# Skeletal Muscle Perfusion During Exercise Using Gd-DTPA Bolus Detection

Anders T. Nygren,[1] Dan Greitz,[2] and Lennart Kaijser[1]

[1]Department of Medical Laboratory Sciences & Technology, Division of Clinical Physiology, Huddinge University Hospital, Huddinge, Karolinska Institutet, Sweden
[2]MR Research Centre, Karolinska Hospital, Stockholm, Karolinska Institutet, Sweden

## ABSTRACT

The study was performed to evaluate if skeletal muscle perfusion can be determined during exercise using an IV bolus injection of Gd-DTPA. A fast spoiled gradient echo sequence (T1 weighted) was used with intermittent imaging during one-legged plantar flexion at different workloads. Between repetitive flexions, a 2-sec rest allowed magnetic resonance imaging (MRI) of the lower legs and measurements of the blood flow in the popliteal artery by ultrasonography for subsequent calculation of muscle perfusion. Maximal signal intensity, upslope and downslope of the bolus, mean transit time, and integrated curve area were measured within regions of interest bilaterally. The skeletal muscle perfusion estimated by ultrasonography increased in the exercising leg from $4 \ ml \cdot 100 \ g^{-1} \cdot min^{-1}$ at rest to 38 ml at low, 86 ml at medium, and $110 \ ml \cdot 100 \ g^{-1} \cdot min^{-1}$ at high workload. The $SI_{max}$ increased from $1.38 \pm 0.12$ to $1.58 \pm 0.15$ and the negative slope of the peak nonsignificantly from $- 2.38 \pm 1.75$ to $- 12.05 \pm 9.71$. All obtained MRI parameters could visually separate the muscles into exercising, nonexercising, and presumably low active muscles. It is concluded that the signal intensity curve using a fast spoiled gradient echo sequence did not overall quantitatively mirror the perfusion, evaluated as the blood flow measured by ultrasonography. However, the signal intensity seemed to follow the blood flow velocity within a limited range of $15–60 \ cm \cdot sec^{-1}$, corresponding to $35–90 \ ml \cdot 100 \ g^{-1} \cdot min^{-1}$. Nonetheless, it might be useful when studying ischemia or endothelial dysfunction in skeletal muscles during exercise.

KEY WORDS: Exercise; Gd-DTPA; Human; MRI; Perfusion; Skeletal muscle.

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## INTRODUCTION

Impaired perfusion of the lower extremities is a documented finding in patients with chronic heart failure (1), as it is in patients with peripheral artery disease (e.g., intermittent claudication), and may contribute to exercise intolerance. It is important that we can offer methods that can accurately measure regional skeletal muscle perfusion to evaluate the reason of impaired exercise tolerance and to localize areas of reduced perfusion. This also makes it possible to follow the effect of treatment, including physical training, medical, or invasive interventions. Our noninvasive methods of today are limited as to quantitate perfusion in regional skeletal muscles.

During the last years several reports have indicated that magnetic resonance imaging (MRI) using Gd-DTPA as an extravascular tracer can quantitatively assess tissue perfusion. The underlying mechanism for the correlation of the T1-weighted signal with tissue perfusion is a contrast enhancement by gadolinium due to its paramagnetic influence on water molecules. The gadolinium molecule will interact with the water molecules, both extra- and intracellularly. The achieved signal increase in the tissue is influenced by the presence of gadolinium in blood vessels and also in the extravascular space because Gd-DTPA is known to have a high rate of diffusion into the extravascular space. It is also clear that the signal intensity is not only influenced by the concentration of Gd. The used relaxativity agent, its volume of distribution, and the movement of water will probably also contribute to the signal enhancement (2).

The extravascular deposition of Gd-DTPA could make the substance less well suited for quantitative measurements of tissue perfusion due to unknown distribution volume and kinetics of the Gd-DTPA bolus. Nevertheless, several reports have indicated that the Gd-DTPA bolus kinetics can be used to assess regional tissue perfusion. For quantitative measurements, a modified Kety equation is commonly used (3) with determination of the capillary transfer constant. This mathematical approach has been used in the measurement of myocardial perfusion (4,5). A semiquantitative analysis of the signal-intensity curve, especially the characteristics of the upslope, has also been applied (6–8). The semiquantitative approach has also been used to estimate local renal ischemia (9,10). Graded ischemia induced in skeletal muscles by manometer cuff inflation and examination of the post-ischemic hyperemia with MRI has been performed (11), but no reports have presented perfusion in skeletal muscle at rest and during a graded dynamic exercise. This study was performed to evaluate whether skeletal muscle perfusion during exercise can be determined using Gd-DTPA bolus injection. Duplex ultrasonography in the popliteal artery was performed in both legs for quantification of the blood flow at rest and at different exercise levels.

## MATERIALS AND METHODS

### Subjects

Four healthy students were included, two men and two women, mean age 25 years (range 23–26). The Ethics Committee of Karolinska Institutet approved the study.

### Exercise Protocol

A specially designed movable foot ergometer was made in nonmagnetic materials so that the ergometer could be placed either on an examination bed or in the magnet. The ergometer was made for one-legged plantar flexion with the right foot. The subjects were in the supine position on a bed with one foot placed on the ergometer footplate. On the MRI slide the ergometer was stabilized by strings and adjusted with an aluminium cord against the MRI bed to prevent backward movements of the MRI slide during exercise with the weight-loaded ergometer. A cotton cord was attached to the footplate and was lined backward over a wheel and attached to an aluminium plate near the floor. Lead weights could be placed on the plate to allow graded exercise. Three subjects exercised at 4-, 14-, and 22-kg load (low, medium, and high workload) and one subject at medium and high workload. During one-legged exercise with the right calf (E-leg), the contralateral foot (N-leg) was in a fixed position.

For ultrasonographic measurements at all loads, the exercise was performed on the same day. Measurements started at rest and continued at low, medium, and high workloads with a 20-min rest between the different workloads. The exercise time was approximately 9 min at each workload. The E-leg performed graded plantar flexion exercise at 1 Hz. After 3 min of continuous exercise, the subjects performed an intermittent exercise with short breaks. Five flexions were followed by a 2-sec rest for ultrasonography or MR measurements. The MRI studies were performed on three separate days, using the same protocol.

### Duplex Ultrasonography

Pulsed Doppler recording of blood flow velocity in the popliteal artery at rest and during graded one-legged

exercise was performed using an ultrasound machine (HDI, Ultramark 9, ATL Ultrasound, Bothell, WA) equipped with a phased-array transducer (pulsed Doppler 2 MHz). The sampling volume was placed proximal to the branching of the gastrocnemic artery using a size that included most of the vessel diameter. The mean velocity was assessed using software (ATL) for automatic tracing. The diameter of the vessel lumen at rest was measured and used for calculations of the volume blood flow (ml · min$^{-1}$) ($\pi$ × vessel radius$^2$ [cm$^2$] × mean velocity [cm · sec$^{-1}$] × 60]. Heart rate was registered on a three-lead electrocardiogram recorder. To estimate the perfusion of the calf muscles, the obtained volume blood flow as mentioned above was used together with an approximate total muscle volume calculated with MRI on one subject.

## Magnetic Resonance Imaging

### In Vitro Study

Imaging was performed with a 1.5-T magnet using a birdcage quadrature head coil with a uniform field (Signa, General Electric, Milwaukee, WI). A phantom study was performed to ensure that the T1 sequence was sensitive to the concentration of Gd-DTPA (GdDTPA-BMA, Nycomed AB). In vitro concentrations of Gd-DTPA in NaCl from 0.039 to 3.333 mmol/l were prepared. A fast spoiled gradient echo sequence was used with a short TR and TE to reduce the effect of saturation and T2* (TR 9.7 msec, TE 4.6 msec, field of view 30 × 15 cm, matrix 256 × 128, slice thickness 10 mm). The matrix was set by 256 frequency-encoding and 128 phase-encoding steps, giving an in-plane resolution of 1.2 × 1.2 mm. Flip angles a with 10-degree interval from 90 to 10 degrees were tested. Number of excitations (NEX) differed using one, two, or three NEX at the different flip angle. The pulse sequence, fast spoiled gradient with flip angle 50 degrees and 3 NEX, was chosen after the in vitro study because it had the highest linear relationship with Gd-DTPA concentrations in the expected signal intensity range and best signal-to-noise ratio. This sequence was then used in the perfusion study. Gd-DTPA tubes attached to the N-leg during perfusion scanning confirmed the pulse sequence linearity from the in vitro study.

### In Vivo Study

Lower limb imaging was performed using parameters as described above with simultaneous imaging of right and left leg. The lower legs were placed through the head coil with the feet on the ergometer. To ensure that imaging was performed at the same location of the limb in all examinations, the isocenter of the imager was adjusted to a fixed distance from the medial knee joint. Single-slice imaging was performed at the level with the largest cross-sectional area (CSA) at mid-calf level. Multiple short-axis imaging (slice thickness 5 mm, slice interval 20 mm) was performed in one subject covering the lower limb to estimate total calf muscle volume. Forty-six slices were achieved, and manual planimetry performed on 13 slices allowed calculation of individual slice area, radius, and cylindrical volume. Between the imaged slices extrapolated cylindrical volumes were obtained. The cylindrical volumes were then summed and used as the approximate calf muscle volume. The specific density of the muscle was approximated to 1.0 and used when calculating the perfusion (ml · 100 g$^{-1}$ · min$^{-1}$); [measured volume blood flow (ml · min$^{-1}$) / calf volume (ml)] × 100.

Serial imaging was performed during exercise with an interval between sampling points of 7 sec, including 2 sec to acquire the image during the short interruption of exercise. After the first 10 initial baseline images during exercise, a hand-injected bolus of Gd-DTPA (Omniscan™, GdDTPA-BMA, 0.1 mmol · kg$^{-1}$) was given, and an additional 60 images were obtained. The injection was done as fast as possible and lasted approximately 3 sec. The exercise time at each load was approximately 9 min. Two subjects performed an additional exercise at high workload with Gd-bolus injection at the end of the exercise and immediate postexercise imaging.

Image analysis included manual planimetry of the CSA of the lower leg, excluding subcutaneous fat and including the tibia. Regional CSA of individual muscles were obtained by using the high-signal intensity induced by Gd-DTPA. Selected muscles were in the E-leg m. gastrocnemius medial portion, including m. plantaris (E-Gm) and both medial and lateral gastrocnemius (E-G), m. soleus (E-S), and in the N-leg m. tibialis anterior (N-T). A region of interest (ROI) of approximately 50 mm$^2$ was placed within both legs for measurement of signal intensities, medially in m. gastrocnemius (G), centrally in m. soleus (S) and m. tibialis anterior (T), excluding visible vessels.

The measured signal intensity during the loads was corrected with the baseline value, and a signal intensity time curve was used for analysis. Analysis of the signal intensity time curves included maximum intensity (SI$_{max}$) during the appearance of the bolus. The upslope of the peak was defined as the slope of the line, using the peak and the image before, and downslope using the image after the peak. The mean transit time and calculated integrated area was measured within 110 sec after the bolus

injection. An ROI of 2, 8, and 16 mm² was also placed in the E-leg within a small artery to define whether the arterial input curve could be used. Software from General Electric was used for calculation of CSA by manual planimetry and SI from multiple slice measurements. Measurements were done in a blinded fashion with name, date, and situation unknown for the examiner.

## Statistical Analysis

All values are expressed as mean ± SD. Statistical significance was evaluated by paired Student's $t$-test. Significant statistical level $p < 0.05$.

## RESULTS

### Ultrasonography

The mean blood flow velocity increased in the E-leg from $2.8 \pm 1.6$ cm · sec$^{-1}$ at rest to $28 \pm 12$ cm · sec$^{-1}$ ($p = 0.07$) at low, $55 \pm 15$ cm · sec$^{-1}$ ($p < 0.05$) at medium, and $77 \pm 19$ cm · sec$^{-1}$ ($p < 0.005$) at high workload. Corresponding blood flow was 60, 533, 1008, and 1484 ml · min$^{-1}$. The velocities did not change in the N-leg except for a nonsignificant numerical increase from $3.2 \pm 1.1$ cm · sec$^{-1}$ at rest to $4.3 \pm 0.8$ cm · sec$^{-1}$ at low, $3.7 \pm 0.7$ cm · sec$^{-1}$ at medium, and $5.6 \pm 1.8$ cm · sec$^{-1}$ at high workload. Corresponding blood flow was 62 ml · min$^{-1}$ at rest and 106 ml · min$^{-1}$ at high workload. Measured CSA of the popliteal artery at rest was $0.30 \pm 0.04$ cm² and was used for calculation of volume flow.

### Magnetic Resonance Imaging

#### Signal Intensities

Signal intensity time curves, obtained in 18 situations, showed a different pattern in different muscles of the exercising and nonexercising legs (Fig. 1, A–C). All signal intensity curves could visually separate the muscles into
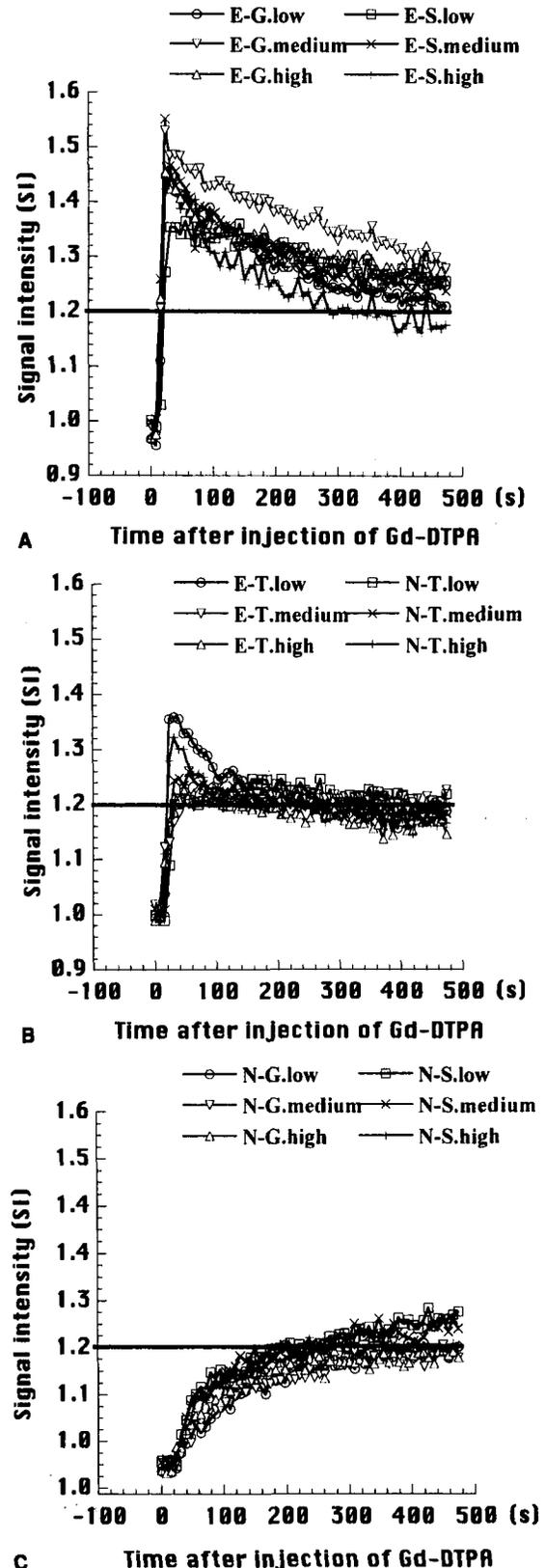
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**Figure 1.** (A) Signal intensity time curves in m. gastrocnemius (G) and m. soleus (S) in the exercising leg (E) at low, medium, and high workload. (B) Signal intensity time curves in m. tibialis anterior (T) in the nonexercising (N) and exercising leg (E) at low, medium, and high workload. (C) Signal intensity time curves in m. gastrocnemius (G) and m. soleus (S) in the nonexercising leg (N) during a contralateral leg exercise at low, medium, and high workload.

A  Time after injection of Gd-DTPA

B  Time after injection of Gd-DTPA

C  Time after injection of Gd-DTPA

three subgroups, exercising (E) and nonexercising (N) m. gastrocnemius and m. soleus (E-G, E-S, N-G, N-S) and m. tibialis anterior in both legs (E-T, N-T). In 10 situations a well-defined peak with a decreased SI could be seen in E-G, E-S, and E-T (at low workload) and in N-T (at low and medium loads). The peak was reached within four images with a duration of one image (2 sec). The mean appearance time was 39.5 sec at low and 31.6 sec at medium and high workload with an individual range of 15.8 and 47.4 sec depending on muscle group and workload. In two situations (E-T at medium and high workloads) an increased SI without a peak but a plateau within 50 sec without a decline could be seen. A continuously increasing SI during the whole scanning period of 500 sec was seen in the remaining six situations (N-G and N-S). When imaging immediately after high-intensity exercise, the bolus appeared within the same time but was longer, including five images (12 sec), than during exercise. The $SI_{max}$ was higher in the postexercise than the exercise image within the exercising muscles E-G and E-S but unchanged in E-T in the same subjects (Fig. 2). An arterial input function could not be obtained because the SI in the small artery had a low signal-to-noise ratio and was probably influenced by pulsatile artifacts.

The only parameter that changed significantly be-

tween loads was $SI_{max}$ between low and medium workload in E-S. $SI_{max}$ increase from 1.38 ± 0.12 to 1.58 ± 0.15 ($p < 0.5$), whereas a nonsignificant change in negative slope of the peak was seen in E-S from - 2.38 ± 1.75 to - 12.05 ± 9.71 ($p = 0.08$) (Table 1). The $SI_{max}$ was linearly correlated with the mean blood flow velocity in E-leg within the limited range of 15–60 cm · $sec^{-1}$, corresponding to 35 and 90 ml · 100 $g^{-1}$ · $min^{-1}$ (Fig. 3).

## CSA, Calf Muscle Volume, and Perfusion

The CSA of the E-leg was unchanged at low workload, 85 ± 11.2 $cm^2$, increased by 2.8 % to 90.9 ± 8.57 $cm^2$ ($p < 0.05$) at medium and by 6.4% to 94.1 ± 8.57 $cm^2$ ($p < 0.05$) at high workload. At lower workloads it increased relatively more in m. gastrocnemius than in m. soleus. The increase at medium workload was, in relation to the maximal increase, 80% in E-G, 39% in E-Gm, and 31% in E-S. The CSA was unchanged in the N-leg at low workload (84.4 ± 13.1 $cm^2$) and decreased nonsignificantly by 0.5% at medium and by 1.8% at high load despite an increase in N-T by 8.8% at medium and by 14.9% at high load.

The blood flow was 53 ml · min $^{-1}$ at rest, 500 ml at low, 1200 ml at medium, and 1500 ml at high workload.
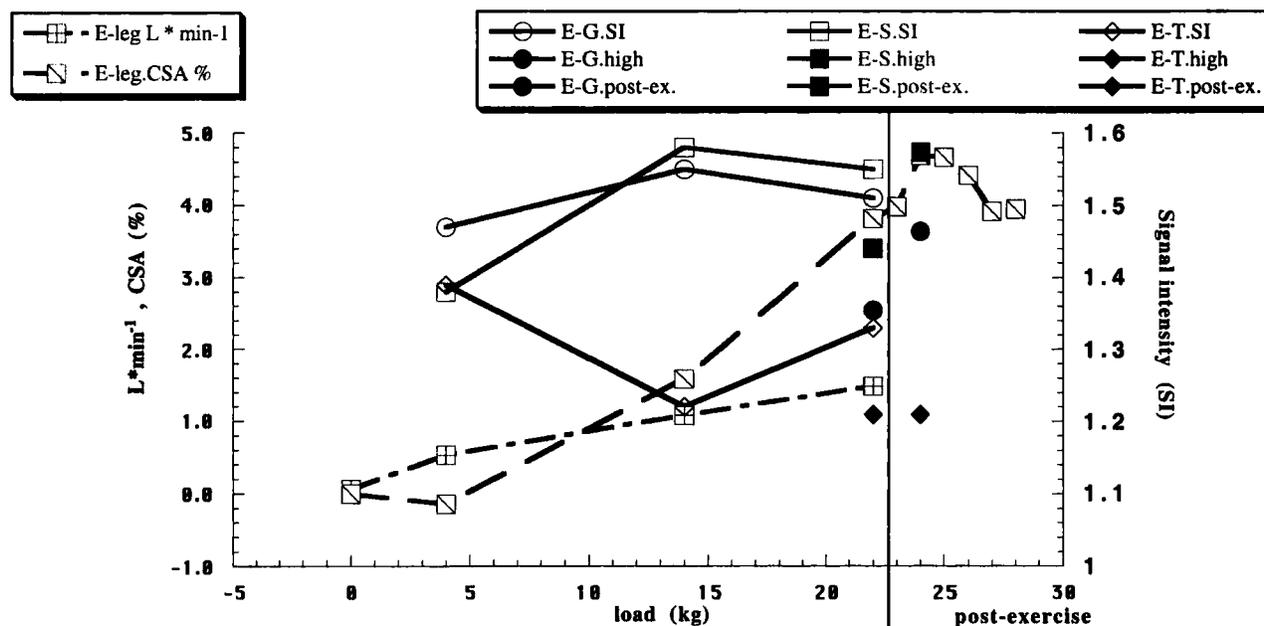


**Figure 2.** Blood flow (E-leg, l/min) and change of the cross-sectional area (dE-leg) in the exercising leg. Maximal signal intensity at different workloads in m. gastrocnemius (E-G.SI). Maximal signal intensity at immediate postexercise imaging (E-G.post-ex.) and the corresponding signal intensity during high workload (E-G.high).

*Table 1*

*Maximum Signal Intensity (SI), Mean Transit Time (MTT), Integrated Area (Area), Upslope and Downslope of the Bolus in Exercising (E) and Nonexercising (N) Leg*

| | E-G | E-S | E-T | N-G | N-S | N-T |
|---|---|---|---|---|---|---|
| **SI** | | | | | | |
| Low | 1.47 ± 0.053 | 1.38 ± 0.12 | 1.39 ± 0.06 | 1.05 ± 0.05 | 1.11 ± 0.08 | 1.23 ± 0.136 |
| Medium | 1.55 ± 0.08 | 1.58 ± 0.15* | 1.22 ± 0.16 | 1.04 ± 0.06 | 1.12 ± 0.06 | 1.27 ± 0.15 |
| High | 1.51 ± 0.16 | 1.55 ± 0.14 | 1.33 ± 0.16 | 1.06 ± 0.09 | 1.07 ± 0.05 | 1.33 ± 0.17 |
| **MTT** | | | | | | |
| Low | 63.06 ± 5.01 | 66.16 ± 6.84 | 61.96 ± 4.43 | 96.13 ± 35.71 | 76.17 ± 10.25 | 68.99 ± 6.50 |
| Medium | 64.18 ± 3.17 | 62.30 ± 5.94 | 70.20 ± 10.31 | 83.50 ± 5.60 | 77.83 ± 6.16 | 70.26 ± 8.35 |
| High | 63.60 ± 2.94 | 61.81 ± 6.37 | 69.40 ± 11.41 | 82.74 ± 6.48 | 79.02 ± 3.85 | 67.10 ± 9.36 |
| **Area** | | | | | | |
| Low | 4.80 ± 0.31 | 4.11 ± 1.06 | 3.74 ± 0.71 | 0.68 ± 0.45 | 1.31 ± 0.70 | 2.28 ± 1.14 |
| Medium | 5.43 ± 0.57 | 4.94 ± 0.78 | 2.32 ± 1.52 | 0.72 ± 0.38 | 1.16 ± 0.56 | 2.59 ± 1.27 |
| High | 4.50 ± 1.06 | 4.45 ± 0.95 | 2.45 ± 1.03 | 0.95 ± 0.76 | 1.03 ± 0.08 | 3.06 ± 1.40 |
| **Upslope** | | | | | | |
| Low | 0.35 + 0.05 | 0.28 + 0.10 | 0.32 + 0.10 | 0.02 + 0.01 | 0.04 + 0.02 | 0.13 + 0.06 |
| Medium | 0.42 + 0.14 | 0.45 + 0.16 | 0.15 + 0.22 | 0.00 + 0.00 | 0.02 + 0.02 | 0.09 + 0.06 |
| High | 0.44 + 0.14 | 0.45 + 0.19 | 0.11 + 0.07 | 0.02 + 0.02 | 0.02 + 0.01 | 0.16 + 0.09 |
| **Downslope ($10^{-2}$)** | | | | | | |
| Low | −4.70 ± 0.27 | −2.38 ± 1.75 | −3.08 ± 0.85 | 2.06 ± 2.55 | 0.99 ± 2.37 | −2.50 ± 1.86 |
| Medium | −7.73 ± 4.67 | −11.95 ± 9.03 | −4.37 ± 2.16 | 4.57 ± 3.83 | 1.60 ± 4.60 | 0.86 ± 3.86 |
| High | −7.98 ± 7.23 | −12.05 ± 9.71 | −2.41 ± 4.07 | 1.50 ± 1.23 | 3.73 ± 1.76 | −3.58 ± 3.17 |

Values are means ± SD. Regional muscles groups are denoted G (gastrocnemius), S (soleus), and T (tibialis anterior) and are presented in respect to low, medium, and high workloads.
*$p < 0.05$.

Calf muscle bulk volume was at rest 1300 ml, measured in one subject. Applying the change in CSA at respective workload resulted in a calf muscle volume of 1300 ml at low and 1400 ml at medium and high workload. This gives an approximate skeletal muscle perfusion of 4 ml · 100 $g^{-1}$ · $min^{-1}$ at rest and 38 ml at low, 86 ml at medium, and 110 ml · 100 $g^{-1}$ · $min^{-1}$ at high workload.

## DISCUSSION

The signal intensity curve overall did not mirror the muscle perfusion, estimated by ultrasonography. However, the different parameters from the signal intensity time curve could visually separate the muscles into three different groups as exercising, presumably low active, and resting muscles. Muscles used for plantar flexion of the foot are m. gastrocnemius and m. soleus. The subjects noticed that during exercise they had to stabilize the pelvic and body position on the table, especially during exercise at high intensity. This low-graded isometric activation of the calf included probably m. tibialis anterior and

could induce the intermediate increased SI and is therefore named a low active muscle. M. gastrocnemius and m. soleus in the resting leg are considered as resting muscles. $SI_{max}$, upslope, downslope, and area separated best between low and medium workload. They could not separate between muscle perfusion at medium and high workload. An arterial input function could not be obtained because the SI in the small artery had a low signal-to-noise ratio and was probably influenced by pulsatile artifacts, thereby excluding the possibility of calculating relative distribution volume and quantitative perfusion using a modified Kety equation.

The calculated perfusion by ultrasonography has some major limitations in our study because the calf muscle volume was not measured in all subjects. The blood flow that was measured in the popliteal artery would underestimate the local muscle perfusion as in a low active muscle group such as m. tibialis anterior as indicated by the obtained increased SI (Table 1). Other limitations are that the variation coefficient when measuring volume flow by ultrasonography using this setup is not known and we did not measure the diameter of the vessel lumen during
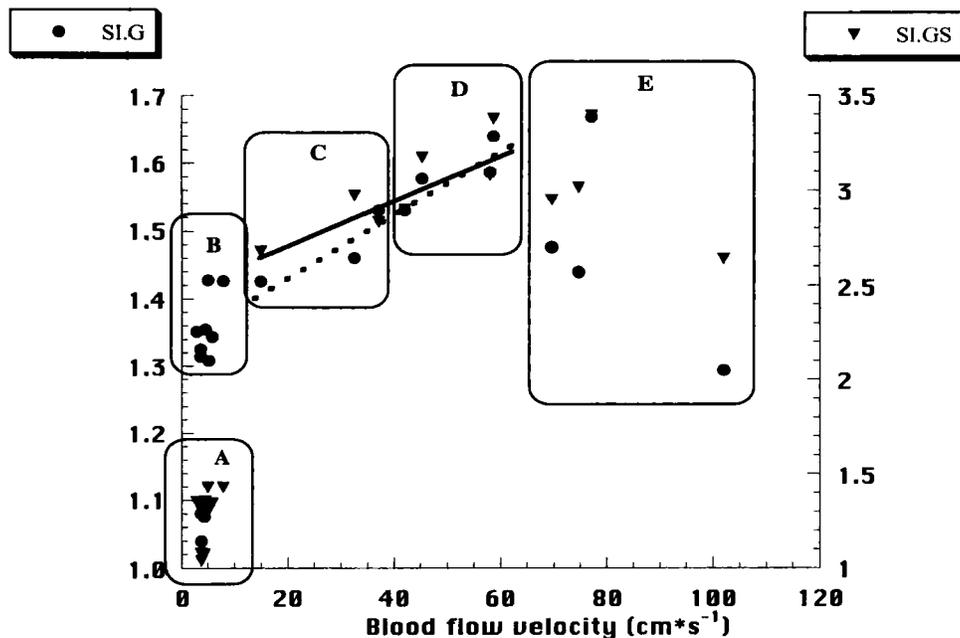
**Figure 3.** Individual maximal signal intensity (SI) as a function of the blood flow velocity in the popliteal artery (cm ·sec⁻¹) m gastrocnemius (G) and m. soleus (S) in the exercising and the nonexercising leg. The Y1-axis representing the SI in G and the Y2-axis the SI in G and S (SI.GS). The muscles are grouped with respect to the presumed activation as resting (A), low activate (B), and exercising muscles at low (C), medium (D), and high (E) workloads. A linear correlation was found in exercising muscles within a limited blood flow velocity range of 15–60 cm · sec⁻¹, $R = 0.946$ (SI.G, dotted line), $R = 0.852$ (SI.GS).

exercise. Our findings indicate, however, despite these limitations, that the blood flow increased as expected with dynamic muscle exercise with a more than 20-fold increased blood flow (12). A linear correlation of SI to blood flow was seen in the exercising muscles up to an upper limit of 60 cm · sec⁻¹, corresponding to 90 ml · 100 g⁻¹ · min⁻¹. The increase in SI was small and approximately 15% compared with the twofold increase in blood flow. One reason could be a poor temporal resolution and an insufficient detection of the bolus due to the time interval between the images. However, this does not seem to be the explanation because the timing of the peak SI was similar during exercise as with imaging immediately after exercise. The finding that $SI_{max}$ was higher after than during exercise is not obvious. CSA increased during the first minute after exercise, probably as a result of a post-exercise hyperemic filling (Fig. 2) that might increase the signal intensity, but this cannot explain the insufficient discrimination between medium and high workload in exercising muscles.

Another reason for the low correlation of Gd bolus to high flow could be the increased water content in the muscle. We presented in a previous study (13) indications

that of the increased CSA at high workload, 50% could result from increased water content. The remaining 50% would represent the increased intravascular blood volume related to hyperemia. In the present study the CSA increased from resting by 3% at medium and 6% at high workload. Whether the additionally increased extravascular volume during high flow alone would explain the inability of SI to follow the blood flow is not settled, but unlikely. The hyperosmolar exercising muscle increases the fluid flux during intense exercise, an event that is probably paralleled by an increased extravascular bolus deposition of gadolinium. It is not settled to what degree changes of the tissue osmolarity and gadolinium concentration would alter the signal intensity. A nonlinear peak response to extracellular contrast agents has been reported (14), suggesting that the T1 enhancement could be significantly affected by the water exchange between the different compartments. The short TR (9.7 msec) used in this study could reduce the effect of water exchange (15). A more detailed review concerning the effect of water exchange is detailed elsewhere (2). A more conceivable explanation could be that the transit time of the bolus in tissue is highly shortened due to the increased

perfusion and consequently highly shortened in comparison with the arterial inflow, a phenomenon known as the central volume theorem (16). The blood flow velocity in the capillary is much lower than in a large artery, approximately 1 mm $\cdot$ sec$^{1}$ at rest (17), as compared with 4 cm $\cdot$ sec$^{-1}$ in the popliteal artery in our study, and is unknown during exercise. The transit time in the capillaries could be in theory, during a high intensity exercise, too short and thereby restrict the diffusion of Gd-DTPA into the extravascular space.

It is concluded that the signal intensity curve overall does not mirror the perfusion, estimated from the blood flow measured by ultrasonography. However, the signal intensity in exercising muscles seemed to follow the blood perfusion within a limited blood flow range of 15–60 cm $\cdot$ sec$^{-1}$, corresponding to 35–90 ml $\cdot$ 100 g$^{-1}$ $\cdot$ min$^{-1}$. Semiquantitative perfusion measurements might be useful when studying induced ischemia in skeletal muscles during exercise.

## ACKNOWLEDGMENTS

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