DCE-MRI Assessment of Hepatic Arterial Infusion Chemotherapy in Patients with Unresectable Primary Liver Cancer

M. Muruganandham[1], L. Schwartz[2], N. Kemeny[3], W. Jarnagin[4], D. Haviland[3], J. Dyke[5], J. Koutcher[6]

[1]Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY, United States, [2]Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, United States, [3]Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, United States, [4]Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, United States, [5]Weill Cornell Medical College, New York, NY, United States, [6]Medical Physics, Radiology & Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, United States

Introduction: Primary liver cancer incidence and mortality rate have both increased substantially in the United States over the past several years (an estimated 14,270 deaths out of 18,920 cases expected to be diagnosed in 2004)[1]. Although complete resection remains most effective therapy, it is not possible in many patients. Liver directed therapy, in which chemotherapeutic agents were delivered locally to the tumor through a surgically implanted hepatic artery infusion (HAI) pump, has been explored to enhance the therapeutic outcome[2]. Dynamic contrast-enhanced MRI (DCE-MRI) measure of tumor perfusion status is emerging as a promising approach to monitor tumor response to treatments. The present study reports preliminary results on the utility of DCE-MRI to assess HAI chemotherapy in patients with unresectable primary liver cancers.

Methods: ***Patients and Treatment:*** A total of 49 MR examinations were performed in 13 patients with unresectable primary liver cancer (12 intrahepatic cholangiocarcinoma(ICC), 1 hepatocellular carcinoma(HCC)). MR scans were acquired before (baseline) and every 2 months after the start of therapy. Chemotherapy (Fluoxuridine(FUDR) + Dexamethasone(DEX)) was administered via intra-hepatic pump by continuous infusion over 14 days on a 4-week cycle basis in all patients. ***MR imaging:*** Studies were performed on a 1.5T GE Signa scanner. The dynamic fast multi-phase gradient echo (SPGR) sequence with TR/TE/θ = 9/2/30^0, 15.63 RBW, 30-34 cm FOV, 256x128 matrix was used to acquire a single slice through tumor center. Two different image acquisition protocols were used. Protocol-I: In the initial 6 patients, 30-40 axial images were acquired at a rate of 1sec/image in a single breath hold block and a total of 3 such blocks (with ~10 sec gap) were repeated to obtain 90-120 time points. In Protocol-II, single slice images in the coronal plane were acquired under shallow breathing for a total of ~5 min (1.34 sec/image, 225 time points). After obtaining 5 baseline images, Gd-DTPA (0.1 mmol/kg) was injected intravenously as bolus using a power injector. ***Data analysis:*** Data were exported to a Sun Ultra 20 workstation and analyzed using in-house software written in IDL 6.0 (Research Systems Inc., Boulder CO.). Time intensity curves (TIC)were analyzed for each voxel in the image. The initial uptake slope was used for characterization of the response to the bolus. Calculation of the initial slope used a 5-point sliding linear regression applied to the first 2 minutes of the TIC. A baseline signal intensity (SI) value, SI_{pre}, was calculated as the mean intensity of 3 points prior to injection. The percent increase/minute for each voxel was then calculated according to equation, % SI/min = (Slope/SI_{pre})*100. In addition, the data were analyzed using a two-compartment model incorporating rate constants of Gd-DTPA between the lesion to plasma compartments (k_{ep}) and elimination by the plasma (k_{el}) [3,4]. The parameters A (amplitude) and K_{ep}, which describes the contrast transfer between the lesion and plasma compartments were fit independently. Bi-dimensional tumor measurements (greatest diameter and maximal perpendicular to it) were used to estimate lesion size and response. With respect to the baseline lesion size, response was evaluated as - complete response(CR): disappearence of all target or non target lesions, partial response(PR): ≥30% reduction, progressive disease(PD): ≥20% increase over point of maximum regression, stable disease(SD): neither belong to PR nor PD.

Results: Two patients (1 deceased, 1 with scan-artifacts at baseline) were excluded from the present analysis. In all analyzed cases, the median follow-up was 4 months (range 2-12 months). During their last follow-up 5 had PR, 3 had SD at the lesion site and 3 patients have completed only their first follow-up scan and their study is ongoing. Comparison of the lesion size (lines) and TIC slope (bars) from 4 representative patients (Fig.1) show that the post-treatment changes in tumor perfusion (TIC slope) observed at early (2 months) time point clearly predict the treatment response as opposed to the bi-dimensional tumor measurements. In addition, the pre-treatment (BL) slope values were found to be >300 (% increase/min) in all responders and it is below this empirical value in non-responders. Similar trends were observed with the estimated compartmental model parameter Akep (data not shown).

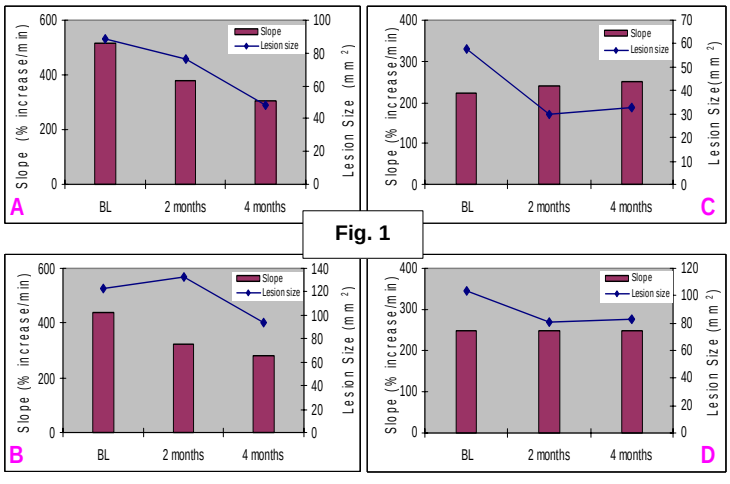

Fig. 1

Discussion: The preliminary results presented here suggest that the early changes in tumor perfusion and vascular permeability due to HAI chemotherapy may better predict treatment response in primary liver cancers. Pre-treatment tumor perfusion level appears to be an important factor in predicting outcome of therapy. Further analysis on intra-tumor perfusion heterogeneity may offer a more complete assessment.

References: 1). NCI fact sheet 2003. 2). Kemeny NE & Fata F. Lancet Oncol 2001; 2: 418-428. 3). Hoffman U et.al. Magn Reson Med 1995; 33:506-14. 4). Dyke JP et.al Radiology. 2003; 228(1):271-8.