Clinical applications of arterial spin labeling perfusion in diagnosis of neoplastic brain lesions

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Learning objectives

- The aim of this educational poster is to emphasize the possibilities of arterial spin labeling perfusion (ASL) imaging in an assessment of perfusion in different types of primary brain tumors.
- We want to point out the possibility of ASL as a completely non invasive MR perfusion imaging method in differentiating between the most common high-grade and low-grade infiltrative brain tumors in adults as well as between tumor recurrence and treatment sequels.
Background

Arterial spin labeling (ASL) is a completely noninvasive magnetic resonance method for assessment of perfusion of different types of pathological brain conditions.

Well established and widely used, in clinical practice and research, methods for brain perfusion evaluation are dynamic susceptibility weighted contrast (T2W*DSC) MR imaging, CT perfusion, and nuclear medicine single photon emission computed tomography and positron-emission tomography (1). These "state of the art" techniques use exogenous materials as a diffusible tracers for estimation of brain perfusion and its parameters.

Unlike these methods ASL perfusion imaging (ASL-PI) does not use exogenous substances, but endogenous arterial water as an absolutely freely diffusible tracer.

Therefore ASL, compared with standard perfusion techniques, is much safer, especially in pediatric patients, those with renal failure, where the risk of nephrogenic systemic fibrosis, after injection of gadolinium agents, is significantly elevated, older patients and those after chemotherapy, where adequate intravenous line cannot be provided (2, 3). Since it is completely non invasive, and does not require contrast agent nor radiation, ASL could be repeated as many times as needed.

The main disadvantage of ASL-PI has been limitation in quantification of perfusion parameters such as cerebral blood flow (CBV), cerebral blood volume (CBV), mean transit time (MTT) etc. Some limited success has been achieved in the field of quantification of CBF based on ASL perfusion map, but it has not been introduced into clinical practice, yet. Therefore ASL perfusion images could be used as an additional tool to conventional MR imaging in the evaluation of brain neoplasms providing information of relative hypo- and hyperperfusion of these lesions (4).
Findings and procedure details

ASL perfusion imaging were performed on a clinical 1.5T MR imager with a product transmit/receive head coil. After conventional MR imaging protocol (sagittal T1W, axial T2W/FLAIR/DWI/SWI and coronal T2W images) ASL PI was performed with ASL_3D sequence with following parameters: perfusion mode FAIR Q II, TR 4000ms, TE 36ms, TI 1990ms, ET 21, BW 752 Hz/px, slice thickness 3mm, acquisition time 3,16min.

The perfusion pattern of each tumor is described, in a comparison to the surrounding normal brain tissue, as a hyper- or hypovascular, based on a signal intensity of a tumor, when we use black-white maps. If we use colour maps, the semiquantitative information could be given, according to colour. Dark colours (blue) represent hypovascular zone, and vascularisation grows over green, yellow to red colour, representing the highest perfusion.

Brain tumors may occur at any age, but many types of tumors are most common in a certain age group. In adults, gliomas, meningiomas and schwannomas are the most common types of primary brain tumors (5).

1. Meningioma (Figure 1)

Meningioma is the second most common primary brain tumor in adults, with an incidence of 15-20%. Most typical meningiomas are slowly growing neoplasms that are histologically benign although their location may make complete resection difficult. Vivid contrast enhancement of meningioma arises from the absence of a true blood-brain barrier (6). Meningiomas are hypervascular tumors that derive their blood supply from the dural vessels (7).

2. Schwannoma (Figure 2)

The incidence of cerebollo-pontine angle Schwannoma account approximately 8-10% of all primary brain neoplasms. Among the masses of pontocerebellar angle, vestibular Schwannoma accounts approximately 75% of the lesions. MR perfusion characteristics of schwannoma/neurinoma depend on the density of the inner vascular network, while the contrast enhancement is a consequence of damaged blood- brain barrier (8).

3. Pituitary macroadenoma (Figure 3)
Pituitary adenoma is the most common intrasellar mass, accounting for at least half of all tumors of this location (9). As small pituitary adenoma grows, it extends in suprasellar cistern and, sometimes even in anterior or medial cranial fossa. These tumors, when solid, express the same imaging characteristics as a normal pituitary gland with strong contrast enhancement caused by an absence of a blood-brain barrier. Density of blood vessels within pituitary adenomas vary among different types. Adenomas can present as hypo- or hyperperfused mass (10). It was found that the richest vascular network can be found in adenomas expressing follicle-stimulating hormone (11).

4. Low grade and high grade gliomas - astrocytomas (Figures 4, 5, 6, 7 and 8)

Gliomas are the most common primary brain tumors in adults, with an incidence around 65%. The latest WHO classification divides astrocytomas into circumscribed astrocytomas (grade I), diffuse astrocytomas (grade II), anaplastic astrocytomas (grade III), and GBM (grade IV) on the basis of histologic criteria and gross/imaging appearance (12).

Low grade gliomas are a heterogenous group of brain tumors that sometimes is difficult to differentiate form high grade gliomas on conventional MRI.

With MRI with gadolinium contrast administration, it is possible to be moderately confident of tissue diagnosis.

However, in up to 30% of cases of what appears to be low grade gliomas are in fact grade III or grade IV tumours (13).

Spectroscopic analysis of the MRIs can help to clarify diagnosis but certainly cannot be definitive. Radiological diagnosis of a "low grade glioma" can therefore pose a dilemma.

5. Radiation necrosis (Figure 9)

Radiation therapy is an important part of the treatment of high-grade gliomas. One of the most severe complication of a radiotherapy, sometimes when combined with a chemotherapy, is radiation necrosis, that can occur at any time after radiation therapy (from 6 months to many years following radiotherapy).

Radiation necrosis has been described in depth in the neurooncological literature, but its diagnosis is still a challenging issue because its radiological pattern is frequently indistinguishable from that of tumor recurrence, especially in contrast enhancing primary tumors (14).
Compared with T2W DSC imaging, ASL imaging is found to be more accurately in distinguishing recurrent high-grade glioma from radiation necrosis (15).
**Fig. 1:** Axial T2W (A), and contrast enhanced T1W images in coronal (B) and axial (C) planes show tentorial meningioma, with enhanced "dural tail" (arrow in B) and extending to either side of the tentorium. ASL PI (D) show a hypervascular pattern of meningioma; arrow in D shows basilar artery near meningioma.

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Fig. 2: Axial T2W (A) and T1W contrast enhanced images (B) show a schwannoma of right vestibulocochlear nerve (CN VIII) with signs of degeneration in the central part of the tumor. ASL perfusion images (C and D) show increased vascularisation of both, cisternal and intracanalicular (arrow in C) solid components of the tumor and decreased vascularisation of the central part of the tumor.

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Fig. 3: Sagittal T1W (A) and sagittal and coronal contrast enhanced T1W images (C and D) show pituitary macroadenoma with extension in the right cavernous sinus. ASL PI (D) shows increased vascularisation of the aforementioned intrasellar mass (arrow in D).

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Fig. 4: Axial T2W FLAIR (A) image shows infiltrative lesion of corpus callosum (CC) with the expansion of splenium and without contrast enhancement within the lesion (B), consistent with gliomatosis cerebri. There are some post-radiation changes mixed with infiltration in corona radiata bilaterally. ASL PI (C and D) show a hypovascular pattern of lesion of CC, confirmed on T2W*DSC images (low rCBF - image E, and low rCBV - image F).

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Fig. 5: Small infiltrative lesion is seen in the tectal plate on T2W FLAIR axial image (arrow in A), with no contrast enhancement (arrow in B). Arrow in C (ASL PI) point to a small hypovascular lesion of mesencephalon, consistent with low grade tectal glioma, confirmed on long echo (135ms) MR spectroscopy (D).

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Fig. 6: Axial T2W FLAIR image (A) show infiltrative lesion of the right temporal lobe, without significant contrast enhancement (B), confirmed to be a low grade glioma on MR spectroscopy with long echo - 135ms (C). ASL PI (D) as well as T2W*DSC rCBF and rCBV maps (E and F) show relatively low perfusion of the lesion.

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Fig. 7: Axial T2W and FLAIR images (A and B) show infiltrative lesion of the left frontal lobe, without significant contrast enhancement (C). MR spectroscopy with log echo (TE 135ms) and voxel placed in the central (D) and peripheral part of the lesion (E) show different grades of tumor. ASL PI (F) shows hypervascular pattern consistent with high grade tumor (WHO Gr. III).

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Fig. 8: Axial T2W FLAIR and T1W with a gadolinium contrast agent images (A and B, respectively) show infiltrative lesion of both frontal lobes and centrum semiovale with transcallosal spread (C) and restricted diffusion (D and E). ASL PI shows hypervascular lesion consistent with glioblastoma multiforme (WHO Gr. IV).

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**Fig. 9:** MR imaging after surgical resection, radiation, and chemotherapy for left occipital glioblastoma multiforme. Axial T2W image (A) show parenchymal defect of the left occipital lobe and large zone of edema in the left occipital and temporal lobes. Axial T1W image after contrast administration (B) shows an area of contrast enhancement, with decreased vascularisation on ASL PI (C) and with no significant diffusion restriction (D and E). MR spectroscopy with long echo - TE 135ms (F) shows decreased peaks of Cho, Cr and NAA, with increased peak of lipid, consistent with radiation necrosis. High peak located around 3.8ppm most probably represents mannitol, administered as an anti-edema drug.
Conclusion

• ASL PI is a completely noninvasive MR procedure that can be helpful as an additional imaging tool for evaluation of different types of brain tumors, even without quantification of perfusion parameters, such as CBF or CBV.
• Since ASL does not require contrast administration it should be a method of choice for assessment of brain perfusion in children, elderly patients, patients with impaired renal function, and all other where gadolinium contrast is contraindicated.
• MR imaging with ASL PI should be a part of imaging protocol it patients after chemoirradiation, especially in those treated for high grade gliomas, where radiation necrosis or tumor recurrence is likely to happen.
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