



2025 IEEE
Symposium Series on
Computational Intelligence



CAS-GAN for Contrast-free Angiography Synthesis

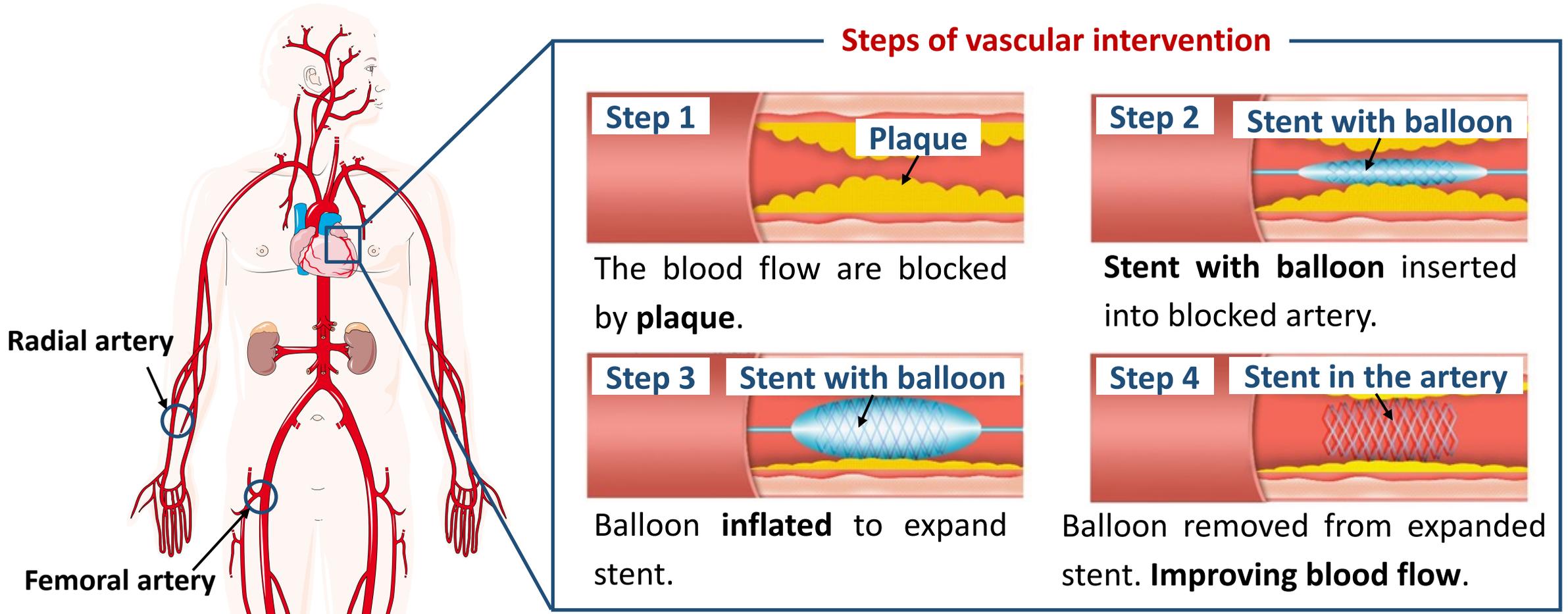
De-Xing Huang, X. Zhou*, M. Gui, X. Xie, S. Liu, S. Wang, H. Li, T. Xiang, Z.-G. Hou*

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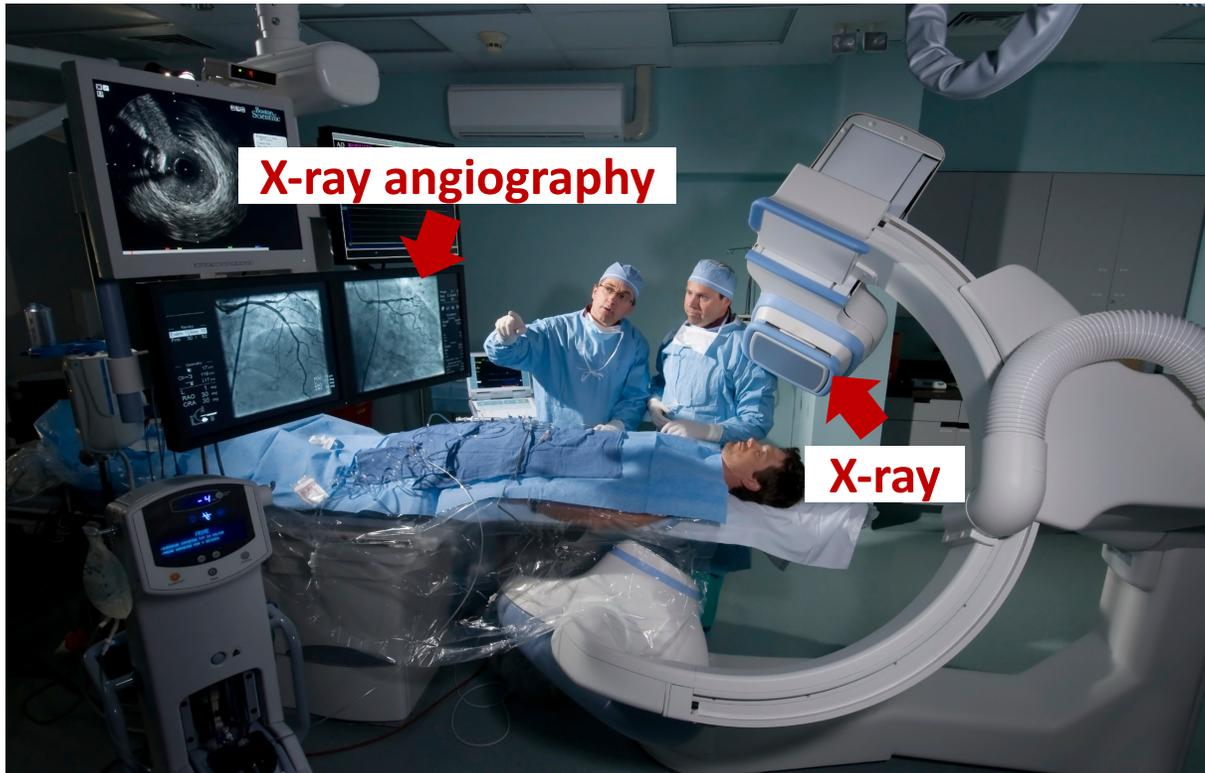
Background

- **Vascular intervention** is a minimally invasive treatment of cardiovascular diseases.



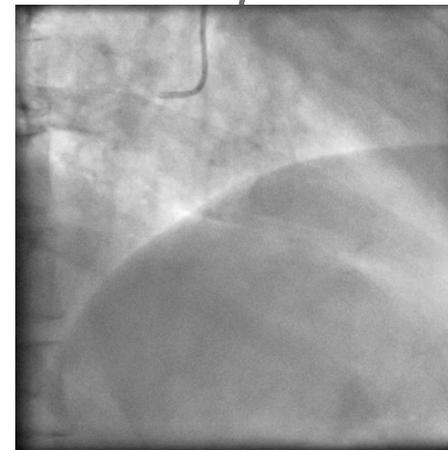
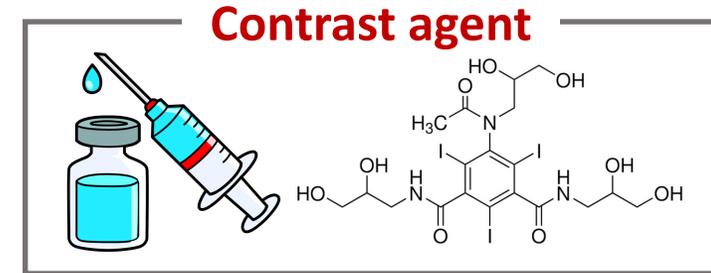
Background

- Currently, **X-ray angiography** is a **must** for guiding cardiologists to locate vascular lesions.

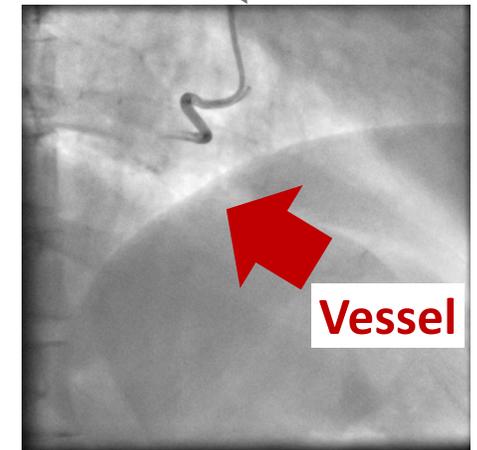


Vascular interventional procedures

(From: <https://www.dicardiology.com/>)



Non-contrast X-ray



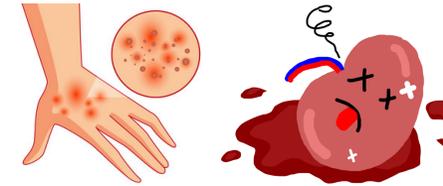
X-ray angiography

Vessel

- H. Zhao *et al.*, "Large-scale pretrained frame generative model enables real-time low-dose DSA imaging: An AI system development and multi-center validation study," *Med*, 6(1): 100497, 2025.

Motivation

- Contrast agents pose **significant health risks** for patients.



ARTICLE INFO

O. Clavier et al. / *EClinicalMedicine* 1 (2018) 54–61

ABSTRACT

Background: Iodinated and gadolinium-based contrast media (ICM, GBCM) induce immediate hypersensitivity (IH) reactions. Differentiating allergic from non-allergic IH is crucial; allergy contraindicates the culprit agent for life. We studied frequency of allergic IH among ICM or GBCM reactions.

Methods: Patients were recruited in 11 hospitals between 2005 and 2009. Clinical symptoms, plasma histamine and tryptase concentrations, and skin tests were recorded. Allergic IH was diagnosed by intradermal tests (IT) with the culprit ICM diluted 1:10, "provoked allergic" IH by positive IT with open ICM and non-allergic IH by negative IT.

Findings: Among 243 skin tested patients (ICM = 209; GBCM = 36), allergic IH to ICM was identified in 41 (19.0%) and to GBCM in 10 (27.8%). Skin cross-reactivity was observed in 13 patients with ICM (GBCM) and 5 with GBCM (50%). Allergy frequency increased with clinical severity and histamine and tryptase concentrations ($p < 0.0001$). Cardiovascular signs were strongly associated with allergic, non-allergic IH was observed in 152 patients (62% ICM/38% GBCM/18). Severity grade was lower ($p < 0.0001$) and reaction delay longer (13.6 vs 5.6 min; $p < 0.01$). Potentially allergic IH was diagnosed in 42 patients (17.1% ICM/34% GBCM). The delay, severity grade, and mediator release were intermediate between the other groups.

Interpretation: Allergic IH accounted for ~10% of cutaneous reactions, and ~30% of life-threatening ones. GBCM and ICM triggered comparable IH reactions in frequency and severity. Cross-reactivity was frequent, especially for GBCM. We propose considering skin testing with pure contrast agent, as it is more sensitive than the usual 1:10 dilution criteria.

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REVIEWS

Understanding and preventing contrast-induced acute kidney injury

Michael Fähring*, Erdmann Seeliger*, Andreas Potzack and Pontus B. Persson

Abstract Contrast-induced acute kidney injury (CI-AKI) occurs in up to 30% of patients who receive iodinated contrast media and is generally considered to be the third most common cause of hospital-acquired AKI. Accurate assessment of the incidence of CI-AKI is obscured, however, by the use of various definitions for diagnosis, the different populations studied and the prophylactic measures put in place. A deeper understanding of the mechanisms that underlie CI-AKI is required to enable reliable risk assessment for individual patients, as their medical histories will determine the specific pathways by which contrast media administration might lead to kidney damage. Here, we highlight common triggers that prompt the development of CI-AKI and the subsequent mechanisms that ultimately cause kidney damage. We also discuss effective protective measures, such as rapidly acting oral hydration schemes and loop diuretics, in the context of CI-AKI pathophysiology. Understanding of how CI-AKI arises in different patient groups could enable a marked reduction in incidence and improved outcomes. The ultimate goal is to shape CI-AKI prevention strategies for individual patients.

The first report of contrast-induced acute kidney injury (CI-AKI) dates back to over half a century ago and prompted research that has led to more than 3,000 publications. Today, the predicted number of patients suffering from kidney damage caused by contrast media reaches the millions. CI-AKI is generally considered to rank third among the causes of hospital-acquired AKI, explain why patients with various pre-existing conditions respond differently to the damaging effects of contrast media, and shed light on present and future prevention strategies.

Research in Context

Evidence Before This Study

Immediate hypersensitivity (IH) reactions to iodinated contrast media have been an everlasting problem for radiologists. Severe reactions have been rare, happen seldomly, and are difficult to handle by an imaging team, which is often not trained or experienced in managing unexpected severe reactions. This leads to a poor prognosis when vasoactive drugs are not immediately used in patients experiencing anaphylactic shock or cardiac arrest. Many studies have attempted to decipher the underlying mechanisms involved in the hope of circumventing them. For decades, a true allergic mechanism was discounted by the community, who have advocated non-specific, so-called "pseudo-allergic" or "pseudo-allergic" reactions, and identified risk factors such as "previous reaction", "anxiety", and "sensitivity to drugs". Several preventative protocols have been tested, mainly based on antihistaminic drugs and corticosteroids. However, these do not prevent severe reactions and anaphylactic shocks, which are called "breakthrough reactions". Gadolinium chelates used as contrast agents for Magnetic Resonance

these studies included retrospective cases tested years after the reaction, or lacked precise clinical history, name of culprit agent, or were misad immediate and delayed reactions. Measurements of plasma histamine and tryptase were not performed. Only a few allergic reactions to gadolinium-based contrast agents have been described as clinical cases. We conducted the first prospective study of IH reactions to iodinated or gadolinium-based agents. It needed to be multicenter, since the incidence of severe reactions is so low, in order to include a few hundred reactions over the term of the study. Based on an incidence of 0.1% moderate and severe reactions, we included 25 centers from across France that were able to provide allergy testing 30min after the reaction. We assumed that each center could perform at least 7000 injected examinations per year, meaning that 600,000 examinations could be obtained over a 3-year period, so that we could recruit 600 reactions. However, after two years, the inclusion rate was lower than expected, and we decided to continue the study for a total of 4.5 years. Between 2005 and 2009, 243 patients presenting with IH reactions to iodinated or gadolinium-based contrast media using included. After appropriate medical treatment, blood sampling for

Contrast-induced acute kidney injury occurs in up to 30% of patients who receive iodinated contrast media.

Acute kidney injury (AKI)

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Lancet Discovery Science, 1: 51-61, 2018.

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Nature Reviews Nephrology, 13(3): 169-180, 2017.

More volume
Higher AKI incidence

Contrast volume (mL)	Rate of acute kidney injury (%)
101-150	6.5%
151-200	6.5%
201-250	6.8%
251-300	7.5%
301-350	8.1%
351-400	8.8%
>400	10.3%

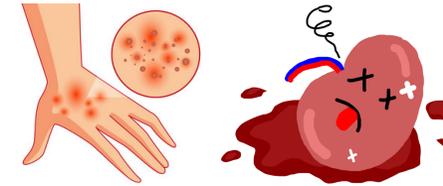
High AKI risk
No volume reduction

Acute kidney injury risk (decile)	Mean contrast volume (mL)
1	~200
2	~200
3	~200
4	~200
5	~200
6	~200
7	~200
8	~200
9	~180
10	~180

• A. P. Amin *et al.*, "Association of variation in contrast volume with acute kidney injury in patients undergoing percutaneous coronary intervention," *JAMA Cardiol.*, 2017, 2(9): 1007-1012. 4/15

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However, after two years, the inclusion rate was lower than expected, and we decided to continue the study for a total of 4.5 years. Between 2005 and 2009, 249 patients fulfilling with IH reactions to iodinated or gadolinium-based contrast media were included. After appropriate medical treatment, blood sampling for

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Nature Reviews Nephrology, 13(3): 169-180, 2017.

Vessels are invisible in non contrast X-ray!

Non-contrast X-ray

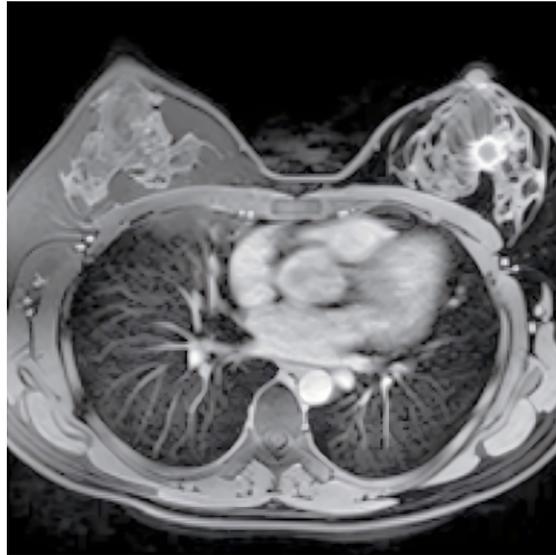
Contrast-free X-ray angiography

Solution

- Generative models can create **photorealistic images** based on specific constraints.



A photo of Bakklandet in Trondheim, 4k, photorealistic

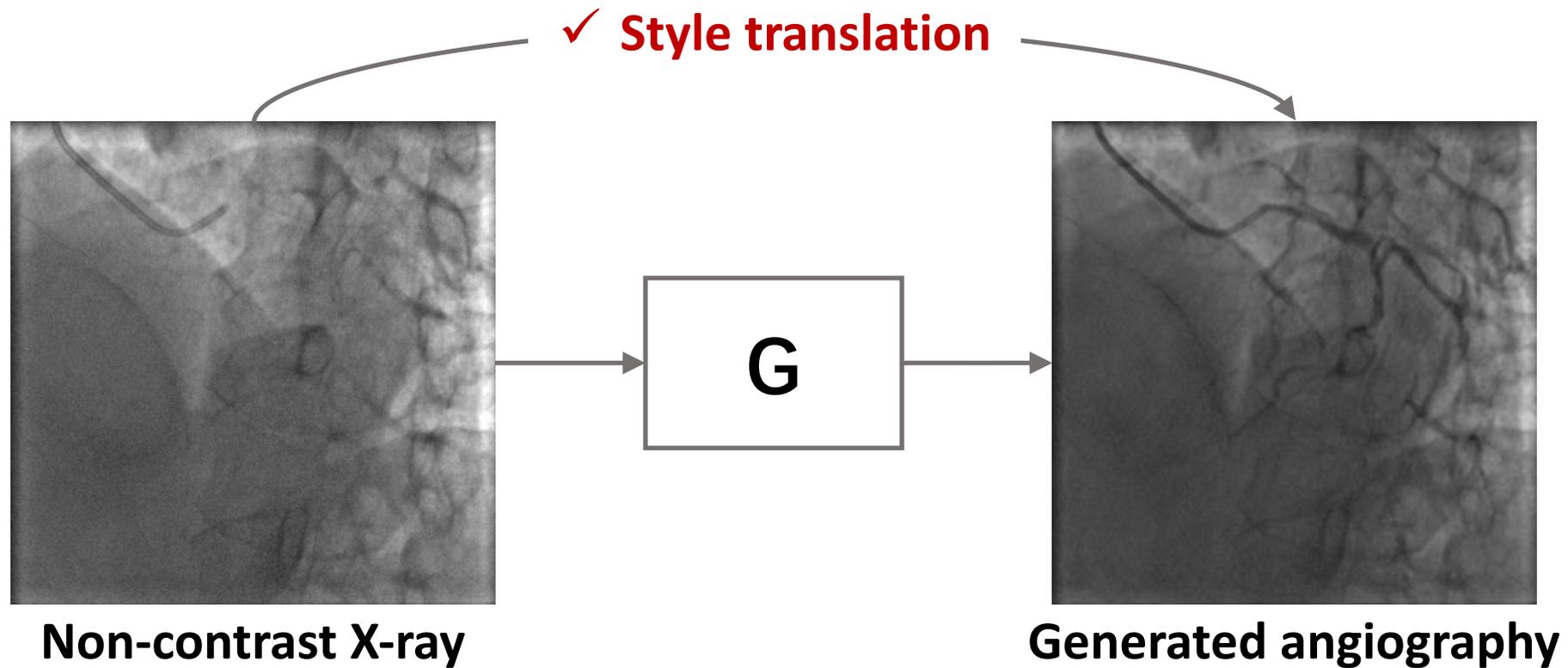


MRI: breast tumor with HER2 mutation from the view of T1c

 Can we use generative models as “virtual contrast agent”?

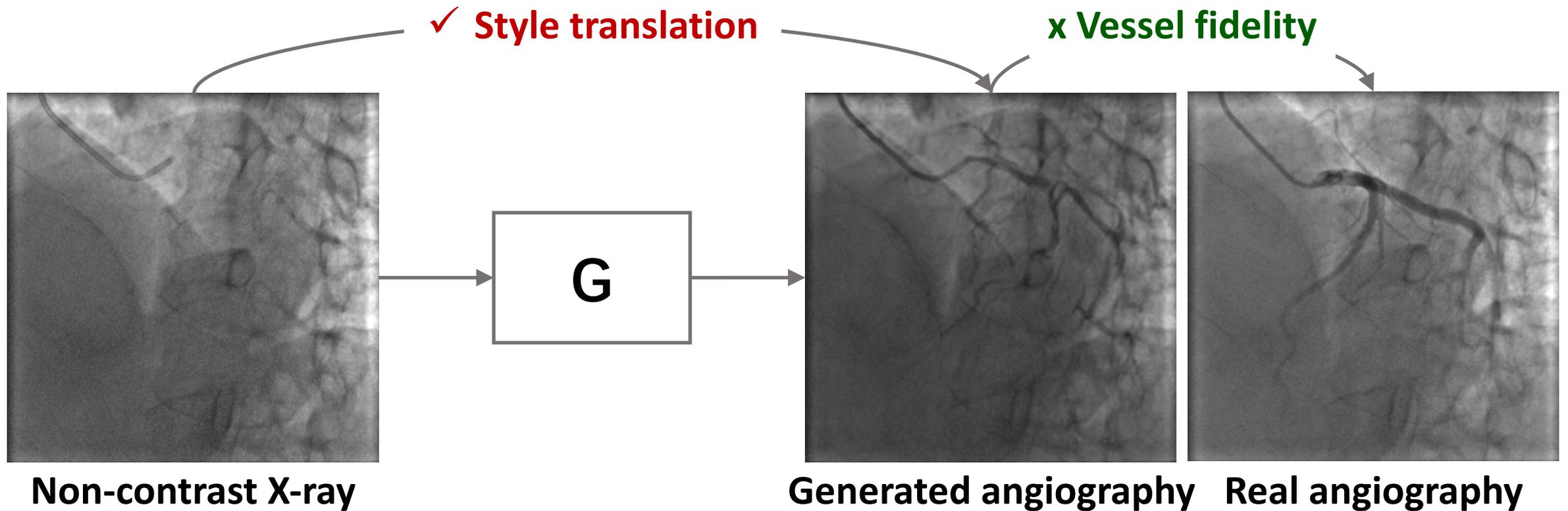
Challenge

- Current methods focus on **style translation** but fail to preserve **vessel fidelity**.



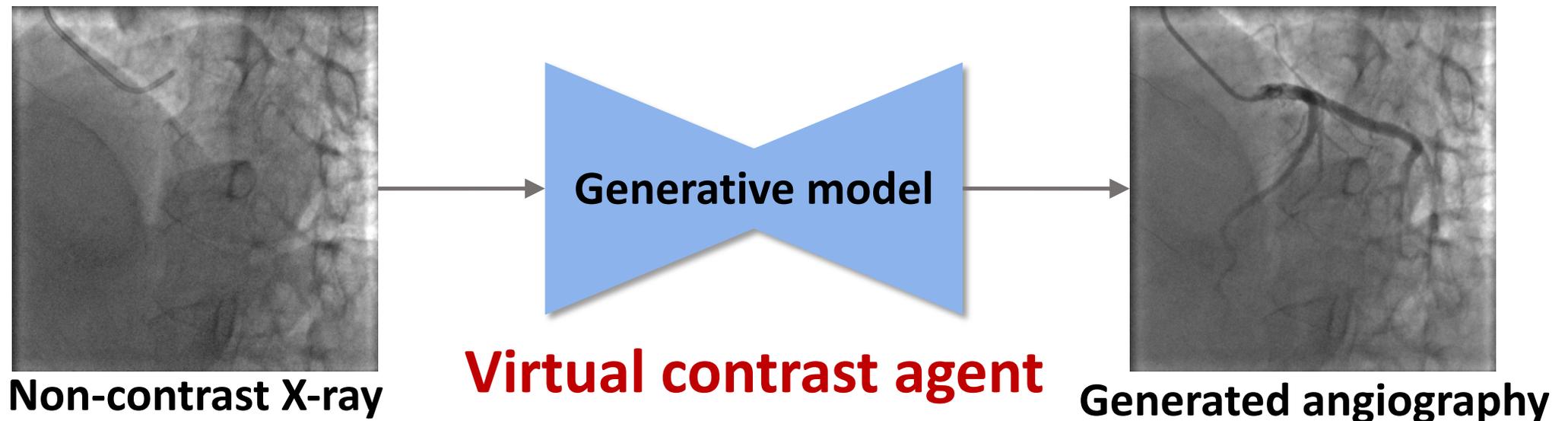
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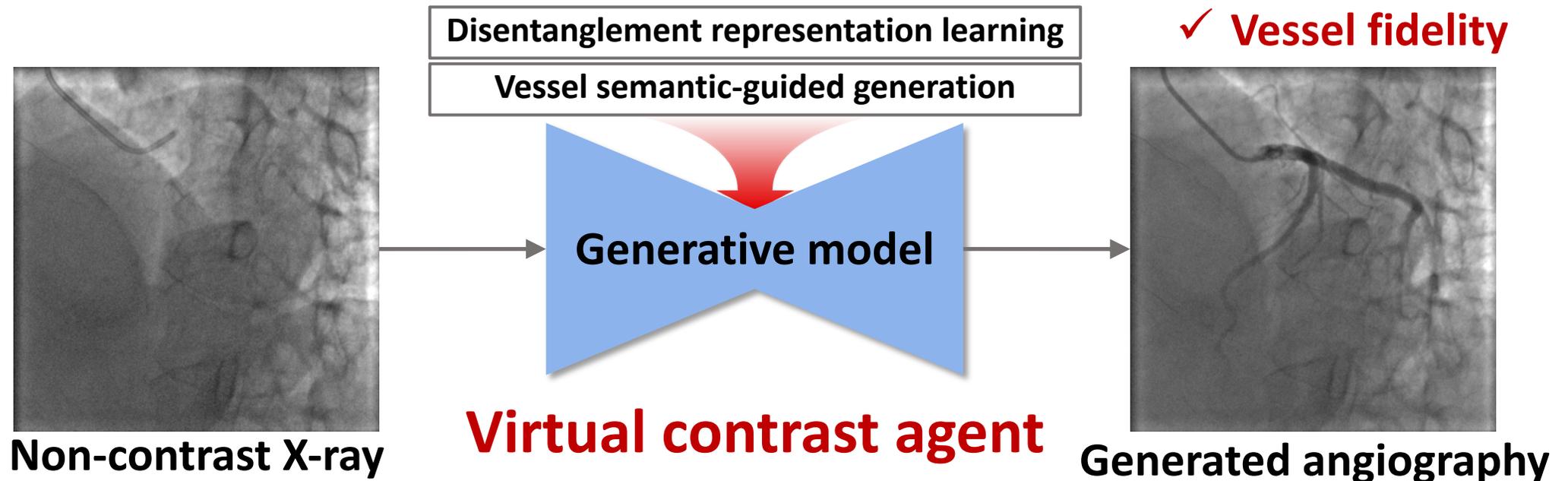
Contributions of this work

- ✓ Novel **generative model** for more accurate contrast-free X-ray angiography synthesis.



Contributions of this work

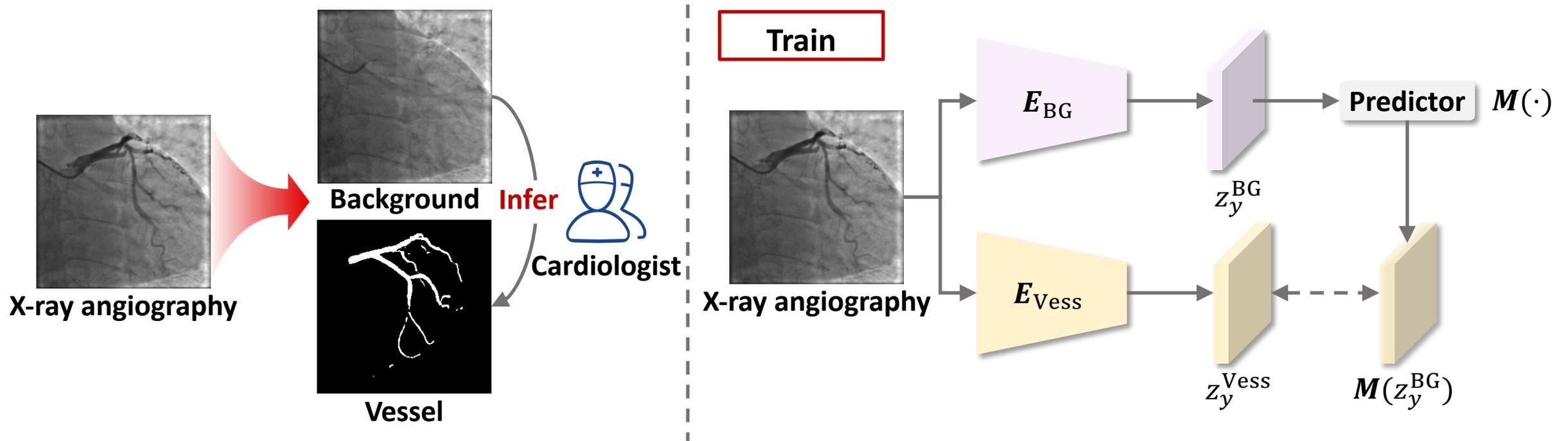
- ✓ Novel **generative model** for more accurate contrast-free X-ray angiography synthesis.
- ✓ Novel **disentanglement representation learning** approach for capturing relationships between anatomical and vessel features.
- ✓ Novel **vessel semantic-guided generation process** for X-ray angiography synthesis with enhanced attention mechanism and loss function.



Part I: Disentanglement Representation Learning

**Novel representation learning approach
inspired by cardiologists**

Part I: Disentanglement Representation Learning



- **Disentanglement encoding**

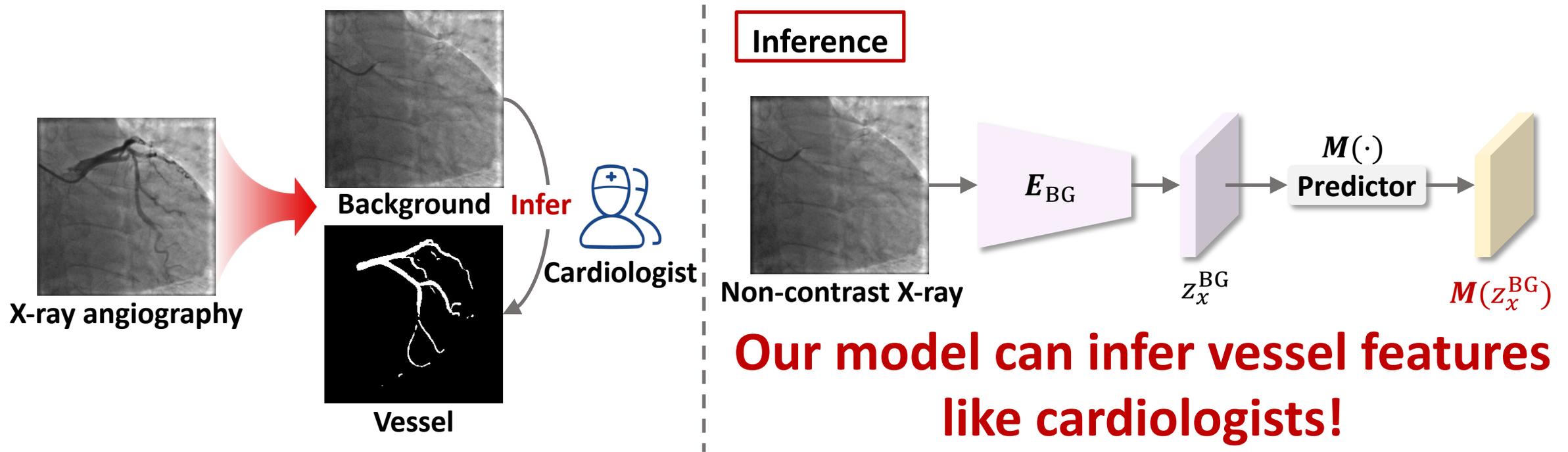
For an X-ray angiography (y), using the background encoder (E_{BG}) and vessel encoder (E_{Vess}) to extract its background (z_y^{BG}) and vessel (z_y^{Vess}) features.

$$z_y^{BG} = E_{BG}(y), z_y^{Vess} = E_{Vess}(x)$$

- **Explicitly formulating the relationship between background (z_y^{BG}) and vessel (z_y^{Vess}) features**

$$\mathcal{L}_{Pred} = \mathbb{E}_{y \sim y} \left\{ \left| M(z_y^{BG}) - z_y^{Vess} \right|_1 \right\}$$

Part I: Disentanglement Representation Learning



- Infer vessel (z_x^{Vess}) features from background (z_x^{BG}) features

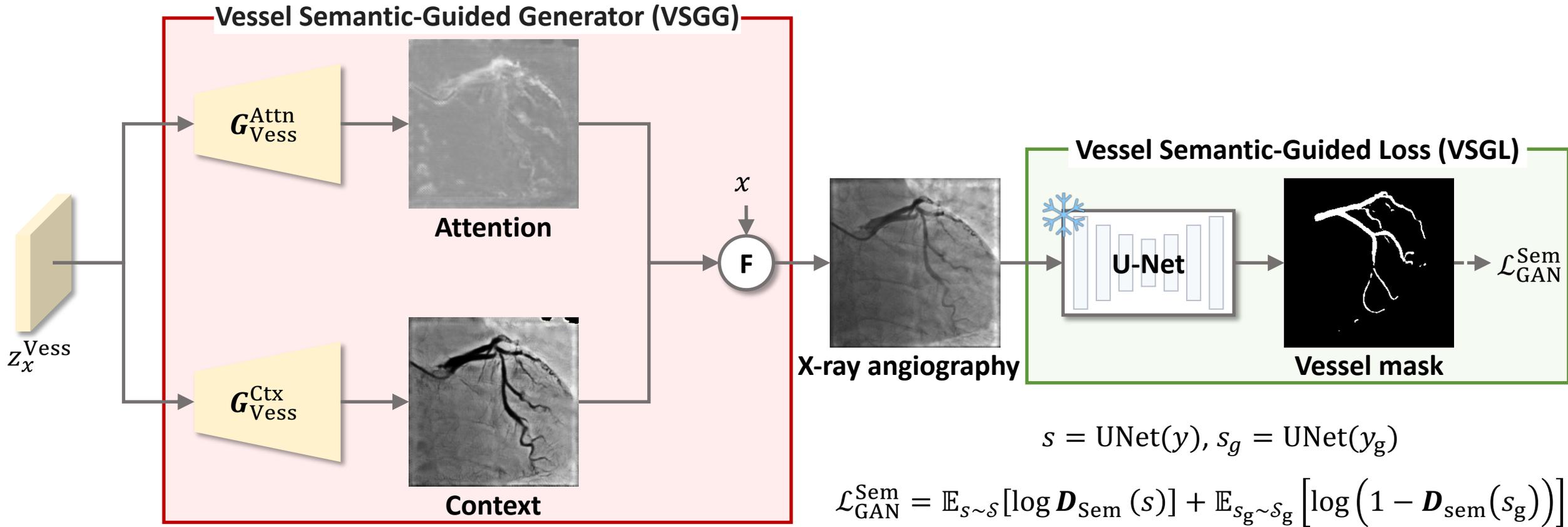
For a non-contrast X-ray (x), using the background encoder (E_{BG}) to extract its background (z_x^{BG}) features. Then, the predictor is utilized infer vessel features (z_x^{Vess}) based on background (z_x^{BG}) features.

$$z_x^{BG} = E_{BG}(x), z_x^{Vess} = M(z_x^{BG})$$

Part II: Vessel Semantic-Guided Generation

**Novel angiography generation process focuses on
vascular details**

Part II: Vessel Semantic-Guided Generation



$$A_g = G_{\text{Vess}}^{\text{Attn}}[M(z_x^{\text{BG}})], C_g = G_{\text{Vess}}^{\text{Ctx}}[M(z_x^{\text{BG}})]$$

$$y_g = x \odot (1 - A_g) + C_g \odot A_g$$

$$s = \text{UNet}(y), s_g = \text{UNet}(y_g)$$

$$\mathcal{L}_{\text{GAN}}^{\text{Sem}} = \mathbb{E}_{s \sim \mathcal{S}} [\log D_{\text{Sem}}(s)] + \mathbb{E}_{s_g \sim \mathcal{S}_g} [\log (1 - D_{\text{Sem}}(s_g))]$$

• H. Tang *et al.*, "AttentionGAN: Unpaired image-to-image translation using attention-guided generative adversarial networks," *IEEE Trans. Neural Networks Learn. Syst.*, 34(4): 1972-1987, 2021.

• O. Ronneberger *et al.*, "U-Net: Convolutional networks for biomedical image segmentation," in *Proc. MICCAI*, 2015: 234-241.

Main Results – Comparisons with SOTAs

- The proposed CAS-GAN significantly outperforms baselines in both FID and MMD.

Evaluation metrics

- **Frechet Inception Distance (FID)**

$$\text{FID} = \|\mu - \hat{\mu}\|_2^2 + \text{Tr} \left\{ \Sigma + \hat{\Sigma} - 2(\Sigma\hat{\Sigma})^{\frac{1}{2}} \right\}$$

- **Maximum Mean Discrepancy (MMD)**

MMD

$$\begin{aligned} &= \frac{1}{n(n-1)} \sum_{i \neq j} k(f_i^R, f_j^R) + \frac{1}{m(m-1)} \sum_{i \neq j} k(f_i^G, f_j^G) \\ &\quad - \frac{2}{mn} \sum_{i=1}^n \sum_{j=1}^m k(f_i^R, f_j^G) \end{aligned}$$

Table I. Quantitative comparisons with SOTAs.

Method	FID ↓	MMD (×10) ↓
CycleGAN [ICCV' 17]	6.54	0.28
UNIT [NeurIPS' 17]	9.99	<u>0.22</u>
MUNIT [ECCV' 18]	8.87	0.33
CUT [ECCV' 20]	7.09	0.26
AttentionGAN [TNNLS' 21]	<u>6.34</u>	0.31
QS-Attn [CVPR' 22]	7.20	0.24
StegoGAN [CVPR' 24]	10.80	2.26
CAS-GAN [Ours]	5.87	0.16

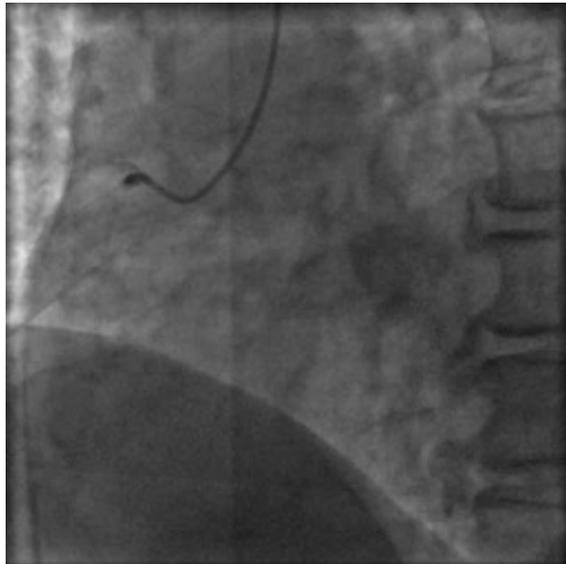
- Best results are highlighted in **bold** and second best are underlined.

• M. Heusel *et al.*, “GANs trained by a two time-scale update rule converge to a local Nash equilibrium,” in *Proc. NeurIPS*, 2017.

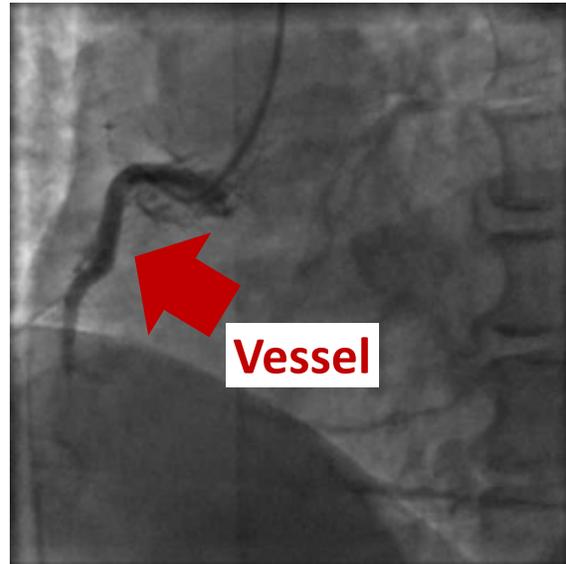
• A. Gretton *et al.*, “A kernel two-sample test,” *J. Mach. Learn. Res.*, 13(1): 723-773, 2012.

Main Results – Comparisons with SOTAs

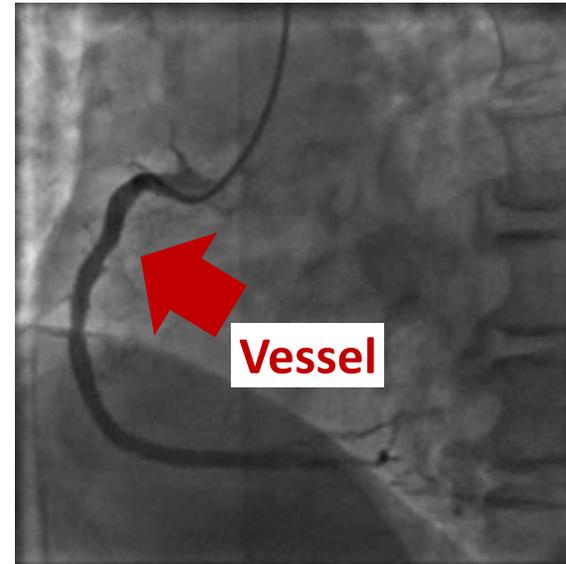
- Case 1: CAS-GAN can effectively **preserve structural consistency** of vessels.



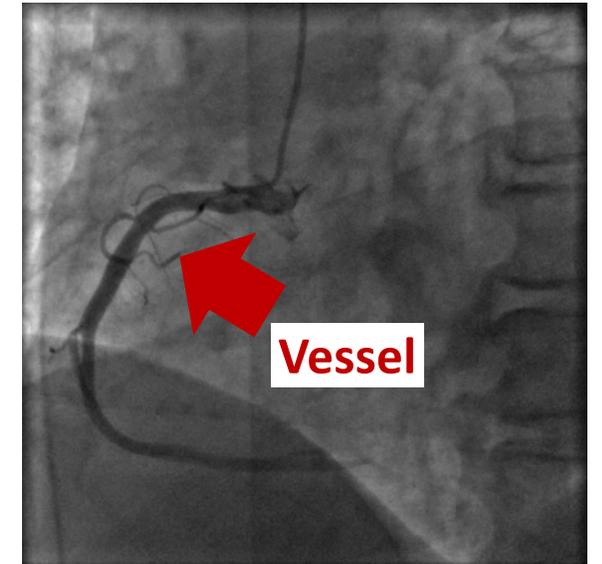
Non-contrast X-ray



AttentionGAN
(TNNLS' 21)



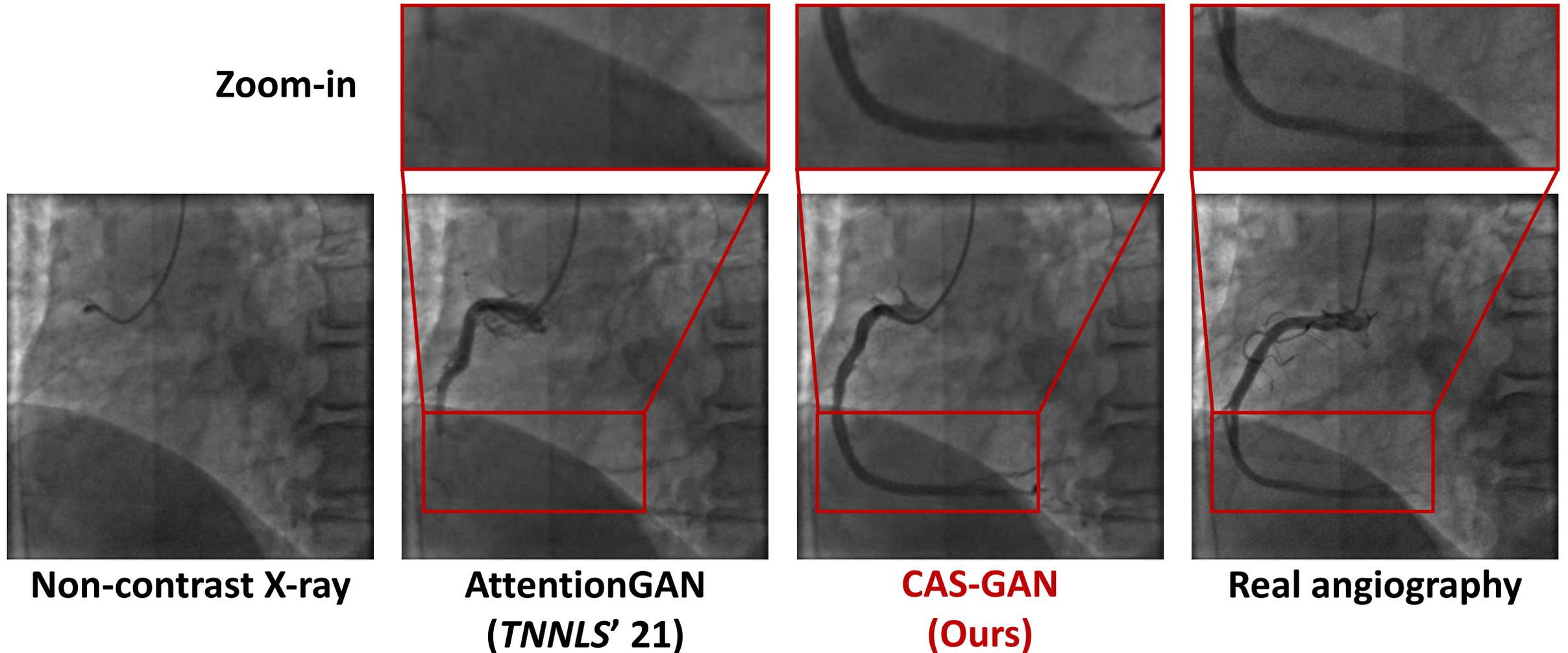
CAS-GAN
(Ours)



Real angiography

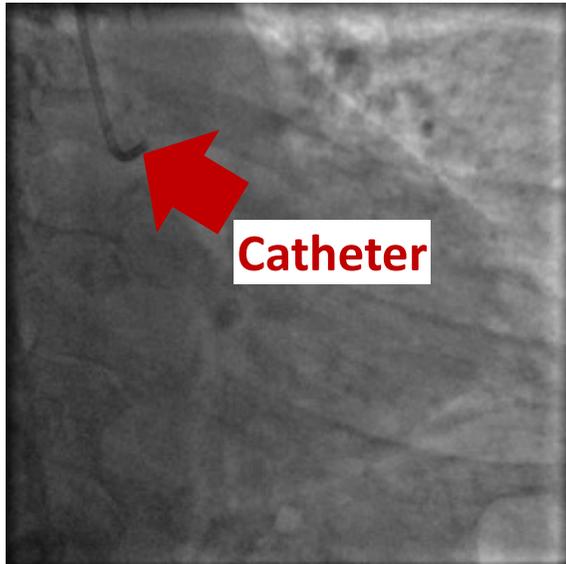
Main Results – Comparisons with SOTAs

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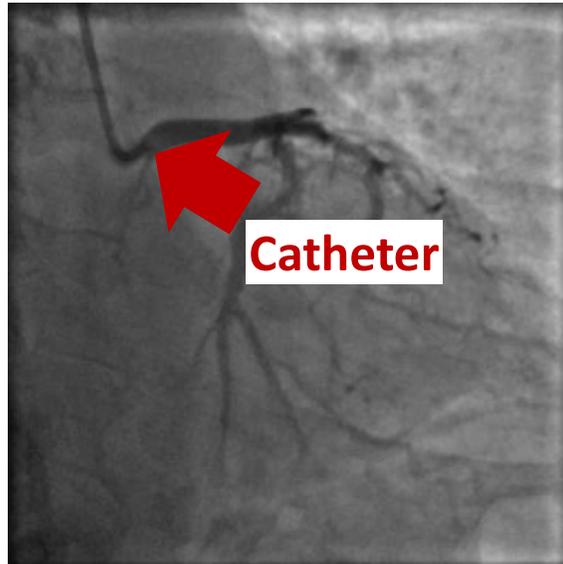
Main Results – Comparisons with SOTAs

- Case 2: CAS-GAN can **accurately synthesis critical vessel bifurcations**.



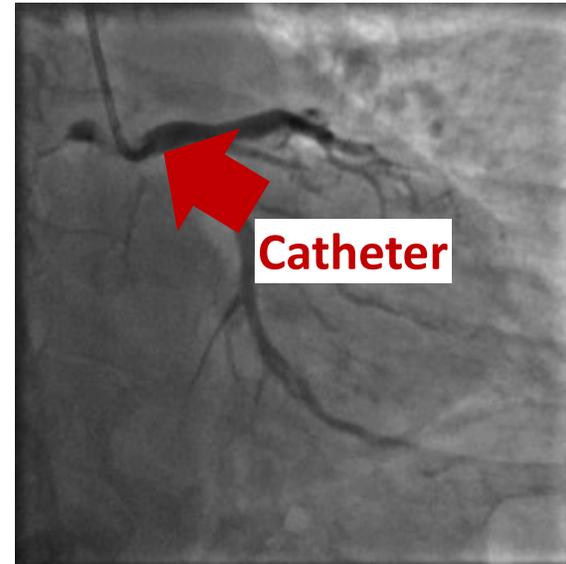
Catheter

Non-contrast X-ray



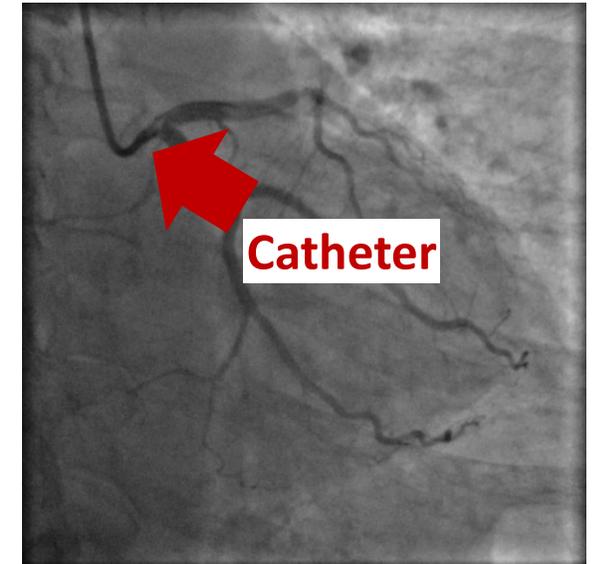
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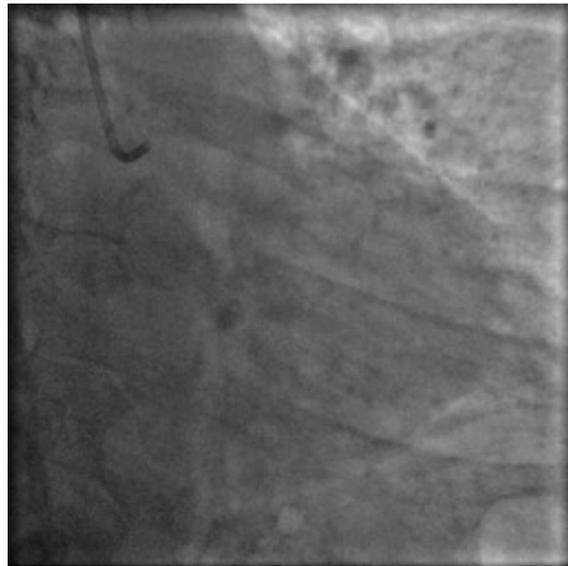
Catheter

Real angiography

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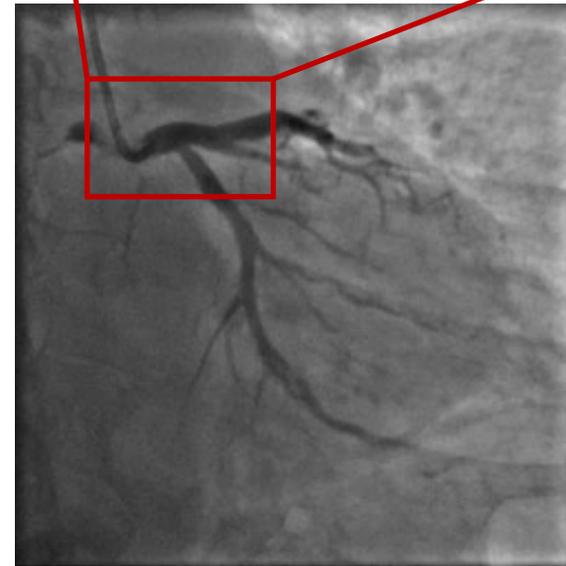
Zoom-in



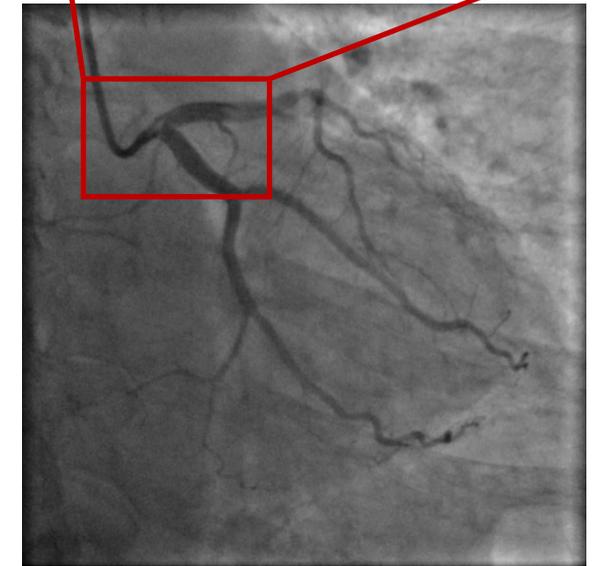
Non-contrast X-ray



AttentionGAN
(TNNLS' 21)



CAS-GAN
(Ours)



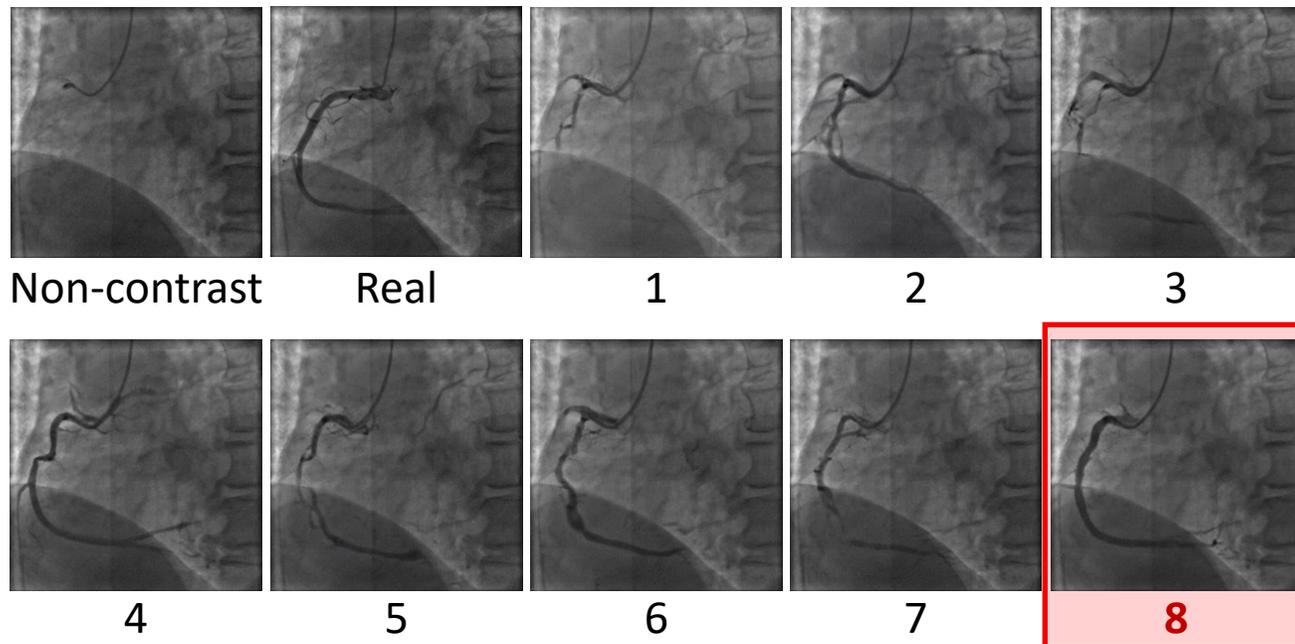
Real angiography

Main Results – Ablation Studies

Table II. Effects of several designs.

Index	DRL	VSGG	VSGL	FID ↓	Δ
1				7.14	+1.27
2			✓	8.59	+2.72
3		✓		6.57	+0.70
4		✓	✓	5.98	+0.11
5	✓			6.87	+1.00
6	✓		✓	6.70	+0.83
7	✓	✓		5.93	+0.06
8	✓	✓	✓	5.87	—

- DRL: Disentanglement representation learning
- VSGG: Vessel semantic-guided generator
- VSGL: Vessel semantic-guided loss



Each module within the CAS-GAN plays an integral role in precisely generating vascular structures

Summary

- ✓ This is the **first attempt** to utilize a generative model for **contrast-free angiography synthesis**, offering a promising way to reduce reliance on contrast agents.
- ✓ The **disentanglement representation learning approach** and **vessel semantic-guided generation process** can ensure high fidelity of generated images.
- ✓ In future works, CAS-GAN will be validated on a **large-scale dataset**, and **downstream applications** will be conducted in vivo animal experiments.

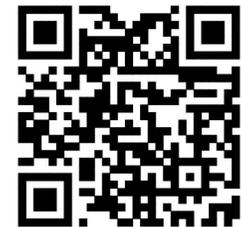


2025 IEEE
Symposium Series on
Computational Intelligence



Thanks! & QA

Email: huangdexing2022@ia.ac.cn



arXiv



Poster