IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 23, Issue 11 Ser. 7 (November. 2024), PP 37-42
www.iosrjournals.org

In-Vitro Model-Based Performance Testing Of A Self-Expanding Clot Retrieval Device

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Abstract
The Clot Retrieval Device is designed to restore blood flow in patients suffering from acute ischemic stroke by effectively removing thrombus in neuro vasculature. This research article presents an in-vitro simulation test methodology aimed at evaluating the performance, safety, and efficiency of this thrombectomy device. The simulation replicates clinical conditions, offering insights into device performance before clinical application. The device's self-expanding mesh structure, designed with giant-baby cells, has demonstrated superior thrombus retrieval efficiency while minimizing damage to vascular tissue. The test methodology involves creating blood clot analogs that mimic human thrombi, followed by testing the device's retrieval efficacy under controlled simulated conditions. Research results indicate that the device demonstrates high retrieval success rates, contributing to improved clinical outcomes for stroke patients.

Keywords: *Clot Retrieval Device, Acute Ischemic Stroke, In-vitro Simulation, Thrombus, Neurovasculature, Thrombectomy, Giant-baby cells and Thromboss Retrieval*

Date of Submission: 15-11-2024 Date of Acceptance: 25-11-2024

I. Introduction

One of the primary causes of morbidity and mortality worldwide is cerebrovascular illness, especially ischemic stroke (Hameed, 2017). When the blood arteries in the brain thin or obstruct, an ischemic stroke happens. The goal of the Clot Retrieval Device is to improve patient safety and clot removal methods. By using the Clot Retrieval device to remove thrombus, blood flow in the neuro-vasculature is restored (Liu, 2023).

Before any clinical application, the development of in-vitro simulations are essential for imposing the performance of such device's in controlled environment. The creation of in-vitro simulations is necessary to force the operation of such devices in a controlled setting prior to any clinical application. An in-vitro simulation test for the Clot Retrieval device is described in this article. When there is a blockage that prevents blood flow to the brain, an ischemic stroke happens (Campbell, 2022). An ischemic stroke might result in irreversible brain damage or even death if blood flow doesn't return promptly enough. The self-expanding mesh structure of the Clot Retrieval device allows it to efficiently engage and remove clots from the neurovasculature (Fitzgerald, 2021). Prior to clinical application, an in-vitro simulation test methodology is required to evaluate its performance under controlled conditions.

II. Literature Review

Acute ischemic stroke is the leading cause of death worldwide. In order to overcome this, clot retrieval device particularly stent was developed focusing on advancements and trends in their design and clinical application in managing acute ischemic strokes (Aamir Hameed, 2017).

Recently Mechanical thrombectomy is one of the most important method used to treat acute ischemic stroke for large vessel occlusion. Prior to clinical application, in-vitro simulation test methodology has become common and convenient method for mechanical thrombectomy research. This simulations helps researchers to assess device performance in controlled condition before clinical application, thereby enhancing the predictive accuracy of preclinical studies (LiuR, 2023). Stent retrievers are novel endovascular devices that provide vessel recanalization through thrombus retrieval mechanical thrombectomy (Marmagkiolis, 2015).

The importance of mechanical thrombectomy in acute ischemic stroke, marking a significant shift towards interventional approaches in stroke management was depicted. This study laid the foundation for device developers to focus on optimizing the clot retrieval process, aiming to enhance first-pass success rates and reduce complications (Elgendy, 2015).

In addition, the critical role of fluid dynamics in testing neurovascular device has been depicted by several studies (Perrira, 2022). The use of anatomically accurate models along with blood-mimicking fluids like

saline solution allows researchers to simulate different clot types and vessel geometries, providing crucial insights into device performance under varied conditions.

This device differs as it consists of unique giant-baby cell design that promises enhanced clot engagement and removal efficiency. Literature on in-vitro models emphasizes the importance of such simulations in predicting device performance while minimizing the need for early animal testing.

III. Material Method

The in-vitro simulation model of a Neurovasculature was designed to replicate the neurovascular environment where the Clot Retrieval device is deployed. The test setup included:

- **Clot replica**: Artificial thrombus created with biocompatible materials, replicating clot consistency.
- **Fluid dynamics**: Used saline solution with viscosity similar to blood flow.
- **Device deployment**: Clot retrieval device designed as self-expanding stents with a mesh structure that captures and traps the blood clot was deployed into the simulation model where artificial clot was formed, and once in position, it was expanded to engage the clot. The entire system was than withdrawn, bringing the trapped clot along with it.

Key Device Specifications

- **Material**: Superelastic Nitinol tube
- **Radiopaque Markers**: Pt/Ir coil markers
- **Device Design**: Stratified mesh with giant-baby cells
- **Delivery Wire**: Nitinol tapered wire with PTFE coating
- **Sheath Length**: 650 - 750 mm

The in-vitro simulation test for the Clot Retrieval Device involves replicating conditions within human vasculature to evaluate the device's performance in clot retrieval. Here's a structured approach to conducting this simulation:

1. Setup of the Simulation Environment

- **Material**: The model was typically made of silicone materials to replicate the compliance and mechanical properties of human blood vessels.
- **Geometry**: The vascular model had anatomically accurate dimensions, including bifurcations and tortuous pathways, to simulate realistic conditions.

2. Preparation of the Clot

- **Clot Composition**: Synthetic clot was created to simulate human thrombi. These vary in composition to test the device under different clot types.
- **Clot Placement**: The clot was placed in a specific location within the vascular model, typically where an occlusion would occur in a stroke patient.

3. Flow Simulation

- **Blood-Mimicking Fluid**: A blood analog fluid with similar viscosity and flow characteristics was circulated through the vascular model. This helps in assessing how the device performs in conditions mimicking in vivo blood flow.
- **Flow Rate**: The flow rate was controlled to match physiological conditions of the cerebral arteries.

4. Introduction of the Device

a. Device Deployment Preparation

- **Accessing the Vascular Model**: A microcatheter system, typically guided by a steerable guidewire, was introduced into the simulated vascular environment. The catheter was carefully advanced to navigate through the tortuous pathways of the vascular model, just as it would in a human patient.

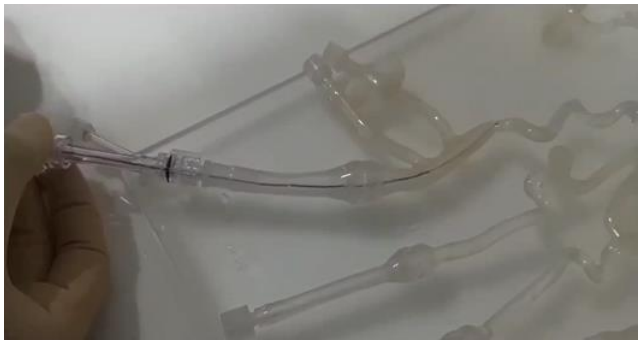

Figure 1: Insertion of guidewire and catheter at desired position

- **Positioning**: The operator carefully positioned the microcatheter tip just proximal (upstream) to the location of the clot in the vascular model. The guidewire was than withdrawn, leaving the microcatheter in place, ready for device deployment.

b. Clot Retrieval Device Introduction

- **Loading the Device**: Connected the hemostatis valve with micro-catheter. The Clot Retrieval Device, which is typically a stent retriever designed to engage clots, was loaded into the microcatheter.

Figure 2: Connecting the hemostasis valve with micro-catheter

- **Advancement through the Catheter**: Lossened the RHV and advanced the introducer sheath until its firmly seated in the hub of microcatheter. Tightened the hemostasis valve. The device was advanced through the microcatheter system by pushing it forward using a delivery wire. As it moves through the catheter, it remains constrained in its collapsed form to allow smooth passage.

Figure 3: Advancing the introducer sheath

- **Navigation through the Vasculature**: The operator ensured that the device does not encounter any undue friction or obstacles while navigating the tortuous pathways of the vascular model, using slight adjustments in the catheter to steer through difficult bends or curves.

c. Deployment at the Clot Site

- **Reaching the Occlusion**: Once the device tip was positioned at the clot site, the operator slowly pulled back the microcatheter while maintaining the position of the clot retrieval device. This action exposes the stent retriever, allowing it to expand within the vessel.

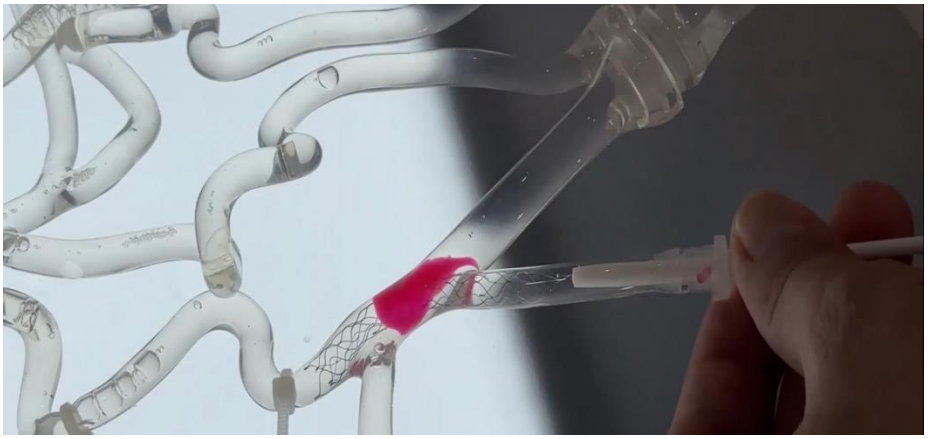

Figure 4: Positioning of microcatheter tip at the location of clot

- **Engagement of the Clot:** As the Clot Retrieval device was expanded, it deployed its mesh-like structure that encases and interlocks with the clot material. This interaction ensures firm engagement of the clot within the stent's structure, ready for retrieval.

5. Clot Retrieval Process

a. Device Activation and Clot Engagement

- **Stent Expansion**: After the Clot Retrieval device was fully deployed, the stent retriever expands to its intended size, pressing against the vessel walls. This expansion is critical for clot engagement, as it embeds the clot into the interstices of the stent's mesh.

b. Initiating Clot Retrieval

- **Slow Withdrawal**: The operator began to slowly withdraw the device, pulling it back through the vascular model while maintaining continuous force on the retrieval wire. The goal was to maintain engagement with the clot throughout the withdrawal process, ensuring it is removed as a whole unit.

Figure 5: Full Clot capture and retrieval

- **Maintaining Device Stability**: The microcatheter was often used in tandem to help provide stability and prevent loss of the clot during retraction.

c. Challenges during Retrieval

- **Resistance from Tortuous Pathways**: While the device was being withdrawn, the vascular model contained bends and bifurcations. The operator skillfully navigated these regions without dislodging or fragmenting the clot.
- **Prevention of Clot Fragmentation**: During withdrawal, particular care was taken to prevent fragmentation of the clot, which could lead to smaller emboli traveling distally (in a patient, this can cause secondary strokes). In the simulation, visual and mechanical feedback indicated whether the clot remains intact.

d. Successful Clot Removal

- **Full Clot Capture**: A successful retrieval involved the removal of the clot intact, with no residual clot material left in the vascular model. The Clot Retrieval device was able to completely extract the thrombus, without significant fragmentation or vessel wall damage.

- **Inspection of the Device and Clot**: After the clot was removed, both the clot and the device were inspected. The clot was firmly attached to the stent retriever, demonstrating proper engagement. Any loose fragments or incomplete clot capture would suggest a performance issue with the device.

e. Post-Retrieval Flow Assessment

- **Flow Restoration Check**: Once the clot was removed, the fluid flow through the vascular model was restored. The fluid flow in the model was assessed to ensure that it mimics successful reperfusion, similar to what would be observed in a human patient after clot removal.
- **Aspirating Residual Debris**: In some cases, aspirating the region around the clot site using a catheter may help remove any residual clot fragments or emboli that could compromise the success of the procedure.

6. Evaluation of Performance

- **Success of Clot Removal**: Evaluated whether the device was able to retrieve the clot in one pass (first-pass success). Measured if any clot fragments were left behind.
- **Embolic Fragmentation**: Assessed if any distal embolization or clot fragmentation occurred during the retrieval process. This is critical as it can lead to secondary strokes in patients.
- **Vessel Wall Interaction**: Checked for damage to the vascular model (simulating vessel injury) that could occur due to excessive force or friction by the device.

7. Repeat with Different Conditions

- Tested the device under various conditions:
- Different types of clots (e.g., hard, soft, or mixed clots).
- Different vessel geometries (straight vs. tortuous pathways).
- Different occlusion locations (proximal vs. distal arteries).

This in-vitro test helps to validate the Clot Retrieval Device's performance before progressing to clinical trials or further regulatory evaluation.

IV. Results

Table: 1 Test Parameters and Observations

Sr. No.	Test Parameter	Observation
01	Kink Resistance Test	The catheter does not kink or lose its ability to deliver the device properly through narrow or curved vessels.
02	Device Deployment Testing	The device deployed smoothly without resistance or malfunction.
03	Retrieval Testing	The device remained undamaged and functional after repeated retraction and deployment cycles.
05	Vessel Wall Integrity	The synthetic vascular model showed no signs of mechanical damage, suggesting that the device applies safe forces during navigation and clot retrieval without risking vessel injury.
06	Success of Clot Removal	The device was able to retrieve the clot in one pass (first-pass success).
07	Embolic Fragmentation	No distal embolization or clot fragmentation occurred during the retrieval process.

The results of these tests collectively evaluated the performance, safety, and reliability of clot retrieval devices. Study revealed kink resistance, smooth deployment, retrieval durability, vessel wall safety and first-pass success that demonstrates it can significantly improve clinical outcomes for patients suffering from acute ischemic strokes. The Clot Retrieval Device has shown ease in deployment over clot with ease of the withdrawal of the clot through micro catheter and guide catheter and restore the blood flow in the blocked artery after the procedure. These tests are essential in validating the functionality and safety of clot retrieval devices. They ensure that the device can perform under various conditions without causing harm to patients.

V. Discussion

During deployment and retrieval, the device’s unique, self-expanding architecture allows it to easy expand and contract inside the vessel. Combination of giant and a baby cell improved the device’s effectiveness and safety. Throughout the radiopaque marker at equal distance on device enhance the visibility during the procedure. The nitinol core wire with PTFE coating (hydrophilic) reduces friction. The in-vitro simulation revealed that the Clot Retrieval Device was able to engage and retrieve thrombi effectively by the help of an aforementioned developed clot retrieval device.

VI. Conclusion

The Clot Retrieval Device effectively tackled a number of significant issues that come with neurovascular thrombectomy. First, a noteworthy accomplishment of the device is its capacity to sustain high first-pass success rates, in which the clot is recovered intact in a single effort. Because prompt and thorough clot removal is necessary to prevent brain tissue damage and lower the risk of additional problems, this is very crucial in practical practice. Because a high first-pass success rate reduces the length of ischemia, it preserves brain function and lessens disability, which is directly correlated with better patient outcomes. The in-vitro simulation methodology demonstrated in this study has successfully validated the efficacy and safety of the Clot Retrieval Device in removing thrombi from the neurovasculature. By replicating realistic clinical conditions, the simulation provided a comprehensive understanding of the device performance in terms of deployment, clot engagement and retrieval. The in-vitro simulation methodology validated its performance, demonstrating that the giant-baby cell design allows for superior clot engagement, improving the likelihood of first pass success- a crucial factor in minimizing the duration of ischemia and enhancing patient outcomes. This in-vitro testing is an essential step in the preclinical validation process that helps to identify any potential issues and optimize device performance before advancing to clinical trials. These findings lay the foundation for further clinical testing, ensuring its readiness for real-world applications. The results of this study suggest that the device could become key tool in the management of acute ischemic stroke, potentially reducing patient morbidity and mortality by offering a safer, more effective means of restoring blood flow in the neurovasculature.

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