

Plaque vulnerability in patients with high- and moderate-grade carotid stenosis – comparison of plaque features on MRI with histopathological findings

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Summary

BACKGROUND: Plaque vulnerability plays an important role in determining the risk of subsequent cerebrovascular events in patients with carotid stenosis. Plaque morphology magnetic resonance imaging (MRI) can be used to assess plaque vulnerability. We therefore set out to examine the diagnostic accuracy of plaque morphology MRI compared with histopathological findings as gold standard in moderate- to high-grade carotid stenosis at our centre.

METHODS: A total of 36 patients with moderate- to high-grade carotid stenosis underwent plaque morphology MRI with a multisequence protocol (time of flight sequence, dark blood T1- [native and post-gadolinium] and T2-weighted sequence with fat suppression). The status of the fibrous cap, calcification, lipid-rich necrotic core (LRNC) and intraplaque haemorrhage (IPH) were assessed by means of qualitative MR analysis of plaque characteristics and compared with the histopathological findings. Detection statistics (sensitivity, specificity), chi-squared test, Cohen's kappa (κ), percentage of agreement and phi coefficient (ϕ) were determined.

RESULTS: Carotid stenosis was symptomatic (transient ischaemic attack, amaurosis fugax or ischaemic stroke in the territory of the stenosed carotid artery) in 25 patients (69.5%). Twenty-eight patients (77.8%) had a high-grade and eight patients (12.2%) a moderate-grade stenosis. Significant congruence between MRI and histology was found for plaque calcification (89% histology, 75% MRI, $\kappa = 0.364$, $p = 0.013$), for LRNC (89% histology, 53% MRI, $\kappa = 0.245$, $p = 0.025$) and IPH (75% histology, 53% MRI, $\kappa = 0.314$, $p = 0.035$). In a subgroup of patients with symptomatic stenosis, the agreement for LRNC and IPH was slightly better (LRNC $\kappa = 0.390$, $p = 0.014$; IPH $\kappa = 0.386$, $p = 0.045$). Status of the fibrous cap, essentially ulceration,

did not show any significant agreement ($\kappa = 0.032$, $p = 0.842$). There was significant correlation between LRNC on MRI and symptomatic carotid stenosis ($\phi = 0.339$, $p = 0.042$).

CONCLUSION: Plaque morphology MRI is capable of identifying the main components of atherosclerotic plaques with moderate to good accuracy as compared with histopathological findings as gold standard. LRNC seems to be a useful marker of plaque vulnerability and warrants its use in clinical decision making.

Keywords: carotid plaque morphology, carotid stenosis, plaque characteristics, vulnerable plaque, high-resolution magnetic resonance imaging

Introduction

Stroke is the third leading cause of death and the most common cause of long-term disability [1]. Cerebral embolism from carotid artery plaque due to plaque rupture is an important pathophysiological mechanism of ipsilateral stroke [2]. It is well established that surgical treatment such as carotid endarterectomy reduces the risk of stroke in patients with symptomatic high-grade carotid stenosis [3]. The treatment of asymptomatic carotid stenosis is more controversial. Thus it is crucial to identify patients who are at risk for carotid artery embolism resulting in ipsilateral stroke. Traditionally, the degree of stenosis has been used to assess the risk of thromboembolism from carotid plaques [4–8]. However, nowadays the importance of plaque morphology features as an additional factor for vulnerability is well-accepted [2, 9–11]. Plaque morphology components indicating plaque vulnerability are a thin or disrupted fibrous cap, a large lipid-rich necrotic core (LRNC), neovascular growth and intraplaque haemorrhage (IPH) [12, 13], whereas calcification is considered as a component of plaque stability [14]. Magnetic resonance

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imaging (MRI) has been shown to identify the various plaques features. In patients at risk for an ipsilateral stroke, noninvasive imaging techniques, especially MRI, may play an important role in therapeutic decision making [15]. Although multisequence MRI is already well-established in the analysis of carotid plaque characteristics, this method was relatively new at our centre and not yet frequently used as standard procedure to determine patients at risk of ipsilateral stroke. We therefore set out to define the diagnostic accuracy of plaque morphology MRI in comparison with histopathological findings as gold standard. Secondly we compared the subgroups of symptomatic and asymptomatic patients and also the correlation between each plaque component and the presence of neurological symptoms.

Patients and methods

Study population

Patients with symptomatic and asymptomatic high- and moderate-grade carotid stenosis were included. A sample size calculation was not performed. Patients were drawn from the population of a larger study analysing plaque morphology on MRI and clinical outcome [16]. Patient data were gathered retrospectively up to April 2015 at Inselspital, University Hospital of Bern. The cantonal ethics committee of the canton of Bern approved the study setting and all patients gave their informed consent.

Study setting and methods

We compared carotid plaque characteristics on 3-Tesla carotid plaque MRI with histology as gold standard. This was to analyse the diagnostic accuracy of MRI for assessing the various plaque components compared to histopathological findings. Secondly we analysed both the agreement in detecting plaque criteria between MRI and histology in subgroups of symptomatic and asymptomatic patients and the correlation between particular plaque components and the presence of neurological symptoms. Inclusion criteria were a preoperative plaque morphology MRI and intraoperative plaque resection for further analysis. The decision to perform carotid surgery was made individually by interdisciplinary consent and was not in the scope of our study. The degree of stenosis was determined by duplex ultrasound based on the NASCET method [3, 17], with high grade stenosis defined as $\geq 70\%$ and moderate grade 30 to 60% stenosed lumen. A stenosis was defined as symptomatic if patients had suffered from a transient ischaemic attack, amaurosis fugax or an ischaemic stroke in the territory of the stenosed carotid artery up to 6 months before inclusion in the study.

MRI protocol

The entire image analysis was done by MLM and MEK as described previously [16]. They were blinded to the status of the patient (asymptomatic/symptomatic) and the results of the histological analysis. Plaques with imaging features of a thin/disrupted fibrous cap, a large lipid-rich necrotic core (LRNC) or intraplaque haemorrhage (IPH) were considered “vulnerable” [12, 13].

The following imaging protocol was used for the evaluation of the carotid plaques:

The carotid artery was imaged using a 3-T MRI system (Magnetom TrioTim syngo, VB15, Siemens, Erlangen, Germany) with a four-channel phased array surface coil (Machnet BV, Eelde, The Netherlands). A coronal sequence was used to localise the carotid bifurcation and its plaque distribution and was followed by an axial 3D multislab time of flight (ToF) angiography (TR/TE 22/3.86 ms, FOV read 200 mm, FOV phase 83.3%, slice thickness 0.65 mm, averages 1). This was followed by three pulse-triggered, double inversion recovery, turbo spin echo dark-blood sequences in order to avoid artefacts from the inflowing blood: (1) nonfat-saturated T1-weighted images (WI) (TR/TE 400/ 8.6 ms, 10 slices, slice thickness 3 mm, FOV read 150 mm, FOV phase 100%, averages 2); (2) fat-saturated sequence T2WI (TR/TE 700/52.0 ms, 10 slices, slice thickness 3 mm, FOV read 150 mm, FOV phase 100%, averages 3), and (3) contrast-enhanced (CE) fat-saturated T1WI after intravenous gadolinium (TR/TE 400/ 8.6 ms, 10 slices, slice thickness 3 mm, FOV read 150 mm, FOV phase 100%, averages 2). With a zero-filled Fourier transform applied to all sequences, a voxel size of $0.5 \times 0.5 \times 3.0$ mm was achieved. The carotid bifurcation was used as a landmark for matching the four different sequences at each slice location. Plaque components were characterised according to previously published criteria based on relative tissue signal intensities in comparison with the adjacent sternocleidomastoid. Details of the criteria were as follows: calcifications were of hypointense signal intensity in all sequences; the signal intensity of the lipid-rich necrotic core with IPH depended on the age of the haemorrhage: IPH type I (fresh) was hyperintense in ToF and T1WI and hypo-/isointense in T2WI and CE-T1WI, whereas IPH type II (recent) was hyperintense in all sequences. The LRNC without IPH was isointense in ToF, hyperintense in T1WI, of variable intensity on T2WI and hypointense in CE-T1WI. The dominant component of the plaque was determined by visual assessment. The status of the fibrous cap was dichotomised into two groups: thick and intact caps and thin or disrupted caps. A thick fibrous cap was characterised by a uniform dark band adjacent to the lumen on ToF images that showed strong enhancement on CE-T1WI and a smooth luminal surface on all images. In thin fibrous caps, the dark band adjacent to the lumen on ToF was missing and there was no enhancement adjacent to the lumen on CE-T1WI, but a smooth luminal surface on all images. The fibrous cap was considered ruptured when the dark band adjacent to the lumen was missing or discontinuous on ToF images, the signal at the site of the presumed rupture was hyperintense on ToF images and the surface was irregular on the images of all sequences.

Plaque resection

Carotid endarterectomy was performed using a standard non-patch technique [18]. During surgery every effort was made to completely resect the plaque in one piece. However, an incision longitudinally to the plaque is necessary for removal. Therefore nonadherent fibrous cap / thrombus may be altered during removal.

Histological analysis

The histological analysis was carried out blinded to status of the patients (symptomatic/asymptomatic) and the results of the plaque analysis in MRI.

Carotid endarterectomy specimens were processed according to standard protocols and histological slides were stained with haematoxylin-eosin and Elastica-van-Gieson stain.

For each specimen the following histological features were assessed on haematoxylin-eosin-stained slides and classified as present or absent: calcification, LRNC (defined by the presence of foamy macrophages and/or cholesterol crystals), IPH (defined by the presence of haemosiderin pigment or fresh haemorrhage deemed unrelated to the surgical procedure), fibrous cap ulceration (defined by discontinuity in the fibrous cap with tissue reaction, namely clotting and thrombus formation at the site of rupture). If there was no indication of tissue reaction, the plaque was considered intact. Continuity of the intima and atrophy of the tunica media were assessed on Elastica-van-Gieson-stained slides.

Comparison of plaque characteristics on MRI and histology

We compared the following plaque morphology components: calcification, LRNC, ulceration of the fibrous cap and IPH. Congruence of MRI and the histopathological correlates was analysed, as well as the prognostic value of preoperative MR plaque imaging to estimate the vulnerability of the carotid plaque. Plaque sections were not exactly matched to slices in MRI, resulting, however, in an absolute qualitative analysis of the whole plaque. We also compared plaque morphology characteristics and baseline factors between symptomatic and asymptomatic carotid stenosis. IPH was reported if fresh or recent blood residues were found. Older residues or chronic haemorrhage were not included. The size of LRNC was estimated visually both histologically and on MRI, and categorised as small and large.

Statistical analysis

Continuous variables were expressed as mean \pm 1 standard deviation (SD) ranges. Detection statistics (sensitivity, specificity) were evaluated and the chi-squared test for contingency tables was used to compare nominal variables (plaque components). A value of $p < 0.05$ was considered to indicate a significant difference. The diagnostic accuracy measures were calculated by percentage of agreement and Cohen's kappa (κ). Kappa was defined as fair from 0.21 to 0.40 and moderate from 0.41 to 0.60. The phi coefficient (ϕ) was used to show correlation of nominal variables. Correlation was assumed to be moderate if $\phi > 0.3$ and good if $\phi > 0.5$. Statistical analysis was performed by using IBM SPSS Statistics software version 25.

Results

Demographic and baseline characteristics

In total 36 patients were included. Demographic and baseline characteristics are summarised in [tables 1 and 2](#). Mean age (\pm SD) was 71.5 ± 8.68 years. Seven patients (19.4%) were female. Twenty-five (69%) patients had a symptomatic ipsilateral carotid stenosis. A high-grade stenosis was found in 28 patients (78%).

Plaque morphology components

[Table 3](#) shows the comparison of the different plaque components between histological and MRI analysis. LRNC was found in 32 patients (89%) on histological and in 19 patients (52.8%) on MRI analysis. MRI showed a moderate sensitivity (59%) and an excellent specificity (100%). Cohen's kappa showed fair but significant congruence ($\kappa = 0.245$, $p = 0.025$) between MRI and histological findings. When we divided LRNC into subgroups of large versus small lipid core, there was relatively low congruence between the two groups: fair but insignificant congruence for large lipid cores ($\kappa = 0.204$, $p = 0.201$) and absolutely no congruence ($p = 1$) for small lipid cores.

Table 1: Patient baseline characteristics.

| Characteristic | n (%) | |
|--|------------------------------|-------------|
| Mean age \pm standard deviation, years | 71.5 \pm 8.68 | |
| Women | 7 (19.44%) | |
| Vascular risk factors | Arterial hypertension | 23 (63.89%) |
| | Smoking | 12 (33.33%) |
| | Diabetes mellitus | 6 (16.67%) |
| | Hypercholesterolaemia | 28 (77.78%) |
| | Coronary artery disease | 5 (13.89%) |
| | Atrial fibrillation | 2 (5.56%) |
| Current medical treatment | Antithrombotic treatment | 31 (86.11%) |
| | Oral anticoagulation therapy | 2 (5.56%) |
| | Antihypertensive treatment | 26 (72.22%) |
| | Statin therapy | 30 (83.33%) |

Table 2: Carotid stenosis characteristics.

| Characteristics | n (%) | |
|------------------------------|----------------------------|-------------|
| Grade of carotid stenosis | High (>70%) | 28 (77.78%) |
| | Moderate (50–69%) | 8 (22.22%) |
| Symptomatic carotid stenosis | 25 (69.44%) | |
| | Transient ischaemic attack | 9 (25%) |
| | Stroke | 14 (38.88%) |
| | Amaurosis fugax | 2 (5.55%) |

Calcification was found in 89% in the histological analysis and 75% on MRI. MRI showed moderate to high sensitivity (81.25%) and specificity (75%) in predicting plaque calcification. Congruence was fair and statistically significant ($\kappa = 0.364$, $p = 0.013$).

IPH appeared in 75% in histological analysis and in 52.78% on MRI. Sensitivity (62.96%) and specificity (77.78%) of MRI analysis were moderate to high. A significant fair correlation was found ($\kappa = 0.314$, $p = 0.035$).

There was a relatively low prevalence of ulceration of the fibrous cap in histological analysis (27.78%), whereas MRI showed disrupted plaque in 47.22%. Sensitivity (50%) and specificity (53.85%) were poor and there was no significant congruence between MRI and histology ($\kappa = 0.032$, $p = 0.842$).

Figure 1 shows a carotid plaque with LRNC and IPH in the direct comparison of MRI and histological analysis in the same patient.

Plaque morphology components in symptomatic and asymptomatic carotid stenosis

We made the same accuracy tests in subgroups of patients with symptomatic carotid stenosis ($n = 25$) and patients without neurological symptoms ($n = 11$). Detailed results are shown in tables 4 and 5.

There was the same trend as in the total study population, with significant and even higher levels of congruence for LRNC ($\kappa = 0.390$, $p = 0.014$) and IPH ($\kappa = 0.386$, $p = 0.045$). For calcification, slightly lower congruence was found ($\kappa = 0.339$), which was close to significant ($p = 0.065$).

In the asymptomatic subgroup calcification showed moderate ($\kappa = 0.421$) but not significant congruence ($p = 0.087$). The remaining plaque components did not show any significant results or trends.

Correlation of plaque morphology with the presence of neurological symptoms

When comparing plaque morphology characteristics with the presence of cerebral ischaemic symptoms, we found significant correlation ($p = 0.042$) for the plaque morphology feature of LRNC on MRI. Tables 6 and 7 show detailed results of both MRI and histology. LRNC was found more frequently on MRI in symptomatic patients ($n = 16$, 64%) than asymptomatic patients ($n = 3$, 27.3%). Phi coefficient (ϕ) showed moderate but significant correlation ($\phi = 0.339$, $p = 0.042$). The division into large and small LRNC did not result in significant correlation.

When the other plaque morphology features (ulceration, IPH and calcification) were compared with neurological symptoms, no sufficient significance could be proved for either MRI or histology. However, ulceration was more often seen on MRI in symptomatic patients ($n = 14$, 56% of symptomatic patients) than in asymptomatic ($n = 3$, 27.3% of asymptomatic patients) although with no statistically significance ($p = 0.112$).

Histological analysis did not show significant correlation between any of the vulnerability criteria (LRNC, IPH, ulcerated fibrous cap) and cerebral ischaemic symptoms.

Discussion

The main findings in this comparison of qualitative plaque analysis on MRI with histological analysis as the reference standard were statistically significant agreements between plaque calcification, LRNC and IPH. With significant results in three of the four plaque features examined, this study shows a relatively good accuracy of MRI in detecting carotid plaque components.

Plaque vulnerability

For assessing the vulnerability of a carotid plaque, the intraplaque components prone to rupture are of great interest. IPH and a large LRNC are known risk factors for plaque ulceration [12, 13], whereas plaque calcification is associated with plaque stability [14]. Various studies focused on the correlation of carotid plaque components and the presence of cerebral ischaemic symptoms. Complex atherosclerotic carotid plaques (type VI in the modified American Heart Association [AHA] classification by Naghavi [19]) with a large lipid core, thin or ruptured surface, haemorrhage or thrombus formation were shown to be more common in patients with symptomatic carotid stenosis [20, 21]. Several studies showed that a ruptured fibrous cap detected by MRI was associated with recent history of stroke or transient ischaemic attack [22, 23]. Ulceration was also more frequently found in the symptomatic cohort of our patients (56 vs 27%). However, congruency between MRI and histological findings was not significant for ulceration ($p = 0.112$). This may be explained by our stricter definition of an ulcerated fibrous cap, whereby we assumed a state of ulceration only if the plaque showed tissue reaction (thrombus formation) in the histological sections.

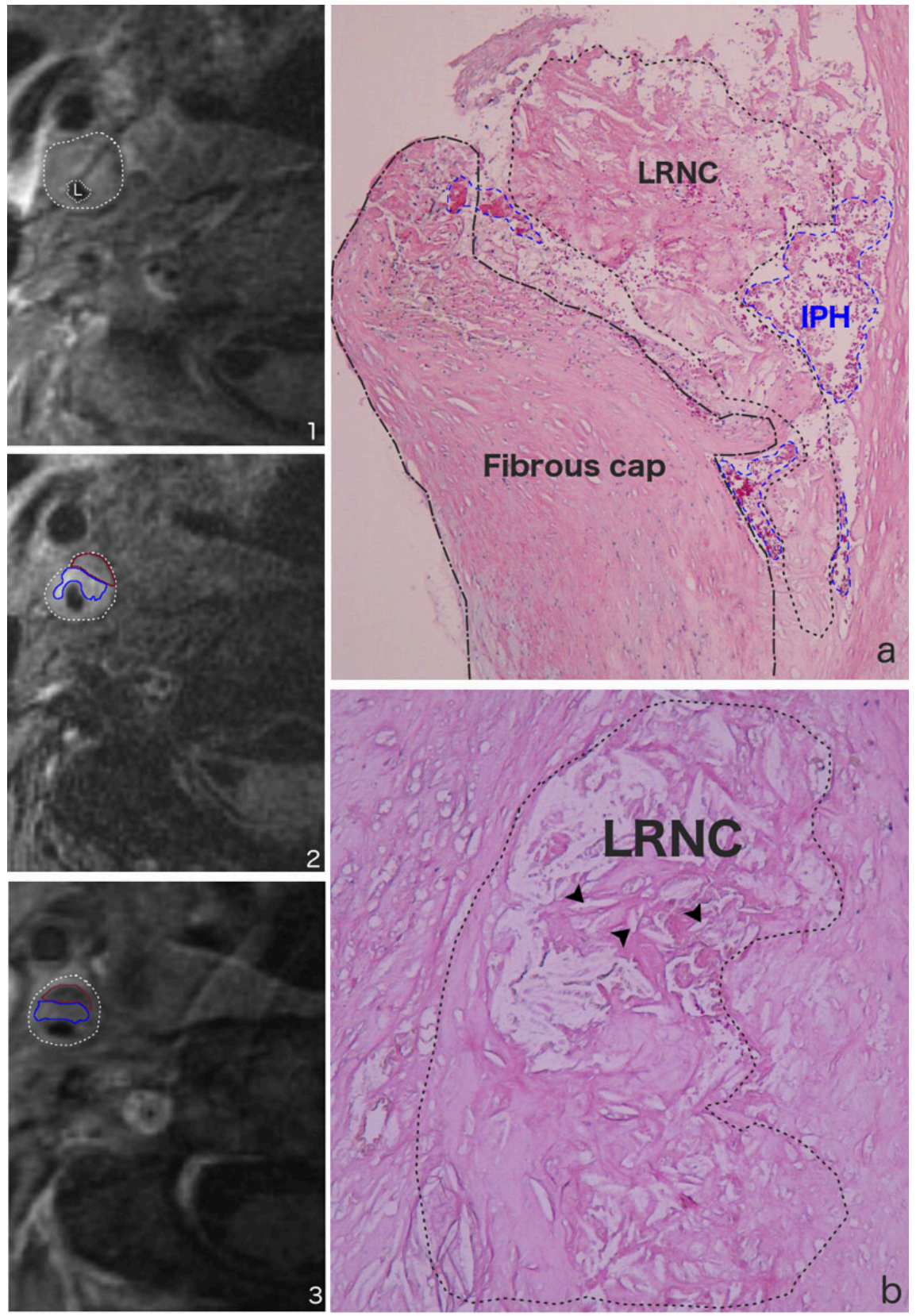
Retrospective [24] and prospective [25] studies showed a strong correlation between IPH and cerebral ischaemic symptoms. In our analysis we could prove that LRNC was significantly more frequent in plaques of patients with

Table 3: Plaque morphology components and congruency between histology and MRI ($n = 36$).

| | | Prevalence histology n (%) | Prevalence MRI n (%) | Sensitivity (%) | Specificity (%) | Significance* (p-value) | % agreement | Cohen's κ |
|----------------------------|--------------------|----------------------------|----------------------|-----------------|-----------------|-------------------------|-------------|------------------|
| LRNC [†] | Total | 32 (88.89%) | 19 (52.78%) | 59.39% | 100% | 0.025 | 63.89% | 0.245 |
| | Large [‡] | 14 (38.88%) | 11 (30.56%) | 46.86% | 77.27% | 0.201 | 63.89% | 0.204 |
| | Small | 18 (50.00%) | 8 (22.22%) | 22.22% | 77.78% | 1.000 | 52.78% | 0.031 |
| Calcification [†] | | 32 (88.89%) | 27 (75.00%) | 81.25% | 75.00% | 0.013 | 80.56% | 0.364 |
| IPH [†] | | 27 (75.00%) | 19 (52.78%) | 62.96% | 77.78% | 0.035 | 66.67% | 0.314 |
| Ulceration [†] | | 10 (27.78%) | 17 (47.22%) | 50.00% | 53.85% | 0.842 | 55.78% | 0.032 |

IPH = intraplaque haemorrhage; LRNC = lipid-rich necrotic core; MRI = magnetic resonance imaging 95% confidence interval: sensitivity 38.07–69.49; specificity: 65.24–88.65 * p-value refers to Cohen's κ . † plaque components were identified and quantified visually in both analyses. ‡ size of lipid cores was estimated surface. Large LRNC was defined as continuous lipid core being the predominant aspect of the plaque.

Figure 1: MRI appearance of a vulnerable internal carotid artery (ICA) plaque with lipid-rich necrotic core (LRNC) and intraplaque haemorrhage (IPH) (1 to 3) and the histological correlate (a, b) in the same patient. T1-weighted precontrast, non-fat-suppressed image showing a predominantly hyperintense plaque, vessel lumen marked with L (1), T2-weighted (2) and post-gadolinium T1, fat-suppressed sequences (3) showing partial suppression of the plaque signal at the anterior aspect of the plaque suggesting that this is the lipid-rich part of the plaque (red area), while the rest of the plaque, which remains hyperintense in all sequences represents the intraplaque haemorrhage (blue area). ICA with lipid core and broken fibrous cap. In between intraplaque haemorrhage (blue area) (a). Typical crystalloid shape of washed out lipid collections in the lipid rich necrotic core of the plaque, marked with arrows (b).



cerebral ischaemic symptoms (64 in symptomatic vs 27% in asymptomatic patients, $p = 0.042$). These findings are in line with different studies where LRNC was associated with symptomatic carotid stenosis and ipsilateral stroke [16, 26]. A large study comparing stable and vulnerable plaques, according to the AHA criteria, also showed a significantly higher lipid content (LRNC) in vulnerable plaques [27]. A significant correlation between IPH and cerebral symptoms, even though IPH is described as one of the compositional characteristics of vulnerable plaques [28, 29], could not be proved in our analysis. It is not entirely clear why histological findings, defined as the gold standard, did not show a correlation to ischaemic symp-

toms despite there being quite good congruence of plaque components between MRI and histology. This discrepancy might be partially explained by lack of congruence on the presence of ulceration – a component that is strongly associated to plaque vulnerability.

Plaque composition

Other studies with histological validation determined that multi-contrast high-resolution-MRI can characterise plaque morphology [30], as well as plaque components such as LRNC, IPH, calcification and the fibrous cap [31]. More recently, Xia et al. showed that multi-contrast high-resolution MRI (3.0 Tesla) has a high accuracy in detection

Table 4: Plaque morphology components and congruency between histology and MRI in symptomatic patients (n = 25).

| | | Prevalence histology n (%) | Prevalence MRI n (%) | Sensitivity (%) | Specificity (%) | Significance* (p-value) | % agreement | Cohen's κ |
|---------------|-------|----------------------------|----------------------|-----------------|-----------------|-------------------------|-------------|-----------|
| LRNC | Total | 22 (88%) | 16 (64%) | 72.73% | 100% | 0.014 | 76.00% | 0.390 |
| | Large | 11 (44%) | 9 (36%) | 45.45% | 71.43% | 0.383 | 60.00% | 0.172 |
| | Small | 11 (44%) | 7 (28%) | 27.27% | 71.43% | 0.943 | 52.00% | -0.013 |
| Calcification | | 22 (88%) | 19 (76%) | 81.82% | 66.67% | 0.065 | 80.00% | 0.339 |
| IPH | | 18 (72%) | 15 (60%) | 72.22% | 71.43% | 0.045 | 72.00% | 0.386 |
| Ulceration | | 7 (28%) | 14 (56%) | 57.14% | 44.44% | 0.94 | 48.00% | 0.012 |

IPH = intraplaque haemorrhage; LRNC = lipid-rich necrotic core; MRI = magnetic resonance imaging 95% confidence interval: sensitivity 43.13–75.75; specificity: 56.74–85.06 * p-value refers to Cohen's κ.

Table 5: Plaque morphology components and congruency between histology and MRI in asymptomatic patients (n = 11)

| | | Prevalence histology n (%) | Prevalence MRI n (%) | Sensitivity (%) | Specificity (%) | Significance* (p-value) | % agreement | Cohen's κ |
|---------------|-------|----------------------------|----------------------|-----------------|-----------------|-------------------------|-------------|-----------|
| LRNC | Total | 10 (90.91%) | 3 (27.27%) | 30.00% | 100% | 0.521 | 36.36% | 0.072 |
| | Large | 3 (27.27%) | 2 (18.18%) | 33.33% | 87.50% | 0.425 | 72.73% | 0.233 |
| | Small | 7 (63.64%) | 1 (9.09%) | 14.29% | 100% | 0.428 | 45.45% | 0.108 |
| Calcification | | 10 (90.91%) | 8 (72.73%) | 80.00% | 100% | 0.087 | 81.82% | 0.421 |
| IPH | | 9 (81.81%) | 4 (36.36%) | 44.44% | 100% | 0.237 | 54.55% | 0.225 |
| Ulceration | | 3 (27.27%) | 3 (27.27%) | 33.33% | 75.00% | 0.782 | 63.64% | 0.083 |

IPH = intraplaque haemorrhage; LRNC = lipid-rich necrotic core; MRI = magnetic resonance imaging 95% confidence interval: sensitivity 21.46–57.00; specificity 85.38–100.00 * p-value refers to Cohen's κ.

Table 6: Correlation between plaque components in MRI and neurological symptoms (n = 36).

| | | Prevalence symptoms n (%) | Prevalence component n (%) | Sensitivity (%) | Specificity (%) | Correlation (φ) | Significance* (p-value) |
|---------------|-------|---------------------------|----------------------------|-----------------|-----------------|-----------------|-------------------------|
| LRNC | Total | 19 (52.78%) | 16 (44.44%) | 66.67% | 25.00% | 0.339 | 0.042 |
| | Large | 11 (30.56%) | 9 (25.00%) | 81.82% | 36.00% | 0.178 | 0.285 |
| | Small | 8 (22.22%) | 7 (19.44%) | 87.50% | 35.71% | 0.210 | 0.209 |
| Calcification | | 27 (75.00%) | 19 (52.80%) | 70.37% | 33.33% | 0.035 | 0.835 |
| IPH | | 19 (52.78%) | 15 (41.67%) | 78.95% | 41.18% | 0.218 | 0.191 |
| Ulceration | | 17 (47.2%) | 14 (39.9%) | 82.35% | 42.11% | 0.265 | 0.112 |

IPH = intraplaque haemorrhage; LRNC = lipid-rich necrotic core; MRI = magnetic resonance imaging 95% confidence interval: sensitivity 71.63–84.26; specificity 30.61–40.50 * p-value refers to correlation.

Table 7: Correlation between plaque components in histology and neurological symptoms (n = 36).

| | | Prevalence symptoms n (%) | Prevalence component n (%) | Sensitivity (%) | Specificity (%) | Correlation (φ) | Significance* (p-value) |
|---------------|-------|---------------------------|----------------------------|-----------------|-----------------|-----------------|-------------------------|
| LRNC | Total | 32 (88.89%) | 22 (61.11%) | 66.67% | 25.00% | -0.043 | 0.798 |
| | Large | 13 (36.11%) | 10 (27.78%) | 76.92% | 34.78% | 0.122 | 0.464 |
| | Small | 18 (50.00%) | 11 (30.56%) | 61.11% | 22.22% | -0.181 | 0.278 |
| Calcification | | 32 (88.89%) | 10 (27.78%) | 66.67% | 25.00% | -0.043 | 0.798 |
| IPH | | 27 (75.00%) | 18 (50.00%) | 66.67% | 22.22% | -0.104 | 0.531 |
| Ulceration | | 10 (27.78%) | 7 (19.44%) | 70.00% | 30.77% | 0.007 | 0.964 |

IPH = intraplaque haemorrhage; LRNC = lipid-rich necrotic core; MRI = magnetic resonance imaging 95% confidence interval: sensitivity 63.83–72.19; specificity 22.62–30.71 * p-value refers to correlation.

of common plaque components, in a larger study population ($n = 817$) [27].

In the analysis of studies comparing of *in-vivo* MRI with histological examination as the gold standard, it is necessary to distinguish between qualitative and quantitative analysis. Saam et al. [31] evaluated 31 MRI subjects by a quantitative analysis (four histological sections of 0.5 mm were matched to one MR slice of 2 mm) and found good to strong correlation of LRNC, IPH and calcifications (Pearson's coefficient from 0.66 for IPH to 0.75 for LRNC, all with $p < 0.001$). Our correlation was not as strong but showed the same trend: Calcification ($\kappa = 0.364$, $p = 0.013$), LRNC ($\kappa = 0.245$, $p = 0.025$) and IPH ($\kappa = 0.314$, $p = 0.035$) showed stronger correlation than the status of the fibrous cap.

Study limitations

One limitation of this study was the relatively small patient cohort ($n = 36$). Furthermore, our analysis was simply qualitative, which meant that for histological analysis sections with the most representative presence of plaque components were chosen and accorded to MRI. However, the quality of our analysis can be considered as good, because the histological reprocessing of the whole plaque ended in a selection of the most significant sections.

Conclusions

At our centre, high-resolution preoperative MRI can identify plaque components with adequate safety in symptomatic and asymptomatic carotid stenosis. Plaque characteristics detected on MRI may therefore be used for risk stratification of ipsilateral stroke for patients with carotid artery plaque, especially in asymptomatic patients and symptomatic patients with low- to moderate-degree stenosis. LRNC seems to be a useful marker of plaque vulnerability and its use in clinical decision making is warranted. Further research, especially in larger multicentre trials is needed to prove the accuracy of MRI in detecting carotid plaque components for clinical use. Furthermore, it will be interesting to follow the use of new post-processing imaging techniques, such as quantitative susceptibility mapping or diffusion-weighted imaging, in analysis of carotid plaque components.

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Potential competing interests

The authors declare no conflict of interest.

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