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# Reply to comments on "State of the art in magnetic resonance imaging of hepatocellular carcinoma": the role of DWI

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## Author's reply

We were very pleased to read the comments from Dr Granata and colleagues in Radiology and Oncology about our article "State of the art in magnetic resonance imaging of hepatocellular carcinoma".[1] As highlighted, the diffusion weighted imaging (DWI) plays a key role as a qualitative and quantitative method in the detection of hepatocellular carcinoma (HCC), mostly for small (< 20 mm) or well-differentiated HCC with atypical post-contrast imaging patterns[2], helping differentiate benign from malignant focal hepatic lesions, and also allowing the evaluation of treatment response to systemic and locoregional therapies in hepatic malignancies.

DWI is an MRI sequence which provides useful information especially in the absence of intravenous contrast media.[3] In this context, the intravoxel incoherent motion (IVIM) model is based on the fact that perfusion exists inherently in DWI voxels and influences the measurement of the apparent diffusion coefficient (ADC), allowing qualitative and quantitative assessment. It can be used in the differentiation between benign and malignant hepatic nodule, such as focal nodular hyperplasia and HCC.[4] Furthermore, a few recent studies showed that there is a correlation between the histopathological grade and prognosis of HCC and DWI, demonstrating that significantly lower ADC values in poorly differentiated tumors with a shorter recurrence-free survival and a cut-off value of 1.175 x $10^{-3}$ $mm^2/s$ to predict microvascular invasion.[5,6]

Regarding Diffusion kurtosis imaging (DKI), we also recognize its current role in the evaluation of non-Gaussian water diffusion, providing better information in heterogeneous tissues such as large HCCs, even in the post-treatment studies. Wang *et al*. suggested that a mean Kurtosis value cut-off of 0.917 has a good sensitivity, specificity and diagnostic accuracy in the prediction of microvascular invasion, as the ADC value commented above.[7] However, to our knowledge there is not enough evidence to correlate the quantitative parameters obtained with DWI and IVIM with HCC physiopathology or pathologic subtypes. This is possibly due to the discrepancy in the current spatial resolution of DWI/IVIM and pathologic findings, the currently described correlations are significant but underline a gap of knowledge between what is observed at MRI and what is observed at pathology. The hope is that IVIM may be able to describe subcategories of HCCs of among the pathologic descriptors allowing for better treatment tailoring and prognostic assessment.

Finally, it is important to emphasize that all the information obtained from DWI is complementary and does not replace the use of intravenous contrast agents, Hectors *et al*. proved that these

sequences offer non-redundant data on flow and perfusion inside the tumor, probably due to the change in the microvascular supply, although they presented moderate to strong correlation in the surrounding liver.[8]

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