Tumor Blood Flow Measurement by Pseudo-Continuous Arterial Spin Labeling (pCASL) in Head and Neck Cancer; Comparison to Dynamic Contrast Enhanced MRI

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Authors: N. Fujima¹, D. Yoshida¹, Y. Suzuki², H. Sugimori³, K. K. Tha¹, S. Terae¹, H. Shirato¹, ¹Sapporo/JP, ²Tokyo, 108-8507/JP, ³Sapporo hokkaido/JP

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Purpose

Tumor blood flow (TBF) is considered to be one of important biological information for the assessment of head and neck squamous carcinoma (HNSCC). Several reports have indicated clinical utility of TBF for the evaluation of HNSCC as prognostic factor, or early detection of treatment effect (1). For the measurement of TBF using MRI, dynamic contrast enhanced (DCE) perfusion or dynamic susceptibility contrast (DSC) perfusion was commonly used. However these methods require rapid injection of contrast media; therefore repetitive scanning is sometimes difficult.

On the other hands, pseudo continuous arterial spin labeling (pCASL) technique has been introduced for noninvasive measurement of tissue blood flow, especially reported brain or kidney (2, 3). If TBF measurement of HNSCC using pCASL is successfully performed, it will be useful for noninvasive assessment of TBF.

The aim of this study is to evaluate the reliability of TBF measurement in HNSCC using pCASL by comparing to DCE perfusion MRI.
Methods and Materials

Subjects

Fifteen patients were evaluated retrospectively with following inclusion criteria (1) the patient was diagnosed HNSCC histopathologically, (2) MR scanning was performed before treatment, (3) MR scanning of both pCASL and DCE perfusion were performed within the same examination. Patients included 13 males (mean age, 64 years; range, 45-79 years) and 2 females (49 and 53 years old respectively). The primary lesions of these 15 patients included maxillary sinus in 6 patients, tongue in 5 patients, and oropharynx in 4 patients.

Imaging protocol

All MR imaging was performed by using a 3.0 Tesla unit (Achieva TX; Philips Medical Systems, Bests, the Netherlands) with a 16-channel neurovascular coil. Not only pCASL and DCE perfusion but also post contrast enhanced T1WI was obtained for each tumor delineation to determine tumor region of interest (ROI).

Acquisition of pCASL was performed by using multi-shot spin-echo echo-planar imaging. Parameters of pCASL were as follows; labeling duration, 1650 ms; post label delay, 1280 ms; TR, 3619 ms; TE, 18 ms; FA, 90 degree; FOV, 230_230 mm; 80_80 matrix; slice thickness, 5 mm×15 slices; scanning time, 5' 05.

Acquisition of DCE perfusion was performed by using 3D-T1 fast field echo (T1-FFE) sequence. Parameters of DCE perfusion were as follows; TR, 6.1 ms; TE, 1.5 ms; flip angle, 15 degree; dynamic duration, 3.2 s; dynamic phase, 64 phases; matrix, 256 x 256 in 24 x 24 cm FOV (pixel size, 0.94 x 0.93mm); slice thickness, 3mm x31 slices; scanning time, 3' 51.

Data analysis for TBF mapping

TBF calculation using pCASL was conducted by past reported equation (4) (Fig. 1 on page 5 with adjustment of blood/tissue partition coefficient from brain tissue to HNSCC (5);

Where f is TBF, #M is difference signal between the control and label acquisition, R₁a is the longitudinal relaxation rate of blood (0.67 s⁻¹), # is the labeling time (1.65 s), # is the post labeling delay time (1.28 s), # is the labeling efficiency (0.85), # is the blood/tumor-tissue water partition coefficient (1.0 g/ml), and M₀ is equilibrium magnetization
of tumor tissue (estimated from signal intensity of control image and tumor longitudinal relaxation rate).

TBF calculation using DCE perfusion was performed based on deconvolution method like a CT perfusion analysis with the adjustment of signal intensity in DCE time intensity curve, described in past reports (6, 7).

Mathematical software (MATLAB, version 2012a) was used for the calculation of TBF value both pCASL and DCE perfusion.

Image analysis

Whole tumor ROI

Each tumor was delineated with polygonal ROI on post contrast enhanced T1WI by board-certified neuroradiologist. Delineated ROI was copied and placed on TBF map calculated by pCASL and DCE perfusion respectively (Fig. 2 on page 5). Each TBF of pCASL or DCE perfusion in each patient was determined as mean of TBF value in delineated ROI.

Central and Peripheral ROI in the tumor

In each tumor, ten mm$^2$ square ROI was also placed on central and peripheral lesion respectively by one neuroradiologist. One ROI was placed on central lesion. Two ROIs were placed on peripheral lesion. In placing on central lesion, ROI was placed not to contain necrotic (non-contrast enhanced) area. These square ROIs were also copied and placed on TBF map of both pCASL and DCE perfusion (Fig. 3 on page 6, Fig. 4 on page 6). Mean TBF value in each ROI was determined as each focal TBF of central or peripheral lesion in the tumor. Peripheral TBF was determined as mean value of two square ROIs.

Statistical analysis

Correlation of measured TBF between pCASL and DCE was analyzed using Pearson’s correlation coefficients ($r < 0.2$, poor correlation; $r = 0.2-0.4$, fair correlation; $r = 0.41-0.6$, moderate correlation; $r = 0.61-0.8$, good correlation; $r > 0.81$, excellent correlation). Pearson’s correlation test was performed in whole lesion, central lesion, and peripheral lesion in the tumor respectively. The level of significance was set at $P < 0.05$. 
Fig. 1: The equation used for calculation of TBF value in each HNSCC by acquired data from pCASL. This equation was referred by ASL quantification model described by Ze Wang, et al. Where \( f \) is TBF, \( \Delta M \) is difference signal between the control and label acquisition, \( R_{1a} \) is the longitudinal relaxation rate of blood (0.67 s\(^{-1}\)), \( \# \) is the labeling time (1.65 s), \( \# \) is the post labeling delay time (1.28 s), \( \# \) is the labeling efficiency (0.85), \( \# \) is the blood/tumor-tissue water partition coefficient (1.0 g/ml), and \( M_0 \) is equilibrium magnetization of tumor tissue (estimated from signal intensity of control image and tumor longitudinal relaxation rate).

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**Fig. 2:** Delineation of whole tumor ROI; Each tumor was delineated with polygonal ROI on post contrast enhanced T1WI by board-certified neuroradiologist. Delineated ROI was copied and placed on TBF map calculated by pCASL and DCE perfusion respectively.

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**Fig. 3:** ROI placement of central lesion in tumor; Ten mm² square ROI was placed on central lesion in the tumor by board-certified neuroradiologist. In placing central lesion, ROI was placed not to contain necrotic area. This square ROI was copied and placed on TBF map of both pCASL and DCE perfusion.

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Fig. 4: ROI placement of peripheral lesion in tumor; ten mm² square ROI was placed on peripheral lesion by board-certified neuroradiologist. Two ROIs were placed on peripheral lesion. These square ROIs were copied and placed on TBF map of both pCASL and DCE perfusion.

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Results

In 15 patients, mean TBF in whole tumor was 132±39 ml/min/100g in TBF map calculated by pCASL, and was 142±35 ml/min/100g in TBF map calculated by DCE perfusion. Good correlation was observed between TBF of pCASL and DCE perfusion (r=0.72, p<0.05) (Fig. 5 on page 9). In addition, TBF of peripheral lesion in the tumor was 134±37 ml/min/100g in pCASL, and 137±33 ml/min/100g in DCE perfusion respectively. Good correlation was also observed between TBF of pCASL and DCE perfusion (r=0.74, p<0.05) (Fig. 6 on page 9).

On the other hands, TBF of central lesion in the tumor was 65±33 ml/min/100g in pCASL, and was 109±25 ml/min/100g in DCE perfusion. Statistical significant correlation was observed between TBF of pCASL and DCE perfusion, however, it was not good but moderate correlation (r=0.58, p<0.05) (Fig. 7 on page 10, Fig. 8 on page 11).
**Fig. 5:** Comparison in whole tumor ROI; good correlation was observed between TBF of pCASL and DCE with statistical significance ($r=0.72$, $p$
Fig. 6: Comparison in peripheral lesion of the tumor; good correlation was observed between TBF of pCASL and DCE with statistical significance ($r=0.74$, $p$}
Fig. 7: Comparison in central lesion of the tumor; moderate correlation was observed between TBF of pCASL and DCE with statistical significance ($r=0.58$, $p$...
Fig. 8: Around the central necrotic area, TBF map of pCASL shows lower perfusion (arrow) compared to that of DCE perfusion. This discrepancy was probably considered due to underestimation of pCASL by arterial transit delay.

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Conclusion

TBF measurement by pCASL was successfully performed. In addition, good correlation was observed in TBF value between pCASL and DCE perfusion; measured TBF value by pCASL was considered to be reliable from this result. Several studies assessing correlation of blood flow between pCASL and MR DSC / DCE perfusion were already reported especially in brain or kidney (2, 8). These studies indicated good correlation was observed between pCASL and DSC / DCE perfusion. Like these reports, this study indicated good correlation of measured TBF value between pCASL and DCE perfusion. Therefore, pCASL can be used with sufficient reliability in the case of HNSCC as well as lesion of brain or kidney.

However, focal TBF value of central lesion in the tumor was not observed good correlation but moderate correlation. We guess the cause of this was probably that signal intensity of pCASL was underestimated because of transit delay of feeding arterial blood. Arterial transit delay of central lesion in the tumor was often observed by digital subtraction angiography (DSA), probably because tumor central located deeper lesion and arterial blood supply is considered to be delay compared to other lesion. Therefore, Central lesion of the tumor should be carefully treated to avoiding misleading of TBF estimation. To use longer post labeled delay time will be effective for this problem, however scanning time became long, and moreover signal to noise ratio (SNR) will be decrease in other tumor lesion whose arterial transit is rapid by changing post labeled delay time. It is necessary to determine appropriate delay time in obtaining TBF map to decrease signal loss by transit delay effect without decreasing SNR of other lesion much.

In conclusion, pCASL can be useful tool for noninvasive assessment of TBF in patients with HNSCC, however TBF underestimation by arterial transit delay should be carefully treated.


Personal Information

Noriyuki Fujima, MD, PhD, Department of Radiology, Department of Radiology, Hokkaido University Graduate School of Medicine, Hokkaido, Japan;

Noriyuki.Fujima#mb9.seikyou.ne.jp