Dynamic Contrast Enhanced (DCE) -MRI and 18Fluoromisonidazole (18F MISO) PET Imaging in head and neck squamous cell carcinoma: Initial evaluation of perfusion and hypoxia in nodal metastasis

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Introduction
The tumor microenvironment in squamous cell carcinoma of the head and neck (HNSCC) plays a critical role in malignant tumor progression and treatment resistance. Among the microenvironment parameters that have shown to be relevant for treatment outcome are tumor cell hypoxia and proliferation. The DCE-MRI data provides insight into the tumor microenvironment (1). With proper compartmental modelling, the data may yield results on tumor-vessel permeability, and extracellular-extravascular volume fraction, i.e. data relating to the tumor microenvironment. Targeting hypoxia as a marker of outcome in HNSSC has shown its promises and challenges. The radiopharmaceuticals containing imidazole moiety such as 18F-misonidazole (18F-MISO) has shown promise as a potential agent for hypoxia imaging (2). The present study has been designed to compare perfusion and hypoxic status of the nodal metastasis in HNSCC using Dynamic Contrast Enhanced (DCE) -MRI and 18Fluoromisonidazole (18F MISO) PET imaging prior to treatment.

Materials and Methods
Tumor perfusion and hypoxia was assessed in 9 HNSCC patients with nodal metastasis using DCE-MRI and 18 F MISO PET imaging prior to chemotherapy and radiation therapy. Perfusion data was acquired on a 1.5 Tesla G.E. MRI scanner (GE, Milwaukee, WI). The study consisted of MR imaging using a neuro vascular phased array coil. Antecubital vein catheters delivered a bolus of 0.1mmol/kg gadodiamide (Omniscan) at 2 ml/sec, followed by saline flush. Dynamic perfusion studies were acquired on the nodes using a fast multi-phase spoiled gradient echo (FMSPLGR) sequence and parameters described previously (3). These parameters provided a temporal resolution between 3-6 sec/image which was sufficient to observe the initial uptake of Gd-DTPA into the region. Data was analyzed using software previously written (4) to display and analyze data using IDL 5.4 (Research Systems Inc., Boulder Co). The two compartment model analysis (5, 6) measured the rate constants of the contrast agent transfer between the lesion and plasma compartments (kep) and elimination by the plasma (kel). Each patient was assigned a single MR imaging parameter of uptake slope and compartmental data using IDL 5.4 (Research Systems Inc., Boulder Co). The two compartment model analysis (5, 6) measured the rate constants of the contrast agent transfer between the

Results and Discussion
Evaluation of the preliminary result supports the hypothesis that hypoxic tumors have poor perfusion.

Figure 1A-C show the contrast enhanced MR image, the characteristic time intensity curve for tumor tissue and the parametric image of the Akp parameter. Figure 1D-E exhibit the 18F MISO uptake in the same node. All the 9 nodes studied had perfusion and hypoxia data measured by DCE-MRI and 18F MISO signal intensity respectively. Out of the 9 nodes; 4 nodes showed no 18F MISO uptake (score=0), 3 had mild uptake (score=1), 2 had moderate uptake (score=2) and none had severe uptake (score=3). The SUV measurements for the nodes that showed mild or moderate uptake ranged from 2.0 to 3.2. For the nodes that showed no hypoxia on PET imaging, the histogram analysis of the Akp parameter had mean value of amplitude= 0.09, mode= 9.4, and median=9.98. The nodes that showed mild or moderate 18F MISO uptake the mean values were: amplitude=0.23, mode=4.1, and median=5.85. The histogram analysis showed that the node values were able to differentiate between hypoxic nodes versus the non hypoxic nodes (P=0.029) (Figure2). The hypoxic nodes (poorly perfused nodes) had lower Akp values compared to the nodes that had no hypoxia (well perfused nodes). The initial evaluation of the preliminary result supports the hypothesis that hypoxic tumors have poor perfusion.

References

Acknowledgment
This study was funded by the NIH grant RO1 CA115895-01A.

Figure 2. Graph shows the histogram analysis of the Akp parameter for the nodes versus the 18F MISO PET uptake score for the nodes.