European Journal of Radiology 83 (2014) 806–810

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Non-invasive assessment of intratumoral vascularity using arterial spin labeling: A comparison to susceptibility-weighted imaging for the differentiation of primary cerebral lymphoma and glioblastoma

J. Furtner[a,e,*], V. Schöpf[a,1], M. Preusser[b,e,2], U. Asenbaum[a,3], R. Woitek[a,3], A. Wöhrer[c,e,4], J.A. Hainfellner[c,e,4], S. Wolfsberger[d,e,5], D. Prayer[a,e,6]

[a] Department of Biomedical Imaging und Image-guided Therapy, Medical University of Vienna, Austria
[b] Department of Medicine I, Division of Oncology, Medical University of Vienna, Austria
[c] Institute of Neurology, Medical University of Vienna, Austria
[d] Department of Neurosurgery, Medical University of Vienna, Austria
[e] Comprehensive Cancer Center-Central Nervous System Tumors Unit (CCC-CNS), Medical University of Vienna, Austria

ARTICLE INFO

Article history:
Received 5 December 2013
Received in revised form 8 January 2014
Accepted 15 January 2014

Keywords:
Glioblastoma
Primary CNS lymphoma
Arterial spin labeling
Susceptibility-weighted imaging
Intratumoural susceptibility signals

ABSTRACT

Using conventional MRI methods, the differentiation of primary cerebral lymphomas (PCNSL) and other primary brain tumors, such as glioblastomas, is difficult due to overlapping imaging characteristics.

This study was designed to discriminate tumor entities using normalized vascular intratumoral signal intensity values (nVITS) obtained from pulsed arterial spin labeling (PASL), combined with intratumoral susceptibility signals (ITSS) from susceptibility-weighted imaging (SWI).

Thirty consecutive patients with glioblastoma ($n = 22$) and PCNSL ($n = 8$), histologically classified according to the WHO brain tumor classification, were included. MRIs were acquired on a 3 T scanner, and included PASL and SWI sequences. nVITS was defined by the signal intensity ratio between the tumor and the contralateral normal brain tissue, as obtained by PASL images. ITSS was determined as intratumoral low signal intensity structures detected on SWI sequences and were divided into four different grades.

Potential differences in the nVITS and ITSS between glioblastomas and PCNSLs were revealed using statistical testing. To determine sensitivity, specificity, and diagnostic accuracy, as well as an optimum cut-off value for the differentiation of PCNSL and glioblastoma, a receiver operating characteristic analysis was used.

We found that nVITS ($p = 0.011$) and ITSS ($p = 0.001$) values were significantly higher in glioblastoma than in PCNSL. The optimal cut-off value for nVITS was 1.41 and 1.5 for ITSS, with a sensitivity, specificity, and accuracy of more than 95%. These findings indicate that nVITS values have a comparable diagnostic accuracy to ITSS values in differentiating glioblastoma and PCNSL, offering a completely non-invasive and fast assessment of tumoral vascularity in a clinical setting.

* Corresponding author at: Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria. Tel.: +43 1 40400 4818; fax: +43 1 40400 4898.

E-mail addresses: julia.furtner@meduniwien.ac.at (J. Furtner), veronika.schoepf@meduniwien.ac.at (V. Schöpf), matthias.preusser@meduniwien.ac.at (M. Preusser), ulrika.asenbaum@meduniwien.ac.at (U. Asenbaum), ramona.woitek@meduniwien.ac.at (R. Woitek), adelheid.woehrer@meduniwien.ac.at (A. Wöhrer), johannes.hainfellner@meduniwien.ac.at (J.A. Hainfellner), stefan.wolfsberger@meduniwien.ac.at (S. Wolfsberger), daniela.prayer@meduniwien.ac.at (D. Prayer).

[1] Tel: +43 1 40400 5751.
[2] Tel.: +43 1 40400 4457.
[3] Tel.: +43 1 40400 4818.
[4] Tel.: +43 1 40400 5501.
[5] Tel.: +43 1 40400 2565.
[6] Tel.: +43 1 40400 4895.

0720-048X/$ – see front matter © 2014 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ejrad.2014.01.017

1. Introduction

Primary cerebral lymphoma (PCNSL) is a rare but increasingly seen brain tumor entity, with a low incidence of about 3–4% of all primary brain tumors [1–3].

Using conventional MRI methods, the differentiation between cerebral lymphomas and other primary brain tumors, such as the considerably more frequently occurring glioblastomas, can sometimes be difficult because MR findings in cerebral lymphomas often overlap with the typical imaging findings in other tumorous brain lesions. However, a precise diagnosis is important to establish optimal therapy planning and to determine the prognosis.

Previously published data indicate that advanced imaging methods are able to increase the diagnostic accuracy in the differentiation of cerebral lymphomas and high-grade gliomas.

Neovascularization in glioblastomas is known to be pronounced in contrary to cerebral lymphomas. PCNSLs, only to a small extent, present with a slightly increased microvascular density and elevated VEGF (vascular endothelial growth factor) levels [4]. Liao et al. demonstrated significantly higher mean vessel density, labeled by anti-CD34, in glioblastoma than PCNSL [5]. Therefore, dynamic susceptibility contrast-enhanced perfusion has been investigated as a potentially useful tool to differentiate between these tumor types, and results have shown a typically lower rCBV (relative cerebral blood flow) in PCNSL compared to high-grade gliomas [6–8].

Susceptibility-weighted imaging (SWI) in high-field MRI has been recently reported to be a promising tool for non-invasive glioma grading, reflecting microvascularity, as well as areas of macro- and micronecrosis or microbleeding [9]. Furthermore, Radbruch et al. and Peters et al. described the possibility of differentiating between glioblastomas and lymphomas based on intratumoral susceptibility signals (ITSS) [10,11]. Another recently published marker for tumor vascularization based on pulsed arterial spin labeling (PASL) measurements, using low inversion times, is the normalized intratumoral signal intensity value (nVITS), which has been shown to correlate with glioma grade [12]. The advantage of this method is that it reflects only arterial vessels, and is not affected by blood products, necrosis, or calcification, in contrast to SWI.

The purpose of the present study was to determine the utility of nVITS values obtained from PASL to differentiate between PCNSL and glioblastomas in a routine clinical setting, and to compare the diagnostic accuracy of this new method with the accuracy of ITSS values obtained from SWI. This could ultimately result in a totally non-invasive method to differentiate lymphoma and glioblastoma.

2. Methods

2.1. Patients

We enrolled 30 consecutive patients in this study from July 2010 to July 2013. Eight presented with PCNSL and 22 with new-onset glioblastoma. The local Institutional Ethics Review Board this prospective study. Written, informed consent was obtained from all patients after the nature, scope, and possible consequences of the examination had been explained to them. The study was performed in accordance with the current guidelines of the Declaration of Helsinki.

3. Imaging

The MRI examinations were obtained on a whole-body 3 Tesla Trio system (Siemens Medical Solutions, Erlangen, Germany), with actively shielded imaging gradients, in conjunction with an eight-channel head coil. All sequences were aligned parallel to the midline structures and covered from the base of the skull to the vertex.

The routine MR imaging protocol included an axial T2-weighted, fluid attenuated inversion recovery (FLAIR) sequence, a coronal T2-weighted turbo spin echo sequence, and an axial T1-weighted sequence pre- and post intravenous contrast media application (0.1 mmol/kg body weight of a gadolinium-based contrast agent). Additional scanning included an SWI and multi-slice PASL sequences.

For PASL imaging, a quantitative imaging of perfusion using a single subtraction with interleaved thin-slice TI_1 periodic saturation (Q2TIPS) arterial spin labeling sequence with a proximal inversion with a control for off-resonance effects (PICORE) tagging scheme was used. For a detailed description of the PICORE technique, please see Wong et al. [13]. Imaging parameters for the PASL sequence were as follows: TE = 11 ms; TR = 2750 ms; field of view = 192 × 100 mm; number of slices = 14; slice thickness = 6 mm; slice gap = 1.5 mm; flip angle = 90°; number of measurement repetitions = 25. No crusher gradients were used. PASL perfusion MRI sequences were performed at an inversion time of 370 ms, based on previously published data [12]. The PASL sequence had an acquisition time of 1 min and 19 s. Due to the known T1 shortening effect of gadolinium-based contrast agents, which results in a reduction of the signal-to-noise ratio, the PASL data was acquired before the application of contrast media [14].

The susceptibility-weighted sequence was a flow-compensated 3D gradient echo sequence, and the imaging parameters were as follows: TE = 20 ms; TR = 28 ms; field of view = 230 × 230 mm; number of slices = 80; slice thickness = 1.75 mm; slice gap = 0 mm; flip angle = 15°. The SWI sequence had an acquisition time of 3 min 52 s.

The overall acquisition time for the anatomical images and the additional PASL and SWI sequences was about 25 min.

4. Data analysis

4.1. Arterial spin labeling

The data were transferred to an off-line workstation (Siemens Leonardo workplace, Erlangen, Germany) and *z*-transformed for postprocessing. To define the tumor localization and extension, the FLAIR and T1 postcontrast sequences were used, as suggested by RANO criteria [15]. These images were then assigned to co-registered PASL images. To approximate the whole tumor volume, tumor regions of interest (mean 1254 mm^2; range, 405–2778 mm^2) were manually drawn, at each imaging slice, by an experienced neuroradiologist who was blinded to the tumor histopathology. Areas with extended necrosis were attempted to be spared. The mean signal intensity value of each slice of one tumor was used to calculate the average mean signal intensity of the tumor regions of interest. To avoid inter- and intra-individual differences in brain vascularization, nVITS values were calculated. Therefore, a region of interest of equal size was positioned at each slice exactly in the contralateral healthy hemisphere to calculate the average mean signal intensity of the contralateral normal brain tissue.

4.2. Susceptibility-weighted imaging

Based on the previously published data of Park et al., ITSS was determined as intratumoral linear or dot-like low signal intensity structures detected on susceptibility-weighted images [9]. As suggested, ITSS were divided into four different grades: grade 0, no ITSS; grade 1, 1–5 ITSS; grade 2, 6–10 ITSS; and grade 3 > 10 ITSS. Intratumoral macrohemorrhages or calcifications were excluded using the conventional MRI sequences (FLAIR, T1-, and T2-weighted images).