Rectal cancer at 3.0T: correlation of DCE-MRI findings with tumor angiogenesis

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Introduction: Tumor angiogenesis is an essential process for tumor growth, proliferation, and metastasis. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is increasingly advocated for assessing tumor vascularity. The purpose of this study is to correlate enhancement patterns of rectal cancer on DCE-MRI with tumor angiogenesis on immunohistochemistry (IHC).

Materials and Methods: DCE-MRI was performed in 38 patients with histologically confirmed rectal cancer at 3T (GE Signa Excite, Milwaukee, Wisconsin, U.S.A.) using an 8-channel phased-array surface coil. Bowel preparation included laxative cleansing, distension with sodium chloride enema and anisodamine to reduce peristalsis. Multiphase axial 3D SPGR with fat suppression was performed with 14-16 second temporal resolution for a total data acquisition time = 4-6 minutes, initiated simultaneously with intravenous injection of 0.1 mmol/kg Gd-DTPA at 3 mL/sec. The time-intensity curve (TIC) was obtained using a region-of-interest of 50 mm^2 covering the center of the tumor excluding cystic or necrotic area. Peak enhancement ratio (ER_{peak}) and time to peak enhancement (T_{peak}) for each tumor were determined.

After resection, microvascular density (MVD) and vascular endothelial growth factor (VEGF) expression was determined using immunohistochemistry (IHC) stain on selected specimens (n = 24). Normal rectal mucosa from the same patient population (n = 6) were also examined for MVD and VEGF as control. The correlation of MVD and VEGF with functional parameters of DCE-MRI including TIC pattern, $ER_{peak,}$ and T_{peak} were analyzed using SPSS 11.5 software. Independent samples T-test, one-way ANOVA, Chi-square Test, Pearson correlation analysis and Spearman grade correlation analysis were performed. $P < 0.05$ was considered to be statistically significant.

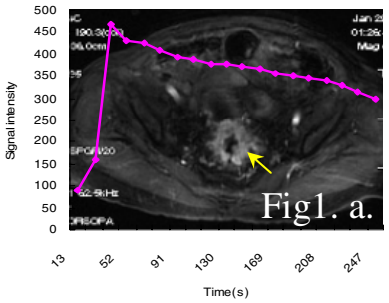
Results: Time-intensity curves were classified into four types according to time to peak enhancement and contrast wash out: type A with early enhancement (T_{peak} <80s) and gradual washout; type B with late enhancement (T_{peak} >80s) and gradual washout; type C with late enhancement followed by plateau phase; type D gradual rising with no peak. The enhancement of primary adenocarcinoma (n = 33) was heterogeneous, with 88% (n = 29) showing either type A (n = 18) or type B (n = 11) enhancement. For signet cell cancer/mucinous carcinoma with the worst differentiation (n = 5), the patterns of TIC were variable from type B to type D with type D only seen in signet cell cancer (n = 1).

MVD was significantly correlated with VEGF ($p < 0.01$) with r = 0.49. VEGF expression was positive in 66.7% of rectal cancer (n = 16) but none in normal mucosa. In VEGF positive group, the mean value of MVD was 92 ± 36, significantly higher than that of VEGF negative group (mean value = 64 ± 32, $p < 0.05$). The expression of MVD and VEGF was significantly different between normal rectal mucosa and rectal cancer ($p < 0.05$) and between tumors with and without lymph node metastasis ($p < 0.05$).

Among 24 rectal cancers examined with IHC staining, most time-intensity curves were type A (n = 15, Fig1) and type B (n = 7, Fig2). MVD was significantly higher for tumors with Type A (93 ± 39 vs. 61 ± 7, $p < 0.05$) enhancement. T_{peak} negatively correlated with MVD (r = -0.48, $p < 0.05$). T_{peak} of VEGF positive group was 77 ± 34 s, significantly earlier than that of VEGF negative group (131 ± 51 s, $p < 0.05$).

Conclusions: MVD and VEGF represent the degree of tumor angiogenesis and are helpful in distinguishing malignant lesions, defining infiltration, and predicting metastasis and prognosis of rectal cancer. Data from this study show the functional parameters of DCE-MRI correlated with the level of MVD and VEGF expression. This information is helpful to evaluate tumor angiogenesis in vivo and the sequence/analysis can be easily incorporated into routine examinations.

References: 1.Kanematsu M. Top Magn Reson Imaging, 2005,16:67-75. 2.Leach MO. Breast Cancer Res, 2001,3:22-27. 3.Tuncbilek N. Breast J, 2003,9:403-408. 4.Daldrup Link HE. Radiology,2003,229:885-892. 5.George ML. Br J Surg, 2001,88:1628-1636. 6.Roka M. Radiology, 2000,217: 841-848. 7.Wang B. Acta Radiol, 2005,46:353- 358. 8.de Lussanet QG. Radiology, 2003,229:429-438. 9.Turetschek K. Radiology, 2001,218:562-569



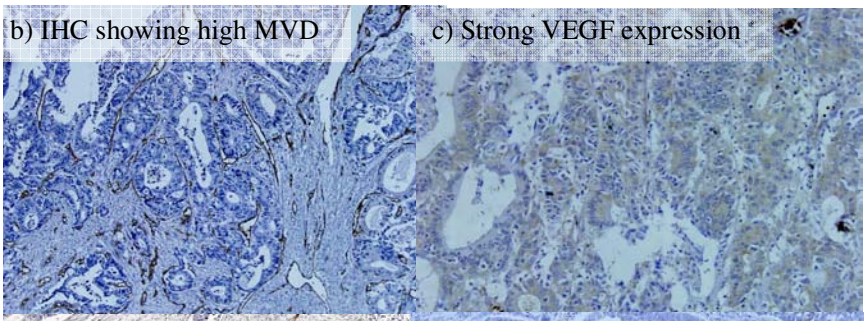
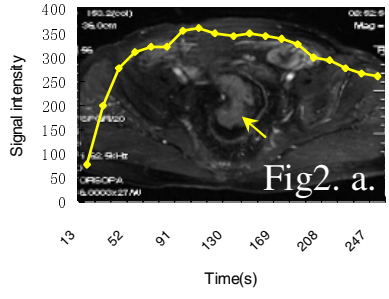


Fig1. a) Arterial phase DCE-MRI shows rectal CA (arrow) with type A TIC, b) IHC with CD34 shows high MVD and c) strong VEGF expression.



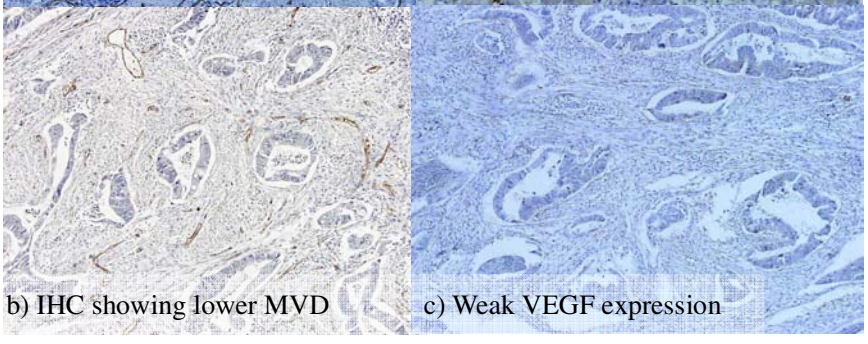


Fig2. a) Arterial phase DCE-MRI shows rectal CA (arrow) with type B TIC, b) IHC with CD34 shows lower MVD and c) weak VEGF expression.