Effects of carbogen breathing on tissue oxygenation and perfusion in head en neck tumors as measured by MRI.

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Introduction

Recent studies show that treatment results in advanced head and neck tumors can be improved successfully by accelerated radiotherapy with carbogen and nicotinamide (ARCON) [1]. Breathing carbogen may induce both increased tissue oxygenation and blood flow [2,3]. In this study gradient recalled echo (GRE) MRI and Gadolinium (Gd) contrast MRI techniques were combined to investigate the effect of carbogen breathing on tumor oxygenation and tumor perfusion.

Patients and Methods

MR imaging was performed on a 1.5 T Siemens Vision whole body system. Six patients (hypopharynx carcinoma n=2; larynx carcinoma n=4) were each studied twice, with and without carbogen breathing (2% CO_2; 98% O_2). The time between the two sessions was at least 24 hours. Gd was administered by intravenous bolus injection (0.5 mM, 2.5 ml/s). In the first session T1, T2, PD weighted images were recorded and Gd tissue uptake was monitored with a temporal resolution of 2 seconds (FLASH, TR=50 ms, TE=4.4 ms, α=60, 7 mm slice) for 90 seconds. In the second session GRE images (16 echo FLASH, TR=65 ms, TE=6-51 ms, α=20, 5 mm slice) were recorded for 14 minutes whilst breathing air, subsequently carbogen breathing was started and GRE images were recorded for another 6 minutes, followed by Gd contrast enhanced imaging as in the first session. T2* values were calculated from the GRE imaging data.

The T1 weighted Gd contrast image data and PD weighted images were used to calculate Gd concentration (a.u.) [4]. The dynamic Gd concentration data was analyzed using the compartmental model of Larsson [5]. The arterial input function $C_p(t) = A_1 \cdot exp^{-a1 \cdot t} + A_2 \cdot exp^{-a2 \cdot t}$ was fitted to the data from the last part of the Gd bolus passage only, as temporal resolution did not allow accurate determination of the maximum of the bolus. The function

$C_t(t) = f \cdot K^{trans} \cdot [(A_1/(k_{ep}-a_1)) \cdot exp^{-a1 \cdot t} + (A_2/(k_{ep}-a_2)) \cdot exp^{-a2 \cdot t} - (A_1/(k_{ep}-a_1)+A_2/(k_{ep}-a_2)) \cdot exp^{-kep \cdot t}]$

was fitted to the data (C_t: concentration Gd (mM); k_{ep}: rate constant (s^{-1}); K^{trans}: transfer constant $K^{trans} = k_{ep} \cdot v_e$ (s^{-1}); v_e: extravascular extracellular space [6]). Factor f is a scaling factor and is dependent on the MR method used and the relaxation properties of the tissue. Gd uptake curves were calculated from regions of interest in well-perfused parts of the tumor. Also, the arterial input curve was calculated from pixels in the vertebral artery and the carotid artery. To test the reproducibility of the method also neck muscular tissue of all patients was analyzed in the same way.

Results and Discussion

The average T2* in the tumor was 28 ms and 31 ms whilst breathing air and breathing carbogen respectively. This carbogen-induced T2* increase was shown to be significant (ANOVA, split plot design; $p<0.05$) and corresponds well to previously reported measurements of T2* [7] and carbogen-induced T2* changes [2].

Typical results of the Gd uptake curve in tumor tissue and the arterial input function whilst breathing air are shown in figure 1. The biexponential arterial input function was used to describe the last part of the bolus and the biodistribution of Gd. The clearance of Gd by the kidneys was assumed to be negligible in the time span of the measurement (90 s). The rate constant for neck muscular tissue showed little variation among all patients (standard deviation < 10%). No significant difference was found between the rate constants of Gd uptake whilst breathing air and carbogen, k_{ep} (tumor, air) / k_{ep} (tumor, carbogen) = 1.04 (± 0.1). Since this kind of tumor seems to be well perfused, breathing carbogen may not induce perfusion effects in these tumors. The combined results suggest that the T2* increase whilst breathing carbogen is due to improved oxygenation of tumor tissue, as no perfusion changes were detected by Gd contrast enhanced MR imaging.

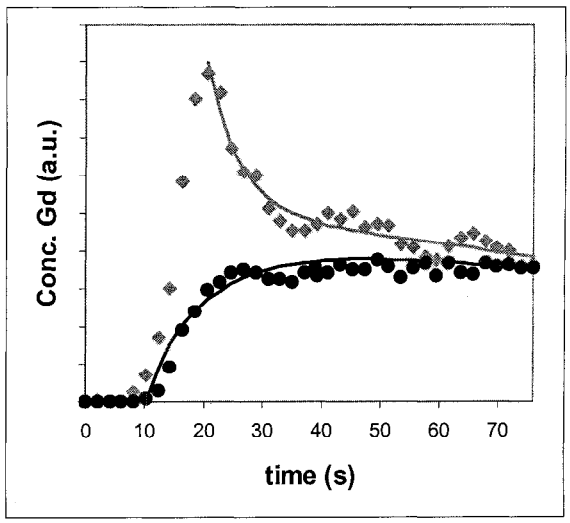

Figure 1. Gd uptake curve in well-perfused tumor tissue (black) and the arterial input function (gray). Fit parameters: $A_1 = 7.66 \cdot 10^3$ a.u.; $A_2 = 1.02 \cdot 10^4$ a.u.; $a_1 = 0.19$ s^{-1}; $a_2 = 0.005$ s^{-1}; $f \cdot K^{trans} = 0.057$ $mM \cdot (a.u. \cdot s)^{-1}$; $k_{ep} = 0.061$ s^{-1}.

References

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