

## DCE-MRI before and after induction chemotherapy in squamous cell carcinoma of the head and neck

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**Introduction:** Squamous cell carcinoma of the head and neck (HNSCC) accounts for more than 85% of head and neck cancers. Worldwide, around 600,000 patients are diagnosed with head and neck cancer each year, with 5-year survival of ~50%. In advanced (stage 3/4) disease, aggressive treatment in our centre is by induction chemotherapy (IC) followed by chemoradiotherapy but ~30% of patients show no response to IC and their identification would spare unnecessary treatment. Dynamic contrast-enhanced CT has been used to predict treatment response in HNSCC (1), and DCE-MRI is increasingly being used in this patient group (2,3). This study measured DCE-MRI parameters at baseline and after 2 cycles of IC with the aim of establishing what changes occur in the microvascular environment during this treatment. We present DCE-MRI parameters correlated with response to IC determined by RECIST.

**Methods:** Fifty patients were recruited to this study, which was approved by the local ethics committee. Patients were imaged at 1.5 T (Siemens Avanto) using the head and neck coil, before and after two cycles (patients received 3 cycles in total) of IC (docetaxel, cisplatin, 5-FU). Haematocrit was measured before each MR study. The imaging protocol included axial high resolution T<sub>2</sub>w and saturation-recovery turboFLASH images (TI = [37, 100, 250, 1000, 2500, 3900] ms, TE/α = 1.63 ms / 12°, FOV = 22 cm, 20 x 5 mm slices, 256x256 matrix) for measurement of T<sub>1</sub>, followed by location-matched VIBE images (TR/TE/α = 2.63/1.05 ms/18°) at a temporal resolution of 2.3 s for a total of 7 minutes. During the dynamic series, 0.1 mmol/kg Gadovist was injected using a power injector at 2 ml/s, followed by a saline flush at 2 ml/s.

The tumour and up to 3 lymph nodes were outlined on the T<sub>2</sub>w images, and these ROIs were transferred to both the SR-FLASH and dynamic series. T<sub>1</sub> was measured for the tumour and node ROIs by fitting the SR-FLASH signal equation, and signal intensity vs time curves for tumour and node ROIs were converted to concentration vs time curves using these T<sub>1</sub> values. The arterial input function was measured for each patient visit using a manually drawn ROI within the internal carotid artery, and corrected for haematocrit to give a plasma input function. The 2-compartment exchange model (2CXM, (4)) and 2-compartment uptake model (2CUM, (4)) were fitted to the tumour and node uptake curves to obtain estimates of plasma flow (F<sub>p</sub>), permeability-surface area product (PS), plasma volume (v<sub>p</sub>), extravascular-extracellular volume (v<sub>e</sub>, 2CXM only) and mean transit time (MTT). For each curve, the most appropriate model from these two was chosen using an F-test (5). RECIST measurements were also made on the T<sub>2</sub>w images to divide the patients into responders (complete or partial response) and nonresponders (stable disease). A paired t-test was used to assess changes in DCE-MRI parameters pre and post-treatment within the groups.

**Results:** A total of 37 patients underwent both DCE-MRI scans, resulting in 37 tumour and 49 node ROIs. The F-test identified the 2CUM as the most appropriate model in 6 pre-, 8 post-treatment tumours, 14 pre- and 22 post-treatment nodes. In these patients, v<sub>e</sub> was not compared between visits, and 2CUM estimates for F<sub>p</sub>, PS and v<sub>p</sub> were used for comparison between pre and post-treatment. In all other cases, 2CXM parameters were compared. RECIST criteria identified 25 responders and 12 non-responders. Mean parameter values ± standard deviation for parameters pre and post treatment in the two groups are shown in figure 1 for both tumours and nodes. There was a significant increase in v<sub>e</sub> (tumour p=0.001, node p=0.02) in responders only, but no significant differences in other parameters.

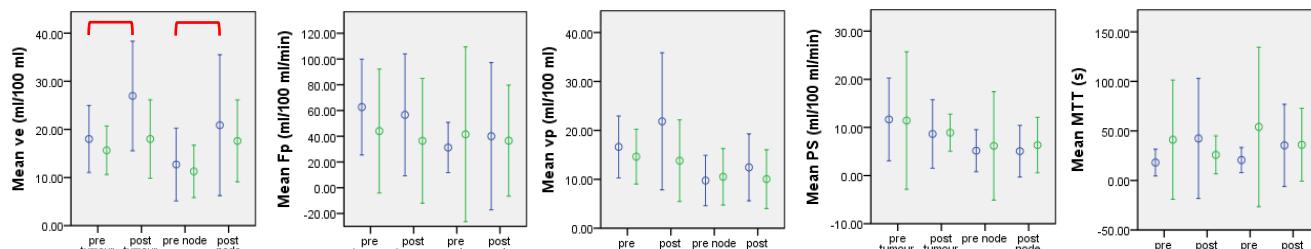


Figure 1 – Mean ± sd for all parameters pre and post 2 cycles of induction chemotherapy, responders in blue, nonresponders in green. Significant differences in v<sub>e</sub> shown by red bracket (paired t-test)

**Discussion:** To our knowledge, this is the largest reported series of patients undergoing DCE-MRI to assess the effect of IC in HNSCC. The significant increase in v<sub>e</sub> in responders could be due to apoptosis resulting in a larger distribution volume for the tracer. The parameters shown to change during early therapy in previous work (F<sub>p</sub>, v<sub>p</sub>, MTT) (1,2) showed no changes in this cohort, but these two studies had conflicting findings, for example v<sub>p</sub> changed in opposite directions. A different tracer kinetics model was used in (3) to show significant changes due to IC but this study used PET as the indicator of response rather than RECIST, which may be more sensitive. In (2), parameter changes were associated with local tumour control at a median of 10 months, but volume change (the basis for RECIST) during early chemoradiotherapy was not predictive for long-term outcome. Current work is focusing on histological analysis of HPV status and tumour hypoxia in these patients, which will be available shortly.

**Conclusion:** In this large cohort, there was a significant change in v<sub>e</sub> in responders to IC but not in nonresponders.

**References:** (1). Petralia G, Preda L, Giugliano G, et al. Perfusion computed tomography for monitoring induction chemotherapy in patients with squamous cell carcinoma of the upper aerodigestive tract: correlation between changes in tumor perfusion and tumor volume. *J. Comput. Assist. Tomogr.* 2009; 33:552–9. (2). Cao Y, Popovtzer A, Li D, et al. Early prediction of outcome in advanced head-and-neck cancer based on tumor blood volume alterations during therapy: a prospective study. *Int. J. Radiat. Oncol. Biol. Phys.* 2008 1; 72:1287–90. (3). Powell C, Schmidt M, Borri M, et al. Changes in functional imaging parameters following induction chemotherapy have important implications for individualised patient-based treatment regimens for advanced head and neck cancer. *Radiother. Oncol.* 2013; 106:112–7. (4). Sourbron S, Ingrisch M, Siefert A, Reiser M, et al. Quantification of cerebral blood flow, cerebral blood volume, and blood-brain-barrier leakage with DCE-MRI. *Magn. Reson. Med.* 2009; 62:205–17. (5). Ewing JR, Brown SL, Lu M, et al. Model selection in magnetic resonance imaging measurements of vascular permeability: Gadomer in a 9L model of rat cerebral tumor. *J. Cereb. Blood Flow Metab.* 2006; 26:310–20