Hepatocellular Carcinoma (HCC): Correlation between MultiHance™ - enhanced magnetic resonance (MR) imaging and pathological findings

INTRODUCTION: MultiHance™ (Gadobenate dimeglumine, Gd-BOPTA) is a liver-specific MR contrast agent which is targeted to hepatocytes (1). In a recent study in patients with HCC, 0.1 mmol/kg MultiHance™, coupled with dynamic and delayed, static imaging, was shown to improve the characterization of HCC lesions both in patients with cirrhosis and in patients with no underlying liver disease (2). In delayed imaging of HCC, non unequivocal behavior of contrast enhancement has been observed, with a marked improvement in liver-lesion contrast-to-noise ratio seen in some cases and a patchy, inhomogeneous washout of contrast from lesions in others.

The present study formed part of the phase III clinical evaluation of MultiHance™ and was aimed at identifying those factors, intrinsic and extrinsic to primary malignant focal liver lesions, that might influence and thus explain this variable enhancement pattern. Specifically, attempts were made to retrospectively correlate MultiHance™-enhanced MR imaging with the anatomical and pathological characteristics of histologically proven HCC lesions.

PATIENTS AND METHODS: A total of 34 patients (20 M/14 F, mean age: 64.2 years) with HCC were assessed. HCC diagnosis was always confirmed by core biopsy and histology. In all, 22 patients were classified as Child A, 9 as Child B and 1 as Child C cirrhosis. Two patients had no signs of underlying conditions. Correlation with anatomical and pathological features was carried out in 28 cases directly on the resected lesion, and in 6 cases on the basis of at least 3 core biopsies. In 12 cases the diameters of the lesions fell in the range from 1 to 3 cm, in 9 cases from 3 to 5 cm, and in 3 cases from 5 to 7 cm. In the remaining 10 cases, lesions were greater than 7 cm in diameter. Histological analysis of the lesions took into account: a) the degree of cellular differentiation; b) the degree of fatty metaplasia; c) the degree of tissue necrosis; and d) the presence or absence of peliosis and bile.

MR imaging was performed at 1.5T before and at 60-120 min after the administration of 0.1 mmol/kg MultiHance™ (10 ml/min). The following sequences were used: T1-WSE (TR/TE 500-600/15), T2-WSE (TR/TE 2000/90), and T1-WGE (TR/TE/FA 80/4/70°) and images were obtained for all patients along the axial plane (slice thickness: 8-10 mm; 2 mm interval; matrix size: 192 x 256; rectangular FOV: 350 x 420 mm). Qualitative and quantitative evaluations of the images were performed and correlated with histologic findings. The quantitative evaluation, performed on T1-WGE images, looked at a) the % increase of liver enhancement after MultiHance™ administration, b) the contrast/noise (C/N) ratio between lesion and liver parenchyma before and after MultiHance™ administration, and c) the C/N increase after MultiHance™ administration. The qualitative analysis considered the morphologic features of the lesions as well as the visual variation of the liver-to-lesion contrast before and after MultiHance™ administration.

RESULTS: In terms of lesion differentiation, 14/34 HCC (41.1%) were histologically classified as well differentiated, 11/34 (32.3%) as moderately differentiated and 9/34 (26.4%) as poorly differentiated. Fatty metaplasia was present in 23/34 HCC (67.6%), necrosis in 77/34 HCC (64.7%), peliosis in 21/34 HCC (61.7%) and bile in 13/34 HCC (38.2%).

In 6/34 (17.6%) cases the pre-contrast C/N (C/Npre) was positive and in 28/34 (82.3%) cases, negative. The change in C/N after MultiHance™ administration (C/Npost/C/Npre) was for the better in 23/34 patients (67.6%). In terms of lesion conspicuity, an improvement was seen post-contrast for 12/34 patients (35.3%), while no change was noted for 16/34 patients (47%) and a slightly worse conspicuity for 6/34 patients (17.6%). The 12/34 patients for whom an improved lesion conspicuity was observed post-contrast also demonstrated an improved post-contrast C/N and a C/Npost/C/Npre value of greater than 2. In these patients, the mean lesion diameter was 5.06 ± 4.17 cm, the degree of fatty metaplasia 8.6 ± 11.7%, and the degree of intra-lesional necrosis, 13.9 ± 13.4%. Peliosis and bile were present in these lesions in 11/12 (92%) and 4/12 (33.3%) cases, respectively. In this group 10/12 patients were classified as Child A and 2/12 as Child B.

For the 16/34 patients showing no change in lesion conspicuity, the C/N ratio was shown to be variable and the C/Npost/C/Npre value to fall between -1.22 and 1.97. The mean lesion diameter in this group was 6.6 ± 3.6 cm, the degree of fatty metaplasia 16 ± 25.3%, and the degree of intra-lesional necrosis, 10.9 ± 12.5%. Peliosis was observed in 10/16 HCC (62.5%) and bile in 6/16 HCC (37.5%). In 2/16 patients there was no evidence of underlying liver disorder, while of the remaining 14 patients 9 were classified as Child A and 5 as Child B.

Finally, for the 6/34 patients showing slightly worse post-contrast lesion conspicuity, a concomitant reduction in the C/N ratio was also observed along with a C/Npost/C/Npre value that was in all cases ≤0.54. The mean diameter of these lesions was 4.18 ± 3.29 cm, the degree of fatty metaplasia 48.3 ± 31.8%, and the degree of intra-lesional necrosis was 7.5 ± 11.7%. Peliosis was observed in 4/6 (66.6%) cases and bile in 3/6 (50%) cases. In all, 3/6 patients in this group were classified as Child A, 2/6 as Child B and 1/6 as Child C.

Overall, the enhancement of the moderately differentiated lesions (69.2 ± 42.7 %) was greater than that of well differentiated and poorly differentiated lesions (46.4 ± 26.5% and 42.4 ± 20.6%, respectively).

CONCLUSION: This study has demonstrated that HCC lesion enhancement with MultiHance™ is influenced by the dimensions of the lesion, the degree of vascularization and by the degree of correlation with the level of necrosis. Moreover, inhomogeneous contrast washout, leading to reduced C/N, is due to a greater degree of intra-lesional fatty metaplasia.

REFERENCES: