Reviewer's report

Title: "Early identification of brain injury in infants with hypoxic ischemic encephalopathy at high risk for severe impairments: accuracy of MRI performed in the first days of life"

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Reviewer: Peter Filan

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Early identification of brain injury in infants with hypoxic ischemic encephalopathy at high risk for severe impairments: accuracy of MRI performed in the first days of life"

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Reviewer comments

The question raised in this paper is certainly relevant, when an MRI is performed in the context of an infant with HIE does the scan reflect the true degree of injury or normality. In addition many centres face limitations of availability and accessibility to neonatal MR imaging that influence when the scan can be performed and performed safely. The advent of therapeutic hypothermia can also influence clinician's decisions as to when they perform the scan.

My main concerns are as follows

1) There is an overemphasis throughout the paper from the abstract through to the discussion on the timing of the MRI and its role in end of life decisions/ redirection of care. The timing of the MRI and its accuracy is a relevant question primarily, for clinical prognostication and parental discussions, for the majority of infants who survive. Time critical decision making regarding redirecting care are relatively uncommon, even in western societies. I would broaden the discussion to reflect this.

2) Although a picture sometimes tells a thousand words, an MRI is not necessarily essential in order to redirect care. The clinical assessment I believe is still useful despite discussions in the literature about how hypothermia may have influenced its role. The paper mentions that all infants had aEEG monitoring but do not discuss the role of aEEG / EEG in time critical redirection of care decisions. The current consensus is that failure of the aEEG / EEG to improve by 48 hours or more is indicative of a poor prognosis. The sensitivities and specificities of aEEG / EEG are equal to if not superior to MRI in numerous papers and summarised in Pediatrics 2013 van Laerhoven (reference 9). Whilst EEG not the topic of the paper perhaps this could be briefly discussed and again
pointing to my concern re the message that MRI not always essential although usually performed, this point is relevant to units where MRI may not be as immediately accessible on site.

3) Is the topic of this paper a primary aim of this prospective observational study or a sub study of a larger project? I ask this as only 15 of the 40 infants with moderate to severe encephalopathy had 2 scans; if it was the primary question then I would have expected a better 2 scan result even allowing for deaths and drop outs due to transfers to other hospitals.

4) The ratio of moderate to severe encephalopathy cases seems to be reversed, is this correct and if so why, does it reflect local cooling practice. You allude to this in discussion but I would expand the sentence.

5) Numbers in the study are still relatively small, but is it possible to comment on the few scans where the MR scores did change from scan 1 to scan 2 in relation to region of injury, this may not be possible within the word limits and small numbers

Minor revisions
Although generally well written and structured there are some misspellings or sentences that require rewriting throughout the paper, other necessary corrections listed below

Abstract
Background: with the ones-change to with the scans, this also occurs in the main text background
Results – extensions – change to extent

Main text of paper
Background: trails – trials
redirection of care a better term than treatment withdrawal, other wise refer to withdrawal of life sustaining treatment
“risk” that the “neonate” will survive: ?/ say possibility that the infant will survive

MR imaging oxymeter – oximeter

Results; line one “significant” encephalopathy, this qualitative word not necessary in results section
Clarify why only 33 of 40 infants had one scan and why only 15 had two scans
5of 9 moderate cases were scanned, should this be 5 of 14, perhaps a flow chart on this would be useful

MR imaging end of paragraph - HI should read HIE

Discussion: as pointed by Wilkinson - change to as described
it is “both” ethical – better to say it is considered
Is it still unclear how cooling impacts on MR imaging, I'm not sure but the TOBY cooling trials have published on the utility of MR after cooling

page 11 we couldn’t – change to we could not

Tables
Table 1: p value for pH is this correct or should it be 0.64
Table 3: needs to ordered better eg according to grade on encephalopathy or pattern of injury and does RM1 and RM 2 refer to 1st and 2nd MRI, if so then change the abbreviation to MR1 and MR2 and list below the table

Figures
Title of figure 1 seems to have been truncated. may be a print error

References
good, up to date

Overall worthy of publication with some revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.