Editors' Note: In response to Dr. Sabour's and Dr. Morrow's comments on the reliability and accuracy of skeletal muscle imaging in limb-girdle muscular dystrophies, Drs. ten Dam et al. respond and provide 2 additional tables summarizing the positive and negative likelihood ratios as well as test characteristics of uninformative scans. These important additional data were not included in the original publication because of space constraints.

Chafic Karam, MD, and Robert C. Griggs, MD

RELIABILITY AND ACCURACY OF SKELETAL MUSCLE IMAGING IN LIMB-GIRDLE MUSCULAR DYSTROPHIES

Siamak Sabour, Tehran, Iran: ten Dam et al. evaluated the reliability and accuracy of skeletal muscle CT to correctly identify different muscular dystrophies manifesting with limb-girdle weakness.¹ They reported that the overall interobserver agreement was poor ($\kappa = 0.27$), with markedly higher scores for Becker muscular dystrophy (BMD) ($\kappa = 0.51$) and Bethlem myopathy ($\kappa = 0.59$). For reliability analysis for qualitative variables, weighted kappa should be used with caution because kappa has its own limitations.^{2–5} They also reported that sensitivity was 40%, specificity 58%, positive predictive value 77%, and negative predictive value 21%. These results do not reflect acceptable validity. The authors should have used positive and negative likelihood ratio (LR+ and LR–) as well as odds ratio (OR) (true/false) to completely evaluate validity or diagnostic accuracy.^{2–5} As the authors concluded, muscle CT might be an adjunct to the clinical diagnosis of BMD and Bethlem myopathy. This conclusion may be misleading due to inappropriate or incomplete use of the relevant validity and reliability analysis.

Author Response: Leroy ten Dam, Anneke J. van der Kooi, Menno van Wittingen, Rob J. de Haan, Marianne de Visser, Amsterdam: The authors thank Dr. Sabour for his comments. We did not use weighted kappa to investigate the interrater agreement because the multiple diagnostic scoring categories studied are not ordinal. We also studied more than 2 observers so we used Fleiss generalized kappa (see Methods¹) as a measure of overall concordance of multiple raters using nominal scoring

categories.⁶ We are aware that this unweighted kappa approach gives a conservative estimate of the interobserver agreement due to the multiple scoring categories and have stressed this disadvantage in the Discussion.

We did calculate the LR+ and LR– and the OR, but did not present this data in the article due to space limitations. We now supply the LR + LR– and diagnostic OR as additional information (table 1). The LR+ and diagnostic OR are markedly higher and LR– is markedly lower in BMD and Bethlem myopathy compared to the other groups, which supports our conclusion that muscle CT might be an adjunct to the clinical diagnosis of BMD and Bethlem myopathy, but not for the other limb-girdle muscular dystrophies. However, we still believe that the reliability is too low for individual clinical decision-making and therefore skeletal muscle imaging is insufficient for use in clinical practice.

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1. Ten Dam L, van der Kooi AJ, van Wittingen M, de Haan RJ, de Visser M. Reliability and accuracy of skeletal muscle imaging in limb-girdle muscular dystrophies. *Neurology* 2012;79:1716–1723.
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Table 1 Positive and negative likelihood ratio and diagnostic odds ratio

Category	LR+	LR–	Odds ratio
Overall	0.95	1.04	0.92
BMD	7.22	0.10	72.55
LGMD2C-F	2.81	0.84	3.32
LGMD2I	0	0	0
LGMD1B	1.28	0.99	1.29
LGMD2A	2.11	0.96	2.19
Bethlem myopathy	22.5	0.10	216
LGMD2L	0	1.03	0
Miscellaneous	2.79	0.53	5.29

Abbreviations: BMD = Becker muscular dystrophy; LGMD = limb-girdle muscular dystrophy; LR+ = the proportion of sensitivity/(1 – specificity); LR– = the proportion of (1 – sensitivity)/specificity; odds ratio = the proportion of (LR+/LR–).

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Jasper M. Morrow, Mary M. Reilly, Michael G.

Hanna, London: The authors' analysis of using pattern on imaging in isolation to diagnose subtypes of LGMD¹ highlights the lack of strong data in this area. The overview of the pattern of muscle involvement in LGMD is a fair summary of the available literature. However, the patterns described for LGMD2I, LGMD1B, LGMD2A, and LGMD2L are very similar, with overall posterior greater than anterior thigh involvement and predominant medial gastrocnemius and soleus involvement in the calf. It is therefore not surprising that both interobserver agreement and sensitivity/specificity for these diagnoses are low. Conversely, the patterns described for Bethlem and Becker are more distinctive, accounting for the higher reliability and sensitivity for these diagnoses.

The exclusion of uninformative scans because they revealed too little or too much pathology is not reflective of real-world usage. The authors outline this in the Discussion but could have provided analysis with these scans included. While the role of imaging in congenital myopathies with rigidity of the spine is well known,² systematic analysis of a greater number of patients is needed to assess if any imaging features are useful in distinguishing subtypes of LGMD.

Author Response: Leroy ten Dam, Anneke J. van der Kooi, Menno van Wattering, Rob J. de Haan, Marianne de Visser, Amsterdam: We agree with Morrow et al. that more data are needed on patterns of muscle involvement in the subtypes of LGMD. In our Discussion,¹ we noted that most studies in which these patterns are described include relatively small cohorts, ranging from 7 LGMD2L³ and LGMD2A patients⁴ to 22 laminopathy patients.⁵

The patterns described for LGMD1B, LGMD2A, LGMD2I, and LGMD2L are similar, which contributes to the disappointing test characteristics found in these groups. However, the more distinctive pattern of muscle involvement found in the sarcoglycanopathies (LGMD2C–F) group did not result in higher test characteristics, suggesting that there are more factors responsible for the low test characteristics.

We excluded uninformative scans to calculate the accuracy of muscle imaging in LGMDs under optimal conditions. As stated in our Discussion, we agree

Table 2 Test characteristics including uninformative scans^a

Category	Prevalence	Prevalence all scans	Sensitivity	Sensitivity all scans	Specificity	Specificity all scans	PPV	PPV all scans	1 – NPV	1 – NPV all scans
Overall	86/110 (78)	118/150 (78)	34/86 (40)	34/118 (29)	14/24 (58)	14/32 (44)	34/44 (77)	34/52 (65)	52/66 (78)	84/98 (86)
BMD	23/110 (21)	28/150 (19)	21/23 (91)	21/28 (75)	76/87 (87)	11/122 (91)	21/32 (66)	21/32 (66)	2/78 (3)	7/118 (6)
LGMD2C-F	9/110 (8)	11/150 (7)	2/9 (22)	2/11 (18)	93/101 (92)	131/139 (94)	2/10 (20)	2/10 (20)	7/100 (7)	9/140 (6)
LGMD2I	3/110 (3)	4/150 (3)	0/3 (0)	0/4 (0)	96/107 (90)	135/146 (92)	0/11 (0)	0/11 (0)	3/99 (3)	4/139 (3)
LGMD1B	18/110 (16)	26/150 (17)	1/18 (6)	1/26 (4)	88/92 (96)	120/124 (97)	1/5 (20)	1/5 (20)	17/105 (16)	25/145 (17)
LGMD2A	15/110 (14)	24/150 (16)	1/15 (7)	1/24 (4)	92/95 (97)	123/126 (16)	1/4 (25)	1/4 (25)	14/106 (13)	23/146 (16)
Bethlem myopathy	10/110 (9)	14/150 (9)	9/10 (90)	9/14 (64)	96/100 (96)	132/136 (97)	9/13 (69)	9/13 (69)	1/97 (1)	5/137 (4)
LGMD2L	8/110 (7)	11/150 (7)	0/8 (0)	0/11 (0)	99/102 (97)	136/139 (97)	0/3 (0)	0/3 (0)	8/107 (7)	11/147 (7)

Abbreviations: BMD = Becker muscular dystrophy; LGMD = limb-girdle muscular dystrophy; NPV = negative predictive value; PPV = positive predictive value.
^a Values are n (%).

that this does not reflect clinical practice and therefore, as suggested by Morrow et al., we have provided the test characteristics that include uninformative scans (table 2). The test characteristics of BMD and Bethlem myopathy are still markedly better compared with the other LGMDs. When calculating the reliability of muscle imaging, no scans were excluded.

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1. ten Dam L, van der Kooi AJ, van Waddingen M, de Haan RJ, de Visser M. Reliability and accuracy of skeletal muscle imaging in limb-girdle muscular dystrophies. *Neurology* 2012;79:1716–1723.
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CORRECTION

Vision assessment using the NIH Toolbox

In the article “Vision assessment using the NIH Toolbox” by R. Varma et al. (*Neurology*® 2013;80:S37–S40), there is an error in the references. The author in reference 12 should read Hays R. The authors regret the error.

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Reliability and accuracy of skeletal muscle imaging in limb-girdle muscular dystrophies

Siamak Sabour, Leroy ten Dam, Jasper M. Morrow, et al.

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