Novel Method of Quantifying Pulmonary Vascular Resistance by Use of Simultaneous Invasive Pressure Monitoring and Phase-Contrast Magnetic Resonance Flow

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Background—Pulmonary vascular resistance (PVR) quantification is important in the treatment of children with pulmonary hypertension. The Fick principle, used to quantify pulmonary artery flow, may be a flawed technique. We describe a novel method of PVR quantification by the use of magnetic resonance (MR) flow data and invasive pressure measurements.

Methods and Results—In 24 patients with either suspected pulmonary hypertension or congenital heart disease requiring preoperative assessment, PVR was calculated by the use of simultaneously acquired MR flow and invasive pressure measurements (condition 1). In 19 of the 24 patients, PVR was also calculated at 20 ppm nitric oxide +30% (condition 2) and at 20 ppm nitric oxide +100% oxygen (condition 3), with the use of the MR method. This method proved safe and feasible in all patients. In 15 of 19 patients, PVR calculated by Fick flow was compared with the MR method. At condition 1, Bland-Altman analysis revealed a bias of 2.3% (MR > Fick) and limits of agreement of 50.2% to 45.5%. At condition 2, there was poorer agreement (bias was 28%, and the limits of agreement were 151.3% to 95.2%). At condition 3, there was very poor agreement (bias was 54.2%, and the limits of agreement were 174.4% to 66.0%).

Conclusions—We have demonstrated the feasibility of using simultaneous invasive pressure measurements and MR flow data to measure PVR in humans. (*Circulation*. 2004;110:826-834.)

Key Words: vasculature • magnetic resonance imaging • catheterization

Pulmonary hypertension is characterized by narrowing and occlusion of the small pulmonary arteries and increased pulmonary vascular resistance (PVR).1 PVR can be calculated by invasively measuring pulmonary artery pressure and flow. The calculated PVR and the response of PVR to nitric oxide (NO) and oxygen are used to assess suitability for surgery of patients with congenital heart disease and the need for vasodilator therapy in patients with pulmonary vascular disease.2,3

Currently, catheter manometers are used to measure pressure, whereas the Fick principle is used to quantify flow. However, the Fick principle cannot be considered a “gold standard.”4–6

The Fick principle requires measurement of hemoglobin, aortic and pulmonary artery oxygen saturations and partial pressures, and oxygen consumption. This dependency on multiple measurements leads to the accumulation of individual measurement errors and is a considerable source of inaccuracy.4–6 The accuracy and precision of the Fick principle is further reduced in patients with large intracardiac shunts and high pulmonary blood flow as the result of the reduced pulmonary arteriovenous oxygen content difference.4–6 Reliable PVR quantification is vital in this group of patients because they are likely to develop pulmonary vascular disease. The use of high-concentration oxygen as a pulmonary vasodilator further reduces the reliability of the Fick principle. This is a severe limitation because response to vasodilators is important in making treatment decisions about medical therapy.3

Other methods of invasive flow quantification (eg, indicator dilution and thermodilution techniques) also suffer from reduced reliability in the presence of cardiac shunts or valvular regurgitation.7

An additional problem with current techniques is the requirement for fluoroscopic guidance when placing and manipulating catheters. Exposure to medical radiation is increasingly being recognized as a significant health risk for both patients and healthcare professionals.8,9
There is a need for a method of flow quantification that allows accurate and reproducible measurement of PVR, with less exposure to x-ray radiation. Velocity-encoded phase-contrast magnetic resonance (MR) enables quantification of blood flow in major vessels. Cardiac output and the pulmonary-to-systemic flow ratio (Qp:Qs) measured with the use of this technique have been shown to be accurate. In addition, phase-contrast MR has been validated in numerous phantom experiments. However, it has not been previously possible to obtain invasive pressure and MR flow data simultaneously.

We have set up a program of MR-guided diagnostic cardiac catheterization in children and adults with suspected pulmonary hypertension. This technique allows simultaneous acquisition of invasive pressure and MR flow data with less exposure to x-ray radiation. The aim of the present study is to evaluate the practicality of this novel technique and compare it with the traditional method. We describe the first 24 patients to be studied in our facility.

Methods

Study Population

The study population consisted of 24 children and adults (median age, 6.4 years; range, 0.23 to 42.4 years) with either suspected pulmonary hypertension or congenital heart disease requiring preoperative assessment of PVR. All patients referred to our unit were included, with no exclusion criteria. Patient demographics, heart rate, surface area, estimated systolic pulmonary artery pressure, diagnosis, and reason for catheterization are shown in Table 1. All patients were in sinus rhythm. The local research ethics committee approved the study. Informed consent was given either by the patient or a parent or guardian (for patients under the age of 16 years).

Cardiac Catheterization

Subjects underwent cardiac catheterization in an MR interventional suite (1.5 T Intera I/T MRI scanner; maximum gradient performance, 30 mT/m amplitude; slew rate, 150 T/m per second; Philips Medical Systems) with x-ray backup (BV Pulsera cardiac x-ray unit, Philips Medical Systems) in the same room (XMR suite). General anesthesia was induced and maintained with propofol, and uncuffed endotracheal tubes were used in patients younger than 12 years of age. Catheter advancement was carried out either under MR guidance or by using a combination of x-ray and MR guidance, depending on ease of catheter manipulation. Angiographic catheters (4F to 6F) with carbon dioxide-filled balloons were used for all procedures, allowing visualization in both imaging modalities.

MR Catheter Visualization

All imaging was performed with the use of an adult or pediatric 2-element phase-array coil (Flex L, Flex M; Philips Medical Systems) for signal reception and the body coil for signal transmission. An interactive steady-state free precession sequence (echo time, 1.45 ms; repetition time, 2.9 ms; matrix, 128×128; field of view, 250 to 350 mm; 10 to 14 frames per second; flip angle, 45°; slice thickness, 6 to 8 mm; free breathing acquisition) was used to visualize the catheter balloon during manipulation within the heart and great vessels. The imaging plane could be manipulated in real time into any plane to follow the catheter.

PVR Data Collection

PVR data were collected in all 24 patients at baseline (30% oxygen) by means of the MR and Fick methods; 30% oxygen was used at baseline to compensate for the relative hypoxia associated with anesthesia. In 19 patients in whom assessment of response to vasodilators was clinically indicated according to our hospital policy, PVR was also calculated at 30% oxygen and 20 ppm of NO (condition 2) and at 100% oxygen and 20 ppm of NO (condition 3), by using both the MR and Fick methods.

Pressure data (main pulmonary artery and pulmonary wedge or left atrium) was collected in all 24 patients during image acquisition with the use of standard fluid-filled catheters coupled to a computerized data recording system (5S collect system, Datex Ohmeda).

MR Flow Quantification

Pulmonary artery flow data were acquired through the use of a flow-sensitive fast-field echo sequence (repetition time, ~9 ms; echo time, ~5 ms; matrix, 128 to 192×256, field of view, 250 to 350 mm; flip angle, 15°; slice thickness, 5 to 7 mm; free breathing acquisition, number signal averages of 3; retrospective gating, 20 to 40 phases; in-plane and through-plane resolution optimized to patient size). A dedicated nonlinear phase correction filter, based on Chebichev polynomials (Philips Medical Systems), was used to correct for phase errors introduced by eddy currents and Maxwell terms. In addition, the image plane was centered in the bore of the magnet to further reduce the phase errors. Image planes were located at the midpoint of the pulmonary artery or at the midpoint of the superior vena cava in patients with bidirectional cavopulmonary shunts. In the patient with a Waterston shunt, the pulmonary flow was defined as the difference between the preshunt and postshunt flow in the ascending aorta.

Fick Flow Measurement

In the 19 patients who underwent Fick flow measurement in response to vasodilators, blood samples were obtained from the pulmonary artery and the aorta or left atrium pulmonary vein, depending on anatomy. The oxygen saturations and partial pressures of these samples were measured (A-vox Systems Inc). This allowed quantification of oxygen content incorporating oxygen bound to hemoglobin and dissolved plasma oxygen. In conditions 1 and 2, oxygen consumption was measured with the use of a paramagnetic metabolic monitor (Deltrac, Datex Ohmeda); however, in condition 3, exposure to 100% oxygen made it impossible to measure oxygen consumption with the use of the metabolic monitor. Therefore, the oxygen consumption immediately before commencement of 100% oxygen was used. In 4 patients, technical difficulties with acquisition of oxygen consumption (ie, endotracheal leak) or oxygen content measurement invalidated calculation of pulmonary artery flow. These 4 patients were excluded from the comparison between Fick and MR quantification of PVR.

MR Validation In Vitro

A 25-mm-diameter distensible rubber tube embedded in methylcel-lulose gel was used to assess the accuracy and precession of phase-contrast MR. Pulsatile flow (1 to 8.7 L/min) and ECG gating were generated with the use of an animal bypass machine (Harvard Apparatus Inc). A solution of glycerol (40%) and water (60%) was used to mimic the MR (T1=850 ms, T2=170 ms) and viscous properties of blood. Accuracy was assessed by comparing a range of flow rates, quantified by means of the same MR sequence as used in the human study and with the use of the graduated cylinder and stopwatch method. For a given flow rate, the heart rate and stroke volume corresponded to expected values for age-appropriate patients with similar cardiac output. Precision was assessed by comparing repeated phase-contrast MR flow quantification at low, medium, and high flow rates. In addition, 10 phase-contrast MR measurements at high flow rate were made with the catheter in situ to assess the effect of the catheter on accuracy and precision.

Data Analysis

Averaged pulmonary blood stroke volume was calculated with phase-contrast MR data by means of a semiautomatic vessel edge detection algorithm (Flow, Medis), with operator correction. Pulmonary artery blood flow is the product of pulmonary blood stroke volume and heart rate. In all patients, each scan (n=62) was analyzed by 2 different researchers (blinded to each other’s results and to results derived from invasive oximetry) to test interoperator variabili-
TABLE 1. Patients’ Ages, Surface Areas, Heart Rates, Diagnoses, Reasons for Investigation, Additional MR Findings, and Baseline PVRs

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Surface Area, m²</th>
<th>Heart Rate</th>
<th>Diagnosis</th>
<th>Reason for Investigations</th>
<th>Additional MR Assessment</th>
<th>PVR RMR, WU/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.75</td>
<td>1.08</td>
<td>99</td>
<td>Tricuspid atresia, VSD</td>
<td>Previous catheter PA pressure 45/12 mm Hg. Preoperative assessment.</td>
<td>Tricuspid atresia, ASD, VSD, RV hypoplasia.</td>
<td>4.1</td>
</tr>
<tr>
<td>2</td>
<td>0.87</td>
<td>0.41</td>
<td>131</td>
<td>Large VSD</td>
<td>Presented late without symptoms. Estimated SPAP 84 mm Hg</td>
<td>Perimembranous subaortic VSD.</td>
<td>2.3</td>
</tr>
<tr>
<td>3</td>
<td>19.46</td>
<td>1.83</td>
<td>86</td>
<td>VSD</td>
<td>Estimated SPAP 55 mm Hg. No symptoms of PH.</td>
<td>Muscular VSD.</td>
<td>2.0</td>
</tr>
<tr>
<td>4</td>
<td>4.24</td>
<td>1.47</td>
<td>63</td>
<td>VSD, ASD</td>
<td>Previous catheter PA pressure 78/28 mm Hg. Hypopnea.</td>
<td>Large VSD. Dilated pulmonary arteries.</td>
<td>3.0</td>
</tr>
<tr>
<td>5</td>
<td>3.55</td>
<td>0.59</td>
<td>76</td>
<td>Scimitar syndrome, PH</td>
<td>Estimated SPAP 55 mm Hg. Symptoms of PH.</td>
<td>Very small RPA. No right-sided pulmonary veins seen.</td>
<td>7.4</td>
</tr>
<tr>
<td>6</td>
<td>6.76</td>
<td>1</td>
<td>109</td>
<td>Chronic lung disease, PH</td>
<td>Dilated RA and RV. TR. Estimated SPAP 110 mm Hg.</td>
<td>Normal pulmonary artery and venous anatomy.</td>
<td>13.8</td>
</tr>
<tr>
<td>7</td>
<td>1.76</td>
<td>0.46</td>
<td>100</td>
<td>AVSD repaired, residual VSD</td>
<td>Late AVSD repair. Estimated SPAP 94 mm Hg.</td>
<td>Residual VSD. No pulmonary artery or venous anatomy.</td>
<td>4.6</td>
</tr>
<tr>
<td>8</td>
<td>37.99</td>
<td>1.4</td>
<td>83</td>
<td>AV discordance, mitral atresia, PH</td>
<td>Symptoms of PH. Estimated SPAP 104 mm Hg.</td>
<td>Dilated RA and LA. Large muscular midtrabecular VSD.</td>
<td>4.5</td>
</tr>
<tr>
<td>9</td>
<td>9.47</td>
<td>0.89</td>
<td>115</td>
<td>Chronic lung disease, diaphragmatic hernia</td>
<td>Symptomatic requiring oxygen. Dilated RA and RV.</td>
<td>Normal pulmonary artery and venous anatomy.</td>
<td>2.0</td>
</tr>
<tr>
<td>10</td>
<td>0.52</td>
<td>0.35</td>
<td>93</td>
<td>Large complete AVSD</td>
<td>No symptoms or signs of heart failure. Estimated SPAP 90 mm Hg.</td>
<td>Complete AVSD. Large ventricular component.</td>
<td>3.3</td>
</tr>
<tr>
<td>11</td>
<td>0.47</td>
<td>0.31</td>
<td>134</td>
<td>VSD, DORV, PA Band</td>
<td>Low PA band gradient. Estimated SPAP 58 mm Hg.</td>
<td>Loose PA band. VSD.</td>
<td>4.2</td>
</tr>
<tr>
<td>12</td>
<td>0.78</td>
<td>0.3</td>
<td>147</td>
<td>VSD</td>
<td>Preoperative assessment. Estimated SPAP 60 mm Hg.</td>
<td>Large perimembranous VSD.</td>
<td>2.1</td>
</tr>
<tr>
<td>13</td>
<td>0.38</td>
<td>0.25</td>
<td>119</td>
<td>VSD</td>
<td>Estimated SPAP 55 mm Hg. Preoperative assessment.</td>
<td>Small VSD.</td>
<td>1.6</td>
</tr>
<tr>
<td>14</td>
<td>0.23</td>
<td>0.25</td>
<td>129</td>
<td>VSD</td>
<td>Symptomatic requiring oxygen. Estimated SPAP 60 mm Hg.</td>
<td>Multiple VSDs.</td>
<td>2.9</td>
</tr>
<tr>
<td>15</td>
<td>23.6</td>
<td>1.92</td>
<td>63</td>
<td>Connective tissue disease, Ross</td>
<td>Symptomatic. Reduced exercise tolerance. Dilated aorta, homograft narrowing, aortic and pulmonary regurgitation.</td>
<td>10.6</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>15.7</td>
<td>1.42</td>
<td>91</td>
<td>Chronic lung disease, HIV</td>
<td>Symptomatic Estimated SPAP 135 mm Hg.</td>
<td>Normal pulmonary artery and venous anatomy, no shunt.</td>
<td>30.9</td>
</tr>
<tr>
<td>17</td>
<td>4.08</td>
<td>0.98</td>
<td>85</td>
<td>Tetralogy of Fallot repaired, PR</td>
<td>Symptomatic Estimated SPAP 35 mm Hg.</td>
<td>Free PR. No VSD leak.</td>
<td>3.0</td>
</tr>
<tr>
<td>18</td>
<td>10.27</td>
<td>1.01</td>
<td>65</td>
<td>Mitral stenosis, PH</td>
<td>Symptomatic Estimated SPAP 35 mm Hg.</td>
<td>Mitral stenosis. Normal pulmonary veins and arteries.</td>
<td>3.2</td>
</tr>
<tr>
<td>19</td>
<td>1.21</td>
<td>0.35</td>
<td>121</td>
<td>Chronic lung disease, PH</td>
<td>Symptoms of PH. Normal pulmonary artery and venous anatomy.</td>
<td>6.6</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>7.3</td>
<td>0.85</td>
<td>119</td>
<td>ASD</td>
<td>Interprocedure assessment of PVR.</td>
<td>Closure of ASD under XMR guidance.</td>
<td>2.4</td>
</tr>
<tr>
<td>21</td>
<td>3.75</td>
<td>0.70</td>
<td>103</td>
<td>LH, cavopulmonary shunt</td>
<td>Preoperative baseline of PVR before TCPC.</td>
<td>Assessment of branch pulmonary arteries.</td>
<td>2.0</td>
</tr>
<tr>
<td>22</td>
<td>35.24</td>
<td>1.40</td>
<td>59</td>
<td>AVSD</td>
<td>Late closure. Estimated SPAP 93 mm Hg.</td>
<td>Large atrial component to AVSD, little ventricular component.</td>
<td>1.7</td>
</tr>
<tr>
<td>23</td>
<td>20.31</td>
<td>1.29</td>
<td>60</td>
<td>Pulmonary atresia, Waterstone shunt</td>
<td>Symptomatic. Assessment of suitability for TCPC.</td>
<td>Branch PA stenosis (not seen in previous angiograms). Dilated cardiac chambers.</td>
<td>2.9</td>
</tr>
<tr>
<td>24</td>
<td>5.95</td>
<td>0.68</td>
<td>98</td>
<td>Atralil syndrome</td>
<td>Before liver transplantation. Bilateral branch PA stenosis. CO increased in response to dobutamine.</td>
<td>1.1</td>
<td></td>
</tr>
</tbody>
</table>

Patients 1 through 15 underwent vasodilator testing. Estimated systolic pulmonary artery pressure (SPAP) from Doppler ultrasound is included if available. VSD indicates ventricular septal defect; PA, pulmonary artery; ASD, atrial septal defect; RV, right ventricle; RPA, right pulmonary artery; RA, right atrium; TR, tricuspid regurgitation; AVSD, atrioventricular septal defect; LA, left atrium; PR, pulmonary regurgitation; CO, cardiac output; and TCPC, total caval pulmonary connection.

### Statistical Analysis

Data are expressed as means (±SD) unless otherwise stated. A 2-tailed t-test was used to compare x-ray dose in the study and control population, the response to NO, and in vitro flow data. Correlation coefficients and Bland-Altman analysis were used to compare the different methods’ phantom flow quantification (phase-contrast MR versus stopwatch) and interrogator variability. Bias was the mean of the difference between the 2 methods, and agreement was the mean±2 SD.15 Precision was quantified by use of the 95% confidence intervals of the bias and the agreements.15 Correlation coefficients and Bland-Altman analysis were also used to compare the different methods of PVR quantification (Fick versus phase-contrast MR). To allow comparison of the differences between the 2 methods at each of the conditions, the bias, level of agreements,
TABLE 2. Hemodynamic Data at Condition 1 (Baseline), Condition 2 (20 ppm NO), and Condition 3 (20 ppm NO and 100% Oxygen) in the 15 Patients in Whom Fick and MR Were Compared

<table>
<thead>
<tr>
<th>Patient</th>
<th>Condition 1</th>
<th>Condition 2</th>
<th>Condition 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P_{transpulmonary} (mm Hg)</td>
<td>Q_{fick} (L/min)</td>
<td>PVR_{fick} (WU/m²)</td>
</tr>
<tr>
<td>1</td>
<td>18.0</td>
<td>6.1</td>
<td>3.0</td>
</tr>
<tr>
<td>2</td>
<td>18.5</td>
<td>9.5</td>
<td>1.9</td>
</tr>
<tr>
<td>3</td>
<td>12.0</td>
<td>6.3</td>
<td>1.9</td>
</tr>
<tr>
<td>4</td>
<td>14.2</td>
<td>5.2</td>
<td>2.7</td>
</tr>
<tr>
<td>5</td>
<td>20.6</td>
<td>1.9</td>
<td>10.8</td>
</tr>
<tr>
<td>6</td>
<td>34.0</td>
<td>1.8</td>
<td>19.2</td>
</tr>
<tr>
<td>7</td>
<td>27.0</td>
<td>6.3</td>
<td>4.3</td>
</tr>
<tr>
<td>8</td>
<td>39.0</td>
<td>10.4</td>
<td>3.7</td>
</tr>
<tr>
<td>9</td>
<td>4.0</td>
<td>1.9</td>
<td>2.1</td>
</tr>
<tr>
<td>10</td>
<td>21.0</td>
<td>6.9</td>
<td>3.1</td>
</tr>
<tr>
<td>11</td>
<td>15.0</td>
<td>4.4</td>
<td>3.6</td>
</tr>
<tr>
<td>12</td>
<td>21.0</td>
<td>10.5</td>
<td>2.0</td>
</tr>
<tr>
<td>13</td>
<td>6.0</td>
<td>3.1</td>
<td>1.9</td>
</tr>
<tr>
<td>14</td>
<td>17.0</td>
<td>4.2</td>
<td>4.1</td>
</tr>
<tr>
<td>15</td>
<td>18.5</td>
<td>2.7</td>
<td>6.9</td>
</tr>
</tbody>
</table>

P_{transpulmonary} indicates transpulmonary pressure; Q_{fick}, pulmonary blood flow calculated with Fick; Q_{mr}, pulmonary blood flow calculated with phase contrast magnetic resonance; PVR_{fick}, pulmonary vascular resistance calculated using Fick data; and PVR_{mr}, pulmonary vascular resistance calculated using phase contrast magnetic resonance data.

Results

Feasibility
Simultaneous pressure and flow data were obtained in all 24 patients. In 10 patients, catheterization of the pulmonary artery was achieved under MR guidance alone. In 14 patients, catheter advancement was carried out with the use of a combination of x-ray and MR guidance.

X-Ray Exposure
There was a significant difference between the mean x-ray dose received by the 24 patients in this study who underwent XMR-guided cardiac catheterization and control subjects, who underwent traditional cardiac catheterization (mean, 5.8±11.3 Gy cm² versus mean, 38.2±39.2 Gy cm², respectively, P<0.005).

PVR: Phase-Contrast MR
The mean baseline PVR for all 24 patients calculated with the use of phase-contrast MR flow data was 5.1±6.3 WU (Woods units)/m². In the 19 patients in whom the response to vasodilators was assessed, the baseline PVR was 5.9±6.8 WU/m². At condition 2 (20 ppm of NO), the mean PVR fell to 5.2±6.2 WU/m², a fall from baseline of 12% (P=0.049), and at condition 3 (20 ppm NO + 100% O₂), the mean PVR fell to 5.0±6.0 WU/m², a fall from baseline of 15% (P=0.044).

Phase-Contrast MR Validation
The correlation coefficient between flow quantified by use of phase-contrast MR and by use of a graduated cylinder and stopwatch method was 0.99 (P<0.001) (Figure 1). The bias was negligible (−0.02 L/min; precision, −0.10 to 0.06 L/min); an upper level of agreement was 0.26 L/min (precision, −0.11 to 0.40 L/min) and a lower level of agreement was −0.30 L/min (precision, −0.16 to −0.44 L/min). Precision was assessed by measuring the mean and standard error (as a percentage of the mean) of 10 repeated phase-contrast MR measurement at 3 flow rates. At the low flow rate, the phase-contrast MR flow was 0.74 L/min ± 0.7%; at the medium flow rate, the flow was 2.92 L/min ± 0.4%; and at the high flow rate, the flow was 5.05 L/min ± 1.2%. The mean flow rate with the catheter in situ was 5.19 L/min ± 0.9%, which was not statistically different from the flow rate without the catheter (P=0.1). Interoperator variability was minimal, with a bias of 0.02 L/min (precision, −0.01 to 0.05 L/min), an upper level of agreement of 0.22 L/min (precision, 0.16 to 0.27 L/min), and a lower level of agreement of −0.18 L/min (precision, −0.13 to −0.24 L/min).

PVR: Phase-Contrast MR Versus Fick
In the 15 patients in whom comparison between phase-contrast MR and Fick was made (Table 2), the mean PVR at baseline was 4.7±4.6 WU/m² with the use of Fick-derived flow data and 4.6±3.5 WU/m² with the use of phase-contrast MR flow data. At condition 2, the mean PVR measured with the use of Fick was 3.3±3.2 WU/m² and the PVR with the use of phase-contrast MR was 3.7±2.1 WU/m². At condition 3, mean PVR fell to 2.4±2.3 WU/m² with the use of Fick and 3.0±1.9 WU/m² with the use of phase-contrast MR flow data. At baseline, the correlation coefficient between the 2 methods was 0.91 (P<0.05) (Figure 2). Bland-Altman analysis revealed a bias of 2.3% (MR PVR > Fick PVR), with a precision of −10.9% to 15.6%, an upper limit of agreement of 50.2% (precision 27.2% to 73.2%), and a lower limit of agreement of −45.5% (precision, −22.6% to −68.5%). At condition 2, the two methods correlated less well (r=0.78,
The bias was 28% (precision, −6.1% to 62.1%), the upper limit of agreement was 151.3% (precision, 92.2% to 210.5%), and the lower limit of agreement was −95.2% (precision, −36.2% to −154.4%). At condition 3, the two methods showed poor correlation (\(r=0.59, P=0.02\)) (Figure 4) and very poor agreement. The bias was 54.2% (MR PVR > Fick PVR), with a precision of 20.1% to 87.5%; the upper limit of agreement was 174.4% (precision, 116.7% to 232.0%) and the lower limit of agreement was −66.0% (precision, −8.4% to −123.6%).

Discussion

We have demonstrated the feasibility of combining invasive pressure measurements and MR flow data to quantify PVR in humans. This technique raises the possibility of a more accurate method of PVR quantification, leading to better treatment of patients with pulmonary hypertension. In addition, this technique is straightforward to carry out, leads to reduced exposure to ionizing radiation, and can be combined with other MR techniques, allowing comprehensive cardiac assessment.
Calculation of PVR is essential in the treatment of patients with suspected pulmonary hypertension. Unfortunately, the Fick principle, which is used to quantify pulmonary artery blood flow, is an indirect and potentially flawed means of calculating pulmonary flow. This may lead to inaccuracies in PVR quantification, which could adversely affect patient treatment. The development of new methods of simultaneous flow and pressure quantification are therefore an important step.

Velocity-encoded phase-contrast MR is a validated technique that enables quantification of blood flow in major vessels. Our novel facility allows catheter placement under both x-ray and MR within the same interventional suite, allowing the safe combination of invasive pressure measurements and MR flow quantification. In all patients, we demonstrated the feasibility and safety of this new method. Furthermore, in 10 patients, catheter placement was accomplished wholly under MR guidance, thus eliminating x-ray exposure.

Validation of Phase-Contrast MR
Assessment of the accuracy and precision of a diagnostic method requires comparison with a gold standard. There is no in vivo gold standard for flow quantification. There are, however, a number of in vitro studies with nondistensible phantoms that have demonstrated the accuracy and precision of this technique. We have further demonstrated the in vitro accuracy and precision of phase-contrast MR in our

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**Figure 2.** Comparison of PVR calculated with the use of phase-contrast MR flow and Fick-derived flow at condition 1 (baseline). A, Correlation of PVR calculated with phase contrast by use of the two techniques. B, Bland-Altman plot of the difference in PVR calculated by use of the two techniques and mean PVR measured by use of the two methods.
facility by using a flow phantom that replicates in vivo conditions more closely than previous studies. In vivo internal validation of phase-contrast MR by comparison of aortic and pulmonary blood flow or comparison of phase-contrast flow through the pulmonary artery or aorta with the ventricular output measured from short-axis images has also been previously performed.16

**Figure 3.** Comparison of PVR calculated with the use of phase-contrast MR flow and Fick-derived flow at condition 2 (20 ppm of NO). A, Correlation of PVR calculated by use of the two techniques. B, Bland-Altman plot of the difference in PVR calculated by use of the two techniques and the mean PVR measured by use of the two methods.

### Discrepancy Between Fick and Phase-Contrast MR

We have shown reasonable agreement between Fick and phase-contrast–derived PVR at baseline. This corroborates a number of other studies that have found reasonable agreement between phase-contrast MR flow and invasive method of flow quantification (eg, Fick).10,11 However, we found that in the presence of NO, there was less agreement between the 2 methods, and with 100% oxygen and NO there was a large bias and worsening agreement. The Fick principle is known to be inaccurate and imprecise in the presence of high pulmonary blood flow and high concentrations of oxygen.5–6

Our phantom studies demonstrate that phase-contrast MR is accurate at high flow rates. In addition, the oxygen content of pulmonary arterial blood at 100% oxygen is similar to the oxygen content of aortic blood at baseline, where it has been shown that phase-contrast MR is accurate.10 We therefore believe that the worsening agreement between the 2 methods in response to pulmonary vasodilation is due to errors in the Fick method rather than phase-contrast MR and that the Fick method underestimates PVR in the presence of 100% oxygen and 20 ppm of NO. This has important implications for
patient treatment because response to vasodilators is integral to the assessment of patients with pulmonary hypertension.

**Reduced X-Ray Dose**

A further benefit of our MR method is the reduction in exposure to x-ray radiation. This is particularly important in children, who are more susceptible to the carcinogenic effects of x-ray dose. The reduced x-ray dose also allows more frequent invasive assessment of PVR. This will enable better monitoring of the effectiveness of new drug therapies. It also has implications for staff in the catheterization laboratory who may receive a significant cumulative dose in their working lifetime.

**Limitations**

Phase-contrast MR flow is less accurate in patients with either arrhythmias during acquisition or turbulent blood flow; the presence of these is a general limitation of this technique. We did not repeat previous work internally validating phase-contrast MR in our patient population because we did not wish to prolong the procedure times. However, we did demonstrate accuracy and precision of this technique in vitro. We also did not repeat previous work looking at the repeatability of the Fick method to minimize blood sampling, particularly in our younger patients. Finally, MR-guided cardiac catheterization takes longer than traditional techniques. This is partly due to the extra time required for patient preparation and transfer between modalities. However, the
procedure time has fallen, as we have gained experience, to \( \approx 2 \) hours.

**Conclusions**

We have demonstrated the feasibility of performing PVR quantification with the use of a novel MR method. Our facility includes an MR scanner with x-ray backup. We believe that phase-contrast MR is more accurate than Fick in measuring pulmonary blood flow. Although we have gone some way in demonstrating this, definitive proof requires invasive in vivo validation in an animal model of pulmonary hypertension. Reduction or elimination of x-ray radiation, added anatomic and functional information available with MR, and the relative ease and accuracy of phase-contrast MR flow quantification may make this technique the method of choice for invasive measurement of PVR.

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**References**

Novel Method of Quantifying Pulmonary Vascular Resistance by Use of Simultaneous Invasive Pressure Monitoring and Phase-Contrast Magnetic Resonance Flow

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