Supplemental Material

Supplementary Table 1. Imaging parameters for time-of-flight MR angiography and time-resolved MR angiography

	Time-of-flight MR angiography	Time-resolved MR angiography (Time-Resolved Angiography with Interleaved Stochastic Trajectories)
TR/TE	22–23/3–4.02 ms	2.87/1.06 ms
Flip angle	18°	21º
Bandwidth	76.8–82.8 kHz	700 kHz
Number of excitations	1	1
Field-of-view	172×230 mm	300×400 mm
Matrix	448–512×235–303	448×218
Section thickness	0.5–0.6 mm	0.85 mm
Reconstructed voxel size	0.6×0.6×0.6 mm	0.89×0.89×0.85 mm
Number of slabs	11	
Thickness of one slab	16 mm	
Number of slices in one slab	32	
Slab overlap	5.5 mm	
GRAPPA imaging factor		6
Temporal resolution		1.25 s
Total acquisition time	5 min 25–46 s	45 s

MR, magnetic resonance.

Supplementary Table 2. Hyperparameters used in various training settings.

Batch size	2
Learning rate	0.0001
Weight decay	0.0001
Cycle weight	10
Adversarial weight	1
Identity weight	10
Cam weight	1000
Number of channels	64
Image size	256
Number of image channels	3
Number of resblock	4
Number of discriminator layer	6

Supplementary Table 3. SSIM of the synthetic TOF generated from the cycleGAN model without or with gradient-weighted class activation map (GradCAM) in ten patients randomly selected from the validation dataset.

	GradCAM (-)	GradGAM (+)	*p* value
SSIM mean ± standard deviation	0.607 ± 0.019	0.660 ± 0.019	< 0.001

Supplementary Table 4. Grading scales for subjective image quality assessment.

	1	2	3	4	5
Overall image quality	Non-diagnostic	Poor	Fair	Good	Excellent
Noise	Non-diagnostic	Severe	Moderate	Mild	No artifact
Sharpness of vessel margin	Non-diagnostic	Not sharp	A little sharp	Moderately sharp	Satisfyingly sharp
Vascular conspicuity	M1	M2	M3	M4	Distal branches
Venous contamination	Non-diagnostic	Severe	Moderate	Mild	None

Supplementary Table 5. Qualitative and quantitative assessment of the overall image quality using TR-MRA, synthetic TOF-MRA, and TOF-MRA.

					P value*		
	TR	synTOF	TOF	All	TR vs. synTOF	TR vs. TOF	synTOF vs. TOF
No. of patients	198	198	198				
Qualitative analysis**							
Median [IQR]							
Mean ± SD							
Overall image quality	3.00 [2.00;3.00]	4.00 [4.00;4.00]	4.00 [4.00;5.00]	< 0.001	< 0.001	< 0.001	< 0.001
	2.59 ± 0.54	4.01 ± 0.63	4.44 ± 0.53				
Noise	3.00 [2.00;3.00]	5.00 [4.00;5.00]	4.00 [4.00;5.00]	< 0.001	< 0.001	< 0.001	1.000
	2.71 ± 0.63	4.50 ± 0.55	4.46 ± 0.52				
Sharpness of vessel margin	2.00 [2.00;2.00]	4.00 [4.00;4.00]	5.00 [5.00;5.00]	< 0.001	< 0.001	< 0.001	< 0.001
	2.20 ± 0.40	4.00 ± 0.59	4.86 ± 0.34				
Vascular conspicuity	3.00 [2.00;3.00]	3.00 [3.00;3.00]	4.00 [3.00;4.00]	< 0.001	0.456	< 0.001	< 0.001
	2.75 ± 0.52	2.88 ± 0.54	3.52 ± 0.59				
Venous contamination	3.00 [3.00;4.00]	5.00 [5.00;5.00]	5.00 [5.00;5.00]	< 0.001	< 0.001	< 0.001	1.000
	3.33 ± 0.84	4.99 ± 0.14	5.00 ± 0.00				
Quantitative analysis, median [IQR]							
SNR (M1)	27.00 [21.00;36.00]	55.50 [38.00;73.00]	54.50 [36.00;80.00]	< 0.001	< 0.001	< 0.001	1.000
SNR (M2)	24.50 [19.00;32.00]	40.00 [26.00;56.00]	41.00 [29.00;59.00]	< 0.001	< 0.001	< 0.001	0.358
SNR (M3)	16.00 [11.00;21.00]	17.00 [10.00;28.00]	30.00 [20.00;45.00]	< 0.001	1.000	< 0.001	< 0.001
SNR (BA)	19.00 [14.00;26.00]	37.00 [25.00;50.00]	67.00 [46.00;97.00]	< 0.001	< 0.001	< 0.001	< 0.001
SNR (PCA)	18.00 [13.00;24.00]	34.00 [23.00;48.00]	59.00 [41.00;77.00]	< 0.001	< 0.001	< 0.001	< 0.001
Noise	14.50 [10.00;25.00]	3.00 [2.00;4.00]	10.00 [7.00;14.00]	< 0.001	< 0.001	< 0.001	< 0.001
		Between synTOF and TOF					
PSNR (dB), median [IQR]		15.56 [14.82;16.42]					
SSIM, median [IQR]		0.67 [0.65;0.69]					

MRA, magnetic resonance angiography; IQR, interquartile range; SD, standard deviation; TR, time-resolved MRA; TOF, time-of-flight; synTOF, synthetic TOF; SNR, signal-to-noise ratio; PSNR, peak signal-to-noise ratio; SSIM, structural similarity.

*Friedman test and Bonferroni correction were applied to the Wilcoxon signed-rank test for pairwise comparisons.

** The mean ± SD is for a comprehensive comparison between groups. The data are non-normally distributed, and the p-value was analyzed based on the non-normal distribution.

Supplementary Table 6. Interobserver agreements for qualitative and quantitative assessment of overall image quality among TR-MRA, synTOF, and TOF results.

	Weighted Kappa or intraclass correlation coefficient (95% CI)		
	TR-MRA	synTOF	TOF
Qualitative analysis			
Overall image quality	0.805 (0.727, 0.883)	0.887 (0.834, 0.940)	0.830 (0.761, 0.899)
Noise	0.937 (0.894, 0.980)	0.849 (0.787, 0.911)	0.799 (0.725, 0.874)
Sharpness of vessel margin	0.703 (0.594, 0.813)	0.906 (0.848, 0.963)	0.768 (0.650, 0.887)
Vascular conspicuity	0.738 (0.641, 0.836)	0.905 (0.844, 0.966)	0.907 (0.856, 0.959)
Venous contamination	0.921 (0.880, 0.962)	1.000 (1.000, 1.000)	1.000 (1.000, 1.000)
Quantitative analysis			
SNR (M1)	0.997 (0.996, 0.998)	0.927 (0.905, 0.944)	0.989 (0.986, 0.992)
SNR (M2)	0.993 (0.990, 0.995)	0.954 (0.939, 0.965)	0.990 (0.986, 0.992)
SNR (M3)	0.997 (0.996, 0.998)	0.971 (0.961, 0.978)	0.990 (0.986, 0.992)
SNR (BA)	0.997 (0.997, 0.998)	0.972 (0.963, 0.979)	0.991 (0.988, 0.993)
SNR (PCA)	0.985 (0.980, 0.988)	0.928 (0.906, 0.945)	0.976 (0.968, 0.982)
Noise	0.950 (0.934, 0.962)	0.883 (0.848, 0.910)	0.991 (0.988, 0.993)

CI: confidence interval;: time-of-flight; synTOF: synthetic TOF; SI: signal intensity; MRA, magnetic resonance angiography; IQR, interquartile range; SD, standard deviation; TR, time-resolved MRA; synTOF, synthetic TOF; SNR, signal-to-noise ratio

Supplementary Table 7. Comparisons of diagnostic performance of 4D and synthetic TOF for detecting aneurysm or stenosis

	TOF	4D	synTOF	P value		
Number of patients	198	198	198	TOF vs. 4D	TOF vs. synTOF	4D vs. synTOF
Detection of aneurysm						
Positive	12	6	6	0.031	0.031	1.000
Sensitivity (95% CI)		0.50 (0.21, 0.79)	0.50 (0.21, 0.79)			
Specificity (95% CI)		1.00 (0.98, 1.00)	1.00 (0.98, 1.00)			
Positive predictive value (95% CI)		1.00 (0.54, 1.00)	1.00 (0.54, 1.00)			
Negative predictive value (95% CI)		0.97 (0.93, 0.99)	0.97 (0.93, 0.99)			
Accuracy (95% CI)		0.97 (0.94, 0.99)	0.97 (0.94, 0.99)			
Area under the curve (95% CI)		0.750 (0.684, 0.809)	0.750 (0.684, 0.809)			
Detection of stenosis (> moderate degree)						
Positive	44	33	38	0.001	0.031	0.063
Sensitivity (95% CI)		0.75 (0.60, 0.87)	0.86 (0.73, 0.95)			
Specificity (95% CI)		1.00 (0.98, 1.00)	1.00 (0.98, 1.00)			
Positive predictive value (95% CI)		1.00 (89.42, 1.00)	1.00 (0.91, 1.00)			
Negative predictive value (95% CI)		0.93 (0.89. 0.96)	0.96 (0.92, 0.98)			
Accuracy (95% CI)		0.94 (0.90, 0.97)	0.97 (0.94. 0.99)			
Area under the curve (95% CI)		0.875 (0.821, 0.918)	0.932 (0.887, 0.963)			

CI: confidence interval; TOF: time-of-flight; synTOF: synthetic TOF; TR, time-resolved MRA; synTOF, synthetic TOF

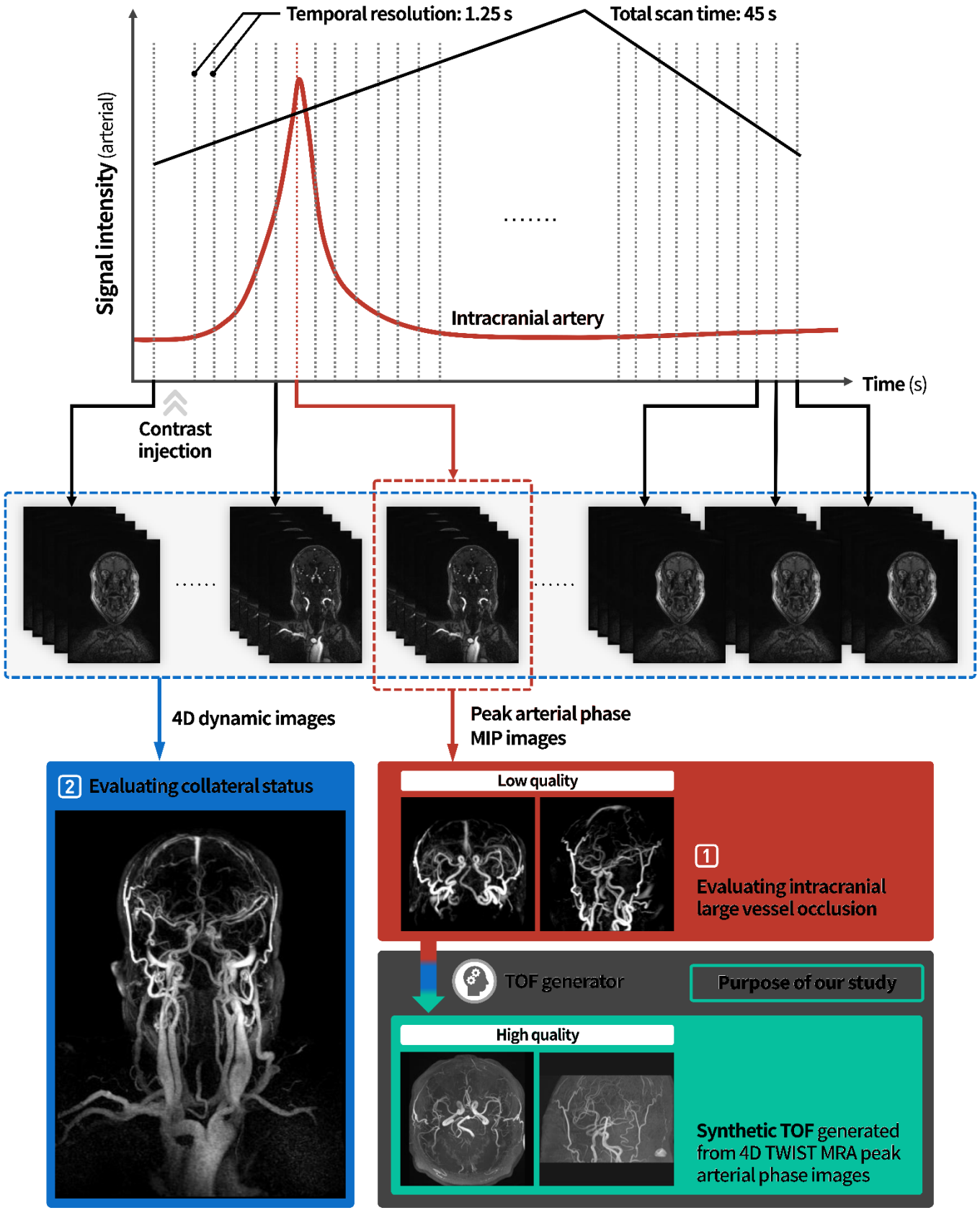
Supplementary Table 8. Imaging optimality of each MRA sequence in 20 randomly selected patients.

		Optimal sequences for diagnosis			Best sequence for diagnosis			Selecting TOF sequence		
		TR	synTOF	TOF	TR	synTOF	TOF	TR	synTOF	TOF
No. of cases		20	20	20	20	20	20	20	20	20
Reader 1	Resident (1 y)	2	20	19	0	14	6	0	13	7
Reader 2	Resident (1 y)	0	20	20	0	9	11	6	11	3
Reader 3	Resident (2 y)	0	20	20	0	13	7	0	11	9
Reader 4	Resident (3 y)	3	17	19	1	9	10	3	8	9
Reader 5	Resident (3 y)	0	20	20	0	5	15	0	17	3
Reader 6	Resident (4 y)	0	20	20	0	5	15	0	17	3
Reader 7	Resident (4 y)	1	18	18	0	15	5	0	6	14
Reader 8	Neuroradiologist (6 y)	0	20	18	0	10	10	0	15	5
Reader 9	Neuroradiologist (10 y)	0	10	10	0	4	16	0	20	0
Reader 10	Neuroradiologist (11 y)	4	18	20	0	4	16	0	3	17
Reader 11	Neuroradiologist (11 y)	1	18	18	0	0	20	0	0	20
Reader 12	Neuroradiologist (11 y)	2	20	20	0	4	16	0	4	16
Reader 13	Neuroradiologist (12 y)	1	15	19	0	4	16	0	3	17
Reader 14	Neuroradiologist (12 y)	0	20	20	0	4	16	0	3	17
Reader 15	Neuroradiologist (17 y)	0	20	20	0	2	18	0	9	11
Reader 16	Neuroradiologist (20 y)	9	20	20	0	1	19	1	19	0
Median [IQR]		0.50 [0.00;2.00]	20.00 [18.00;20.00]	20.00 [18.50;20.00]	0.00 [0.00;0.00]	4.50 [4.00;9.50]	15.50 [10.00;16.00]	0.00 [0.00;0.00]	10.00 [3.50;16.00]	9.00 [3.00;16.50]
P value*			< 0.001			< 0.001			< 0.001	
TR vs. synTOF			< 0.001			< 0.001			0.001	
TR vs. TOF			< 0.001			< 0.001			0.003	
synTOF vs. TOF			1.000			0.279			1.000	

MRA, magnetic resonance angiography; IQR, interquartile range; SD, standard deviation; TOF, time-of-flight; synTOF, synthetic TOF; TR, time-resolved MRA

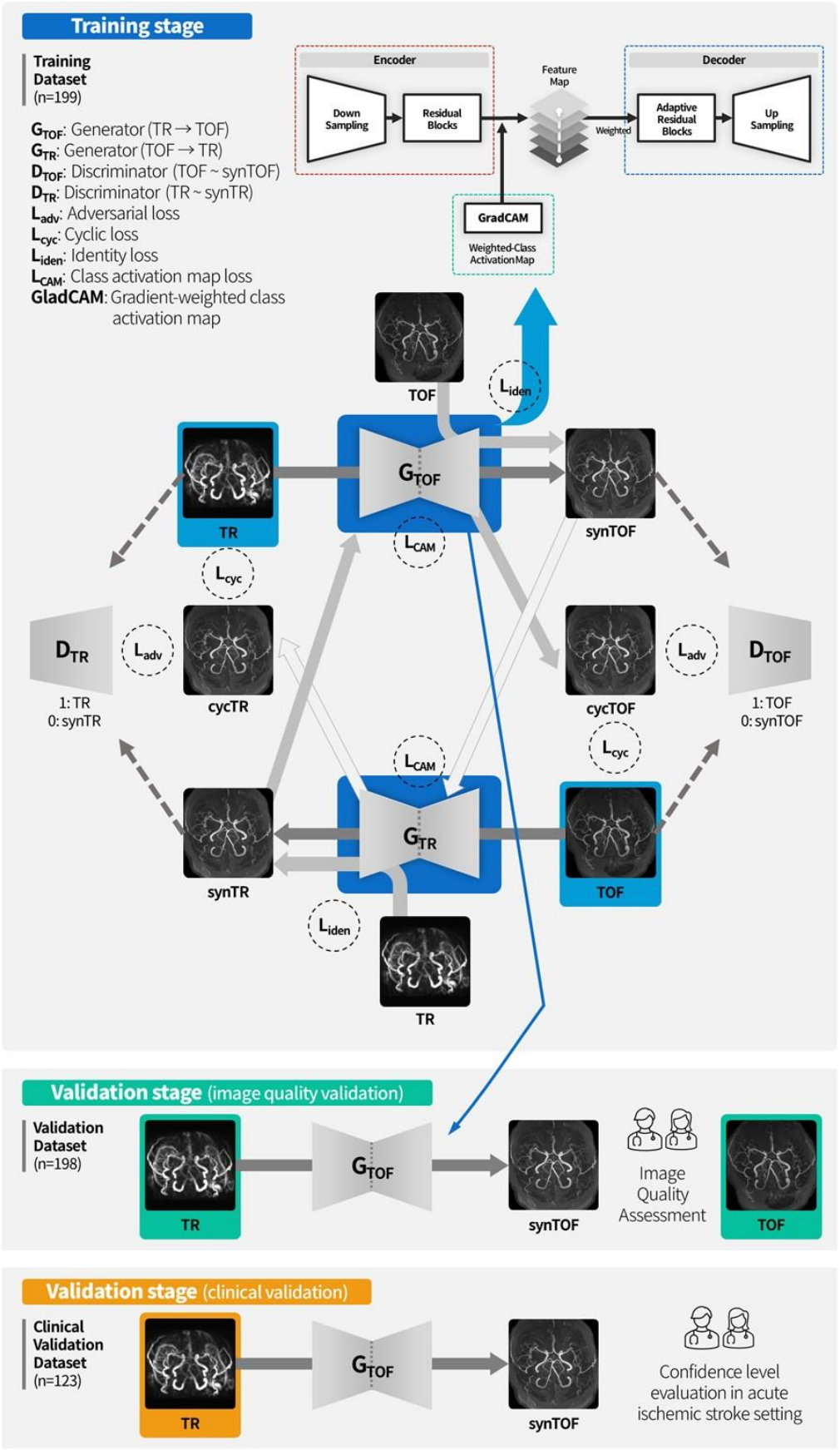
*Friedman test and Bonferroni correction were applied to the Wilcoxon signed-rank test for pairwise comparisons.

Supplementary Figure 1. Role of time-resolved magnetic resonance angiography (TR-MRA) in the evaluation of acute ischemic stroke and the purpose of our study

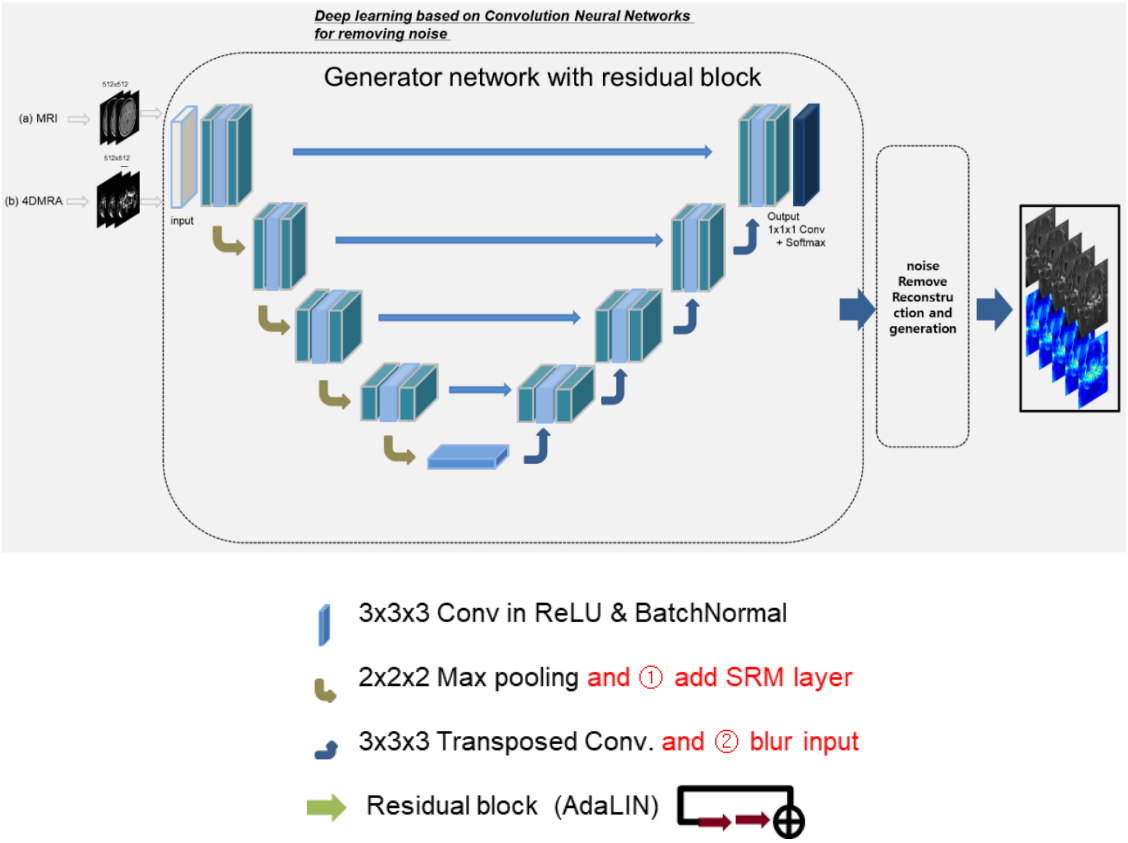


Supplementary Figure 2. Schematic view of the proposed optimized cycle-consistent generative adversarial network architecture for synthetic TOF generation model during the training and validation stages

TR-MRA, time-resolved MRA; TOF, time of flight MRA; synTOF, synthetic TOF

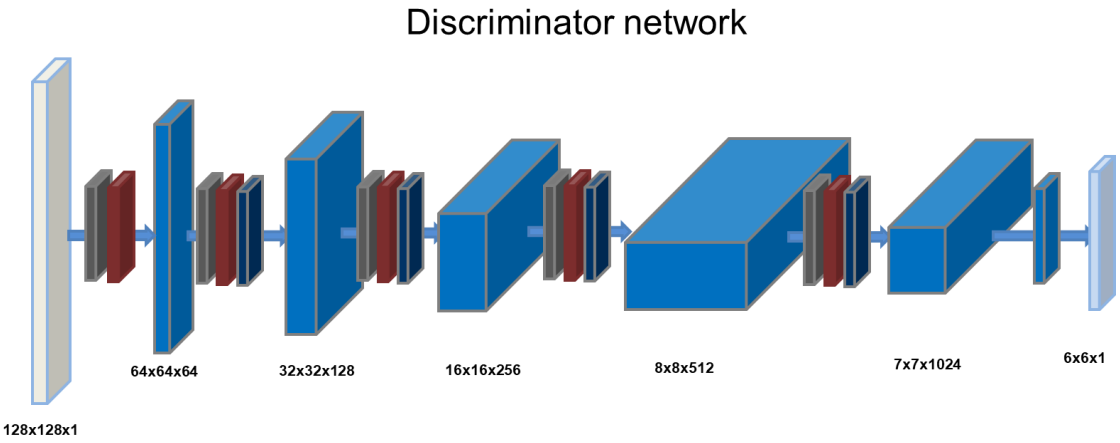


Supplementary Figure 3. Architecture of the generator. It is based on the ResNet structure. It includes a style-based recalibration module (SRM layer) and incorporates blur input in the residual block for up-sampling. AdaLIN comprises fully connected layers and LeakyReLu activation layers. The generator in this architecture consists of four layers, including two convolutional layers with ReLU activation and instance normalization. These convolutional layers use a 3 × 3 kernel and a stride of 2 and are up-sampled using nearest-neighbor interpolation. The first layer has 64 convolutional filter channels, and this number doubles in each subsequent layer, reaching 1024 in the final layer. To improve style transfer and image translation with various changes in shape and texture, the network includes AdaLIN, which adjusts the ratio between instance normalization (IN) and layer normalization (LN) in residual blocks. For better reconstruction of synthetic TOF images, modifications were made to the residual block and residual-AdaIN block within a single generator. Specifically, the residual block was changed from instance normalization to batch normalization and a style-based recalibration module (SRM) layer was incorporated for style pooling. Additionally, the residual-AdaIN block was introduced in the blur processing during the up-sampling step. These improvements were demonstrated using bidirectional image translation and offer several advantages that can help overcome the limitations of existing models such as cycleGAN, CUT, or U-GAT-IT.

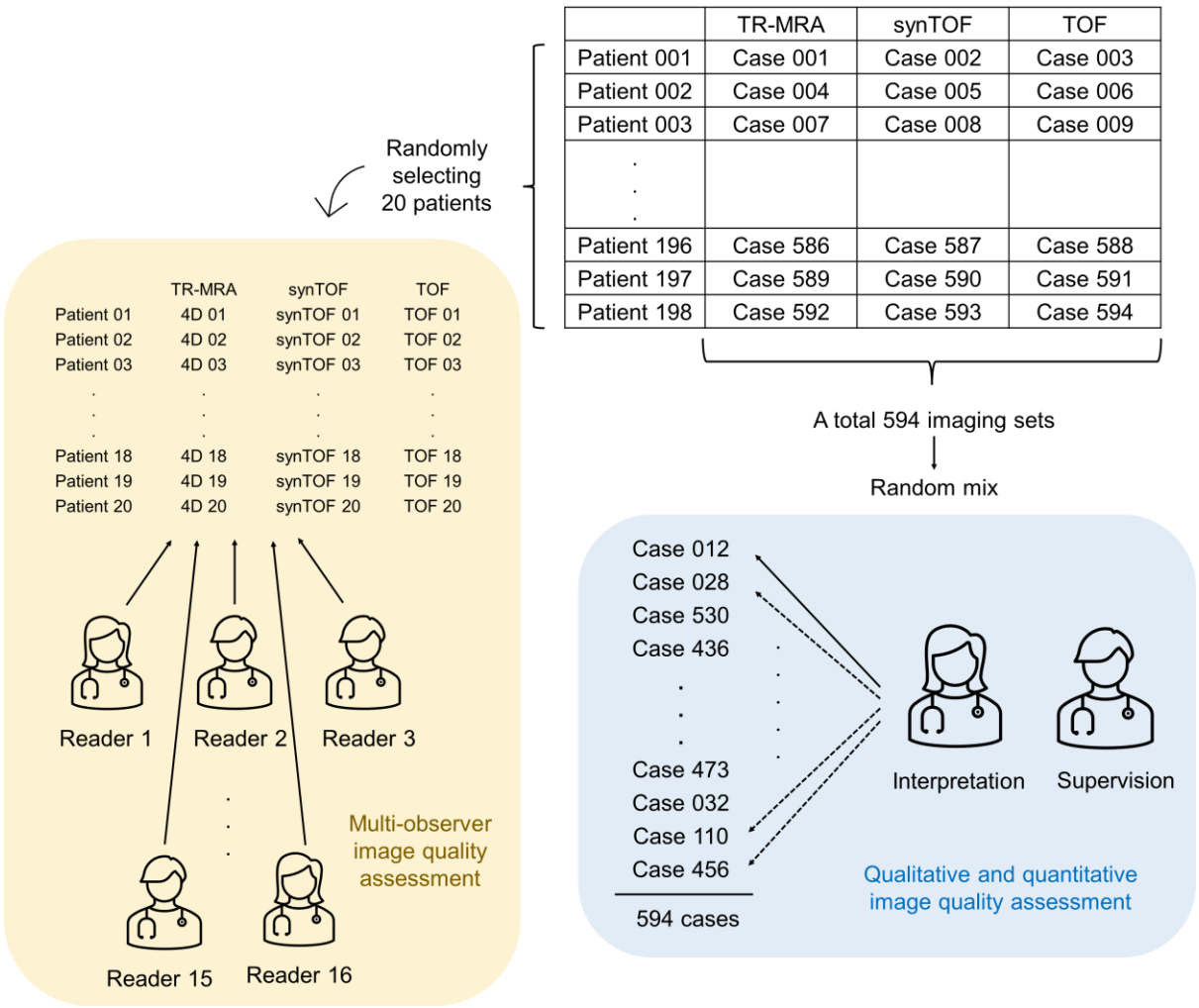


Supplementary Figure 4. The architecture of the discriminator follows a PatchGAN design. Each number in the diagram represents the dimensions (height, width) and number of channels in the feature map. The colored boxes represent the individual layers in the network. In this architecture, the first four convolutional layers have a stride of 2, while the subsequent convolutional layers have a stride of 1. The initial convolutional layer takes 1-channel images as input and produces 64-channel feature maps. As these feature maps progress through each subsequent convolutional layer, the number of channels doubles. The final output is obtained by reducing the number of channels to one in the last layer. The discriminator loss, referred to as "ldisc (G, F, Dx, Dy)," includes LSGAN (Least Squares GAN) losses and is calculated using the discriminator's output as follows:

$$l_{disc}(G, F, D_x, D_y) = \mathrm{E}_{y\sim P_y}[\|D_Y(y)\|_1] + \mathrm{E}_{x\sim P_x}[\|1 - D_Y(G(x; F(c)))\|_1] + \mathrm{E}_{x\sim P_x}[\|D_X(x)\|_1] + \mathrm{E}_{y\sim P_y}[\|1 - D_X(G(y; C_x))\|_1] \quad (1)$$



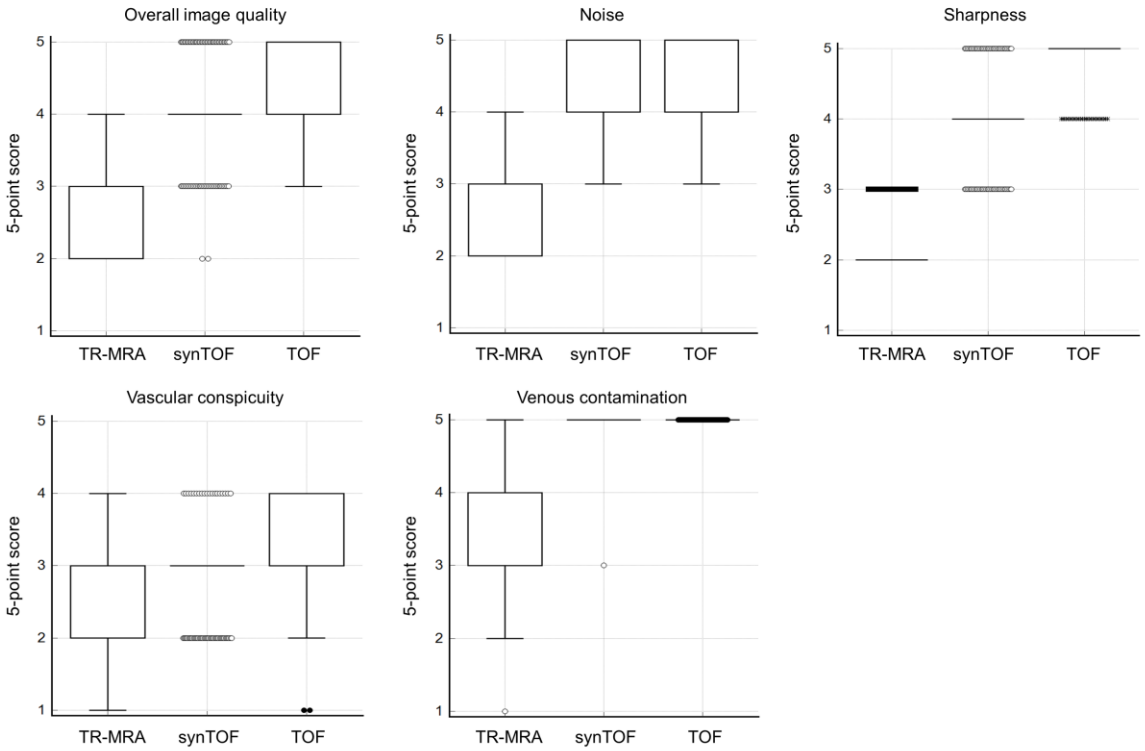
Supplementary Figure 5. Design for image interpretation.



Supplementary Figure 6. Box and whisker plots for qualitative assessment with TR-MRA, synTOF, and TOF: (a) overall image quality, (b) noise, (c) sharpness, (d) vascular conspicuity, and (e) venous contamination.

TR-MRA, time-resolved MRA; synTOF, synthetic TOF-MRA; TOF, time-of-flight; MRA, magnetic resonance angiography

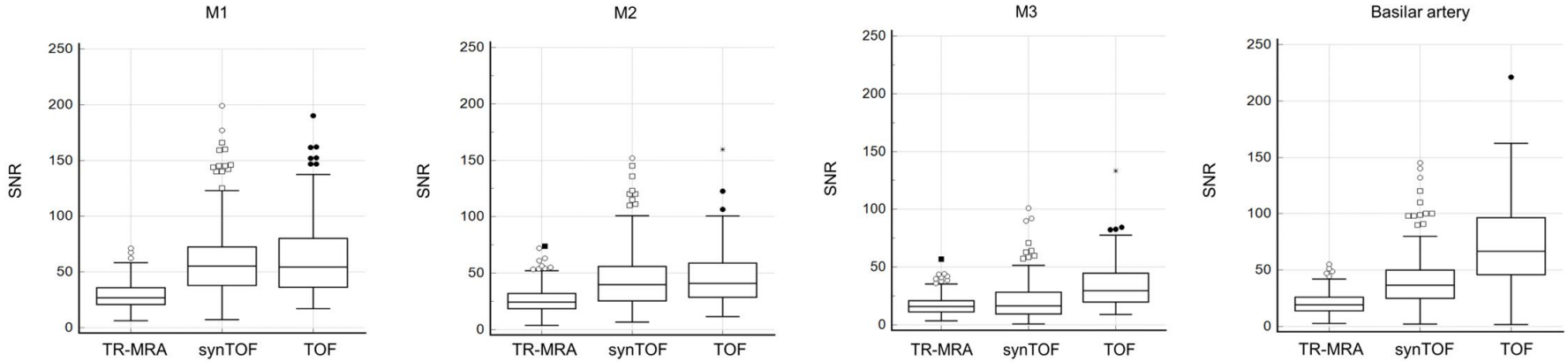
Lines in boxes = median values; Boundaries of boxes = 25th and 75th percentiles, with whiskers extending from the median to ± 1.5 × interquartile ranges and outliers beyond the whiskers are represented by points.



Supplementary Figure 7. Box and whisker plots for the signal-to-noise ratio of middle cerebral artery (M1, M2, and M3 segments) and basilar artery with TR-MRA, synTOF, and TOF: (a) M1, (b) M2, (c) M3, and (d) BA.

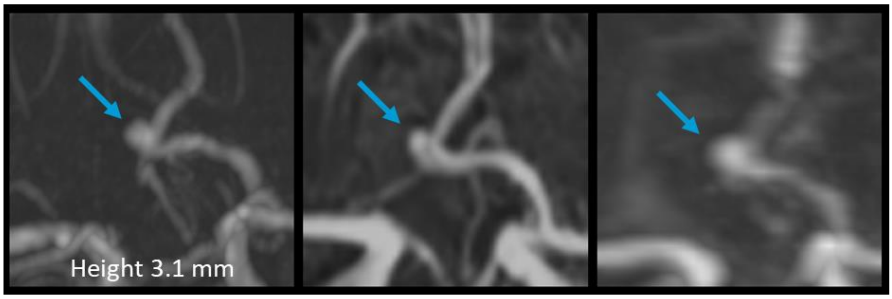
TR-MRA, time-resolved MRA; synTOF, synthetic TOF-MRA; TOF, time-of-flight MRA

Lines in boxes = median values; Boundaries of boxes = 25th and 75th percentiles, with whiskers extending from the median to ± 1.5 × interquartile ranges and outliers beyond the whiskers represented by points.



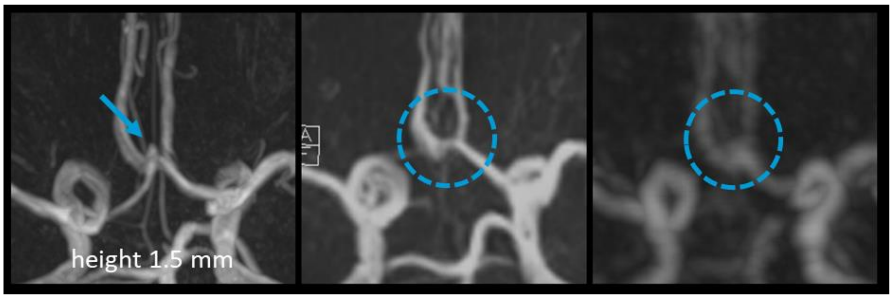
Supplementary Figure 8. Representative images of TOF, synTOF, and TOF in patients with intracranial aneurysm

Female, 82 years old Anterior communicating artery aneurysm



	TOF	synTOF	4D
Aneurysm	Positive	Positive	Positive

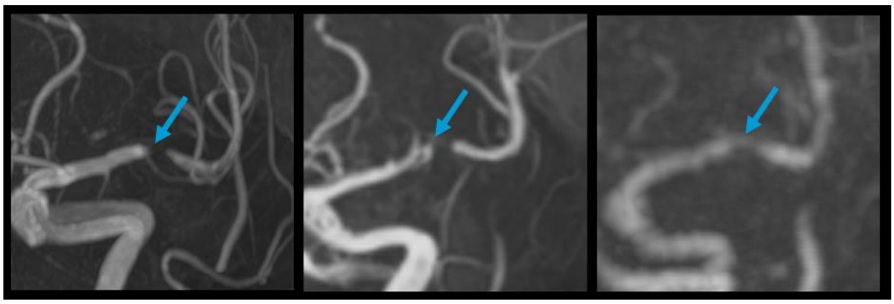
Male, 72 years old Anterior communicating artery aneurysm



	TOF	synTOF	4D
Aneurysm	Positive	False negative	False negative

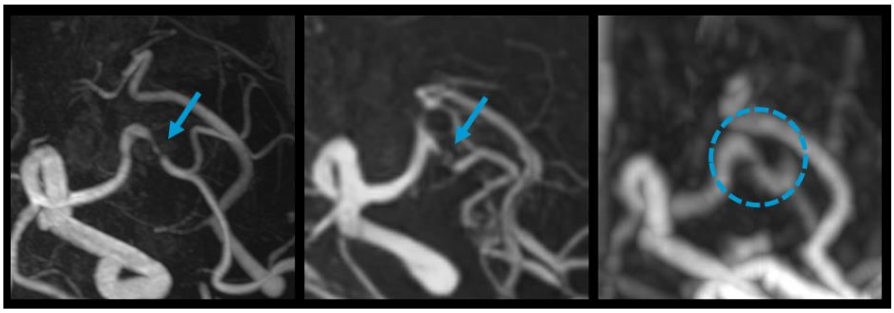
Supplementary Figure 9. Representative images of TOF, synTOF, and TOF in patients with intracranial arterial stenosis over moderate degree

Male, 47 years old — Left M1 stenosis



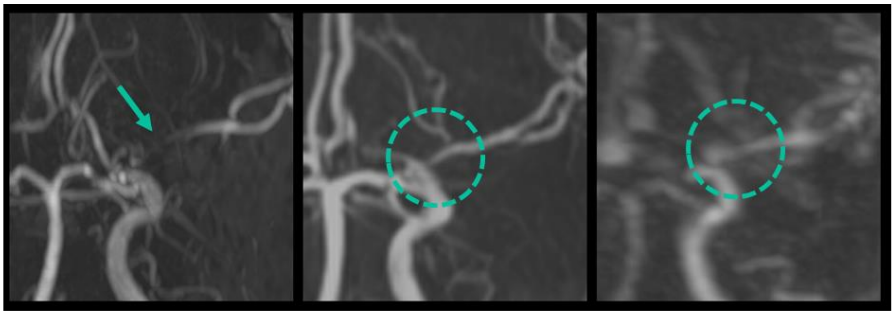
	TOF	synTOF	4D
Presence of stenosis	Positive	Positive	Positive

Male, 62 years old — Left M2 stenosis



	TOF	synTOF	4D
Presence of stenosis	Positive	Positive	False negative

Male, 62 years old — Left M1 stenosis



	TOF	synTOF	4D
Presence of stenosis	Positive	False negative	False negative

Supplementary Figure 10. Diagnostic confidence level of TR-MRA only vs. TR-MRA and synTOF.

TR-MRA, time-resolved MRA; synTOF, synthetic TOF-MRA