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Susceptibility Imaging in Glial Tumor Grading; Using 3 Tesla Magnetic Resonance (MR) System and 32 Channel Head Coil

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: Susceptibility weighted imaging (SWI) is a velocity compensated, high-resolution three-dimensional (3D) spoiled gradient-echo sequence that uses magnitude and filtered-phase data. SWI seems to be a valuable tool for non-invasive evaluation of central nervous system gliomas. Relative cerebral blood volume (rCBV) ratio is one of the best noninvasive methods for glioma grading. Degree of intratumoral susceptibility signal (ITSS) on SWI correlates with rCBV ratio and histopathological grade. This study investigated the effectiveness of ITSS grading and rCBV ratio in preoperative assessment.

Material/Methods: Thirty-one patients (17 males and 14 females) with histopathogical diagnosis of glial tumor undergoing routine cranial MRI, SWI, and perfusion MRI examinations between October 2011 and July 2013 were retrospectively enrolled. All examinations were performed using 3T apparatus with 32-channel head coil. We used ITSS number for SWI grading. Correlations between SWI grade, rCBV ratio, and pathological grading were evaluated. ROC analysis was performed to determine the optimal rCBV ratio to distinguish between high-grade and low-grade glial tumors.

Results: There was a strong positive correlation between both pathological and SWI grading. We determined the optimal rCBV ratio to discriminate between high-grade and low-grade tumors to be 2.21

Conslusions: In conclusion, perfusion MRI and SWI using 3T MR and 32-channel head coil may provide useful information for preoperative glial tumor grading. SWI can be used as an accessory to perfusion MR technique in preoperative tumor grading.

MeSH Keywords: Glioma • Magnetic Resonance Imaging • Neuroradiography

PDF file: http://www.polradiol.com/abstract/index/idArt/900374

Background

Preoperative magnetic resonance (MR) examination has a very important role in detection and differential diagnosis of intracranial tumors, decisions with regard to planning of treatment and surgery, as well as guidance for stereotactic biopsy procedure. Although conventional MRI provides helpful information about intracranial tumors, it is inadequate for tumor characterization and grading. In order to further evaluate the internal structure of the tumor and improve preoperative grading, various MRI techniques are being used, such as MR perfusion, MR spectroscopy and diffusion MR [1–3].

Malignant potential is proportional to the extent of neovascularity in intracranial tumors. Furthermore, intratumoral necrosis and hemorrhage are the factors associated with poor prognosis. Perfusion of the lesions can be indirectly estimated using dynamic susceptibility contrast (DSC) perfusion MR. Contrast enhancement in conventional T1-weighted images most likely results from disruption of the blood-brain barrier. However, perfusion imaging may

demonstrate intratumoral neovascularity. The relative tumor blood volume (rCBV) ratio increases with increasing vascularity; thus, it can be used for grading [1,4,5].

Susceptibility-weighted imaging (SWI) is a velocity compensated high-resolution 3D spoiled gradient-echo sequence that utilizes magnitude and filtered-phase information [6]. Filtered phase image could be used to distinguish hemorrhage from calcification. SWI minimum intensity projection (MinIP) images can be particularly useful in vascular disorders [2,7]. However, the SWI technique is generally time consuming and therefore, it is not used in routine neuroradiology practice. With the advent of parallel imaging techniques and clinical 3T MRI systems, imaging time has been shortened to reasonable durations [6–8].

Previous studies indicate that SWI technique is superior to conventional MRI with regard to assessment of glial tumors and provides valuable information in terms of tumor grading [2,3,9,10]. SWI may demonstrate internal architecture and intratumoral susceptibility signal (ITSS) caused by vascularization, hemorrhage or necrosis that cannot be shown by conventional MRI. Pinker et al. [3] reported that ITSS identified using SWI correlated with the results of positron emission tomography (PET) and histopathological examination. Park et al. [9] suggested that intratumoral ITSS could indicate vascularity, hemorrhage, or necrosis. They also reported that SWI was correlated with the findings in DSC perfusion MRI and histopatological grade.

High-grade glial tumors are usually characterized by increased vascularity and hemorrhages within the lesions. There is a well-known correlation between SWI findings and both intratumoral hemorrhaging and vascularity [2]. There are many grading systems for glial tumors using SWI technique [8,11,12]. However, there is no consensus with regard to the superiority of some grading systems over another. The degree of (ITSS) on SWI correlates with rCBV ratio and histopathological grade [8,11]. This study investigated the usefulness of SWI grading and rCBV ratio for preoperative tumor grading.

Material and Methods

Patients

Thirty-one patients (17 males and 14 females) with histopathogically diagnosed glial tumors that had undergone routine cranial MRI, SWI, and DSC perfusion MRI scanning between October 2011 and July 2013 were retrospectively enrolled. The study protocol was approved by the local ethics committee and all patients gave written informed consent before the procedure. None of the patients have undergone radiotherapy, chemotherapy or surgical treatment of the lesion before the MR examination. There were no reported serious adverse events due to MR examination or use of contrast agents. An experienced neuropathologist graded the gliomas according to WHO 2007 classification [13].

MR imaging protocol and image analysis

ITSS number was used for SWI grading according to the definition of Park et al. [9]. All examinations were performed using the clinical 3T MR imaging system (Achieva; Philips Healthcare, Best, Netherlands) with a 32-channel head coil. For conventional MR study, axial 3D turbo field echo (TR/TE=8.1/3.7 ms), axial T2-weighted turbo spin-echo (TR/TE=3000/80 ms), and axial post-contrast 3D- Turbo field echo sequences were acquired.

Venous BOLD imaging, which is a flow-compensated T2*-weighted, 3D gradient-echo sequence, was used. Imaging parameters were as follows: TR/TE, 21/29 ms; flip angle, 10°; FOV, 220×220 mm; section thickness, 0.6 mm; ETL, 1 k-space; NEX 2. Source images were axial and reformatted using MinIP technique with section thickness of 4 mm and –1 mm gap (scanning time: 6 minutes).

DSC MR perfusion imaging was performed using gradient-echo echo-planar sequences during the administration of a standard dose (0.2 ml/kg of body weight) of gadoteratemeglumine (Dotarem, Guerbet, Villepinte, France) at a rate of 4–5 ml/s using an MR-compatible power injector (Medrad, Spectris Solaris EP MR Injection System). The bolus of contrast was followed by a 40-ml bolus of saline that was administered at the same injection rate. The detailed imaging parameters for DSC MR perfusion were as follows: image number: 960, TR/TE: 1513/40 ms; flip angle: 75°; FOV: 224 mm; and Voxel size: 2.33/2.33/5 mm, slice thickness/gap: 5/0 mm, dynamic number 40, and scan time 1.05 min. Arterial input function model was used for DSC data processing. Middle cerebral artery (MCA) was selected as an arterial input for assessing CBV maps. For obtaining normalized values, the corresponding region on the contralateral hemisphere was used and rCBV ratios were evaluated.

For image analysis, ITSS number was used as reported by Park et al. [9]. Standard SWI minIP reformatted images of 31 patients were analyzed by two radiologists blinded to histopathological diagnoses. The strength of ITSS was divided into 4 grades: grade 0 was defined as no ITSS, grade 1 was defined as 1–5 ITSS, grade 2 was defined as 6–10 ITSS, and grade 3 was defined as ≥11 ITSSs within the maximum ITTS seen in tumor slices [9,11]. SWI grades 0 and 1 were accepted as low-grade and 2 and 3 were considered high-grade. Gliomas were classified into two groups as low-grade (grade 1 and 2) and high-grade (grade 3 and 4) according to WHO 2007 classification. ITSS due to calcifications was not taken into account during image analysis. Coarse intratumoral calcifications were excluded using computed tomography (CT). Image analysis was performed with Extended MR workspace (Version 2.6.3.2, 2009, Philips Medical Systems) using special application tools, such as ''neuro perfusion'' and ''volume imaging'' for DSC-PMRI and SWI, respectively.

Statistical analysis

SPSS v. 13 for Windows (SPSS Inc, Chicago, Illinois, USA) was used for statistical analyses. Categorical data were expressed as numbers and percentages, while continuous data were expressed as means ± standard deviations. Categorical variables were compared using Pearson's chi-square and Fischer's exact tests. The agreement between radiological and pathological grading was assessed using Kappa coefficient. Continuous variables were compared

Table 1. Patients list, pathologic grades, SWI grades and rCBV ratios.

Patient No	Age/gender	Pathologic diagnose	WHO 2007 pathologic grade	rCBV	SWI grade
1	68/M	GBM	4	4.40	3
2	57/M	GBM	4	4.13	2
3	26/F	GBM	4	3.00	3
4	61/F	GBM	4	3.78	3
5	56/F	GBM	4	6.58	3
6	71/M	GBM	4	3.13	3
7	58/M	GBM	4	8.15	3
8	56/M	GBM	4	5.77	3
9	51/F	GBM	4	1.89	3
10	48/F	GBM	4	2.80	3
11	57/F	GBM	4	2.94	3
12	57/F	GBM	4	2.88	3
13	74/F	GBM	4	5.13	3
14	55/F	GBM	4	7.14	3
15	52/M	GBM	4	4.67	3
16	72/M	GBM	4	6.05	3
17	46/M	GBM	4	3.39	3
18	62/M	GBM	4	3.84	3
19	48/F	Astrocytoma	3	2.27	1
20	24/F	Oligodendroglioma	2	0.72	0
21	45/M	Oligodendroglioma	2	0.91	1
22	53/F	Oligodendroglioma	2	1.19	0
23	33/M	Oligodendroglioma	2	1.26	3
24	47/M	Oligodendroglioma	2	1.32	1
25	64/M	Oligodendroglioma	2	0.81	0
26	59/M	Oligodendroglioma	2	1.83	0
27	59/M	Oligodendroglioma	2	2.32	1
28	41/M	Oligodendroglioma	2	2.13	0
29	37/M	Oligodendroglioma	2	1.09	0
30	24/F	Mixedoligoastrocytoma	2	1.01	1
31	46/F	Astrocytoma	2	2.15	2

Table 2. Demographical features of patients with low and high grade tumors.

WHO grade	Low grade	High grade	p
Gender (M/F)	8/4	9/10	0.46
Age (mean ±SD)	44.3±13.2	56.6±11	0.009

SD – standard deviation; M – male; F – female.

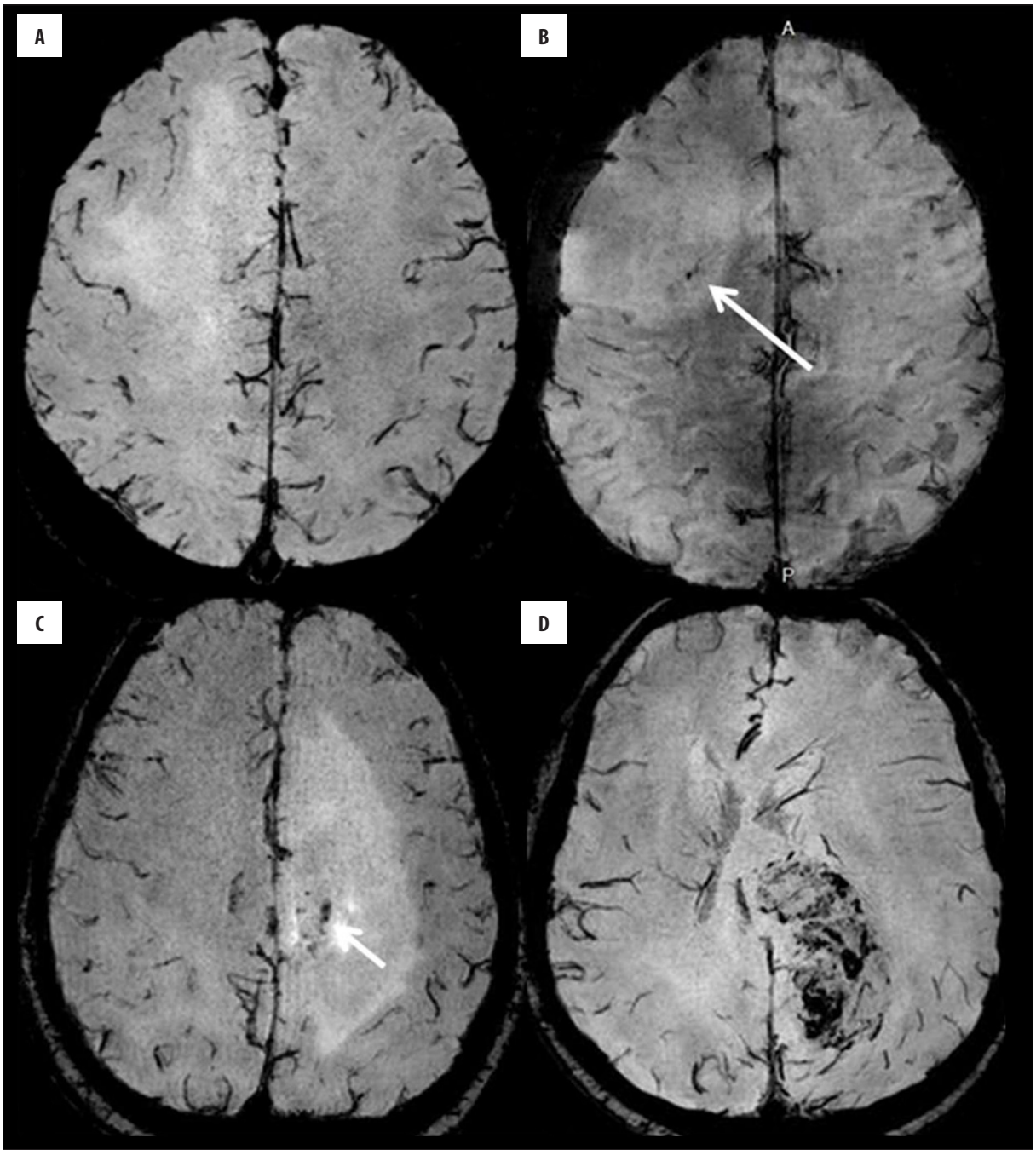

Figure 1. SWI grades based on ITSS numbers. (**A**) Right frontal tumor (oligodendroglioma) – no ITSS in the tumor, SWI grade 0; (**B**) Right frontal tumor (oligodendroglioma) – one ITSS (arrow), SWI grade 1; (**C**) Left frontoparietal tumor (astrocytoma) – more than five ITSS in the tumor (arrow), SWI grade 2; (**D**) Left parietal tumor (glioblastoma) – numerous ITSS in the tumor, SWI grade 3.

with Student's t-test. Correlations between SWI grade, rCBV ratio, and pathological grading were evaluated with Spearman's correlation analysis. We considered a coefficient of 0.1–0.3 as weak, 0.3–0.5 as moderate, and >0.5 as strong correlation and p value of less than 0.05 as statistically significant. Receiver operator characteristics (ROC) analysis was performed to determine the optimal rCBV ratio to distinguish high-grade from low-grade glial tumors.

Results

Of the 33 tumors, 12 were low-grade (10 oligodendrogliomas, 1 astrocytoma, 1 mixed oligoastrocytoma) and 19 were high-grade (18 glioblastomas, 1 anaplastic astrocytoma) (Table 1). The patients with high-grade tumors were older, while there was no statistically different difference with respect to gender (Table 2). All patients underwent surgery or stereotactic biopsy after the MR examination and the diagnoses were confirmed histopathologically. Most of the low-grade gliomas were oligodendrogliomas.

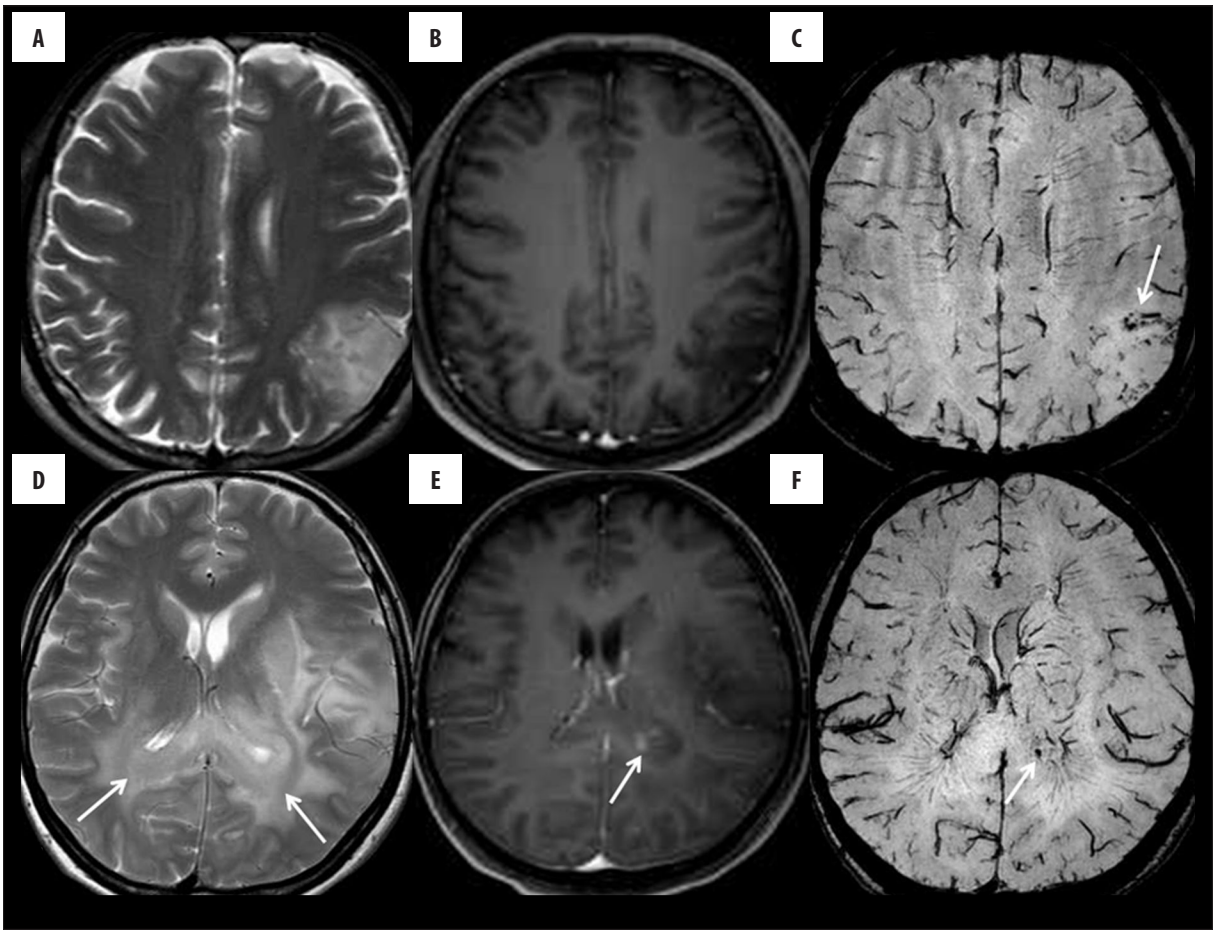

Figure 2. Left parietal oligodendroglioma. T2-weighted imaging shows hyperintense lesion (**A**) and there is no contrast enhancement shown in T1-weighted imaging (**B**). More than ten ITSS within the tumor and SWI grade 3 (**C**) From the other side, a butterfly astrocytoma (WHO grade 3); T2 weighted imaging demonstrates a bilateral hyperintense lesion (arrows) (**D**). There is minimal, punctate contrast enhancement (arrow) in the left side of corpus callosum (**E**), one ITSS (arrow) and SWI grade 1 (**F**).

Nearly all of the oligodendroglimas seemed homogenous and only one oligodendroglioma contained a coarse calcification. None of the oligodendrogliomas contained remarkable cystic areas.

The SWI grades were mostly grade 3 (n=18). SWI grades of 0, 1 and 2 were seen in 6, 5 and 2 patients, respectively (Figure 1). Only 2 of 20 tumors considered high-grade according to SWI grading were histopathologicaly verified to be low-grade. On the other hand, among 19 high-grade tumors according to histopathology, only one was graded low according to SWI grading (Figure 2). There were strong, positive correlations between pathological grade and both SWI grade ($r=0.87$, $p<0.001$) and rCBV ratio ($r=0.83$, $p<0.001$, Figure 3). There was a strong agreement between SWI and pathological gradings (Kappa=0.793, $p<0.001$, Table 3).

Nearly all of the low-grade tumors were oligodendrogliomas (n=10) and almost all high-grade tumors were glioblastomas. In SWI evaluation seventeen glioblastomas were evaluated as ITSS grade 3. One glioblastoma was evaluated as grade 2. Three of ten olidendrogliomas were evaluated as grade 1 and six oligodendrogliomas I grade 0. Only one oligodendroglioma showed more than ten ITSS, like glioblastomas, and was evaluated as grade 3.

Mean rCBV ratios were significantly higher for pathologically high-grade tumors (Table 4). Optimal rCBV ratio to discriminate between high-grade and low-grade tumors was found to be 2.21 (area of under the curve 0.982, $p<0.001$, sensitivity 94.7%, specificity 91.7%, positive predictive value 94.7%, negative predictive value 91.7%, Figure 4).

Discussion

Venous BOLD is a kind of SWI sequence that uses susceptibility contrast. A long scanning time due to long echo sequence time at 1.5T and high resolution is sometimes a limitation of SWI [8]. 3T MR system with increased contrast-to-noise ratio (CNR), multichannel coils and parallel imaging methods have reduced acquisition times [2,7,8,14] . Moreover, sensitivity encoding (SENSE) technique suppressed the susceptibility artifact [15,16]. In this study we used a 3T MR system, 32-channel head coil and SENSE parallel imaging method. Therefore, acquisition time was reduced to nearly six minutes. 3D venous BOLD image thickness was 0.6 mm. Acquisition time may be reduced to a more reasonable time provided that the image thickness is increased. Source MR images were processed at a workstation and created standard minIP reformatted images.

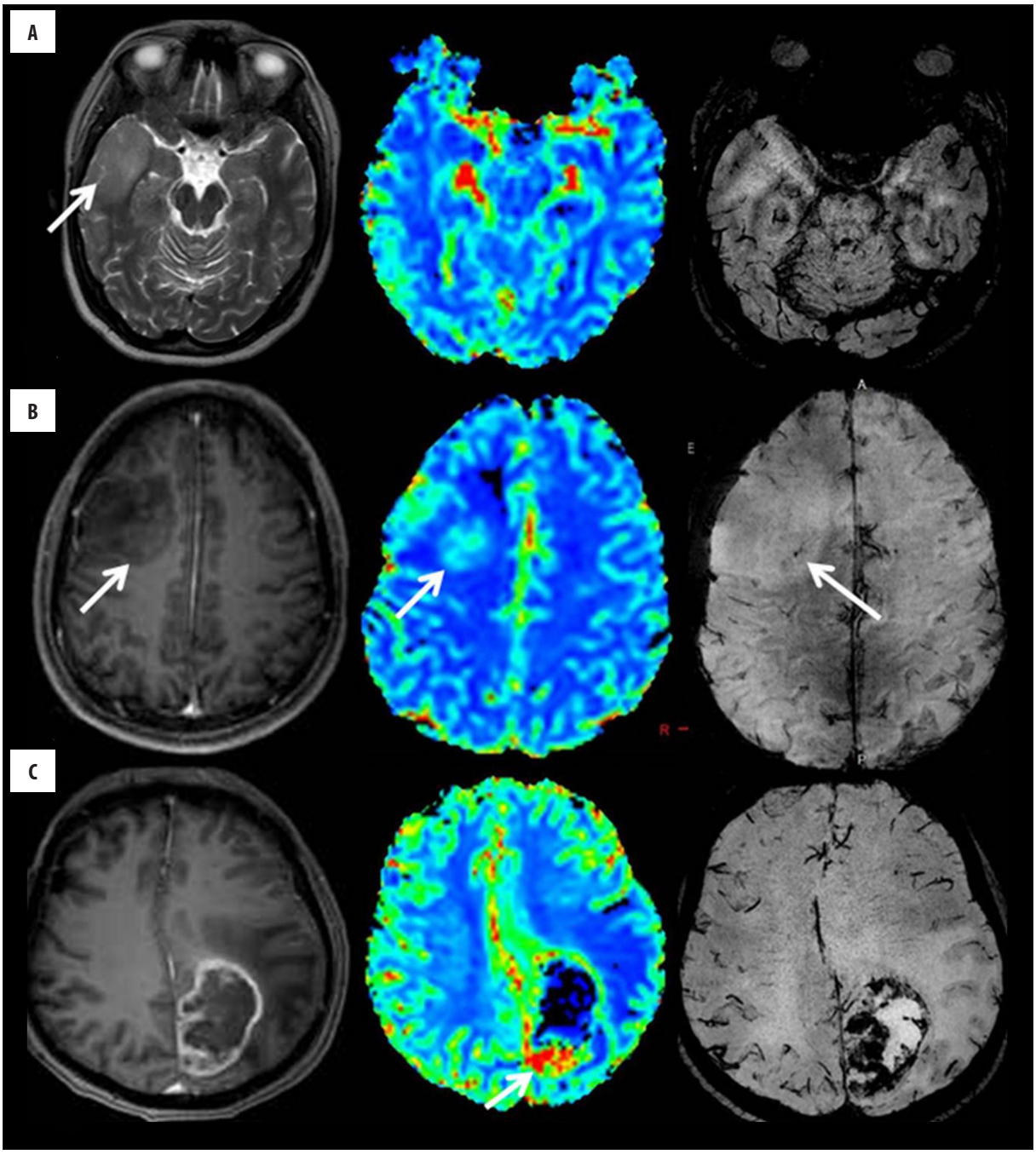

Figure 3. (**A**) Right temporal oligodendroglioma – the tumor is slightly hyperintense in T2-weighted imaging (arrows); no ITSS in the tumor, SWI grade 0 and no perfusion anomalies. (**B**) Right frontal WHO grade 2 oligodendroglioma – T1 weighted imaging shows perceivable contrast enhancement (arrow). CBV map shows moderate hyperperfusion (arrow), rCBV ratio is 2.32. There is one ITSS (arrow) and SWI grade is 1. (**C**) Left parietooccipital glioblastoma - T1-weighted imaging shows rim enhancement, CBV map demonstrates significant hyperperfusion on the posterior side of the tumor, rCBV ratio is 3.78. There are numerous ITSS (arrow), SWI grade is 3.

SWI minIP images improved visualization of hypointense susceptibility signals such as venous structures or hemorrhages [6,17].

Most significant finding of this study is a strong, positive correlation between pathological grade and both SWI grade and rCBV ratio. We found the rCBV ratio cutoff value for high-grade gliomas to be 2.21 in this study. This is slightly higher than the values determined in previous studies, which suggested cutoff values between 1.75 and 2.00 [1,4,18]. In this study most of the low-grade tumors were oligodendrogliomas (10 of 12 low-grade tumors). We suggest that the rCBV ratio for low-grade oligodendrogliomas could be higher than for low-grade astrocytomas [19].

In most of cases, MR perfusion is can clearly differentiate low-grade from high-grade gliomas and is one of the most preferred MR techniques for the evaluation of

Table 3. The agreement between SWI and pathological grade.

		Pathological grade		Total
		Low	High	
SWI grade	Low	10	1	11
	High	2	18	20
Total		12	19	31

Table 4. pathologic grade and rCBV ratios.

	Min–Max rCBV	Mean rCBV ±SD	P
Low grade	0.72–2.32	1.4±0.56	<0.001
High grade	1.89–8.15	4.3±1.74	

Min – minimum; Max – maksimum; Sd – standart deviation.

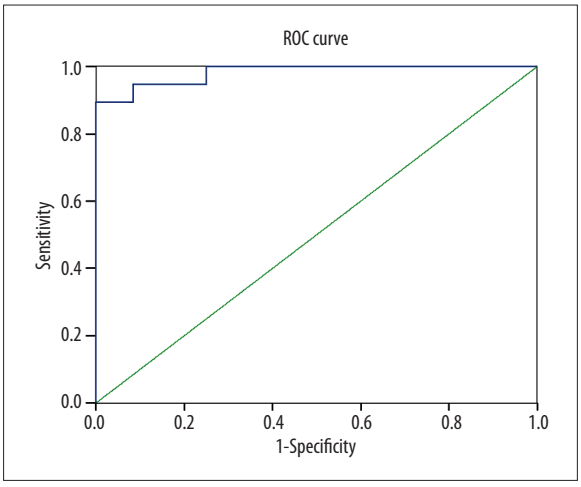

Figure 4. ROC curve analyses. Area under the ROC curve is equal to 0.982, p value <0.001, 95% confidence interval: (0.95–1.02). For the cut-off value of 2.21206 sensitivity is % 94.7 and specificity is 91.7%; ositive predictive value 94.7%, ad negative predictive value 91.7%.

gliomas. SWI and rCBV ratio provides similar results with respect to glial tumor grading [6,9]. Recently, many studies have shown that SWI could be used for tumor evaluation [2,3,8,9,11]. Li et al. [2] reported that SWI could show intratumoral hemorrhage and vascularity better than other MR sequences. They also suggested that intratumoral hemorrhage and vascularity were significantly increased in high-grade glial tumors compared with the low-grade lesions. However, they did not define any quantitative limits to distinguish between low- and high-grade tumors. Hori et al. [8] compared three different SWI grading methods and reported that the ratio of ITSS area within the tumor to the total tumor area was more useful in terms of grading than other parameters. In one of their studies, Park et al. [9] classified the ITSSs according to morphologies and compared SWI grades with rCBV ratios. There are many types of ITSS sources, like hemorrhage, necrosis, and angiogenesis. Although it seems helpful to classify ITSS according to morphology, it is a subjective method due its user-dependent and complex nature. We believe that such a distinction is not necessary because hemorrage, necrosis, and angiogenesis are all indicators of potential malignancy. Therefore, we did not use this method in our study.

SWI is a quite useful technique that provides valuable information about vascular disorders, neurologic disorders, and tumor grading. Intracranial iron deposition, which can be seen in various neurodegenerative disorders, and multiple sclerosis plaques may be demonstrated by using filtered phase images. Microhemorrhages in ischemic stroke may be overlooked in conventional sequences, but may be demonstrated with SWI minIP reformatted images. SWI can distinguish between blood and calcification when magnitude and filtered phase images are used together [6,20]. Lobel et al. [21] compared 3D SWI sequence with T2* gradient echo images in patients with diffuse intrinsic pontine gliomas. They proposed that, although T2* gradient echo images were not able to distinguish a calcification from hemorrhage demonstrated by CT, SWI could distinguish them properly when filtered phase images and magnitude images were used together. In this study we could not make this distinction because we did not utilize any phase filtering methods. We detected intratumoral calcifications with CT studies. Diagnostic contribution of contrast material is controversial in SWI. Park et al. have reported that use of contrast material does not contribute to additional diagnostic accuracy [8,11]. SWI may be preferred to DSC perfusion MRI when use of contrast material is contraindicated due to other conditions, such as chronic renal failure.

Stereotactic biopsy and histopathological evaluation is gold standard for the diagnosis and planning therapy of glial tumors. Internal structure of the tumor may not be homogeneous, thus stereotactic biopsy may give false results. Glial tumors can be globally evaluated by MR examination. Furthermore, sometimes stereotactic biopsy cannot be performed due to tumor localization [1–3]. There are numerous MR techniques for preoperative glial tumor evaluation, like perfusion MR, ADC map, and MR spectroscopy [18].

One limitation of this study may be due to the lack of adequate number of grade 3 tumors. Although there were 19

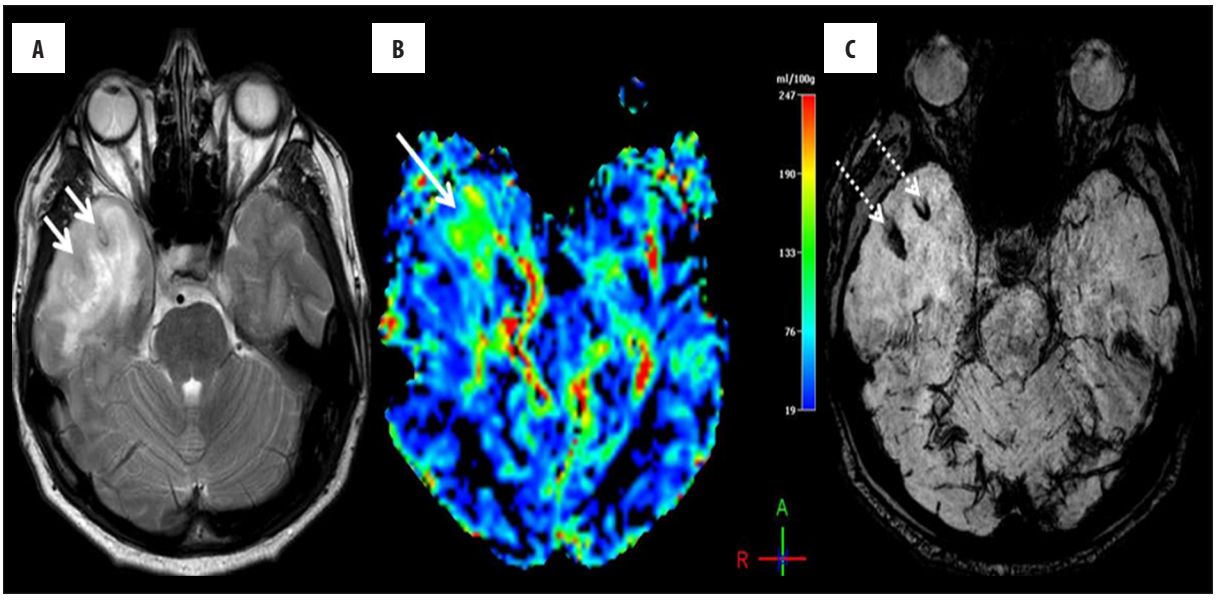

Figure 5. Right temporal oligodendroglima, (**A**) T2-weighted imaging shows hyperintense lesion and two slightly hypointense small areas (arrows). (**B**) CBV map shows moderate hyperperfusion (arrow). (**C**) SWI shows two ITSS but this ITSSs originated from a coarse calcification and was verified by CT. There are no other ITSS and SWI grade is 0.

high-grade glial tumors, there was only one grade 3 tumor. This could be the reason for excellent correlation between SWI grade and histopathologic grade obtained in our study. A small number of astrocytomas constitutes another limitation. Oligodendrogliomas may include much more areas of cystic and calcific degeneration than low-grade diffuse astrocytomas. Moreover, in low-grade oligodendrogliomas the rCBV ratio could be higher than in low-grade diffuse astrocytomas. In this study, all but one of the low-grade tumors seemed homogenous, while another contained a coarse calcification (Figure 5).

Conslusions

In conclusion, SWI using 3T MR system and 32-channel head coil may provide quite useful information for preoperative glial tumor grading. There seems to be a strong correlation between pathological grading and that assessed with SWI. SWI may be used to provide additional information complementary to DSC perfusion MR in preoperative tumor grading. Especially in situations when the use of contrast material is contraindicated, SWI may be of benefit in evaluation of glial tumors.

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