Intra-neuromuscular ultrasound (NMUS) was pursued because it is readily available, inexpensive, painless, radiation-free, highly reliable, can demonstrate atrophy, and can measure muscles of critical importance in those with ALS. It can also contribute to the personalization of treatment in an incredibly heterogenous disease. For example, a patient with bulbar onset ALS will benefit more from tracking geniohyoid measurements, whereas it would be more appropriate to track changes in the tibialis anterior in a patient with lower extremity onset.

Future studies could include:
- Measurement of muscle volume to obtain a more complete impression of muscle atrophy
- Longitudinal studies with large sample sizes
- Evaluation of echogenicity and its change in relation to muscle size over time
- Comparison of multi-center studies with patient reported outcomes to determine if NMUS may be more responsive than other modalities

Future investigations of NMUS as a biomarker for ALS should be pursued because it is readily available, inexpensive, painless, radiation-free, highly reliable, can demonstrate atrophy, and can measure muscles of critical importance in those with ALS. It can also contribute to the personalization of treatment in an incredibly heterogenous disease. For example, a patient with bulbar onset ALS will benefit more from tracking geniohyoid measurements, whereas it would be more appropriate to track changes in the tibialis anterior in a patient with lower extremity onset.

Future Directions

Figure 1. Technique for measuring muscle thickness.

(A) Geniohyoid (B) Biceps/brachialis (C) Tibialis anterior
(D) Diaphragm at expiration (E) Diaphragm at inspiration

Table 1. Inter-rater and intra-rater reliability of NMUS.

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Group 1 Inter-rater CC</th>
<th>p-value</th>
<th>Group 1 Intra-rater CC</th>
<th>p-value</th>
<th>Group 2 Inter-rater CC</th>
<th>p-value</th>
<th>Group 2 Intra-rater CC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geniohyoid</td>
<td>0.90</td>
<td>&lt;0.001</td>
<td>0.83</td>
<td>&lt;0.001</td>
<td>0.97</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Bicep</td>
<td>0.99</td>
<td>&lt;0.001</td>
<td>0.97</td>
<td>&lt;0.001</td>
<td>0.97</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Bicep</td>
<td>0.99</td>
<td>&lt;0.001</td>
<td>0.97</td>
<td>&lt;0.001</td>
<td>0.97</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Diaphragm (Expiration)</td>
<td>0.94</td>
<td>&lt;0.001</td>
<td>0.92</td>
<td>&lt;0.001</td>
<td>0.91</td>
<td>&lt;0.001</td>
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</tr>
<tr>
<td>Right Diaphragm (Expiration)</td>
<td>0.88</td>
<td>&lt;0.001</td>
<td>0.90</td>
<td>&lt;0.001</td>
<td>0.82</td>
<td>0.004</td>
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<tr>
<td>Right TA</td>
<td>0.84</td>
<td>0.003</td>
<td>0.83</td>
<td>0.003</td>
<td>0.93</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right TA</td>
<td>0.92</td>
<td>&lt;0.001</td>
<td>0.92</td>
<td>&lt;0.001</td>
<td>0.92</td>
<td>0.002</td>
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<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>0.99</td>
<td>&lt;0.001</td>
<td>0.99</td>
<td>&lt;0.001</td>
<td>0.99</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results

- Mean age: 23.5 years in Group 1 and 66.1 years in Group 2
- 70% were female in Group 1; 50% were female in Group 2
- Mean age: 23.5 years in Group 1 and 66.1 years in Group 2
- Average ratio of the diaphragm on inspiration to expiration was 1.87:1 in healthy controls, and 1.34:1 in ALS patients

Conclusions

- The total inter-rater CC of all muscles in Group 1 was 0.99 with a 2.15% average difference between measurements.
- The total intra-rater CC of all muscles in Group 1 was 0.99 with a 2.20% average difference between measurements.
- The total inter-rater CC of all muscles in Group 2 was 0.99 with a 1.68% average difference between measurements.
- NMUS is a highly reliable diagnostic technique. In this study, reliability was higher than the reported reliability of two widely used ALS biomarkers, ALSFRS-R™ and FVC™, even though one of the ultrasonographers was a student with limited NMUS experience.

References