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Neck vessel cross sectional area measured with MRI: scan-rescan reproducibility for longitudinal evaluations

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Abstract

Background and Purpose—The cross-sectional area (CSA) of common carotid arteries-internal carotid arteries (CCA-ICAs), vertebral arteries (VAs) and internal jugular veins (IJVs) is influenced by aging. However, the neck vessel CSA can be affected by other factors as well, including subject positioning, hydration and respiration, especially in longitudinal studies. This study aimed to assess scan-rescan reproducibility of CCA-ICAs, VAs and IJVs CSA measurements in order to evaluate their feasibility for longitudinal CSA assessments, and to apply the segmentation method on a longitudinal pilot dataset.

Methods—Two set of 2D Neck Magnetic Resonance Angiography (MRA) images were acquired on a 3T scanner from two separate datasets: 9 healthy individuals (HI) were scanned 5 days apart (scan-rescan dataset), and 12 HI were acquired 5 years apart (baseline-follow-up dataset). CCA-ICAs, VAs and IJVs were segmented along the whole vessel length between C3 and C7 intervertebral spaces. Repeated measure analysis of covariance, adjusted for cervical level and sample, and Wilcoxon signed-rank sum test were used to assess the scan-rescan and baseline-follow-up CSA differences. Intra-class correlation coefficient (ICC) was also computed to evaluate scan-rescan reliability.

Results—No significant CSA differences were found for the scan-rescan and baseline-follow-up CSA comparisons, using the whole vessel length or single cervical level measurements. ICC analysis showed good degree of scan-rescan reproducibility (considering whole vessel measures:

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ICC>0.9, p-value<0.001 for CCA-ICAs, ICC>0.6, p-value<0.001 for VAs and ICC>0.7, p-value<0.001 for IJVs).

Conclusions—Scan-rescan reproducibility of CCA-ICAs, VAs and IJVs CSA measurements is high, making longitudinal studies feasible.

Keywords

scan-rescan reproducibility; magnetic resonance angiography; internal jugular vein; internal carotid artery; vertebral artery; cross-sectional area

Introduction

Internal carotid arteries (ICAs) branch from the common carotid artery (CCA), and together with vertebral arteries (VAs), are the vessel pathways responsible for the blood supply to the brain. On the other hand, internal jugular veins (IJVs) are the main routes for the extra-cranial venous drainage in supine position.^{1,2} Since hydraulic resistance of blood vessels is inversely proportional to their radius,^{3–5} measuring the cross-sectional area (CSA) of CCA-ICAs, VAs and IJVs can give indirect information about resistance to brain inflow and outflow, respectively.

Occlusions or flow reduction in these ascending and descending pathways can impair cerebral perfusion. It is well established that occlusive disease and low flow in ICAs, if associated with an insufficient VA and collateral supply, can result in brain hypoperfusion and lead to cerebral ischemia.⁶ However, neck vessel alterations seem to be linked not only to stroke and cerebrovascular diseases. A recent study showed lower arterial CSA of CCA-ICAs and VAs, and higher frequency of secondary neck vessels in patients with multiple sclerosis (MS).⁷ Also, in the last decade morphological and hemodynamic alterations of IJVs were observed in neurological diseases such as MS,^{8–10} transient monocular blindness,¹¹ normal-pressure hydrocephalus,¹² idiopathic sudden sensorineural hearing loss and Meniere's disease.¹³ Although the link between these neurological diseases and morphological/hemodynamic alterations in neck vessels is still under debate, more investigations are warranted in order to clarify the role of extra-cranial supply and drainage circuits related to these pathologies.

Different imaging techniques can be used to measure the CSA of neck vessels, such as conventional angiography, digital subtraction angiography, computed tomography angiography, ultrasound, contrast-enhanced magnetic resonance angiography (MRA) and time-of-flight (TOF) MRA.^{14–19} Among these techniques, ultrasound and TOF MRA are non-invasive imaging techniques and can be used to scan also healthy individuals (HIs) without rising ethical concerns related to the use of exogenous contrast agents.²⁰ Furthermore, comparing TOF MRA to ultrasounds, the previous has the additional advantages of allowing less operator dependent acquisition and of providing an entire 3D image as outcome.²¹ Thus, on TOF MRA images, vessel CSA can be measured a posteriori on any axial slice within the field of view (FOV).

Independently of the acquisition technique used, the CSA evaluation of CCA-ICAs, VAs and IJVs is performed at different levels identified by some anatomical landmarks (e.g. intervertebral cervical level, cricoid cartilage level, thyroid gland level, vessel bifurcation, etc.).^{17,18,22,23} However, IJV CSA varies along the course of the vessel in HIs.²⁴ Therefore, performing few IJV CSA measures only at different cervical levels might not be representative of the CSA along the whole vessel length. In order to overcome this limitation, a recent MRI-based study proposed to segment the IJVs along the whole vessel course.¹⁹ In order to do this, a semi-automatic segmentation procedure, taking advantage of edge seeking and 3D propagation algorithms, was used. Furthermore, a normalization method was introduced to perform slice-by-slice comparison and allow group-based statistical analysis. This approach was reported to be characterized by high intra- and inter-operator reproducibility.¹⁹

In addition to great intra- and inter-subject anatomical variability of extra-cranial venous pathways,^{24–26} the measurement of the IJV CSA can be influenced by several factors, such as positioning, hydration, respiration, and body mass index.^{27–29}

Furthermore, in some cross-sectional studies, both neck veins and arteries CSA have been reported to vary with aging. Specifically, a positive correlation between age and IJV CSA was observed in HIs.^{22,30} An age-related trend of increasing CCA-ICAs and VAs diameter was also reported.^{31,32} However, to the best of our knowledge, a comprehensive longitudinal study investigating CCA-ICAs, VAs and IJVs CSA altogether in HIs has not been yet performed. In order to validate longitudinal CSA comparison, it is essential to assess the reproducibility of the measures utilized.

Therefore, in this study, we aimed at assessing scan-rescan reproducibility of CCA-ICAs, VAs and IJVs CSA measurements performed on TOF MRA images, by using a previously described segmentation method that assesses the whole vessel length between C3 and C7 intervertebral spaces.¹⁹ Furthermore, we aimed at applying the segmentation method to a 5-year longitudinal pilot dataset of HIs.

Methods

Subjects

Twenty-one HIs with no history of neurological and cerebrovascular disease were included in this study. The subjects were recruited among hospital personnel (scan-rescan dataset), or participated, as controls, in the prospective study of cardiovascular, environmental and genetic factors in patients with MS (baseline-follow-up dataset).^{33–35} All subjects were scanned twice: 9 out of 21 were acquired 5 days apart (scan-rescan dataset) and 12 out of 21 were scanned 5 years apart (baseline-follow-up dataset).

The study was approved by local Institutional Review Board and it was conducted in accordance with the ethical principles of the Helsinki Declaration. Written informed consent was obtained from all participants.

MRI acquisition

Magnetic resonance imaging (MRI) data was acquired using a 3T GE Signa Excite HD 12.0 Twin Speed 8-channel scanner (General Electric, Milwaukee, WI, USA) using an 8-channel head and neck (HDNV) coil. The 2D neck TOF MRA was acquired with the following parameters: repetition time (TR)=14ms, echo time(TE)=4.3ms, flip angle=70°, bandwidth=121.094 kHz, number of contiguous axial slices varying from 80 to 150, slice thickness=1.5mm, distance factor=1.5mm, axial resolution=0.430×0.430mm², and axial FOV= 220×220mm². A sagittal localizer was used to position the MRA FOV, so that all the cervical levels between C3 and C7 were included. No pre-saturation band was used in order to acquire both veins and arteries in the same image. All the subjects were asked to breath normally during the scans.

MRI processing

Image quality control—All the acquired images were visually inspected by an expert operator in order to exclude bad quality scans.

Segmentation: Since bones structures are better visualized on the localizer image rather than on the MRA, the identification of the limits of all the cervical levels between C3 and C7 was performed on the localizer image. Specifically, by using FSLView tool from FMRIB's Software Library (FSL; <http://www.fmrib.ox.ac.uk/fsl>), 6 markers were positioned on each sagittal localizer image, on all the intervertebral spaces between C3 and C7 (i.e. C2–C3, C3–C4, etc). The localizer image was registered to the corresponding MRA with FLIRT FSL tool,^{36,37} taking advantage of the orientation information only (usesqform option). After visually assessing the registration outcome, the estimated registration parameters were used to transform the cervical marker coordinates into the MRA space. The z-coordinates of the registered markers identified the slice of the MRA image where the limits of the cervical levels of interest (from C3 to C7) were located.

CCA-ICAs, VAs and IJVs were segmented on all the acquired MRA images, on their whole length between C2–C3 and C7-T1 markers. Since the ICA branches from the CCA, ICA and CCA were considered as part of the same region of interest (ROI), they were referred to as CCA-ICA. The CCA was segmented on the slices below the CCA bifurcation, while ICA was segmented above it. The segmentation was performed with Jim 6.0 software package (Xinapse Systems, UK, <http://www.xinapse.com/>), by semi-automatic ROI contour definition on a single axial slice and its 3D propagation on the whole vessel length, as described previously.¹⁹ Only the flow area of the vessel (hyperintense area) was segmented. If no flow could be identified, contours were not drawn for that vessel on a particular slice.

Once the entire CCA-ICAs, VAs and IJVs were defined, the corresponding CSA was automatically computed for all the segmented slices. The CSA was considered equal to zero for all the non-segmented slices.

Resampling: The number of segmented slices for each subject depended on the position of C2–C3 and C7-T1 markers that was specific for each segmented MRA image. Therefore, in order to compare corresponding slice-by-slice CSA values at the group level, the CSA-to-

slices curves were resampled using Matlab (MATLAB Release 2013b, The MathWorks, Inc., Natick, Massachusetts, USA) with the following approach. For each subjects, the segmented slices were classified according to the cervical level to which they belonged. For each cervical level, the number of samples for the resampling was defined as the average number of slices segmented for that level among the subjects of the group. Resampling was performed on each cervical level, considering the first and the last segmented slices of the same cervical level of all the subjects of the group as corresponding samples. Scan-rescan and baseline-follow-up were processed as independent datasets. CSA medians and interquartile range (IQR) across subjects were calculated both for each sample and for each level, considering all the corresponding samples together.

Statistical analysis

Statistical analysis was performed with SPSS (version 24; IBM Corp., Armonk, NY, USA). Age and sex differences between the scan-rescan and baseline-follow-up datasets were assessed with Student's t-test and Fisher's exact test, respectively. Either Kolmogorov-Smirnov test or Shapiro-Wilk test were used to assess normality (more or less than 50 observations, respectively). After performing a logarithmic transformation to normalize the CSA data distribution, scan-rescan and baseline-follow-up CSA differences were tested with repeated measure analysis of covariance (rmANCOVA), where cervical level and sample (i.e. the index taking into account the slice level after the resampling) were used, as covariates. Wilcoxon signed-rank sum test was used to compare scan-rescan and baseline-follow-up median CSA values on each cervical level separately. Intra-class correlation coefficient (ICC), with corresponding 95% confidence interval (CI) and p-values, was computed to test for CSA systematic differences between scan and rescan CSA measures. The ICC was estimated for all the vessels, both considering each cervical level separately and the whole vessel measures together. The agreement was considered poor for ICC lower than 0.40, fair for ICC between 0.40 and 0.59, good between 0.60 and 0.74 and excellent for values higher than 0.75.^{38,39}

P-values < 0.05 were considered statistically significant, and p value < 0.1 a trend, using two-tailed test.

Results

Subjects

Scan-rescan and baseline-follow-up subject groups were sex-matched (scan-rescan group: females/males=8/1; baseline-follow-up group: females/males=11/1) but not age-matched (p=0.035; scan-rescan group: mean±standard deviation(std) age=30.9±9.0 years; baseline-follow-up group: mean±std age=44.7±16.5 years).

Image quality control

All the acquired scans were classified as good quality images. Therefore, no scans were excluded from the study.

Feasibility of segmentation and resampling

Right CCA-ICA, VA and IJV were identified and segmented on all the MRA images. As regards the left side, all the vessels were segmented with the exception of the left IJV on one MRA image since it was not visible. An example showing the segmented ROIs on the sagittal, coronal and axial plan is reported in Figure 1. The number of slices segmented on average in the two considered cohorts was 56 and 54 for the scan-rescan dataset and the baseline-follow-up dataset, respectively. Specifically, samples were distributed among the cervical levels of interest as follows: 11 samples for C3, C4, C5 and C6, and 12 samples for C7 level for the scan-rescan dataset; 11 samples for C3 and C4, 10 samples for C5 and C6, and 12 samples for C7 level for the baseline-follow-up dataset.

Scan-rescan reproducibility assessment

No significant differences were found between scan-rescan CSAs for any of the vessels. There was a trend for scan-rescan difference for right IJV at C4 level only ($p=0.051$). The lack of differences was observed for the whole vessel length measures, as well as for single cervical level measures (Table 1). Furthermore, ICC analysis showed a good degree of reproducibility between scan and rescan CSA values for all the vessels ($p<0.01$) (Table 2). Considering the whole vessel measures, an excellent agreement ($ICC>0.75$) was found for CCA-ICAs and IJVs, and a good agreement ($ICC>0.60$) was observed for VAs (Table 2). At single cervical levels, good or excellent agreement was obtained for CCA-ICAs and IJVs at all the levels, for left VA between C4 and C7 and for right VA at C6 and C7. The lowest ICC values were observed for right VA at C3, C4 and C5 ($ICC=0.471, 0.387, 0.563$ respectively). Scan and rescan CCA-ICAs, VAs and IJVs CSA-to-samples curves are shown in Figure 2.

Baseline-follow-up longitudinal analysis

Bilateral CCA-ICAs, VAs and IJVs showed comparable CSA values between baseline and follow-up at 5 years, for the whole vessel length measures, as well as for a single cervical level measures (Table 3). CCA-ICAs, VAs and IJVs CSA-to-samples curves based on baseline and follow-up cases are represented in Figure 3.

Discussion

This study assessed the scan-rescan reproducibility of major arterial and venous neck vessels (CCA-ICAs, VAs and IJVs) CSA measures, using the whole vessel length method.¹⁹ Good scan-rescan reproducibility was found for all the considered vessels.

The high ICC values obtained for bilateral CCA-ICAs, VAs and IJVs when considering the measures of the whole length, highlighted the good agreement between scan and rescan CSA measurements. This finding is in accordance with the reported absence of significant differences in CSA measures of 5-days-apart scans. The trend for scan-rescan difference was observed only for right IJV at C4 ($p=0.051$), however, there was an excellent ICC obtained for right IJV at the same level ($ICC=0.776$) confirming the reproducibility of the measure. The quite poor ICC values that were obtained at some cervical levels for VAs could be attributed to the small size of these vessels that may make the CSA values more susceptible to small differences. However, the highly significant ICC p-values and the absence of

significant differences between scan and rescan VA CSA measures support an acceptable scan-rescan reproducibility for VA CSA measures. As expected, the highest ICC was obtained for CCA-ICAs, characterized by larger CSA and lower variability.

Comparing the CSA IQR values of the CCA-ICAs, VAs and IJVs, it can be observed that the arterial pathways showed lower variability across subjects when compared to IJVs. Furthermore, comparing scan-rescan group CSA median values of baseline-follow-up cohort, IJVs showed less reproducible values with respect to arteries. These findings confirm a higher inter-subject variability that characterizes the extra-cranial venous drainage system, as reported previously.^{25,26} It should also be considered that differences in age and cardiovascular risk factors between the baseline and follow-up might have influenced the IJV CSA median differences between the two analyzed datasets.²² Unfortunately, the small sample size prevented us from exploring this possibility further.

The intra-subject IJV CSA variability was also higher than that of CCA-ICAs and VAs, as one HI had the left IJV visible on the first MRA, but not on the second one acquired five days later (see Figure 1). Changes in position or hydration are more likely responsible for this discrepancy.^{27,28} Despite this single case, we showed a high scan-rescan reproducibility at the group level, rendering longitudinal studies feasible also for the IJVs.

The CSA-to-samples charts (Figures 1 and 2) display the IJVs CSA variability along the neck, confirming the non-cylindrical geometry of the IJVs, as previously reported.^{19,24} Therefore, the common methodological choice of performing few CSA measures at specific anatomical landmark levels (e.g., C3, C5–C6, C7 level, cricoid cartilage level, thyroid gland midlevel) is probably not a very accurate methodological approach for longitudinal studies. On the other hand, the segmentation method used in this study propagated the vessel borders on all the slices between C3 and C7, giving more representative and complete information regarding the IJV CSA.

When comparing the IJV CSA median measures obtained in this study with previous ones,^{19,22,24,40} several aspects have to be taken into account. Firstly, the already mentioned high inter-subject variability that characterize IJV CSA can lead to very different CSA values, especially when dealing with a small sample size. The differences in IJVs CSA median values obtained for scan dataset and baseline one within this same study support this assumption. In addition, considering CSA measures gained with disparate acquisition and segmenting techniques can introduce further variability and impair the comparison.⁴⁰ Finally, the anatomical landmarks where CSA measures reported by literature were performed, are not always the same (e.g. intervertebral cervical levels, cricoid cartilage level, thyroid gland level). All of these factors render difficult a direct comparison between the IJV CSA measurements and those reported in the previous studies. However, when compared to a recent study performed with the same acquisition and segmenting technique,¹⁹ baseline dataset showed very similar CSA values for IJVs (comparing those mean CSA values with our median ones at corresponding cervical levels: 45.3 mm² vs 44.0 mm² at C3, 54.1 mm² vs 54.2 mm² at C4, 62.2 mm² vs 63.1 mm² at C5, 66.6 mm² vs 66.3 mm² at C6, 66.9 mm² vs 59.4 mm² at C7). Beyond the abovementioned factors influencing overall variability, the trend for lower CSA values could also be related to the experimental design choice of

segmenting only the flow hyper-intense area. Differently from the arteries for which the flow is generally homogeneous, the veins more frequently present with low flows and refluxes that weaken the signal and reduce the brightness of vessels. The CSA variability along the IJV, the high inter-subject differences and the dependence of IJV CSA measures on the acquisition technique used to collect the data question the utility of defining venous stenosis in terms of absolute thresholds.

The CCA-ICA CSA values derived in the present study are comparable to those described previously.^{23,41} Focusing on CCA-ICAs CSA-to-samples curves (Figures 2 and 3), the CSA increase between C3 and C4 can be explained as a result of CCA bifurcation. A previous study measuring the CSA 2cm proximally to the CCA bifurcation, reported a diameter equal to 7.1 mm and 7.7 mm, on average for 25 year old women and men, respectively and a diameter equal to 6.8 mm and 8.3 mm, on average for 45 year old women and men, respectively.⁴² Assuming a circular geometry, these diameters correspond to CCA CSA of 39.6mm² and 46.5mm² 25 year old women and men, respectively, and of 36.3mm² and 54.1mm² for 45 year old women and men, respectively. Another study that measured CCA CSA 2cm proximally to the bifurcation, on six group of women of different ages, showed an average diameter of 7mm for the 26.4-year-old-on-average group and of 6.9mm for the 47.8-year-old-on-average group, corresponding to 38.5mm² and 37.4mm² CSA respectively.²³ In our study, for scan-rescan group we obtained a median left CCA-ICA CSA of 37.5mm² at C4 and of 37.4mm² at C5, and a median right CCA-ICA CSA of 34.3mm² and 35.8mm² at C4 and C5, respectively. Furthermore, for baseline-follow-up group we reported a median left CCA-ICA CSA of 37.1mm² at C4 and of 35.4mm² at C5, and a median right CCA-ICA CSA of 38.7mm² and 36.7mm² at C4 and C5, respectively. Therefore, considering the age of the recruited subjects (30.9 and 44.7 years old on average, for scan-rescan and baseline-follow-up groups, respectively) and the higher prevalence of women in both the datasets considered in this study (females/males=8/1 and 11/1, for scan-rescan and baseline-follow-up groups, respectively), our CCA-ICA CSA results are in line with the literature. In addition, by segmenting the arterial CSA directly, the measure is more accurate than computing it from diameter, assuming a circular geometry. Similarly, for VAs, a mean diameter of 4.5mm was reported in previous studies,⁴³ which corresponds to a CSA of 15.9mm², and is comparable to our scan-rescan dataset CSA values (scan left VA median CSA=15.7mm², scan right VA median CSA=16.3mm²; rescan left VA median CSA=15.3mm², rescan right VA median CSA=16.1mm²) and baseline-follow-up ones (baseline left VA median CSA=15.4mm², baseline right VA median CSA=15.4mm²; follow-up left VA median CSA=15.7mm², follow-up right VA median CSA=15.7mm²).

Considering the baseline-follow-up dataset, no significant differences were observed comparing any of the vessels over 5 years, both at single cervical levels and on the whole vessel length. This result is in contrast with the evidence showing age-related changes of CCA-ICAs, VAs and IJVs CSA in previous studies.^{22,31,32} However, these studies were conducted recruiting subjects from a wide age span and were cross-sectional in their design. Therefore, 5 years might be not sufficient time frame to observe noticeable changes in the CSA of CCA-ICAs, VAs and IJVs, especially in young subjects, as utilized in this study. Measuring the CSA of the neck vessels on a larger group of HIs is recommended to confirm these preliminary longitudinal findings. Furthermore, since previous cross-sectional studies

proved the dependence of the neck vessels CSA on age,^{22,30–32} future longitudinal CSA assessment should be conducted using heterogeneous age groups.

There are some limitations of the study, which have to be considered. First, a previous work comparing contrast enhanced MRA and TOF MRA showed that the former depicts the vascular anatomy more completely than the latter.⁴⁰ Nevertheless, in this study we preferred using TOF MRA because it allows to gain a 3D volume of the neck vasculature in non-invasive way. Accordingly, this technique is more adaptable to studies that involve HIs. Another limitation that has to be taken into account is that the procedure is not entirely operator-independent, since the segmentation is not completely automated. However, the operator's contribution was limited only to the contour selection on a single axial slice and to the ROI quality control. Furthermore, a previous work showed that this segmentation procedure is highly reproducible, both for the same operator and among different ones.¹⁹ The resampling step can be considered as another potential source of error. However, since the measurements are made on each 1.5mm-thick slice and the number of segmented slices is similar among the subjects, CSA-to-slice curves are not subsampled. Although a linear trend of CSA measure between two neighboring slices is assumed, the potential bias is small because of the low slice thickness. Finally, it should also be taken into consideration that since the CSA is measured on axial slices, we are assuming that the vessels are perpendicular to the axial plane. Although this can be considered almost true for the majority of the course of the considered vessels, future CSA assessment studies should be performed correcting for the angle existing between the vessel longitudinal axis and the z axis.

Conclusions

The scan-rescan reproducibility of the CCA-ICAs, VAs and IJVs CSA measures obtained via TOF-MRI with the whole vessel segmentation method is high. Furthermore, the importance of measuring the CSA on the whole vessel course and comparing corresponding levels is highlighted. In conclusion, the described method could be used to assess changes in future longitudinal studies on larger cohorts of subjects.

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Figure 1. Region of interest segmentation

A-anterior; CCA-common carotid artery; ICA-internal carotid artery; IJV-internal jugular vein; L-left; MRA-magnetic resonance angiography; P-posterior; R-right; ROI-region of interest; VA-vertebral artery.

Sagittal, coronal and axial view (C5–C6 level) of the CCA-ICAs, VAs and IJVs ROIs segmented on the MRA are shown in red, purple and blue respectively.

Figure 2. Cross sectional area (CSA) measurements of the CCA-ICAs, VAs and IJVs for the scan-rescan dataset

CCA-common carotid artery; CSA-cross-sectional area; ICA-internal carotid artery; IJV-internal jugular vein; IQR-interquartile range; VA-vertebral artery.

The scan median CSA (in blue), the rescan median CSA (in red) and the respective IQR (bars) are represented for all the samples, along C3 and C7 cervical levels.

Figure 3. Cross sectional area (CSA) measurements of the CCA-ICAs, VAs and IJVs for the baseline-follow-up dataset

CCA-common carotid artery; CSA-cross sectional area; ICA-internal carotid artery; IJV-internal jugular vein; IQR-interquartile range; VA-vertebral artery.

The baseline median CSA (in blue), the follow-up median CSA (in red) and the respective IQR (bars) are represented for all the samples, along C3 and C7 cervical levels.

Table 1

Comparison between scan-rescan cross-sectional area measurements.

Vessel	Cervical level	Scan CSA [mm ²] Median (IQR)	Rescan CSA [mm ²] Median (IQR)	p-value
Left CCA-ICA	C3	19.8 (5.9)	20.2 (5.1)	0.767
	C4	37.5 (20.6)	37.2 (20.0)	0.594
	C5	37.4 (5.5)	36.0 (7.7)	0.515
	C6	33.4 (4.7)	33.4 (6.3)	0.859
	C7	33.6 (8.1)	33.6 (7.5)	0.859
	Whole	32.5 (13.0)	33.1 (15.2)	0.890
Right CCA-ICA	C3	18.0 (4.9)	18.9 (6.3)	0.515
	C4	34.3 (15.5)	33.6 (16.2)	0.767
	C5	35.8 (6.4)	37.0 (7.0)	0.173
	C6	32.5 (8.3)	33.0 (8.7)	0.767
	C7	32.4 (11.7)	32.3 (11.8)	0.953
	Whole	30.8 (12.6)	31.0 (14.6)	0.762
Left VA	C3	15.6 (5.8)	15.7 (5.1)	0.594
	C4	16.1 (3.3)	15.8 (3.3)	0.678
	C5	15.6 (6.5)	15.8 (4.1)	0.678
	C6	15.3 (6.6)	14.4 (4.7)	0.374
	C7	15.6 (4.5)	14.8 (3.7)	0.678
	Whole	15.7 (5.6)	15.3 (4.1)	0.466
Right VA	C3	15.9 (2.4)	16.0 (3.1)	0.767
	C4	16.0 (2.8)	16.1 (3.6)	0.953
	C5	17.8 (3.7)	16.3 (3.4)	0.441
	C6	15.4 (3.9)	15.9 (4.3)	0.767
	C7	16.5 (3.5)	16.3 (4.4)	0.441
	Whole	16.3 (3.2)	16.1 (3.8)	0.169
Left IJV	C3	26.9 (21.9)	20.4 (34.0)	0.594
	C4	27.7 (37.0)	21.7 (33.9)	0.678
	C5	27.3 (47.5)	25.8 (33.5)	0.953
	C6	21.1 (56.8)	23.6 (37.6)	0.953
	C7	18.5 (77.0)	28.9 (50.3)	0.859
	Whole	24.4 (43.7)	23.6 (37.1)	0.128
Right IJV	C3	48.1 (13.0)	42.4 (18.2)	0.139
	C4	50.5 (23.1)	41.7 (25.2)	0.051
	C5	47.3 (25.3)	44.4 (21.9)	0.515
	C6	37.1 (29.9)	41.8 (27.7)	0.767
	C7	49.8 (34.3)	52.5 (51.7)	0.594
	Whole	46.6 (26.3)	44.7 (27.4)	0.307

CCA-common carotid artery; CSA-cross sectional area; ICA-internal carotid artery; IJV-internal jugular vein; IQR-interquartile range; VA-vertebral artery.

Scan-rescan CSA group medians and IQR on each cervical level are reported. Scan-rescan differences were tested on each level using Wilcoxon signed-rank sum test and with repeated measures analysis of covariance of the whole vessel length, corrected for the cervical level and the sample. P-values<0.05 were considered significant.

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Table 2

Intra-class correlation coefficients between scan and rescan cross-sectional area measures.

Vessel	Cervical level	ICC	95% CI		p-value
			Lower bound	Upper Bound	
Left CCA-ICA	C3	0.834	0.750	0.890	<0.001
	C4	0.826	0.741	0.883	<0.001
	C5	0.730	0.597	0.818	<0.001
	C6	0.782	0.675	0.853	<0.001
	C7	0.850	0.781	0.898	<0.001
	Whole	0.904	0.885	0.919	<0.001
Right CCA-ICA	C3	0.813	0.718	0.876	<0.001
	C4	0.837	0.757	0.891	<0.001
	C5	0.660	0.493	0.771	<0.001
	C6	0.740	0.613	0.825	<0.001
	C7	0.828	0.748	0.882	<0.001
	Whole	0.908	0.891	0.923	<0.001
Left VA	C3	0.408	0.108	0.606	0.006
	C4	0.634	0.455	0.754	0.006
	C5	0.807	0.713	0.871	<0.001
	C6	0.619	0.433	0.744	<0.001
	C7	0.620	0.444	0.740	<0.001
	Whole	0.639	0.570	0.698	<0.001
Right VA	C3	0.471	0.204	0.649	0.001
	C4	0.387	0.088	0.589	0.001
	C5	0.563	0.349	0.706	0.008
	C6	0.760	0.643	0.839	0.008
	C7	0.760	0.649	0.836	<0.001
	Whole	0.651	0.584	0.707	<0.001
Left IIV	C3	0.642	0.458	0.763	<0.001

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Vessel	Cervical level	ICC	95% CI		p-value
			Lower bound	Upper Bound	
	C4	0.790	0.681	0.861	<0.001
	C5	0.883	0.815	0.925	<0.001
	C6	0.886	0.821	0.928	<0.001
	C7	0.942	0.911	0.963	<0.001
	Whole	0.831	0.795	0.860	<0.001
Right IJV	C3	0.741	0.610	0.828	<0.001
	C4	0.776	0.666	0.849	<0.001
	C5	0.680	0.523	0.785	<0.001
	C6	0.773	0.662	0.848	<0.001
	C7	0.812	0.725	0.872	<0.001
	Whole	0.790	0.749	0.824	<0.001

CCA-common carotid artery; CI-confidence interval; CSA-cross sectional area; ICA-internal carotid artery; ICC-intra-class correlation coefficient; IJV-internal jugular vein; VA-vertebral artery.

Scan-rescan ICC, its 95% CI and p-values on each cervical level and for the whole vessels are reported. The agreement was considered poor for ICC lower than 0.40, fair for ICC between 0.40 and 0.60, good between 0.60 and 0.75 and excellent if higher than 0.75. P-values<0.05 were considered significant.

Table 3

Comparisons between baseline-follow-up cross-sectional area measurements.

Vessel	Cervical level	Baseline CSA [mm ²] Median (IQR)	Follow-up CSA [mm ²] Median (IQR)	p-value
Left CCA-ICA	C3	29.0 (15.3)	31.9 (16.2)	0.347
	C4	37.1 (11.3)	37.3 (9.9)	0.583
	C5	35.4 (7.2)	34.7 (6.3)	0.659
	C6	33.2 (7.0)	34.0 (6.9)	0.308
	C7	33.3 (6.8)	32.8 (8.2)	0.433
	Whole	33.6 (8.5)	34.4 (9.0)	0.282
Right CCA-ICA	C3	29.0 (14.6)	32.5 (19.6)	0.060
	C4	38.7 (9.5)	39.5 (7.0)	0.754
	C5	36.7 (7.7)	37.3 (5.4)	0.583
	C6	35.7 (6.4)	36.0 (5.5)	0.937
	C7	36.1 (7.0)	36.8 (9.1)	0.875
	Whole	35.8 (9.1)	36.9 (8.5)	0.820
Left VA	C3	16.2 (5.5)	15.7 (6.1)	0.158
	C4	15.9 (6.2)	16.2 (7.2)	0.937
	C5	15.4 (6.6)	16.0 (7.2)	0.388
	C6	14.5 (6.9)	15.1 (7.5)	0.388
	C7	14.8 (7.3)	15.2 (7.7)	0.530
	Whole	15.4 (6.6)	15.7 (6.8)	0.390
Right VA	C3	15.4 (5.7)	15.9 (5.9)	0.875
	C4	16.0 (6.2)	15.9 (5.4)	0.695
	C5	15.5 (6.9)	15.5 (7.3)	0.754
	C6	14.9 (6.2)	15.3 (7.3)	0.530
	C7	15.0 (6.5)	15.1 (9.1)	0.209
	Whole	15.4 (6.4)	15.7 (6.8)	0.663
Left IJV	C3	44.0 (42.1)	39.2 (46.0)	0.530
	C4	54.2 (40.4)	57.2 (33.7)	0.480
	C5	63.1 (48.6)	58.1 (34.0)	0.530
	C6	66.3 (54.3)	54.6 (50.8)	0.239
	C7	59.4 (74.0)	60.2 (57.0)	0.209
	Whole	53.0 (51.6)	53.8 (46.4)	0.858
Right IJV	C3	50.0 (26.7)	57.6 (36.2)	0.583
	C4	57.9 (24.1)	59.6 (33.3)	0.638
	C5	53.5 (44.4)	58.6 (32.2)	0.695
	C6	47.2 (56.0)	54.2 (43.8)	0.638
	C7	56.0 (70.5)	68.5 (58.7)	0.638
	Whole	54.3 (47.0)	59.2 (39.4)	0.762

CCA-common carotid artery CSA-cross sectional area; ICA-internal carotid artery; IJV-internal jugular vein; IQR-interquartile range; VA-vertebral artery.

Baseline-follow-up CSA group medians and IQR on each cervical level are reported. Baseline-follow-up differences were tested on each level using Wilcoxon signed-rank sum test and with repeated measures analysis of covariance of the whole vessel length, corrected for the cervical level and the sample. P-values<0.05 were considered significant.

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