

# A comparison of thrombus preparation methods for experimental mechanical thrombectomy

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**Abstract**— Animal models used to test mechanical thrombectomy devices mostly use autologous blood to prepare *ex vivo* thrombi that are then injected back into the animal. In this study, we compared the thrombi produced from multiple thrombus preparation methods in terms of their histological characteristics, injectability, and radiopacity.

**Clinical Relevance**— A better understanding of clots used for preclinical testing can lead to improved thrombectomy devices.

## I. INTRODUCTION

Mechanical thrombectomy is the preferred treatment for large vessel occlusions causing ischemic stroke. Most *in vivo* preclinical testing of thrombectomy devices is performed in the swine carotid [1] by extracting blood, forming a clot, and injecting the clot back into the carotid (branches) to create arterial occlusion. Histological analyses of thrombi extracted from ischemic stroke patients show a layered pattern of fibrin, cellular components, and erythrocyte-rich bands [2]. Various ‘clot-production’ techniques have been described to generate experimental thrombi that emulate this structure [3,4]. In this study we tested these methods, and additionally evaluated the effect of collagen exposure, on thrombus composition.

## II. METHODS

A total of eight thrombus samples were prepared by

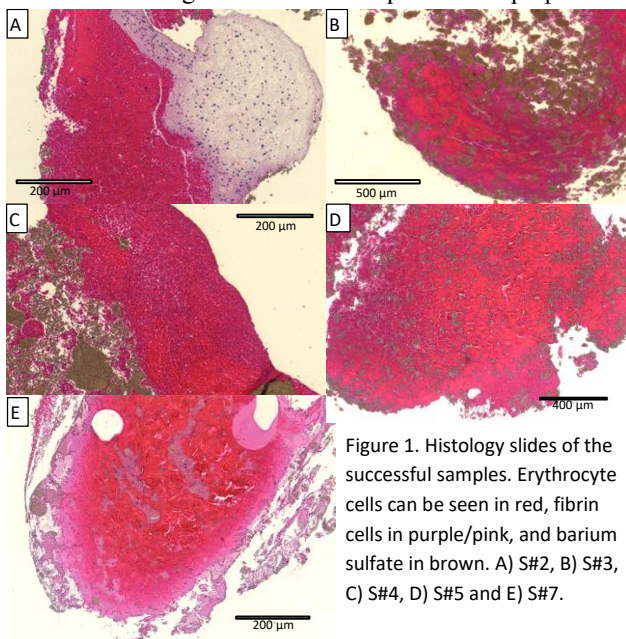


Figure 1. Histology slides of the successful samples. Erythrocyte cells can be seen in red, fibrin cells in purple/pink, and barium sulfate in brown. A) S#2, B) S#3, C) S#4, D) S#5 and E) S#7.

drawing arterial blood from a femoral sheath placed during IACUC approved procedures in two domestic swine. All samples (S#) contained 1 mL of blood and 0.1 g of barium sulfate (HiMedia Labs, #GRM1342). Except for S#2, which was incubated in a 1 mL syringe, all samples were incubated in silicone tubes ( $d=3.175$  mm). Sample preparation protocols were:- **S#1**: 2 I.U. of bovine thrombin (Biopharm Laboratories, #91-055), incubated at 37°C for 1 hour (hr); **S#2**: rotated in syringe for 20s, 22°C for 2hrs; **S#3**: 2 I.U. thrombin, 4mg fibrinogen (Fisher Scientific, #AAJ6327603), **S#4**: 2 I.U. thrombin, placed on a motorized wheel rotated at 30rpm at 37°C for 15 minutes; **S#5**: 37°C for 1hr; **S#6**: 2 I.U. thrombin, 4-0 catgut suture, 37°C for 1hr; **S#7**: 2 I.U. thrombin, 4mg fibrinogen, 4-0 catgut suture, 37°C for 1hr; **S#8**: 2 I.U. thrombin, 4-0 catgut suture, rotated at 30rpm at 37°C for 15 mins. After incubation, half of each sample was placed in formalin for histological processing and subsequent H&E staining. The other half was injected through a 6F catheter and then imaged under X-ray.

## III. RESULTS

Of the eight samples, only five produced clots (S#2,3,4,5,7). Samples S#2 (protocol from [3]) and S#7 (thrombin, fibrinogen, and catgut suture) showed the greatest evidence of layering similarity to patient thrombi (Fig. 1). The other 3 samples also showed some layering but were more erythrocyte-rich and amorphous. All clots could be injected through a catheter without loss of structural integrity. Other than S#5, which had homogenous radiopacity, the distribution of barium sulfate was poor to uneven in all other samples.

## IV. DISCUSSION & CONCLUSION

Brief (order of seconds) rotation of blood in a syringe, incubation at room temperature, the addition of fibrinogen, and use of catgut sutures (collagen) may produce experimental thrombi that are closest in structure to those recovered from stroke patients. The most traditional protocol used in the literature (S#1 from [1]) did not produce a clot in our experiments. The reproducibility of our methodology including generation of homogenous radiopacity needs to be evaluated with larger sample sizes.

## ACKNOWLEDGMENT

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