

Development and application of AI enabled automated drug delivery system for TACE guided by DSA

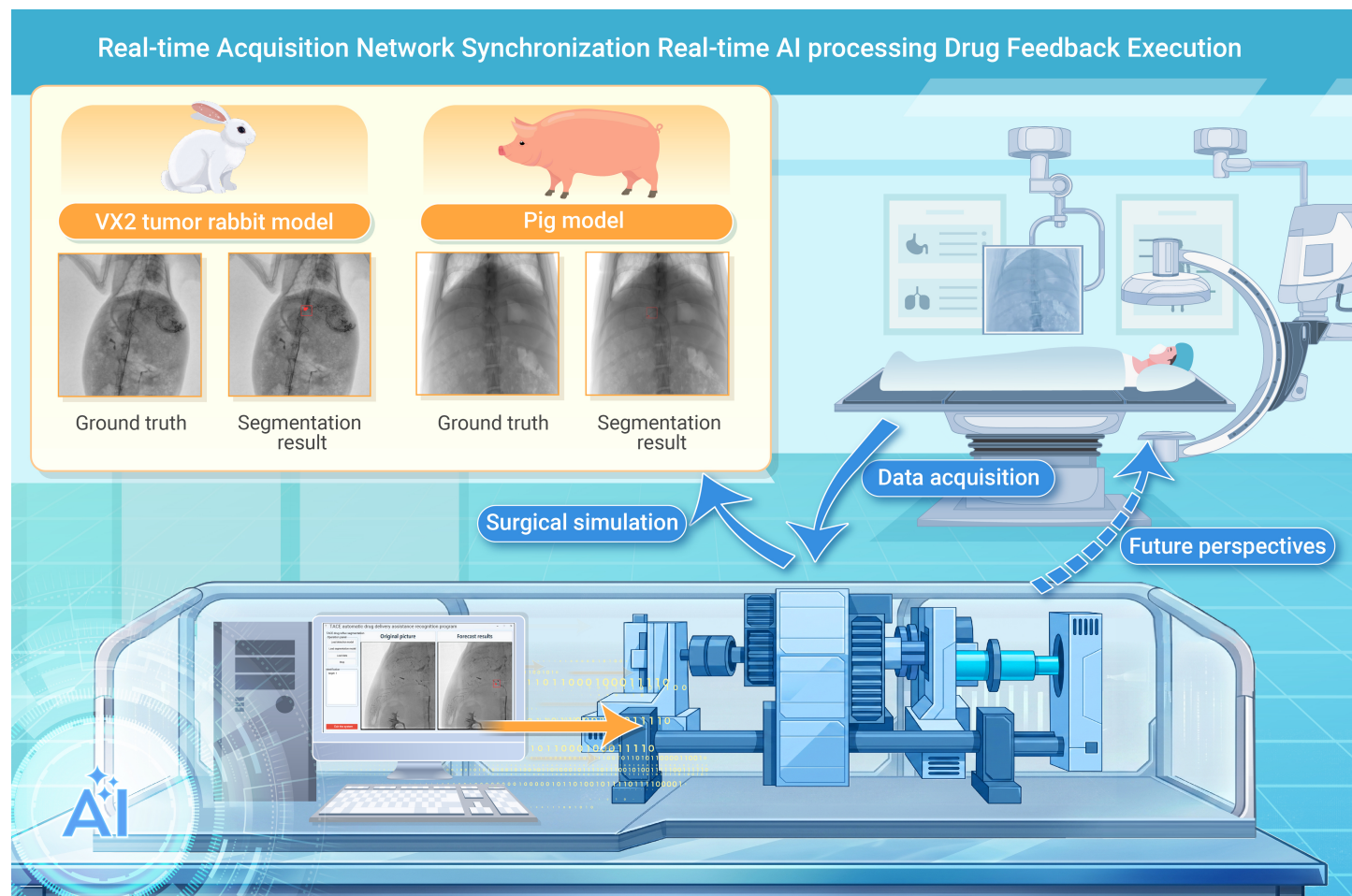
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GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- We developed an intelligent drug delivery system to enhance safety and precision in liver cancer therapy.
- It enables automated drug delivery control through real-time imaging monitoring.
- The system detects blood flow changes and adjusts dosing to reduce drug reflux.
- Results show more stable injection, faster response, and strong adaptability.
- It may reduce radiation exposure and improve clinical treatment outcomes.

Development and application of AI enabled automated drug delivery system for TACE guided by DSA

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Transarterial chemoembolization (TACE) is an important treatment modality for unresectable hepatocellular carcinoma. Real-time monitoring of drug injection and reflux during the procedure is a critical factor influencing both therapeutic efficacy and radiation dose exposure for interventional radiologists. However, existing automatic injection devices lack high-dimensional, real-time closed-loop feedback. To overcome these limitations, we developed AI-FlowTACE, an intelligent drug delivery system that integrates real-time monitoring, adaptive dynamic flow regulation, and precision braking control. AI-FlowTACE can be seamlessly incorporated into clinical workflows to acquire intraoperative DSA images in real time. By analyzing imaging feedback through an embedded Artificial Intelligence (AI) module, the system autonomously guides the injector to achieve adaptive drug delivery. The model architecture achieved segmentation AUCs of 98.15% and 97.23% in two external validation cohorts. In an in vitro simulated vascular model, AI-FlowTACE demonstrated markedly more stable injection performance than manual administration, with the cumulative error consistently maintained within 0.02 mL. In three highly sensitive rabbit blood-flow models, the system achieved drug-adjustment response times of 0.83 s, 0.70 s, and 0.82 s, respectively. In in vivo experiments using a porcine model with human-like vascular anatomy, the response time was 0.8 s, indicating excellent adaptability and feasibility. Furthermore, in real TACE procedures, simulated comparisons with manual injection further validated the system's adaptive reflux-adjustment capability, while demonstrating a 20% reduction in additional radiation exposure.

INTRODUCTION

Transarterial chemoembolization (TACE) is currently one of the most important therapeutic approaches for unresectable hepatocellular carcinoma.¹⁻³ Depending on tumor burden and biological characteristics, TACE enables the flexible selection of chemotherapeutic or radioactive embolic agents, which are superselectively delivered into the tumor-feeding arteries to achieve individualized treatment.⁴⁻¹² Stagnation of blood flow and drug reflux within the target vessels are indicative of complete tumor embolization. Although physicians can perform real-time monitoring under digital subtraction angiography (DSA) guidance, manual drug injection during TACE may lead to premature reflux when the injection rate is too rapid or unstable, resulting in an increased risk of nontarget embolization and radiation-induced injury.¹³⁻¹⁸

Existing high-pressure injectors can be programmed with parameters such as flow rate and total injection volume, thereby enabling quantitative and constant-rate delivery.^{19,20} However, purely mechanical injectors lack information-processing capabilities and real-time closed-loop feedback mechanisms, making it difficult to maintain optimal drug delivery in complex hemodynamic environments.²¹⁻²⁴ Therefore, endowing drug delivery systems with intelligent perception and control stability remains a key challenge in optimizing the TACE injection process. Some intelligent infusion pumps rely on drug databases to reference static knowledge, allowing for cross-threshold configuration and the inclusion of pressure sensors to receive low-dimensional feedback. Nonetheless, such approaches struggle to handle high-dimensional and multimodal data—such as imaging information—and remain constrained by excessive dependence on manually defined thresholds, frequent false

alarms, and complicated user interfaces.²⁵ Moreover, these systems still lack dynamic optimization and learning capability. Deep learning models, through supervised learning, are capable of efficiently processing high-dimensional and complex data such as medical images, as well as integrating multimodal clinical information.^{26,27} Combined with automated control technologies, artificial intelligence models can further ensure the stability of key procedural operations.²⁸⁻³¹ Therefore, by designing a series of TACE guided labels, constructing a high-dimensional information machine vision perception module for DSA images, and based on this, building a feedback decision-making system that accommodates medical knowledge, the precise administration of mechanized drug delivery equipment is guided, providing a new idea for the automated drug delivery of TACE.

In this study, we developed AI-FlowTACE (AI-powered Flow-regulated TACE System), which is an automatic drug delivery system with local pharmacokinetic feedback that integrates static knowledge reference and dynamic adaptive feedback (Figure 1). Based on 50,909 intraoperative real-time DSA videos (0.4–264s), the system incorporates a multi-stage deep learning-based drug delivery monitoring algorithm coupled with a high-precision mechanical injection device, enabling real-time monitoring, adaptive dynamic flow regulation, and precision braking during TACE procedures. We validated the system's injection stability across multiple embolic agents using in vitro simulated vascular models, tumor-bearing animal models, and human-like physiological models, assessing its sensitivity in flow recognition and control, as well as its feasibility in complex, human-like vascular environments. Additionally, simulated comparative experiments were performed in six real TACE procedures to evaluate AI-FlowTACE's capability for reflux detection and reduction of radiation exposure under real-world clinical conditions. Our study presents the first imaging perception-based, closed-loop automated drug delivery framework for TACE, introducing a deep learning-driven paradigm of real-time intelligent control that holds promise for broader applications in interventional radiology.

MATERIALS AND METHODS

This study was conducted in accordance with the Declaration of Helsinki and was reviewed and approved by the institutional ethics committee (Ethics Approval No. 2024PS1227K). DSA fluoroscopic imaging sequences were retrospectively collected. As the images were obtained during routine clinical practice, the requirement for informed consent was waived.

Study design and datasets

Among the 8,407 patients initially screened, DSA images were excluded from analysis for those with missing or incomplete clinical data ($n = 3,110$), incomplete imaging records ($n = 1,099$), or poor image quality ($n = 526$) (Figure 2). Finally, this study included DSA imaging data from a total of 3,672 patients who underwent TACE between January 2017 and May 2025. For the drug reflux region detection dataset, the internal cohort comprised 1,622 patients, and the external cohort comprised 2,050 patients. We further selected patients with clearly visible reflux manifestations from this cohort to construct a drug reflux segmentation dataset. The internal cohort consisted of 273 patients (1,269 video clips, 21,062 frames), covering different stages of hepatocellular carcinoma (HCC), while the external cohort included 408 patients (872 video clips, 57,888 frames). To account for inter-device variability

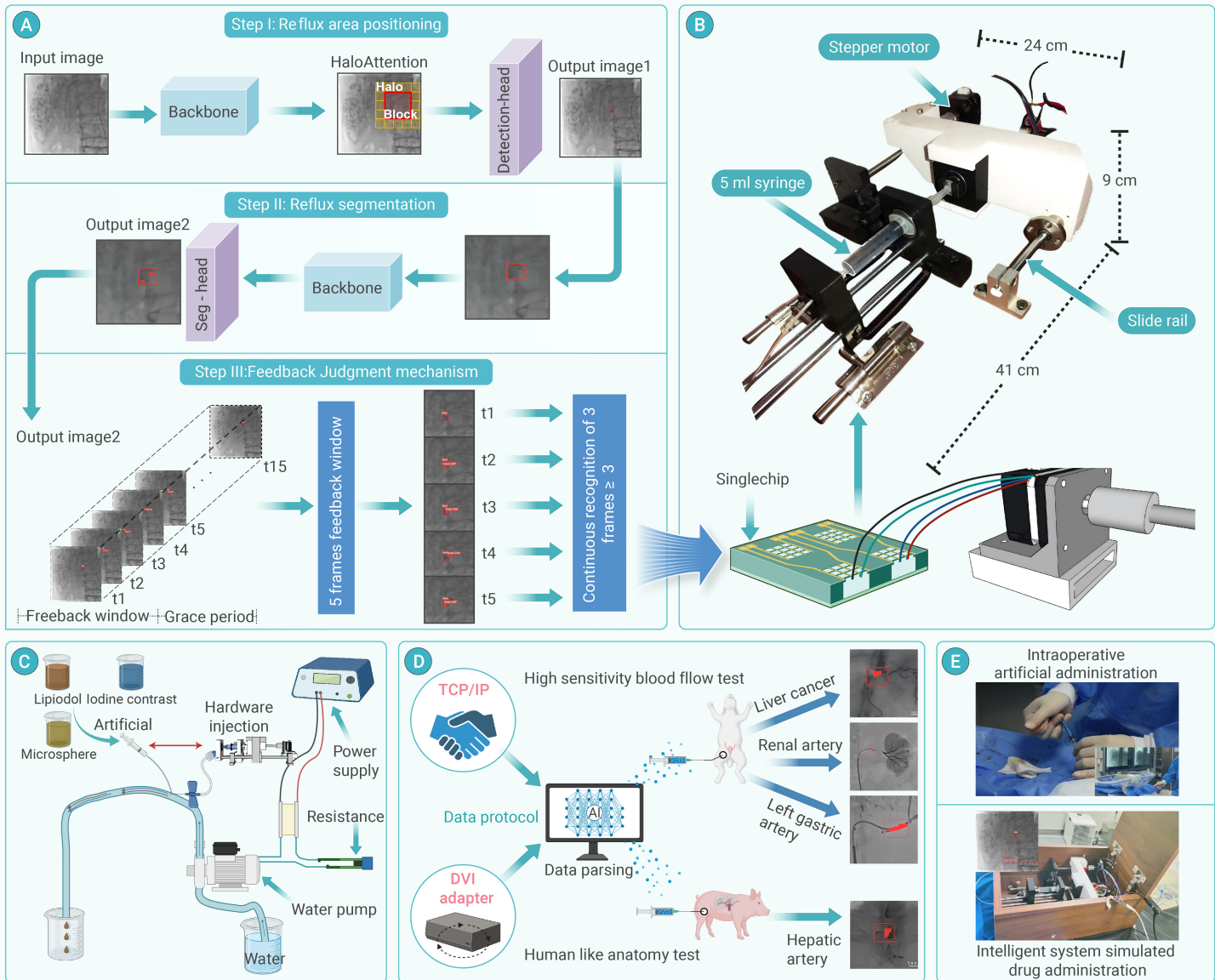


Figure 1. Process of AI-FlowTACE (A) The two-stage model architecture of YOLO Attention+PA-FPN automatically locates and segments abnormal reflux drugs caused by mismatched infusion and blood flow rates on 2D-DSA perspective slices. Through a feedback signal flow mechanism of continuous three frame recognition, the AI recognition results are efficiently converted into downstream drug feedback pathways, driving hardware response in real-time; The setting of the buffer period effectively filters out short-term fluctuation signals, avoiding frequent adjustments caused by transient anomalies in the system. (B) The injection device (41 cm in length, 24 cm in width, and 9 cm in height) integrates a microcontroller to achieve real-time reception of upstream drug delivery signals and efficient conversion of motor drive instructions. The stepper motor drives the transmission mechanism through a coupling, driving the injector to achieve high-precision and controllable automatic injection rate. (C) A simulation system based on self-priming pump, pipeline, and pressure display module is built, and glycerol, silicone oil, and microspheres are used to simulate iodine oil, iodine contrast agent, and microsphere suspension, respectively. Add organic dyes to visually observe the fluid injection process of artificial and AI FlowTACE. (D) Verify the effectiveness of AI FlowTACE in vivo environment using rabbit model with high blood flow sensitivity and pig model with complex vascular background. (E) Conduct simulated clinical comparative experiments in real surgery to evaluate the performance differences of human-machine injection and the substantial benefits of reducing the radiation load of interventional doctors.

and enhance model robustness, the data were acquired using DSA equipment from Siemens, Philips, Shimadzu, and Neusoft.

Imaging acquisition and annotation

Using Picture Archiving and Communication System (PACS), we obtained videos of drug injection during TACE procedures, capturing the hepatic proper artery and its branches under fluoroscopy. Each DSA video contained 15–18 frames, and fluoroscopic sequences larger than 512×512 pixels were resized to this dimension (Supplemental Materials S1). Two authors (Y.X. and Y.Y.), each with over three years of interventional surgery experience, annotated the DSA images using Labelme software (<http://github.com/wkentaro/labelme>). The annotated regions corresponded to the catheter tip located at the edge of the rectangular annotation box—drug presence within this region was considered reflux. Subsequently, refluxing drug droplets within the rectangular box were labeled, and Cohen's Kappa coefficient was used to assess inter-

annotator consistency. Finally, the annotations were reviewed by two experienced interventional radiology experts (H.W. [10 years of clinical experience] and M.N. [13 years of clinical experience]) (Figure S1). The acquired DSA images were then augmented (Supplemental Materials S2), followed by Min-Max normalization and Gaussian denoising to remove random noise from the images.

Deep learning algorithm

The model was first fine-tuned on the large-scale public dataset ImageNet to adapt to low-contrast scenarios in DSA images, such as overlapping catheters, blood vessels, and tissue. The deep learning algorithm for dynamic drug flow management adopts a Convolutional Neural Network (CNN)-based two-stage architecture.³² According to DSA imaging, drug reflux is intuitively defined as the clear retrograde flow of contrast or embolic agents on normal forward arterial blood flow, extending beyond the tip of the microcatheter

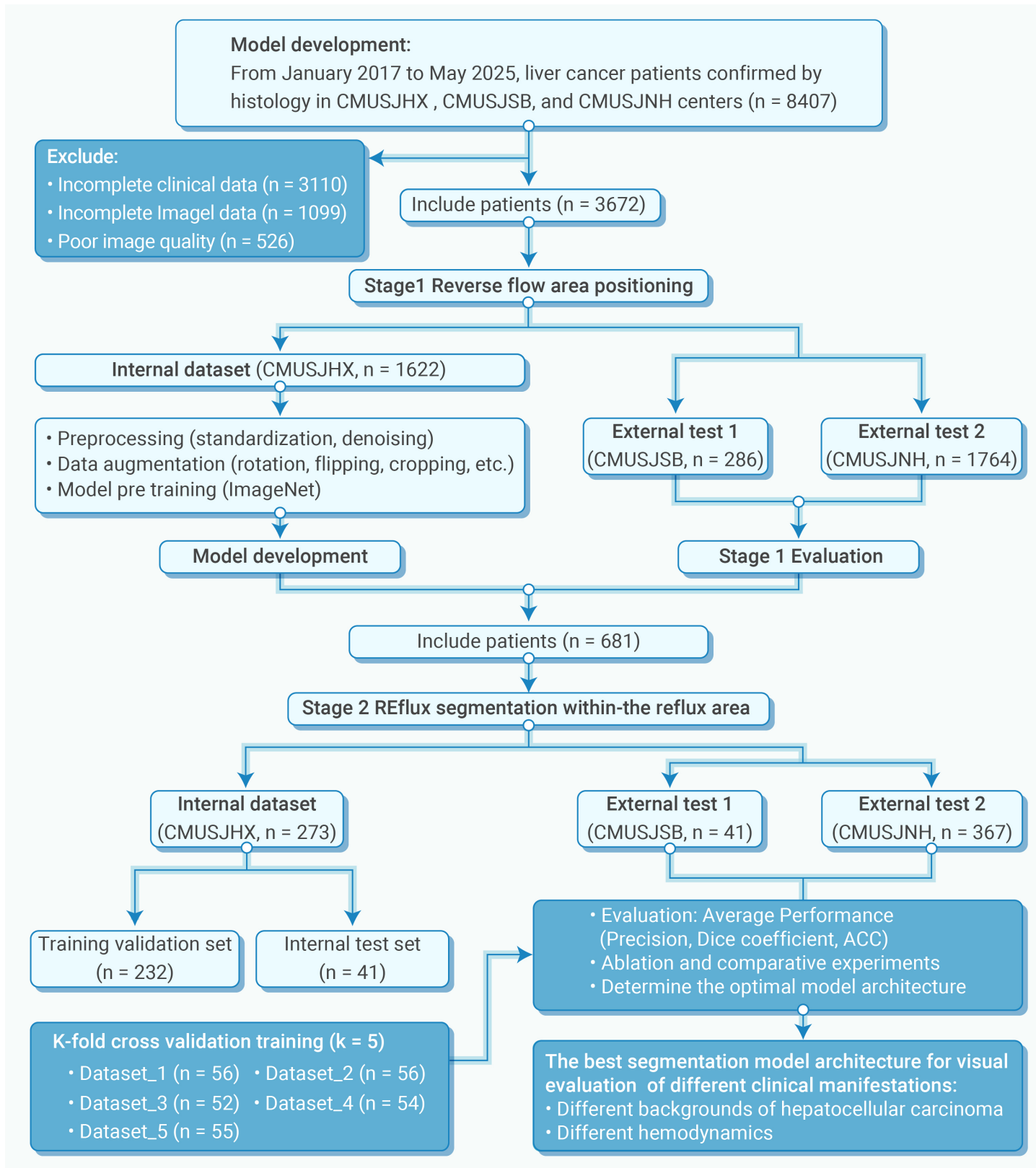


Figure 2. The inclusion and exclusion criteria for this study The development of the deep learning (DL) model for this system includes two stages: the first stage is for locating the backflow area, and the second stage is for training and testing the backflow segmentation within the backflow area. In the first stage, imaging data from 2,050 patients will be used to evaluate the accuracy of reflux area localization in two external test sets (CMUSJSB, CMUSJNH). Subsequently, 681 patients with reflux imaging findings were selected from the first stage queue, and their accuracy and generalizability in the reflux drug segmentation task were validated using five fold cross validation in the internal queue and two external test sets, thereby verifying the credibility and generalization ability of the model.

towards the proximal end and lasting for at least 3 consecutive DSA frames. Two experienced interventional radiologists unanimously validated this visual assessment. In the first stage, for detecting regions of drug reflux in 2D-DSA images, we constructed an object detection network incorporating a local self-

attention mechanism—designed to adaptively enhance detection sensitivity while maintaining computational efficiency.³³ Firstly, identify the tip of the microcatheter and establish a dynamic candidate reflux local region of interest (ROI). Then, the detected bounding boxes are sent to the second stage,

which uses PA-FPN (Path Aggregation Feature Pyramid Network) to construct a segmentation network (Supplemental Materials S3), strictly segmenting the backflow target at the pixel level within this constrained region framework. Across a multi-level evaluation framework, we not only evaluated the segmentation adaptability and accuracy of the model at the patient level without overlap in different clinical scenarios, but also quantified its generalization ability in two external queues with different data sources. In addition, an exploratory analysis was conducted on a small subset of ambiguous or unclear reflux cases ($n = 2$), which were not included in the primary evaluation due to the absence of a reliable reference standard. These cases were used to qualitatively assess model behavior under indeterminate conditions.

Based on this, a time-series feedback mechanism with a 1-second cycle was established. During the first one-third of each cycle, five frames were evenly sampled as the feedback window to segment drug droplets within the reflux regions of each frame. To prevent sporadic reflux from excessively affecting dosage adjustments, the alert threshold was set to three consecutive frames with positive droplet segmentation. Considering the actual response characteristics of the device, the remaining portion of the cycle was treated as a buffer period, during which images were not processed, providing the injection pump sufficient time to interpret and execute the feedback signals.

Hardware development

The development process of the self-designed intelligent injection hardware system encompassed multiple stages, including 3D structural modeling, 3D printing fabrication, integration of the core control unit, and motor drive module construction (Figure 3, Supplemental Materials S4). The 3D printing process is strictly used for rapid prototyping of external machines and mechanical transmission components. Its strong generalization in rabbits, pigs, and humans relies entirely on adaptive algorithm software, rather than specific anatomical customization for different vascular environments or species. The functional components of the injection pump were precisely modeled using SketchUp software and fabricated layer by layer with Polylactic Acid (PLA) material, followed by assembly. PLA is a renewable polymer with high mechanical strength at room temperature and excellent biodegradability. Flow rate control of the injection pump was achieved through a micro-controller unit (MCU) integrated with a stepper motor driver circuit. Based on real-time recognition results, the AI module generated feedback signals that were received by the MCU, which parsed the serial communication signals via a driver expansion board and adaptively adjusted the stepper motor speed across multiple flow-rate levels according to preset parameters (Supplemental Materials S5, Table S1).

To validate the hardware performance and assess its practical applicability, we independently constructed an *in vitro* simulated vascular model. This model, equipped with a self-priming pump, tubing system, and pressure display module, reproduced the hemodynamic characteristics of blood flow. Using simulated mixtures of Lipiodol, Iodine contrast medium, and Microspheres, we compared the performance between manual injection and the intelligent injection device, thereby comprehensively evaluating the system's adaptability to different fluid properties and its flow control precision. In the Supplemental Materials S6, the physical properties of three injectable drugs are systematically described.

In vivo animal experiment validation

The *in vivo* experiments in this study were conducted in the laboratory of the Neusoft Medical Digital Angiography System R&D Center to verify the closed-loop control effectiveness of the network-based TACE intelligent drug delivery system (Supplemental Materials S7). After general anesthesia, New Zealand white rabbits underwent femoral artery puncture and catheterization into the common hepatic artery. Under real-time guidance of the NeuAngio 30F DSA system, iodized oil delivery through the hepatic artery was performed (Supplemental Materials S8), verifying the interaction performance of AI-FlowTACE in a hepatic tumor environment, which serves as the primary clinical target analog for TACE.^{34–36} In addition, to assess the adaptability of AI-FlowTACE across diverse hemodynamic environments, additional experiments were conducted in the left renal artery (representing a high-

flow, low-resistance system) and the left gastric artery (modeling a small-caliber, tortuous vessel with high peripheral resistance) in selected rabbits.

Another *in vivo* experimental setup, more closely resembling human anatomy, was established at the Genesis MedTech Interventional Catheter Center using porcine models. Three types of agents—Lipiodol, Iodine contrast agent, and Microspheres—were administered via the hepatic artery to evaluate the injection performance of AI-FlowTACE. At this stage, a differentiated data access strategy was implemented: DSA device image signals were output through a DVI port, converted via a DVI-to-HDMI cable, routed through a USB KVM SWITCH (2×1) adapter, and finally imported into a local server for AI processing. This setup enabled stable image acquisition and algorithm-driven operation using standard hardware connections.

All experiments were approved by the Institutional Animal Ethics Committee and conducted in strict accordance with relevant animal experimentation regulations (Ethics Approval No. 2024PS1354K).

Comparison of intraoperative man-machine delivery simulation

We further investigated the potential of AI-FlowTACE to serve as a substitute in real clinical drug delivery procedures. To this end, we designed a retrospective simulation strategy based on intraoperative imaging to establish a performance comparison framework between AI-FlowTACE and manual operation. At the CMUSJNH center, full-process videos of physicians performing drug delivery during actual TACE procedures were recorded (Figure S2), along with synchronized intraoperative DSA images, to quantitatively assess the dynamic characteristics and response delays of manual delivery. Subsequently, the corresponding patients' DSA images were input into the intelligent drug delivery system to perform a simulated AI-FlowTACE-based delivery process without human intervention, enabling reconstruction and comparison of human-machine performance within the same clinical scenario. The experiment included three operators with different levels of experience (Y.X. [3 years of interventional experience], Y.L. [6 years of interventional experience], H.W. [16 years of interventional experience]) and six patient datasets (Table S2), with each operator assigned two independent cases, covering both inter-operator variability and intra-operator fluctuations.

Evaluation metrics

For reflux region detection, mean average precision (AP) was used to evaluate the overall performance of different models at various Intersection over Union (IoU) thresholds. For drug droplet segmentation, IoU, Precision, Recall, Dice coefficient, Accuracy, and Area Under Receiver Operating Characteristic (AUC) were calculated at the patient level for each dataset, and their 95% confidence intervals were calculated. Five-fold cross-validation was performed to ensure model performance consistency across different data subsets. Continuous variables are analyzed using analysis of variance, and categorical variables are tested using chi square test. All statistical analyses were conducted using SPSS (version 23.0; IBM) and Python (version 3.11.2; Python Software Foundation). Radiation exposure was quantitatively evaluated using the microsievert (μ Sv) metric. For the mechanical performance evaluation of the automated injection system, precision metrics including the Maximum Instantaneous Error and Root Mean Square Error (RMSE) were utilized (Supplemental Materials S9). Using linear mixed effects model (LMM) to correctly explain the clustering properties and repeated measurements of data in operator equipment comparisons.

RESULTS

Clinical characteristics of dataset

The clinical characteristics of included participants are summarized in Table S3. In the reflux region localization dataset, which contained 50,909 DSA videos from 3,672 patients, the mean ($\pm$ SD) age in the internal cohort was 60 ± 10.4 years, and 73.7% (1,196 of 1,622) were male.

In the reflux segmentation dataset, comprising 2,141 DSA videos from 681 patients, the reflux occurrence rates in the internal cohort and the two external cohorts were 42.2%, 22.8%, and 35.6%, respectively. In addition, differences were observed in frame acquisition rates, with external cohort 2 operating at 11 FPS, while the internal and external cohort 1 both approached 15 FPS.

Across all cohorts, Siemens systems were used most frequently; Neusoft equipment appeared only in external test set 1, whereas Shimadzu systems

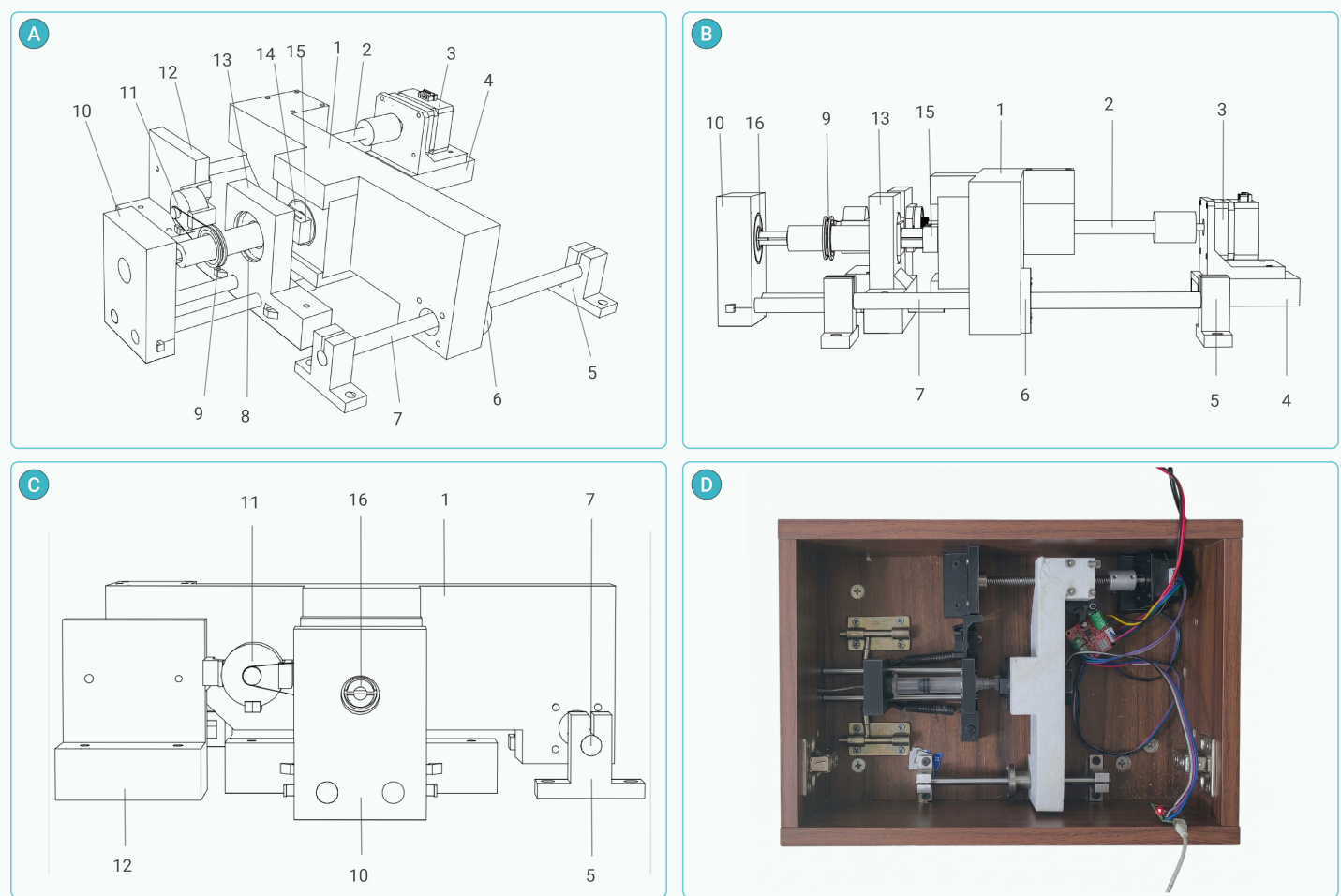


Figure 3. Intelligent injection hardware device CAD three view and physical drawing (A–C) displays the CAD overall drawing, left view, and front view of the intelligent injection hardware device in three dimensions (1. Large horizontal seat; 2. Screw kit: Screw, Nut seat, Horizontal bearing, Coupling; 3. Stepper motor; 4. Motor seat; 5. Optical axis bracket; 6. Slide rail bearing; 7. Slide rail; 8. Thrust ball bearing; 9. Belt ring; 10. Front seat; 11. Motor motor; 12. Motor bracket; 13. Rear seat; 14. Ball bearing; 15. Rear clip; 16. Front clip). (D) The hardware entity diagram of the intelligent injection device is roughly as follows: after the system sends instructions, the injection device's microcontroller receives the instructions through the Type-C serial port. Then, the microcontroller parses the instructions and calculates the motor control parameters. The motor drives the expansion board to receive and convert signals, and the motor executes motion according to the time and speed matched by the driving signal.

were exclusively used in external test set 2. Further details are provided in Table 1.

Performance of two-stage architecture and cross center validation

In the first stage of the model architecture, a bounding box was generated to localize the reflux region (Figure 4A). The baseline YOLOv8 model achieved an AP50 of 89.3% and an AUC of 80.74%. After incorporating a local self-attention mechanism, the final model achieved an AP50 of 94.1% and an AUC of 86.29%, markedly outperforming YOLOv8, YOLO9, YOLO10, YOLO11, and RT-DETR models. Although the number of model parameters increased to 3.22M, the inference speed remained excellent at 165 FPS, second only to the YOLOv8 baseline (Table S4). In the reflux segmentation stage, Figure S3A shows the ROC curves obtained from five folds (Fold-one to Fold-five) in the internal cohort. The areas under the curve (97.79%, 98.03%, 99.69%, 99.36%, and 97.14%) demonstrated highly accurate and consistent predictions. Moreover, both the precision-recall (PR) curves and confusion matrices for each fold exhibited high agreement (Figure S3B–G).

By calculating Cohen's kappa coefficient, we further validated the agreement between model predictions and manual annotations, yielding a kappa value of 0.83, which indicates a strong concordance and supports the model's reliability and accuracy. Additionally, Table S5 compares the performance of direct reflux segmentation versus the two-stage approach, showing that the latter achieved significantly better results, underscoring the necessity and effectiveness of the first-stage localization process (Table S6 shows the exact number of patients and total video frames assigned to the training and validation sets for each fold in the five fold cross validation fold).

The generalizability of the proposed deep learning (DL) model architecture was evaluated across two external cohorts—comprising 57,888 2D-DSA images—and data from four different angiography system manufacturers. As shown in Figure 4B, for the first-stage reflux region localization task, the model's performance was assessed on both external datasets, and the corresponding precision-recall (PR) curves confirmed its robustness across diverse data sources, achieving areas under the curve (AUCs) of 97.14% and 92.94%, respectively (The learning curve is shown in Figure S4). Furthermore, the model demonstrated consistent performance in the second-stage reflux segmentation across both external cohorts (Table S7). In terms of ROC analysis, the proposed two-stage DL architecture achieved a 10% improvement in AUC compared to direct single-stage segmentation (Figure 4C). Supplemental Materials VideoS1 also presents a representative example of video-based segmentation. A stratified analysis across the four major DSA system manufacturers involved in the external datasets revealed excellent cross-platform adaptability, with AUC values ranging from 86.5% to 96.46% (Figure 4D). Additionally, the model architecture demonstrated ultrafast feedback response times—from reflux recognition to injection command issuance—across all cohorts. As shown in Figure 4E–G, the response times were extremely short and consistently centered around 0.12 s, regardless of age group, hepatitis status, or Child–Pugh classification. To further evaluate model behavior in ambiguous scenarios, we analyzed a subset of unclear reflux cases ($n = 2$). Representative examples are provided in Supplemental Materials VideoS2. In these cases, reflux-like signals were typically transient, weak, and lacked temporal persistence. While occasional short-lived or precursor-like patterns were observed, they did not develop into sustained

Table 1. Clinical characteristics of reflux segmentation dataset in reflux area.

Characteristic	Internal dataset (CMUSJHX)	External test 1 (CMUSJSB)	External test 2 (CMUSJNH)	P_value
Dynamic angiograms	21062	3862	54026	..
No.of DSA videos	1269	90	782	..
No.of patients	273	41	367	..
Age (y) [†]	61±10.6	60±11.4	62±9.9	<0.001*
Male patients	199 (72.9)	33 (80.5)	281 (76.6)	<0.001**
Body mass index [†]	23.5±4.4	23.5±3.1	24.1±3.2	<0.001*
Child-pugh	..	..	..	..
A	231 (84.6)	26 (63.4)	324 (88.3)	..
B	37 (13.5)	15 (36.6)	39 (10.7)	..
C	5 (1.9)	0	4 (1)	..
Manufacturer	..	..	..	..
Siemens	112	0	245	..
Philips	161	39	2	..
Neusoft	0	2	0	..
Shimadzu	0	0	120	..
Reflux frame ratio(%) [†]	42.2±55.9	22.8±16.9	35.6±27.1	<0.001*
DSA Video FPS [†]	14.7±1.7	14.8±1.1	11±3.1	<0.001*

Note: Data in parentheses are percentages. Body mass index is calculated as weight in kilograms divided by height in meters squared. The reflux frame ratio is the number of frames with reflux in DSA video divided by the total number of frames.

*The three datasets were compared using the analysis of variance test.

**The three datasets were compared using chi square test

“..”indicates not applicable.

†Data are means ± SDs.

reflux events. Correspondingly, model predictions in these scenarios were generally of lower confidence and did not meet the predefined criteria for clearly visible reflux.

Table S8 further illustrates the feasibility of multi-platform deployment using data from external cohort 1. Under high-performance GPU conditions, the model achieved 29.26 FPS and an AUC of 91.42%, providing strong support for real-time inference. Even under computationally constrained conditions, the system maintained robust performance: the CPU and embedded development board (NVIDIA Jetson Orin Nano) achieved 11.62 FPS / 9.38 FPS and AUCs of 91.62% / 91.42%, respectively—demonstrating the model's adaptability and efficiency across varying hardware configurations.

Hardware response characteristics

In the in vitro vascular simulation system, glycerol, silicone oil, and 300 μm microspheres were proportionally mixed to simulate Lipiodol, Iodine contrast agent, and Microsphere suspensions, respectively, with the addition of organic dyes to facilitate direct visualization of the fluid injection process (Figure S5). Under identical conditions, the drug delivery performance of the intelligent injection device (Figure 5A) was compared with that of two interventional operators—Operator A (Y.X.) and Operator B (Y.L.) (Figure 5B)—for the three simulated drug types (Iodine contrast agent, Lipiodol, and Microspheres).

The results indicated that the stability of manual injection was significantly influenced by the physical properties of the injected fluid. Under Lipiodol conditions, Operator A exhibited an injection rate fluctuation of 0.066 mL/s with a maximum cumulative dose error of 0.199 mL, whereas Operator B achieved lower variability (maximum error = 0.056 mL, rate fluctuation = 0.08 mL/s) but still demonstrated intermittent instability with a range [E] close to 0.2 mL (Figure 5C). Under Iodine contrast agent conditions, Operator A displayed the largest fluctuations, with an injection rate variation of

0.24 mL/s, a maximum cumulative dose error of 0.616 mL, a fluctuation range (range [E]) of 0.616 mL, and an RMSE of 0.436 mL. Operator B performed more stably, showing an injection rate fluctuation of 0.16 mL/s, a maximum cumulative error of 0.187 mL, a range [E] of 0.222 mL, and an RMSE of 0.132 mL (Figure 5D). During Microsphere injection, Operator A's injection rate fluctuated up to 0.28 mL/s, yet the dose error remained the lowest among the three drug conditions (maximum cumulative dose error = 0.123 mL, range [E] = 0.123 mL, RMSE = 0.075 mL). In contrast, Operator B demonstrated pronounced irregularity, with both the maximum error and range [E] reaching 0.305 mL and an RMSE as high as 0.196 mL (Figure 5E).

In comparison, the intelligent injection device maintained a nearly constant injection rate of 0.04 mL/s across all three drug conditions, with the cumulative error consistently within 0.02 mL, effectively representing bias-free output (Table S9).

In vivo validation of AI-FlowTACE

Through the integration of TCP/IP protocol and DVI signal conversion, we achieved an organic combination of data communication, AI processing, and automated control, successfully deploying an efficient closed-loop intelligent drug delivery system. In reflux detection tests conducted within rabbit hepatic vasculature, AI-FlowTACE demonstrated excellent performance (Figure 6A), achieving an AUC of 94.68% and Precision of 66.5%; in left renal artery conditions, the model reached AUC 91.71% and Precision 98.6%; and in the left gastric artery, an AUC of 85.81% and Precision of 76.3%, with corresponding drug adjustment response times of 0.83s, 0.7s, and 0.82s, respectively (measured as the interval from reflux detection to injector adjustment initiation). Additional performance metrics are provided in Table S10. Regarding injection performance, the hardware device operated stably in vivo, with smooth and consistent gear-shift curves (Figure 6B), confirming its reliable performance across various conditions. Supplemental Materials VideoS3

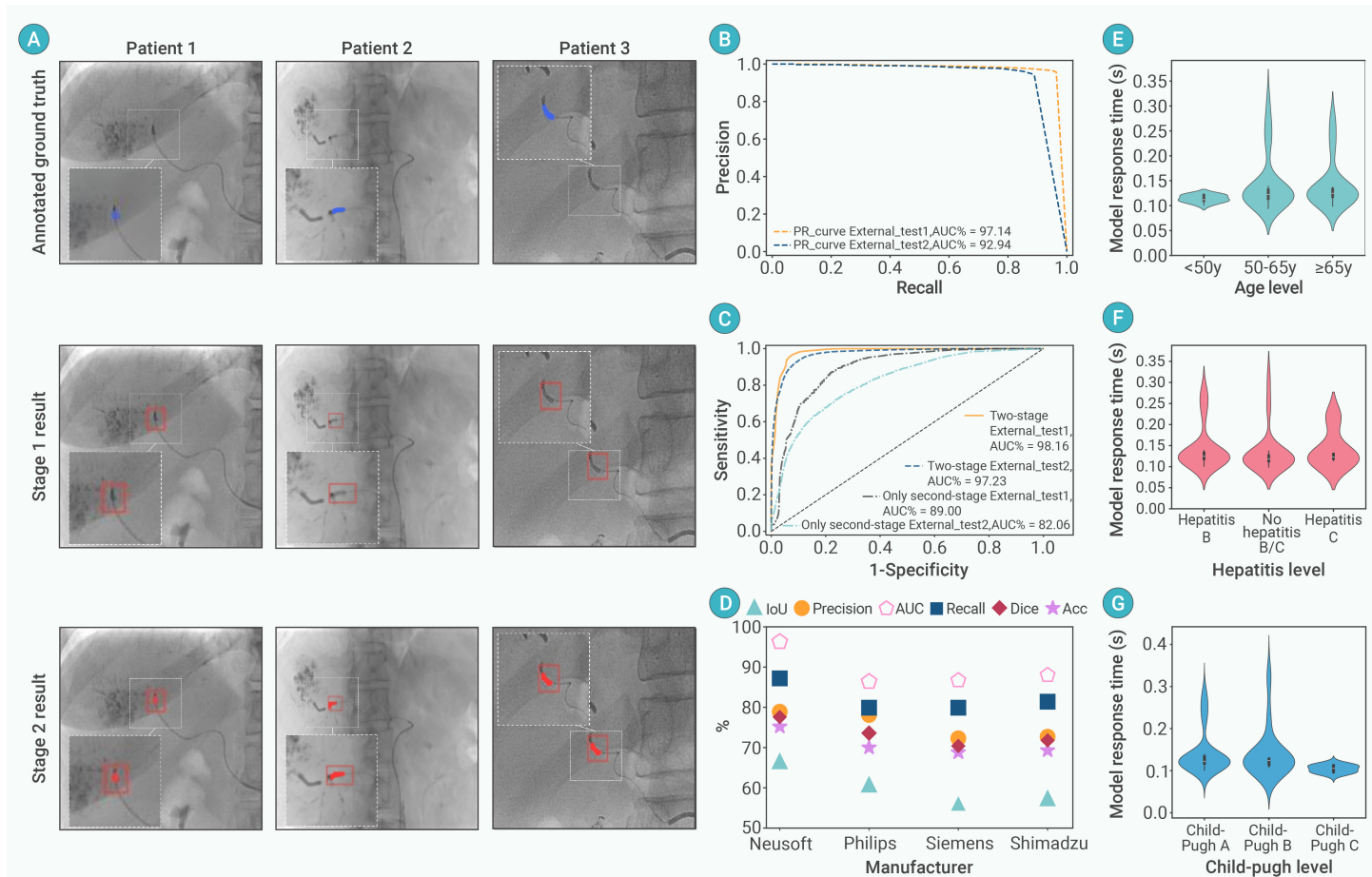


Figure 4. Multi level evaluation system for segmentation performance of two-stage model architecture (A) The first panel displays the true background of the annotations, with darker blue indicating a clear reference for abnormal reflux. The second panel displays the red detection boxes generated in the first stage of the model architecture. The third panel displays the output of the second stage of the model architecture, which segmented the backflow within the detection box generated in the first stage. Patient 1-3 demonstrated the accurate extraction of abnormal reflux drugs using DL models in female patients aged 59 with hepatitis C-related liver cancer (Child Pugh score 6, grade A, lesion located in segment S4 of the liver), male patients aged 37 without hepatitis (Child Pugh score 8, grade B, segment S5 of the liver), and male patients aged 46 with hepatitis B-related cancer (Child Pugh score A, tumor located in segment S4 of the left lobe of the liver). (B) For the localization of the first stage reflux area, the model architecture is based on the detection PR curves of external test 1 and external test 2. (C) Comparison of Receiver Operating Characteristic (ROC) curves between the two-stage segmentation network and the segmentation network with only the second stage in external tests 1 and 2. (D) The dot plot shows the performance of two-stage DL networks under four different scanner manufacturers, ACC=Accuracy, Dice=Dice coefficient. (E-G) Comparative analysis of the response time (identification of reflux feedback mechanism judgment issuance of medication adjustment rate instructions) of the model architecture for two external test queues distributed in Age, Hepatitis, and Child-pugh levels.

include a visualization video of segmentation in the animal model. The device's feedback performance was also fully validated in real-time in vivo drug delivery: it automatically adjusted injection schemes based on model feedback signals and achieved an average reaction time of 0.7 s. Experimental videos ([Supplemental Materials VideoS4](#)) demonstrate how the injector dynamically switches gears according to reflux changes during different feedback windows.

Furthermore, in porcine experiments simulating human-like vascular anatomy, AI-FlowTACE again exhibited strong reflux recognition performance (Figure 6C), achieving an AUC of 93.03%, Precision of 93.7%, and a drug adjustment response time of only 0.8s (Table S10). During hepatic arterial administration of Lipiodol, Iodine contrast agent, and Microspheres, the system maintained stable injection performance (Figure 6D). Using the DVI-based data transfer strategy (Figure 6E), the system successfully completed the recognition-decision-execution closed-loop drug delivery workflow. The delivery system operated entirely in a third-party monitoring mode, ensuring no interference with existing clinical procedures. Once surgery began, the AI processing module automatically identified key frames of the drug delivery process and dynamically overlaid prediction results onto the video stream.

To further integrate the delivery system into real-time surgical workflows, we developed a graphical user interface (GUI) application based on PySide6 (Qt6 framework), providing automated image analysis and interactive user control. Figure 6F illustrates the workflow of the Windows-based GUI application, named "TACE Automatic Drug Delivery Assistance Recognition Program." The software was deployed on a standardized workstation

equipped with an Intel® Core™ i5 3.7 GHz CPU and an NVIDIA GeForce RTX 4060 Ti GPU. Live video streams served as input to the AI model for intelligent image analysis, with prediction outputs visualized through the interactive interface.

Intraoperative man-machine delivery simulation results

As shown in Figure 7A, time-injection dose curves for each patient revealed that all operators exhibited delayed responses or failed to adjust injection behavior promptly. The slope differences before and after the intersection points on the curves indicate reflux events where operators did not reduce the injection rate. Notably, the less experienced Operator A (Y.X.) failed to adjust during eight reflux incidents across two TACE procedures, whereas the more experienced operators—Operator B (Y.L.) and Operator C (H.W.)—had only three such instances. Operator C experienced two missed adjustments in the first case, but this number decreased to one in the second.

A comparative analysis of human-machine drug delivery rates revealed that AI-FlowTACE consistently achieved higher uniformity and stability (injection rate SD = 0.003) compared with manual injection, which exhibited substantial fluctuations (SD = 0.057). The variability was especially pronounced for the less experienced Operator A, whose injection rate showed the greatest instability (SD = 0.072) and poor procedural continuity (Figure 7B). Meanwhile, AI-FlowTACE demonstrated timely rate adjustments after reflux events, achieving an average response time of 0.78 s (Figure 7C). The senior operator, Operator C, also showed a short and stable adjustment

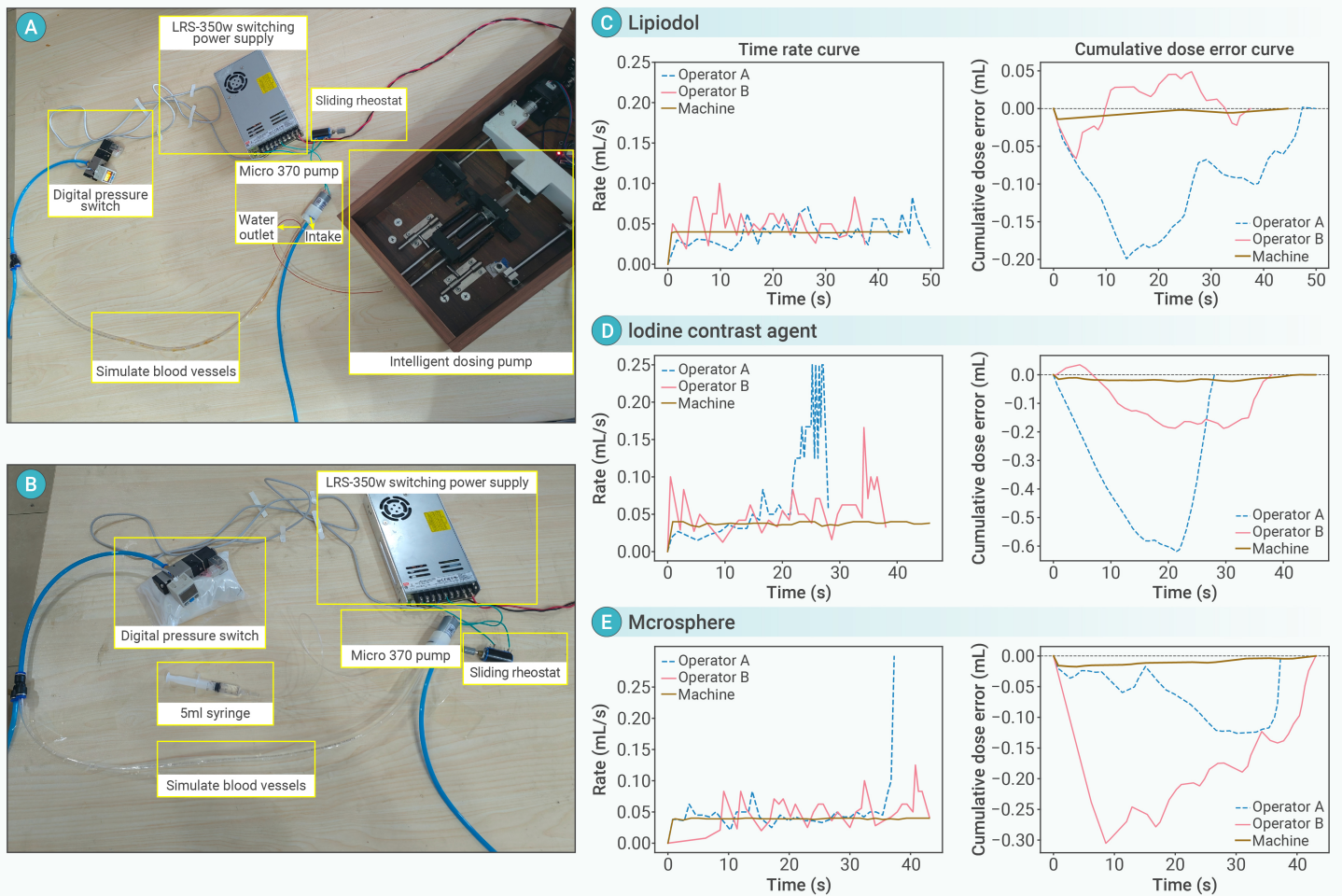


Figure 5. Human machine injection performance in in vitro simulated vascular simulation model (A) The testing scenario of intelligent injection device in an in vitro fluid simulation system. (B) The evaluation scenario for manual injection involves manually pushing a 5ml syringe. (C-E) Under different simulated drug conditions (Lipiodol, iodine contrast agent, Microsphere), the performance of the intelligent device and two surgeons' push injection was evaluated. The left column shows the injection time rate curve, which shows significant rate fluctuations and staged fluctuations during manual injection (Operator A: 0.068 ± 0.061 mL/s, Operator B: 0.053 ± 0.025 mL/s), while the intelligent device maintains a nearly constant target rate (0.038 ± 0.002 mL/s) in all three types of drugs; The right column shows the cumulative dose error curve for iodine contrast agent (Operator A has a maximum instantaneous error of 0.616 mL and RMSE of 0.436 mL; Operator B has a maximum instantaneous error of 0.187 mL and RMSE of 0.132 mL); Lipiodol (Operator A has a maximum instantaneous error of 0.199 mL and an RMSE of 0.436 mL; Operator B has a maximum instantaneous error of 0.056 mL and an RMSE of 0.031 mL); Microsphere (Operator A has a maximum instantaneous error of 0.123 mL and an RMSE of 0.075 mL; Operator B has a maximum instantaneous error of 0.305 mL and an RMSE of 0.196 mL), while the intelligent device always controls the cumulative error within 0.02 mL, exhibiting almost zero deviation output.

response time (0.94 ± 0.35 s), indicating the ability to promptly regulate injection flow, whereas Operator A and Operator B displayed slower reactions, particularly Operator A (1.1 ± 0.36 s). Adjusting for repeated measurements and within-case variability using a linear mixed-effects model, overall manual operation exhibited a statistically significant response delay of 0.23 seconds compared with the AI-FlowTACE system (95% CI: 0.12–0.34; $P < 0.001$) (Table S11).

Further analysis of intraoperative injection rates in six patients (Figure 7D) showed that AI-FlowTACE maintained low coefficients of variation, ranging from 0.19 to 0.28, reflecting high consistency and controllability. In contrast, manual injection showed marked variability, with coefficients ranging from 0.94 to 1.69—particularly in Operator A's group, which reached 1.69, indicating that manual delivery is highly susceptible to operator experience and environmental factors, making stable control difficult to achieve.

Importantly, under an average total radiation dose of $3.71 \mu\text{Sv}$ during the TACE procedure, the drug delivery phase alone accounted for approximately $0.66 \mu\text{Sv}$ (Figure 7E). This implies that replacing manual injection with AI-FlowTACE could eliminate approximately 20% of additional radiation exposure, translating into a substantial clinical safety benefit by reducing radiation burden on interventional radiologists.

DISCUSSION

The embolization efficacy of TACE has long been constrained by human

factors.^{37,38} Under video-guided procedures, physicians often struggle to promptly detect reflux on DSA images and make precise adjustments, due to limitations in individual recognition speed and reaction time. Furthermore, when embolic agents exhibit high viscosity, manual injection becomes labor-intensive and difficult to maintain at a stable rate. In addition, interventional radiologists face potential safety risks from radiation exposure. To address these challenges, we integrated deep learning-based image analysis with automated control technology to achieve real-time reflux recognition and stable flow regulation during drug delivery, thereby establishing a fully AI-coordinated closed-loop system that enables partial automation of TACE and reduces intraoperative radiation exposure. AI-FlowTACE has been validated across three experimental platforms—an in vitro simulated vascular model, in vivo animal experiments, and real-world simulated clinical studies—demonstrating strong clinical translational potential as an intelligent alternative to manual drug delivery.

Reflux recognition remains one of the most challenging aspects of the TACE drug delivery process.^{39,40} Due to the small droplet volume and poor contrast under DSA imaging, operators often struggle to detect reflux signals in a timely manner—particularly during the early onset of reflux or under unstable injection conditions, when the signals are weak and difficult to discern within a short period. Moreover, during the injection of high-viscosity agents (such as Lipiodol), drug flow becomes sluggish, and the resulting reflux images appear blurred and indistinct, causing operators to frequently

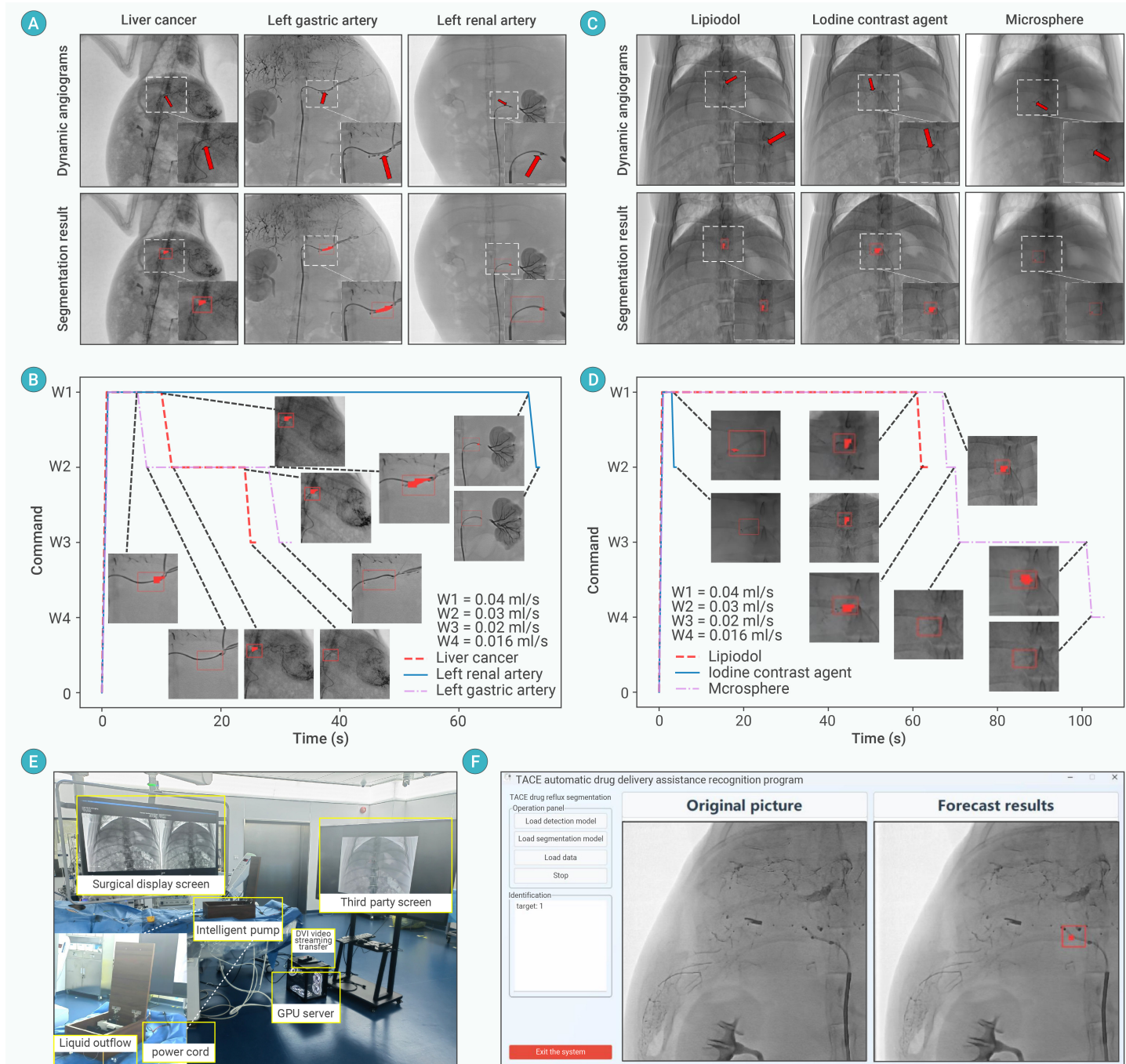


Figure 6. In vivo environment validation of AI FlowTACE (A) Visualization verification of intubation images of liver cancer blood supply artery, left gastric artery, and left renal artery in rabbits, with each example containing the original image and the model output reflux segmentation image. (B) In the three site administration experiment of the rabbit model, the gear change curve of the injection device was observed. (C) Visual validation of iodine oil, iodine contrast agent, and microsphere administration was performed on the hepatic artery of a pig model. (D) The gear change curve of the automatic delivery of three types of drugs by the injection device in the human like dissection experiment of pigs. (E) In the pig experiment, the DVI switching strategy was applied, and the system fully implemented the closed-loop process of recognition decision execution, successfully completing the entire process of drug delivery and real-time feedback adjustment. (F) The supporting graphical user interface (GUI) application is developed on the Windows platform based on PySide6, which receives real-time video streams and performs image analysis. The image recognition effects in the figure correspond to the red rectangular box for locating and detecting the reflux area, and the red mask for the reflux segmentation within the reflux area.

miss the early signs of reflux.^{41–44} At the same time, transient physiological reflux events—which occasionally occur during TACE—can trigger excessive operator alertness, even though clinically significant reflux typically lasts several seconds. Such overreactions may disrupt the operator's judgment and procedural continuity.^{45–48} Even when reflux is recognized, delayed human response still poses a potential risk of nontarget embolization. Given that the response time of humans to complex dynamic visual stimuli (recognizing reflux on DSA) and subsequent physical movements (adjusting / stopping injections) is typically between 1 and 2 seconds (even experienced interventional physicians), and is highly susceptible to physician fatigue and expe-

rience levels. AI FlowTACE addresses these challenges by continuously tracking and real-time analyzing imaging signals, achieving AUCs of 97.14% and 92.94% under the PR curve on an external dataset, and shortening the overall drug adjustment response time to 0.78 seconds. In addition, in clinical practice, although reflux may occur rapidly, the accumulation of hemodynamic resistance before severe non targeted reflux usually occurs within one or more cardiac cycles. Our 0.33s sampling window is frequent enough to intervene when the reflux signal lasts for three consecutive frames, enabling it to distinguish between transient physiological reflux and persistent pathological reflux, effectively capturing these reflux precursors while ensuring safe

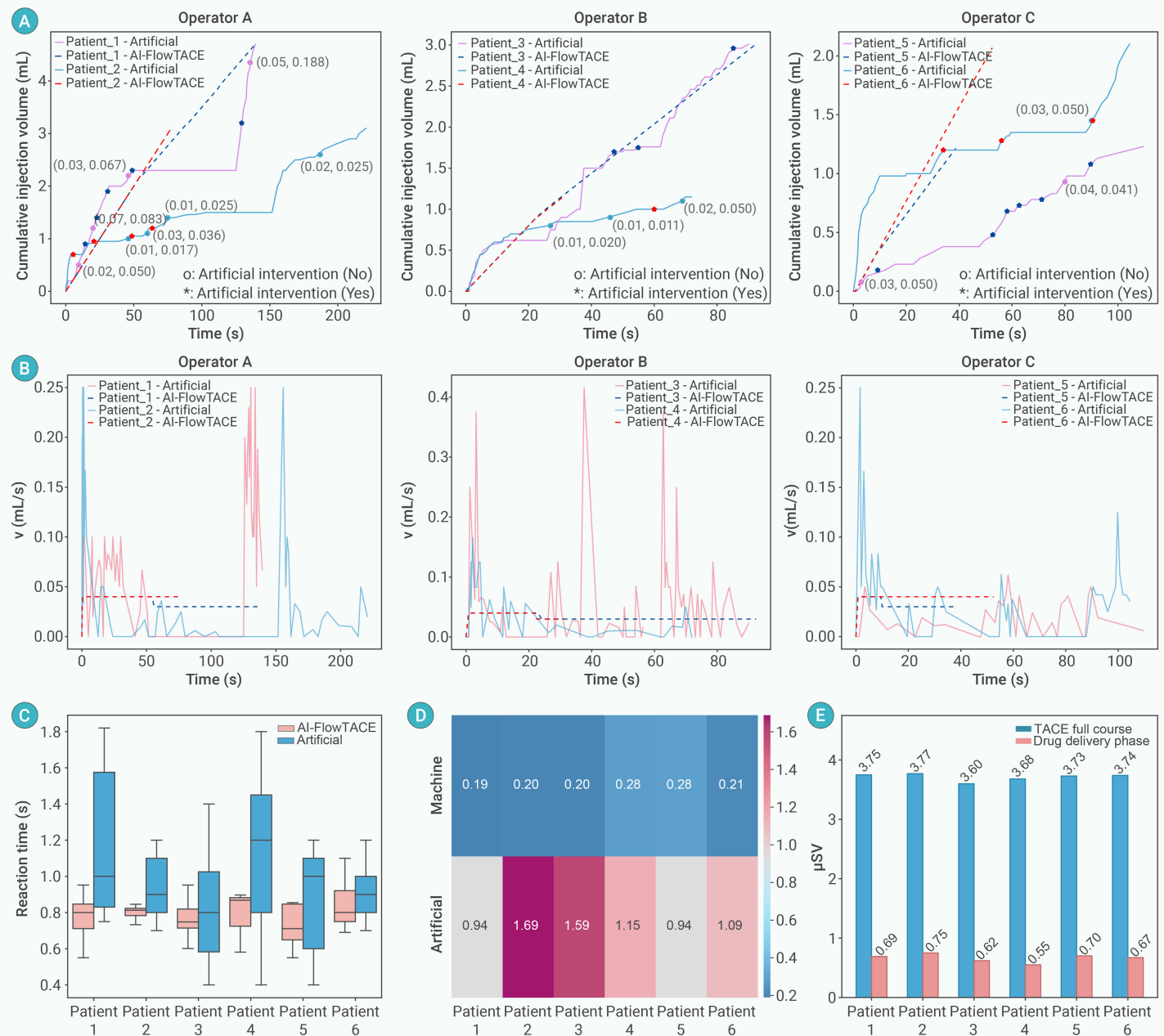


Figure 7. Comparative performance of human-machine drug delivery simulation in real surgery (A) Three operators (Operator A; Operator B; Operator C) presented the time injection dose curves for their respective patients, with parentheses ("o") at the intersection representing the slope change (rate) of the curve, indicating that no corresponding changes in medication behavior were made. "o" The surgeon here intervened in the reflux. (B) Comparison between the injection time rate curves of three surgeons for their respective patients and the simulated administration curves of the intelligent drug delivery system. Comparison between the injection time rate curves of three surgeons for their respective patients and the simulated administration curves of the intelligent drug delivery system. (C) Comparison of intraoperative administration time and system response time of AI FlowTACE administration in 6 patients. (D) Thermogram of the coefficient of variation of the rate of artificial and machine administration. (E) The radiation dose administered throughout the 6 surgical procedures was compared with the radiation dose during the administration phase.

and stable mechanical drive.

During manual operation, the injection process often becomes a struggle between resistance and inertia. High-viscosity embolic agents such as Lipiodol tend to cause jerky and unstable flow, while low-viscosity Microsphere suspensions can easily accelerate uncontrollably.^{49–51} The differing rheological properties of these agents significantly affect the stability of manual injection, leading to local hemodynamic disturbances that increase the risk of nontarget embolization and contribute to uncertainty in embolization efficacy—all of which may compromise patient outcomes.^{52–55} Among the three simulated embolic agents, both interventional operators exhibited noticeable fluctuations in injection stability, particularly with high-viscosity Iodine contrast agent analogs, where injection rate variations reached 0.24 mL/s and 0.16 mL/s, respectively. Even the more experienced Operator B could not fully eliminate dosing deviations, with an error range approaching 0.2 mL. In

contrast, when injecting the lower-viscosity microsphere analog, the less experienced Operator A managed to limit dose fluctuations to approximately 0.1 mL. By comparison, AI-FlowTACE maintained a consistent injection rate of 0.04 mL/s across all viscosity conditions, with the cumulative dose error range (range [E]) consistently kept within 0.02 mL, reflecting near-perfect delivery precision. This superior stability arises from two key factors:

(1) AI-FlowTACE receives real-time feedback from DSA image monitoring on a per-second scale rather than relying on pressure sensing, thereby eliminating human-induced dose variability and acceleration loss caused by differences in embolic agent viscosity; and (2) the high-precision motor-driven mechanism, equipped with a linear rail and bearing system, ensures that the syringe plunger moves smoothly along a straight trajectory, maintaining stable and accurate drug delivery throughout the procedure.

At present, most commercial automatic syringes used in the fields of inter-

vention and radiology are open-loop systems. They deliver liquids at a predetermined fixed rate without the need for real-time hemodynamic feedback and with a large range of dose errors.^{11,56–59} In the dynamic environment of TACE, as the embolization endpoint approaches, vascular resistance increases unpredictably. Due to the inability of standard open-loop syringes to visually or hemodynamically identify impending reflux, if doctors do not manually discontinue them in a timely manner, they have a high risk of non-targeted embolism.⁶⁰ To bridge this critical technological gap, our AI-FlowTACE system introduces a closed-loop paradigm tailored specifically for the complex hemodynamics of TACE. By integrating real-time visual feedback, our system achieved a rapid adjustment response time of approximately 0.78 seconds. In addition, unlike traditional systems that struggle to handle different fluid viscosities, AI-FlowTACE dynamically compensates for resistance. It maintains a highly stable injection rate of 0.04 mL/s and strictly limits the cumulative dose error to within 0.02 mL, even when dispensing high viscosity drugs such as iodized oil. In clinical practice, this autonomous adaptation provides significant advantages by actively preventing reflux and standardizing precise drug delivery.

In the rabbit model of liver tumors, structural changes in liver blood vessels may occur due to tumor growth, leading to vascular stenosis and reduced blood flow velocity, which can easily cause reflux. Under such circumstances, achieving stable and consistent injection is crucial to ensure drug delivery accuracy and efficiency; therefore, we first performed sensitivity testing of the AI-FlowTACE system in this setting.^{61–63} Building on these results, we extended validation to vascular environments with different hemodynamic characteristics. The renal artery, originating from the abdominal aorta, functions as a major filtration vessel with a dense capillary network and large branches.⁶⁴ In contrast, the left gastric artery has a finer diameter and a more complex branching pattern, with blood flow often influenced by gastric wall contractions. Accordingly, we simulated two distinct hemodynamic conditions: one with high flow velocity and low pressure, and another with low flow velocity, low pressure, and high pulsatility.⁶⁵ Under these respective conditions, AI-FlowTACE achieved AUCs of 91.71% and 85.81% and Precisions of 98.6% and 76.3%. These results were obtained without additional model fine-tuning, demonstrating that the machine vision module not only maintains high accuracy but also exhibits strong cross-scenario robustness and background-independent detection capability.

Although differences in morphology exist between humans and pigs, their hepatic segmental anatomy is highly consistent, and pigs can be operated on using clinical-grade DSA systems. Therefore, the porcine model is widely recognized as the gold standard for validating surgical procedures.^{66,67} In this physiologically relevant environment—closely resembling human hemodynamics and anatomy—AI-FlowTACE successfully completed the entire operational process, achieving accurate embolization endpoint identification (AUC = 93.03%) and a rapid drug adjustment response time of 0.8 s, comparable to that observed in simulated settings. Furthermore, results from real intraoperative simulations revealed that, even though interventional radiologists remain highly focused and strive for precise, consistent injections under complex clinical conditions, delayed adjustments still occurred when reflux was subtle or rapidly developing—even among experienced operators. In contrast, AI-FlowTACE, leveraging a real-time image-driven deep learning algorithm, autonomously identified reflux and performed closed-loop flow rate adjustments, surpassing the limits of human reaction speed. This automation significantly shortened injection duration and reduced radiation exposure by approximately 20%, translating into a substantial clinical safety benefit through decreased radiation burden on interventional radiologists. However, it should be noted that the initial stage of surgery (including microcatheter navigation and precise placement) still requires manual, bedside operations. Therefore, although the system greatly reduces the cumulative radiation dose for surgeons, it does not completely eliminate the exposure of the entire surgery. In addition, although patients are inevitably exposed to radiation during any fluoroscopy guided interventional therapy, AI FlowTACE provides secondary radiation benefits. Its accurate adaptive dosing mechanism minimizes the time for doctors to manually adjust repeatedly, which in turn reduces the total fluoroscopy time and indirectly lowers the overall radiation burden on patients.

This study demonstrated excellent injection performance of AI-FlowTACE

across multiple species models and intraoperative simulations. It should be emphasized that AI-FlowTACE is fundamentally designed as an active control system with independent decision-making and mechanical execution capabilities, rather than a passive monitoring or alarm device that relies on human operators. In our *in vivo* animal experiments, the system successfully achieved fully automated closed-loop drug delivery without any human intervention. Although our current clinical validation using human data is still indirect. Since AI FlowTACE is an autonomous actuator rather than a simple diagnostic aid, applying its active control capability directly to human patients requires rigorous prospective clinical trials and strict ethics committee approval, which is beyond the scope of this preliminary translational study. Therefore, current human data assessment is an important and secure engineering concept validation. Future research will focus on exploring these necessary ethical and regulatory approaches. Secondly, due to the lack of reliable foundational facts, vague or unclear reflux events were not included in the preliminary analysis. This exclusion may introduce a certain degree of selection bias and may lead to overestimation of model performance. However, our exploratory evaluation of representative fuzzy cases suggests that these signals are typically short-lived, weak, and not temporarily persistent, making them unlikely to be clinically feasible or affect treatment decisions. Therefore, their impact on the overall clinical utility of the model is expected to be limited. Another limitation is the inherent subjectivity in visually assessing reflux on 2D DSA images, despite using inter-observer consensus and Kappa coefficients. To provide a more objective benchmark, future studies will incorporate precise quantitative validations, such as *in vitro* phantom experiments. Given the high risk of endovascular intervention therapy, the interventional physician must retain the ultimate authority over the procedure. In the event of unexpected clinical events, it is crucial to integrate a manually controlled fail safe mechanism. However, certain limitations remain under specific conditions. In particular, under special physiological states such as arteriosclerosis, hypotension, or high-flow hemodynamics,^{68,69} drug flow within vessels may exhibit nonlinear patterns, requiring operators to perform intermittent injections and observe physiological responses. These nonstandard scenarios fall beyond the current scope of system validation, and the delivery performance of AI-FlowTACE under such conditions remains uncertain. Although AI-FlowTACE has shown high adaptability in DSA imaging involving conventional contrast agents and embolic materials, novel therapeutic agents may display distinct flow dynamics and imaging characteristics in future clinical practice,^{70,71} potentially posing new challenges to the system's continuous monitoring capability. This will necessitate real-time updates and optimization of the AI-FlowTACE perception module. In resource-limited settings—such as mobile medical units or primary surgical environments—the system must not only maintain high operational efficiency but also offer enhanced portability.^{72,73} This requires the intelligent module to be based on a low-power, compact computational architecture design.⁷⁴ Ensuring that AI-FlowTACE continues to operate stably and reliably in such constrained environments will be a crucial focus of future research. And the sample size for the operator and equipment validation phase is relatively limited, involving only 3 surgeons and 6 surgeries. In the future, larger scale, multi center interventional radiologist cohorts need to be involved for validation to further confirm the universality of our system's advantages over manual operation.

By integrating algorithmic intelligence with hardware innovation, this study developed AI-FlowTACE, an automated drug delivery system that combines sensitive perception with stable injection control, demonstrating the feasibility of intelligent closed-loop drug delivery. In the next step of our work, we plan to conduct Phase I/II prospective, multicenter, randomized controlled trials (RCTs) to compare AI FlowTACE assisted surgery with traditional manual TACE. The main endpoints of the trial will focus on safety and surgical efficiency, specifically assessing the incidence of adverse events (such as non-targeted embolism or reflux), total surgical time, and reduction in operator radiation dose. The secondary endpoint will evaluate clinical efficacy, including technical success rate and objective tumor response. To ensure absolute patient safety, the trial design will incorporate strict stopping rules, independent data, and continuous monitoring by the Safety Monitoring Board (DSMB), as well as mandatory integration of the aforementioned manual one button emergency stop function during all AI assisted injections

CONCLUSION

According to our research findings, the AI FlowTACE system has successfully overcome the key limitations of traditional manual injection and existing mechanical injection systems in hepatic artery chemoembolization through adaptive, stable, and precise drug delivery control. Therefore, this system has enormous clinical potential, especially in the field of interventional oncology. It can serve as the core tool for the next generation of automated image-guided drug delivery systems, providing a more precise, safe, and efficient treatment plan for clinical practice.

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AUTHOR CONTRIBUTIONS

M.N. and H.W. conceptualized, designed, and supervised this study. T.D., Y.X. and Y.W. are responsible for the development, validation, and analysis of model architecture, as well as the construction and debugging of hardware. Y.Y. and Y.L. provide support and assistance for the conduct of animal experiments. Y.H., X.X. and B.F. are responsible for clinical deployment and establishing network communication. M.N., H.W., T.D., C.L., B.F. provided support for the analysis and participated in the discussion of the results. Y.X., T.D. and C.L. wrote the initial draft of the paper and obtained and verified the basic data reported in the paper. All authors had full access to all the data in the study and accept the responsibility to submit it for publication. All authors read and approved the final version of the manuscript.

DECLARATION OF INTERESTS

Y.H., X.X., and B.F. are employees of Neusoft Medical Systems Co., a company that may have a commercial interest in the results of this research and technology. The other authors declare no conflicts of interest.

ETHICAL STATEMENT AND PATIENT CONSENT

This study was approved by the Institutional Ethics Committee of Shengjing Hospital affiliated with China Medical University. For the retrospective analysis of clinical images, the committee granted approval and officially waived the requirement for written informed consent because the data were collected retrospectively from routine clinical practice (Ethics Approval No. 2024PS1227K). Furthermore, all animal experiments were approved by the same committee (Ethics Approval No. 2024PS1354K) and were conducted in strict accordance with relevant guidelines and regulations for the care and use of laboratory animals.

DATA AND CODE AVAILABILITY

The DSA image data reported in this study cannot be deposited in a public repository because they contain sensitive information that could compromise patient privacy. Deidentified patient-level clinical and outcome data will be provided upon reasonable request. In addition, summary statistics describing these data have been deposited at supplementary tables and are publicly available as of the date of publication. Source code for the deep learning model is available at: <https://github.com/xiongyin666/AI-FlowTACE>. Any additional information required to reanalyze the data reported in this work paper is available from the lead contact upon request.

SUPPLEMENTAL INFORMATION

It can be found online at <https://doi.org/10.59717/j.xinn-oncol.2026.100009>