Combination of high-resolution susceptibility-weighted imaging and the apparent diffusion coefficient: added value to brain tumour imaging and clinical feasibility of non-contrast MRI at 3 T

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ABSTRACT. The purpose of this study was to determine the benefit of high-resolution susceptibility-weighted imaging and the apparent diffusion coefficient for brain tumour imaging, and to assess the clinical feasibility of using a non-contrast MR protocol at 3 T. 73 patients with intra-axial tumours were enrolled into the study. Two experienced neuroradiologists reviewed three MRI sessions: (i) a non-contrast protocol including high-resolution susceptibility-weighted images and apparent diffusion coefficient; (ii) a contrast protocol including MR perfusion images; and (iii) combined contrast and non-contrast protocols. The two observers categorised tumours as glial or non-glial tumours, and then subcategorised the gliomas into low-grade or high-grade tumours. For semi-quantitative analysis, a scoring system based on the degree of intra-tumoral susceptibility signals and the visual apparent diffusion coefficient was used. The two observers diagnosed accurate tumour pathology in 52 (71%) of 73 tumours in the first review, 55 (75%) of 73 tumours in the second review and 61 (84%) of 73 tumours in the third review. The addition of the non-contrast protocol to the contrast protocol significantly differentiated glioblastoma multiforme and metastatic tumours, which was not possible with the contrast protocol alone. The sensitivity, specificity, positive predictive value and negative predictive value for glioma grading with the non-contrast protocol were 83.2%, 100%, 100% and 79.3%, respectively. The addition of both high-resolution susceptibility-weighted imaging and the apparent diffusion coefficient improved the diagnostic performance of the contrast MR protocol for brain tumour imaging and could be feasible in selected patients who cannot tolerate a contrast agent.

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Contrast-enhanced (CE) conventional MRI, which is commonly used in the evaluation of brain tumours, is usually included as part of the routine brain tumour imaging protocol in most institutions. Although conventional MRI with gadolinium-based contrast agents is useful for the detection and structural characterisation of brain tumours, enhancement after gadolinium reflects disruption of the blood–brain barrier rather than a true assessment of tumour vascularity [1, 2]. Recently, a number of advanced MRI techniques, such as MR perfusion, have been developed to provide biological and physiological information for the assessment of brain tumours [3, 4]. Dynamic susceptibility contrast (DSC) MR perfusion imaging has provided physiological information that allows the evaluation of neovascularity and angiogenesis in brain tumours [5, 6].

High-resolution susceptibility-weighted MR imaging (HR-SWI) is a three-dimensional gradient-echo technique that is sensitive to local tissue magnetic susceptibility and is blood oxygen level dependent [7–9]. This new imaging

technique has largely been used for the detection of micro-venous structures, as well as for the detection of extravascular blood products [10, 11]. The development of 3 T MR scanners and parallel imaging techniques has enabled an increase in the speed, coverage and signal-to-noise ratio of MR images. Therefore, this new technique could be suitable for the examination of patients with various brain disorders in order to obtain high spatial resolution with a reasonable acquisition time.

As has been demonstrated in previous reports, HR-SWI has the potential to assess non-invasively the intratumoral microvasculature associated with fast-growing tumours [12, 13]. Diffusion-weighted imaging (DWI) provides information about tumour cellularity and structural integrity by measuring differences in the apparent diffusion coefficient (ADC) [14, 15]. HR-SWI and DWI do not require contrast administration. Although gadolinium-based contrast agents are widely used in the clinical setting for the assessment of brain tumours, HR-SWI and DWI can be integrated easily into a conventional MR examination at any time, as long as no contrast agent is administered. A non-contrast MR protocol can also be applied to patients in whom are contrast agents contraindicated or who cannot tolerate a bolus injection of contrast medium.

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The purpose of this study was to determine the benefit of HR-SWI and the ADC for brain tumour imaging protocols, including MR perfusion imaging, and to assess the clinical feasibility of the use of non-contrast MR protocols, including HR-SWI and the ADC, at 3 T.

Methods and patients

Study population

Between May 2006 and February 2009, 73 consecutive patients with histologically proven intra-axial brain tumours were enrolled into the study. All study patients underwent HR-SWI, DWI and DSC MR perfusion imaging, as well as conventional structural MRI, before undergoing a surgical biopsy and/or resection. There were 31 male and 42 female patients, and the age of the patients ranged from 19 to 75 years, with a mean age of 43 years. An experienced neuropathologist performed the histopathological evaluation. All tumours were pathologically proven by means of either a stereotactic resection ($n=47$) or a stereotactically guided biopsy ($n=26$) and were classified in accordance with the revised World Health Organization (WHO) system of brain tumours [16].

MRI protocol

MRI was performed using a 3 T system (Achieva; Philips Medical Systems, Best, the Netherlands) with an eight-channel head coil and sensitivity encoding (SENSE). Our brain tumour imaging protocol included the following MR sequences: axial fast spin-echo T_2 weighted imaging (repetition time (TR)/echo time (TE), 3000/80 ms), axial spin-echo T_1 weighted imaging (TR/TE, 495/10 ms), conventional gradient-echo image (T_2^* weighted), DWI, HR-SWI, DSC MR perfusion, and contrast-enhanced axial and coronal T_1 weighted imaging. Axial DWI was performed using a single-shot spin-echo echo-planar sequence with the following parameters: b -value, 1000 s mm⁻²; field of view (FOV), 220 × 220 mm; matrix size, 128 × 128; section thickness, 5 mm; and total acquisition time, 1 min 24 s.

HR-SWI was performed according to the technique previously described [9, 10]. The detailed image parameters for HR-SWI were as follows: flow-compensated three-dimensional gradient-echo sequence; TR/TE, 24/34 ms; flip angle, 10°; FOV, 200 × 200 mm; matrix, 332 × 332; section thickness, 3 mm; slab thickness, 135 mm; and total acquisition time, 4 min 2 s.

DSC MR perfusion imaging was performed with gradient-echo echo-planar sequences during the administration of a standard dose of 0.1 mmol kg⁻¹ of gadolinium dimeglumine (Magnevist; Schering, Berlin, Germany) per kilogram of body weight at a rate of 4 ml s⁻¹ with an MR-compatible power injector (Spectris; Medrad, Pittsburgh, PA). The bolus of contrast material was followed by a 20 ml bolus of saline that was administered at the same injection rate. The detailed imaging parameters for DSC MR perfusion were as follows: TR, 1407 ms; TE, 40 ms; flip angle, 35°; FOV, 24 cm; and matrix, 128 × 128. The total acquisition time for DSC MR perfusion imaging was 1 min 30 s.

DSC MR perfusion imaging was performed using the same section orientations and coverage as those used for conventional MRI and HR-SWI. The temporal resolution of our DSC MR perfusion technique was ~1.42 s. All imaging data were transferred from the scanners to an independent PC for quantitative analysis. Perfusion parametric maps were obtained by using a dedicated software package (Nordic ICE; Nordic Imaging Lab, Bergen, Norway). After eliminating recirculation and leakage of contrast agent with γ -variate curve fitting, the relative cerebral blood volume (rCBV) was computed by means of a numeric integration of the curve.

Image analysis

The benefit of using HR-SWI and ADC in a brain tumour imaging protocol was assessed. In addition, the diagnostic performance of a non-contrast-enhanced (NCE) protocol and the diagnostic performance of a CE MRI protocol were compared for the differentiation and grading of intra-axial tumours. Each observer reviewed the MR images of 73 intra-axial tumours 3 times. Three review sessions were spaced 4 weeks apart to avoid recall bias, and each review session consisted of qualitative and (semi-)quantitative analyses (Figure 1).

In the first review, the observers were given the NCE MRI protocol, including T_2 weighted images, T_1 weighted images, DWI with the ADC, conventional gradient-echo images (T_2^* weighted images) and HR-SWI. For the qualitative analysis, two observers independently categorised the tumours as glial or non-glial, and then subcategorised the gliomas into low-grade or high-grade tumours. As a last step, the observers attempted to make a histopathological diagnosis of the tumour type based on conventional MRI findings, the intratumoral susceptibility signal (ITSS) seen on HR-SWI and the visual ADC. A final decision was achieved by consensus.

The ITSS was defined as being from either low-signal tubular structures or dot-like structures with or without conglomeration within a tumour, as depicted on HR-SWI. Intratumoral calcifications and haemorrhage, which could cause similar findings to the ITSS, were excluded based on the findings of conventional MR images with or without gradient-echo image and susceptibility artefacts, as seen on DWI.

For the semi-quantitative analysis, the two observers assessed independently the degree of the ITSS and the visual ADC scores for glioma grading. The degree of the ITSS was divided into four grades. Grade 0 was defined as no ITSS; grade I as 1–5 dot-like or tubular ITSSs; grade II as 6–10 dot-like or tubular ITSSs; and grade III as ≥ 11 dot-like or tubular ITSSs in the selected imaging slice that visually showed the maximum frequency of the ITSS within a tumour (Figure 2). For statistical purposes and quick analyses, combined with the ITSS grade on HR-SWI, the ADC of all tumours was scored visually. For scoring of the visual ADC, the interpretation was based on the appearance of normal white matter and cerebrospinal fluid (CSF). A four-point scoring system was as follows: an ADC less than the white matter indicated a low ADC (four points); an ADC equal to the white matter indicated a medium ADC (three points); an ADC greater

Figure 1. Diagram of three MR imaging review sessions used in the present study.

than the white matter and less than the CSF indicated a high ADC (two points); and an ADC equal to the CSF indicated a very high ADC (one point).

In the second review, the reviewers were given the CE MRI protocol, including T_2 weighted images, T_1 weighted images, conventional gradient-echo images (T_2^* weighted images), DSC MR perfusion and CE T_1 weighted images. The step of qualitative analysis was the same as for the first review session. For the quantitative analysis, regions of interest that contained the complete tumour were drawn in each section according to the combined overlay and underlay information, with care taken to avoid areas of necrosis, cysts or non-tumour macrovessels that were evident on the CE T_1 weighted images. T_2 high signal intensity areas thought to represent tumour tissue were used to define the outermost tumour margin. Histograms were then generated by classifying the normalised CBVs in each region of interest into a predefined number of bins. Finally, the maximum value of the normalised $rCBV_{max}$ was recorded onto the x-axis of the histogram.

In the third review, the reviewers were provided with both the NCE and CE MRI protocols. To compare the benefit of the NCE protocol with the CE protocol for brain tumour imaging, the third review was performed with qualitative analysis alone. The observers recorded the time needed to perform the analysis of each review session. The level of interobserver variability was assessed for the ITSS, ADC scoring and $rCBV_{max}$ measurements. The qualitative and semi-quantitative results of the three review sessions were compared with the pathological tumour classification and grade. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of each imaging protocol were calculated for the correct identification of glial and non-glial tumours, and for low- and high-grade gliomas.

Statistical analysis

The relationship between qualitative imaging diagnosis or grading and the final pathological diagnosis was

analysed using the Pearson χ^2 test for statistical significance. The intraclass correlation coefficient (ICC) was used to determine the level of interobserver variability in the semi-quantitative analyses of two imaging protocols. Receiver operating characteristic (ROC) curve analyses were performed to determine the optimum thresholds and diagnostic accuracy of NCE and CE MRI protocols for determining high-grade tumours. This analysis permitted the determination of the sensitivity, specificity, PPV and NPV associated with each quantitative parameter of HR-SWI, the ADC maps and DSC MR perfusion images as a function of the threshold value used to identify high-grade and low-grade gliomas. We analysed the Pearson χ^2 and ICC using the SPSS statistical package (version 13.0; SPSS, Chicago, IL) and the ROC curve using the MedCalc statistical package (MedCalc Software, Mariakerke, Belgium). The areas under the ROC curves were compared among the MRI protocols. All p -values were two-tailed, with $p=0.05$ being the criterion for statistical significance.

Results

Pathological diagnosis

The final pathological diagnoses comprised 25 non-glial tumours and 48 glial tumours. Of the 25 non-glial tumours, there were 15 metastatic tumours, 7 lymphomas and 3 central neurocytomas. Of the 48 glial tumours, there were 12 low-grade astrocytomas (WHO grade II), 4 low-grade oligodendrogliomas (WHO grade II), 7 anaplastic astrocytomas (WHO grade III) and 25 glioblastoma multiforme (GBMs; WHO grade IV).

Added value of HR-SWI and the ADC to brain tumour imaging protocols

The additional acquisition time for HR-SWI and DWI with the ADC was 5 min 26 s. The two observers diagnosed accurate tumour pathology in 52 (71%) of 73

Figure 2. The grade of intratumoral susceptibility signals (arrows) on a high-resolution susceptibility-weighted image. (a) grade 1. (b) grade 2. (c) grade 3.

tumours in the first review, 55 (75%) of 73 tumours in the second review and 61 (84%) of 73 tumours in the third review. ITSSs were seen in 25 (100%) of 25 GBMs, in 4 (57%) of 7 anaplastic astrocytomas, in 11 (73%) of 15 metastatic tumours and in 1 (33%) of 3 central

neurocytomas. There was no evidence of ITSS in low-grade astrocytomas, low-grade oligodendrogliomas or lymphomas. Table 1 shows the comparison of ITSS grade, mean visual ADC score and mean $rCBV_{max}$ among each pathological tumour type. The CE protocol

Table 1. Comparison of ITSS grade, mean visual ADC score and mean rCBV_{max} among each pathological tumour type

Tumour pathology	ITSS grade				Mean visual ADC score	Mean rCBV _{max}
	0	I	II	III		
Low-grade astrocytoma (n=12)	12(100%)	0(0%)	0(0%)	0(0%)	2.0	1.72
Low-grade oligodendroglioma (n=4)	4(100%)	0(0%)	0(0%)	0(0%)	2.0	2.63
Anaplastic astrocytoma (n=7)	4(57%)	3(43%)	0(0%)	0(0%)	2.4	3.36
Glioblastoma multiforme (n=25)	0(0%)	1(4%)	3(12%)	21(84%)	3.6	5.67
Metastasis (n=15)	4(27%)	2(13%)	3(20%)	6(40%)	3.1	5.92
Lymphoma (n=7)	7(100%)	0(0%)	0(0%)	0(0%)	3.7	1.82
Central neurocytoma (n=3)	2(67%)	1(33%)	0(0%)	0(0%)	3.0	3.12

ADC, apparent diffusion coefficient; rCBV_{max}, relative cerebral blood volume; ITSS, intratumoral susceptibility signal.

was not able to differentiate significantly between GBMs and metastatic tumours ($p=0.0721$, Pearson's χ^2 test; Table 2). However, the CE protocol with adjunct HR-SWI and the ADC was able to differentiate significantly between GBMs and metastatic tumours, with a sensitivity of 84.0% and a specificity of 60.0% ($p=0.0392$, Pearson's χ^2 test; Table 1). The CE protocol with adjunct HR-SWI and the ADC was also able to differentiate significantly between GBMs and lymphomas, with a sensitivity of 86.7% and a specificity of 100.0% ($p<0.0001$, Pearson's χ^2 test; Table 2). Table 2 shows the p -values of the three MRI protocols for the differentiation of the specific pathological types of intra-axial tumours.

Qualitative analyses of the NCE and CE MR protocols

Based on qualitative analysis, the differentiation between glial and non-glial tumours using the NCE protocol was statistically significant, with a sensitivity of 77.5% and a specificity of 82.6% ($p=0.0295$, Pearson's χ^2 test; Table 2; Figures 3 and 4). The CE protocol also significantly differentiated between glial and non-glial tumours, with a sensitivity of 89.2% and a specificity of 85.7% ($p=0.0252$; Table 2; Figures 3 and 4). For qualitative glioma grading with pathological correlation, both protocols differentiated between low-grade and high-grade gliomas, with statistical significance (Figure 4). The sensitivity and specificity for the determination of high-grade gliomas were 85.2% and 95.6%, respectively, with the NCE protocol, and 93.1% and 87.9%, respectively, with the CE protocol.

Quantitative analyses of the NCE and CE MR protocols

For quantitative analysis, the interobserver agreement between the two reviewers was excellent for the measurement of the ITSS degree (ICC=0.93), ADC scoring (ICC=0.96) and rCBV_{max} (ICC=0.81). For the NCE MR protocol, the sensitivity, specificity, PPV and NPV were 83.2% (95% confidence interval (CI)=80.2–94.5%), 100% (95% CI=54.1–100.0%), 100% and 79.3%, respectively (Table 3; Figure 5a). The optimal threshold values for rCBV_{max} (for the CE protocol) demonstrated a sensitivity, specificity, PPV and NPV of 93.6% (95% CI=81.5–98.7%), 87.5% (95% CI=59.1–98.1%), 91.6% and 86.7%, respectively (Table 3; Figure 5b). ROC curve analyses showed no significant difference in the area under the curve between the NCE and CE MRI protocols (Figure 5c).

Discussion

One of the major findings from the present study is that the combination of HR-SWI and the ADC could provide additional information for the differentiation of glial and non-glial tumours. The ITSS, as depicted on HR-SWI, could significantly differentiate GBMs from lymphomas and low-grade gliomas, with a specificity of 100%. In our study, an ITSS was never seen in a lymphoma or low-grade glioma. The combination of no ITSS and a low ADC can be very specific for the diagnosis of a lymphoma. The CE protocol with adjunct HR-SWI and the ADC could differentiate GBMs from solitary metastatic tumours. In our study, both GBMs

Table 2. p -Values for the qualitative differentiation between specific pathological groups of intra-axial tumours: comparison of non-contrast-enhanced MR protocol, contrast-enhanced MR protocol, and contrast-enhanced MR protocol with adjunctive HR-SWI and ADC

Tumour pathology	Non-contrast protocol	Contrast protocol	Contrast protocol + HR-SWI and ADC
Glioblastoma vs metastasis	0.0653	0.0721	0.0392
Glioblastoma vs lymphoma	0.0002	0.0037	<0.0001
Glial vs non-glial tumours	0.0295	0.0252	0.0012
High- vs low-grade gliomas	0.0057	0.0015	0.0002

Data were calculated using Pearson χ^2 test for qualitative analyses.

HR-SWI, high-resolution susceptibility-weighted imaging; ADC, apparent diffusion coefficient.

Figure 3. Comparison between non-contrast-enhanced and contrast-enhanced MR protocols in a 72-year-old man with a pathologically proven lymphoma. (a) Transverse contrast-enhanced T_1 weighted image demonstrates strong contrast enhancement in the corresponding lesion. (b) Corresponding apparent diffusion coefficient (ADC) map shows a medium ADC (white arrow; visual ADC scoring of 3 points). (c) Corresponding high-resolution susceptibility-weighted image demonstrates no intratumoral susceptibility signal (ITSS) (black arrow; ITSS of grade 0). The lack of ITSS is an unusual finding in high-grade glioma. (d) Transverse gradient-echo dynamic susceptibility contrast MR perfusion image with contrast leakage-corrected relative cerebral blood volume (CBV) map shows the lesion with relatively high perfusion (arrowhead, maximum relative CBV of 1.77).

Figure 4. Comparison between non-contrast-enhanced and contrast-enhanced MR protocols in a 67-year-old man with a pathologically proven glioblastoma multiforme. (a) Transverse contrast-enhanced T_1 weighted image demonstrates strong contrast enhancement in the corresponding region of peripheral solid tumour. (b) Corresponding apparent diffusion coefficient (ADC) map shows a medium ADC (white arrows; visual ADC scoring of 3 points). (c) Corresponding high-resolution susceptibility-weighted image demonstrates high-grade intratumoral susceptibility signals (ITSSs) (black arrows; ITSS of grade III). The high-grade ITSS and low or medium ADC are typical findings in high-grade glioma. (d) Transverse gradient-echo dynamic susceptibility contrast MR perfusion image with contrast leakage-corrected relative cerebral blood volume (CBV) map shows the lesion with high perfusion (maximum relative CBV of 5.13).

Table 3. Sensitivity, specificity, PPV and NPV of non-contrast and contrast MR protocols for quantitatively determining high-grade glioma (WHO grades III and IV) according to their threshold values

Protocol	Criterion	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Noncontrast MR protocol	≥ 3	90.9	92.3	95.2	85.7
	≥ 4	83.2	100.0	100.0	79.3
Contrast MR protocol	> 1.92	96.3	82.2	87.2	91.5
	> 2.12	93.6	87.5	91.6	86.7

Data were calculated using receiver operating characteristic curve analyses for quantitative analyses. The criterion for non-contrast MR protocol was determined based on the grade of intratumoral susceptibility signals and the visual scoring of the apparent diffusion coefficient.

PPV, positive predictive value; NPV, negative predictive value; WHO, World Health Organization.

and solitary metastatic tumours demonstrated the presence of an ITSS within a tumour. However, the ITSS grade was lower in the metastatic tumours than in GBMs. With the depiction of a high ITSS grade ($\geq$ grade II), it was possible to differentiate between GBMs and solitary metastatic tumours.

The second major finding of our study is that the diagnostic performance of the NCE protocol for the differentiation of intra-axial tumours was comparable to that of the CE protocol. We demonstrated that the NCE MRI protocol could qualitatively differentiate between glial and non-glial tumours and between high- and low-grade gliomas. For example, lymphomas showed high

Figure 5. Diagnostic performance of non-contrast-enhanced and contrast-enhanced MR protocols for determining high-grade glioma (WHO grades III and IV) according to their threshold values. (a) Plot vs criterion values of the NCE MR protocol for determining high-grade glioma (WHO grades III and IV). (b) Plot vs criterion values of the CE MR protocol for determining high-grade glioma (WHO grades III and IV). (c) Receiver operating characteristic (ROC) curve analysis of the NCE and CE MR protocols for correctly identifying high-grade glioma (WHO grades III and IV). The area under the ROC curve for the NCE protocol is 0.95 (95% confidence interval=0.82–0.99) and that for the CE protocol is 0.94 (95% confidence interval=0.81–0.99). rCBV, relative cerebral blood volume; ITSS, intratumoral susceptibility signal.

cellularity on an ADC map and a relatively low grade of ITSS when compared with high-grade gliomas. For quantitative glioma grading, the sensitivity, specificity, PPV and NPV with the use of the NCE protocol were similar to the corresponding values obtained with the CE MRI protocol, including MR perfusion. Moreover, the specificity and PPV were actually high with the use of the NCE protocol, as a positive ITSS and a low ADC were rarely seen in the low-grade tumours in this study. MR perfusion parameters could be a challenge for the grading of oligodendrogliomas. However, four cases of low-grade oligodendrogliomas in this study did not show an ITSS, and this finding was helpful to differentiate low-grade from high-grade oligodendrogliomas.

As a hallmark of brain tumour imaging is the performance of serial imaging, often with intervening surgery and radiation therapy, the uniform application of HR-SWI and the ADC for non-contrast tumour imaging will be limited because of the presence of susceptibility from introduced blood products. Therefore, our results suggest that the NCE MR protocol, including HR-SWI and the ADC, could be an alternative method for screening brain tumours and for initial glioma grading in patients who have a contraindication to contrast medium or who cannot tolerate the bolus injection of contrast medium.

Several previous studies have reported that, when using HR-SWI to evaluate brain tumours, contrast administration could shorten the T_1 relaxation times of the blood, and therefore the extra phase shift could improve signal cancellation in a shorter acquisition time, resulting in a shorter scan time [8, 17, 18]. However, in most institutions, brain tumour imaging protocols usually include contrast enhancement studies, such as CE T_1 weighted images and perfusion MR images. Moreover, DSC MR perfusion imaging has been reported to provide a non-invasive assessment of tumour vascularity that is not available with the use of conventional MRI, and comparisons between rCBV and histological sections have demonstrated a significant correlation between tumour vascularity and maximum tumour rCBV [19–21]. Thus, in clinical practice, combined HR-SWI and contrast enhancement do not provide any advantage over MR perfusion in terms of diagnostic accuracy or acquisition time for glioma grading. In the present study, we performed HR-SWI without contrast administration, and the accuracy for the diagnosis and grading of gliomas was comparable between the NCE and CE protocols. Thus, as diagnostic accuracy is comparable between the NCE and CE MRI protocols, the NCE protocol may be used in routine brain tumour imaging in selected patients. A bolus injection of contrast agent is poorly tolerated in some patients, especially paediatric patients. Moreover, DSC MR perfusion imaging can be affected by changes in the blood–brain barrier and tumour permeability [22]. A NCE MRI protocol has the advantage of being completely non-invasive, and the protocol could be integrated into a conventional MR examination at any time, without preparation of a power injector. Moreover, HR-SWI and ADC results are available immediately after acquisition, with only minimal post-processing, and do not require additional PC-based post-processing, as is required for DSC-MR perfusion.

With the advent of 3 T MR scanners and parallel imaging techniques, the acquisition time of HR-SWI is not excessive when compared with that of MR perfusion imaging. In our imaging protocol, HR-SWI allowed coverage of the whole brain with a 4 min acquisition time. Combining post-processing time and acquisition time, there was no significant difference in the time before image interpretation between the NCE and CE MR protocols.

Our study has several limitations. We did not sub-categorise high-grade gliomas into grades III (anaplastic astrocytoma) and IV (GBM) because of the small number of grade III tumours. Moreover, a relatively small sample size of low-grade tumours (grade II) compared with high-grade tumours (grades III and IV) can lead to over-estimation of the specificity and PPV for the differentiation between high- and low-grade tumours. Further studies with a larger number of grade II and III gliomas should be performed to validate the quantification with the NCE protocol. The quantification of the ITSS can be subjective and is not an interval or ratio scale variable, which would have been more amenable to quantitative statistical analysis. Although a previous study has shown that the ITSS correlated with pathological findings of tumour vascular proliferation, we did not exclude the possibility of other vascular pathologies, such as arteriovenous shunts, contributing to the ITSS. However, the CE protocol has this same limitation, and this finding rarely affects the diagnosis or grading of brain tumours. Moreover, the application of an invasive procedure to exclude other vascular pathologies does not make sense for the diagnosis or grading of brain tumours. Fundamentally, as a hallmark of brain tumour imaging is the performance of serial imaging, often with intervening surgery and radiation therapy, the uniform application of HR-SWI and ADC for noncontrast tumour imaging will be limited because of the presence of susceptibility from introduced blood products.

Conclusions

In conclusion, the addition of both HR-SWI and the ADC could improve the diagnostic performance of a contrast MR protocol for brain tumour imaging. The diagnostic accuracy of the NCE MR protocol, including HR-SWI and the ADC, for both the initial diagnosis and the grading of intra-axial tumours is comparable to that of the CE MR protocol. In terms of image acquisition time and only minimal post-processing, the use of the NCE MR protocol could be feasible in selected patients who have a contraindication to contrast medium or who cannot tolerate a bolus injection of contrast medium.

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