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***Reply:***

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## REPLY:

We thank Professors Linda de Vries and Frances Cowan for their interest in our recent publication, “Validation of an MRI Brain Injury and Growth Scoring System in Very Preterm Infants Scanned at 29- to 35-Week Postmenstrual Age.”<sup>1</sup> In their correspondence, the authors expressed concern about our example presented in On-line Fig 2, which they said we presented as “grade 2 white matter injury (WMI).” They correctly pointed out that the example shows connatal cysts and not cystic periventricular leukomalacia (PVL), an observation with which we entirely agree. They were concerned that connatal cysts are “still being misinterpreted as cystic WMI.”

We would like to confirm that nowhere in our publication or on-line material have we called this example in On-line Fig 2, WMI. We have not labeled it cystic PVL or inferred that in the text or on-line material. The exact descriptions in the text are “white matter abnormality,” “cystic degeneration,” or “cystic lesion.” In On-line Tables 1 and 2, this scoring category is called “cerebral WM, cystic lesion.” The scoring system was descriptive and not interpretive—that is, if a cyst was observed, then it was scored without interpretation of the pathogenesis or etiology. This descriptive approach was undertaken to improve the reproducibility of the scoring system, especially in cases in which the pathogenesis or etiology of a lesion was unclear. We agree that it is of paramount importance that clinicians do not interpret our example as cystic PVL; thus, we have amended the caption of On-line Fig 2 to “Bilateral connatal cysts, classified as cerebral WM, cystic lesion, focal bilateral, score 2 (axial T2)” to ensure the utmost clarity.

The authors also commented on On-line Figs 11, 12, and 14, in which they suggest that “germinal matrix hemorrhages are scored as deep gray matter injury.” We agree that germinal matrix hemorrhages are evident in these images; however, from the available images, we think that a secondary involvement of the deep GM (head of caudate) is very likely and, in any case, cannot be excluded, hence our scoring of the images of these subjects as focal bilateral deep GM signal abnormality. An additional coronal image that relates to On-line Fig 12 is included here as On-line Fig 12B, to demonstrate caudothalamic groove germinal matrix hemorrhages, in which extension into the adjacent caudate head is likely. The deep GM subscale score demonstrated strong associations with both motor and cognitive outcomes in our article.

We include 2 additional images from the same subject used in On-line Fig 7, to clarify the involvement of WM in addition to the germinal matrix hemorrhage in this case. We believe that signal abnormality from the additional T1 images supplied, despite the low quality, can support the presence of linear hyperintensity involving the white matter next to the more evident germinal matrix hemorrhage, along with a slightly enlarged ventricle.

We are not presenting this scoring system as a diagnostic tool but rather as an assessment in which our methodology has demonstrated predictive validity. Compared with MR imaging at term-equivalent age in preterm infants, certain features are specific to the earlier imaging time point, such as hemorrhagic lesions, which present unique challenges to scoring. Our choice of

being very sensitive in our scoring may have led to a tendency to overestimate germinal matrix hemorrhages populating part of the putamen and caudate, for example. We believe this is better than the alternative of potentially underestimating the impact of germinal matrix hemorrhages on adjacent tissue structures. We think that our approach is sensitive and descriptive in a new and challenging area and an important first step in developing robust and validated MR imaging scoring tools for use in this population.

## REFERENCE

1. George JM, Fiori S, Fripp J, et al. **Validation of an MRI brain injury and growth scoring system in very preterm infants scanned at 29- to 35-week postmenstrual age.** *AJNR Am J Neuroradiol* 2017;38:1435–42 CrossRef Medline

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