Radiomics analysis of MR neonatal brain: will it be the Rosetta stone for predicting the poor psychomotor outcome in preterm newborns?

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The prediction of neurodevelopmental outcome (NDO) in premature infants is one of the major issues in neonatology [1]. With the advent of non-invasive imaging techniques such as ultrasound and, more efficaciously, MR, a growing amount of data have been progressively collected on premature brain and its disorders, but even with the most accurate and state-of-the-art imaging techniques the presence of an apparently normal premature brain at term equivalent age (TEA) cannot exclude an abnormal NDO [2].

Researchers have tried to analyze premature brain with almost all the most advanced MR techniques, looking for some biomarkers not directly observable with standard techniques. Diffusion tensor imaging (DTI) and neurite orientation dispersion and density imaging (NODDI) metrics exhibit lower fractional anisotropy (FA) and higher orientation dispersion index (ODI) in children born very preterm than those in full-term children, providing additional information of the impact of prematurity and white matter microstructure on cognitive outcomes up to 6 years of age [3]. According to Duerden and colleagues [4], tract-based spatial statistics, a diffusion MR imaging analysis method, performed at TEA, seemed to be a promising predictor of neurodevelopmental outcomes in children born very preterm up to 18 months.

Using neonatal deformation-based morphometry and neonatal DTI, Ullman and colleagues [5] identified, in the preterm brain, regions around the insula and putamen associated with skills important for childhood mathematical achievement. Increased tissue volumes in these regions during the neonatal

period seem to be associated with better early mathematics in preterm children.

Recently, an artificial neural network, a segment of artificial intelligence, with one hidden layer, called feedforward neural network (fNN), was used to predict the neurodevelopmental outcome of very preterm neonates at 12 months corrected age by using biomarkers of cerebral MR proton spectroscopy (1H-MRS) and DTI at TEA. According to the authors, fNNs might be able to predict motor and cognitive development of preterm infants up to 12 months corrected age [6].

All these interesting and complex studies, and many similar others suffer some intrinsic limitations. First of all, the complexity of post-processing procedures does not allow considering them readily available for clinical purposes; secondly, the results are expressed in terms of probability and not referred to a single case; and last, but not least, all these groups of preterm newborns consider both infants with normal brain on conventional MR and infants with white matter injuries (WMI), making it impossible to understand what the problem is in the apparently normal brain MR of premature infants who exhibit a poor NDO.

From a practical point of view, neuroradiologists challenged with predicting the premature NDO have first to exclude any structural abnormalities on conventional MRI, and Cayan-Rand and colleagues from Sick Kids in Toronto demonstrated how a very simple classification of white matter injuries on conventional MRI in preterm infants can predict cognitive outcomes in 90% and motor outcomes in 85% of the cases [7]. Still, we know from the seminal article by Woodward and colleagues [2] that up to 15% of premature infants with no WMI on MRI at term equivalent age suffer from NDO at corrected age of 2 years.

In this issue of *European Radiology*, Shin and colleagues [8] evaluated preterm newborns at TEA by means of radiomics analysis in order to evaluate its potential as a predictor for poor NDO. In spite of 45 out of 46 neonates having no significant WMI on conventional MRI, the radiomics

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analysis showed a good performance for predicting a poor NDO at 12 months of corrected age.

Radiomics is something still obscure for the vast majority of radiologists; it seems like a black box in which all the numbers related to any acquired images are magically processed to obtain some other numbers, the biomarkers, that can potentially correlate with some clinical feature. The main idea of radiomics is that among the millions of data acquired in a standard MR study, there is something not perceivable by our senses, but still with some relationship with brain structure, that can be disclosed only by some mathematical calculations. In other words, MR images contain a sort of secret numerical alphabet that we cannot read without the aid of a powerful computing machine.

In the study of Shin and colleagues, from a semi-automatic segmentation on the WM region carried out on the simple T1-weighted and T2-weighted images, were initially extracted 1906 features from which the top 20 relevant features were used to build prediction models based on T1-weighted images (T1WI) and T2-weighted images (T2WI), respectively, whereas for another model based on a combination of T1WI and T2WI the top 10 relevant features of each of T1WI and T2WI were used.

The prediction model performed best with T1WI which shows upon analysis an area under curve (AUC) of 0.92, sensitivity of 84.6%, specificity of 78.8%, and accuracy of 80.4%.

In this study, the number of infants studied is relatively low; and like all the other studies with advanced MR techniques, it suffers from a complex and time-consuming post-processing pipeline, limiting its application in a clinical setting. From the practical point of view, however, it should be considered that all data stem exclusively from standard T1WI and T2WI only, with a very simple acquisition protocol. The presence of only one case with moderate to severe WMI is then the really good news in order to reduce the 15% of false negatives in predicting poor NDO still reported on standard MR sequences.

We are expecting future confirmations on these interesting data, hoping radiomics could definitely help us in understanding the mysterious alphabet hidden in the standard MRI acquisition sequences.

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