

ORIGINAL RESEARCH

Exploring the efficacy of cyclic vs static aspiration in a cerebral thrombectomy model: an initial proof of concept study

Scott Simon,¹ Casey Paul Grey,² Trisha Massenzo,² David G Simpson,³ P Worth Longest^{4,5}

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/neurintsurg-2013-010941>).

¹Department of Neurosurgery, Pennsylvania State University, Hershey, Pennsylvania, USA

²Department of Biomedical Engineering, Virginia Commonwealth University, Richmond, Virginia, USA

³Department of Anatomy and Neurobiology, Virginia Commonwealth University, Richmond, Virginia, USA

⁴Department of Mechanical Engineering, Virginia Commonwealth University, Richmond, Virginia, USA

⁵Department of Pharmaceutics, Virginia Commonwealth University, Richmond, Virginia, USA

Correspondence to

Casey Paul Grey, Department of Biomedical Engineering, Virginia Commonwealth University, 401 West Main Street, P.O. Box 843067, Richmond, VA 23284-3067, USA; greycp@vcu.edu

Received 14 August 2013

Revised 24 October 2013

Accepted 27 October 2013

Published Online First

14 November 2013

ABSTRACT

Background and purpose Current technology for endovascular thrombectomy in ischemic stroke utilizes static loading and is successful in approximately 85% of cases. Existing technology uses either static suction (applied via a continuous pump or syringe) or flow arrest with a proximal balloon. In this paper we evaluate the potential of cyclic loading in aspiration thrombectomy.

Methods In order to evaluate the efficacy of cyclic aspiration, a model was created using a Penumbra aspiration system, three-way valve and Penumbra 5Max catheter. Synthetic clots were aspirated at different frequencies and using different aspiration mediums. Success or failure of clot removal and time were recorded. All statistical analyses were based on either a one-way or two-way analysis of variance, Holm–Sidak pairwise multiple comparison procedure ($\alpha=0.05$).

Results Cyclic aspiration outperformed static aspiration in overall clot removal and removal speed ($p<0.001$). Within cyclic aspiration, Max Hz frequencies (~ 6.3 Hz) cleared clots faster than 1 Hz ($p<0.001$) and 2 Hz ($p=0.024$). Loading cycle dynamics (specific pressure waveforms) affected speed and overall clearance ($p<0.001$). Water as the aspiration medium was more effective at clearing clots than air ($p=0.019$).

Conclusions Cyclic aspiration significantly outperformed static aspiration in speed and overall clearance of synthetic clots in our experimental model. Within cyclic aspiration, efficacy is improved by increasing cycle frequency, utilizing specific pressure cycle waveforms and using water rather than air as the aspiration medium. These findings provide a starting point for altering existing thrombectomy technology or perhaps the development of new technologies with higher recanalization rates.

INTRODUCTION

Thrombectomy devices for use in ischemic stroke have undergone a stepwise evolution as each generation of technology becomes more effective without increasing complications. Despite progress, the best thrombectomy technology currently only achieves recanalization in approximately 85% of cases.¹ In the interest of positive patient outcomes after ischemic events, the continued development of thrombectomy technology should be encouraged as it is necessary until successful recanalization is assured in all cases.²

Current thrombectomy techniques focus on applying endovascular disruptive forces to facilitate the removal of occluding thrombi. This can involve

mechanical entrapment and extraction of clots via a deployable mesh-like device (eg, stent retrievers)³ or, in suction thrombectomy (the topic of this study), an aspiration source (eg, pump, large-gauge syringe)^{4–7} is used to dislodge clots from the vasculature so they can be removed via a catheter. Each is performed under either static suction, generated by a pump or syringe, or flow arrest using a proximal balloon. While these techniques are moderately successful,⁸ we propose the idea that applying a more nuanced or sophisticated aspiration pressure profile could improve current recanalization rates. The logic behind this idea is that, generally, cyclic changes in force induce material fatigue.⁹ In this way, subjecting clots to material fatigue via cyclic aspiration might reduce their required load-to-failure (theoretically enabling the removal of more entrenched clots) and the time-to-failure given a specific load (theoretically reducing the time to reperfusion) with obvious benefits to the patient.^{10 11}

Simply defined by Wiley, ‘Fatigue refers to the modification of the properties of a material due to the application of stress cycles whose repetition can lead to fracture’.⁹ Unlike most real-world examples of fatigue, such as the de Havilland Comet 1 plane crash in 1954 where material fatigue was unintended and undesirable,¹² increasing the likelihood of clot failure through fatigue mechanisms is exactly the goal of this study.

Knowing that a clot is simply an occlusive material possessing measurable material properties (albeit dynamic ones),¹³ and that cyclic loading facilitates material failure through fatigue mechanisms,^{9 12} we hypothesized that the introduction of cyclic aspiration forces in suction thrombectomy would generate clot fatigue. We further hypothesized that, by fatiguing the clot, we could measurably improve aspiration performance compared with the static forces characteristic of current suction thrombectomy techniques.⁶ Moreover, as failure in fatigue is a function of total load cycles,¹⁴ we hypothesized that increased aspiration frequencies would lead to increased treatment efficacy. To test our hypotheses, we evaluated the efficacy of novel cyclic suction thrombectomy force profiles against the current static suction thrombectomy force profile through their performance in aspirating synthetic clots in a flow model.

METHODS**The cyclic impact aspiration technique**

The model depicted in figure 1 involved performing cyclic impact aspiration by placing a three-way valve



CrossMark

To cite: Simon S, Grey CP, Massenzo T, et al. *J NeuroInterv Surg* 2014;**6**:677–683.

Basic science

(Harvard Apparatus, Holliston, Massachusetts, USA) between a vacuum source (Penumbra aspiration pump, Penumbra, Alameda, California, USA) and the catheter (Penumbra 5Max reperfusion catheter) to establish open continuity between the vacuum source, the catheter tip and air (the aspiration medium) when the valve was opened. Temporarily closing the valve to air (eg, with an index finger) allowed the pump to establish a vacuum at the catheter tip. Subsequently removing the finger reopened the system to air and rapidly diminished the vacuum at the catheter tip. Impact aspiration is performed by repeatedly opening and closing the valve to air so that cyclic pressure profiles are developed at the catheter tip. Additional tests were performed by changing the aspiration medium to water (incompressible fluid) rather than air (compressible fluid). This was accomplished by submerging the three-way valve in water. Care was taken to ensure that the system was primed with the aspiration medium before experimentation.

Additionally, using this model allows modification of the frequency profile and also the pressure profile. We describe two general ways to cycle aspiration pressure at a specific frequency. Down-cycling (DC) involves a brief pressure-relieving impulse in each cycle with a majority of time spent at maximum treatment pressure (see Results section, figure 2A,B). Up-cycling (UC) involves a brief pressurizing impulse in each cycle with a majority of time spent at minimum treatment pressure (see Results section, figure 2A,B). At frequencies higher than 2 Hz the pressure plateau characteristic of DC aspiration was not possible via manual control, so we considered all aspiration above 2 Hz to be UC as it consisted of very brief pressurization impulses.

Clot removal flow model analysis

Synthetic polyurethane clots (Concentric Medical, Mountain View, California, USA) were extruded with a cylindrical template cut to a specific clot size (see Results section) using Traceable Digital Calipers (Control Company, Friendswood, Texas, USA). They were then placed in a flow model consisting of a Penumbra 5Max reperfusion catheter (1.37 mm tip internal diameter) inside rigid plastic tubing (2.5 mm internal diameter, 4 mm outside diameter) submerged in water. The clots were positioned directly adjacent to the catheter tip and exposed to either suction alone (Penumbra aspiration pump) or cyclic aspiration via our impact aspiration technique (note that the model did not include afferent flow). The test was performed until either the clot was removed or 5 min had elapsed. If the clot was not completely cleared within 5 min (the standard dwell time of current stent retrievers), the trial was considered unsuccessful. To observe a successful trial video please see <http://stroke.ahajournals.org>. With regard to the ADAPT technique as described by Turk *et al.*,¹⁵ we did not attempt to withdraw the aspiration catheter after partial engagement. It is important to note that the synthetic clot changes in consistency (and, presumably, mechanical properties) within several days after opening,

therefore only freshly opened packages were used in experimentation.

Aspiration pressure analysis

Pressure profiles were generated by placing an Equus 3620 Innova Vacuum Gauge (Equus Products, Irvine, California, USA) distal to the three-way valve during experimentation. Using reduced speed playback of the vacuum gauge fluctuations, we were able to record the pressures generated during static aspiration and 15 cycles of impact aspiration at frequencies of 1 and 2 Hz, as well as a third group labeled 'Max Hz' where the experimenter cycled the system as fast as possible. The 'Max Hz' category was necessary to capture impact aspiration performance at higher frequencies while acknowledging that accurately reproducing frequencies above 2 Hz was not possible with our manual technique. The actual frequency for the 'Max Hz' trials was determined by dividing the number of cycles by the time elapsed. Limitations in our ability to manually control the pressure cycling prevented us from testing a wider range of frequencies. After noticing the increased efficacy of the UC impact aspiration technique and with limited synthetic clot available, we focused our efforts on obtaining as much data on the UC technique in order to facilitate statistical analysis of the results.

Statistical analysis

All statistical analyses were based on either a one-way (static loading vs cyclic loading and UC impact aspiration clot clearance trials) or two-way analysis of variance (all other analyses), Holm-Sidak pairwise multiple comparison procedure ($\alpha=0.05$).

RESULTS

Cyclic loading: cycle dynamics

Pressure cycle dynamics for each system are approximated in figure 2. The Penumbra pump acting alone provided an adequate pump-down time, rapidly creates and maintains a vacuum (figure 2A–C, dotted line).⁶ DC and UC cyclic aspiration are shown in figure 2A,B.

Aspiration pressure dynamics

The Penumbra system alone creates a rapidly developing static pressure curve that reaches a peak value of -24.5 in Hg. Cyclic aspiration creates a dynamic pressure curve where the pressure cycles between a maximum and minimum value at a specific frequency (maximum and minimum relating to the magnitude of pressure). Impact aspiration cycles between -23.8 (SD 0.09) in Hg and 0 (SD 0) in Hg at 1 Hz, between -22.0 (SD 0.11) in Hg and 0 (SD 0) in Hg at 2 Hz and between -18.9 (SD 0.8) in Hg and -5.0 (SD 2.42) in Hg at Max Hz (~ 6.3 Hz) (figure 2). The relationship between frequency and pressure differential for the three impact aspiration values is remarkably linear with linear curve-fitting yielding an equation of $y=47.654x - 653.4$ with an r^2 value of 1.

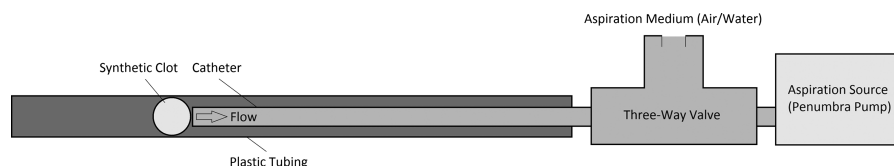


Figure 1 Aspiration flow schematic. For static load aspiration the three-way valve was modified so that continuity existed only between the catheter and the aspiration source. For cyclic load aspiration the three-way valve was modified so that open continuity existed between the catheter, the aspiration medium and the aspiration source. In this way it was possible to manually cycle the aspiration pressure at the catheter tip by repeatedly covering and uncovering the valve port open to the aspiration medium.

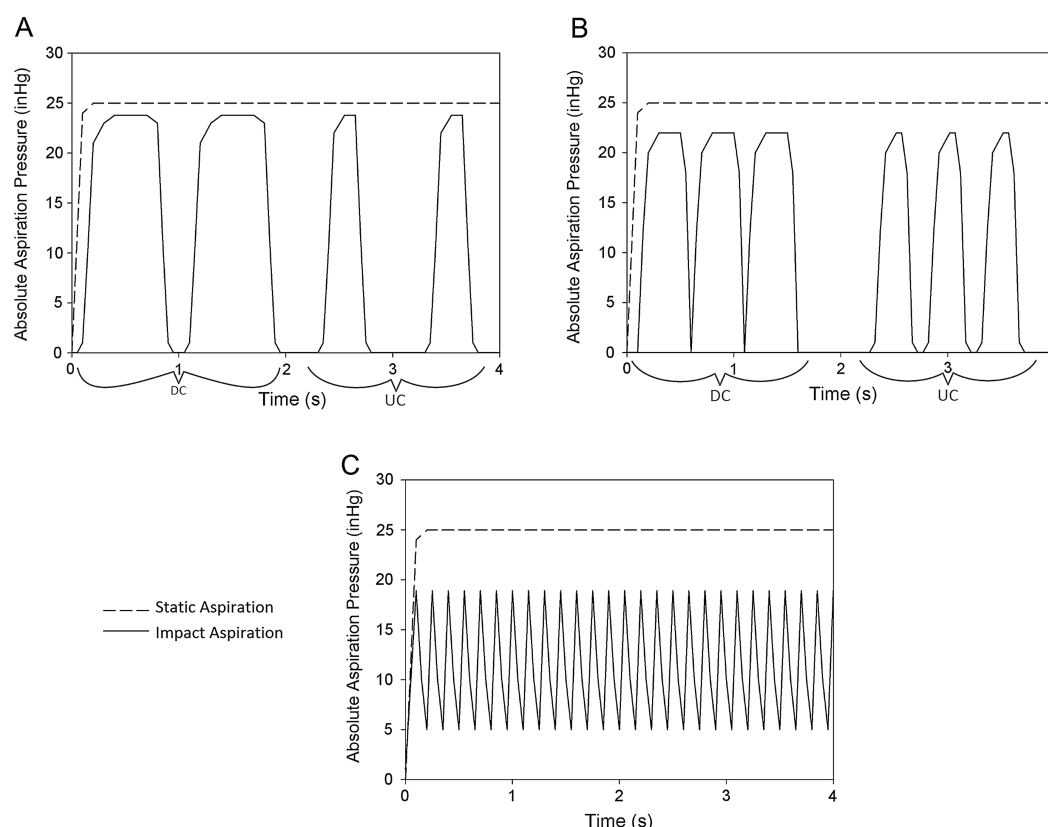


Figure 2 Examples of down-cycling (DC) and up-cycling (UC), two cyclic aspiration pressure profiles used in this study. DC involves brief pressure-relieving impulses while UC involves brief pressurizing impulses. The Penumbra pump produces a static pressure profile (A–C, dotted lines) whereas, in impact aspiration, the pressure profile dynamically changes (A–C, solid lines). (A) 1 Hz DC (first two cycles) and UC (last two cycles) pressure profiles. (B) 2 Hz DC (first three cycles) and UC (last three cycles) pressure profiles. (C) Max Hz pressure profile (~6.3 Hz). While the differences between DC and UC pressure profiles may seem trivial, the UC pressure profile significantly outperformed the DC pressure profile in both clot clearance time and clearance success rate ($p < 0.001$).

Clot sizing

By systematically increasing the synthetic clot diameter until the Penumbra system could no longer successfully clear the clots from the flow model, we created a thrombectomy model in which suction alone would be an insufficient treatment. Synthetic clots with a diameter of 2.16 mm and a length of 3 mm satisfied the criteria and were used in all experiments.

Strategy for analyzing aspiration success

Examining the data as a whole brings to light the complex interplay between the variables (static aspiration, cyclic aspiration and, within cyclic aspiration, frequency, aspiration medium and pressure waveform) and the ultimate results (overall clot clearance rate and clot clearance time). In the following sections we systematically examine how each individual variable affects the experimental results.

Static loading versus cyclic loading

Aspiration with the Penumbra pump alone failed to clear a single clot ($n=10$) whereas the combined clearance rate of impact aspiration was 91.43% (64 cleared, $n=70$). Impact aspiration was significantly better at clearing clots from the flow model than static aspiration with the Penumbra pump ($p < 0.001$).

Cyclic loading: frequency comparison

Impact aspiration had successful clearance rates of 84% (1 Hz, $n=25$), 100% (2 Hz, $n=25$) and 90% (Max Hz, $n=20$) and clearance times of 35.1 (SD 22.8) s (1 Hz, $n=21$), 40.7 (SD 55.4) s (2 Hz, $n=25$) and 7.8 (SD 6.8) s (Max Hz, $n=18$). Aspirating at Max Hz was significantly faster at clearing clots than at 1 Hz ($p < 0.001$) or 2 Hz ($p = 0.024$). There were no significant differences between frequencies when considering the general ability to clear clots from the flow model.

Cyclic loading: aspiration medium comparison

When air was used as the aspirating medium, impact aspiration had an overall clearance rate of 85% ($n=40$) and an average clearance time of 34.7 (SD 49.3) s ($n=34$). When water was used as the aspirating medium, impact aspiration had an overall clearance rate of 100% ($n=30$) and an average clearance time of 23.8 (SD 22.7) s ($n=30$). Impact aspiration using water as the aspirating medium was significantly more effective at clearing clots than when air was used as the aspirating medium ($p = 0.019$). There were no significant differences between the two aspirating mediums in clearance time.

Cyclic loading: cycle dynamics comparison

Using DC pressure profiles in impact aspiration resulted in a clearance rate of 60% ($n=10$) and an average clearance time of

Basic science

80.7 (SD 94.8) s (n=6). Using UC pressure profiles resulted in a clearance rate of 96.67% (n=60) and an average clearance time of 24.3 (SD 24.8) s (n=58). Compared with DC, UC pressure profiles were both significantly more effective in the general ability to clear clots from the flow model ($p<0.001$) and significantly faster at clearing the clots from the flow model ($p<0.001$).

UC impact aspiration clot clearance trials

Max Hz cycling with water as the aspiration medium was significantly faster than 1 Hz cycling with either air ($p=0.015$) or water as the aspiration medium ($p=0.025$). While clearance time clearly trended downwards with increasing aspiration frequency, no other differences were found to be statistically significant (figure 3).

DISCUSSION

From our results we believe that cyclic loading may eventually supplant static loading as the base aspiration profile for the treatment of ischemic stroke. Although none were observed in this study, in the interest of preventing the distal migration of thrombi, impact aspiration would have to be performed either in conjunction with continuous aspiration or as a stand-alone treatment with a minimum frequency such that a vacuum is maintained throughout testing. In this study ~6.3 Hz (Max Hz) was the only frequency that maintained uninterrupted net aspiration pressure as both 1 Hz and 2 Hz had minimum pressures of 0 in Hg. Implementing a pressure-controlling device would allow flexibility in aspiration frequency due to the increased control over minimum pressure. As with current static aspiration techniques, we believe cyclic aspiration would pair successfully with supplemental treatment methods such as the use of a separator wire.

Cyclic versus static loading

While the dips in the pressure-time curve (figure 2) show that cyclic loading delivers less total force to the clot than static

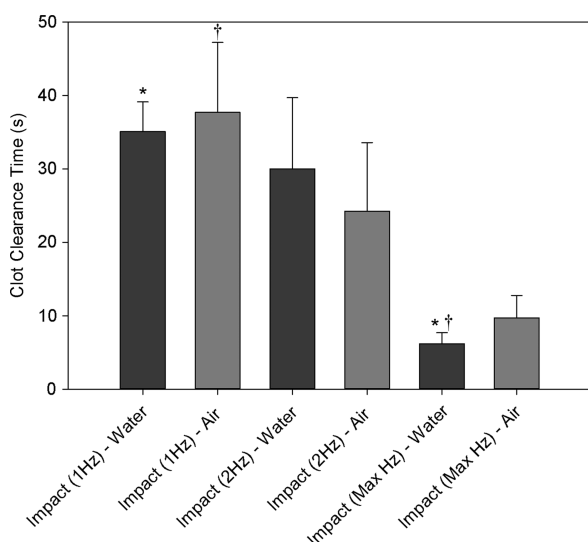


Figure 3 Up-cycling (UC) impact aspiration clot clearance times with SE bars. A one-way analysis of variance was used to determine the relationship between different UC impact aspiration groups and their performance with regard to clot clearance time. Significant differences are marked with * and †.

loading, we found that cyclic loading is superior to static loading in clearing clots from our flow model ($p<0.001$). The discrepancy between total force delivered and experimental outcome indicates that the dynamics of loading play a significant role in the success of the procedure.

Frequency

While Max Hz cycling was not 100% successful in this study (it is worthwhile to note that all clearance failures occurred with air as the medium), the downward trend in clot clearance time shown in figure 3 is a good indicator that increasing frequency is the correct path to more effective treatments. We believe that additional dimensions of frequency and amplitude modulation may be added to this technique in which their values are temporally adjusted to increase treatment efficacy.

UC versus DC

The more efficacious UC method differs from DC impact aspiration in that its pressure dynamics are characterized by two rapid perturbations (pressure on and off) with virtually no static loading between them. DC impact aspiration, on the other hand, has a relatively long static loading period between its two perturbations. In this study it appeared that the prolonged static force actually decreased the efficacy of the technique. We therefore believe the mechanism of successful clot disruption lies in the perturbations applied to the clot, not in the static force.

Air versus water

In our clot model, why might a closed system containing water be more effective at clearing clots than one containing air? An analysis of hydraulics (dealing with liquids such as water) and pneumatics (dealing with gases such as air) reveals that the likely answer is that water is non-compressible and therefore transfers the changes in pressure actuated at the valve to the catheter tip much more faithfully than highly compressible air. Krivits states that 'Aspects that make a hydraulic actuator useful are the low compressibility of hydraulic fluids and high stiffness which leads to an associated high natural frequency and rapid response ... [conversely] owing to the compressibility characteristics of the air and high friction force, the pneumatic actuator system is very highly nonlinear, and the system parameters are time variant with changes in the environment.'¹⁶ Our experimental design did not allow for the sophisticated type of measurements required to prove this general principle by recording the detailed pressure transitions between recorded highs and lows. Nonetheless, using these principles to attempt to interpret the data, it is possible to construct a theoretical pressure curve for both water and air that explains the observed results (figure 4). It is likely that the pressure reaches maximum and minimum more quickly with water, providing more total time at maximum pressure, more abrupt pressure perturbations and steeper pressure development slopes in the ramping phases. This is detailed in our theoretical perturbation curves and provides an explanation for increased efficacy with water as the aspiration medium.

Impact aspiration as a departure from current techniques

A technique that bears some similarity to the topic of this study is ultrasound augmented fibrinolysis. The ultrasonic oscillations in this technique, delivered transcranially or via a catheter, are designed to increase the penetration of fibrinolytic agents into the clot so that the clot breaks up and flows distally.¹⁷⁻¹⁹ The benefits of ultrasound augmented fibrinolysis, however, may not outweigh the increased risk of hemorrhage.¹⁷ By comparison,

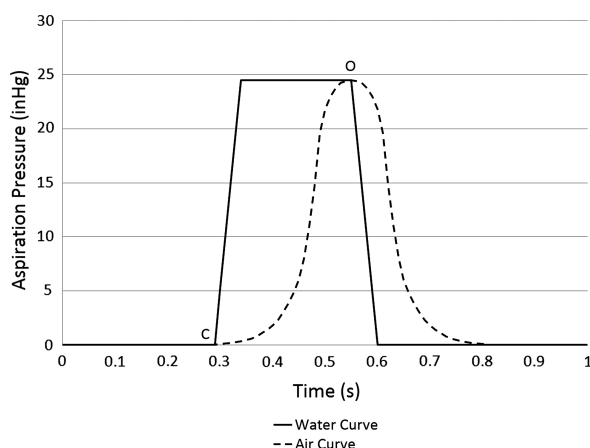


Figure 4 Theoretical perturbation curves when using air or water as the aspiration medium. 'C' and 'O' represent the points in a cycle where the valve is closed (initiating pressure) and opened (relieving pressure), respectively.

impact aspiration employs much lower frequency and higher amplitude oscillations aimed at mechanically dislodging and disrupting the clot so that it can be aspirated from the vessel.

Possible risks

There may be concerns regarding an increased risk of hemorrhage, especially in light of reports of increased hemorrhage

after the application of ultrasound in stroke treatment.¹⁷ While these risks are possible, the risks associated with ultrasound treatment appear to be frequency dependent, with kHz frequencies posing a much larger risk than MHz.²⁰ On the other hand, physiological frequencies of ~1–3 Hz are part of normal circulation where the natural elasticity of the vessel walls allows for safe expansion and contraction. We hypothesize that there is a range of unsafe frequencies where the risk of compromising vessel walls is increased, leading to increased rates of hemorrhage. This unsafe range (~kHz)²⁰ would be characterized by frequencies too high to allow the vessel walls to elastically accommodate the perturbations, rendering their deformation as plastic, and amplitudes large enough to cause significant mechanical damage. Above this unsafe frequency range (eg, MHz frequencies) the amplitudes are not large enough to cause significant wall damage, accounting for the decreased rate of hemorrhage, although these frequencies are associated with increased thermal tissue damage.²¹ Impact aspiration uses low frequency mechanical perturbations that should not exceed local elastic limits. Alternatively, it is possible that high frequency vibrations may lie within the harmonic resonance frequencies of the surrounding blood vessels. This could result in unintentional amplification of the source signal²² to magnitudes that are high enough to cause tissue damage. While testing would have to confirm that the perturbations associated with impact aspiration do not increase the risk of hemorrhage, low frequency perturbations should be sufficiently similar to physiological circulatory frequencies not to result in increased rates of hemorrhage.

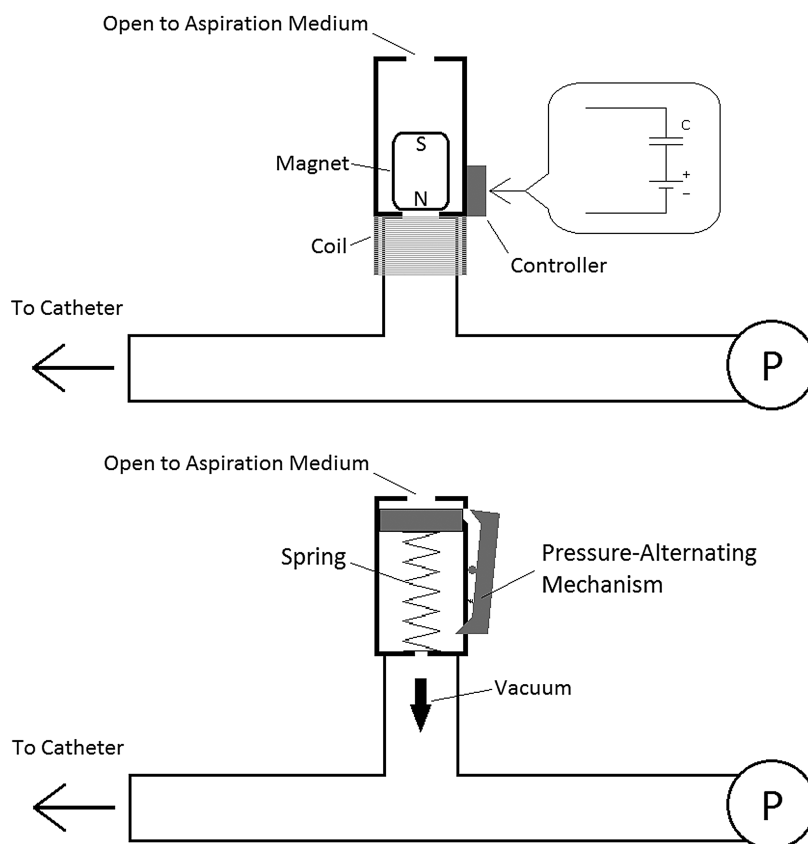


Figure 5 Concept impact aspiration device designs. The top device employs an electromagnetic pressure controlling mechanism while the bottom device employs a simple mechanical pressure controlling mechanism. Additional designs are detailed online in the supplementary figures I–III (please see <http://stroke.ahajournals.org>).

Basic science

Distal emboli in cerebral thrombectomy are a significant concern, and not all currently available methods appear to be equal in this regard.¹⁵ As the pressure curves reveal, higher frequency oscillations were more effective at removing the synthetic clot in this limited experimental model and also never returned to 0 mm Hg. This technique can therefore be optimized to provide uninterrupted net reverse flow to prevent distal migration. The limited model and data produced in this paper are to inform further research and not to recommend that practitioners immediately adopt a new model or technique. That being said, it is not hard to extrapolate that high frequency oscillation of the suction source would be at a similar risk for distal emboli as current Penumbra aspiration that is low risk because there is always reverse flow in the system. Additionally, throughout the study no distal emboli were observed.

Limitations of experimental clot material

The polyurethane clot material used in this study was taken from a training course for the TREVO device. This material was also used during MERCI training courses. Using clinical experience as a reference, qualitative evaluation revealed that the bulk mechanical properties were similar to that of clots successfully removed during thrombectomy cases. While our clot model is only an approximation of a biological clot, Chueh *et al*²³ conceded that 'it is currently not possible with these models to represent the entire diversity of the human specimens that we measured'. The study by Chueh *et al* also encountered limitations including the small number of human samples (n=9), the sampling bias inherent in testing only successfully removed specimens, the inability to test calcified specimens and the untested hypothesis that specimens from carotid plaques will manifest the properties of future middle cerebral artery clots. Given these limitations and the material variability of clots, it was not possible to conclude that one or another type of clot was ideal for testing. Chueh *et al* appropriately state that finding such a material 'is the focus of our future research'. While the search for the ideal thrombectomy clot model undoubtedly continues, we believe an approximated clot model is appropriate for exploratory research in order to highlight possible efficacy differences between thrombectomy techniques.

Next steps with this technology

The narrow purpose of this experiment is not to recommend a new method that surgeons should attempt in patients based on this study alone. Nonetheless, all current methods involve either flow arrest or static aspiration pressure, which begs the question if oscillation of the pressure source could produce a better result. Representing the first step to answering this question, we set out in this study to determine whether, given the approximate sizes, materials and forces encountered in the majority of cerebral thrombectomy cases, oscillating the suction source increases the efficiency of clot removal. In order to truly identify aspiration dynamics as the critical factor, we performed this work in a simplified model with all other variables held constant.

Only now, with these pilot data established, does it seem prudent to embark on future research to classify further how the many variables involved—for example, frequency, differential amplitude range, pressure waveform—can be optimized. Furthermore, these data make it worthwhile to develop a device that can vary the frequency and pressure more precisely. This will allow much more detailed examination of suction variation that might be able to be a stand-alone technique or to augment current techniques by replacing flow arrest or static suction (figure 5).

Complete testing of all types of clot with many different suction profiles will undoubtedly require computer modeling (eg, computational fluid dynamics with fluid-solid interactions). It is our opinion that, only when this type of data has been gathered and analyzed, of which the data presented here are the initial step, can meaningful and preclinical animal testing be performed.

CONCLUSION

We demonstrate that cyclic loading with our impact aspiration technique significantly outperforms static loading with the Penumbra pump at clearing synthetic clots in an experimental model. Within our impact aspiration technique, aspirating at a higher frequency (eg, 6.3 Hz vs 1 Hz) using the UC pressure waveform and water as the aspirating medium is the most effective way to clear synthetic clots from the flow model.

Acknowledgements The authors would like to thank Paul Grey for discussions on harmonics.

Contributors All authors contributed to the design, writing, editing and approval of this manuscript. SS and CPG performed the experimental testing.

Competing interests US and international patents pending.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- Dávalos A, Pereira VM, Chapot R, *et al*. Retrospective multicenter study of Solitaire FR for revascularization in the treatment of acute ischemic stroke. *Stroke* 2012;43:2699–705.
- Fiehler J, Söderman M, Turjman F, *et al*. Future trials of endovascular mechanical recanalization therapy in acute ischemic stroke patients: a position paper endorsed by ESMINT and ESNR. Part I: Current situation and major research questions. *Neuroradiology* 2012;54:1293–301.
- Bösel J, Hacke W, Bendszus M, *et al*. Treatment of acute ischemic stroke with clot retrieval devices. *Curr Treat Options Cardiovasc Med* 2012;14:260–72.
- Kreusch AS, Psychogios M, Knauth M. Techniques and results—Penumbra aspiration catheter. *Tech Vasc Interv Radiol* 2012;15:53–9.
- Kang D, Hwang Y, Kim Y, *et al*. Direct thrombus retrieval using the reperfusion catheter of the Penumbra system: forced-suction thrombectomy in acute ischemic stroke. *AJNR Am J Neuroradiol* 2011;32:283–7.
- Simon SD, Grey CP. Hydrodynamic comparison of the Penumbra system and commonly available syringes in forced-suction thrombectomy. *J Neurointerv Surg* 2014;6:205–11.
- The Penumbra Pivotal Stroke Trial Investigators. The penumbra pivotal stroke trial: safety and effectiveness of a new generation of mechanical devices for clot removal in intracranial large vessel occlusive disease. *Stroke* 2009;40:2761–8.
- Barreto AD, Alexandrov AV. Adjunctive and alternative approaches to current reperfusion therapy. *Stroke* 2012;43:591–8.
- Bathias C, Pineau A. *Fatigue of materials and structures fundamentals*. London: ISTE, Hoboken, NJ: John Wiley, 2010.
- Saver JL. Time is brain—quantified. *Stroke* 2006;37:263–6.
- Khatir P, Abruzzo T, Yeatts SD, *et al*. Good clinical outcome after ischemic stroke with successful revascularization is time-dependent. *Neurology* 2009;73:1066–72.
- Withey PA. Fatigue failure of the de Havilland comet I. *Eng Failure Anal* 1997;4:147–54.
- Brown AEX, Litvinov RI, Discher DE, *et al*. Multiscale mechanics of fibrin polymer: gel stretching with protein unfolding and loss of water. *Science* 2009;325:741–4.
- Mršnik M, Slavič J, Boltežar M. Frequency-domain methods for a vibration-fatigue-life estimation—application to real data. *Int J Fatigue* 2013;47:8–17.
- Turk AS, Spiotta A, Frei D, *et al*. Initial clinical experience with the ADAPT technique: a direct aspiration first pass technique for stroke thrombectomy. *J Neurointerv Surg* 2014;6:231–7.
- Krivits IL. *Pneumatic actuating systems for automatic equipment structure and design*. Hoboken, NJ: CRC Press, 2006.
- Kelley RE, Martin-Schild S. Ischemic stroke: emergencies and management. *Neurol Clin* 2012;30:187–210.
- Alexandrov AV. Ultrasound enhancement of fibrinolysis. *Stroke* 2009;40:S107–10.
- Saqqur M, Uchino K, Demchuk AM, *et al*. Site of arterial occlusion identified by transcranial Doppler predicts the response to intravenous thrombolysis for stroke. *Stroke* 2007;38:948–54.

- 20 Barlinn K, Barreto AD, Sisson A, *et al.* CLOTBUST-hands free: initial safety testing of a novel operator-independent ultrasound device in stroke-free volunteers. *Stroke* 2013;44:1641–6.
- 21 Monteith S, Sheehan J, Medel R, *et al.* Potential intracranial applications of magnetic resonance-guided focused ultrasound surgery. *J Neurosurg* 2013;118:215–21.
- 22 Gao F, Zheng Y, Feng X, *et al.* Thermoacoustic resonance effect and circuit modelling of biological tissue. *Appl Phys Lett* 2013;102:063702.
- 23 Chueh JY, Wakhloo AK, Hendricks GH, *et al.* Mechanical characterization of thromboemboli in acute ischemic stroke and laboratory embolus analogs. *AJNR Am J Neuroradiol* 1108;32:1237.



Exploring the efficacy of cyclic vs static aspiration in a cerebral thrombectomy model: an initial proof of concept study

Scott Simon, Casey Paul Grey, Trisha Massenzo, David G Simpson and P Worth Longest

J NeuroIntervent Surg 2014 6: 677-683 originally published online November 14, 2013
doi: 10.1136/neurintsurg-2013-010941

Updated information and services can be found at:
<http://jnis.bmj.com/content/6/9/677>

Supplementary Material

Supplementary material can be found at:
<http://jnis.bmj.com/content/suppl/2013/11/14/neurintsurg-2013-010941.DC1.html>

These include:

References

This article cites 21 articles, 11 of which you can access for free at:
<http://jnis.bmj.com/content/6/9/677#BIBL>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections

Articles on similar topics can be found in the following collections
[Basic science](#) (48)

Notes

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://group.bmj.com/subscribe/>