Reproducibility of pulmonary blood flow measurements by phase-contrast MRI using different 1.5 T MR scanners at two institutions

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Abstract
Background: Magnetic resonance imaging (MRI) can be beneficial for diagnosis of disease by offering quantitative information. However, reproducibility can be a major problem when there is a numerical threshold in multi-institution, multi-vendor situations.

Purpose: To measure pulmonary blood flow with phase-contrast (PC) imaging using two different MR scanners (1.5 T) at different institutions in the same participants and to examine the reproducibility of the measurements.

Material and Methods: Participants were 10 healthy volunteers (5 men; age range, 27–36 years). The measurements included the mean and maximal blood velocities, the mean blood flow volume, and the acceleration time and volume (AT and AV), derived from the time-flow curve of the PC-MRI. Simultaneously obtained maximal, minimal, and mean areas from regions of interest set in the pulmonary artery were also calculated. In order to calculate the reproducibility of the quantitative variables, intra-class correlation coefficients (ICCs) were employed. When an adequate ICC was obtained, Bland–Altman analysis was conducted to identify any systematic bias.

Results: The ICCs were almost perfect for the mean blood flow volume and the AV \( (r = 0.82 \text{ and } 0.80) \), and were substantial in the mean and maximal areas, and the AT \( (r = 0.63, 0.74, \text{ and } 0.64, \text{ respectively}) \). However, there was a fixed bias in the area measurement between the two scanners. Also, the AV had a proportional bias.

Conclusion: Our results reveal that various indices derived from PC-MRI on different MR scanners are promising as common indices for pulmonary flow assessment. Research and clinical use of PC-MRI for the pulmonary artery is expected to extend to multi-institution situations.

Keywords
Magnetic resonance imaging (MRI), phase-contrast MRI, pulmonary artery, flow measurement, reproducibility, multi-vendor

Introduction
Magnetic resonance imaging (MRI) can provide excellent information about various diseases. It can also give beneficial information for diseases by offering quantitative information. However, reproducibility can be a major problem when we set a numerical threshold to use for clinical practice in multi-institution, multi-vendor situations. There are few studies that test the efficacy of a common index using MRI in different institutions and from different vendors. To our knowledge by a literature review, available common quantitative criteria across different vendors were only

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reported for apparent diffusion coefficient (ADC) values of various abdominal organs (1), liver magnetic resonance elastography (2), knee articular cartilage damage in osteoarthritis (3), and blood and cerebrospinal fluid flow quantification by phase-contrast MRI (PC-MRI) (4).

PC-MRI has been established as a non-invasive technique for the characterization of blood flow, usually in large vessels (5). PC-MRI can demonstrate hemodynamics in the pulmonary arterial system by measuring the blood flow rate non-invasively. It is thought that it could be used as a substitute for echocardiography and angiography (6–8). Pulmonary arterial hypertension (PAH) may be caused by idiopathic PAH, chronic thromboembolic pulmonary hypertension, or pulmonary hypertension due to left-sided heart and lung disease. Recently, treatment of PAH has advanced substantially including different types of special drugs and surgical procedures such as pulmonary endarterectomy and balloon pulmonary angioplasty (9). We consider that PC-MRI may be useful for the evaluation of the treatment effects of these new methods. If reproducibility in the measured values derived from PC-MRI across different MR scanners can be confirmed, it may be useful as a general test to evaluate pulmonary blood flow.

In the present study, the aim was to measure pulmonary blood flow in the same participants using a PC acquisition on two different 1.5 T MR scanners and examine the reproducibility of the measurements.

### Material and Methods

The institutional review board of each institution approved this prospective, multi-institution study and informed consent was obtained. The goal of the study was to determine the reproducibility of pulmonary blood flow measurements obtained with a PC acquisition on two different 1.5 T systems (Magnetom Avanto: Siemens HealthCare, Erlangen, Germany and Achieva: Philips Healthcare, Best, The Netherlands) in our institutions. The participants were 10 healthy, non-smoking volunteers (5 men; age range, 27–36 years) with no history of cardiac or respiratory disease.

In each institution, a PC-MRI was performed by retrospective ECG triggering with free breathing. The pulse sequences and the other parameters for the respective MR scanners are listed in Table 1. The flow was measured perpendicular to the vessel, resulting in a double-oblique slice orientation, and the region of interest (ROI) was set in the pulmonary artery truncus (Fig. 1) by a single researcher with 5 years of experience in diagnostic radiology. The measurements included the mean and maximal blood velocities, the mean blood flow volume, the acceleration time and volume (AT and AV), the maximal change of flow rate during ejection (M), and the M/AV derived from time-flow curve of the PC-MRI. Each image of the 32 frames per beat was obtained simultaneously, and the maximal, minimal, and mean areas of the ROI set in the pulmonary artery were calculated automatically. The maximal and minimal areas are almost analogous to the images of the systolic and diastolic phases. The examinations were performed on two different MR scanners in different institutions and the interval between both examinations was less than 1 month. The blood velocity, flow volume, and area were calculated automatically by software when the ROI was traced and the time-flow curve was also obtained automatically. The AT, AV, M, and M/AV were calculated by waveform analysis software (Flex Pro7.0, WEISANG, Ingbert, Germany).

### Statistical analysis

In order to calculate the reproducibility of the quantitative variables, intra-class correlation coefficients (ICCs) were employed by use of Statistical Package for the Social Sciences (SPSS) software, version 19 (SPSS Inc., Chicago, IL, USA). An ICC of more than 0.80 was defined as “almost perfect” and that from 0.61 to 0.80 as “substantial” (10). In addition, a Bland–Altman analysis was performed for the indices with adequate ICCs (substantial and almost perfect) to identify any systematic bias (MedCalc, Ostend, Belgium). A P value <0.05 was considered significant.

### Results

The ICCs were almost perfect for the mean blood flow volume and the AV (r = 0.82 and 0.80), and

| Pulse sequence     | Avanto | Achieva |
|--------------------|--------|---------|
| TR/TE (ms)         | 27.25/3.14 | 12/8.5  |
| FOV (mm)           | 260    | 240     |
| Matrix             | 256×256 | 256×256 |
| Number of acquisitions | 3     | 2       |
| Temporal resolution (frames/heart beat) | 32 | 32 |
| Segmentation factor | 4     | 2       |
| Slice thickness (mm) | 6     | 6       |
| Receiver bandwidth (Hz/pixel) | 391 | 398.6   |
| Flip angle (°)    | 30     | 30      |
| Velocity encoding (cm/s) | 150 | 200     |

FFE, fast field echo; FLASH, fast low angle shot; FOV, field of view; PC-MRI, phase-contrast MRI.
were substantial in the mean and maximal areas, and the AT (r = 0.63, 0.74, and 0.64, respectively) (Table 2). By the Bland–Altman analysis, the limits of agreement were small in all indices. However, there was a fixed bias in the area measurement between the two scanners. Most plots distributed from the x-axis in the negative direction, meaning the measured area obtained by the Avanto was smaller than that by the Achieva. In addition, the AV had a proportional bias (Fig. 2).

![Localizing images with a horizontal cross-section of the pulmonary artery trunk (PT). The flow was measured perpendicular to the vessel, resulting in a double-oblique slice orientation (a, b). (c) Magnitude and (d) velocity images of the pulmonary trunk were obtained and the ROI was set in the pulmonary artery truncus (open circle). The velocity image contains velocity flow data.](image)

**Table 2.** Values of ICC for each index derived from PC-MRI.

| Measurements               | Avanto (mean ± SD) | Achieva (mean ± SD) | ICC value | P value |
|----------------------------|--------------------|---------------------|------------|---------|
| Mean blood flow rate (mL/cm) | 18.4 ± 3.3         | 15.1 ± 2.8          | 0.49       | 0.005   |
| Maximal blood flow rate (mL/cm) | 76.4 ± 10.7       | 103.9 ± 30.1        | 0.31       | 0.057   |
| Mean blood flow (mL)       | 83.5 ± 15.2        | 86.1 ± 15.3         | 0.82*      | 0.001   |
| Mean area (cm²)            | 4.6 ± 0.6          | 5.2 ± 0.8           | 0.63*      | 0.001   |
| Maximal area (cm²)         | 5.8 ± 0.9          | 6.4 ± 1.0           | 0.74*      | 0.001   |
| Minimal area (cm²)         | 3.5 ± 0.5          | 4.2 ± 0.7           | 0.31       | 0.111   |
| AT (ms)                    | 142.2 ± 19.7       | 149.8 ± 19.4        | 0.64*      | 0.014   |
| AV (mL)                    | 26.2 ± 5.1         | 27.7 ± 7.6          | 0.80*      | 0.001   |
| M/AV (L/S²)                | 130.1 ± 25.6       | 129.3 ± 25.3        | 0.39       | 0.134   |

AT, acceleration time; AV, acceleration volume; M, maximal change of flow rate during ejection.
*Almost perfect.
*Substantial.
Discussion

The quantitative indices of PC-MRI for the pulmonary artery were used to assess PAH. In patients with PAH, the AT was shorter, the mean and maximal velocities and the AV were decreased, and the mean and maximal areas and the M/AV were increased. The mean velocity was correlated with the mean pulmonary artery pressure, and the AT, AV and M/AV were correlated with pulmonary artery resistance (11,12). Therefore, these
indices are expected to be useful in the therapeutic evaluation of patients with PAH. Clarification of the reproducibility of pulmonary blood flow measurements in a multi-institutional and multi-vendor situation is important for clinical applications. From our results, research and clinical usage of PC-MRI for the pulmonary artery can be seen as consistent across different scanners and institutions.

In this study, the indices under investigation can be divided into three categories: (i) blood velocity and flow volume; (ii) morphological area measurements of pulmonary arteries; and (iii) the indices obtained from the time-flow curve. In the category of blood velocity and flow volume, the mean flow volume had a high ICC score and no systemic bias using the Bland–Altman analysis. It is considered to be an excellent general index for pulmonary arterial flow. However, the mean and maximal velocities turned out to be inappropriate for a multi-vendor study. The velocity threshold was set at 150 cm/s and 200 cm/s at the respective institutions. The noise in the velocity image is determined by the flow-encoding velocity and the signal-to-noise ratio of the magnitude images. The better the encoding velocity matches the real velocity of the ROI, the more precise the measurement becomes. Noise in velocity images increases with larger velocity threshold values. We speculate that the velocity threshold of 200 cm/s from one of our institutions was too large and created more noise although they used 200 cm/s routinely for estimation of velocity of both thoracic aorta and pulmonary trunk simultaneously. In fact, the values of the velocity obtained at 200 cm/s were consistently larger than those at 150 cm/s (not shown in this paper). If we had used the same appropriate threshold value for the velocity, the mean and maximal velocities might have been useful indices for a multi-vendor study.

With regard to the morphological area measurements, the mean and maximal areas had relatively high scores in the ICCs analysis but those of the minimal area were low. As previously mentioned in the literature, the signal intensity is strong enough in the systolic phase, in other words the maximal area, to place the ROI easily whereas the low signal intensity of the minimal area during the diastolic phase likely affected the measurement. Moreover, the indices of the area measurement had a fixed bias on the Bland–Altman plot. Therefore, these measurements need to be used with caution. Regarding the indices obtained from the time-flow curve, the ICCs of the AT and AV were high scores. However, it would be better not to use the AV because our results indicated a proportional bias (correlation coefficient; $r = -0.635$, $P = 0.048$).

The present study has several limitations. First, the institutions where the MRI was performed were a considerable distance apart. Therefore, the participants' overall status might have changed between the time when the examination was performed in their hometown versus when it was performed at the other institution after arriving by air. The numerical value associated with pulmonary flow could have changed even though they were healthy volunteers. In fact, data from one volunteer are fairly different (not shown).

Second, the images for the quantification of PC-MRI must be acquired at a right angle to the blood flow. Placement of this plane in the pulmonary artery was usually carried out manually, so measurement error could occur between institutions due to different individual placement. Nevertheless, the operator bias in this current study may be low because the same person placed the ROI on the PC images from both institutions.

Third, the parameters of PC-MRI were set as the best sequence by the individual experience at each institution. For example, the velocity threshold was different; 150 cm/s versus 200 cm/s as mentioned before. Another important difference was the length of TR that determined the temporal resolution. The Philips scanner (TR, 12 ms) has more than three times the temporal resolution of the Siemens scanner (TR, 27.5 ms). Even if the velocity encoding images were less than 32 frames set in a cardiac cycle, the retrospectively interpolated methods applied to the nearest-neighbor images demonstrated the entire cardiac cycle efficiently.

From the data of the present study, the temporal resolution of the images did not generate a discrepancy between the two sets of imaging data. That being said, these different MR parameters might influence the similarity of indices made from each PC-MRI acquisition. It was thought that we should have decided on the appropriate parameters in advance using a phantom.

Fourth, there were 10 participants, which may be too small to evaluate minor differences between the MR scanners. If the participant number were to be increased, the similarities in each dataset might be more accurately obtained. Nevertheless, we believe that our data can provide good evidence for the reproducibility of PC-MRI at least from different scanners of two institutions.

In conclusion, our results reveal that various indices derived from PC-MRI on our different MR scanners are promising as common indices for pulmonary flow assessment. Research and clinical usage of PC-MRI for assessment of PAH treatment is expected to be open to multi-institution and multi-vendor situations.

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