Blood Oxygenation Level–Dependent Magnetic Resonance Imaging of the Skeletal Muscle in Patients With Peripheral Arterial Occlusive Disease

Hans-Peter Ledermann, MD; Anja-Carina Schulte, PhD; Hanns-Georg Heidecker, MD; Markus Aschwanden, MD; Kurt A. Jäger, MD; Klaus Scheffler, PhD; Wolfgang Steinbrich, MD; Deniz Bilecen, PhD, MD

Background—Blood oxygenation level–dependent (BOLD) magnetic resonance imaging (MRI) has been used to measure T2* changes in skeletal muscle tissue of healthy volunteers. The BOLD effect is assumed to primarily reflect changes in blood oxygenation at the tissue level. We compared the calf muscle BOLD response of patients with peripheral arterial occlusive disease (PAOD) to that of an age-matched non-PAOD group during postischemic reactive hyperemia.

Methods and Results—PAOD patients (n = 17) with symptoms of intermittent calf claudication and an age-matched non-PAOD group (n = 11) underwent T2*-weighted single-shot multiecho planar imaging on a whole-body magnetic resonance scanner at 1.5 T. Muscle BOLD MRI of the calf was performed during reactive hyperemia provoked by a cuff-compression paradigm. T2* maps were generated with an automated fitting procedure. Maximal T2* change (ΔT2* max) and time to peak to reach ΔT2* max for gastrocnemius, soleus, tibial anterior, and peroneal muscle were evaluated. Compared with the non-PAOD group, patients revealed significantly lower ΔT2* max-values, with a mean of 7.3 ± 5.3% versus 13.1 ± 5.6% (P < 0.001), and significantly delayed time-to-peak values, with a mean of 109.3 ± 79.3 versus 32.2 ± 13.3 seconds (P < 0.001).

Conclusions—T2* time courses of the muscle BOLD MRI signal during postocclusive reactive hyperemia revealed statistically significant differences in the key parameters (ΔT2* max; time to peak) in PAOD patients compared with age-matched non-PAOD controls. (Circulation. 2006;113:2929-2935.)

Key Words: peripheral vascular disease ■ atherosclerosis ■ diagnosis ■ hemoglobin ■ muscles ■ magnetic resonance imaging ■ perfusion

Atherosclerosis is the leading cause of morbidity and mortality in Western industrialized countries. Peripheral arterial occlusive disease (PAOD) is an important clinical manifestation of atherosclerosis and a very important prognostic factor with respect to patients’ survival.1,2 It includes a wide spectrum of symptoms that range from intermittent claudication to critical limb ischemia. The primary pathophysiological mechanism of PAOD is a decrease of the peripheral blood pressure due to stenosis and occlusions along the arteries of an extremity, which results in impaired blood flow in the dependent tissue, such as musculature and skin. In routine clinical practice, ankle or toe pressure measurements are widely available, important techniques to judge peripheral blood supply but are only rough instruments and have several limitations. Conversely, radiography and magnetic resonance (MR) angiography (MRA) are imaging techniques to delineate the peripheral macrovasculature and to localize arterial lesions.3–6 However, sometimes additional data about the oxyhemoglobin content in the deep structures of the end tissue are warranted in the decision-making process about whether to improve blood flow via interventional procedures, such as angioplasty or bypass surgery. To bridge this gap, transcutaneous Po2 measurements have been introduced into clinical practice. This technique, however, is restricted to the superficial structures of the skin.7,8

With the discovery of the blood oxygenation level–dependent (BOLD) effect in the brain, new insight into the blood oxygenation of living tissue became feasible.9,10 It is generally accepted that BOLD magnetic resonance imaging (MRI) is sensitive to the concentration of paramagnetic deoxyhemoglobin and thus to the relative oxyhemoglobin content at microvascular level. It is assumed that the disproportional blood inflow during neuronal activation leads to an increase of the slightly diamagnetic oxyhemo-
globin at the postcapillary side, which is responsible for a signal gain in T2*-weighted MR sequences.\textsuperscript{11,12} This technique allows high spatial resolution mapping of the BOLD response within the tissue of interest. However, the BOLD signal is also influenced by changes in perfusion, oxygen extraction rate, and blood volume within the region of interest (ROI). For functional brain studies, its individual contributions have been described in detail previously.\textsuperscript{13}

Recently, BOLD MRI of the skeletal muscle in healthy volunteers has been introduced, and different paradigms, such as exercise, ischemia, postocclusive reactive hyperemia, and oxygen ventilation, have been used to provoke measurable BOLD signal alterations.\textsuperscript{14–17} As in neurofunctional studies, it is assumed that the muscle BOLD response originates predominantly from changes in tissue oxygenation.\textsuperscript{18–20} To date, BOLD MRI of the human skeletal muscle has been performed with physiological arterial blood supply. No data about impaired blood flow conditions, such as those encountered in patients with PAOD, are presently available.

Thus, the purpose of the present study was to measure the BOLD response in the calf muscle in symptomatic PAOD patients during postocclusive reactive hyperemia and to compare this response pattern with that of an age-matched non-PAOD group. A single-shot multiecho echo planar imaging (EPI) sequence was applied to assess pure T2* changes of the BOLD signal.

### Methods

#### Patient Selection

Seventeen patients (mean age 63.4±11.6 years; 10 males) with intermittent claudication (stage II of Fontaine classification) and 11 age-matched control subjects (mean age 64±6.7 years; 6 males) with no manifestation of PAOD underwent BOLD MRI of the calf muscle. The PAOD patients were recruited from the Department of Angiology, University Hospital Basel. Patients had restrictions of muscle. The PAOD patients were recruited from the Department of

### Table 1. Demographic Data

<table>
<thead>
<tr>
<th></th>
<th>PAOD Patients (n=17)</th>
<th>Age-Matched Controls (n=11)</th>
<th>2-Tailed t Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age, y</td>
<td>63.4±11.6</td>
<td>64.0±6.7</td>
<td>P=0.84</td>
</tr>
<tr>
<td>Male/female, n</td>
<td>10/7</td>
<td>6/5</td>
<td>0</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>24.7±5.0</td>
<td>24.1±3.0</td>
<td>P=0.68</td>
</tr>
<tr>
<td>ABI</td>
<td>0.6±0.2</td>
<td>1.1±0.1</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>135±14</td>
<td>138±15</td>
<td>P=0.80</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>83±12</td>
<td>83±10</td>
<td>P=0.94</td>
</tr>
<tr>
<td>Pain intensity*</td>
<td>3.1±0.8</td>
<td>Not evaluated</td>
<td>0</td>
</tr>
<tr>
<td>Side measured (left/right), n</td>
<td>13/4</td>
<td>10/1</td>
<td>0</td>
</tr>
</tbody>
</table>

BMI indicates body mass index.

Values are mean±SD or n.

*Scored on a 1 to 10 analogue scale, where 1=no pain and 10=maximum pain.

Cuff Compression Paradigm for Reactive Hyperemia

Reactive hyperemia was provoked with a cuff-compression paradigm. A conventional leg sphygmomanometer (15×75 cm) was fixed at mid-thigh level. Cuff compression with a pressure of 50 mm Hg above the individual brachial systolic blood pressure was applied during the ischemic phase for 360 seconds. Cuff compression was performed manually and was changed within 5 seconds. BOLD MRI measurements started contemporaneously with cuff deflation and continued for 360 seconds. Cuff deflation was initiated by fast opening of the air valve.

Subjective discomfort or pain perception of the patients was recorded after MRI with an analogue visual scale that ranged from 1 to 10,\textsuperscript{21} in which 1 was graded as no discomfort, and 10 was graded as maximal, unbearable pain.

### MRI Protocol

All MRI measurements were performed on a 1.5T scanner (Sonata, Siemens Medical Solution, Erlangen, Germany) with a peripheral vascular array coil. Patients and controls were investigated in the supine position. To evaluate T2* effects, a single-shot multiecho EPI sequence was applied to assess pure T2* changes of the BOLD signal.

### Table 2. Summary of Clinical Data

<table>
<thead>
<tr>
<th></th>
<th>PAOD Patients (n=17)</th>
<th>Age-Matched Controls (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking history</td>
<td>14 (82)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>4 (24)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>9 (53)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>8 (47)</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5 (29)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid-lowering agent</td>
<td>4 (24)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Blood-pressure drug</td>
<td>7 (41)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Heparin/vitamin K antagonist</td>
<td>3 (18)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Aspirin/clopidogrel</td>
<td>6 (35)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Values are n (%).
sequence with fat suppression and a temporal resolution of 1 measurement per second was used.\textsuperscript{22,23} Four axial slices with a slice thickness of 5 mm and an imaging gap of 2.5 mm were positioned in the upper calf at maximal diameter. Imaging parameters were as follows: field of view 380×238 mm; matrix size 128×80 mm; repetition time 1000 ms; and effective echo time with 4 echo images 16, 38, 61, and 83 ms. EPI images were supplemented with anatomic reference images of the corresponding 4 slices with a standard T1-weighted spin-echo sequence.

**Data Analysis**

T2* effects and initial signal intensity effects were separated by a pixel-by-pixel least-square fit of monoexponential decay to the signal intensities (S) of the 4 echo images \((T_{E1} \ldots)\). Parameter maps of T2* reflecting the true BOLD signal were generated from the multiecho EPI data according to the following equation

\[
S(I_0, T_{E1} \ldots) = I_0 \cdot \exp(-T_{E1}/T_2^*)
\]

where \(I_0\) refers to the initial signal intensity, which is modulated by perfusion, proton density, and T1, and \(T_2^*\) refers to effective echo time.

An ROI analysis was performed on the T2* maps with the statistical parametric mapping software BrainVoyager (Brain Innovation BV, Maastricht, the Netherlands). T2* time courses were extracted from rectangular ROIs within soleus, gastrocnemius, anterior tibial, and peroneal muscle. The size of the ROI was \(\sim \)90 pixels in the soleus, 100 pixels in the gastrocnemius, 40 pixels in the anterior tibial, and 50 pixels in the peroneal muscle. The ROIs were chosen to exclude pixels of large arteries and veins.

Further data analysis was performed for each muscle group separately with self-developed MATLAB (Mathworks, Natick, Mass) routines. Individual T2* time courses were normalized with respect to the average T2* value during the first 3 seconds after cuff deflation. To characterize the resulting normalized T2* time courses during reactive hyperemia, 2 parameters were determined: maximal T2* change \((\Delta T2_{\text{max}})\) and time to peak (TTP), i.e., the elapsed time between cuff deflation and maximal T2* change. \(\Delta T2_{\text{max}}\) and TTP values were calculated for each of the 4 muscles separately. In addition, mean \(\Delta T2_{\text{max}}\) and mean TTP were determined by averaging \(\Delta T2_{\text{max}}\) and TTP in all analyzed ROIs of the 4 muscles, irrespective of the muscle group.

Statistical analysis was performed with an unpaired, 2-sided Student \(t\) test to determine significant differences in \(\Delta T2_{\text{max}}\) and TTP between patients and the control group. The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

**Results**

BOLD MRI measurements were performed successfully. In all participants, suprasystolic cuff compression of the thigh was well tolerated. The patients’ scoring of discomfort ranged from 2 to 4 (mean 3.1±0.8), which reflects only mild to moderate discomfort due to cuff compression. Significant calf motion during the measurements was not observed.

Figure 1 illustrates the averaged and normalized T2* time courses in the anterior tibial, peroneal, soleus, and gastrocnemius muscle of PAOD patients and non-PAOD controls during 360 seconds of postocclusive reactive hyperemia. In both groups, all 4 muscles showed an increase in T2* after cuff deflation, followed by a nonlinear decline after peaking at TTP. When the T2* time courses of both investigated groups were compared, 2 relevant differences were observed: First, the \(\Delta T2_{\text{max}}\) values were significantly reduced in PAOD patients compared with the age-matched non-PAOD group \((P<0.001)\), with a mean \(\Delta T2_{\text{max}}\) of 7.3±5.3% versus 13.1±5.6%. Second, TTP values in the patient group were significantly delayed \((P<0.001)\). In healthy controls, the T2* time course reached its maximum after 32.2±3.3 seconds, whereas a considerable prolongation in TTP to 109.3±79.3 seconds was observed in the patient group.

In Figure 2, the individual TTP values of all 17 patients and 11 age-matched non-PAOD control subjects are plotted versus the corresponding \(\Delta T2_{\text{max}}\). TTP and \(\Delta T2_{\text{max}}\) of each individual were averaged over the 4 calf muscles. The distribution of TTP and \(\Delta T2_{\text{max}}\) was clearly different for PAOD patients and age-matched non-PAOD control subjects, which demonstrates a change in these 2 key parameters.

Analysis of the different calf muscles revealed quantitative differences in the T2* time courses. For both groups, the highest \(\Delta T2_{\text{max}}\) was found in soleus muscle (controls 19.0±5.2%, patients 10.5±6.3%). Rather low \(\Delta T2_{\text{max}}\) values were observed in the anterior tibial muscle (controls...
8.8 ± 2.4%, patients 5.3 ± 4.4%). Comparable results were found for the TTP values. High TTP values were assessed in the soleus muscle (controls 35.3 ± 15.3 seconds, patients 118.4 ± 82.7 seconds), low TTP values in the tibial anterior muscle (controls 31.9 ± 13.6 seconds, patients 103.9 ± 88.4 seconds). The key parameters $\Delta T2^*_{\text{max}}$ and TTP for the investigated calf muscles are summarized in Table 3.

The relation of ABI to TTP is plotted for the PAOD patients and non-PAOD control subjects in Figure 3. For the non-PAOD group with ABI values > 1, TTP values were ≤ 50 seconds or below. In the PAOD group, ABI values were < 1 and, with 1 exception, TTP values were > 50 seconds. In this group, the increase in TTP was accompanied by a decrease in ABI and vice versa.

**Discussion**

Functional MRI studies of the brain have demonstrated that the blood oxygenation level is inversely proportional to the T2* relaxation of the MR signal and can thus be used as a marker for the oxygenation level of tissue.24,25 Recently, application of the BOLD effect has been extended to other tissue sites, e.g., to assess oxygenation of the human heart26–28 and skeletal muscles.14,18,29 However, the origin of the BOLD effect in the skeletal muscle and its dynamic response to muscle work or ischemia is still an underinvestigated field of research and presently is not fully understood. In particular, the influence of an underlying vascular disease and its impact on muscle BOLD response has not yet been elucidated.

In the present study, we investigated symptomatic PAOD patients who had intermittent claudication with BOLD MRI and compared the results with an age-matched non-PAOD group. A postocclusive reactive hyperemia paradigm with cuff compression was applied to evoke $\Delta T2^*$ changes in the calf muscles. Cuff compression interrupted arterial inflow and venous outflow completely, and the fast cuff inflation (within 5 seconds), the contribution of the BOLD effect of venous filling was kept as low as possible. This cuff-compression approach was well tolerated in all PAOD patients, who reported only minor

**TABLE 3. Summary of $\Delta T2^*_{\text{max}}$ and TTP Values of the PAOD Patients and the Control Group for All 4 Investigated Calf Muscles Separately**

<table>
<thead>
<tr>
<th></th>
<th>Patients (n=17)</th>
<th>Controls (n=11)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta T2^*_{\text{max}}$ %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soleus muscle</td>
<td>10.5 ± 6.3</td>
<td>19.0 ± 5.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gastrocnemius muscle</td>
<td>8.7 ± 4.4</td>
<td>15.1 ± 4.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peroneal muscle</td>
<td>4.6 ± 3.8</td>
<td>9.5 ± 2.6</td>
<td>&lt;0.030</td>
</tr>
<tr>
<td>Tibial anterior muscle</td>
<td>5.3 ± 4.4</td>
<td>8.8 ± 2.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean $\Delta T2^*_{\text{max}}$</td>
<td>7.3 ± 5.3</td>
<td>13.1 ± 5.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TTP, s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soleus muscle</td>
<td>118.4 ± 82.7</td>
<td>35.3 ± 15.3</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Gastrocnemius muscle</td>
<td>103.1 ± 58.5</td>
<td>34.6 ± 14.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peroneal muscle</td>
<td>112.0 ± 89.8</td>
<td>26.9 ± 8.5</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Tibial anterior muscle</td>
<td>103.9 ± 88.4</td>
<td>31.9 ± 13.6</td>
<td>&lt;0.020</td>
</tr>
<tr>
<td>Mean TTP</td>
<td>109.3 ± 79.3</td>
<td>32.2 ± 13.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The difference in these parameters between groups was statistically significant for all muscles.
discomfort. In general, manual cuff compression is an easily applicable and technically simple method that does not require a specifically designed MR-compatible device, only a conventional leg sphygmomanometer cuff.

Application of the cuff-compression technique might be superior to treadmill paradigms, because this paradigm (1) is independent of the patient’s compliance, (2) can be standardized, and (3) is less hampered by motion artifacts of the leg. Additionally, in the case of treadmill studies, only specific calf muscles are activated, whereas cuff compression induces a general reactive hyperemia in all calf muscles.

We used a multiecho EPI sequence to measure pure T2* changes, which reflect alternations in blood oxygenation and exclude effects from blood inflow. Contrary to multiecho EPI, the BOLD signal change of conventional single-shot EPI is related to changes in T2* and initial signal amplitude/initial signal intensity. The latter is influenced by several parameters such as inflow (perfusion), changes in T1, and baseline drifts. A monoexponential fit to multiecho EPI enables a separation of oxygenation-related changes in T2* and other effects.

It is assumed that the main source of the T2* increase in BOLD MRI is related to a disproportional inflow of oxyhemoglobin during reactive hyperemia. The rapid T2* increase after cuff deflation with peak values after 30 seconds in the non-PAOD group in the present study is identical to previous reports with young healthy volunteers. However, the present study revealed significant differences in the key parameters T2*max and TTP in PAOD patients compared with the age-matched non-PAOD group. The T2* time course in PAOD patients revealed a significant reduction in ΔT2*max and a more than 2-fold prolongation of the TTP value.

We assume that the prolongation of TTP in PAOD patients is mainly caused by the impaired inflow of freshly oxygenated blood into the microvasculature of the calf muscles. However, the reduction of ΔT2*max in PAOD patients must be interpreted with care, because several aspects, including O2 extraction, vascular autoregulatory mechanism, and blood volume effects, must be taken into account. First, the continuous O2 extraction of skeletal myocytes is one of the mechanisms that influences oxyhemoglobin content at the capillary level during postischemic hyperemia. This O2 exchange is driven by diffusion and is a time-consuming process. In PAOD patients, impaired blood flow provides a longer contact time between the capillary blood, myoglobin, and oxygen-consuming myocytes. Therefore, more efficient deoxygenation of oxyhemoglobin is expected, leading to a higher final concentration of deoxyhemoglobin. This circumstance might contribute to an overall reduction in ΔT2*max. Compared with oxygen-consuming myocytes, myoglobin presumably plays a minor role in O2 extraction because of its low tissue concentration. Further investigations such as with near-infrared spectroscopy are needed to elucidate the interplay between oxyhemoglobin and deoxyhemoglobin. Furthermore, PAOD is accompanied by a reduction in perfusion reserve due to preexisting vasomotor relaxation or vessel wall rigidity. From neurofunctional studies, it is known that steno-occlusive disease of the carotid artery elevates the baseline condition for the BOLD contrast due to this relaxation process and compromises ΔT2*max. A similar phenomenon of vasomotor relaxation for the peripheral arteries was recently demonstrated by 201Tl scintigraphy in patients with long-standing diabetes mellitus. In that case, vessel wall rigidity might have played the major role.

With regard to the human brain, it is generally accepted that the BOLD response and its ΔT2* magnitude are closely correlated with blood volume within the ROI. A similar but presumably higher impact on ΔT2* changes can be expected for the human musculature. This can be inferred by an increase of arterial blood flow and the large venous reservoir within the calf. However, its contribution to ΔT2* changes has not yet been elucidated but might be accessible with a blood-pool contrast agent.

Animal studies have demonstrated that chronic ischemia damages capillaries and causes a reduction of the total capillary density in muscle tissue, a process that presumably occurs in PAOD patients. This overall reduction in blood volume may also contribute to the decrease in the ΔT2* change.

Qualitatively, a trend was observed for ABI and TTP values. With some exceptions, an increase in the TTP value was accompanied by a decrease in the ABI. Patients with very low ABIs demonstrated long TTP values. This phenomenon is conclusive, because ABI indicates the severity of the underlying PAOD with arterial lesions along the peripheral runoff.

The results of the present study revealed different T2*max and TTP values for the individual calf muscles in both groups. The highest T2*max values were observed in the soleus muscle, a finding that has been reported previously. The soleus muscle belongs to the slow-twitch oxidative tissue, which has a higher capillary density and therefore a higher blood volume than fast-twitch glycolytic (white) muscles such as the gastrocnemius. However, it is not clear whether the larger T2*max in the soleus arises from its greater capillary density, the orientation of its capillaries relative to the magnetic field, or both.

We assume that all of the described mechanisms interact and contribute to the decline in ΔT2*max in PAOD patients during reactive hyperemia. However, the individual extent of the different contributions is still unknown and beyond the scope of the present study. Future investigations of the BOLD effect in human skeletal muscle must be performed to elucidate its underlying mechanisms.

In the present study, we have demonstrated a significant change in the muscle BOLD response of PAOD patients in the key parameters ΔT2*max and TTP during reactive hyperemia. Muscle BOLD functional MRI might provide additional information about PAOD; however, its clinical impact with regard to its sensitivity and specificity must be determined in further prospective studies. Furthermore, muscle BOLD MRI may facilitate the objective assessment of responses to drug treatment or may play a role in the evaluation of new drugs. It might also allow monitoring of
the therapeutic success of interventional or vascular surgical procedures in the near future.

In conclusion, calf muscle BOLD MRI revealed significant differences in symptomatic PAOD patients compared with an age-matched control group during postocclusive reactive hyperemia. BOLD MRI of the calf muscles has the potential to provide a means to noninvasively monitor the success of therapy directly in the organ that is supplied by the arteries in PAOD patients.

Disclosures

None.

References


33. Hsu HB, Sun SS, Chen JJ, Tsai JJ, Kao CH, ChangLai SP. Usefulness of thallium-201 muscle scan to investigate perfusion reserve in the lower limbs of patients with systemic lupus erythematosus. Rheumatol Int. 2004;24:291–293.

34. Hsu HB, Sun SS, Chen JJ, Tsai JJ, Kao CH, ChangLai SP. Usefulness of thallium-201 muscle scan to investigate perfusion reserve in the lower limbs of patients with systemic lupus erythematosus. Rheumatol Int. 2004;24:291–293.

35. Hsu HB, Sun SS, Chen JJ, Tsai JJ, Kao CH, ChangLai SP. Usefulness of thallium-201 muscle scan to investigate perfusion reserve in the lower limbs of patients with systemic lupus erythematosus. Rheumatol Int. 2004;24:291–293.


**CLINICAL PERSPECTIVE**

Peripheral arterial occlusive disease (PAOD) is a widely prevalent manifestation of atherosclerosis. The limitation in perfusion to the skeletal musculature is responsible for clinical symptoms ranging from symptomatic claudication to limb-threatening ischemia. With magnetic resonance imaging (MRI), a single-shot multiecho planar imaging sequence was used to evaluate the blood oxygenation level–dependent (BOLD) signal change during reactive hyperemia in symptomatic PAOD patients, as a measure of oxygen delivery to the leg muscle tissue. Comparison of the key parameters time-to-peak BOLD signal and maximal T2* change revealed significant differences between the PAOD patients and an age-matched healthy, elderly referent population. A close relation between ankle-brachial index and time to peak was also elucidated, whereby ankle-brachial index values <1 were accompanied by an increase in time to peak and vice versa. The clinical impact concerning the sensitivity and specificity of muscle BOLD MRI for PAOD detection must be determined in future prospective studies. However, muscle BOLD MRI may facilitate the objective assessment of responses to drug treatment or may play a role in the evaluation of the effectiveness of new drugs or therapies, such as angiogenesis or interventional therapies, in patients with PAOD. This approach may provide a more sensitive index for appreciation of therapeutic effects, given that it evaluates tissue-level changes in oxygen delivery rather than flow in larger vessels.
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