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 HNSCC has shown its promises and challenges. The radiopharmaceuticals containing imidazole moiety such as ^{18}F-misonidazole (^{18}F-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 ^{18}Fluoromisonidazole (^{18}F 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} FMISO 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 (FMSPGR) 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 (k_{ep}) and elimination by the plasma (k_{el}). Each patient was assigned a single MR imaging parameter of uptake slope and compartmental model (Ak_{ep}) on the basis of the histogram analysis (amplitude, mode and median) of all individually fit tumor voxels. For ^{18} FMISO PET imaging, F18-flouride was produced by the cyclotron by proton irradiation of an enriched O-18 water target in a small-volume titanium chamber. 11.0 mCi of ^{18}F-MISO was administered by IV and image acquisition at the PET/CT scanner started after 2 hours of the injection. PET/CT images were reconstructed with the standard reconstruction array processor and corrected for attenuation. ^{18} FMISO images were transferred to a workstation for image analysis.^{18}FMISO uptake by the tumor was scored 0-3; no uptake (score= 0), mild (score=1), moderate (score=2), or severe (score=3), using visual analysis. This was followed by the evaluation of CT and PET/CT images. Further semi-quantitative analysis included calculation of tumor-to-muscle ratios and SUV measurements. Whole blood samples collected from each patient were counted in a calibrated multichannel gamma well counter and the blood activity was expressed in as µCi/ml, decay corrected to time of injection.

Results and Discussion

Figure 1A-C show the contrast enhanced MR image, the characteristic time intensity curve for tumor tissue and the parametric image of the Ak_{ep} and fig. 1D-E exhibit the ^{18}FMISO uptake in the same node. All the 9 nodes studied had perfusion and hypoxia data measured by DCE-MRI and ^{18}FMISO signal intensity respectively. Out of the 9 nodes; 4 nodes showed no ^{18}FMISO 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 Ak_{ep} parameter had mean value of amplitude= 0.09, mode= 9.4, and median=9.98. The nodes that showed mild or moderate ^{18}FMISO uptake the mean values were: amplitude=0.23, mode=4.1, and median 5.85. The histogram analysis showed that the mode 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 Ak_{ep} 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

1. Z. Wang, M.Y. Su et al, Technol Cancer Res Treat, 1, 29 (2002).
2. C. Van de Weile, C. Lahorte et al, Intl J Radiat Oncol Biol Phys, 55, 5 (2003).
3. A. Shukla-Dave, H. Stambuk et al, Proc.Intl. Soc..Magn. Reson Med., 2931, (2006).
4. J.P. Dyke, D.M. Panicek et.al., Radiology, 228, 271 (2003).
5. U. Hoffman, G. Brix et. al., Magn Reson Med, 33, 506 (1995).
6. G. Brix, W. Semmler et.al., J Comput Assist Tomogr, 15, 621 (1991).

Acknowledgment

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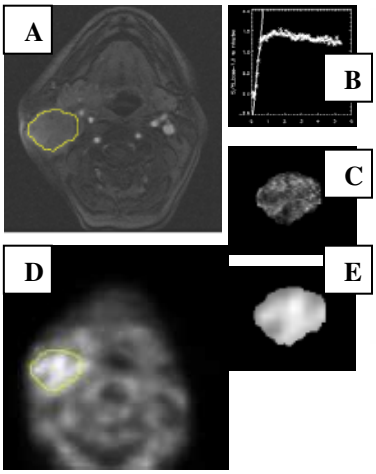

Figure 1A) Post contrast MR image with region of interest (ROI) marked, 1B) graph exhibits the change in signal over time in the ROI, 1C) parametric image of the node with Ak_{ep} parameter, 1D) ^{18}FMISO PET image with ROI marked, and 1E) ^{18}FMISO PET image showing uptake in the ROI.

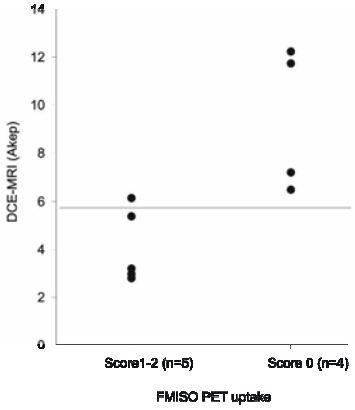

Figure 2. Graph shows the histogram analysis of the Ak_{ep} parameter for the nodes versus the ^{18} FMISO PET uptake score for the nodes.