

Intra-arterial high signals on arterial spin labeling perfusion images predict the occluded
internal carotid artery segment

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Informed consent

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Conflict of interest statement

We declare that we have no conflict of interest.

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1 **Abstract**

2 **Introduction**

3 Arterial spin labeling (ASL) involves perfusion imaging using the inverted magnetization
4 of arterial water. If the arterial arrival times are longer than the post-labeling delay,
5 labeled spins are visible on ASL images as bright intra-arterial high signals (IASs); such
6 signals were found within occluded vessels of patients with acute ischemic stroke. The
7 identification of the occluded segment in the internal carotid artery (ICA) is crucial for
8 endovascular treatment. We tested our hypothesis that IASs on ASL images can predict
9 the occluded segment.

10 **Methods**

11 Our study included 13 patients with acute ICA occlusion who had undergone
12 angiographic and ASL studies within 48 hr of onset. We retrospectively identified the
13 IAS on ASL images and angiograms and recorded the occluded segment and the number
14 of IAS-positive slices on ASL images. The ICA segments were classified as cervical (C1),
15 petrous (C2), cavernous (C3), and supraclinoid (C4).

16 **Results**

17 Of 7 patients with intracranial ICA occlusion, 5 demonstrated IASs at C1-C2, suggesting
18 that IASs could identify stagnant flow proximal to the occluded segment. Among 6

1 patients with extracranial ICA occlusion, 5 presented with IASs at C3-C4, suggesting that
2 signals could identify the collateral flow via the ophthalmic artery. None had IASs at
3 C1-2. The mean number of IAS-positive slices was significantly higher in patients with
4 intra- than extracranial ICA occlusion.

5 **Conclusion**

6 IASs on ASL images can identify slow stagnant- and collateral flow through the
7 ophthalmic artery in patients with acute ICA occlusion and help to predict the occlusion
8 site.

9

10 Key words: magnetic resonance imaging, arterial spin labeling, internal carotid artery
11 occlusion, occluded segment

12

1 **Introduction**

2 Acute ischemic stroke due to acute internal carotid artery (ICA) occlusion is often
3 associated with severe and persistent neurological deficits and a high mortality rate.
4 Among stroke patients who received tissue plasminogen activator (tPA) therapy 71.3%
5 had unfavorable outcomes, as did 79.4% who did not undergo thrombolysis (modified
6 Rankin scale, mRS: 3-6) [1]. Four randomized controlled trials [2-5] showed that
7 endovascular treatment was superior to intravenous recombinant tPA (iv-rtPA) therapy
8 alone and to standard care.

9 The outcome was worse in patients with acute intra- than extracranial ICA
10 occlusion [6]. This may reflect a difference in the amount of collateral circulation.
11 Intracranial ICA occlusion tends to be treated endovascularly with Merci thrombectomy
12 (Stryker), a penumbra system (Penumbra, Inc.) or a stent retriever [Solitaire (Covidien),
13 Trevo (Stryker)]. As the endovascular treatment of extracranial ICA occlusion first
14 requires angioplasty by balloon or stent, the occluded segment must be known before
15 such therapy. However, magnetic resonance angiography (MRA) cannot be used to
16 diagnose the occluded ICA segment because all signals disappear.

17 With arterial spin labeling (ASL), perfusion can be visualized and the cerebral
18 blood flow (CBF) can be quantified. ASL uses magnetically labeled arterial blood water

1 protons as endogenous tracer particles [7, 8]. If the arterial arrival time exceeds the
2 post-labeling delay, labeled spins are visible as bright intra-arterial high signals (IASs)
3 known as the arterial transit artifact [9]. The post-labeling delay time defines the time
4 required for spins to travel from the labeling plane or volume to the imaged slice;
5 typically it is between 1,500 and 2,000 ms. Bright intravascular signals, attributable to
6 slow-flowing blood on ASL images, have been observed upstream of major vessel
7 occlusion sites [10, 11].

8 Based on these findings, we hypothesized that the detection of stagnant flow using
9 a sequence other than MRA would be useful to identify the occluded ICA segment. We
10 investigated whether IASs on ASL images help to distinguish between acute intracranial-
11 and extracranial ICA occlusion and compared differences in the flow pattern, the location
12 of IASs, and the length of IASs-positive sites in patients with acute ICA occlusion. Here
13 we show that IASs are useful for identifying the occlusion site.

14

1 **Methods**

2 **Subjects**

3 Our institutional review board approved this retrospective study. Written
4 informed consent was obtained from all patients or their relatives. Unless contraindicated,
5 assessment with 3T magnetic resonance imaging (MRI) is the first-line diagnostic tool for
6 stroke patients in our center. On March 1, 2012 we added ASL to the MRI protocol. From
7 March 1, 2012 to July 31, 2015, 572 consecutive patients with acute ischemic stroke or
8 transient ischemic attacks were admitted to our stroke care unit. Of these, 55 with acute
9 ICA occlusion were seen within 48 hr after stroke onset; 37 patients underwent MRI and
10 a good ASL image was acquired. In 13 patients we were able to diagnose the ICA
11 occlusion segment on post-ASL angiographs; these patients are the study subjects in our
12 retrospective study.

13

14 **Clinical backgrounds and characteristics**

15 The patients' age, sex, National Institutes of Health Stroke Scale (NIHSS) score at
16 admission, the score based on diffusion weighted imaging - the Alberta Stroke Program
17 Early Computed Tomography Score (DWI-ASPECTS [12]), their vascular risk factors
18 including atrial fibrillation, hypertension, diabetes mellitus, and dyslipidemia, the time

1 from onset to MRI, and the time from MRI to angiography were recorded. The stroke
2 etiology was assessed based on the classification of Adams et al. [13].

3

4 **MRI examination**

5 MRI studies were acquired on a 3T MRI scanner (Discovery MR 750; GE
6 Healthcare, Milwaukee, WI) equipped with an 8-channel phased-array head coil. For
7 ASL we followed the method of Dai et al. [14].

8 ASL perfusion imaging was performed with pseudo-continuous labeling,
9 background suppression, and a stack-of-spirals 3D fast spin echo imaging sequence. The
10 parameters for ASL imaging were 512 sampling points on 8 spirals, field of view (FOV)
11 24 cm, reconstructed matrix 64 x 64, TR 4632 ms, TE 10.5 ms, NEX 2, labeling duration
12 1500 ms, post-labeling delay 1525 ms, slice thickness 4 mm, number of slices 36, total
13 acquisition time 3 min 30 sec. For MRA they were FOV 22 cm, matrix 512 x 224, TR 30
14 ms, TE 2.8 ms, flip angle 17°, slice thickness 1.2 mm, number of slices 66.

15

16 **Image analysis**

17 IASs were defined as spot-like or vessel-like bright hyperintensity areas within an
18 artery on ASL images (Figs. 1Ba-d). The ICA segments were classified as C1: cervical-,

1 C2: petrous-, C3: cavernous-, C4: supraclinoid (Gibo et al. [15]). To determine the ICA
2 segment harboring the slice visualized on ASL images we referred to the contralateral
3 normal ICA on MRA images.

4 Two neuroradiologists who were not involved in the care of the patients
5 independently reviewed all ASL data for the presence or absence of IASs and the
6 involved ICA segment. They were blinded to clinical information and angiographic data.
7 Their judgments were used to calculate inter-rater agreement. The recorded consensus
8 judgments reflected the unanimous decision of the 2 neuroradiologists plus 2 other
9 readers. IASs were recorded as present only by unanimous decision. If there was
10 disagreement, IASs were judged as absent. The involved ICA segment was also identified
11 only on the basis of a unanimous decision by the 4 readers. The consensus judgments
12 returned for ASL findings were used for further analysis. IASs were assessed based on
13 ASL studies performed at the time of admission. Acute ICA occlusion was diagnosed
14 when the artery was invisible on MRA images and when there were symptoms
15 compatible with the non-visualized artery.

16

17 **Statistical analysis**

1 Statistical analysis was performed using SPSS (IBM Statistics 22) with standard
2 statistics. Inter-rater agreement for identifying IASs and the ICA segment was assessed
3 using kappa (κ) statistics. Chi-square analysis or Fisher's exact test was used to compare
4 binary variables. The Mann-Whitney U test was used to compare differences in the mean
5 number of IASs. Values are expressed as the median (first to third interquartile).
6 Statistical differences were considered significant at $p < 0.05$.

7

1 **Results**

2 *Patient characteristics, site of ICA occlusion, and treatment*

3 The median age of our 13 study subjects was 76 years (interquartile range 70-84
4 years), 3 were female, the median NIHSS score at presentation was 15 (12-18), and the
5 median interval from onset to MRI was 406 min (269-645) (Table 1). ASL images of all
6 13 patients showed hypoperfusion in the MCA territory and the median DWI-ASPECTS
7 was 9 (8-11), indicating a large ischemic penumbra in all patients. The occluded segment
8 was intracranial in 7 patients (C2-, C3-, C4 segment of the ICA); 6 underwent
9 embolectomy. Of the 6 patients with extracranial (C1) occlusion, 2 received iv-rtPA
10 treatment and in 5 a carotid artery stent was placed before other procedures. Hypertension
11 was diagnosed in 9 patients (intracranial ICA occlusion: n = 6, extracranial ICA
12 occlusion: n = 3), atrial fibrillation in 4 (intracranial ICA occlusion: n = 3, extracranial
13 ICA occlusion: n = 1), diabetes mellitus in 3 (intracranial ICA occlusion: n = 2,
14 extracranial ICA occlusion: n = 1), and dyslipidemia in 2 (intracranial ICA occlusion: n =
15 1, extracranial ICA occlusion: n = 1). Patients with intracranial ICA occlusion tended to
16 have a higher incidence of risk factors.

17

18 *Inter-observer agreement for IAS detection*

1 Two neuroradiologists, not involved in the care of patients, independently
2 reviewed all ASL data for the presence or absence of IASs. Inter-observer agreement for
3 the evaluation of IASs was excellent ($\kappa = 0.97$).

4

5 ***Angiographic and ASL findings in patients with intracranial ICA occlusion***

6 MRA images of the 7 patients with intracranial ICA occlusion were inspected for
7 the presence of ICA signals. All affected ICA signal in 6/7 cases were not identified
8 except only a single patient who presented with occlusion in the C4 segment. Thus, MRA
9 alone was inadequate for the prediction of the occluded ICA segment. The angiographic
10 pattern on digital subtraction angiography (DSA) images was different among our 7
11 patients with intracranial ICA occlusion; 5 presented with C4 occlusion (cases 1-5) and 2
12 with occlusion below C3 (cases 6 and 7).

13 ***C4 segmental occlusion:*** The occlusion site in 5 of 7 patients (71%) with intracranial
14 ICA occlusion was at the C4 segment. Figure 1 shows representative MRI and DSA
15 findings in patients with C4 segmental occlusion. The DWI-ASPECTS was 8 (Fig. 1Aa)
16 and ASL revealed reduced perfusion in all of the MCA territory (Fig. 1Ab). Figure 1B
17 shows DSA images obtained in the early and late phases. On angiographs, the left
18 intracranial ICA (C4) was occluded from just above the origin of the posterior

1 communicating artery (PcomA) (Figs. 1Ba and 1Bb). We observed patency at the origin
2 of the ICA and slow stagnant flow along the ICA extra- to intracranially into the
3 ophthalmic artery and the PcomA. All 5 patients with C4 occlusion manifested slow flow
4 along the ICA from the extra- to the intracranial ICA on DSA images. Figure 1Bc
5 presents schemas of the occlusion site and the blood flow on angiographs; in Figure 1C,
6 we present ASL images showing IASs within the C1-C4 segments of the left ICA,
7 reflecting slow stagnant flow within the ICA. Figure 1D shows schemas of the occlusion
8 site on angiographs and the area positive for IASs on ASL images.

9 ***Occlusion at sites lower than C3:*** The occlusion site in 2 of 7 (29%) patients with
10 intracranial ICA occlusion was in a segment lower than C3. Figure 2 presents examples
11 of MRI and DSA findings. The DWI-ASPECTS was 10 (Fig. 2Aa) and ASL showed
12 reduced perfusion in all of the MCA territory (Fig. 2Ab). DSA images obtained in the
13 early and late phases are shown in Figure 2B. Angiography revealed occlusion of the left
14 ICA (C3) and collateral flow through the ophthalmic artery in the late phase (Figs. 2Ba
15 and 2Bb). Although the origin of the ICA was patent, we observed ICA flow arrest
16 because there was no outflow. Anterograde flow in the ICA through the ophthalmic artery
17 was slow. The schemas in Figure 2Bc show the occlusion site and the blood flow on
18 angiographs. On ASL images there were IASs within the C4 segment of the left ICA,

1 reflecting antegrade flow in the ICA through the ophthalmic artery (Fig. 2C). Schemas
2 of the occlusion site and the area positive for IASs on ASL images are presented in Figure
3 2D. In another patient with occlusion lower than the C3 segment we obtained the same
4 DSA findings.

5

6 *Angiographic and ASL findings in patients with extracranial ICA occlusion*

7 There were 6 patients with extracranial ICA occlusion. On MRA images all ICA
8 signals were not identified in all cases. Figure 3 shows representative MRI and DSA
9 findings in patients with extracranial ICA occlusion. DWI and ASL scans revealed a large
10 ischemic penumbra in the MCA territory (Figs. 3Aa and 3Ab). On angiographs we
11 observed occlusion at the left ICA origin (C1) (Fig. 3Ba). Before balloon-angioplasty at
12 the origin of the ICA we noted slow ante- and retrograde flow in the ICA through the
13 ophthalmic artery (Fig. 3Ba); after balloon-angioplasty there was recanalization above
14 the ICA origin (Fig. 3Bb). Schemas showing the occlusion site and the blood flow pattern
15 on angiographs are presented in Figure 3Bc. ASL obtained before balloon-angioplasty
16 detected IASs in the C3-C4 segments of the left ICA, reflecting slow ante- and retrograde
17 flow through the ophthalmic artery (Fig. 3C). Schemas of the occlusion site and the area
18 positive for IASs on ASL images are presented in Figure 3D. Among 6 patients with

1 extracranial ICA occlusion, 5 manifested collateral flow in a short length of the ICA from
2 C3 to C4 through the ophthalmic artery. No patients with extracranial ICA occlusion
3 demonstrated stagnant flow in the C1-C2 segments of the ICA.

4

5 *IAS-positive slices on ASL images at each occluded segment*

6 Our angiographic findings indicate that the range and site of stagnant and slow
7 flow within the ICA differed in patients with intracranial- and extracranial ICA occlusion.
8 Therefore, we examined the relationship between the number and location of
9 IAS-positive slices and the occluded ICA segment to determine whether IASs on ASL
10 images differentiated between intra- and extracranial ICA occlusion.

11 Figure 4 shows the number of slices and the IAS-positive segment in patients with intra-
12 and extracranial ICA occlusion. The number of IAS-positive slices was significantly
13 higher in the former (average 8.3 vs. 2.0 slices: $p < 0.05$). This observation is consistent
14 with angiographic findings that patients with intracranial ICA occlusion manifested a
15 wide range of stagnant- and slow flow in the ICA. No IASs were observed at C1 and C2
16 in patients with extracranial ICA occlusion.

17

1 *Accuracy and value of IASs at C1-C2 on ASL images for diagnosing intracranial ICA*
2 *occlusion*

3 Based on angiographic evidence for stagnant flow in the C1-C2 segments of the
4 ICA, we hypothesized that IASs in these segments were predictive of intracranial ICA
5 occlusion. Table 2 shows the value of IASs at the C1-C2 segments on ASL images for a
6 diagnosis of intracranial ICA occlusion. The IAS-positive ratio in C1-C2 segments was
7 significantly higher in patients with intra- than extracranial ICA occlusion (5/7 vs. 0/6).
8 The sensitivity, specificity, positive- and negative predictive value, and the accuracy of
9 these IASs was 71%, 100%, 100%, 75%, and 85%, respectively, indicating that IASs at
10 the C1-C2 segments of the ICA are predictors of intracranial ICA occlusion.
11

1 **Discussion**

2 We found that almost all patients with intracranial ICA occlusion manifested slow
3 stagnant flow in the C1-C4 segments of the ICA on DSA images; patients whose ICA
4 occlusion was extracranial showed collateral flow in a narrow range (C3-C4) through the
5 ophthalmic artery but no stagnant flow in the C1-C2 segments of the ICA. As on
6 angiograms, we detected IASs in the C1-C4 segments on ASL images of patients with
7 intracranial ICA occlusion. Notably, most of these patients manifested IASs not only in
8 the C3-4- but also in the C1-C2 segments of the ICA. In contrast, in patients with
9 extracranial ICA occlusion, we detected IASs in the C3-C4 segments. These observations
10 indicate that IASs on ASL studies reveal slow stagnant- or collateral flow in patients with
11 acute ICA occlusion and help to identify the occlusion site.

12 The endovascular treatment of patients with acute ICA occlusion has been
13 successful. Saver et al. [5] reported that 47% of patients treated endovascularly had a
14 favorable outcome (mRS 0-2). However, the therapeutic strategy to address intra- and
15 extracranial ICA occlusion is different. In most patients with extracranial ICA occlusion,
16 the occluded site was at the ICA origin and 83% of their patients required angioplasty;
17 none with intracranial ICA occlusion did. Consequently, the preoperative prediction of

1 the occlusion site is crucial to determine whether angioplasty at the origin of the ICA is
2 required.

3 Elsewhere our group documented that in the presence of acute middle cerebral
4 artery occlusion, the sensitivity of IASs is higher than the susceptibility vessel sign on
5 T2*-gradient echo images [16]. However, no MRI findings demonstrating the occluded
6 ICA segment have been reported. While the susceptibility vessel sign on T2*-gradient
7 echo images can reveal acute endovascular clots in other vessels [17], susceptibility
8 artifacts at the skull base or clots outside the scan range on such images make it difficult
9 to detect this sign in patients with acute ICA occlusion. Due to the lack of ICA signals,
10 MRA was not able to depict the occlusion site in the current study. While carotid
11 ultrasound can distinguish between vessel occlusion and patency at the origin of the ICA,
12 it requires special techniques and too much time in emergency situations. MRI, on the
13 other hand, is useful for predicting the occluded site and in addition, it yields information
14 such as the infarct volume and CBF.

15 We tested our hypothesis that IASs on ASL images are useful for detecting the
16 occluded ICA segment. We now demonstrate that the sensitivity, specificity, and
17 accuracy of IAS detection in the C1-C2 segments for a diagnosis of intracranial ICA
18 occlusion were high (71%, 100%, and 85%, respectively). However, in 2 patients with

1 intracranial ICA occlusion there were no IASs at C1-C2; the occluded- was lower than
2 the C3 segment and angiographs showed flow arrest at C1-C2 and collateral flow through
3 the ophthalmic artery. Anatomical features may explain this observation; under normal
4 conditions, no vessels branch from the cervical (C1) segment of the ICA. The
5 caroticotympanic and the vidian artery branch from the petrous (C2)- and the
6 meningohipophyseal trunk and the inferolateral trunk branch off the cavernous (C3)
7 segment of the ICA. The ophthalmic- and anterior choroidal artery, and the PcomA
8 branch from the supraclinoid (C4) segment. As vessels branching from the C2-C3
9 segments are very small, they tend not to be visualized on angiographs. If the C2-C3
10 segment is occluded, vessels cannot provide collateral flow to the brain. This elicits flow
11 arrest in the C1-C2 segments. We demonstrate that the presence of IASs in the C1-C2
12 segments is highly specific and useful for diagnosing intracranial ICA occlusion.

13 IASs and arterial transit artifacts are influenced by the post-labeling delay time
14 [18]. Alsop et al. [19] recommended a post-labeling delay of 2000 ms for the accurate
15 assessment of the CBF because a wide range of pathologies may not have been identified
16 before imaging. A post-labeling delay of approximately 1500 ms has been applied in
17 studies to investigate the presence and importance of intravascular high signals [11, 16].
18 As a longer post-labeling delay time on ASL studies detects slower flow [20], it may

1 increase the sensitivity for IASs. Other imaging parameters such as the labeling approach,
2 background suppression, and crusher gradients may affect the appearance of IASs on
3 ASL studies. In our and earlier investigations, pseudo-continuous ASL (PCASL) was the
4 labeling approach. The application of consecutive radiofrequency pulses on PCASL
5 studies instead of a single short pulse or a limited number of pulses in pulsed ASL
6 (PASL) and background suppression may show IASs more clearly. Crusher gradients are
7 used for quantification by suppressing the intravascular signal. However, as they may
8 remove important clinical information such as the presence of delayed flow and
9 arteriovenous shunting [19], we did not use crusher gradients. Stack-of-spirals 3D fast
10 spin echo imaging is insensitive to susceptibility MRI artifacts [21] and it may attenuate
11 susceptibility artifacts from bone in the skull base. Diagnostically it may therefore be
12 superior to the susceptibility vessel sign on T2*-gradient echo images.

13 Our study has some limitations. As we included only patients with
14 angiographically-confirmed acute ICA occlusion, our sample size was small and we
15 cannot exclude bias in the analysis of retrospective data. Although there were no
16 false-positive findings, such results can be obtained in patients with severe ICA stenosis.
17 Since IASs represent slow antegrade arterial flow, in patients with severe stenosis they
18 may be visible in a distal segment. Our findings should be confirmed in a large cohort.

- 1 Also, the therapeutic intervention procedures may have affected the hemodynamics.
- 2 Nonetheless, we confirmed that symptoms of all patients did not change from the MRI to
- 3 the angiography in this study.
- 4

1 **Conclusions**

2 We show that IASs on ASL images can be used to identify the sites of slow
3 stagnant- and collateral flow in patients with acute ICA occlusion. Our findings confirm
4 the high sensitivity, specificity, and accuracy of IASs in the C1-C2 segments for a
5 diagnosis of acute intracranial ICA occlusion. Additional studies are underway to
6 determine the usefulness of IAS detection for the diagnostic work-up and treatment of
7 patients with ischemic stroke.

8

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1 **Figure Legends**

2

3 **Fig. 1**

4 **Representative angiographic- and MRI findings in a patient with ICA occlusion at**
5 **the C4 segment**

6 A 70-year-old man presented with aphasia and right hemiparesis (case 3).

7 A: DWI (a) and ASL (b) indicated a large penumbral area.

8 a: High-intensity signals in the insula, anterior MCA cortex, and anterior MCA
9 territory (DWI-ASPECTS: 8).

10 b: ASL showed reduced perfusion in all of the MCA territory.

11 B: Early- (a) and late phase (b) of left common carotid angiography and schema of
12 the occlusion site and the blood flow (c).

13 a: Left common carotid angiograph showing patency at the origin of the ICA
14 (arrow).

15 b: In the late phase of left common carotid angiography there is slow stagnant
16 flow along the ICA from the C4- to the C1 segment (arrows).

17 c: Schema of the blood flow seen on digital subtraction angiographs (black
18 arrow, blood flow; solid portion, occlusion site).

1 C: Upper panels, ASL; lower panels, MRA of the ICA on the normal side (the lines
2 correspond with the ASL image). ASL shows IASs in the left ICA in segments C4
3 (a), C3 (b), C2 (c), and C1 (d). (IAS: arrow)
4 D: Schema of ASL images (the occlusion site is solid, the IAS-positive segment is
5 hatched).

6

7 **Fig. 2**

8 **Representative angiographic- and MRI findings in a patient with ICA occlusion at**
9 **the C3 segment**

10 An 81-year-old woman presented with aphasia and consciousness disturbance (case 6).

11 A: DWI (a) and ASL (b) indicated a large penumbral area.

12 a: High intensity signals were shown in the lenticular nucleus (DWI-ASPECTS:
13 10).

14 b: ASL showed reduced perfusion in all of the MCA territory.

15 B: Early- (a) and late phase (b) of left common carotid angiography and schema of
16 the occlusion site and blood flow (c).

17 a: Left common carotid angiograph showing patency at the origin of the ICA
18 (arrow).

1 b: In the late phase of left common carotid angiography there is collateral flow
2 into the C4 segment of the ICA through the ophthalmic artery (arrow).

3 c: Schema of the blood flow seen on DSA images (black arrow, blood flow;
4 solid portion, occlusion site).

5 C: Upper panels, ASL; lower panels, MRA of the ICA on the normal side (the lines
6 correspond with the ASL image). ASL shows IASs in the left ICA in segment C4
7 (a). (IAS: arrow)

8 D: Schema of ASL images (the occlusion site is solid, the IAS-positive segment is
9 hatched).

10

11 **Fig. 3**
12 **Representative angiographic- and MRI findings in a patient with extracranial ICA**
13 **occlusion**

14 An 84-year-old man with a history of symptomatic left ICA stenosis presented with
15 aphasia and right hemiparesis (case 8).

16 A: DWI (a) and ASL (b) indicated a large penumbral area.
17 a: High intensity signals were shown in the insula ribbon, the MCA cortex lateral
18 to the insula ribbon, and the lateral MCA territory (DWI-ASPECTS: 8).

1 b: ASL showed reduced perfusion in all of the MCA territory.

2 B: Left common carotid angiograph obtained before (a) and after balloon

3 angioplasty (b) and schema of the occlusion site and blood flow (c).

4 a: Occlusion at the origin of the ICA and collateral flow through the ophthalmic

5 artery (arrow).

6 b: Left ICA stenosis (arrow).

7 c: Schema of the blood flow seen on DSA images (black arrow, blood flow;

8 solid portion, occlusion site).

9 C: Upper panels, ASL; lower panels, MRA of the ICA on the normal side (the lines

10 correspond with the ASL image). ASL shows IASs in the left ICA in segments C4

11 (a) and C3 (b). (IAS: arrow)

12 D: Schema of ASL images (the occlusion site is solid, the IAS-positive segment is

13 hatched).

14

15 **Fig. 4**

16 **The number of IAS-positive slices and segments in each patient**

17 The occluded segment in patients 1-7 was in the intracranial ICA (1-5: C4 segment; 6 and

18 7: lower than the C3 segment). The occluded segment in patients 8-13 was the

1 extracranial ICA. Although 5 of 7 patients with intracranial ICA occlusion had IASs at
2 segments C1 and C2, no IASs were observed at C1 and C2 in patients with extracranial
3 ICA occlusion. The number of IAS-positive slices on ASL images was significantly
4 higher in patients with intracranial- than extracranial ICA occlusion (average 8.3 vs. 2.0
5 slices: $p < 0.05$). Data were analyzed with the Mann-Whitney *U*-test.

6

1 **Table 1**

2 **Patients and treatments**

Case No	Age, Sex	Initial NIHSS	Etiology	Onset to MRI (minutes)	DWI-ASPECTS	IV tPA therapy	Occlusion segment*	ICA flow arrest	Past History	Endovascular procedure
1	88, M	11	ATBI	701	11	-	C4,M1distal	-	HT	Balloon angioplasty
2	75, M	21	CE	645	6	-	C4	-	HT, AF	Penumbra
3	70, M	18	CE	269	8	-	C4	-	AF	Merci→Penumbra
4	86, F	16	CE	406	8	-	C4	-	HT, AF, DL	Penumbra
5	67, M	13	CE	305	10	-	C4-M1 proximal	-	HT,DM	Trevo
6	81, F	15	other**	632	10	-	C3	+	HT, DM	Penumbra→Trevo
7	90, M	10	CE	323	11	-	C3-M1 proximal	+	HT	Trevo
8	84, M	16	ATBI	602	8	-	C1, M1 distal		HT	CAS→Penumbra
9	76, M	12	CE	1640	11	-	C1-C3		HT, AF	Penumbra
10	73, M	14	ATBI	261	8	-	C1, M1 distal		DL	CAS→Solitaire
11	67, F	28	ATBI	75	8	+	C1, M1 distal		-	CAS→Penumbra
12	78, M	23	ATBI	654	9	-	C1, M1 proximal		HT, DM	CAS→Penumbra
13	55, M	10	ATBI	83	11	+	C1, C4		-	CAS→Penumbra

3

4 *Includes long and tandem lesions.

5 **Embolism based on the Trousseau syndrome

6 Abbreviations: ATBI, atherothrombotic brain infarction; DWI-ASPECTS, diffusion

7 weighted imaging - the Alberta Stroke Program Early Computed Tomography Score; AF,

8 atrial fibrillation; C1, supraclinoid-, C2, cavernous-, C3, petrous-, C4, cervical segment

9 of the ICA; CAS, carotid artery stenting [penumbra, aspiration system (Penumbra

10 Alameda), Merci, Merci retriever system (Concentric Medical, Mountain View), Trevo,

11 stent retriever system (Stryker Neurovascular), Solitaire, stent retriever system (eV3

- 1 Neurovascular)]; CE, cardioembolism; DL, dyslipidemia; DM, diabetes mellitus; HT,
- 2 hypertension; M1, middle cerebral artery, horizontal segment
- 3

1 **Table 2 Value of IASs on ASL images for diagnosing intracranial ICA occlusion**

2

3 Assessment of IAS at the C1-C2 segments in ICA

	n	%
5 Sensitivity	5/7	71
6 Specificity	6/6	100
7 Positive predictive value	5/5	100
8 Negative predictive value	6/8	75
9 Accuracy	11/13	85

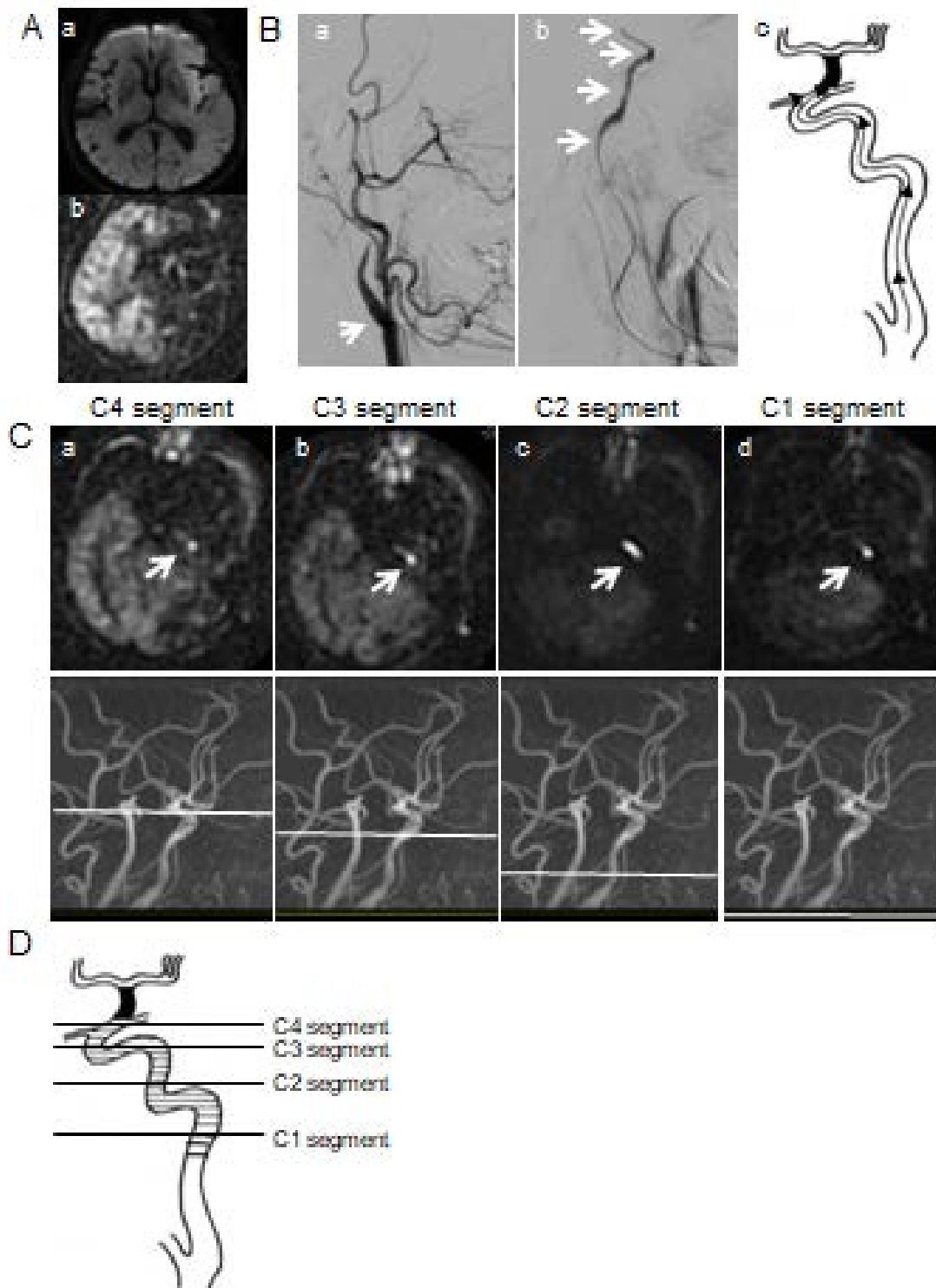
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11 The incidence of IAS-positive C1 and C2 segments was significantly higher in patients

12 with intra- than extracranial ICA occlusion (5/7 vs. 0/6).

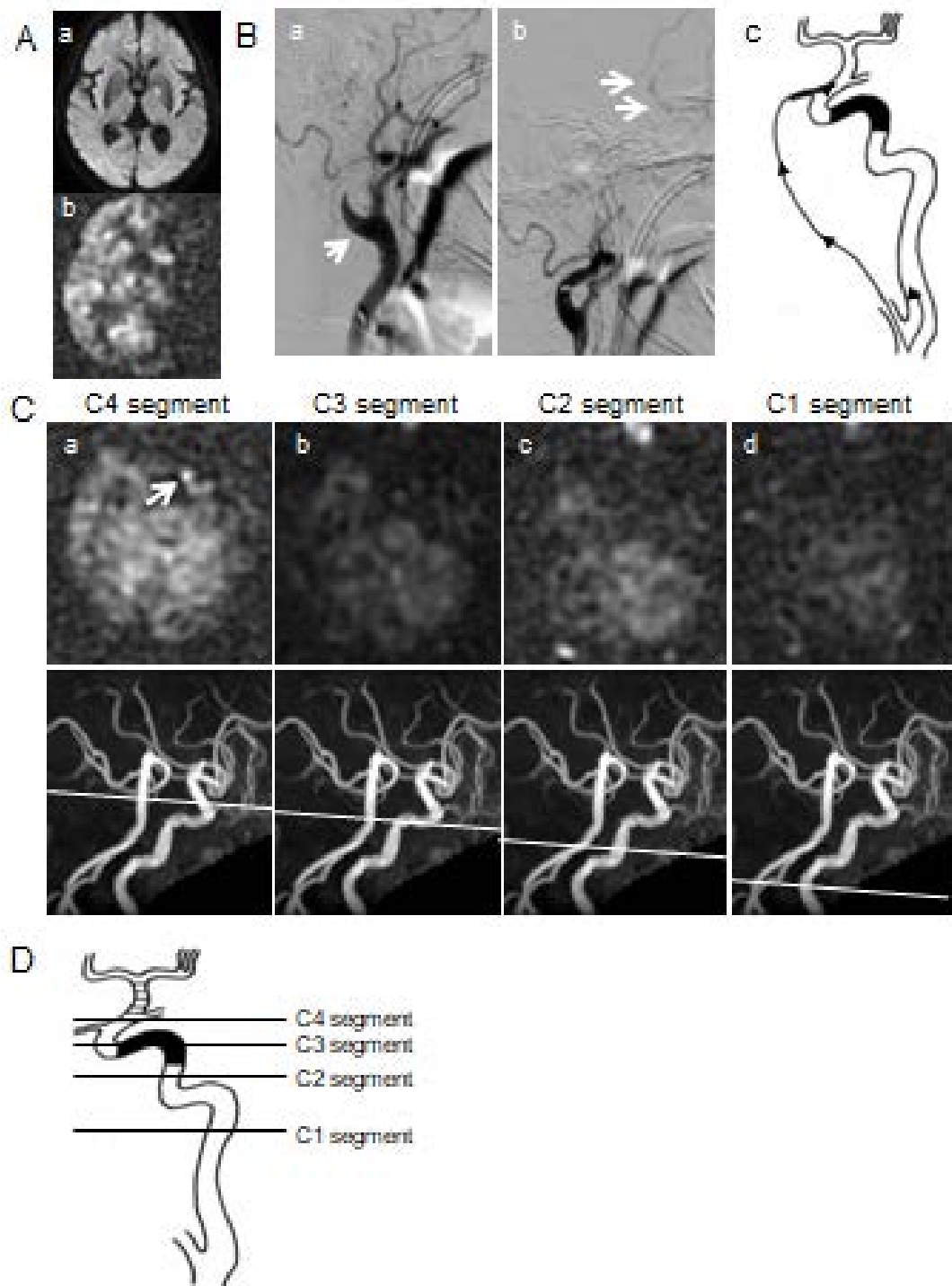
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Fig. 1



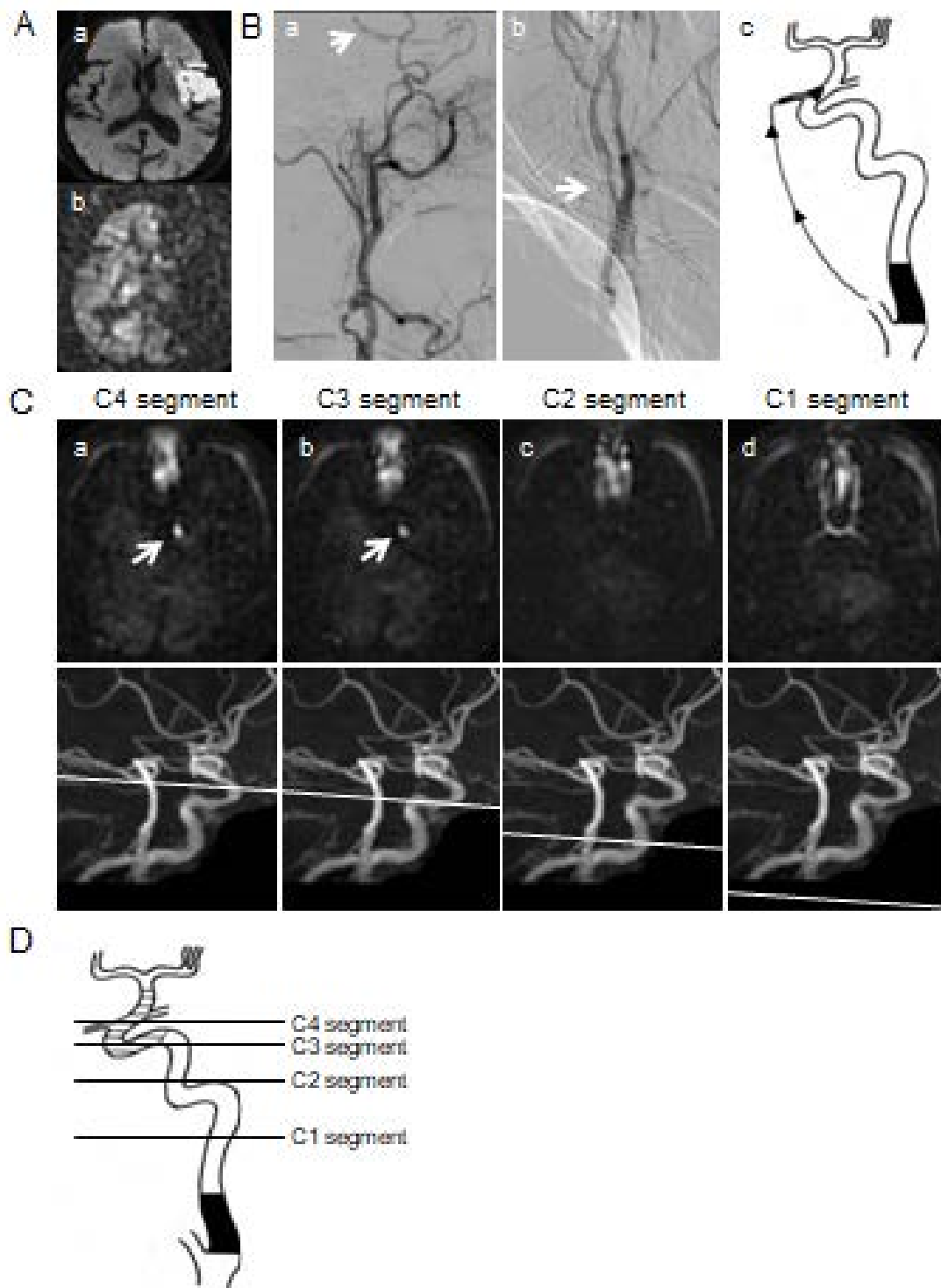
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Fig. 2



1
2

Fig. 3



1
2

Fig. 4

