

Inter-Observer Reliability of Fused Time-of-Flight MR Angiography and 3D Steady State Sequence versus 3D Contrast Enhanced Images in Evaluation of Neurovascular Compression

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Abstract

Purpose: Is to evaluate the accuracy of fused 3D time-of-flight (TOF) MR angiography and 3D Steady-State sequence (FIESTA) versus 3D contrast-enhanced T1 weighted images in evaluation of neurovascular compression via an inter-observer agreement protocol. **Methods:** Patients presented with trigeminal neuralgia, tinnitus, or facial hemispasm were examined using 3D-TOF-MRA, 3D-FIESTA, and 3D contrast-enhanced T1WI of the cerebellopontine angle to assess neurovascular compression. Two independent readers assessed the location, signal alteration, offending vascular structure, and grade of neurovascular compression using fused 3D-TOF-MRA and 3D-FIESTA versus contrast-enhanced T1 weighted images. The Kappa test for interobserver agreement was done. **Results:** The final study cohort consisted of 56 patients (42 females and 14 males) with a mean age of 38.25 ± 1.94 . AICA was the offending vessel for 32 (57.1%) patients. The most common offending nerve was the trigeminal nerve in 26 patients, followed by facial/vestibulocochlear complex in 18 patients, and solely the 8th nerve in 12 patients. All three grades of compression were encountered in this study with percentages of 48.2% (27/56), 30.3% (17/56), and 21.4% (12/56) for grades I, II, III respectively. Fused TOF and steady-state images, and contrast-enhanced images showed perfect agreement for detection of the side of compression, the relation between nerve and vascular loop, offended neural segment, and offend-

ing vessel, while showing good agreement regarding the degree of compression. **Conclusion:** Fused TOF and steady-state images provide sufficient data to diagnose and grade microvascular compression syndromes comparable to contrast-enhanced images.

Keywords

Neurovascular Compression, Trigeminal Neuralgia, Microvascular Decompression, Tinnitus, Vertigo, Hemifacial Spasm

1. Introduction

Neurovascular compression syndromes are due to the presence of conflict between a vascular loop and one of the cranial nerves at the root entry/exit zone in the cerebellopontine angle. Hemifacial spasm was first described in the literature in 1875 in a case of vertebral artery aneurysm compressing the facial nerve, while the concept of neurovascular compression, as per current concept, was first described by McKenzie in 1936 and more investigated and pioneered by Jannetta [1]. The anatomic proximity of these nerves to the vascular tree correlates the clinical presentation to the expected anatomical abnormality as classified by Rhoton's neurovascular bundles [2]; trigeminal nerve is related to and commonly compressed by the superior cerebellar artery, while facial and vestibulocochlear nerves are related to the anterior inferior cerebellar artery. The inferior neurovascular bundle includes the lower four cranial nerves and the posterior inferior cerebellar artery.

Clinical presentation varies according to the severity of compression, symptoms include trigeminal neuralgia, hemifacial spasm, vertigo, tinnitus, and glossopharyngeal neuralgia according to the compressed nerve [1] [3] [4] [5]. Neurovascular compression syndromes remained a diagnosis of exclusion in early surgical practice with an incidence of irrelevant surgical evidence and outcome, with advances in neuroradiological studies, the diagnosis was more radiologically confirmed in a number of studies comparing preoperative imaging to intraoperative findings [6]. Preoperative diagnosis is essential to avoid unnecessary exploratory surgeries. Formerly MRI role was limited to rule out causative pathologies e.g. tumor, multiple sclerosis, and infection. MR angiography was then applied to visualize abnormal neurovascular proximity [7], while in 2004 Naraghi *et al.* [8] introduced the concept of the constructive interface in steady-state (CISS) where the CSF cisterns are seen hyperintense, thus visualizing the neurovascular structures accurately in a non-invasive maneuver.

Earlier, diagnosis of neurovascular compression syndromes was mainly clinical, introduction of conventional MRI to detect proximity between nerves and vascular structures was helpful, however, not diagnostic since no MR vascular imaging panel was feasible. In certain situations, conventional diagnostic angio-

graphy was performed, to compare course of vascular structures on both sides, but this was not a reproducible tool as an invasive maneuver. Currently, the routine MRI protocol for NVC syndromes includes 3D post-contrast T1WI, high-resolution T2 in steady-state sequences, and 3D Time of Flight MR angiography (TOF MRA). We propose an evaluation tool based on both 3D TOF MRA fused to high-resolution T2 in steady-state using FIESTA (Fast Imaging Employing Steady-State Acquisition) sequence without the need for contrast administration. Successful interpretation of the results would rule out the post-contrast images thus avoiding the patient's unnecessary intravenous contrast administration. The purpose of this study is to assess the inter-observer reliability of fused TOF MRA and FIESTA versus 3D contrast-enhanced T1WI sequence in the evaluation of neurovascular compression syndromes.

2. Patients and Methods

2.1. Study Population

Between July 2019 to July 2020, all patients with clinical suspicion of cranial nerve compression by clinical examination who were referred for MRI evaluation were included in the study. Patients presented by trigeminal neuralgia not explained by head and neck clinical examination, tinnitus not improved by usual management, or facial hemispasm. All patients underwent history taking, clinical examination for possible causes of the symptoms, and conventional MRI imaging to rule out other causes than neurovascular compression. Patients with contraindication to contrast administration were excluded. Patients having nerves pathology including high signal intensity and enhancement as well as patients having space-occupying lesions or arteriovenous malformations in the vicinity of the clinically affected nerves were excluded.

2.2. Magnetic Resonance Imaging

All patients included in this study were examined using a 1.5-T MR imaging scanner (GE SIGNA EXPLORER) using 16 channel neurovascular head and neck coil, for assessment of the neurovascular compression, all patients were examined using 3D FIESTA on the posterior fossa (TR/TE: 6.8/2.7, flip angle: 60, thickness 1 mm with overlapping 0.5 mm & NEX: 2), 3D TOF (TR/TE: 28/4, flip angle: 20, thickness 1.2 mm with overlapping 0.6 mm & NEX: 1) and 3D axial FSPGR post-contrast (TR/TE: 7/2.1, flip angle: 12, thickness 1 mm with overlapping 0.5 mm & NEX: 1) after administration of contrast dose of 0.05 mmol/kg using Gadoterate meglumine through 20 gauge peripheral venous cannula. The axial plane was defined as perpendicular to the floor of the fourth ventricle and the posterior border of the brainstem; the coronal plane was parallel to these structures.

2.3. Image Analysis

All DICOM data transferred to secondary advantage window workstation GE

ADW 4.7 (volume share 7) images were analyzed. Multi-planer reformatted images were generated for the three sequences (3D FIESTA, TOF-MRA, and post-contrast T1) with a section thickness of 0.5 mm and without an intersection gap. Fusion MR images that combined 3D FIESTA and TOF-MRA were generated on the workstation by choosing the option image fusion after doing drag and drop of the FIESTA image into the TOF-MRA image. 3D FIESTA, TOF-MRA, post-contrast T1, and fusion sequences from all examinations were randomized. Two expert neuro-radiologists (13- and 12-years' experience in neuroradiology) were asked to assess the diagnostic performance of each sequence on the same workstation independently, there results were conducted for inter-observer agreement.

Observers were asked to report the side of the neurovascular compression, the offended vascular structure (artery or vein), the offended neural segment (root entry zone or cisternal portion), the location of vascular structure in relation to the nerve (inferior, lateral, medial, superior or anterior) and degree of compression (Grade I: if the vessel was simply in contact with the nerve but without any visible deformity of the root; Grade II: if there was a displacement and/or a distortion of the root; Grade III: if a clear-cut and marked indentation on the root was present).

2.4. Statistical Analysis

Data were analyzed using IBM SPSS software package version 22.0. Qualitative data were described using numbers and percentages. Quantitative data were described using mean, standard deviation for parametric data after testing normality using the Kolmogorov-Smirnov test. The significance of the obtained results was judged at the (0.05) level. Kappa agreement was calculated for categorical variables with Kappa where results were interpreted as follows: 1) 0.01 - 0.20: slight agreement, 2) 0.21 - 0.40: fair agreement, 3) 0.41 - 0.60: moderate agreement, 4) 0.61 - 0.80: good agreement, and 5) 0.81 - 0.99: 0 perfect agreement.

3. Results

105 patients with clinical suspicion of cranial nerve compression by clinical examination were referred for MRI evaluation. Fourteen patients were excluded due to contraindication to contrast administration, 35 patients were excluded due to space-occupying lesions in the vicinity of the clinically affected nerves. All patients were presented with one of the suspected cranial nerve neuropathic pain or symptoms *i.e.* trigeminal neuralgia, facial hemispasm and vertigo, either due to neurovascular compression or underlying lesion. Course of the disease was variable among the group, ranging from 3 months to 2 years. The final study cohort consisted of 56 patients, 42 (75%) of them were female, age ranged from 17 to 68 years old, and mean age 38.25 ± 1.94 . AICA was the offending vessel for 32 (57.1%) patients, 6 of them were trigeminal nerve compression, while SCA was the offending vessel for 24 (42.9%) patients, 20 of them were trigeminal neuralgia patients.

The most common offended nerve was the trigeminal nerve in 26 patients (Right 12, Left 12, Bilateral 2), followed by facial/vestibulocochlear complex in 18 patients (Right 4, Left 12, Bilateral 2), and solely the 8th nerve in 12 patients (Right 6, Left 4, Bilateral 2). All three grades of compression were encountered in this study with percentages of 48.2% (27/56), 30.3% (17/56), and 21.4% (12/56) for grades I, II, III respectively (**Table 1**). Demonstrative cases of neuro-vascular compression are shown in (**Figure 1** and **Figure 2**).

Kappa agreement test showed perfect agreement for detection of the side of compression, the relation between nerve and vascular loop, offended neural segment, and offending vessel, while showing good agreement regarding the degree of compression, results of the inter-observer agreement are summarized in (**Table 2**).

No signal intensity alteration of the offended nerve was detected by any of the reviewers among the study cases, with 100% agreement.

Table 1. Patients' demographics, affected nerve distribution, compressing vascular loop, and degree of nerve compression among studied cases.

	N = 56	%
Age/years		
Mean \pm SD	38.25 \pm 14.5	
(range)	(17.0 - 68.0)	
Sex		
Male	14	25.0
Female	42	75.0
Nerve affected:		
Trigeminal nerve	n = 26	46.4
Right	12	46.2
left	12	46.2
both	2	7.7
Facial & Vestibulocochlear nerves	n = 18	32.2
Right	4	22.2
left	12	66.7
both	2	11.1
Vestibulocochlear nerve	n = 12	21.4
Right	6	50.0
left	4	33.3
both	2	16.7
Compressing loop		
AICA	32	57.1
SCA	24	42.9
Degree of compression		
Grade 1	27	48.2
Grade 2	17	30.3
Grade 3	12	21.4

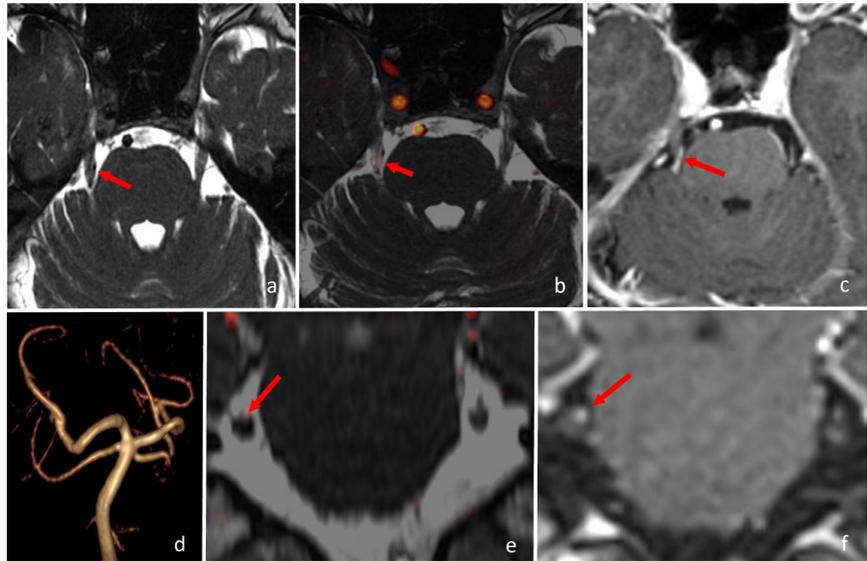


Figure 1. 43 years old female complained of right-side trigeminal neuralgia. (a) Axial FIESTA image at the Meckel's caves level shows linear low signal intensity crossing the right trigeminal nerve (arrowed). (b) Fused axial FIESTA and TOF MRA image at the same level shows the vascular loop crossing the right trigeminal nerve in orange color. (c) Axial contrast enhanced T1 image at the same level shows the enhancing vascular loop crossing the right trigeminal nerve. (d) 3D TOF MRA shows a higher level of the right superior cerebellar artery. (e and f) Fused coronal FIESTA and TOF MRA image, and coronal contrast enhanced T1 image show the relationship between the offending vascular loop and trigeminal nerve, and degree of indentation (type II).

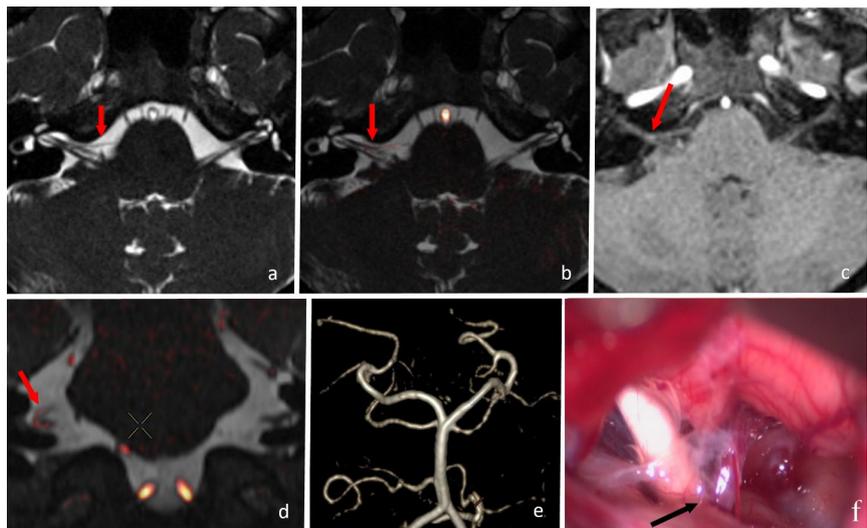


Figure 2. 37 years old male complained of right-side pulsatile tinnitus. (a) Axial FIESTA image through the internal auditory canal shows linear low signal intensity contacting the right vestibulocochlear nerve (arrowed). (b) Fused axial FIESTA and TOF MRA image at the same level shows the vascular loop contacting the right vestibulocochlear nerve in orange color. (c) Axial contrast enhanced T1 image at the same level shows the enhancing vascular loop contacting the right vestibulocochlear nerve. (d & e) Fused coronal FIESTA and TOF MRA image, and 3D TOF MRA show the vascular loop of the right anterior inferior cerebellar artery. (f) Intra-operative image shows the degree of neurovascular compression (type III).

Table 2. Inter-observer agreement for fused Fiesta/TOF and contrast enhanced T1 images in assessment of neurovascular compression.

	MR Sequence	kappa	95% CI	p value	% of agreement
Detection	Fiesta/TOF	1.0	1.0 - 1.0	<0.001*	100
	Contrast T1	1.0	1.0 - 1.0	<0.001*	100
Side affected	Fiesta/TOF	0.95	0.91 - 0.97	<0.001*	96.5
	Contrast T1	0.93	0.78 - 0.98	<0.001*	97.0
Relation between nerve and vascular loop	Fiesta/TOF	0.89	0.83 - 0.96	<0.001*	94.7
	Contrast T1	0.90	0.84 - 0.97	<0.001*	95.8
Offended neural segment	Fiesta/TOF	0.91	0.85 - 0.97	<0.001*	95.9
	Contrast T1	0.89	0.84 - 0.97	<0.001*	94.9
Offending vessel	Fiesta/TOF	0.84	0.68 - 0.91	<0.001*	92.9
	Contrast T1	0.85	0.81 - 0.91	<0.001*	93.5
Degree of compression	Fiesta/TOF	0.74	0.56 - 0.84	<0.001*	85.7
	Contrast T1	0.71	0.49 - 0.81	<0.001*	83.4

4. Discussion

Diagnosis of neurovascular compression syndromes has been one of the neurosurgical challenges, their diagnosis is not definite clinically in several cases. Two theories were adopted in order to explain the associated clinical presentation of neurovascular compression syndromes. One hypothesis supposes that close contact and transmitted pulsation of the offender can lead to focal demyelination, reorganization, and axonal hyperactivity at the junction between the central glial and peripheral nonglial junction [9], while the other theory adopts the concept of hypoperfusion of the offended nerve due to its compression [10]. Accurate diagnosis of neurovascular compression syndromes is essential to avoid unnecessary surgical procedures, to achieve that thorough correlation between clinical presentation and radiological results is the cornerstone to diagnosis [6]. 3D steady-state has been the golden standard to locate neurovascular conflicts due to its high accuracy to visualize structures in the basal CSF cisterns with precise anatomical relations with high resolution [11]. Contrast-enhanced MRA is introduced for better visualization of vascular loops via producing contrast between nerves and offending vessels. The concept of angiography to accurately visualize the offending vessel was adopted by Blitz *et al.* [12] whose study showed two folds positive results than mere steady state. Although Blitz *et al.* used contrast-enhanced angiography, non-contrast TOF is a valid substitute without the need to introduce IV contrast.

Previous studies adopted the concept of dual imaging; steady-state and contrast-enhanced images or TOF, but relied on comparison between images, in this study fused images were produced to give an accurate anatomical picture elimi-

nating the limitation of each imaging modality separately. Inter-observer agreement for fused images protocol achieved a perfect matching regarding the side of compression, the relation between nerve and vascular loop, offended neural segment, and offending vessel, while showed good agreement regarding the degree of compression. This protocol of fused images is adopted in previous reports [13] which matched our results concluding its high sensitivity for diagnosis, while in this study a blinded randomized inter-observer agreement was performed for validation.

Although high spatial resolution steady-state study allows accurate anatomical analysis of vascular and neural structures, it lacks signal differentiation, not only between vessels and nerves. Contrast-enhanced angiography shows vessels in high signal against the low signal CSF, while nerves are seen in an intermediate signal.

The trigeminal nerve is the largest cranial nerve and the most liable to neurovascular compression [14], also its susceptibility to being offended by both AICA and SCA increases its incidence. Our results matched previous studies regarding offending vessels except for negative results which were reported as absent radiological conflict despite clinical and intraoperative findings, which could be attributed to either the venous offender or slice thickness which could skip a small vessel. In this study, no negative results were obtained which is most likely due to the elimination of slice thickness factor via obtaining 3D images for both steady-state and TOF, also offending venous structure is yet to be more investigated, as per Gamaleldin *et al.* [13], cases which were reported to have venous compression showed no findings on preoperative radiological assessment.

Signal intensity alteration of the offended nerve is not properly reported in the literature as a sign of severe compression, though reported by a similar inter-observer study by Gamaleldin *et al.* [13] in 20% of patients, these findings were reported only by one of the two reviewers. Based on the demyelination hypothesis, a number of studies concluded that decreased fractional anisotropy (FA) is strongly associated with NVC syndromes in diffusion tensor imaging (DTI) [15], while recent studies confirmed the same results with other causes of trigeminal neuralgia e.g. multiple sclerosis as well [16], which rules out the value of DTI as a diagnostic tool for NVC syndromes.

Treatment strategies for NVC syndromes include a number of invasive procedures after the failure of best medical treatment, microvascular decompression (MVD) is considered the most durable treatment option that provides immediate pain relief [17], on the other hand, percutaneous rhizotomy has been emerging as a less invasive procedure, thereby rises the importance of preoperative evaluation and surgical results prediction. A number of studies [18] [19] concluded that the degree of compression is the key to postoperative prognosis rather than mere conflict detection, thereby radiological grading is essential to decide a treatment plan and to estimate long term prognosis, as per Leal *et al.* [20], 90% of patients with a higher grade of compression were pain-free within 2

years postoperatively in comparison to only 54% for mild compression. In line with that, Sindu *et al.* [21] reported the highest surgical favorable outcome with the higher compression grade and vice versa. In this study, fused images achieved good inter-observer agreement regarding the degree of compression. Detection of the degree of compression accurately, as well as other parameters, without the need to use contrast, is an important finding of our study, as Ramalho *et al.* [22] reported the potential accumulation of Gadolinium and toxicity due to repeated Gadolinium-enhanced imaging. The limitations of this study are the relatively small number of cases and lack of intra-operative correlation in all cases.

5. Conclusion

Fused TOF and 3D steady-state images are of excellent value to diagnose and classify neurovascular compression syndromes, which is a feasible technique that could substitute contrast-enhanced examination, especially in patients with renal impairment or other contraindication of contrast administration.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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