Title
A regression forest-based automated image analysis technique to estimate GA between 18 and 34 weeks using a single 3D brain volume dataset – a prospective validation.

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Objectives
The scope for estimating gestational age (GA) by US is restricted to 22 weeks. This is a significant problem in low- and middle-income settings where women present late, and where the burden of GA related perinatal mortality is the highest. We hypothesised that morphological development of the fetal cerebral cortex could be used to predict GA, using an automated algorithm requiring a single 3D US volume dataset.

Methods
A supervised machine learning algorithm was developed. Random regression forest analyses were applied to provide a representation of the brain to ‘learn’ which age-specific features and sonographic patterns were best able to discriminate GA. A training-set comprising 150 3D volumes between 138 and 245 days acquired during INTERGROWTH-21st was used. Testing was performed using a prospectively acquired independent validation sample (n=150). Model performance was assessed by comparing absolute values from GA_{model} with GA_{truth} using the systematic difference (SD) and 95% limits of agreement (LOA). Heat-maps were generated to illustrate GA discriminating regions of the brain selected by the model.

Results
The model successfully analysed 138/150 volumes to predict GA_{model}. The systematic difference for GA_{model} compared to GA_{truth} was +0.8 days and 95% LOA were estimated at -10.92 to 10.52 days respectively. The thalamus and Sylvian fissure were consistently highlighted as regions with important GA discriminating features.

Conclusion
Obtaining estimates of GA using automated analysis of a single 3D fetal brain volume dataset is feasible. Preliminary clinical testing suggests that the model is stable. Estimates of model error at 34 weeks are consistent with HC and BPD at ~22 weeks. Further testing using a range of clinical phenotypes is underway.