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### Perfusion magnetic resonance imaging provides additional information as compared to anatomical imaging for decision-making in vestibular schwannoma



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#### ABSTRACT

*Objective:* The added value of perfusion MRI for decision-making in vestibular schwannoma (VS) patients is unknown. MRI offers two perfusion methods: the first employing contrast agent (dynamic susceptibility contrast (DSC)-MRI) that provides information on cerebral blood volume (CBV) and cerebral blood flow (CBF), the second by magnetic labeling of blood (arterial spin labeling (ASL)-MRI), providing CBFimages. The goal of the current study is to investigate whether DSC and ASL perfusion MRI provides complimentary information to current anatomical imaging in treatment selection process of VS. *Methods:* Nine patients with growing VS with extrameatal diameter >9 mm were included (>2 mm/year

and 20% volume expansion/year) and one patient with 23 mm extrameatal VS without growth. DSC and ASL perfusion MRI were obtained on 3 T MRI. Perfusion in VS was scored as hyperintense, hypointense or isointense compared to the contralateral region.

*Results:* Seven patients showed hyperintense signal on DSC and ASL sequences. Three patients showed iso- or hypointense signal on at least one perfusion map (1 patient hypointense on both DSC-MRI and ASL; 1 patient isointense on DSC-CBF; 1 patient isointense on ASL). All patients showed enhancement on post-contrast T1 anatomical scan.

*Conclusion:* Perfusion MR provides additional information compared to anatomical imaging for decisionmaking in VS.

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1. Introduction

Vestibular schwannoma (VS) is a benign tumour that originates from the Schwann's cell of the vestibular nerve, also known as the eighth cranial nerve. The vestibular nerve is located in the cerebellopontine angle, the space between brainstem, cerebellum and

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temporal bone. Clinical complaints of VS generally consist of progressive unilateral hearing loss, vertigo and tinnitus. Tumours that compress the brainstem give more general complaints, such as headache, vision disorders and hypoesthesia of the face. Data from Denmark shows an incidence of 19 VSs per 1 million people per year, these data are seen as most complete because of the referral of all VSs from one country to one single clinic [1]. Diagnosis is made by anatomical MRI examination with or without the use of contrast agent (CA).

Treatment options for VS are radiotherapy, surgery or observation with regularly magnetic resonance (MR) preferable with the use of CA [2]. The choice for treatment is based both upon tumour characteristics and patient characteristics. Such as tumour size, growth rate, heterogeneity of the tumour and hearing loss. The average tumour growth was found to be 1–2 mm per year, but varies [3]. Tumour size is both measured intra- and extrameatal

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Abbreviations: AAO-HNS, American Academy of Otolaryngology-Head and Neck Surgery; ASL, arterial spin labeling; CA, contrast agent; CBF, cerebral blood flow; CBV, cerebral blood volume; DSC, dynamic susceptibility contrast; EPI, echo planar imaging; FA, flip angle; FOV, field of view; Gd, gadolinium; MR, magnetic resonance; MRI, magnetic resonance imaging; PCASL, pseudo-continuous arterial spin labeling; RF, radiofrequency; rCBV, relative CBV; SNR, signal to noise ratio; TR, repetition time; TE, echo time; VS, vestibular schwannoma.

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**Fig. 1.** MR image of left sided vestibular schwannoma. Yellow dotted line is border between intra- and extrameatal portion of the tumour. Size quantified as the largest diameter measurable in the extrameatal portion (red line).

(Fig. 1) [2]. Besides the tumour characteristics the patients preferences are important to decide for a treatment option. If tumour size is stable the frequency of MR is decreased. The preferred treatment option for intrameatal tumours is observation, although occasionally patients with functional hearing are operated to preserve hearing [4]. Tumours localized extrameatal, which are larger than 20 mm are generally spoken, advised to undergo treatment, surgery or radiotherapy. Each treatment option has its specific benefits and side effects. The intention of radiotherapy is to freeze the growth rate; but hearing loss and other cranial nerve pathology are common side effects [5]. Surgery usually results in hearing loss at the operated side and can also affect the function of the facial nerve [6]. In addition infection and haemorrhage are common complications. Patients with small or medium sized tumours can experience a significant decrease of their quality-of-life in each treatment option with relatively small differences in quality-of-life between the treatment groups. It has been shown that not the treatment modality itself, but the actual diagnosis of VS is the main cause of decreasing quality-of-life in patients with VS [7,8]. Observation is becoming the preferred initial treatment policy for VS [8,9]. In order to give an objective advice for patient specific treatment during observation and to decrease side effects during radiotherapy or surgery, it would be of clinical relevance if the growth rate could be predicted.

For brain tumours it is known that vascularization can be measured using perfusion MRI and that it can help in differentiation and staging of brain tumours [10,11]. A tumour with a volume larger than 2 mm<sup>3</sup> is dependent on angiogenesis for growth, since the tumour growth critically depends on influx of oxygen and nutrients [12,13]. Perfusion MRI has been used for early detection and staging of many different tumour types, such as lung cancer and gliomas, although its added value for VS is yet unknown [14,15].

MRI perfusion can be performed by two approaches, one with and the other without the use of CA, i.e. dynamic susceptibility contrast (DSC) MRI and arterial spin labeling (ASL). DSC relies on the intravenous injection of a CA and serial MRI measurement of signal loss during the passage of the bolus through the tissue, using T2 or T2\* weighted sequences. Using this technique, cerebral blood volume (CBV) and cerebral blood flow (CBF) can be calculated. ASL is a non-invasive perfusion MRI method for quantitatively measuring cerebral perfusion, by employing blood itself as an endogenous tracer via inversion of longitudinal magnetization [16]. A difficulty in the depiction of perfusion of VS lies in the magnetic field inhomogeneities near the temporal bone, which could especially affect the measurements of the intrameatal portion of the VS. Such concerns on the imaging quality are probably the reason for the absence of perfusion MRI in many imaging protocols of VS patients. Only a few studies show examples of perfusion MRI in VS, and these studies are limited to single subject examples [11,17].

The goal of the current study is to investigate the additional value of the different perfusion MRI methods to provide information on the vascularization in VS.

#### 2. Material and methods

#### 2.1. Patients

The Leiden University Medical Center is a tertiary referral centre for VS-patients in the Netherlands. Every other week all new patients with VS are being (multidisciplinary) discussed, and patient characteristics are documented in a database. From this database ten patients were selected to be included in this study, based upon the growth rate. Growth was assessed on two consecutive MRI's, where the extrameatal component was measured using the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) criteria (Fig. 1) [2]. This means that in the axial plan on a T1 gadolinium-enhanced sequence the largest diameter was measured in anterior-posterior and medial-lateral dimension. Patients with a growth rate larger than 2 mm/year and a volume increase of more than 20% per year were included following literature procedures [18,19]. A further inclusion criteria was that the extrameatal diameter of the VS needed to be larger than 9 mm; this to guarantee good depiction even when taking the relatively coarse resolution of perfusion MRI sequences into account. Patients with neurofibromatosis type 2 were excluded. The clinical state of the patients on follow-up was documented.

The internal ethical review board of the Leiden University Medical Center approved the study and all subjects provided written informed consent.

#### 2.2. MR protocol

All experiments were performed on a clinical 3T MRI scanner (Achieva 3 T, Philips Healthcare, Best, The Netherlands) equipped with software to enable ASL imaging. Pseudo-continuous labeling was performed with a labeling duration of 1650 ms (1650 RF pulses of 0.5 ms duration). ASL imaging was performed in combination with background suppression, which consisted of a saturation pulse immediately before labeling and inversion pulses at 1680 and 2830 ms after the saturation pulse [20]. This leads to optimal background suppression for the first acquired slice, whereas the background signal in the other slices will gradually increase due to T1-recovery. Imaging was performed with single-shot echo planar imaging (EPI) in combination with parallel imaging (SENSE factor 2.5). In total 17 slices of 5 mm slice thickness were acquired in ascending fashion with an in-plane resolution of  $3 \times 3 \text{ mm}^2$  (TE of 14 ms, TR of 3.9 s). Imaging started 1525 ms after labeling stopped. The total scan was 4 min (Table 1).

For DSC-MRI a single-shot spin-echo echo planar imaging (SE-EPI) sequence with echo time (TE) 30 ms, flip angle (FA)  $90^{\circ}$ , was used to cover an imaging volume of 13 slices for 96 s at a temporal resolution of 1.64 s 15 mL of gadolinium-based CA (Dotarem, Guerbet, France) was injected at a rate of 5 mL/sec followed by a chaser

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