DCEMRI detects effects of tumors on adjacent normal tissue that reflect tumor grade

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Introduction: Dynamic contrast enhanced MRI is used for early detection of cancer, cancer staging, and evaluation of response to therapy. Many studies have compared contrast media dynamics in benign and malignant tumors. However, there have been few MRI studies investigating vasculature of muscles near tumors. Influence of tumors and surrounding muscle may be an important diagnostic marker. Here we used an empirical mathematical model that provides accurate fits to experimental data to compare contrast media uptake and washout rates in muscle far away from and near to tumors.

Materials and Methods: 24 Copenhagen rats were inoculated with either metastatic AT3.1 cells (n = 14) or non-metastatic AT2.1 cells (n = 10). The AT3.1 cells line is a rapidly growing sub-line of the Dunning model and rapidly metastasizes to the lung, while AT2.1 is slower growing with low metastatic potential. To avoid excessive metastases to lung, the rats were imaged within 2-3 weeks after inoculation. T_1-weighted spoiled gradient-recalled-echo images were acquired with a SIGNA 1.5 Tesla MRI scanner. MRI signal from the tissue was detected with a three-inch-diameter surface coil (TR/TE = 15/6 ms, flip angle = 60°, readout bandwidth = 32 kHz, slice thickness = 3 mm, in-plane resolution = 500 µm). A single slice was imaged through the center of the tumor along the long axis of the leg. Gd-DTPA was injected intravenously at a dose of 0.2 mM/kg. Images were acquired before and for one hour after injection, with a time resolution of five seconds. Subsequently, P792 was injected at a dose of 0.05 mM/kg, and images were obtained for an additional hour. P792 was injected second because it washes out more slowly than Gd-DTPA. ROIs were selected in normal muscle far (~10 mm) from the tumor and muscle immediately adjacent to the tumor ROI's. The contrast media concentration as a function of time was calculated in each ROI and fitted using a previously published empirical mathematical model (Fan et al., MRM 2004; 51:487-494).

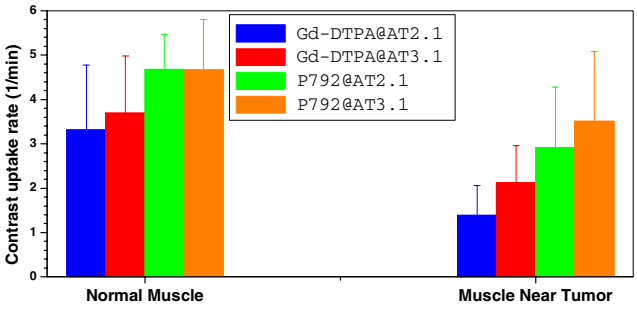

Fig. 1 Contrast uptake rate for muscles.

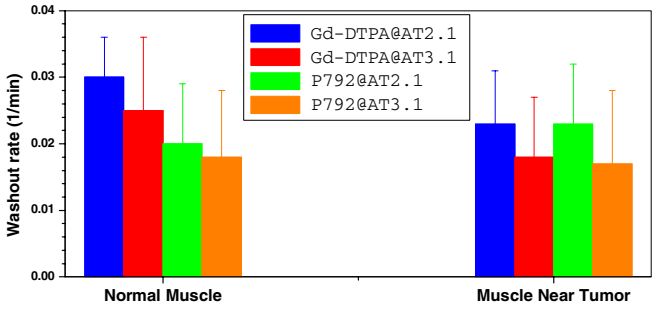

Fig. 2 Contrast washout rate for muscles.

Results: Figures 1 and 2 show the contrast uptake and washout rates in muscle far away from and nearby to metastatic and non-metastatic tumors for Gd-DTPA and P792. Contrast media uptake rate is significantly bigger in normal muscle (3.5 min^{-1}) compared to muscle near tumors (1.8 min^{-1}) for Gd-DTPA data ($p < 10^{-5}$), and in normal muscle (4.7 min^{-1}) compared to muscle near tumors (3.3 min^{-1}) for P792 data ($p < 0.001$). There was clear difference between contrast media washout rate in normal muscle (0.03 min^{-1}) vs. muscle near tumor (0.02 min^{-1}) for Gd-DTPA ($p < 0.01$) but no significant difference for P792 data. Muscle near metastatic tumors had significantly faster uptake ($p < 0.02$) and slower washout ($p < 0.17$) rates than muscle near non-metastatic tumors for Gd-DTPA only.

Discussion: This research demonstrated the influence of cancer on vasculature in surrounding normal tissue. Metastatic tumors had a larger effect on normal tissue than non-metastatic tumors. Uptake and washout rates were slower in muscle near tumors than in muscle far from tumors. This may reflect destruction of normal tissue by invading cancer, cooption of normal vasculature by tumors, and/or an inflammatory response to tumors. Metastatic tumors had a bigger effect on normal tissue than non-metastatic tumors perhaps because they are more invasive. The influence of tumors on surrounding tissue as detected by MRI may provide an additional marker of malignancy that can improve diagnostic accuracy. Pixel-by-pixel analysis should be used in the future analysis to improve sensitivity to effects of tumors on surrounding tissue.