocide (International Speciality Products, UK) and 1.5 wt% agarose gel (Fisher Scientific, Loughborough, UK). After de-gassing under vacuum and leaving overnight, the solution was injected into a polycarbonate tube (inner diameter) with 2 NEX, and 512 (50 pixels across tube’s inner diameter) with 5 NEX. All (G4-KCT-KKA, ECO Gearchem, West Sussex, UK) was used to produce physiologically realistic flow waveforms. An aortic type waveform with peak and average flow rates of 30 mL/s and 15 mL/s was used in all the experiments to give velocities and deformations comparable to those found in vivo. Blood mimicking fluid ($T_1 = 850$ ms, $T_2 = 170$ ms) was used as the working fluid (Shelley Medical Imaging Technologies, Ontario, Canada).

The deformation of the PVA-C phantom was quantified in terms of the diameter variation in the left–right direction. The same measurement was quantified using time-resolved HRDP and was conducted outside the scanner room. To minimize variation in the deformations produced within the phantom inside and outside the scanner room, the distances and elevations of the setup equipment (i.e., between the reservoir, pump, and phantom) were measured and replicated. Because a direct pressure measurement on the PVA-C phantom was not possible due to its high flexibility and relatively fragile nature, the pressure waveform was recorded immediately upstream of the flexible segment by means of a conventional compensated pressure sensor (Sensym, Germany) to ensure that the same deformations were induced.

HRDP was performed using a Pixelink video camera (Pixelink, Ottawa, Canada) mounted perpendicular to the PVA-C phantom. The images were acquired at a rate of 25 frames per second with a pixel size of 28.5 μm. The images were calibrated against a sub-millimeter scale positioned at the same focal distance as the vessel mid-plane. Because PVA-C is a hydrogel and, hence, effectively incompressible and the tube is clamped at its ends so that its length does not change, the deformation of the external diameter recorded by HRDP was converted into variation of the internal diameter by imposing that the tube cross-sectional area is constant.

Image Acquisition

Images were acquired on a 1.5 Tesla (T) whole-body system (Signa HDx, GE Healthcare, Waukesha, WI) using a 3-inch surface coil placed directly on top of the water-filled perspex box. Axial images were acquired using standard 2D cine phase contrast (CPC) and cine gradient echo bright-blood (CBrB) sequences. Flow compensation was used for the CBrB acquisition to minimize intra-voxel phase dispersion. The CPC sequence was not flow compensated.

In addition, a custom-developed cine black-blood (CBB) gradient echo sequence was performed. Flow suppression was achieved using a Hadamard RF pulse to perform symmetrical spatial saturation inferior and superior to the image slice. The saturation bands were prescribed 80 mm thick and centered 60 mm away from the image slice. Flow compensation was not used to maximize dephasing. For all three sequences, 50 temporal phases were reconstructed retrospectively for each R-R interval. Images were acquired using matrix sizes of $256^2$ (25 pixels across the tube’s inner diameter) with 2 NEX, and $512^2$ (50 pixels across tube’s inner diameter) with 5 NEX. All
three sequences were triggered using a simulated ECG produced by the flow simulator. The imaging parameters for the three acquisitions are presented in Table 1.

### Image Postprocessing

A localized region-based active contour, proposed by Lankton and Tannenbaum (21), was used to segment the images. The main idea underlying this class of algorithms is to re-formulate classic region-based active contours onto a local basis so that the contour is driven by local rather than global statistics. The method was implemented in Matlab version 7.5.0 (The Mathworks, Inc., Natick, MA) using the level set formulation (21,22) and with minimal user interaction. Active contour methods start with an initial curve which is iteratively deformed until it reaches the “real” edge of the object being segmented. The initialization step was only performed on the first image in the time series; all subsequent time frames were initialized using the contour from the previous temporal phase. The algorithm is initialized by defining points (ranging from 4 to 8) approximately located on the vessel boundary. Convergence was judged to be achieved for each time frame when the root-mean-square deviation between two consecutive curves was less than $10^{-5}$ mm. Only two parameters (representing the localization radius $r$ and smoothing parameter $\lambda$) were changed by the user to tune the segmentation for each sequence. For consistency, the choice of the two parameters was made on the first time frame for each set of images and all the remaining images in the same time series were segmented using the same set of parameters. The smoothing parameter $\lambda$ was set to 0.1 for all images. The localization radius $r$ was chosen to include as many pixels as possible without intercepting irrelevant image features (21). The value $r$ was changed between 5 to 10 pixels, depending on the pulse sequence used and image SNR. The diameter in the left–right direction was computed as $D_p = D_{ext} - 2t$, where $t$ is the thickness of the tube.

### Statistical Analysis

A Bland-Altman analysis (23) was performed to compare the defined gold-standard HRDP against the diameter in the left–right direction from each of the MR techniques. Bias was calculated as the mean of the differences ($\text{diff}$) between the gold-standard and each technique $[\text{mean}(\text{diff})]$. The 95% limits of agreement (LOA) were defined as the bias $\pm 1.96 \times \text{std}(\text{diff})$.

### Table 1

| Imaging Parameters for CBB, CBrB, and CPC (Listed as 2562/5122 Where Different) |
|-----------------------------------|-----------------|-----------------|-----------------|
| Black blood                       | Bright blood    | Phase contrast  |
| TR (ms)                           | 9.4/18.0        | 9.4/36.1        | 8.5/13.8        |
| TE (ms)                           | 4.2/7.4         | 4.2/13.2        | 4.1/6.3         |
| Flip angle (°)                    | 20              | 20              | 20              |
| Field of view (mm)                | 80              | 80              | 80              |
| Slice thickness (mm)              | 10              | 10              | 10              |
| Flow compensation                 | No              | Yes             | No              |
| VENC (cm/s)                       | n/a             | n/a             | 100             |
| Signal averages                   | 2/5             | 2/5             | 2/5             |
| Views per segment                 | 1               | 1               | 1               |

Figure 1. Diameter (left–right direction) measurements for CBB, CBrB, CPC (magnitude), and the gold standard HRDP for the low (a) and high (b) resolution acquisitions.
where \( \text{stdev}(\text{diff}) \) is the standard deviation of the differences.

The signal-difference-to-noise ratio (SDNR) at the inner-wall/flow interface as defined by Thomas et al (24) was computed as a function of the temporal phase. The SDNR can be considered as a measure of image quality at a given interface. To minimize uncertainties related to the segmentation of the images, the SDNR should be reasonably high and constant over the simulated pulsatile cycle.

\[ \text{Figure 2.} \text{ Bland-Altman plots comparing diameter (left-right direction) from the gold-standard HRDP against CBB, CBrB, and CPC (magnitude) for the low resolution (a: 256 \times 256) and high resolution (b: 512 \times 512) acquisitions.} \]

\[ \text{Figure 3.} \text{ Signal difference to noise ratio (SDNR) at the wall lumen interface as a function of the temporal phase for the low (a) and high (b) resolution acquisitions.} \]
RESULTS

There was good agreement between the experimental setup outside the MR scanner room for HRDP measurements and the experimental setup replicated inside the scanner room as demonstrated by a normalized root-mean-square deviation between pressure measurements inside and outside the scanner room of 0.06%.

The diameters in the left-right direction for CPC (magnitude images), CBB, CBrB, and the defined gold-standard HRDP are plotted over the simulated pulsatile cycle in Figure 1. Bland-Altman plots comparing the gold standard with each MR-derived diameter measurement are shown in Figure 2.

For the 256^2 acquisition, cine bright-blood gave the best results in terms of global agreement, with a bias of 0.073 mm; however, the tube diameter was overestimated for most of the pulsatile cycle, with the distance between the two curves greatest for the systolic phases. The 95% LOA were -0.1 to 0.247 mm. Cine black-blood gave good agreement in the systolic phases, but the diameter was underestimated during the diastolic part of the cycle (bias = -0.086 mm). The 95% LOA were -0.296 to 0.123 mm. CPC systematically underestimated the tube diameter over the pulsatile cycle. The bias was -0.234 mm and the 95% LOA were -0.4 to -0.067 mm. For the 512^2 acquisition, all LOA and biases were reduced. CBB and CBrB were confirmed to be the most accurate with biases of -0.032 and 0.042, respectively. The 95% LOA were -0.209 to 0.146 and -0.11 to 0.194 mm, respectively. For CPC, the bias was -0.155 mm and the 95% LOA were -0.29 to -0.02 mm.

Figure 3 shows the SDNR as a function of the temporal phase for the low and high resolution acquisitions. In the high resolution case, CPC SDNR was similar to CBrB. In the 256^2 acquisition, CBB had the highest mean SDNR value (7.92 ± 1.238) over the pulsatile cycle; CBrB and CPC had a mean SDNR value of 4.87 ± 1.021 and 5.88 ± 1.964, respectively. In the 512^2 acquisition, CBB had a lower SDNR value (4.15 ± 1.823), while CBrB and CPC had a mean SDNR value of 3.91 ± 0.672 and 4.83 ± 0.646, respectively.

Figure 4 shows black-blood, bright-blood and phase-contrast magnitude images corresponding to minimum diastolic and maximum systolic phases for the 256^2 and 512^2 acquisitions. Image contrast between the lumen and the tube wall was higher in the systolic images for both phase contrast and black
in blood. In diastolic images, slow-flow effects in proximity to the wall made segmentation more uncertain. In bright-blood images, flow-related artifacts tended to appear in the systolic phases when velocities were high; however, these artifacts were limited to the bulk of the lumen so that the SDNR was only marginally affected. High resolution images show details of the low velocity region close to the wall for the different sequences: (a) during diastole, when the velocity gradient at the wall was lower, flow suppression for the CBB acquisition was degraded in a relatively thick boundary layer region (white arrow); (b) In CPC images, significant asymmetric ring artifacts appeared in both diastole and systole (black arrows); (c) CBrB images showed very few boundary effects, but systolic image quality appeared worse than the corresponding low resolution case, probably due to the longer TE.

In Table 2, the area variation over the simulated cardiac cycle, the minimum diastolic area, the cross-sectional distensibility coefficient and the compliance coefficient were derived using black-blood, bright-blood, and phase-contrast imaging using a nominal $\Delta P = 100 \text{mmHg}$ for the low and high resolution cases. For the $256^2$ acquisition, black-blood and bright blood gave similar results in terms of area variation and hence compliance coefficient (relative error in CC = 6%). However, the small difference between bright-blood and black-blood-derived diastolic areas (relative error = 5%) translated into a 12% difference on the distensibility coefficient. CPC images gave a 17% increase in compliance and a 15% increase in distensibility compared with CBB. For the $512^2$ acquisition, CBB, CBrB, and CPC-derived distensibility coefficients yielded the same value (0.0027 mmHg$^{-1}$). Deviations of the compliance coefficient from the black-blood-derived value were 3% and 10% when using CBrB and CPC, respectively.

Table 3 shows percentage differences in the compliance and distensibility coefficients with respect to high resolution CBB when using different pulse sequences for the low and high resolution cases. For the CBB acquisition, increasing the pixel size produced an 11.1% and 7.7% decrease in DC and CC, respectively. At both low and high resolution, CBrB agreed best with CBB while CPC-derived values were underestimated with the exception of the high resolution DC.

### DISCUSSION

To the authors' knowledge this study is the first of its kind to report on the accuracy of MR-derived measurements to quantify diameter changes, compliance coefficients, and distensibility coefficients in a tissue-mimicking pulsatile-flow phantom. CPC-magnitude images were found to underestimate the luminal diameter variation curve systematically over the cardiac cycle. CBrB and CBB proved to be in better agreement than CPC with HRDP. CBrB-derived diameters were more accurate in the diastolic phases, while CBB-derived diameters gave the best results in the systolic phases. Increasing spatial resolution improved agreement with HRDP for all sequences.

Although CPC has been used by several investigators to measure arterial distension (10–12), many potential sources of error can affect the extracted area over the cardiac cycle (25). Intra-voxel phase dispersion (IVPD) and partial volume effects can cause partial or even total phase cancellation leading to underestimation of the extracted area. Preprocessing techniques aimed at removing the contribution of static tissue in voxels only partially occupied by flow (26), and semi-empirical correction techniques to improve vessel segmentation (27) have been proposed. A major effort has been made to improve the segmentation algorithms used to derive the area information from CPC images. Conventional edge detection algorithms often fail due to fuzzy boundaries, poor image contrast, and the complex background that characterizes CPC magnitude images. In addition, manual or semi-automatic techniques that are still considered the gold standard, are usually time consuming and highly observer-dependent. Fully automated model-based algorithms which assume a priori knowledge of the velocity profile have been proposed by various groups (28–30), despite the main limitation of this approach that the standard assumptions on the flow profile are not applicable to most arterial segments due to vessel curvature, entrance effects, and complex hemodynamics. Active contours modified to account for the missing edge information and limited spatial resolution have recently been used as a valid alternative (31,32).
this work, a recently proposed localized region-based active contour was used to segment the images, and the MR imaging parameters were carefully selected to optimize image quality. Direct comparison with HRDP showed a systematic underestimation of CBB-derived diameters over the cardiac cycle. CPC magnitude images were characterized by a dark ring (signal void area) close to the wall due to IVPD and partial volume effects. The thickness of the signal void next to the wall was found to vary during the cardiac cycle, and pixel intensities within this region varied as a function of the angular position around the tube. The high resolution acquisition showed additional details of the boundary layer region. In particular, its irregular shape due to complex flow patterns within the tube showed that a posteriori corrections of the extracted contours cannot be based on simple inflation/deflation of the original contours. CPC SDNR showed a peak in proximity to the systolic phases for the low resolution acquisition caused by wash-in effects at high velocities. At high resolution, increased signal inhomogeneity prevailed over the high-flow related signal enhancement resulting in CPC SDNR being more uniform over the simulated cardiac cycle.

In bright-blood images, boundary effects were limited to a much thinner layer in proximity to the wall, and its thickness did not vary significantly during the cardiac cycle compared with CPC.

General signal heterogeneity was seen in higher resolution images as a consequence of the longer TE. To a smaller extent, the same effect was found in high resolution CPC images. CBB SDNR was reasonably high and constant over the cardiac cycle. The slight decrease in mean SDNR for the high resolution case was due to signal reduction in proximity to systole. Although CBB proved to be more accurate than CPC, few authors made use of this technique to evaluate arterial distension and compliance coefficients (13,14). Krug et al compared compliance values obtained using balanced SSFP and FLASH with those derived from phase contrast pulse wave velocity measurements and showed that balanced SSFP agreed best with pulse wave velocity than FLASH (13). However, using our MR system the minimum field-of-view of the balanced SSFP sequence was 180 mm compared with the 80 mm used in this study. Some studies have used spin-echo based sequences for the measurement of compliance (33), but these are time consuming and can only obtain data from one point in the cardiac cycle each time. They can also suffer from poor boundary definition in diastole as we found with our cine black-blood sequence. Because CBB was proved to perform better in low-velocity phases, its application could be particularly valuable in cases where flow velocities are near to zero for much of diastole, as in the aorta for example.

Black-blood images showed better flow suppression during the high-velocity phases. Low-velocity phases were characterized by residual signal, especially close to the wall, leading to underestimation of the luminal area for the diastolic phases. The CBB SDNR was found to be more uniform and have a higher mean at low resolution. Indeed, decreasing the voxel size means that each pixel will contain a smaller range of velocities and, hence, will demonstrate a higher mean signal due to reduced intra-voxel phase dispersion compared with a larger voxel.

Because area measurements cannot be obtained from HRDP, compliance and distensibility coefficients could not be compared directly with the gold standard. In terms of diameters, both high resolution CBB and CBrB were found to be in very good agreement with HRDP, however, while the LOA were comparable for the two sequences, CBB showed the smallest bias. At low resolution, CPC-derived compliance and distensibility coefficients differed by 15% and 17%, respectively, when compared with CBB. When compared with high resolution black-blood, CBrB-derived compliance and distensibility gave the best agreement at both low and high resolution. CPC distensibility and compliance coefficients were underestimated (except DC at high resolution) but within 11% of the high resolution CBB values.

Although the results obtained in this work gave valuable insight into the performance of the different techniques for measuring arterial distension, several limitations must be taken into consideration. The obtained results cannot be generalized to clinical protocols using multiple views per segment, reduced signal averaging, or larger pixel sizes. Although HRDP was not performed in the scanner room, every effort was made to replicate consistent deformations inside and outside the scanner room. For HRDP, a temporal resolution of 25 frames per second, despite introducing minor irregularities in the corresponding diameter curve, was found to be a good compromise between HRDP image quality and smoothness of the resulting diameter curve. Complex flow patterns, such as those found at bifurcations or in the presence of disease (e.g., stenosis, aneurysm), were not simulated.
ACKNOWLEDGMENT

The authors thank Dr. Gordon Campbell for his advice on constructing the PVA-C tube.

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