Objective characterization of disease severity by determination of blood flow reserve capacity of the popliteal artery in intermittent claudication

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Introduction
Blood flow provides important objective information on the hemodynamic significance of vascular lesions in peripheral arterial disease (PAD) [1]. However, blood flow in patients with intermittent claudication might be near-normal due to reduced demand under resting conditions and collateral artery formation [2,3]. In contrast to resting flow, the blood flow reserve capacity (BFRC; defined as the maximum degree of postischemic reactive hyperemia) correlates well with subjective severity of symptoms in patients [4] and stays compromised for a prolonged period of time compared to resting flow during the process of collateral formation [5]. The use of BFRC might therefore improve objective characterization of PAD disease severity and subsequent therapy monitoring compared to resting flow alone. Clinically, BFRC is usually measured using duplex ultrasonography but this method is limited by large interobserver variability in postischemic measurements [6]. The purpose of the current study was to develop a MR method capable of determining resting flow and BFRC of the popliteal artery, using serial velocity encoded 2D MR cine PCA flow measurements. Relevant blood flow reserve parameters were determined and it was evaluated whether these parameters were able to discriminate between patients and healthy volunteers.

Methods
Ten consecutive patients (age range: 50-81 years; 8 men and 2 women) with clinical symptoms of PAD (Fontaine II; intermittent claudication), as well as 10 healthy volunteers with no known or treated PAD symptoms (age range 21-27 years; 3 men and 7 women) were included. All subjects underwent serial ECG-triggered 2D cine phase-contrast MR flow measurements of the popliteal artery (matrix/TR/TE/flip angle/vene/SENSE: 380 x 240 / 9.7ms / 5.8ms / 30° / 100cm/s / 2x; 15 cardiac phases were reconstructed). All scans were performed on a 1.5T clinical scanner (Philips Intera R11.3, Philips Medical systems, Best, NL). A dedicated 128 cm 12-element phased array peripheral vascular coil was used for signal reception. Acquisition duration of 1 scan was heart rate dependent and ranged between 64 ± 9 seconds in patients and 70 ± 11 seconds in volunteers. Three measurements were performed at resting and 10 measurements during reactive hyperemia, as provoked by a previously described cuff inflation/deflation paradigm [7]. Resting flow, maximum flow, BFRC, BFRC-ratio (ratio between BFRC and resting flow), time-to-peak (TTP) and time-to-recovery of resting flow (TTR) were determined by two independent MRI readers (figure 1). All studies were independently analyzed by two readers blinded for the presence of disease. Statistical analysis was performed using an independent-samples t-test. P < 0.05 was considered statistically significant.

Results
Examples of flow measurements in a patient and a healthy volunteer are given in figures 2 and 3. In the table results are listed for patients and healthy volunteers. Patients had much lower resting flow as well as much lower maximum flow compared to healthy volunteers. TTP and TTR, however, were roughly comparable between patients and healthy volunteers. Statistically significant differences between patients and healthy volunteers were found for resting flow and maximum flow, maximum flow and BFRC. The ratio of BFRC to resting flow was unable to discriminate between patients and healthy volunteers. No significant differences were found for TTP and TTR between patients and healthy volunteers, although there was a trend towards prolonged TTP and TTR in patients.

Table 1. Flow parameters (mean ± SD) in patients and healthy volunteers.

<table>
<thead>
<tr>
<th>Table 1. Flow parameters (mean ± SD) in patients and healthy volunteers.</th>
<th>Mean resting flow (mL/s)</th>
<th>Mean maximum flow (mL/s)</th>
<th>Mean BFRC (mL/s)</th>
<th>Mean BFRC-ratio (%)</th>
<th>Mean TTP (s)</th>
<th>Mean TTR (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>Volunteers</td>
<td>p-value</td>
<td>Patients</td>
<td>Volunteers</td>
<td>p-value</td>
<td>Patients</td>
</tr>
<tr>
<td>Reader 1</td>
<td>Reader 2</td>
<td>Reader 1</td>
<td>Reader 2</td>
<td>Reader 1</td>
<td>Reader 2</td>
<td>Reader 1</td>
</tr>
<tr>
<td>6.9 ± 1.6</td>
<td>5.0 ± 1.7</td>
<td>11.0 ± 3.0</td>
<td>11.3 ± 3.3</td>
<td>&lt;0.01</td>
<td>7.1 ± 1.2</td>
<td>7.0 ± 1.2</td>
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<td>BFRC, blood flow reserve capacity; TTP, time-to-peak; TTR, time-to-recover</td>
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</table>

Conclusions
Using 2D MR cine PCA flow measurements it is possible to determine resting flow and BFRC parameters in patients with intermittent claudication and healthy volunteers. A strong reduction in resting flow, maximum flow and BFRC was found in patients with intermittent claudication. This method can potentially be used to supplement MR angiography to objectively characterize PAD disease severity and to monitor therapy efficacy in intermittent claudication.

References
7. Ledermann HP et al. Circulation 2006;113:2929-2935