Associations between magnetic resonance imaging and EMG findings in myopathies

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Objectives: Magnetic resonance imaging (MRI) is a cornerstone in diagnosis of myopathies. The present study sought to elucidate possible associations between electromyography (EMG) findings and histogram parameters derived from clinical MRI in myositis and other myopathies.

Materials and Methods: Twenty six patients with myopathies were included in this retrospective study. Clinical MRI was performed with a 1.5T MRI scanner including T2- and T1-weighted images. EMG analysis was performed during clinical diagnostic workup. The histogram parameters of the MRI sequences were obtained of the same muscle, which was investigated with EMG.

Results: Several correlations were identified between mean duration of the motor unit potentials (MUP) and histogram parameters derived from T1- and T2-weighted images. The highest for T1-weighted images was mode ($r = -0.73$, $P < .0001$) and for T2-weighted images was $p_{25}$ ($r = -0.57$, $P = .022$). There were significant differences for several histogram parameters between muscles with pathological spontaneous activity and without. So, for T1-weighted images, the best discrimination was achieved with mean ($P = .096$), and for T2-weighted images for $p_{10}$ ($P = .05$). Mean SI values derived from T1-weighted images achieved an AUC of 0.84 with a sensitivity of 0.81 and a specificity of 0.86 to discriminate patients with and without pathological spontaneous activity (PSA).

Conclusions: The present study identified strong associations between histogram analysis derived from morphological MRI sequences and the duration of the MUP derived from EMG in myopathies strengthening the fact that both diagnostic modalities can reflect disease state in a similar fashion. Histogram parameters can predict muscles with PSA.

Keywords: electromyography, histogram analysis, magnetic resonance imaging, myopathy, myositis
1 | INTRODUCTION

Autoimmune myositis and myopathy are a heterogeneous group of unknown etiology, which comprises several entities, including inflammatory disorders with more acute edematous behavior or, for example, dystrophic entities with more degenerative behavior and muscle fiber dysfunction.\textsuperscript{1-4} The diagnostic approach is multimodal consisting of clinical examination, serological parameters, needle electromyography (EMG), and histopathology obtained via muscle biopsy as diagnostic gold standard.\textsuperscript{5} Magnetic resonance imaging (MRI) is an important imaging modality for detection of, for example, atrophy, muscle edema or myofasciitis.\textsuperscript{1,5}

Nowadays, MR images are not only evaluated qualitatively by the radiologist but can also be analyzed quantitatively with various approaches.\textsuperscript{6} One common technique is histogram analysis, which issues every voxel of a defined region of interest into a histogram.\textsuperscript{6} By employing this analysis, quantitative biomarkers can be obtained with possible diagnostic and predictive importance. Typically acquired parameters are percentiles, median, mode, skewness, kurtosis, and entropy.\textsuperscript{6}

Previously, some preliminary studies, predominantly in the field of oncologic imaging, showed that histogram parameters derived from MRI are capable to reflect different microstructure characteristics of tumors, such as cellularity and proliferation potential.\textsuperscript{7-10} Furthermore, histogram analysis parameters were able to predict treatment response in longitudinal analyses in several malignancies.\textsuperscript{6,11,12} So, it was discussed that even morphological sequences can reflect tissue features, comprising proliferation potential, cellularity, and nucleic sizes in several malignant tumors.\textsuperscript{7-10}

One important diagnostic modality in clinical neurology practice is EMG.\textsuperscript{13-15} It can be used to detect pathological spontaneous activity (PSA) and to analyze motor unit potentials (MUP).\textsuperscript{13} According to EMG results, muscle disorders can be classified as normal, neuropathic, or myopathic. This approach can further guide to definite diagnosis.\textsuperscript{13}

Presumably, both diagnostic modalities, namely MRI and EMG might be able to reflect microstructure in muscle disorders, such as integrity of muscle fibers and may aid in treatment response evaluation.\textsuperscript{6,13} In fact, some investigations confirmed this hypothesis. For example, it was shown that histogram parameters derived from diffusion-weighted imaging (DWI) can reflect cellularity parameters in muscle lymphomas.\textsuperscript{16} Moreover, in a recent study, associations between apparent diffusion coefficient values derived from DWI and EMG findings were reported, based upon a small patient sample in myositis patients.\textsuperscript{17}

However, it is unclear, whether morphological sequences are also associated with EMG findings in myopathies, when analyzed with a histogram-based approach.

Therefore, the purpose of this study was to elucidate possible associations between histogram analysis parameters derived from morphological sequences and EMG findings in myopathy patients using clinical routine MRI.

2 | METHODS

This retrospective study was approved by the institutional ethic committee (Martin-Luther university of Halle-Wittenberg), and informed consent was waived.

2.1 | Magnetic resonance imaging

Magnetic resonance imaging of the thigh and lower leg was performed using a 1.5-T scanner (Magnetom Vision Sonata Upgrade; Siemens). MRI protocol included T2-weighted fat-suppressed short tau inversion recovery (STIR) images (TR 5490 ms, TE 80 ms, flip angle 150°, slice thickness 10 mm), T1-weighted spin-echo (SE) images without administration of contrast medium (TR 474 ms, TE 11 ms, flip angle 150°, slice thickness 10 mm).

2.2 | Imaging analysis

Magnetic resonance images were transferred in DICOM format and processed offline with custom-made Matlab-based application (The Mathworks). Polygonal regions of interest (ROI) were manually drawn along the contours of the muscle, in which the muscle biopsy was obtained. The ROIs were simultaneously placed on T2-weighted and T1-weighted images on all slides of the muscle to obtain a whole muscle measurement. The images were co-registered to ensure the same ROI placement. No severe motion artifacts were noticed in our patient sample. All measures were performed by one radiologist blinded to the histopathology results (AS, 16 years of general radiological experience). The following histogram parameters were calculated: mean, maximum (max), minimum (min), median, mode, percentiles: 10th, 25th, 75th, and 90th, kurtosis, skewness, and entropy, as described in previous studies.\textsuperscript{7,9} These parameters were each derived from T2-weighted and native T1-weighted images. A patient for illustration purposes is displayed in Figure 1.

2.3 | Electromyography

The written informed consent was given before every EMG procedure. The EMG was recorded by MK using a concentric needle electrode (37 mm, 26G; CareFusion) and by a Multiliner Vision (Viasys) in the Electrophysiology Unit of the Department of Neurology. Motor unit potential (MUP) (amplitude and duration) was measured in each affected muscle. Between 12 MUP and 23 MUP were available per muscle. For MUP recordings, each patient was asked to keep muscle force at a level, where 3 to 5 different MUP could be discerned. The needle was positioned so that MUP with rise times up to 0.5 ms could be obtained for storage and further analysis. Multi-MUP analysis was performed and MUP parameters such as onset, offset, amplitude, and duration were automatically analyzed. Onset and offset were checked carefully and were corrected on screen only when the
automatic analysis clearly failed. Pathological spontaneous activity (PSA), that is, fibrillation potentials, positive sharp waves, or high-frequency discharges, was evaluated as either absent or present. EMG recordings were analyzed for PSA and MUAP variables in each examined muscle. For 2 patients, 2 muscles were evaluated with EMG and MRI. There were the following muscles: tibialis anterior \((n = 14, 50.0\%)\), vastus medialis \((n = 8, 28.6\%)\), and vastus lateralis \((n = 6, 21.4\%)\).

### 2.4 Statistical analysis

Statistical analysis and graphics creation were performed using GraphPad Prism 5 (GraphPad Software, La Jolla, CA, USA). Collected data were evaluated by the means of descriptive statistics (absolute and relative frequencies). Spearman’s correlation coefficient \((r)\) was used to analyze associations between investigated parameters. In discrimination analysis of subgroups, Mann-Whitney test was used. Receiver operator curve (ROC) was used to obtain the area under the curve (AUC), sensitivity, and specificity. In all instances, \(P\)-values < .05 were taken to indicate statistical significance. The Bonferroni correction was used to adjust for multiple testing.

### 3 RESULTS

One hundred and six patients with different muscle disorders were investigated by MRI in our department during the time period 2007 till 2016. Patients were included in this study if they fulfilled the following inclusion criteria:

- Muscle disorder confirmed by histopathology.
- Patients investigated by clinical MRI including the same T1- and T2-weighted images.
- EMG analysis of the same muscle region.

Altogether, 26 patients (11 women, 42.3%) with a mean age 51.4 ± 19.0 years met the inclusion criteria.

The diagnoses were as follows: limb-girdle muscle dystrophy \((n = 5, 19.2\%)\), undetermined myopathy \((n = 4, 15.4\%)\), overlap myositis \((n = 4, 15.4\%)\), necrotizing myositis \((n = 2, 7.7\%)\), polymyositis \((n = 2, 7.7\%)\), Jo-1 syndrome \((n = 2, 7.7\%)\), neurogenic myopathy \((n = 2, 7.7\%)\), inclusion body myositis \((n = 1, 3.8\%)\), anoctamin-5-related myopathy \((n = 1, 3.8\%)\), matrin-3-related myopathy \((n = 1, 3.8\%)\), dermatomyositis \((n = 1, 3.8\%)\), and steroid-induced myopathy \((n = 1, 8\%)\).

The identified EMG findings were as follows (M ± SD): MUP amplitude mean 0.80 ± 0.79 mV, amplitude max 1.6 ± 1.5 mV, mean MUP duration 9.7 ± 1.9 ms.

There were no statistically significant correlations between MRI histogram parameters and mean as well as maximum MUP amplitude. The highest correlation coefficient was p25 derived from T1-weighted images \((r = -.31, P = .11)\) and skewness derived from T2-weighted images \((r = -.31, P = .11)\).

Several correlations were identified between mean MUP duration and histogram parameters derived from T1- and T2-weighted images. The highest for T1-weighted images was mode \((r = -.73, \ldots)\).
Seven of 26 patients had signs of PSA (26.9%). There were significant differences between muscles with PSA and without for several histogram parameters. However, after correction for multiple testing, the results did not remain statistically significant. For T1-weighted images, the best discrimination was achieved with mean testing; the results did not remain statistically significant. For T1- and T2-weighted histogram parameters. However, after correction for multiple significant differences between muscles with PSA and without for several histogram parameters. However, after correction for multiple testing, the results did not remain statistically significant. For T1-weighted images, the best discrimination was achieved with mean $(P = .096, \text{mean } 0.37 \pm 0.17 \text{ for patients with PSA versus } 0.21 \pm 0.09 \text{ without PSA}),$ and for T2-weighted images for $p_{10}$ $(P = .05, \text{mean } 181.2 \pm 125.0 \text{ for patients with PSA versus } 78.7 \pm 53.2 \text{ without PSA, Figure 3). Mean derived from T1-weighted images achieved an AUC of } 0.84 \text{ with a sensitivity of } 0.81 \text{ and a specificity of } 0.86 \text{ to discriminate patients with and without PSA (Figure 4).}$

### 4 | DISCUSSION

The present study identified for the first time strong associations between histogram parameters derived from morphological MRI used in clinical routine and EMG parameters such as PSA and mean MUP duration. These results strengthen the fact that MRI cannot only be assessed qualitatively by the radiologist to identify diseased muscles but also provide novel quantitative imaging biomarkers in muscle disorders. This is especially of interest since both modalities, MRI and EMG, are the cornerstones of clinical diagnostic workup in muscle disorders.\textsuperscript{1,5}

In clinical practice, MRI is of great importance for diagnosing muscle disorders due to its excellent tissue contrast.\textsuperscript{1,5} The benefit was shown for discrimination of different myopathies, guiding biopsy localizations, and monitoring treatment success.\textsuperscript{1,4} Typical imaging findings are muscle edema and fat replacement, expressed by T2-weighted hyperintense areas. Furthermore, nearly all pathophysiological changes can cause T2-relaxation changes. These comprise also fiber necrosis and cell swelling.\textsuperscript{18} Edema and necrosis can be interpreted as signs of acute disease. T1-weighted images are mainly used to detect fatty infiltration of the muscles as a chronic disease sign.\textsuperscript{1,4} Of note, the histogram approach used in the present study can be applied without any more effort into clinical routine, as it was performed on clinically obtained sequences.\textsuperscript{6}

Regarding EMG, it is widely used in the diagnostic workup in myositis patients.\textsuperscript{12-15} Furthermore, it has been shown that also EMG findings can quantitatively reflect muscle alteration.\textsuperscript{13} However, the EMG signal might only display a small area of the muscle surrounding the inserted needle and not the muscle as a whole.\textsuperscript{18} Typical EMG findings in myositis patients are PSA comprising, for example, fibrillations, positive sharp waves, and myotonic discharges.\textsuperscript{13} In acute disease stages with inflammation, a loss of myofibrils leads to MUPs small in amplitude, short in duration, and polyphasic.\textsuperscript{13} It is a known fact that EMG correlates with the clinical presentation in myopathy patients.\textsuperscript{13,18,19} However, the exact underlying tissue alterations causing these phenomena are still unclear, which can be also be stated for MRI.\textsuperscript{18} However, there are first reports that EMG findings well correlate with histopathology.\textsuperscript{20}

It was shown that the amount of fatty degeneration of muscles quantified by MRI correlates with muscle strength score in inclusion body myositis.\textsuperscript{21} Recently, a systematic study investigated associations between muscle MRI and biopsy pathology in facioscapulohumeral muscular dystrophy.\textsuperscript{22} So, edematous muscles assessed by STIR-sequence were associated with histopathologically confirmed inflammation. Muscles with positive STIR and T1-weighted changes were associated with fibrotic changes.\textsuperscript{22} Interestingly, MRI also correlates with the clinical presentation, which was shown for myositis patients.\textsuperscript{22}

Histogram parameters can reflect the microstructure of tissues by issuing every voxel of the MRI into a histogram, and thus, statistical information of the images can be obtained.\textsuperscript{6-12} Thus, in oncologic imaging, it was extensively researched that histogram parameters can reflect microstructure in tumors, which was shown for several tumor entities.\textsuperscript{6-12} There are several different parameters, which can be calculated. Of note, some parameters perform better than others in several studies indicating that every parameter can reflect tissue characteristics in another fashion.\textsuperscript{6}

The concept of histogram parameters can be discussed as several aspects of the drawn ROI are of interest.\textsuperscript{6} The identified correlation between $p_{25}$ derived from T2-weighted images can be seen that especially the part of the muscle with the lowest signal intensity of T2-weighted images is important for the reflection of MUP. Presumably, the higher percentile of the T2-weighted images is more reflective of only edema-related muscle changes.
We identified a strong inverse correlation between the mean MUP duration and histogram parameters derived from T1- and T2-weighted images, whereas the MUP amplitude did not correlate with the investigated imaging findings. In short, a lower signal intensity of the muscles correlates with a longer duration of MUP. The duration is the EMG parameter, which most accurately reflects the area of the motor unit. Presumably, both diagnostic modalities can therefore good display the complex mechanisms of the motor unit of muscles.

Furthermore, a recent study indicated that MUP duration decrease may be more sensitive than MUP amplitude decrease in polymyositis patients, which corroborates the clinical relevance of the reported results. Only one other study investigated associations between clinical MRI and EMG. Positive associations between MUP duration and apparent diffusion coefficient values derived from DWI were identified in myositis patients. This is an additionally obtained sequence, which needs scanning time in clinical work up. The present study identified that conventional MRI sequences can reflect EMG findings as good as diffusion coefficient values without any time loss.

Another interesting point is the ability of especially T1-derived parameters to predict muscles with PSA with a good accuracy. This could help in clinical decision-making to correctly identify muscles to measure with EMG. In a recent study, it was shown that PSA can also be detected on an advanced DWI technique in a similar fashion compared with surface EMG.

There are several limitations of the present study to address. Firstly, it has a retrospective design with known inherent bias. However, imaging and EMG were evaluated blinded and independently to each other to reduce possible bias. Secondly, our patient sample is relatively small and comprises different myopathies. Thirdly, albeit the same muscle was investigated with MRI and EMG, there might be still some local incongruencies between both, which might have an impact on the results. Fourthly, only one radiologist performed the MRI measurements, which might present some inherent bias. However, as shown by previous investigations, the histogram analysis has a high reproducibility and interobserver agreement in several disorders including muscle disorders.

5 | CONCLUSIONS

The present study identified strong associations between histogram analysis parameters derived from morphological MRI sequences and mean MUP duration derived from EMG in myopathies, strengthening the fact that both diagnostic modalities can reflect disease state in a similar fashion. Moreover, histogram parameters are capable to discriminate between muscles with pathological spontaneous activity from those without, which could help in clinical routine to decide which muscle should be evaluated with EMG or taken for muscle biopsy purposes.

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CONFLICT OF INTEREST
None to declare.

DATA AVAILABILITY STATEMENT
The data are available from the corresponding author upon reasonable request.

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