Exploration of change of T2* of metastatic and normal cervical lymph nodes caused by 100% oxygen breathing

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Target audience: Radiologist and oncologist with an interest in cancer imaging

Background: Hypoxia within tumour has been associated with a poorer outcome for radiotherapy treatments [1]. Hypoxia generally arises due to the rapid growth of the tumour and the inability of the tumour vascular system to keep up with oxygen supply needed [2]. Hypoxia increases deoxyhaemoglobin concentration within tissues, which induces a reduction in MRI derived T2* relaxation time [3]. The purpose of this study was to explore T2* changes in cancerous lymph nodes in patients with head and neck squamous cell cancer (SCC) and normal lymph nodes in healthy volunteers; between breathing room air and 100% oxygen, in order to test the hypothesis that cancer involved lymph nodes demonstrate a greater increase in T2* following reversal of hypoxia when patients breathe 100% oxygen.

Material and Methods: Prior to commencement of chemoradiotherapy, we studied the cervical lymph nodes of 21 patients with histological proven squamous cell carcinoma and metastatic neck nodes (N2/3 disease). In addition cervical lymph nodes of 7 healthy volunteers with no history of previous cancer or current infection were also imaged. All participants underwent conventional anatomical T2-weighted MRI. Initial T2* weighted imaging was performed whilst breathing room air, using a conventional multiple-echo gradient echo sequence (echo times 12, 24, 36 and 48 ms) to acquire four axial sets of images. For each participant T2* weighted imaging was repeated within the same session after inhalation of 100% oxygen at 15L/min for four minutes via a face mask, with continued delivery of oxygen during the scan. T2* maps (on room air and 100% oxygen) were derived by performing fits of a standard exponential relaxation model (S = Ke–TE/T2*) to the data on a pixel-by-pixel basis. Two experienced radiologists confirmed and contoured the location of metastatic lymph nodes in patients and normal nodes in healthy volunteers, on 24 ms T2* weighted images with reference to the anatomical T2-weighted MRI sequence. A total of 60 metastatic nodes were examined in patients and 18 normal nodes in healthy volunteers. For each node the entire volume of the node was contoured excluded only cystic areas of necrosis. Contours were automatically transferred from the 24 ms T2* image to air and 100% T2* maps for extraction of quantitative pixel based histographic T2* data. The median, skewness and kurtosis of pixel histograms were derived for each node from the T2* map on air and also the T2* map on 100% oxygen. Quantitative histographic parameters derived from room air T2* maps and from 100% oxygen T2* maps were compared between normal and metastatic nodes. Change in the histographic parameter between the breathing room air and 100% oxygen was calculated for metastatic and normal lymph nodes.

Results: Mean histographic T2* parameters for metastatic and normal nodes are presented in table 1.

	Metastatic Nodes (n=60)			Normal nodes (n=18)		
	Mean of T2* histogram median values (ms)	Mean of T2* histogram skewness	Mean of T2* histogram kurtosis	Mean of T2* histogram median values (ms)	Mean of T2* histogram skewness	Mean of T2* histogram kurtosis
ON ROOM AIR	47.0	0.31	-0.12	43.9	0.73	0.22
ON 100% OXYGEN	33.2	0.55	0.15	47.0	0.95	0.85
Paired t-test p-value	<0.001*	0.002*	0.005*	0.148	0.136	0.160

Table 1: Histographic T2* parameters for metastatic and normal lymph nodes derived from T2* maps acquired with participants on room air and 100% oxygen.

T2* median values of nodal histograms on 100% oxygen compared with room air were significantly lower for metastatic nodes ($p<0.001$) but not significantly different for normal nodes ($p=0.148$). There was a significant difference between normal and metastatic T2* median values of nodal histograms on 100% oxygen (Mann-Whitney $p=0.012$); but not on room air (Mann-Whitney $p=0.549$). T2* nodal histograms became significantly more positively skewed ($p=0.002$) and more peaked with significantly increased kurtosis ($p=0.005$) on 100% oxygen compared with room air. There was no significant change in skewness or kurtosis of normal nodes between room air and 100% oxygen. There was no significant difference in skewness or kurtosis on room air or on 100% oxygen between metastatic and normal nodes (Mann-Whitney $p=0.207$ to 0.744). An illustration of an axial T2 weighted image and corresponding T2* map on air of a patient with a metastatic neck lymph node is given in figure 1.

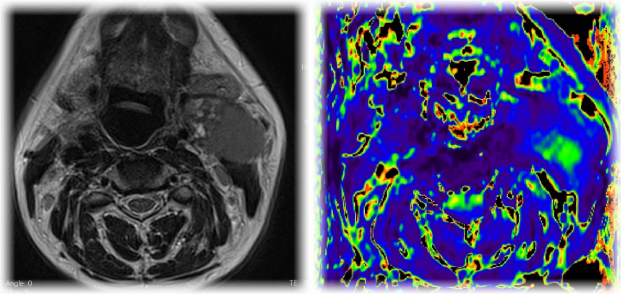

Figure 1: (left) anatomical T2 weighted image demonstrating an enlarged left cervical lymph node; **(right)** corresponding colour T2* map

Discussion: The observed reduction in T2* in metastatic lymph nodes suggests a paradoxical increase in deoxyhaemoglobin concentration on breathing 100% oxygen. However, breathing 100% oxygen has multiple effects on body physiology, including a drop in the cardiac output and an increase in systemic resistance [4]. It is possible that the effect of these changes has a proportionally larger effect on blood flow to metastatic head and neck squamous cell cancer involved lymph nodes which already have an abnormal flow with absence of normal hilar vasculature [5]. The differential response to 100% oxygen inhalation between metastatic and normal nodes could potentially be exploited as a classifier of nodal disease status.

Conclusion: The observed results refute the initial study hypothesis. Further work is needed to ascertain the mechanisms of paradoxical reduction in T2* found in metastatic head and neck squamous cell cancer lymph nodes on breathing 100% and to determine its potential utility for nodal status classification.

References: [1] Nordsmark et al Radiotherapy and Oncology, 1996, Vol.41(1), pp.31-39; **[2]** Padhani et al European Radiology, 2007, Vol.17(4), pp.861-872; **[3]** Punwani et al Adv Exp Med Biol. 1997;413:129-37; **[5]** Daly W Clinical investigation Vol 41 No. 1, 1962; **[5]** Yonetsu K, AJNR 2001 22: 163-169