SYSTEMATIC REVIEW/META-ANALYSIS

Comparison of arterial spin labeling and dynamic susceptibility contrast perfusion MR imaging in pediatric brain tumors: A systematic review and meta-analysis.

Stephanie Vella, Josef Lauri, and Reuben Grech

ABSTRACT

BACKGROUND: Brain tumors are a leading cause of mortality in children. Accurate tumor grading is essential to plan treatment and for prognostication. Perfusion imaging has been shown to correlate well with tumor grade in adults, however there are fewer studies in pediatric patients. Moreover, there is no consensus regarding which MR perfusion technique demonstrates the highest accuracy in the latter population.

PURPOSE: To compare the diagnostic test accuracy of dynamic-susceptibility contrast and arterial spin-labelling, in their ability to differentiate between low- and high-grade pediatric brain tumors at first presentation.

DATA SOURCES: Articles were retrieved from online electronic databases: MEDLINE (Ovid), Web of Science Core Collection and SCOPUS.

STUDY SELECTION: Studies in pediatric patients with a treatment naïve diagnosed brain tumor and imaging including either ASL or DSC or both, together with a histological diagnosis were included. Studies involving adult patient or mixed age populations, studies with incomplete data and those which used dynamic contrast enhanced perfusion were excluded.

DATA ANALYSIS: The sensitivities and specificities obtained from each study were used to calculate the true-positive, true-negative, false-positive, and false-negative count. A case was defined as a histologically proven high-grade tumor. The random-effect model was used to merge statistics. Significance level was set at $p < 0.05$.

DATA SYNTHESIS: Forest plots showing pairs of sensitivity and specificity, with their 95% confidence intervals, were constructed for each study. The bivariate model was applied in order to account for between-study variability. The SROC plots were constructed from the obtained data-sets. The AUC for the SROC of all studies was estimated to determine the overall diagnostic test accuracy of perfusion MRI, followed by a separate comparison of the SROC of ASL versus DSC studies.

LIMITATIONS: Small and heterogenous sample size.

CONCLUSIONS: The diagnostic accuracy of ASL was found to be comparable and not inferior to DSC, thus its use in the diagnostic assessment of pediatric patients should continue to be supported.

ABBREVIATIONS: ASL = arterial spin labelling, DSC = dynamic susceptibility contrast, DCE = dynamic contrast-enhanced, rCBF = relative cerebral blood flow, rCBV = relative cerebral blood volume, MTT = mean transfer time, TR = repetition time, TE = echo time, SROC = summary receiver operating characteristics, HG= high-grade, LG = low-grade, AUC = area under the curve, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses

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From the Medical Imaging Department (Dr. Stephanie Vella, Prof. Reuben Grech), Mater Dei Hospital, Msida, Malta
& the Department of Mathematics and Statistics (Prof. Josef Lauri), Faculty of Science, University of Malta, Msida, Malta
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Please address correspondence to Stephanie Vella, MD, Medical Imaging Department, Mater Dei Hospital, Dun Karm Street, Msida, MSD2090, Malta. stephanie.p.vella@gov.mt.

INTRODUCTION

Brain tumors are the most common solid tumors in the pediatric population with an incidence of 6.14 per 100,000. They are also a leading cause of mortality in this age group, surpassing other cancers and recognized as the top reason for cancer mortality in those aged between 0 and 14 years at diagnosis.(1)(2) Accurate grading of these tumors prior to treatment is clinically important as it allows for appropriate planning of therapeutic approach and prognostication. Whilst the current diagnostic gold standard is histopathology from biopsy or surgical resection, there are a number of cases where surgical access is not feasible or carries high risk. Imaging plays a major role in diagnosis, surgical planning and assessment following treatment. Conventional brain MRI in isolation is often limited in this regard, and often fails to provide sufficient diagnostic test accuracy regarding underlying tumor biology.(3,4) The clinical necessity for an imaging-based assessment of tumor grade in the field of neuro-oncology has led to the development of advanced MRI techniques. Of the modalities providing information on the physiology of tumors, perfusion MRI is a technique aimed at assessing hemodynamic parameters, providing quantitative maps of CBF (cerebral blood flow), CBV (cerebral blood volume) and MTT (mean transfer time), together with vascular permeability parameters.(5)

MRI perfusion has become increasingly relevant in brain tumor assessment, given the established use of anti-angiogenic and anti-vascular therapies(6), as well as for its ability to provide information regarding long-term survival(7) and tumor grade. Traditionally, DSC

(dynamic susceptibility contrast) and arterial spin labeling (ASL), the most widely used techniques, have been thought to have complementary roles in perfusion imaging of brain tumors, with ASL on the one hand being more sensitive to absolute quantification of tumor blood flow, and DSC on the other hand being more sensitive to alterations in tissue permeability and capillary blood volume. Nevertheless, a comparison of their respective ability to assess tumor grade remains a valid research topic due to a number of clinically relevant differences between these techniques.

ASL is a completely non-invasive technique and does not require the administration of gadolinium-based contrast agents. This makes it ideal for scenarios where contrast is contraindicated or best avoided, such as in renal impairment, history of anaphylactic reactions against contrast and pediatric patients in general. This is especially relevant in light of the evidence that administration of contrast results in accumulation of gadolinium in the brain, even in patients without severe renal impairment.(8,9) It is also useful where venous access is difficult or not feasible, as is oftentimes the case in young children, particularly those on chemotherapy. It additionally aids in scenarios where repeated examinations are necessary, such as in cases of failed sedation or patient motion. On the other hand, DSC relies on reasonably high contrast doses, particularly when correcting for leakage effects, and requires the use of a high-flow power injector and large caliber venous access, posing considerable technical challenges in young patients. Bolus delay and dispersion caused by slow injection rates may lead to underestimation of CBF values. Furthermore, in the case of an inadequate study as is quite frequent in young children, it is not possible to repeat DSC in the same examination without a further bolus administration of contrast agent. ASL on the other hand does not require leakage calculation and correction.(10)

As a technique, DSC is extremely vulnerable to image distortion and susceptibility artifacts from interfaces of brain with bone or air, and those resulting from the presence of blood products and calcium.(11) In ASL susceptibility effects causing signal dropout and geometric distortions are comparatively less prominent as shorter echo times are used. It may therefore be better suited in the evaluation of pediatric brain tumors adjacent to the skull base. As pediatric patients possess a higher cerebral water content and overall, more cerebral blood flow than adults, a higher SNR and reduction in artifacts can be afforded in ASL studies in this population.(12)

Whilst these imaging techniques have been well evaluated in adult patients, with a number of studies demonstrating equivalent diagnostic test accuracy of ASL compared with DSC, in terms of distinction between low-grade (LG) and high-grade (HG) tumors, as well as in prognostication (13–20), there is less targeted research specifically relating to pediatric patients and no clear consensus of the clinical role of these techniques. This is especially relevant when considering the fact that the biological features of pediatric brain tumors are unique. The recently published 2021 update of the WHO Classification of Tumors of the Central Nervous System,(21) includes a number of notable changes, whereby the differences between pediatric and adult brain tumors are being increasingly recognized, compelling the undertaking of targeted research in this regard.

The hypothesis underlying our study is that ASL perfusion is comparable to DSC perfusion in its ability to distinguish between LG and HG brain tumors in the pediatric population. The scope was to assess if there is a significant difference in the diagnostic test accuracy of dynamic-susceptibility contrast and arterial spin-labelling, in their ability to differentiate between low- and high-grade pediatric brain tumors at first presentation.

MATERIALS AND METHODS

Criteria for considering studies for inclusion and Search Strategy

The Patients, Interventions, Comparisons and Outcomes (PICO) model was used to define the research question for this study. (22) A summary of the inclusion and exclusion criteria is provided in Table 1. This metanalysis was undertaken in accordance with the Cochrane Handbook for Diagnostic Test Accuracy Reviews (23). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 guidelines (24) were also followed. A systematic search strategy for quantitative data literature was developed. Articles were retrieved from MEDLINE (Ovid), Web of Science Core Collection and SCOPUS (Appendix 1). The search only considered human studies and was limited to studies in the last 10 years. The most recent search for this review was run on 5 August 2022.

Selection of studies

Retrieved hits were transferred onto an online systematic review screening tool. (25) Following the removal of duplicates, the remaining articles were assessed for inclusion independently by two researchers: a consultant and resident specialist in radiology with sub-specialization in neuroradiology, with 10 years' and 1 years' experience in meta-analyses, respectively. In addition, the references from chosen articles were manually reviewed with the aim of identifying any further potentially relevant studies which were not detected in the initial search. The flowchart of retrieval process is presented in Figure 1. Following full-text evaluation, 51 studies were excluded for the following reasons: Eighteen records were review articles or metanalyses lacking original quantitative data. Nine studies did not consider tumor grading but rather disease progression, overall survival or aimed to assess the technical aspects of the perfusion techniques. In seven of the reports the study population was adult, whilst nine of the studies included both adult and pediatric patients with no possibility of separating the respective results. Finally, in seven of the remaining studies, quantitative data values necessary for the statistical analysis, including the sensitivities and specificities obtained were not reported. The respective authors were contacted and requested to provide this information; however, no response was received. Ten studies that included a total of 477 patients were included in the meta-analysis.

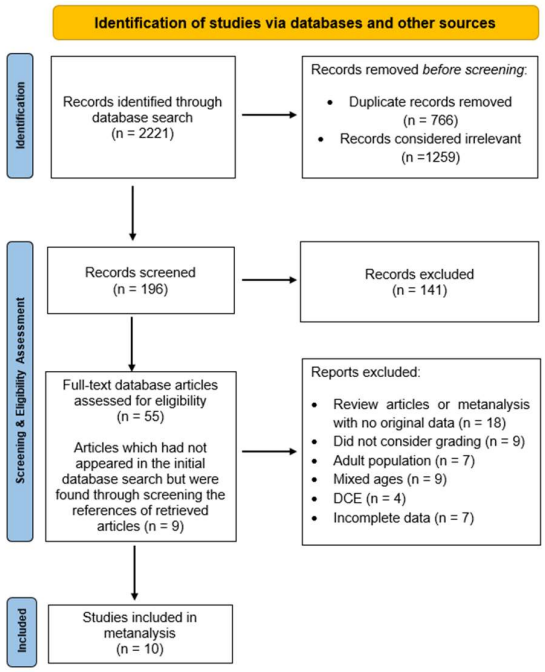

Fig 1. PRISMA flow chart of the study inclusion process.

Data extraction

The following data was extracted independently by two researchers from each of the included studies onto a pre-set sheet:

General information: Study title, first author, journal, country of origin, year of publication and study design (prospective vs. retrospective).
Patient information: Sample size, age range, type of brain tumors being studied and tumor WHO grade.
Imaging information: MR scanner model, manufacturer and field strength, method of MR perfusion performed, ASL technique (pseudo-continuous or pulsed), DSC bolus regime, imaging parameters including TR, TE, slice thickness, matrix size, field of view, flip angle, labelling duration and post-labelling delay (the latter in the case of ASL), region of interest (ROI) evaluation technique and reference region used.
Quantitative results: Data regarding rCBV, rCBF, sensitivity, specificity, summary receiver operating characteristic (SROC) curve with the corresponding area under the curve (AUC) value, extracted based on authors' pre-specified and recommended thresholds.

Critical appraisal tool

Each of the included studies was critically appraised based on the revised Quality Assessment of Diagnostic Accuracy Studies tool (QUADAS 2). (26) Two review authors independently extracted information from each study based on the published articles and any available supplementary material. An adapted template created by the authors of a previously published metanalysis was used in the assessment of included studies (Appendix 2) (27) Any incongruities were dealt with through discussion with a third senior clinician; a consultant radiologist with sub-specialization in neuroradiology with 7 years' experience in meta-analyses.

Data analysis

All analyses were performed using R Statistical Software (v4.2.2 Patched (2022-11-10 r83330).(28) The sensitivities and specificities obtained from each study were used to calculate the true-positive, true-negative, false-positive, and false-negative count. A case was defined as a histologically proven high-grade tumor. A positive index test implied a diagnosis of a high-grade tumor, while a negative test suggested a low-grade tumor. Thus, true positives were correctly diagnosed high-grade tumors, false negatives were high-grade tumors incorrectly labelled as low-grade tumors, true negatives were correctly diagnosed low-grade tumors, while false positives were low-grade tumors incorrectly labelled as high-grade tumors. Between-study heterogeneity variance was measured by tau-squared ($\tau 2$) and I-squared (I2) values. The random-effect model was used to merge statistics. Significance level was set at $p < 0.05$. Forest plots showing pairs of sensitivity and specificity, with their 95% confidence intervals, were constructed for each study using Metafor. (29)

The bivariate model (30) was applied in order to account for between-study variability in estimates of sensitivity and specificity through the inclusion of random effects for the logit sensitivity and logit specificity parameters of the bivariate model. The reitsma function of the mada package was used to generate the bivariate model parameters required to construct the summary receiver operating characteristics (SROC) plot from the obtained data-sets. (31) The area under the curve (AUC) for the SROC of all studies was estimated to determine the overall diagnostic test accuracy of perfusion MRI, followed by a separate comparison of the SROC of ASL versus DSC studies.

RESULTS

The data of the included literature is presented in Table 2 (32–41) and Appendix 3. Collectively, the ten studies included in this metanalysis reported 477 patients with brain tumors. All studies were retrospective and avoided case-control design. The sample size per study was generally adequate and ranged from 19 to 117 cases. Only one study had a sample size of less than 20. (28) The following tumor types were assessed across all studies: gliomas and glioneuronal tumors (n=304), ependymomas (n=41), embryonal (n=115), hemangioblastoma (n=1), germ cell (n=1), craniopharyngioma (n=4), choroid plexus (n=7), pineal (n=3), chordoma (n=1). All cases but one diffuse midline glioma received histological diagnosis. Hence, the bulk of the tumors were of the glial and embryonal groups, which reflects their incidence. The vast majority of the included studies used the 2016 WHO brain tumor classification. DSC was used in three of the included studies, whilst ASL was the perfusion technique assessed in five studies. Two of the included studies used both DSC and ASL. In 4 of the ASL studies, the pulsed technique was used, with the remaining being pseudo-continuous. None of the DSC studies used contrast agent pre-loading. Information regarding arterial input function was only available in two out the five DSC studies, where it was automated. The majority of examinations were performed on a 1.5T scanner (in four studies), one study used a 3T scanner and five studies used both.

The methodological quality assessment of each of the included studies (according to the modified QUADAS-2 criteria) is summarized in Table 3. None of the included studies had low risk of bias and low concern for applicability across all domains, however all were deemed to be of eligible quality. The average rCBV/rCBF values per tumor grade in each included study are presented in Table 4.

With regards to sensitivity of ASL, the between-study heterogeneity variance as measured by $\tau 2$ was negligible, indicating strong homogeneity between the studies. The pooled sensitivity was 0.867 with a 95% confidence interval (CI) equal to [0.806 - 0.911]. In terms of specificity of ASL, although the between-study heterogeneity variance was higher, as estimated by $\tau 2$= 0.536 and I2 = 0.536, these figures were not statistically significant (p value=0.36). The pooled value of the specificity was 0.825 with a 95% CI = [0.687 - 0.910] [Figure 2].

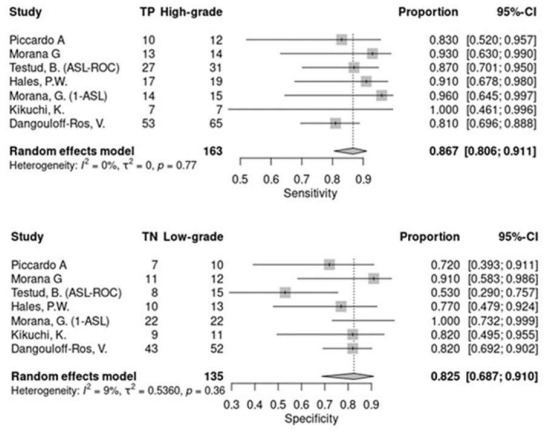

Fig 2. Sensitivity and specificity plots for ASL.

In terms of sensitivity of DSC, I2 was noted to be high at 70%, indicating that more than a half of the variability between the studies was not due to random fluctuations. The between-study heterogeneity variance was estimated at $\tau 2$= 1.928. The pooled value of the sensitivity was 0.888 with a 95% CI = [0.638 - 0.973]. As noted with ASL, the heterogeneity among the DSC studies was greater for specificity than for sensitivity, at least as measured by $\tau 2$= 2.323. The I2 value was practically the same at 69%, with this variance among the studies again noted to be significant (p = 0.01). The pooled estimate of the specificity for these studies was 0.835 with a 95% CI = [0.512 - 0.960] [Figure 3].

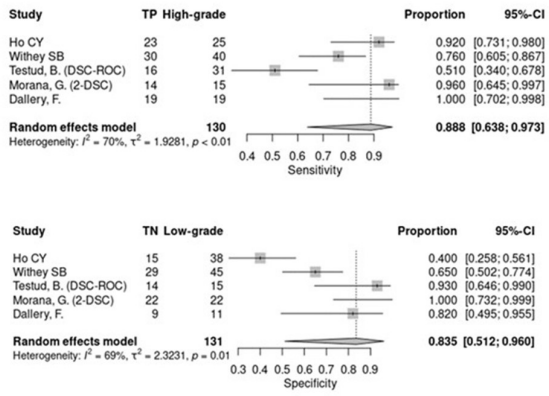

Fig 3. Sensitivity and specificity plots for DSC.

Moderator analyses could not be performed due to an insufficient number of studies. In view of the overall substantial heterogeneity, a random-effects model was used to merge statistics. Meta-analysis of the ten studies using a bivariate model reitsma function was run with its default method of Restricted Maximum Likelihood (reml). The AUC for the SROC was estimated as 0.866. The point estimates for the pooled sensitivity and false positive rates were 0.798 and 0.201, respectively [Figure 4]. The Akaike information criterion (AIC) for the two summary plots were -22.487 for ASL and -4.416 for DSC. This indicates that the ASL plot is a better fit of the data, which is expected given that DSC data comprised a smaller number of studies, and also demonstrated greater heterogeneity [Figure 5]. For ASL, pooled AUC = 0.876, pooled Sensitivity = 0.824, 95% CI = [0.757 - 0.876], pooled false positive rate = 0.204, 95% CI = [0.142 0.285]. For DSC: pooled AUC = 0.861, pooled Sensitivity = 0.789, 95% CI = [0.552 - 0.919], pooled false positive rate = 0.203, 95% CI = [0.081 - 0.425].

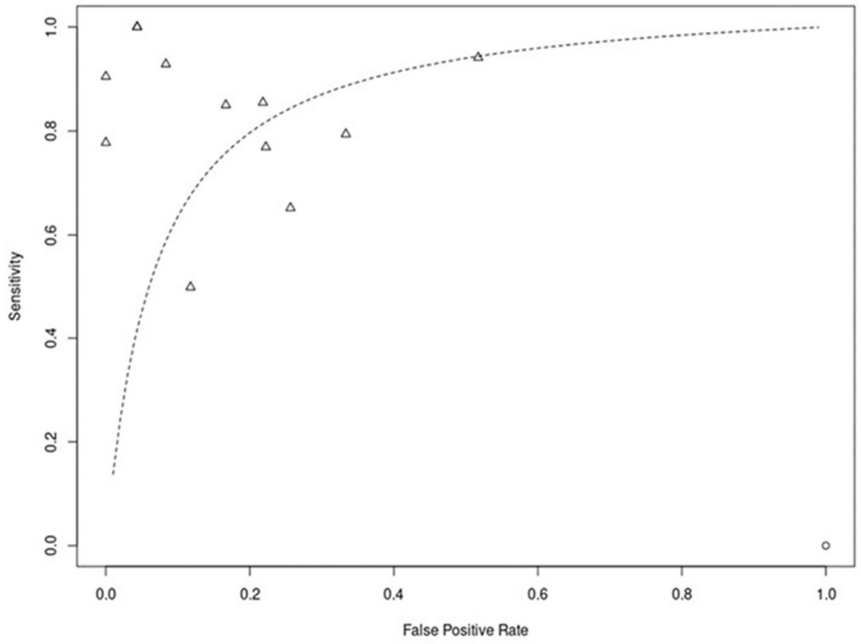

Fig 4. SROC curve (bivariate) for all studies

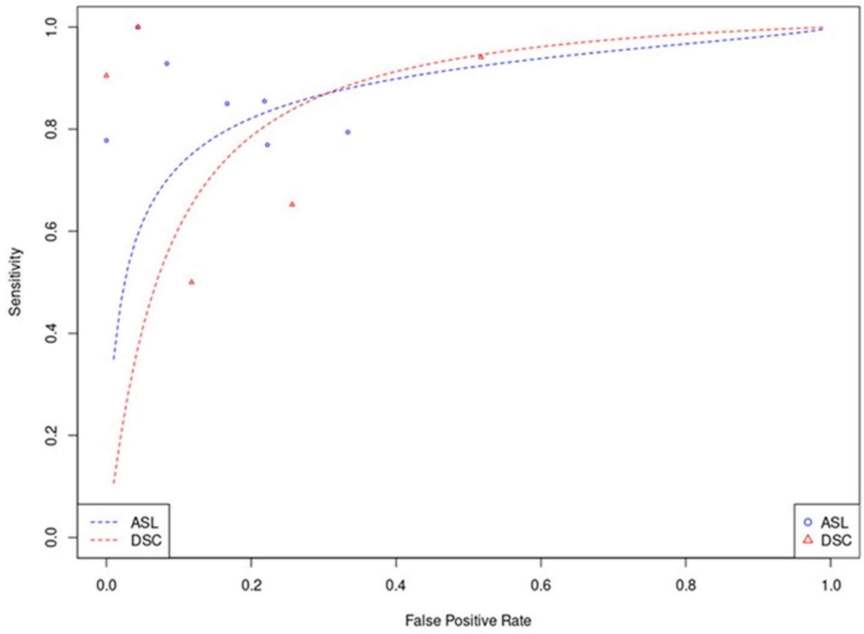

Fig 5. Comparison SROC curves (bivariate) of ASL and DSC

DISCUSSION

This metanalysis confirms that the application of ASL and DSC perfusion MRI confers a good diagnostic accuracy in distinguishing between low- and high-grade brain tumors in the pediatric population, with an AUC estimated at 0.866. This is clinically relevant given that a pre-operative indication of tumor grade is important to guide treatment decisions and strategies, as well as for prognostication.

DSC has been the traditionally used MR perfusion technique. Low-grade tumors are generally less vascularized than high-grade tumors, therefore the hemodynamic parameters measured by DSC would be expected to be significantly increased in the latter. On analysis it was found that the pooled sensitivity and specificity of rCBV obtained by DSC to discriminate between low- and high-grade tumors was 78% and 80% respectively. A limitation of this perfusion technique is the presence of leakage effects, the correction of which has led to a variety of approaches to obtain and process the obtained data. One such approach is the use of a contrast pre-load as has been discussed, however this is rarely done in children. The Boxerman consensus (42), advocates the application of leakage correction in the post-processing and provides guidance to that effect. The approach to leakage correction was not well described in our studies and when it was, did vary somewhat across the studies that were included.

Unlike DSC, perfusion measurements in ASL are not tampered by blood-brain barrier permeability effects. Furthermore, since shorter echo times are used, susceptibility effects leading to signal dropout and geometric distortions are less frequently encountered. ASL does however suffer from low SNR and motion sensitivity. Additionally, measurement of absolute CBF is known to be unreliable due to patient variables, although, even when relative CBF is calculated, variation is still possible due to the difference in pulse sequences and post-processing algorithms which vary in between centers. Recently published consensus guidance regarding the most appropriate implementation for clinical applications and imaging parameters (43) should standardize practice, however several of the included studies comprised cases that preceded these recommendations, also possibly accounting for a proportion of the heterogeneity that was noted. On analysis it was found that the pooled sensitivity and specificity of rCBF obtained by ASL to discriminate between low- and high-grade tumors was 82% and 80% respectively.

There have been a number of studies comparing the performance of ASL and DSC in brain tumor grading in adults (13–20), however given the different biology of pediatric brain tumors, extrapolation of adult study findings to this age group would be inappropriate. A recent study by Morana et al. noted this lacuna in the pediatric population and demonstrated that ASL provides comparable results to DSC in pediatric astrocytic tumors, allowing distinction between low- and high-grade forms.(38) A subsequent study noted moderate abilities of DSC and ASL to distinguish low- and high-grade pediatric brain tumors.(40) There have not been any other such studies which directly compared ASL with DSC, however a number of studies have assessed each technique independently. Through a thorough systematic review, it was aimed to extract the diagnostic data from various studies and assess if there is a significant difference in the performance of these two techniques. From our results it can be surmised that ASL seems to perform better, with a slightly higher pooled sensitivity than for DSC and with both giving the same pooled false positive rate. However, the difference between the two sensitivities was not statistically significant. The confidence interval of the estimate for ASL contains the point estimate for DSC, and vice-versa.

Substantial heterogeneity was noted in this study cohort. One reason for this could be the different tumor types and behaviors. In fact, the initial aim was to limit the analysis to assessment of pediatric gliomas. However, during our search it was noted that a number of studies included other brain tumor types, albeit in much smaller numbers. Gliomas did however account for the majority of cases in our study population. Although the proportion of high versus low-grade tumors was approximately equal in most studies, in one of the studies there were approximately double the number of high-grade tumors compared with low-grade. (40) Additionally, field strengths, parameter settings, post-processing methods and ROI measurement method varied across studies. These factors most likely contributed to the variations noted, however moderator analyses could not be performed due to an insufficient number of studies.

The relatively small sample size/included number of studies is both a reflection of the limited research in this field, and also of the strict methodology standards which were adhered to in order to remain faithful to the review question. Incomplete inclusion of data in publications and lack of author response also contributed. Nevertheless, neuro-oncological imaging is a continuously evolving field and further research in this regard needs to be undertaken, preferably using standardized scanning protocols to reduce heterogeneity. Harmonization of imaging and interpretation techniques is key, leading to clearer comparison between studies with the potential downstream effect of generating a higher level of evidence. Quality assessment revealed a high risk of bias in the index tests of 7 of our included studies, which we consider to be a further limitation.

Lastly, the majority of our studies defined the gold standard of tumor diagnostic assessment as histological/immunohistochemistry grading. However, as highlighted in the recent WHO classification update, the biological behavior and prognosis of brain tumors is becoming increasingly defined through molecular profiling. This modification will need to be considered and evaluated in future studies.

CONCLUSIONS

Whilst DSC has been used more frequently than ASL in the evaluation of brain tumor grade in pediatric patients, the application of ASL is steadily increasing. ASL is a non-invasive technique and does not require the administration of gadolinium-based contrast agents. As the diagnostic accuracy of ASL has been shown to be comparable and not inferior to DSC, its use in the diagnostic assessment of these patients should continue to be supported.

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Table 1: Inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
Study design	Peer reviewed studies based on original data analysis.	Literature which was not published through traditional academic or commercial publishers.
	Published from 2012 onwards.	Literature reviews, case reports or case controls.
Participants	Human subjects below the age of 18.	Adult only or mixed adult and pediatric subjects.
	Diagnosis of brain tumor.	Previously treated with either surgery, radiotherapy or chemotherapy.
	Treatment naïve.	
Index test	ASL and/or DSC MRI perfusion.	DCE (dynamic contrast enhanced) perfusion.
	Availability of result data.	No author response to inquiry for data clarification.
Gold standard test	Histologic assessment following biopsy or resection (except in cases of optic pathway/brainstem glioma).	No histological diagnosis.
	Use of WHO classification for tumor grading.	

Table 2. Characteristics of included studies

First author, Publication year	Region	No. of cases	Median/Mean age	Tumor Grade *n*	Field strength	Perfusion Technique	Diagnostic Parameters
Dallery 2017	France	30	9.4	11 LG, 19 HG	1.5 & 3T GE	DSC	rCBF, rCBV
Dangouloff-Ros 2016	France	117	6.2	52 LG, 65 HG	1.5T GE	ASL	rCBF
Hales 2019	UK	32	4.5	13 LG, 19 HG	1.5 & 3T Siemens	ASL	rCBF
Ho 2014	USA	63	6.3	38 LG, 25 HG	1.5 & 3T Siemens	DSC	rCBV
Kikuchi 2017	Japan	19	6	11 LG, 8 HG	3T Philips	ASL	rCBF
Morana 2017	Italy	26	9.5	12 LG, 14 HG	1.5T Philips	ASL	rCBF
Morana 2018	Italy	37	9	22 LG, 15 HG	1.5T Philips	ASL & DSC	rCBF, rCBV
Piccardo 2019	Italy	22	9	10 LG, 12 HG	1.5T Philips	ASL	rCBF
Testud 2021	France	46	7	15 LG, 31 HG	1.5 & 3T Siemens	ASL & DSC	rCBF, rCBV
Withey 2021	UK	85	8	45 LG, 40 HG	1.5 & 3T Various	DSC	rCBV

Table 3. QUADAS2 methodological quality assessment

Study, Publication year	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Dallery, 2017	+	-	?	?	+	+	+
Dangouloff-Ros, 2016	+	+	+	?	+	+	+
Hales, 2019	+	+	?	?	+	+	+
Ho, 2014	+	-	?	?	+	+	+
Kikuchi, 2017	+	-	?	?	+	+	+
Morana, 2017	+	-	?	?	+	-	+
Morana, 2018	+	-	?	?	+	-	+
Piccardo, 2019	+	-	?	?	?	-	+
Testud, 2021	+	+	?	?	+	-	+
Withey, 2021	+	-	?	?	+	+	+

+ indicates low risk ? indicates unclear risk - indicates high risk

Table 4. **Relative/normalized CBV & CBF values per tumor grade**

Study	No. of cases	Tumor Grade *n*	Perfusion Technique	Diagnostic Parameters	Low-Grade	High-Grade
Dallery	30	11 LG, 19 HG	DSC	rCBF	0.87 ± 0.41	2.37 ± 1.38
2017				rCBV	0.99 ± 0.50	2.69 ± 1.35
Dangouloff-Ros 2016	117	52 LG, 65 HG	ASL	rCBF	0.68 ± 0.24	1.74 ± 1.45
Hales	32	13 LG, 19 HG	ASL	rCBF	n/a	n/a
2019						
Ho	63	38 LG, 25 HG	DSC	rCBV	0.99 ± 0.53	1.48 ± 0.95
2014						
Kikuchi	19	11 LG, 8 HG	ASL	rCBF	0.69 ± 0.81	1.76 ± 0.95
2017						
Morana	26	12 LG, 14 HG	ASL	rCBF	0.81 ± 0.56	2.08 ± 0.98
2017						
Morana	37	22 LG, 15 HG	ASL & DSC	rCBF	0.59 ± 0.27	1.37 ± 0.26
2018				rCBV	0.49 ± 0.33	1.51 ± 0.34
Piccardo	22	10 LG, 12 HG	ASL	rCBF	1.20 ± 0.49	1.89 ± 0.45
2019						
Testud	46	15 LG, 31 HG	ASL & DSC	rCBF, rCBV	n/a	n/a
2021						
Withey	85	45 LG, 40 HG	DSC	rCBV	1.68 ± 1.36	2.54 ± 1.63
2021						

LG=low-grade, HG=high-grade

Appendix 1 – Search String and Strategy

The following search string was used:

("Glioma" OR "neoplasm" OR "neoplasia" OR "tumor" OR "tumour" OR "cancer" OR "malignancy" AND "Brain" OR "Central Nervous System" OR "Cerebral" OR "intracranial" OR "Glial") AND ("paediatric" OR "pediatric" OR "young adult" OR "infant" OR "child" OR "children" OR "adolescent") AND ("perfusion" OR "ASL" OR "arterial spin labelling" OR "arterial spin labeling" OR "arterial spin labeled" OR "dynamic susceptibility contrast" OR "DSC" OR "Perfusion Weighted MRI" OR "MR Perfusion" OR "MRI Perfusion" OR "Spin Labels").

Pubmed Search Strategy

Search number	Query	Sort By	Filters	Search Details	Results	Time
5	#1 AND #2 AND #3		in the last 10 years	((((("Glioma"[All Fields] OR "neoplasm"[All Fields] OR "neoplasia"[All Fields] OR "tumor"[All Fields] OR "tumour"[All Fields] OR "cancer"[All Fields] OR "malignancy"[All Fields]) AND "Brain"[All Fields]) OR "Central Nervous System"[All Fields] OR "Cerebral"[All Fields] OR "intracranial"[All Fields] OR "Glial"[All Fields]) AND ("paediatric"[All Fields] OR "pediatric"[All Fields] OR "young adult"[All Fields] OR "infant"[All Fields] OR "child"[All Fields] OR "children"[All Fields] OR "adolescent"[All Fields]) AND ("perfusion"[All Fields] OR "ASL"[All Fields] OR "arterial spin labelling"[All Fields] OR "arterial spin labeling"[All Fields] OR "arterial spin labeled"[All Fields] OR "dynamic susceptibility contrast"[All Fields] OR "DSC"[All Fields] OR "Perfusion Weighted MRI"[All Fields] OR "MR Perfusion"[All Fields] OR "MRI Perfusion"[All Fields] OR "Spin Labels"[All Fields])) AND (y_10[Filter])	2,826	12:58:29
4	#1 AND #2 AND #3			((("Glioma"[All Fields] OR "neoplasm"[All Fields] OR "neoplasia"[All Fields] OR "tumor"[All Fields] OR "tumour"[All Fields] OR "cancer"[All Fields] OR "malignancy"[All Fields]) AND "Brain"[All Fields]) OR "Central Nervous System"[All Fields] OR "Cerebral"[All Fields] OR "intracranial"[All Fields] OR "Glial"[All Fields]) AND ("paediatric"[All Fields] OR "pediatric"[All Fields] OR "young adult"[All Fields] OR "infant"[All Fields] OR "child"[All Fields] OR "children"[All Fields] OR "adolescent"[All Fields]) AND ("perfusion"[All Fields] OR "ASL"[All Fields] OR "arterial spin labelling"[All Fields] OR "arterial spin labeling"[All Fields] OR "arterial spin labeled"[All Fields] OR "dynamic susceptibility contrast"[All Fields] OR "DSC"[All Fields] OR "Perfusion Weighted MRI"[All Fields] OR "MR Perfusion"[All Fields] OR "MRI Perfusion"[All Fields] OR "Spin Labels"[All Fields])	5,742	12:58:18
3	("perfusion" OR "ASL" OR "arterial spin labelling" OR "arterial spin labeling" OR "arterial spin labeled" OR "dynamic susceptibility contrast" OR "DSC" OR "Perfusion Weighted MRI" OR "MR Perfusion" OR "MRI Perfusion" OR "Spin Labels")			"perfusion"[All Fields] OR "ASL"[All Fields] OR "arterial spin labelling"[All Fields] OR "arterial spin labeling"[All Fields] OR "arterial spin labeled"[All Fields] OR "dynamic susceptibility contrast"[All Fields] OR "DSC"[All Fields] OR "Perfusion Weighted MRI"[All Fields] OR "MR Perfusion"[All Fields] OR "MRI Perfusion"[All Fields] OR "Spin Labels"[All Fields]	252,240	12:57:39
2	("paediatric" OR "pediatric" OR "young adult" OR "infant" OR "child" OR "children" OR "adolescent")			"paediatric"[All Fields] OR "pediatric"[All Fields] OR "young adult"[All Fields] OR "infant"[All Fields] OR "child"[All Fields] OR "children"[All Fields] OR "adolescent"[All Fields]	5,112,674	12:55:43

1	"Glioma" OR "neoplasm" OR "neoplasia" OR "tumor" OR "tumour" OR "cancer" OR "malignancy" AND "Brain" OR "Central Nervous System" OR "Cerebral" OR "intracranial" OR "Glial"	(("Glioma"[All Fields] OR "neoplasm"[All Fields] OR "neoplasia"[All Fields] OR "tumor"[All Fields] OR "tumour"[All Fields] OR "cancer"[All Fields] OR "malignancy"[All Fields]) AND "Brain"[All Fields]) OR "Central Nervous System"[All Fields] OR "Cerebral"[All Fields] OR "intracranial"[All Fields] OR "Glial"[All Fields]	1,141,019	12:55:19

Search number	Query	Sort By	Filters	Search Details	Results	Time
5	#1 AND #2 AND #3	in the last 10 years		((((("Glioma"[All Fields] OR "neoplasm"[All Fields] OR "neoplasia"[All Fields] OR "tumor"[All Fields] OR "tumour"[All Fields] OR "cancer"[All Fields] OR "malignancy"[All Fields]) AND "Brain"[All Fields]) OR "Central Nervous System"[All Fields] OR "Cerebral"[All Fields] OR "intracranial"[All Fields] OR "Glial"[All Fields]) AND ("paediatric"[All Fields] OR "pediatric"[All Fields] OR "young adult"[All Fields] OR "infant"[All Fields] OR "child"[All Fields] OR "children"[All Fields] OR "adolescent"[All Fields]) AND ("perfusion"[All Fields] OR "ASL"[All Fields] OR "arterial spin labelling"[All Fields] OR "arterial spin labeling"[All Fields] OR "arterial spin labeled"[All Fields] OR "dynamic susceptibility contrast"[All Fields] OR "DSC"[All Fields] OR "Perfusion Weighted MRI"[All Fields] OR "MR Perfusion"[All Fields] OR "MRI Perfusion"[All Fields] OR "Spin Labels"[All Fields])) AND (y_10[Filter])	2,826	12:58:29
4	#1 AND #2 AND #3			(((("Glioma"[All Fields] OR "neoplasm"[All Fields] OR "neoplasia"[All Fields] OR "tumor"[All Fields] OR "tumour"[All Fields] OR "cancer"[All Fields] OR "malignancy"[All Fields]) AND "Brain"[All Fields]) OR "Central Nervous System"[All Fields] OR "Cerebral"[All Fields] OR "intracranial"[All Fields] OR "Glial"[All Fields]) AND ("paediatric"[All Fields] OR "pediatric"[All Fields] OR "young adult"[All Fields] OR "infant"[All Fields] OR "child"[All Fields] OR "children"[All Fields] OR "adolescent"[All Fields]) AND ("perfusion"[All Fields] OR "ASL"[All Fields] OR "arterial spin labelling"[All Fields] OR "arterial spin labeling"[All Fields] OR "arterial spin labeled"[All Fields] OR "dynamic susceptibility contrast"[All Fields] OR "DSC"[All Fields] OR "Perfusion Weighted MRI"[All Fields] OR "MR Perfusion"[All Fields] OR "MRI Perfusion"[All Fields] OR "Spin Labels"[All Fields])	5,742	12:58:18
3	("perfusion" OR "ASL" OR "arterial spin labelling" OR "arterial spin labeling" OR "arterial spin labeled" OR "dynamic susceptibility contrast" OR "DSC" OR "Perfusion Weighted MRI" OR "MR Perfusion" OR "MRI Perfusion" OR "Spin Labels")			"perfusion"[All Fields] OR "ASL"[All Fields] OR "arterial spin labelling"[All Fields] OR "arterial spin labeling"[All Fields] OR "arterial spin labeled"[All Fields] OR "dynamic susceptibility contrast"[All Fields] OR "DSC"[All Fields] OR "Perfusion Weighted MRI"[All Fields] OR "MR Perfusion"[All Fields] OR "MRI Perfusion"[All Fields] OR "Spin Labels"[All Fields]	252,240	12:57:39
2	("paediatric" OR "pediatric" OR "young adult" OR "infant" OR "child" OR "children" OR "adolescent")			"paediatric"[All Fields] OR "pediatric"[All Fields] OR "young adult"[All Fields] OR "infant"[All Fields] OR "child"[All Fields] OR "children"[All Fields] OR "adolescent"[All Fields]	5,112,674	12:55:43
1	"Glioma" OR "neoplasm" OR "neoplasia" OR "tumor" OR "tumour" OR "cancer" OR "malignancy" AND "Brain" OR			(("Glioma"[All Fields] OR "neoplasm"[All Fields] OR "neoplasia"[All Fields] OR "tumor"[All Fields] OR "tumour"[All Fields] OR "cancer"[All Fields] OR "malignancy"[All Fields]) AND "Brain"[All Fields]) OR	1,141,019	12:55:19

	"Central Nervous System" OR "Cerebral" OR "intracranial" OR "Glial"	**"Central Nervous System"[All Fields] OR "Cerebral"[All Fields] OR "intracranial"[All Fields] OR "Glial"[All Fields]**		

Web of Science Search Strategy

Database: Web of Science Core Collection

Entitlements:

- WOS.SSCI: 1994 to 2022

- WOS.AHCI: 1994 to 2022

- WOS.ISTP: 1997 to 2022

- WOS.ESCI: 2017 to 2022

- WOS.SCI: 1994 to 2022

- WOS.ISSHP: 1997 to 2022

Searches:

1: ((ALL=((“Glioma” OR “neoplasm” OR “neoplasia” OR “tumor” OR “tumour” OR “cancer” OR “malignancy” AND “Brain” OR “Central Nervous System” OR “Cerebral” OR “intracranial” OR “Glial”))) AND ALL=((“paediatric” OR “pediatric” OR “young adult” OR “infant” OR “child” OR “children” OR “adolescent”))) AND ALL=((“perfusion” OR “ASL” OR “arterial spin labelling” OR “arterial spin labeling” OR “arterial spin labeled” OR “dynamic susceptibility contrast” OR “DSC” OR “Perfusion Weighted MRI” OR “MR Perfusion” OR “MRI Perfusion” OR “Spin Labels”)) Timespan: 2012-01-01 to 2022-08-01 Date run: Fri Aug 05 2022 19:28:03 GMT+0200 (Central European Summer Time) Results: 2266

SCOPUS Search Strategy

(ALL (("Glioma" OR "neoplasm" OR "neoplasia" OR "tumor" OR "tumour" OR "cancer" OR "malignancy" AND "Brain" OR "Central Nervous System" OR "Cerebral" OR "intracranial" OR "Glial")) AND ALL (("paediatric" OR "pediatric" OR "young adult" OR "infant" OR "child" OR "children" OR "adolescent")) AND ALL (("perfusion" OR "ASL" OR "arterial spin labelling" OR "arterial spin labeling" OR "arterial spin labeled" OR "dynamic susceptibility contrast" OR "DSC" OR "Perfusion Weighted MRI" OR "MR Perfusion" OR "MRI Perfusion" OR "Spin Labels"))) AND PUBYEAR > 2011 AND (LIMIT-TO (PUBYEAR , 2023) OR LIMIT-TO (PUBYEAR , 2022)) AND (LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA , "BIOC") OR LIMIT-TO (SUBJAREA , "NEUR"))

Results: 1822

Appendix 2 – Critical Appraisal Tool

Risk of Bias
Patient selection:
• Low if consecutive or reported in years of inclusion together with clear inclusion criteria.
• Unclear if no mention of consecutive series of patients or inclusion/exclusion criteria.
• High if a non-consecutive series was reported and inappropriate inclusion/exclusion criteria were used.
Index test:
• Low if perfusion MRI was interpreted blinded.
• Unclear if no information on blinding but a predefined cut-off was specified for a positive test.
• High if an exploratory cut-off was used and no information on blinding was given.
Reference standard:
• Low if reported on a blinded evaluation and WHO adherence.
• Unclear if no information on blinding was given.
• High if reported on an unblinded evaluation.
Flow and timing:
• Low if less than 30 days between perfusion MRI and histopathology.
• Unclear if not reported.
• High if reported after 6 months.
Applicability Concerns
Patient selection:
• Low if mixed tumour types.
• Unclear if tumour types were not reported or only 1 tumour type was reported.
• High if other comparisons than between high- and low-grade were given.
Index test:
• Low if presented as relative CBF/CBV and pseudo-continuous used if ASL.
• Unclear if CBF/CBV was not normalised.
• High if perfusion metrics other than CBF were presented or if pulsed ASL was used.
Reference standard:
• Low if tumours were classified according to WHO 2007 or later.
• Unclear if WHO was used but the year was unspecified.
• High if no report on the histopathologic diagnosis classification system

Appendix 3 – Study Characteristics

Dallery 2017

Study design and setting,

Retrospective. January 2010 - December 2016. France.

Patient sampling characteristics

Total no. of patients: 30

Average age: 9.4 years. 13 female, 17 male

Tumour types: 22 glioma/glioneuronal, 8 embryonal

Index tests

Perfusion technique: DSC

Perfusion parameters: rCBV

Scanners: 1.5T (Optima MR450W, GE Healthcare, Milwaukee, WI) and 3T (Signa MRHDx, GE Healthcare, Milwaukee, WI)

Acquisition parameters: single shot gradient-echo EPI. At 3T: TR: 1500ms; TE: 30ms; FA, 60°. At 1.5T: TR 1500-2500 ms, TE, 30-65 ms; FA: 60°-90 °. NSA, FOV, Partitions & Matrix: NA

Use of contrast preload: No

Post-processing algorithm: Gamma-variate function

ROI method: Manual ROI in maximal lesion CBV. Normalised to contralateral normal white matter.

Target condition and reference standard

All cases had histological diagnosis. WHO classification 2016. 11 LG, 19 HG.

Dangouloff-Ros, 2016

Study design and setting

Retrospective. March 2011- March 2015. France.

Patient sampling characteristics

Total no. of patients: 117

Median age: 6.2 years (2.6–11.1). 48 female, 81 male

Tumour types: 71 glioma/glioneuronal or neuronal, 12 ependymal, 45 embryonal, 1 haemangioblastoma

Index tests

Perfusion technique: pseudo-continuous ASL

Perfusion parameters: rCBF

Scanners: 1.5T (Signa HD, GE Healthcare, Milwaukee, WI)

Acquisition parameters: TR: 4428ms, TE:10.5ms, PLD: 1025ms; Partitions: 80, FOV: 240mm, Matrix: 512x512; FA: 155°, Acquisition time: 257s

Post-processing algorithm: NA

ROI method: Centred on highest tumour rCBF value. Normalised to normal grey-matter in cerebellum (posterior fossa tumours)/temporal lobe (supratentorial tumours).

Target condition and reference standard

All cases had histological diagnosis. WHO classification 2007. 52 LG, 65 HG.

Hales, 2019

Study design and setting

Retrospective. June 2015- Sept 2017. United Kingdom.

Patient sampling characteristics

Total no. of patients: 32

Median age: 4.8 years (0.4 - 14.5 years). 17 female, 15 male

Tumour types: 24 gliomas/glioneuronal, 7 embryonal, 1 germ cell

Index tests

Perfusion technique: pseudo-continuous ASL

Perfusion parameters: relative/normalised CBF

Scanners: 1.5T (Magnetom Avanto, Siemens, Erlangen, Germany) & 3T (Magnetom Prisma, Siemens, Erlangen, Germany)

Acquisition parameters: 3D gradient-and-spin-echo readout, labelling duration:1800ms, PLD: 1500ms.

Post-processing: Matlab (MathWorks Inc., Natick, MA)

ROI method: Manual ROI in maximal lesion CBF. Normalised to contralateral normal grey matter

Target condition and reference standard

All cases (with the exception of one diffuse midline glioma) had histological diagnosis. WHO classification 2016. 13 LG, 19 HG.

Ho, 2014

Study design and setting

Retrospective. September 2009 - August 2013. USA.

Patient sampling characteristics

Total no. of patients: 63

Mean age: 6.3 years (1.0–16.8). 24 female, 39 male

Tumour types: 36 gliomas/glioneuronal or neuronal, 10 ependymal, 13 embryonal, 1 craniopharyngioma, 1 pineal, 2 choroid plexus papilloma

Index tests

Perfusion technique: DSC

Perfusion parameters: rCBV

Scanners: 1.5T & 3T (Avanto and Verio, Siemens, Erlangen, Germany)

Acquisition parameters: Gradient-echo EPI. TR 1410–2250ms, TE 30–45ms, FA: 90°

NSA, FOV, Partitions & Matrix: NA

Use of contrast preload: No

Post-processing algorithm: NA

ROI method: Manual ROI in maximal lesion CBV. Normalised to contralateral normal white matter.

Target condition and reference standard

All cases had histological diagnosis. WHO classification 2007. 38 LG, 25 HG.

Kikuchi, 2017

Study design and setting

Retrospective. January 2013 - September 2014. Japan.

Patient sampling characteristics

Total no. of patients: 19

Median age: 6 years (2 months –12 years). 9 female, 10 male

Tumour types: 9 glial/glioneuronal, 4 ependymal, 3 embryonal, 2 craniopharyngioma, 1 choroid plexus papilloma

Index tests

Perfusion technique: pseudo-continuous ASL

Perfusion parameters: rCBF

Scanners: 3T (Achieva TX, Philips Healthcare, Best, the Netherlands)

Acquisition parameters: 2-dimensional gradient-echo echo-planar imaging. TR: 4200ms, TE: 8.6ms, NEX: 32, PLD: 1525ms, FOV: 240mm, Matrix: 64x64; Acquisition time: 277s. FA & Partitions: NA.

Post-processing algorithm: NA

ROI method: Manual ROI in maximal lesion CBF. Normalised to contralateral grey matter.

Target condition and reference standard

All cases had histological diagnosis. WHO classification 2016. 11 LG, 8 HG.

Morana, 2017

Study design and setting

Retrospective. Timeframe not specified. Italy.

Patient sampling characteristics

Total no. of patients: 26

Median age: 9.5 years (2–17). 11 female, 15 male

Tumour types: gliomas

Index tests

Perfusion technique: pulsed ASL

Perfusion parameters: rCBF max

Scanners: 1.5T (Intera Achieva; Philips, Best, the Netherlands)

Acquisition parameters: multi-slice single-shot echo planar imaging (EPI) readout with parallel imaging (SENSE factor = 2.3) TR: 4000ms; TE: 25ms; FA, 40°, FOV: 240mm, Matrix: 80x77, 30 label/control pairs; labelling slab thickness: 100mm, 20mm gap, PLD: 1450 - 1800ms, Acquisition time: 245s, Partitions: NA

Post-processing algorithm: NA

ROI method: Manual ROI in maximal lesion CBF. Normalised to contralateral normal white matter.

Target condition and reference standard

All cases had histological diagnosis. WHO classification 2016. 12 LG, 14 HG.

Morana, 2018

Study design and setting

Retrospective. 2010-2016. Italy.

Patient sampling characteristics

Total no. of patients: 37

Median age: 9 years (2–17). 19 female, 18 male

Tumour types: gliomas

Index tests

Perfusion technique: DSC and pulsed ASL

Perfusion parameters: rCBV and rCBF

Scanners: 1.5T (Intera Achieva; Philips, Best, the Netherlands)

Acquisition parameters: *DSC*: T2*-weighted single-shot gradient-recalled echo-planar imaging (GRE EPI). TR: 1912ms, TE: 40ms; FA: 75°, Matrix: 128×128, FOV: 240mm, NEX: 1, Acquisition time: 84s. *ASL*: Signal targeting and alternating radiofrequency (EPISTAR) and multislice single-shot echo planar imaging (EPI) readout with parallel imaging (SENSE factor = 2.3). TR: 4000ms, TE: 25ms, FA: 40°, Matrix: 80×77, FOV: 240mm; 30 label/control pairs; labelling slab thickness: 100mm, 20mm gap, PLD: 1500-1800ms, Acquisition time: 248s. No VC.

Use of contrast preload: No

Arterial input function: Determined automatically using cluster analysis techniques.

Post-processing algorithm: Olea Sphere, version SP 3.0, Olea Medica

ROI method: Manual ROI in maximal lesion CBF. Normalised to contralateral normal grey matter.

Target condition and reference standard

All cases had histological diagnosis. WHO classification 2016. 22 LG, 15 HG.

Piccardo, 2019

Study design and setting

Retrospective. 2010-2018. Italy.

Patient sampling characteristics

Total no. of patients: 22

Median age: 9 years (4 - 17). 10 female, 12 male

Tumour types: gliomas

Index tests

Perfusion technique: pulsed ASL

Perfusion parameters: rCBF max

Scanners: 1.5T (Intera Achieva; Philips, Best, the Netherlands)

Acquisition parameters: Signal targeting and alternating radiofrequency (EPISTAR) and multislice single-shot echo planar imaging (EPI) readout with parallel imaging (SENSE factor = 2.3). TR: 4000ms, TE: 25ms, FA: 40°, Matrix: 80×77, FOV: 240mm; 30 label/control pairs; labelling slab thickness: 100mm, 20mm gap, PLD: 1500-1800ms, Acquisition time: 248s. No VC.

Post-processing algorithm: NA

ROI method: Manual ROI in maximal lesion CBF. Normalised to contralateral normal grey and white matter.

Target condition and reference standard

All cases had histological diagnosis. WHO classification 2016. 10 LG, 12 HG.

Testud, 2021

Study design and setting

Retrospective. May 2015 - January 2020. France.

Patient sampling characteristics

Total no. of patients: 46

Mean age: 7 years. 24 female, 22 male

Tumour types: 28 glioma/glioneuronal, 6 ependymal, 12 embryonal

Index tests

Perfusion technique: DSC and pulsed ASL

Perfusion parameters: rCBV, rCBF

Scanners: 1.5 (Aera, Siemens, Erlangen, Germany) & 3T system (Skyra, Siemens, Erlangen, Germany)

Acquisition parameters: DSC: At 3T: TR: 2350ms; TE: 23ms; FA: 90°. At 1.5T: TR 1610ms, TE; 30ms; FA:90°. ASL: At 3T: labelling duration: 700ms, PLD: 1400 - 1900ms, TR: 5000ms, TE: 18.28ms, FA: 180°. At 1.5T: labelling duration: 700ms, PLD: 1800ms, TR: 4000ms, TE: 36.32ms, FA: 180°. No VC. NSA, FOV, Partitions & Matrix: NA

Use of contrast preload: No

Arterial input function: Determined automatically using cluster analysis techniques.

Post-processing algorithm: Olea Sphere software (v. SP3.0 16, Olea Medical, Canon)

ROI method: Manual ROI in maximal lesion CBV. Normalised to contralateral normal white matter.

Target condition and reference standard

All cases had histological diagnosis. WHO classification 2016. 15 LG, 31 HG

Withey, 2021

Study design and setting

Retrospective. Multicentre – 4 centres. November 2005 - May 2017. UK.

Patient sampling characteristics

Total no. of patients: 85

Mean age: 8 years. 37 female, 48 male

Tumour types: 41 glioma/glioneuronal or neuronal, 27 embryonal, 9 ependymal, 4 choroid plexus tumour, 1 craniopharyngioma, 1 chordoma, 2 pineoblastoma

Index tests

Perfusion technique: DSC

Perfusion parameters: rCBV

Scanners and acquisition parameters: Various as demonstrated below.

Center	1		2	3	4		
Scanner type	Siemens Avanto	Philips Achieva	Siemens Verio	Philips Achieva	Philips Achieva	Philips Achieva	Philips Achieva
Field strength	1.5 T	3 T	3 T	3 T	1.5 T	3 T	3 T
Head coil	12-element head	32-channel	32-channel	SENSE head-8	SENSE-NV-16	SENSE head-8	SENSE head-8
Sequence	GE-EPI	GE-EPI	GE-EPI	GE-EPI	sPRESTO	sPRESTO	GE-EPI
TR (ms)	1,490–1,643	1,830–1,865	1,570	1,666–2,343	16.7–17.2	15.5–16.0	582–1,866
TE (ms)	40	40	29	40	24.7–25.2	23.5–24.0	18.4–40.0
Flip angle (°)	20	20	45	75	7	7	20–40
Slice thickness (mm)	5.0	3.5	3.5	4.0	3.5	3.5	3.5–7.0
No. slices	19–21	30	16	25–35	30–36	30–34	30
No. dynamics	60	60	60	40	60	60	40–60
Field-of-view (mm)	230×230	240×240	220×220	224×224	220×220	230×230	240×240
Matrix	96×96	96×96	64×64	128×128	64–80×64–80	128×128	96×96
SENSE?	Y	Y	N	Y	Y	Y	Y
Temporal resolution (s)	1.5–1.6	1.8–1.9	1.6	1.7–2.3	1.3–1.6	1.2–1.4	0.6–1.9
Total scan time (s)	90–99	110–112	94	67–94	77–94	71–83	70–118
Pre-bolus	Y	Y	N	Y	Y (n=12), N (n=15), NA (n=9)		

ROI method: Manual ROI in maximal lesion CBV. Normalised to contralateral normal white matter.

Target condition and reference standard

All cases had histological diagnosis. WHO classification 2002, 2007, 2016. 45 LG, 40 HG