Reference values for quantitative analysis of Gd-contrast enhancement kinetics in skeletal muscle NMR imaging.

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Introduction: Abnormal skeletal muscle enhancement post Gd-contrast agent (Gd-CA) injection is a commonly recognized feature on NMR images in inflammatory diseases but also in chronic interstitial fibrosis or in conditions where sarcolemma permeability is increased such as in muscle dystrophy (1, 2). Yet, these data have almost always been qualitatively interpreted, and no reference values have ever been acquired in order to determine precisely the abnormality threshold of Gd enhancement. However, when it comes to monitoring lesions severity in longitudinal studies, these benchmarks become mandatory. Our aim here, was to quantify the skeletal muscle relaxivity changes after Gd-CA injection to normal subjects.

Materials and Methods: Twelve healthy volunteers, six male (age range: 22-62 yr) and six female (age range: 22-67 yr) were scanned in a 3T whole-body magnet. Imaging was centered on the thighs. A slice selective inversion-recovery TurboFlash sequence (TR 10s, TI 1.2s, flip angle 8°, TE 1.64ms, FOV 400mm, 5 slices) was run during a 3min baseline period before intravenous injection of 0.1 mmol/kg of Gd-DOTA. Acquisitions were carried on for one hour in order to follow most of the Gd-CA enhancement kinetics. For each slice, regions of interest (ROIs) were drawn on 8 muscles of both thighs and ROI signal intensities were normalized to baseline values.

Using the Gd-DOTA relaxivity constant measured in blood at 3T,, the changes in skeletal muscle relaxivities were calculated for each individual muscle. In order to extract constants proposed by Tofts (3), we simulated the arterial input function (Cp(t)) with data from the literature and using this relation C(t) = VeCp0e-KeKtrans t, with Ktrans = Ktrans/Ve. The concentration Gd-DOTA curve was fitted by a nonlinear fit including the arterial input function (Matlab, Mathworks Software, USA).

Results: The Tofts constants Ktrans, Kep, Ve in healthy subjects were detailed for each muscle in Table 1. No statistically significant difference was detected across muscles or between sexes and age groups.

An example of the use of these benchmarks is shown in Figure 1. A patient with a histologically proven inflammatory myopathy had abnormal values for Ktrans = 0.33, Kep = 0.35 and Ve = 0.93.

Conclusion: This study provides reference values of Gd-CA enhancement kinetics in thigh muscle. These benchmark curves and extracted Tofts constants, will for the first time make it possible to identify unambiguously and objectively pathological enhancements in various conditions. They will also provide quantitative markers mandatory essential to interpretation of longitudinal studies.

Table 1. Description of Gd-DOTA enhancement with Tofts constants in healthy subjects (Mean ±SD).

<table>
<thead>
<tr>
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<th>RF</th>
<th>VI</th>
<th>VL</th>
<th>VM</th>
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<tbody>
<tr>
<td>Ktrans (min⁻¹)</td>
<td>0.089 ± 0.056</td>
<td>0.140 ± 0.091</td>
<td>0.113 ± 0.057</td>
<td>0.148 ± 0.086</td>
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<tr>
<td>Kep (min⁻¹)</td>
<td>0.416 ± 0.301</td>
<td>0.622 ± 0.428</td>
<td>0.546 ± 0.326</td>
<td>0.632 ± 0.386</td>
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<tr>
<td>Ve</td>
<td>0.237 ± 0.060</td>
<td>0.243 ± 0.050</td>
<td>0.227 ± 0.049</td>
<td>0.251 ± 0.047</td>
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