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"Nodule-in-nodule" architecture of hepatocellular carcinoma

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The "nodule-in-nodule" architecture of hepatocellular carcinoma (HCC) is defined by the presence of one or more smaller inner nodules having different imaging features than a larger outer nodule (Fig. 1) [1]. This appearance is a variant of the "mosaic" architecture of HCC, that is defined as the presence of randomly distributed internal nodules or compartments, with different imaging features regarding enhancement, attenuation, intensity, and size [1, 2].

According to the recently released update of Liver Imaging and Reporting Data System (LI-RADS v2018), the nodule-in-nodule architecture represents an ancillary feature favoring HCC in particular. When detected, it may be used to upgrade an observation by one LI-RADS category only, up to LR-4. However, radiologists may apply this feature for such lesions at their discretion [3].

Pathologically, the nodule-in-nodule is suggestive of clonal expansion of more dedifferentiated cells along the hepatocarcinogenesis process compared to the outer nodule. Consequently, the inner nodule is the focus of more progressed neoplastic cells (i.e. HCC) contained within the outer dysplastic nodule [1, 3]. Imaging features of nodule-in-nodule architecture are related to the characteristic histologic growth pattern. On CT and MRI, the inner nodule typically shows HCC-like imaging features, i.e. arterial phase hyperenhancement and washout appearance on portal venous phase (Fig. 2), as opposed to the outer hypovascular dysplastic nodule that does not enhance on arterial phase [4]. A nodule-in-nodule appearance can also be detected by ultrasonography (US), typically as a hyperechoic nodule (expression of HCC with fatty change) containing a well-demarcated hypoechoic nodule inside (expression of cancer tissue without fatty change) [5].

Measurement of lesion size should be made on the entire observation, including the larger outer nodule and not only the smaller inner nodule [4].

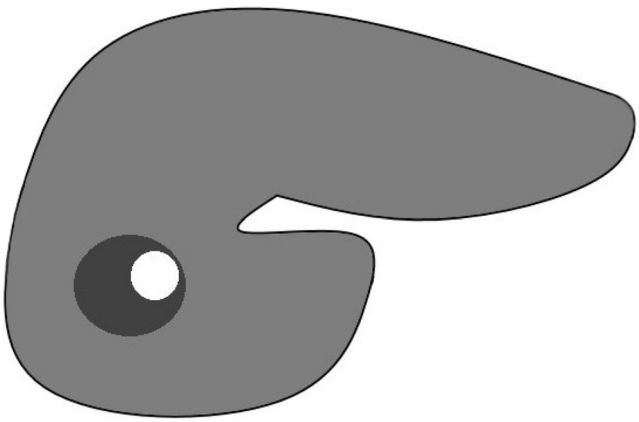

Fig. 1 Schematic representation of nodule-in-nodule architecture of hepatocellular carcinoma. A single nodule is located within a larger mass. The nodule and the larger mass typically have different attenuation/intensity and enhancement

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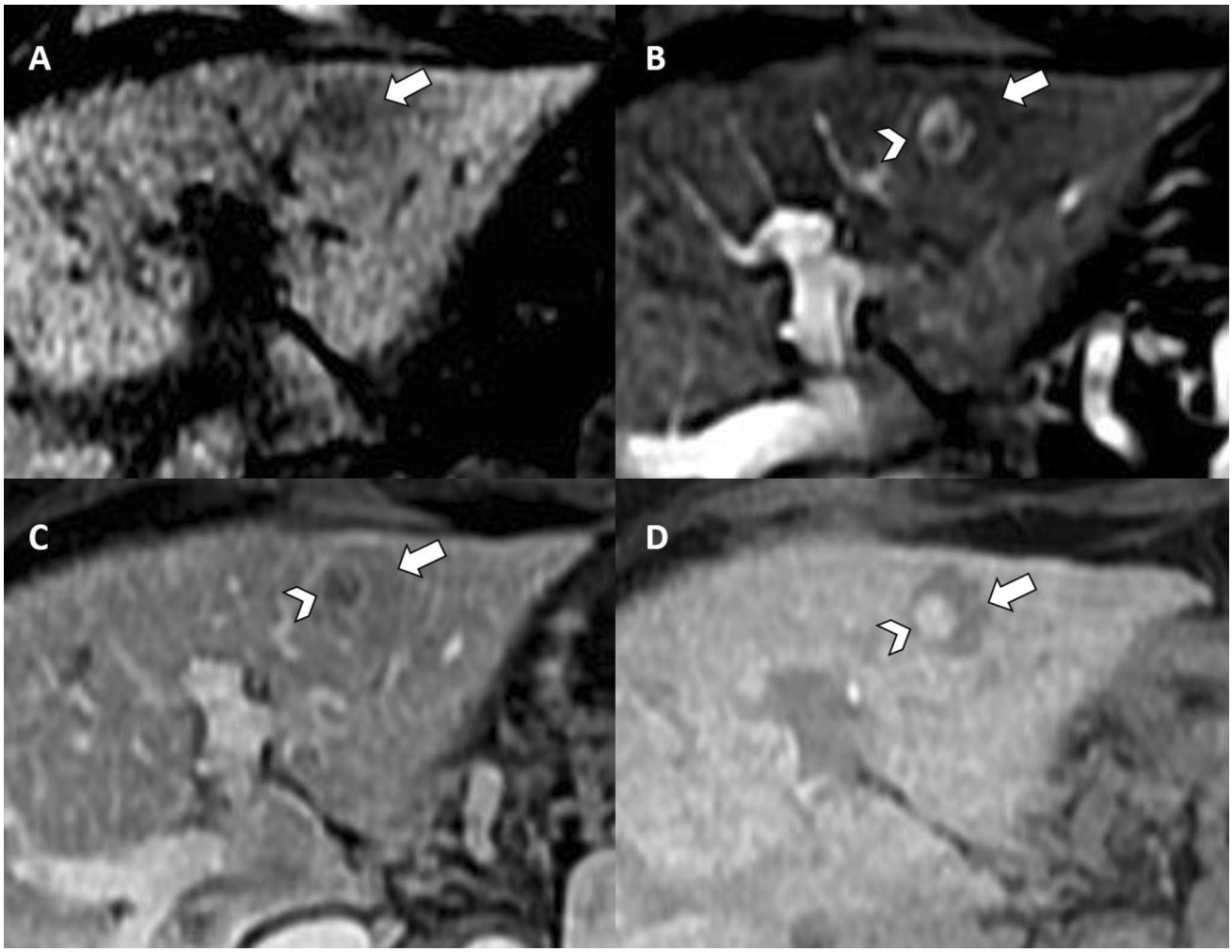

Fig. 2 Gadoxetic acid-enhanced MR images show nodule-in-nodule architecture of hepatocellular carcinoma in an 80-year-old man with hepatitis B cirrhosis. **a** Pre-contrast axial gradient-recalled echo (GRE) T1-weighted fat-saturated MR image shows a hypointense lesion (arrow), size 2.8 cm, in hepatic segment 3. **b** Arterial phase image shows an inner eccentric hypervascular nodule (arrowhead), size 1 cm, within the outer hypovascular nodule (arrow). **c** Portal venous phase image shows washout appearance and enhancing capsule of the inner nodule (arrowhead) within the larger hypointense nodule (arrow). **d** Hepatobiliary phase shows better differentiation between the inner hyperintense nodule (arrowhead) and the outer hypointense nodule (arrow)

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

Informed consent Statement of informed consent was not applicable since the manuscript does not contain any patient data.

Research involving human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

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