# Relationship between microvessel density(MVD) of malignant and benign hepatic lesions and dynamic enhanced MRI

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**INTRODUCTION:** Recent advances in MRI have led to the establishment of fast scan techniques, which, combined with bolus injection of contrast material, allows the acquisition of dynamic enhanced MRI for higher confident detection of HCC. There have been reports on correlation among digital subtraction angiography (DSA), ultrasound angiography (USAG), computed tomography during arterial portography (CTAP) and immunohistochemical findings[1], but the relationship between MVD and dynamic MRI has been seldom reported. In this research, correlation between MVD and dynamic enhanced MRI of hepatic malignant and benign lesions was studied in order to establish a theoretical foundation for evaluation of microvessel wihin these lesions with MRI images, which will give more references to clinical diagnosis or HCC therapy.

**METHODS:** 159 patients underwent dynamic enhanced MRI examination before surgery. MRI was performed with a 1.5T system (Symphony, Siemens) and a phased array coil was used. All the patients underwent axial T1 weighted ( FLASH, TR=123ms, TE=4.8ms), T2 weighted (HASTE, TR=1200ms, TE=57ms) and multiphase dynamic gadolinium-DTPA enhanced(the same sequence as T1 weighted) imaging. The section thickness was 8mm, with an intersection gap of 0.5mm-2mm. The contrast material dose was 0.2 mmol/kg b.w. and was administered as a rapid bolus. Arterial phase images were obtained in the 15s-20s after the start of bolus administration. Portal venous and equilibrium phase images were obtained in the 45s and 90s,respectively. In different phases of the images, signal intensities of lesions($SI_l$), liver parenchyma ($SI_p$) and background noise ($SI_n$) were evaluated, respectively, while obvious vessel and fluid should not be evaluated. Contrast-to-noise ratios(CNR) in all the phases were calculated as CNR=( $SI_l$-$SI_p$)/$SI_n$. All the specimens, including 115 of HCC, 6 of combined hepatocellular and cholangiocarcinoma, 14 of cholangiocellular carcinoma, 3 of focal nodular hyperplasia(FNH), 2 of hepatocellular adenoma, 4 of necrotic liver carcinoma, 3 of chronic liver abscess, 3 of coagulation necrosis, 4 of adenomatous hyperplasia, 2 of angiomyolipoma,6 of inflammatory pseudotumor, 1 of fibroinflamtory necrotic nodule, 1 of eosinophilic granuloma and 1 of neurofibroma, were immunohistochemically stained with monoclonal antibody CD-34. After staining, the tubular, sinusoidal, cystiform or vacuolar structures shaped by endothelial cells or immature endothelial cells, which were stained yellow or brown by CD34, were considered as positive microvessels. In ten high power microscopic views, all the positive microvessels were counted and averaged for MVD. All the pathologic diagnosis were confirmed by both two the pathologists. The lesions were separated into six groups: small HCC (diameter<3cm), normal HCC (diameter>3cm), combined hepatocellular and cholangiocarcinoma, cholangiocellular carcinoma, Group A (FNH, hepatocellular adenoma, adenomatous hyperplasia, angiomyolipoma, eosinophilic granuloma, fibroinflamtory necrotic nodule and neurofibroma) and Group B (necrotic liver carcinoma, chronic liver abscess, coagulation necrosis and inflammatory pseudotumor). Within each group, Pearson correlation was performed for correlation analysis between the MVD and CNRs in arterial, portal venous and equilibrium phases, respectively.

**RESULTS:** Correlation coefficients within the six groups between MVD and CNRs in different phases are shown in Table 1. Shown in Figure 1 are examples of microvessels and MR images of HCC.

**DISCUSSION:** CD34, which is expressed in blood stem cells and neovessel-endothelial cells, is the most distinctive marker for demonstrating vessel-endothelial cells[2], especially for demonstrating sinusoid-like vessels in tumor tissues[3]. The MRI contrast agent, Gd-DTPA, whose pharmacokinetic behavior is similar to the well known iodinated contrast agent used in enhanced CT, urography and angiography, does not penetrate cell membrane and only diffuses into vascular space and interstitial space. Schlemmer *et al*.[4] demonstrated that dynamic contrast-enhanced MRI can provide important information about individual MVD within prostate cancer, but Su *et al*.[5] reported that there was no significant association between dynamic contrast-enhanced MRI and immunohistochemistry based measurements of angiogenesis within breast cancer. Chen *et al*.[6] studied HCC with dynamic spiral CT and found that enhancement imaging features of HCC lesions on CT scanning were correlated with tumor MVD. In this research, MVD of small or normal HCC was correlated with CNRs in images of arterial, portal venous and equilibrium phases, but those of other lesions were not. What caused this diversity probably is: firstly, there was too few cases of the other lesions in this research; secondly, since reports have shown that with small HCC increasing in size and becoming increasingly dedifferentiated, the number of portal tracts apparently decreases and intratumoral arterioles develop, only nodules with blood supply mainly from artery, like HCC or prostate cancer, could demonstrate unified relationship between MVD and CNR; thirdly, because different lesions are with different vascular penetrativity, different tissue density, different interstitial tissue and so on, it is not proper to combine different lesions into one group in studying relationship between MVD and CNR. This phenomenon probably demonstrates that CNR is regulated by many factors besides MVD, and tissular quality may play a more important role than MVD in gross enhancement morphology. CNR of dynamic enhanced MRI could be used to evaluate microvessel within HCC *in vivo* but not within different lesions.

**REFERENCES AND ACKNOWLEDGEMENTS:**

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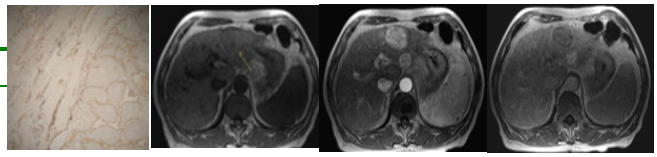
**Table 1:** Correlation between MVD and CNR (Pearson correlation coefficient/*P*)

| | Arterial | Portal | Equilibrium |
|---|---|---|---|
| Small HCC (n=31) | 0.547/0.001 | 0.502/0.004 | 0.395/0.028 |
| ormal HCC (n=78) | 0.386/0.001 | 0.521/0.001 | 0.419/0.001 |
| Combined carcinoma (n=6) | -0.629/0.181 | -0.586/0.222 | -0.479/0.331 |
| Cholangiocellular carcinoma (n=14) | 0.131/0.685 | -0.217/0.499 | -0.408/0.188 |
| Group A (n=14) | -0.041/0.890 | -0.238/0.412 | -0.408/0.148 |
| Group B (n=16) | 0.209/0.436 | 0.618/0.011 | 0.773/0.001 |



**A** **B** **C** **D**

**Figure 1:** HCC in left lobar of liver. A: microvessels, stained by CD34(×40), left part of the figure is cirrhosis; B: MR image, nonenhanced, T1 weighted, CNR=-1.03; C: MR image, arterial phase, CNR=8.02; D: MR image, equilibrium phase, CNR=-2.99