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FULL PAPER

Preoperative evaluation of neurovascular relationship in trigeminal neuralgia by three-dimensional fast low angle shot (3D-FLASH) and three-dimensional constructive interference in steady-state (3D-CISS) MRI sequence

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Objective: The purpose of the study was to evaluate the value of high-resolution three-dimensional fast low angle shot (3D-FLASH) and three-dimensional constructive interference in steady-state (3D-CISS) MRI sequence solely or the combination of both in the visualization of neurovascular relationship in patients with trigeminal neuralgia (TN).

Methods: 65 patients with unilateral TN underwent 3D-FLASH and 3D-CISS imaging were retrospectively studied. Neurovascular relationship at the intracranial segment of trigeminal nerve was reviewed by two experienced neuroradiologists, who were blinded to the clinical details. The imaging results were compared with the operative findings in all patients.

Results: The accuracy and positive rates of the 3D-FLASH + CISS imaging (98.46, 92.31%) in judging the

symptomatic side according to the presence of vascular contacts were higher than those of 3D-CISS (90.77%, 84.62) or 3D-FLASH (89.23, 83.08%) sequence. In addition, the statistical analysis showed the sensitivity and accuracy of 3D-FLASH + CISS imaging was higher than that of 3D-FLASH ($p < 0.05$). The 3D-FLASH + CISS imaging was more accurate in determining the type of offending vessel than 3D-CISS or 3D-FLASH imaging.

Conclusion: The retrospective study demonstrates that the combination of 3D-FLASH with 3D-CISS sequence well delineates the relationship between intracranial segment of trigeminal nerve and adjacent vessels in terms of increased positive rates and accuracy.

Advances in knowledge: The study firstly dealt with the combination of 3D-CISS and 3D-FLASH imaging in TN.

INTRODUCTION

Trigeminal neuralgia (TN) is a common disease in the elderly, with a prevalence of about 50%.¹ It is a unique form of neuropathic pain, seriously affect the life and work of patient, and characterized by recurrent episodes of paroxysmal, electric, and lancinating pain generally in the distribution of one or more branches of the trigeminal nerve.^{2,3} Since Jannetta proposed the theory of microvascular compression, it has been established that neurovascular contact (NVC) is the main cause of TN.³⁻⁵ Preoperative identification of NVC has an impact on the determination of appropriate treatment for TN.

Currently, microvascular decompression (MVD) is considered the most effective treatment for patients with TN after the failure of drug therapy.^{6,7} Indications of MVD needed to be identified, based on demonstration of a vascular compression on preoperative imaging. As we all known, a lot of cases with TN were caused by NVC at the root entry zone of the trigeminal nerve. Furthermore, in several analyses, patients with more severe vascular compression of the trigeminal root have reported greater improvement of their symptoms and greater relief of their long-term pain after MVD.⁸⁻¹¹ Therefore, prediction of NVC using preoperative imaging may be useful

for predicting long-term success and could help guide patient selection for MVD treatment.

Due to poor resolution, conventional imaging techniques are disappointing in preoperative evaluation of the vascular contact with the trigeminal nerve. Recently, a number of high-resolution MRI sequences have been developed, which could be used to evaluate most features of the NVC in patients with TN who are under consideration for MVD. Three-dimensional time-of-flight magnetic resonance angiography (3D-TOF-MRA), three-dimensional constructive interference in steady-state (3D-CISS), and three-dimensional fast imaging employing steady-state acquisition (3D-FIESTA) sequence were mainly used for MRI of trigeminal nerve.^{12,13} The 3D-TOF-MRA imaging could display the larger intracranial arterial.¹⁴ However, it could not display the small tortuous arteries and the veins.¹⁵ The 3D-CISS imaging is a high-spatial-resolution, refocused gradient-echo MRI sequence that is flow compensated.¹⁶ It can clearly display both veins and arteries as low-signal-intensity structures, similar to the trigeminal nerve.¹⁷ Salles et al¹⁸ applied 3D-FIESTA sequence in stereotactic radiosurgery for patients with TN. They confirmed the 3D-FIESTA sequence could provide wonderful visualization of the nerve entry zone and the vasculature surrounding it, and it may be feasible to radiosurgical targeting of specific trigeminal nerve branches.¹⁸

To our knowledge, there was no report about the combination of 3D-CISS and three-dimensional fast low angle shot (3D-FLASH) imaging in TN. In the present study, to preoperatively visualize neurovascular relationship, 3D-FLASH and 3D-CISS sequence was performed on 65 patients with TN. The aims of this study were to evaluate the accuracy and the preoperative diagnostic value of high resolution MRI techniques, the 3D-FLASH and 3D-CISS sequence solely or the combination of both was used to detect the relationship between intracisternal segment of trigeminal nerve and adjacent vessels in patients with TN.

METHODS AND MATERIALS

Patients

The retrospective study was approved by the ethics committee of our hospital and the written informed consent was obtained from all subjects. A total of 65 patients (22 males and 43 females; age range, 35–80 years; mean age, 50 years) with TN that confirmed by clinical diagnosis and surgical findings at our hospital were included during June 2013 to September 2016. The clinical diagnostic criteria for patients with TN were unilateral and had trigeminal innervation episodes of severe electrical shock.³ All of the patients have unilateral, medically intractable TN (left side involvement, $n = 46$; right side involvement, $n = 19$) with median duration of 6.5 years (range, 1.1–20.3 years) All patients underwent preoperative MRI. In addition, patients with recurrent TN, multiple sclerosis, inflammation or intracranial tumors were excluded.

MR imaging procedures

All imaging were performed by using a 1.5 T MR system (NOVUS, Siemens, Erlangen, Germany). Two pulse sequences were used: (1) The 3D-CISS sequence with TR/TE/NEX =

11.34/5.67/2, flip angle = 70°, field of view (FOV) = 160 × 160 mm (read × phase encode), slab thickness = 60.0 mm, section thickness = 0.8 mm, matrix = 256 × 256; (2) the enhanced 3D-FLASH T_1 WI sequence with TR/TE/NEX = 35/7.12/2, flip angle = 25°, field of view (FOV) = 160 × 160 mm (read × phase encode), slab thickness = 60.0 mm, section thickness = 0.8 mm, matrix = 256 × 256, contrast medium gadopentate dimeglumine (GD-DTPA) 0.1 mmol kg⁻¹. All 3D original images were browsed and analyzed. The acquisition slab was oriented transversely on the sagittal and coronal scout images so that both sides of the trigeminal nerve could be included in the image. After obtaining transverse images, coronal reformatted images were also obtained by using a multiplanar reconstruction (MPR) algorithm on the workstation. Based on the 3D-FLASH T_1 WI original images, the maximum intensity projection (MIP) was used to reconstruct blood vessels so that the offending vessels of trigeminal nerve can be displayed.

MRI image analysis

All acquired images were analyzed on the PACS workstation (Neusoft, Shenyang, China) prior to surgery. Two experienced radiologists with 10 years of experience in neuroradiology and radiology evaluated all 3D-CISS and 3D-FLASH images for the presence or absence of NVC independently and separately. The radiologists had completed their training and were blinded to any knowledge of which side the neurovascular contact was located at and operative findings. In addition, the radiologists were familiar with the objectives of this study, specialized in the central nervous system, could accurately judge the relationship between the intracranial nerves and vessels, and the radiologists were very clear about the post processing of images due to the window of the workstation for the radiologists was active. The criteria for determining the presence of vascular contact between the bilateral trigeminal nerves are as following: there is no cerebrospinal fluid between the trigeminal nerve and the blood vessel, and the nerve shows vascular impression, distortion or displacement.¹² The degree of vascular contact with the trigeminal nerve was classified into the following categories: contact (compression, distortion, or deviation of the nerve resulted from vascular compression; simple contact, nerve and blood vessel only existed contact) and noncontact/non-compression type. The steps of analyzing the images were as following: the first step was to singly analyze the 3D-FLASH T_1 WI sequence, the second step was to singly analyze the 3D-CISS sequence, and the third step was to analyze the combination of 3D-FLASH + CISS sequence. When disagreement existed about the presence or absence of NVC, a consensus was reached through discussion. The offending vessels were further determined on the basis of anatomical relation and blood vessel's courser of the upper and lower layers. The examination was regarded as positive if the definite NVC between the trigeminal nerve and a vessel can be seen by 3D-CISS and/or 3D-FLASH sequences, whereas no contact was considered to be negative.

Statistical analysis

Statistical calculations were performed by use of SPSS 16.0 software, (SPSS, Inc., Chicago, IL). χ^2 tests were used to examine the relation between qualitative variables. For all statistical values, a

Figure 1. A 46-year-old female with vascular contact at the left side of the trigeminal nerve. (a) The MPR of 3D-CISS images showed vascular contact (short arrow) at the left of trigeminal nerve (long arrow). (b) The enhanced 3D-FLASH sequence showed two vascular imagings (long arrow and short arrow) around the trigeminal nerve. (c) MIP reconstructions displayed that offending vessels were the superior cerebellar artery (long arrow) and venae petrosa (short arrow), respectively. MIP, maximum intensity projection; MPR, multiplanar reconstruction; 3D-CISS, three-dimensional constructive interference in steady-state; 3D-FLASH, three-dimensional fast low angle shot.

p value of less than 0.05 was considered to indicate a statistically significant difference.

RESULTS

Intraoperative results of neurovascular contact

A total of 65 patients underwent trigeminal microvascular decompression, which were performed by one experienced neurosurgeon via retrosigmoid approach under endoscope.¹⁹ Necessary judgments were made for the identification of offending vessels according to the distribution as well as arrangement. Intraoperative diagnosis identified 61 cases of NVC including 9 cases of multiple vascular contact (Figures 1 and 2) and 52 cases of single vascular contact on intracisternal segment of trigeminal nerve. In addition, the single vascular contact were observed in 31 cases of superior cerebellar artery (Figures 3 and 4), 9 cases of anterior inferior cerebellar artery, 6 cases of verteobasilar artery, and 6 cases of venae petrosa. The multiple vascular contact included 3 cases of superior cerebellar artery + anterior inferior cerebellar artery, 3 cases

of superior cerebellar arteries + venae petrosa, 2 cases of superior cerebellar artery + verteobasilar artery, and 1 case of anterior inferior cerebellar artery + venae petrosa. Furthermore, regarding the remaining 4 cases, intraoperative diagnosis showed no obvious NVC (Figure 5). For the 4 cases found no contact in surgical results, but with very typical clinical symptoms, we concluded that there might not be a causal relationship between NVC and symptoms, or the presence of vascular contact was in the posterior segment of the trigeminal nerve.

Comparison of clinical diagnosis results with preoperative imaging assessment of the symptomatic and asymptomatic side

The 3D-FLASH, 3D-CISS, 3D-FLASH + CISS assessment demonstrated the case of vascular contact in the symptomatic side and asymptomatic side were 54 and 31, 55 and 33, 60 and 35, respectively. By comparing with the surgical results, the

Figure 2. A 39-year-old female with vascular contact at the right side of the trigeminal nerve. (a) The MPR of 3D-CISS images showed vascular contact (short arrow) at the right of trigeminal nerve (long arrow). (b) The enhanced 3D-FLASH sequence showed two vascular imagings (long arrow and short arrow) around the trigeminal nerve. (c) MIP reconstructions displayed that offending vessels were the superior cerebellar artery (long arrow) and venae petrosa (short arrow), respectively. MIP, maximum intensity projection; MPR, multiplanar reconstruction; 3D-CISS, three-dimensional constructive interference in steady-state; 3D-FLASH, three-dimensional fast low angle shot.

Figure 3. A 53-year-old male with vascular contact at the left side of the trigeminal nerve. (a) The MPR of 3D-CISS images showed the vascular contact was at upper edge small vessel (long arrow) of the right trigeminal nerve (short arrow). (b) The enhanced 3D-FLASH sequence showed vascular imaging (long arrow) around the left trigeminal nerve (short arrow). (c) The MIP reconstructions displayed that offending vessel was the superior cerebellar artery (long arrow). MIP, maximum intensity projection; MPR, multiplanar reconstruction; 3D-CISS, three-dimensional constructive interference in steady-state; 3D-FLASH, three-dimensional fast low angle shot.

sensitivity, specificity, and overall accuracy were 83.08, 52.31, 67.69%, respectively for the 3D-FLASH assessment; 84.62, 49.23, 66.92%, respectively for the 3D-CISS assessment; and 92.30, 46.15, 69.23%, respectively for the 3D-FLASH + CISS assessment. Statistical analysis showed that the sensitivity, accuracy, and positive rates of 3D-FLASH + CISS sequence was higher than that of 3D FLASH and 3D-CISS sequence, but there was no statistical significance ($p > 0.05$, Table 1). For patients who were detected with NVC on the asymptomatic side, we registered the information of patients, followed by telephone calls every 6 months to determine whether these patients had clinical symptoms, and accumulated the etiology for future diffusion tensor imaging (DTI) studies of the trigeminal nerve.

Comparison of surgical findings with preoperative assessment of the symptomatic side

The 3D-FLASH sequence diagnosed 54 cases had vascular contact on symptomatic side that the endoscopic findings also was the same, 11 cases had no vascular contact which was different from endoscopic findings that 7 cases of endoscopic vascular contact. The 3D-CISS sequence demonstrated 5 cases

had vascular contact that the endoscopic findings also was the same, 10 cases had no vascular contact which was different from endoscopic findings that 6 cases of endoscopic vascular contact. The 3D-FLASH + CISS sequence indicated 60 cases had vascular contact in symptomatic side that the endoscopic findings also was the same, 5 cases had no vascular contact which was different from endoscopic findings that 1 case of endoscopic vascular contact. By comparing with the surgical results, the sensitivity, specificity and accuracy were 88.52, 100, 89.23%, respectively for the 3D-FLASH assessment, 90.16, 100, 90.77%, respectively for the 3D-CISS assessment, and 98.36, 100, 98.46%, respectively for the 3D-FLASH + CISS assessment. Statistical analysis showed that the sensitivity and the accuracy of 3D FLASH + CISS sequence was higher than that of 3D-FLASH ($p < 0.05$, Table 2).

Responsible vascular type and numbers

The offending vascular type were further determined by 3D-FLASH, 3D-CISS, and 3D-FLASH + CISS sequence, which were compared with intraoperative vascular type. As shown in Table 3, 3D-FLASH + CISS sequence was more accurate in determining the type of offending vessel than 3D-CISS and

Figure 4. A 33-year-old female with vascular contact at the right side of the trigeminal nerve. (a) The MPR of 3D-CISS images showed the vascular contact was at upper edge small vessel (long arrow) of the right trigeminal nerve (short arrow). (b) The enhanced 3D-FLASH sequence showed vascular imaging (long arrow) around the right trigeminal nerve (short arrow). (c) The MIP reconstructions displayed that offending vessel was the superior cerebellar artery (long arrow). MIP, maximum intensity projection; MPR, multiplanar reconstruction; 3D-CISS, three-dimensional constructive interference in steady-state; 3D-FLASH, three-dimensional fast low angle shot.

Figure 5. A 65-year-old male without vascular contact around the trigeminal nerve. The oblique sagittal images of 3D-CISS sequence showed the shape and direction of the normal trigeminal nerve (short arrow), peripheral vessels (long arrow) without vascular contact. 3D-CISS, three-dimensional constructive interference in steady-state.

3D-FLASH sequence alone. In particular, the 3D-FLASH + CISS sequence identified the offending vessels including 31 cases of superior cerebellar artery, 6 cases of vertebrobasilar artery, and 2 cases of superior cerebellar artery + vertebrobasilar artery, which were accordance with intraoperative results. For the diagnosis of the multiple vascular contact, the 3D-FLASH + CISS sequence misdiagnosed 1 case of superior cerebellar artery and anterior inferior cerebellar artery as superior cerebellar artery + petrosal vein, and misdiagnosed 1 case of superior cerebellar artery + venae petrosa as superior cerebellar artery alone. In addition, the analysis of Cohen's Kappa coefficient showed the diagnostic accordance rate between 3D-FLASH assessment and surgical findings, 3D-CISS assessment and surgical findings, 3D-FLASH + CISS assessment and surgical findings was 48.6, 52.3, and 88.4%, respectively.

DISCUSSION

Clinical features and associated examinations are the basis for the diagnosis and treatment of TN. High resolution MRI is considered to be helpful to diagnosis of TN. The conventional MR sequence is not able to clearly depict the relationship between trigeminal nerve and adjacent vessels. However, with the rapid development and the popularity of high resolution MR technology, special sequence of MR imaging can greatly display the relationship between nerve and vessels, and provide a powerful guarantee for the clinical development of MVD.²⁰

The enhanced 3D-FLASH sequence with contrast medium, can not only display the thicker artery steadily, but also depict the smaller arteries and veins, and thus resulting in obvious contrast regarding the signal intensity between the nerves and blood vessels.²¹ The 3D-CISS sequence could show high signal of the cerebrospinal fluid and relatively low signal of nerve and peripheral vessels, which makes the nerve and vessels more clearly and intuitively against the cerebrospinal fluid.^{12,21,22} In this study, the 3D-CISS sequence with small FOV vision and thin-layer scanning (TLS) was used to reconstruct the coronal and oblique sagittal position of the trigeminal nerve, which could clearly show the relationship between trigeminal nerves and vessels, and display the source of offending vessels. The trigeminal nerve trunk and gasserian ganglion could be clearly displayed in all patients. The 3D-CISS sequence could display nerve transposition and bending caused by vascular compression, which was

Table 1. Comparison of surgical results with preoperative imaging assessment of the symptomatic and asymptomatic side

Methods	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value	Positive rates (%)
3D-FLASH	83.08% (54/65)	52.31% (34/65)	67.69% (88/130)	63.53% (54/85)	75.56% (34/45)	65.38% (85/130)
3D-CISS	84.62% (55/65)	49.23% (32/65)	66.92% (87/130)	62.5% (55/88)	76.19% (32/42)	67.69% (88/130)
3D-FLASH + CISS	92.30% (60/65)	46.15% (30/65)	69.23% (90/130)	63.16% (60/95)	85.71% (30/35)	73.08% (95/130)
<i>p-value</i>						
3D FLASH + CISS vs 3D FLASH	0.109	0.483	0.780	0.956	0.260	0.179
3D FLASH + CISS vs 3D CISS	0.170	0.726	0.690	0.923	0.293	0.342

3D-FLASH, three-dimensional fast low angle shot; 3D-CISS, three-dimensional constructive interference in steady-state.

Table 2. Comparison of surgical findings with preoperative assessment of the symptomatic side

Methods	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value	Positive rates (%)
3D-FLASH	88.52% (54/61)	100% (4/4)	89.23% (58/65)	100% (54/54)	36.36% (4/11)	83.08% (54/65)
3D-CISS	90.16% (55/61)	100% (4/4)	90.77% (59/65)	100% (55/55)	40.0% (4/10)	84.62% (55/65)
3D-FLASH + CISS	98.36% (60/61)	100% (4/4)	98.46% (64/65)	100% (60/60)	80.0% (4/5)	92.31% (60/65)
<i>p-value</i>						
3D FLASH + CISS vs 3D FLASH	0.028 ^a	>0.05	0.029 ^a	>0.05	0.106	0.109
3D FLASH + CISS vs 3D CISS	0.052	>0.05	0.052	>0.05	0.143	0.170

D-FLASH, three-dimensional fast low angle shot; 3D-CISS, three-dimensional constructive interference in steady-state.

^a $p < 0.05$.

better than the 3D-FLASH sequence. Although the 3D-CISS sequence displayed the similar signal intensity of the nerves and vessels, it commonly could distinguish them on the basis of the direction of nerves and vessels as well as the MPR reconstruction. However, the 3D-CISS sequence is inferior to the 3D-FLASH sequence regarding the determination of the source of the offending vessels.

The 3D-FLASH and 3D-CISS sequences were used to blindly analyze the vascular contact in the symptomatic side and asymptomatic side of the trigeminal nerve, which was few in the relevant literature reports.¹⁷ The results of comparison between different groups showed the sensitivity of 3D-FLASH + CISS sequence to the pain side was higher than that of the 3D-FLASH sequence, and the specificity was lower than that of 3D-FLASH, but there was no difference in the accuracy of judging the TN side. In addition, 3D-FLASH, 3D-CISS, 3D-FLASH + CISS sequence showed that the proportion of NVC in asymptomatic side was ranged from 47.7 to 53.8%. Peker et al²³ reported there were total of 175 sides (87.5%) with neurovascular compression in 100 patients (200 sides) without symptoms of TN. Therefore, we believed the relationships between NVC and symptoms are still need to be further study, preoperative enhanced 3D-FLASH or 3D-CISS sequence could not accurately determine the TN pain side.

There were several reports about the comparison between the preoperative MRI and surgical results of TN.^{12–15,24} However, due to the different unit imaging sequence and subsequent image processing technology, the sensitivity, the specificity and accuracy were different among these reports.^{25–27} The 3D-FLASH and 3D-CISS sequences imaging, the new generation of volume acquisition and thin-slice MRI technology, have a high resolution to display tiny and complex structure, and can display neurovascular relationship after MPR reconstruction. In this study, the accuracy of 3D-FLASH + CISS sequence determining trigeminal NVC was 98.36%, which was significantly higher than that of the previous literature.^{13,25–27} In addition, the 3D-FLASH sequence could not only display the arteries, but also show the compressed veins. In this study, there were 6 cases of single venae petrosa as offending vessels, and 4 cases of offending vessels involved in venae petrosa, superior cerebellar artery or inferior cerebellar artery. The venae petrosa and its branch accounted for 15.38% in all responsible vessels, which was similar to previous literature.^{12,25,28} Our findings suggested that the use of enhanced scan could display the responsible veins, thereby improving the positive rate of imaging diagnosis.

This study showed that the superior cerebellar artery (31/61, 50.82%) was the main offending vessel, which was consistent with the previous studies.²⁹ The assessment of 3D-FLASH + CISS sequence showed the accuracy of multiple vascular contact was approximately 77.78% (7/9), in which 7 cases were consistent with the surgical operative findings, 2 cases of offending vessel were misjudged as the branches of the anterior inferior cerebellar artery and the venae petrosa, respectively. It might be due to the anterior inferior cerebellar artery is a double branch, and walk shape tortuous, so the branches of the anterior inferior cerebellar artery were misdiagnosed as venae petrosa. Another

Table 3. Preoperative imaging assessment for the accuracy of vascular contact types

Offending vessel	3D-FLASH assessment (<i>n</i> = 65)	3D-CISS assessment (<i>n</i> = 65)	3D-FLASH + CISS assessment (<i>n</i> = 65)	Intraoperative findings (<i>n</i> = 65)
None	11	10	5	4
Single	47	50	52	52
SCA	29	33	31	31
AICA	7	8	10	9
VA	6	6	6	6
VP	5	3	5	6
Multiple	7	5	8	9
SCA + AICA	2	2	2	3
SCA + VP	3	1	4	3
AICA + VP	0	0	0	1
SCA + VA	2	2	2	2

AICA, anterior inferior cerebellar artery; D-FLASH, three-dimensional fast low angle shot; 3D-CISS, three-dimensional constructive interference in steady-state; SCA, superior cerebellar artery; VA, vertebrobasilar artery; VP, venae petrosa.

case of missed diagnosis of venae petrosa might be due to the venae petrosa is close to the petrous bone, and the compression site is located at the proximal Meckel's diverticulum of the trigeminal nerve. The difficult point of 3D-FLASH and 3D-CISS sequence to determine the offending vessels was the diagnosis of arterial composite vein and the branches of venae petrosa. For the composite blood vessels, we believe that the 3D-FLASH sequence followed by postprocessing MPR and MIP reconstruction could continuously and entirely display the branches and the beginning of offending vessels. For the diagnosis of venae petrosa and its branches, we believed that the 3D-FLASH sequence showed they did not originate from the vertebrobasilar artery and injected into the superpetrosal sinuses in the direction of the petrous apex.

However, there were some limitations in this study. Firstly, the sample size was relatively small, because some patients who

worried about the greater risk of surgery were not included. Secondly, we also studied that there was no significant correlation between the degree of nerve compression and the severity of TN, but it was not given more detail due to it was not the ultimate purpose of this study. Thirdly, healthy volunteers were not included. In the future, we will collect more cases and information to improve the diagnostic accuracy of trigeminal NVC and better explain why there are NVC in the healthy side, and better understand what is a causal relationship between NVC and symptoms.

CONCLUSION

The combination of 3D-FLASH with 3D-CISS imaging can clearly depict the relationship between intracisternal segment of trigeminal nerve and adjacent vessels due to which it can provide increased positive rates and accuracy.

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