Rubrica: Technical device

A novel guitar string-like coronary stent method for cerebral aneurysms

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Abstract. *Aims:* To investigate a novel method of stenting using coronary stents for cerebral aneurysms, and to evaluate its performance in a cerebral aneurysm model. *Methods:* The cerebral aneurysm model, which was a viscoelastic model with 3 aneurysms, was investigated. These models had large saccular aneurysms (10 to 12 mm) with an aneurysm entry profile of 3 to 4 mm. Coronary stents (balloon mounted) were used to stent the main artery harbouring the aneurysms. The stents were placed across the mouth of the aneurysms. After placement of the first stent another stent was deployed inside the first stent. The aneurysms were connected to the pressure transducers, which can measure pressure difference across the stent, and the pressure in the main vessel was measured using another transducer. The stents had a strut thickness of about 110 μm. Twenty beats were recorded before stenting and after each stenting in the aneurysms. Average of twenty beats were recorded in one single beat with pressures and time. *Results:* The coronary stents could be deployed across the mouth of the aneurysms. A reduction in the negative peaks was observed after stenting main vessel harbouring the aneurysm. Also, the pressure correlation showed a significant hysteresis in the pressure levels after stenting. By mass-energy equivalence principle, a reduction in energy could lead to reduction in the mass or the size of the aneurysm. Between one and two stents at the mouth of the aneurysm, based on the pressure gradients and the pressure correlation analysis, there were no significant changes. *Conclusion:* There is potential for novel stent method using coronary stents in the treatment of cerebral aneurysm.

Key words: cerebral aneurysms, angioplasty, flow diverter, stent

Un nuovo metodo di stent coronarico simile a una corda per aneurismi cerebrali

Riassunto. *Finalità:* Per indagare su un nuovo metodo di stent utilizzando gli stent coronarici per aneurismi cerebrali e per valutare le sue prestazioni in un modello di aneurisma cerebrale. *Metodi:* È stato studiato il modello di aneurisma cerebrale, che era un modello viscoelastico con 3 aneurismi. Questi modelli presentavano grandi aneurismi sacculari (da 10 a 12 mm) con un profilo di entrata aneurisma da 3 a 4 mm. Stent coronarici (montati su palloncini) sono stati utilizzati per stent l'arteria principale che ospita gli aneurismi. Gli stent sono stati posizionati attraverso la bocca degli aneurismi. Dopo il posizionamento del primo stent è stato distribuito un altro stent all'interno del primo stent. Gli aneurismi erano collegati ai trasduttori di pressione, che possono misurare la differenza di pressione attraverso lo stent e la pressione nel vaso principale è stata misurata usando un altro trasduttore. Gli stent avevano uno spessore del puntone di circa 110 μm. Venti battiti sono stati registrati prima dello stent e dopo ogni stent negli aneurismi. La media di venti battiti è stata registrata in un singolo battito con pressioni e tempo. *Risultati:* Gli stent coronarici potrebbero essere distribuiti attraverso la bocca degli aneurismi. Una riduzione dei picchi negativi è stata osservata dopo l'impianto di stent che ospita l'aneurisma. Inoltre, la correlazione di pressione ha mostrato un'isteresi significativa nei livelli di pressione dopo lo stent. Con il principio di equivalenza massa-energia, una riduzione di energia potrebbe portare alla riduzione della massa o della dimensione dell'aneurisma. Tra uno e due stent alla bocca dell'aneurisma, in base ai gradienti di pressione e all'analisi della correlazione di pressione, non si sono verificati cambiamenti significativi. *Conclusioni:* Esiste la possibilità di un nuovo metodo di stent che utilizza stent coronarici nel trattamento dell'aneurisma cerebrale.

Parole chiave: aneurismi cerebrali, angioplastica, deviatore di flusso, stent

Une nouvelle méthode de stent coronaire semblable à une corde de guitare pour les anévrismes cérébraux

Résumé. *Objectifs:* Étudier une nouvelle méthode de pose d'endoprothèse vasculaire utilisant des endoprothèses coronaires pour les anévrismes cérébraux et évaluer ses performances dans un modèle d'anévrisme cérébral. *Les méthodes:* Le modèle d'anévrisme cérébral, qui était un modèle viscoélastique avec 3 anévrismes, a été étudié. Ces modèles avaient de grands anévrismes sacculaires (10 à 12 mm) avec un profil d'entrée de l'anévrysme de 3 à 4 mm. Des endoprothèses coronaires (montées sur ballon) ont été utilisées pour enduire l'artère principale abritant les anévrismes. Les stents ont été placés en travers de la bouche des anévrismes. Après la mise en place du premier stent, un autre stent a été déployé à l'intérieur du premier. Les anévrismes ont été connectés aux transducteurs de pression, qui peuvent mesurer la différence de pression à travers le stent, et la pression dans le vaisseau principal a été mesurée à l'aide d'un autre transducteur. Les stents avaient une épaisseur de jambe de 110 µm environ. Vingt battements ont été enregistrés avant le stenting et après chaque stenting dans les anévrismes. Une moyenne de vingt battements ont été enregistrés en un seul battement avec des pressions et du temps. *Résultats:* Les stents coronaires pourraient être déployés à travers la bouche des anévrismes. Une réduction des pics négatifs a été observée après la mise en place du vaisseau principal hébergeant l'anévrisme. En outre, la corrélation de pression a montré une hystérésis importante dans les niveaux de pression après la pose d'un stent. Selon le principe d'équivalence masse-énergie, une réduction de l'énergie pourrait entraîner une réduction de la masse ou de la taille de l'anévrisme. Entre un et deux stents à la bouche de l'anévrisme, sur la base des gradients de pression et de l'analyse de corrélation de pression, aucun changement significatif n'a été observé. *Conclusion:* Il existe un potentiel pour une nouvelle méthode de stent utilisant des stents coronaires dans le traitement de l'anévrisme cérébral.

Mots-clés: anévrismes cérébraux, angioplastie, déviateur de flux, stent

Introduction

Cerebral aneurysms are common in clinical practice (1-3). Autopsy studies show an incidence of about 1 to 5% in general population (2). The disease has a common prevalence spread across all age groups (4). Angiographic studies report a prevalence of about 0.65%(5), whereas MRI studies report an incidence of 3 to 5% (6, 7). Also, the estimated incidence of rupture by these aneurysms yielding subarachnoid haemorrhage is about 1/10,000 cases with an incidence of 27,000 cases/yr. in the US alone (2). The rupture rates vary based on the size of the aneurysms (3). The risk of rupture is largely based on the size of the aneurysms with a risk varying from 2.5% for aneurysms less than 7 mm and >50% for aneurysms >25 mm. Women and hypertension have increased the risk of rupture (8). Patient-age inversely and cigarette-smoking correlate with aneurysm risk (9). There is a tendency for familial clustering of these aneurysms (10). The mean observed the one-year risk of rupture was 1.4%. The Finnish and Japanese have 3 to 6 times higher risk of rupture (11).

Rupture of these aneurysms leads to subarachnoid haemorrhages, which often result in high mortality and morbidity. Patients with ruptured aneurysms are usually moribund, and their recovery is also slower. The rupture of these aneurysms is directly related to the size of the aneurysms though ruptures are also seen in smaller aneurysms. Controversy exists regarding the management of this disease (12). At present surgical clipping and endovascular treatment methods are available for therapy (13, 14). Surgical clipping is associated with similar complications in comparison to endovascular methods by studies (15, 16). At present, endovascular coiling and flow diversion stents are commonly used methods of treatment (14). Coiling requires high technical expertise and precision. Endovascular coiling is associated with 7.8% of peri-procedural morbidity and 2% mortality, which is predominantly due to thromboembolic complications. Balloon associated coiling is associated with 9.8% morbidity and 4% mortality. The stent-assisted coiling is associated with 19% peri-procedural complications and 2% mortality. The other option available is multi-layered flow diversion stents (17-23). These stents are multi-layered the trackability is difficult, and the stents are expensive. Also due to their multi-layered build, the cerebral perforators could be occluded during and after deployment and also the restenosis rates are higher. Early and late thromboembolic complications are higher, and these devices have a morbidity rate of 4% and mortality rate of about 4% and overall complication rates of about 16 to 19%. The technical failure rate is about 10% for these devices, and they are usually deployed with 8F sheath through groin puncture. Hence, in this study a single-layered drug-eluting coronary stents were used to evaluate its performance in cerebral aneurysm models, which could be used in 6F femoral sheaths.

Methods

Aneurysm model

Coronary aneurysm model was procured from Elastrat, Geneva, Switzerland. The aneurysm model used in the study is shown in the figure 1. The aneurysm sizes were given in the figure. The experimental set-up of the aneurysms and the cerebral vessel model is shown in figure 2. Six coronary stents (cobalt chromium drug eluting) were selected, and they were planned to deploy in the across the mouth of an aneurysm. The aneurysms were further modified for pressure measurements. Hence, custom-made attachments were made on the wall of the aneurysms for pressure measurements. Pressure probes were placed in the main

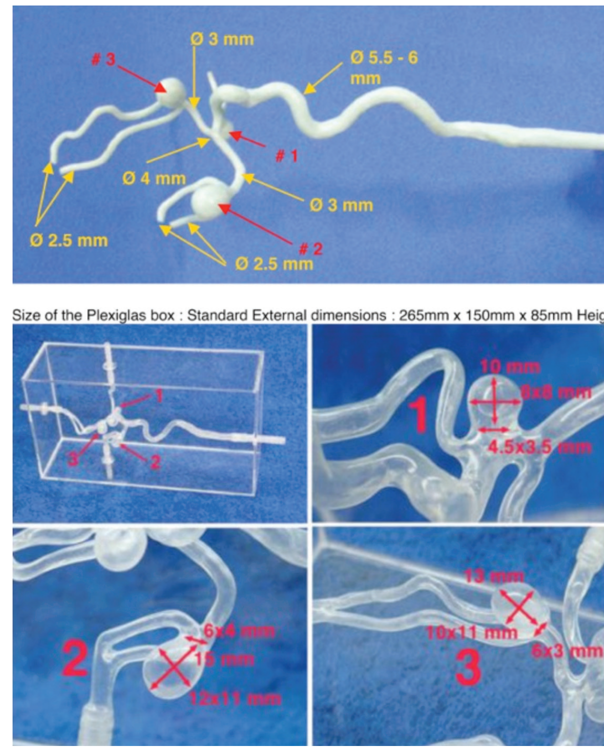

Figura 1. Aneurysm model with dimensions and cerebral arteries

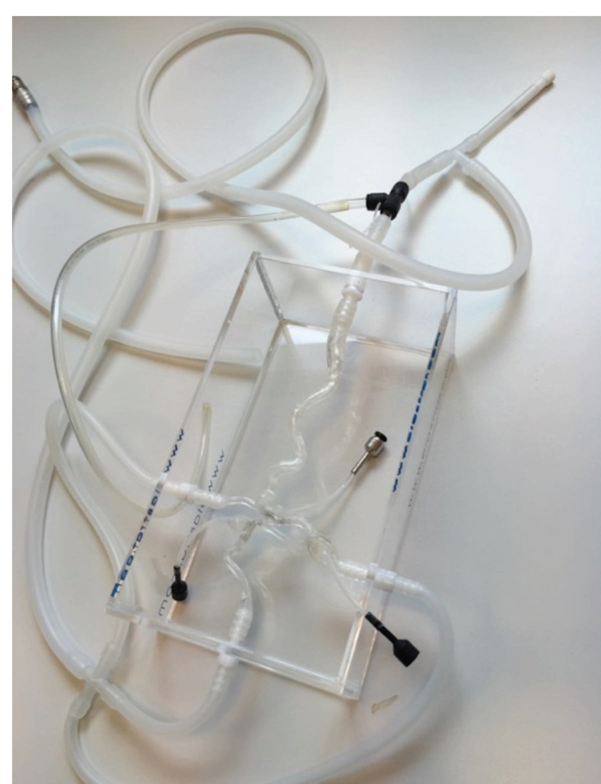

Figura 2. Shows experimental setup used in the study.

vessel. Also, the other side of the pressure transducer was connected to the pressure probe from the aneurysm wall. The model was connected to the continuous pulsatile flow system with a frequency of 72 beats /min.

Right internal carotid artery model including three aneurysm models (Elastrat) was inserted in the simplified pulsatile flow test bench. This tester allows simulating pressure and flow waveforms that approximate physiological conditions. A servo-control data system (Compact DAQ including voltage IO modules - National Instrument) ensured the repeatability of flow monitoring, and of pressure measurements. Gear pump allowed the pulsatile flow in the circuit.

The test consists in evaluating the pressures in aneurysm models under defined physiological flow condition before and after stent deployment at aneurysm inflow orifice. The flow condition was tuned. The pressures in artery model and aneurysm are recorded with a 500 Hz frequency using numerical data acquisition system (Compact DAQ - National Instrument). Then two stents were successively positioned and deployed in front of aneurysm inflow orifice sequentially, and the pressures in artery model and aneurysm were recorded a second time after deployment of the second stent. The instantaneous pressure waveforms were measured and stored 20 times from consecutive cycles. The mean of the cycles was taken and projected into one beat. The test and the pressure circuit used in the study are shown in figure 3.

This procedure was applied to each aneurysm model. Devices were prepared in compliance with preparation operating procedure OLE0916 (Protomedlabs). Prior testing, pressure catheter calibration is performed according to the operating procedure OLE0506 (Protomedlabs). All tests are done following the trial operating procedure OLE1506. Control of bias was done for pressure measurements (accuracy of +/-2 mmHg) and temperature regulation (+/-2°C). While recording the pressures the pressure load was increased from (systolic/diastolic) 120/80 mmHg to 190/110 mmHg and this sequence was maintained in all the nine recordings accurately.

Stent Deployment

The stents were deployed abutting the mouth of the aneurysm. The disposition of the stents appeared like the 'guitar-strings' across the aneurysm. The stents were taken over the 014 BMW wires and were deployed across the aneurysm mouth at balloon infla-

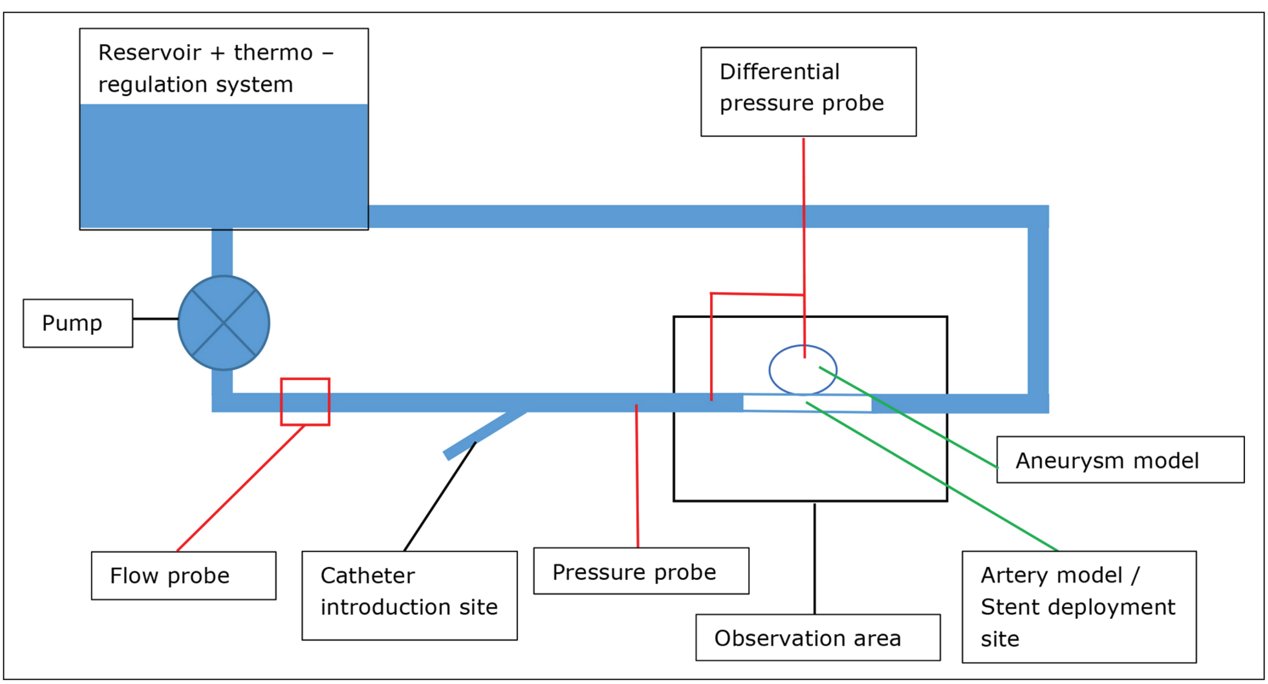

Figura 3. Diagram of mechanical pressure circuit, disposition of the aneurysmal model and placement of pressure probes

tion pressures of 12 to 14 atm. Microcatheters were not used in this technique. Thereafter, the second stent was taken similarly over the 014 wire and deployed by balloon inflation.

Results

The stents could be deployed across the mouth of the coronary aneurysms by over the wire (014) technique (figure 4). The pressure recordings obtained are shown in the pictures (Supplementary figure 1, 2, 3 in Appendix). The pressure recordings were further modified to analyses the positive and negative tracings. The results achieved are shown in the figure 5.

The pressure recordings in the cerebral aneurysms show a lesser tendency for negative dips, which reflects that the chances of the pressure inside an aneurysm being higher than the main vessel would be less. The pressure difference between the main vessel and the aneurysm, however, is not significant. As the pressure (test) circuit is closed, the pressures have to equilibrate. Hence, in the closed-circuit model, the pressure difference may not be significant.

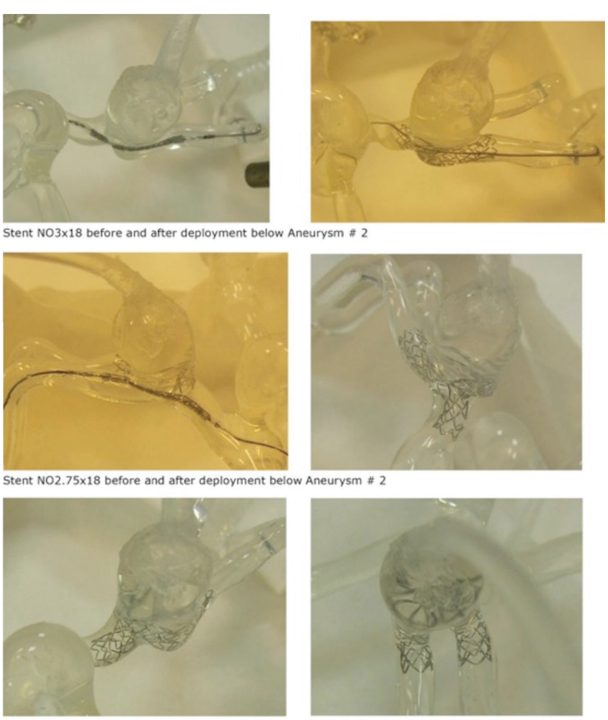

Figura 4. Photographs of experimental setup after deployment of stents across the aneurysm model

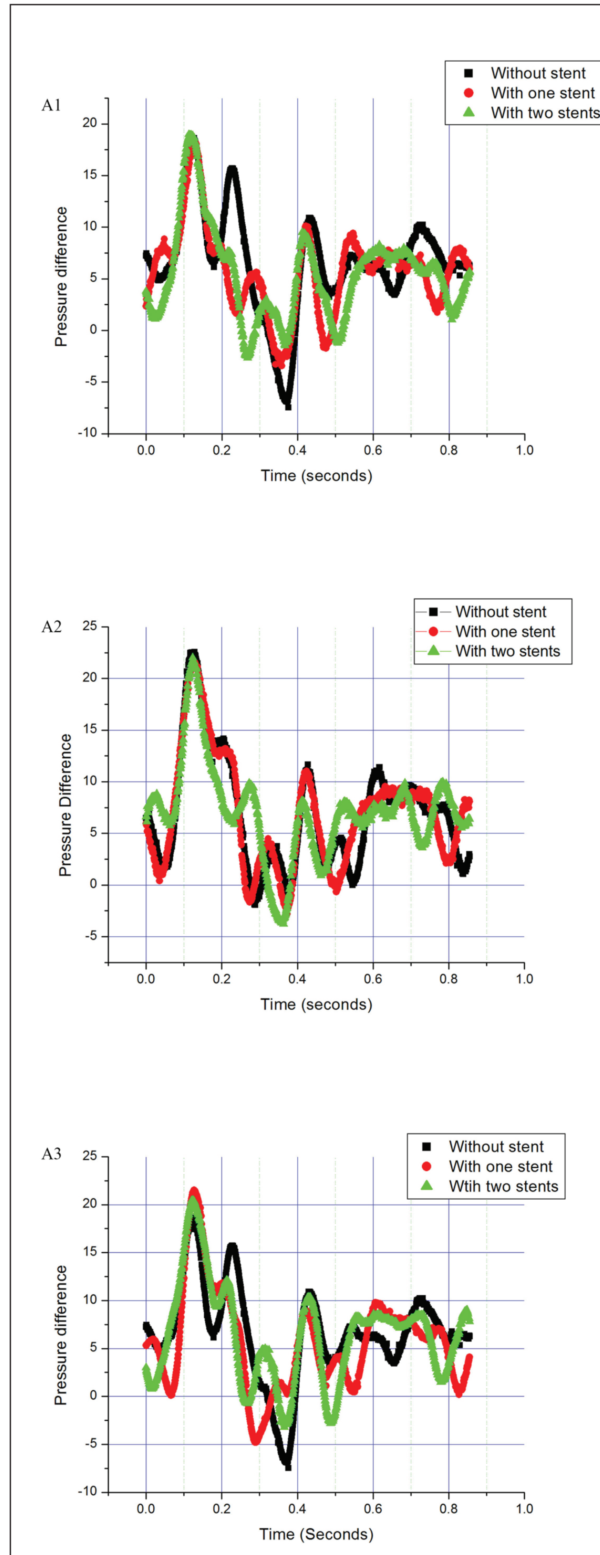

Figura 5. Pressure difference observations between the main vessel and aneurysms

Further analysis was performed with pressure tracings, and the pressure load was given simultaneously. Based on the pressure results correlation graphs were constructed, and further analysis was performed. The pressure correlation graph showed a significant pressure hysteresis, and the hysteresis was not very different from one stent and two stent deployments (Figure 6), which is explicit in the graph. The pressure hysteresis reflects the energy changes after stent deployment. The area inside the hysteresis loop reflects the resistance or the energy saved by the stent. The existing governing flow equations were then analysed, and the results of the obtained analysis were correlated.

Discussion

This study has shown the possible benefits of a novel flow-divider, which is a coronary stent method in the therapy of cerebral aneurysms. This is telescoping coronary stents as a pipeline embolization device instead of the currently available devices. In the past single layered stents were investigated in carotid aneurysms with initial success. However, single layer method was not used clinically as the aneurysm occlusion rates are less than 50%. In the past CFD studies have shown good results with a reduction in velocity of flow inside the aneurysms in a highly porous stent (82%, Wall stent), as well as a decrease in wall shear stress

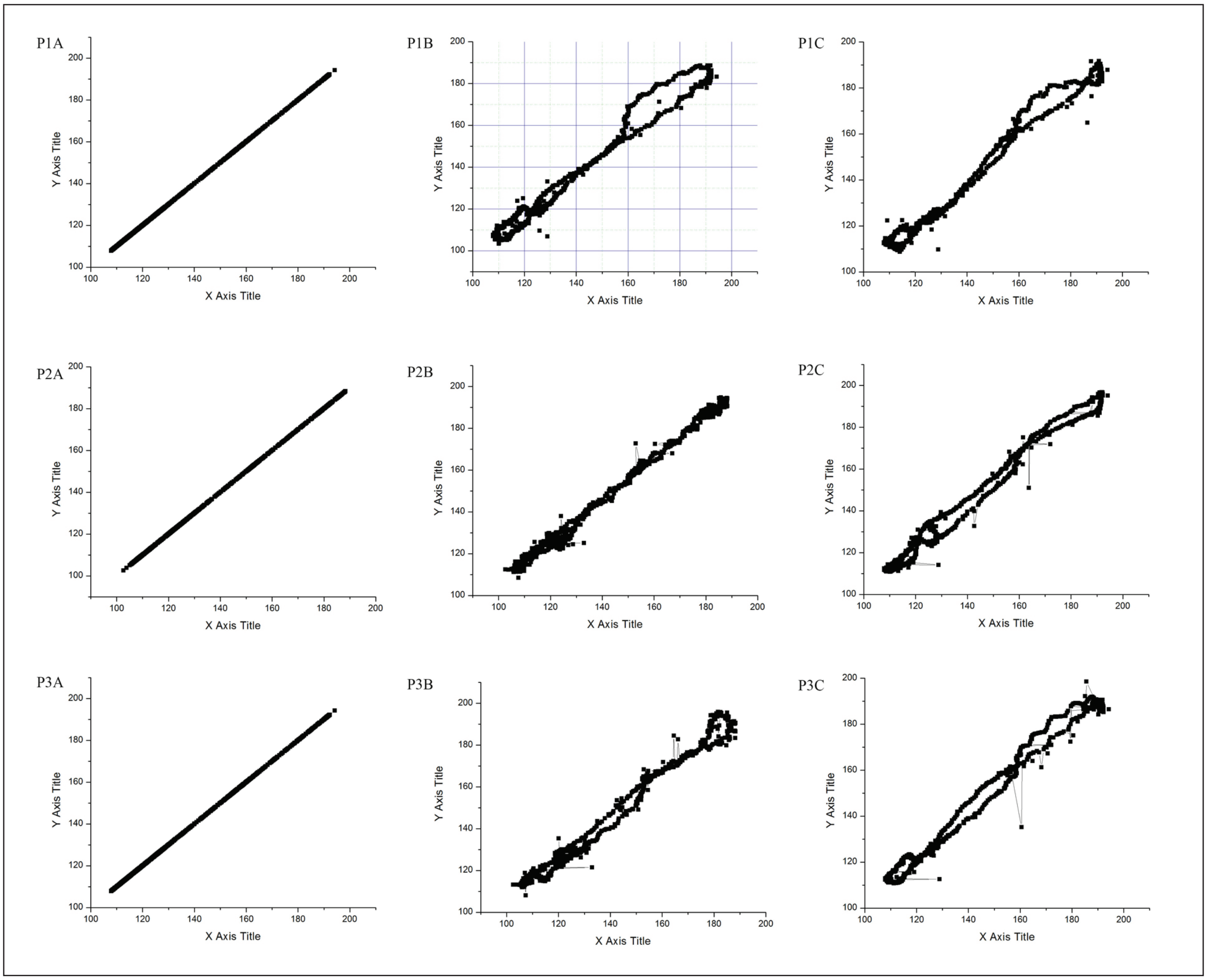

Figura 6. Pressure correlation curves before stenting (left panels), after deployment of one (middle panels) and two stents (right panels)

(24, 25). Also, a comparison of flow diverter stents has shown variations in hemodynamics in the cerebral aneurysms (26).

Hysteresis in pressure-correlation

The pressure correlation graph has shown only marginal pressure hysteresis. However, for the long-term basis, the results are promising as the energy saved (EH) by pressure hysteresis, as an exponential calculation for many days and years could be significant. For example, for one year (EH x72 beats x 60 min x 24 hours x 365 days), which appears significant mathematically. Also, biological remodelling is not taken into consideration in this calculation. If the biological remodelling is introduced the calculation is extrapolated and the energy saved would be higher. The energy saved would correlate with sizes by mass-energy equivalence principle, which is applicable for the fluids also (27). The stent thickness used in this study was 110 μm. The cobalt chromium stent has a Poisson's ratio (transverse contraction strain/longitudinal extension strain) of 0.29. The self-expanding nitinol stents have a Poisson's ratio of about 0.34 and vessel wall has a Poisson's ratio of about 0.5. Hence, a nitinol-based stent could result in better results, but it is speculative at the current moment. A coronary stent with strut thickness of 80 to 90 microns placed across a vessel usually occupies 15 to 20% of the metallic surface area (MSA) of the vessel (28). This porosity varies based on the stent strut thickness. Hence, when this stent is placed across an aneurysm due to the reduction in the effective surface area the velocity of fluid flow across the aneurysm increases, which is according to Bernoulli's principle (A1-As) * V1 = A2 * V2, where As is the area occupied by the stent, and hence V1 increases (29). When the velocity increases the pressure difference (δP) across the artery increases, which is predominantly an increase in δp/δx and the δp/δy reduces. Also, when the strut thickness is increased this metallic surface area increases further, for example, a strut thickness of 110 microns will have a metallic surface area of 23%, and the strut thickness of 140microns can have a metallic surface area of 29%. Therefore, proportionately the velocity of fluid flow tends to increase. The pressure on the wall is given by the mathematical formula, δp/δn = - (δp/δx)*sin(theta) + (δp/δy)*cos(theta). Hence, due to streamlining of flow to certain extent sine (θ) angle increases in the x-axis, and the cos (θ) function in y-axis reduces. However, this flow modification property needs to be verified by computational fluid dynamics.

Technical features

The deployment of the coronary stent has some difficulties since the cerebral vessels are tortuous. However, compared to the flow diversion stents, which are multi-layered the deployment of this coronary stent method as a flow divider method is easier. Flow diversion/pipeline stents are being evaluated in small clinical trials (patient numbers <100) and they have shown a morbidity of 1.6 to 7% and a mortality rate of 4 to 8% (30). This is also confirmed with multi-centric studies (31-36). Also, the device occlusion in the future is about 30%. Delayed parenchymal haemorrhage rates vary between 2% to 8.5% (14). Interestingly the rupture of an aneurysm in the late follow-up is rare (<1%). The thromboembolic complication rate is about 7.5% (34). A high mortality rate for this elective procedure is not very appreciable. Also, a device deployment difficulty rate of about 11 to 21% is observed (30, 35). The coronary stents are drug-coated and have stent thrombosis rates of less than 1% (37). Though a wide range of endovascular devices are upcoming in the market for endovascular treatment of the aneurysms the complication profile is not very attractive (38).

It is worthwhile to study these stents, which are time-tested in the coronaries, and they are a single-layered stent, which is easy to deploy with a low-profile guide catheters (5F or 6F). Interestingly these stents are even compatible with 6F diagnostic catheters, which are more steerable and up to 4mm diameter stents can be deployed using a diagnostic right Judkins catheter. Since these stents are balloon-mounted, it could cause some mechanical damages to the aneurysm wall during deployment, and hence a self-expanding non-balloon mounted nitinol-based stents, which are available commercially (Stentys™) could be evaluated. Alternatively, low-pressure deployments could be evaluated with balloon-mounted stents. Cerebral vessels are more tortuous than coronary vessels, however, this better trackability requirements can be overcome by newer generation of coronary stents which are quite flexible.

Advantages and modifications

The advantage of being single-layered is that the vascular compromise on the perforator branches and the capillaries supplying the normal surrounding brain structures would be lesser. Also, this would result in the lesser incidence of peri-procedural thromboembolic/stroke events. The incidence of cerebral vessel spams during the procedure would be lesser as the stent struts are thinner and single layered compared to flow diversion/pipeline stents. If spasm is a major concern then a self-expanding stent, for example, nitinol based self-apposing stents (Stentys™) could be a better alternative as deployment is simple and it is not balloon mounted (39).

The major advantage of this technique is that it is simple, cost-effective and technically this requires less skill to deploy that other techniques. Complications like perforations, cerebral vasospasms, and stroke risks would be significantly lesser as the metal load is less. Though it is speculative at this current scenario, this technique needs to be tested and validated in animal/human studies with follow-up. Since the coronary stents were tested vastly in the coronaries, it is worthwhile to study in the cerebral aneurysms. If this single layer coronary stent technique reduces the rate of growth of aneurysms, it is appreciable as full aneurysm closure is not always required for a clinical benefit. Technically the expertise required for using the coronary stents is less compared to flow diversion methods and endovascular coils. This technique would be especially useful in mid-range sized aneurysms as the surgical results as well as the endovascular results are associated with higher rate of complications in an asymptomatic individual, which is an apprehension in the day-to-day clinical practice. While the model seems to be useful at the level of carotid siphon aneurysms and post-traumatic and iatrogenic aneurysms, the technical characteristics of the stent make it unlikely that it will work properly in the perforating vessels.

Furthermore, since a high rate of apprehension or reluctance is seen in asymptomatic patients with these aneurysms initially this coronary stent technique can be performed. If there is aneurysm expansion subsequent to this technique, at a later stage, the pipeline devices can be deployed thereafter. The drug-eluting nature of these stents will have the additional advantage of low side branch occlusion and higher perforator patency.

Limitations

The study was performed in-vitro, and the results have to be explored in a live animal model with cerebral aneurysms. Biological remodelling of the vessel wall, which adds more strength to the vessel wall and potential could result in reduced aneurysmal rupture risk, needs to be studied. Computational fluid dynamics study would show more information in this circumstance, which needs to be performed to look for changes in wall shear stress.

Conclusion

There is potential for a novel coronary stent-based flow divider method in the treatment of cerebral aneurysms. Further *in vivo* and *in vitro* studies are required to validate the results.

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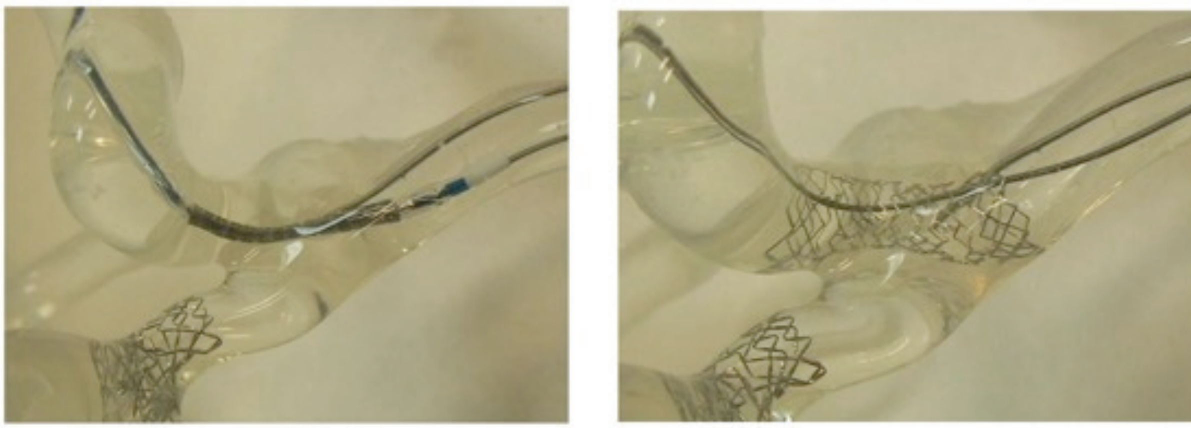
References

1. Gabriel J. E. Rinkel, Mamuka Djibuti, Ale Algra and J. van Gijn. Prevalence and Risk of Rupture of Intracranial Aneurysms. Stroke. 1998; 29: 251-256.
2. Brisman JL, Song JK, Newell DW. Cerebral aneurysms. N Engl J Med 2006; 355: 928-939.
3. Wiebers DO, Whisnant JP, Huston J 3rd, et al. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet 2003; 362: 103-110.
4. Vlak M, Algra A, Brandenburg R, Rinkel G. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. The Lancet Neurology. 2011; 10(7): 626-636.
5. Winn HR, Jane JA Sr, Taylor J, Kaiser D, Britz GW. Prevalence of asymptomatic incidental aneurysms: review of 4568 arteriograms. J Neurosurg 2002; 96: 43-49.

6. Horikoshi T, Akiyama I, Yamagata Z, Nukui H. Retrospective analysis of the prevalence of asymptomatic cerebral aneurysm in 4518 patients undergoing magnetic resonance angiography—when does cerebral aneurysm develop? Neurol Med Chir (Tokyo) 2002; 42: 105-112.
7. Jeon TY, Jeon P, Kim KH. Prevalence of unruptured intracranial aneurysm on MR angiography. Korean J Radiol 2011; 12: 547-553.
8. Morita A, Kirino T, Hashi K, et al. The natural course of unruptured cerebral aneurysms in a Japanese cohort. N Engl J Med 2012; 366: 2474-2482.
9. Juvela S, Poussa K, Lehto H, Porras M. Natural history of unruptured intracranial aneurysms: a long-term follow-up study. Stroke 2013; 44: 2414-2421.
10. Kojima M, Nagasawa S, Lee YE, Takeichi Y, Tsuda E, Mabuchi N. Asymptomatic familial cerebral aneurysms. Neurosurgery 1998; 43: 776-781.
11. Greving JP, Wermer MJ, Brown RD Jr, et al. Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. Lancet Neurol 2014; 13: 59-66.
12. Brown RD Jr, Broderick JP. Unruptured intracranial aneurysms: epidemiology, natural history, management options, and familial screening. Lancet Neurol 2014; 13: 393-404.
13. Thompson B, Brown R, Amin-Hanjani S, et al. Guidelines for the Management of Patients With Unruptured Intracranial Aneurysms. Stroke. 2015; 46: 2368-2400.
14. Pierot L, Wakhloo A. Endovascular Treatment of Intracranial Aneurysms: Current Status. Stroke. 2013; 44: 2046-2054.
15. Taheri Z, Harirchian MH, Ghanaati H, et al. Comparison of endovascular coiling and surgical clipping for the treatment of intracranial aneurysms: A prospective study. Iranian Journal of Neurology. 2015; 14: 22-28.
16. Ruan C, Long H, Sun H, et al. Endovascular coiling vs. surgical clipping for unruptured intracranial aneurysm: A meta-analysis. British journal of neurosurgery. 2015; 29: 485-492.
17. Flow Diversion for Intracranial Aneurysm Management: A New Standard of Care. Fawaz al Mufti, Krishna Amaluru, Chirag D Gandhi, Charles J. Prestigiacomo. Neurotherapeutics. 2016; 13: 582-589.
18. Sadasivan C, Cesar L, Seong J, et al. An original flow diversion device for the treatment of intracranial aneurysms: Evaluation in the rabbit elastase-induced model. Stroke. 2009; 40: 952-958.
19. Nelson PK, Lylyk P, Szikora I, Wetzel SG, Wanke I, Fiorella D. The pipeline embolization device for the intracranial treatment of aneurysms trial. AJNR Am J Neuroradiol. 2011; 32: 34-40.
20. Szikora I, Berentei Z, Kulcsar Z, et al. Treatment of intracranial aneurysms by functional reconstruction of the parent artery: The budapest experience with the pipeline embolization device. Am J Neuroradiol. 2010; 31: 1139-1147.
21. Becske T, Kallmes D, Saatci I, et al. Pipeline for uncoilable or failed aneurysms: Results from a multicentre clinical trial. Radiology. 2013; 267: 858-868.
22. Kallmes D, Hanel R, Lopes D, et al. International retrospective study of the pipeline embolization device: A multicentre aneurysm treatment study. American journal of neuroradiology. 2014; 36: 108-115.
23. Kallmes DF, Brinjikji W, Boccardi E, et al. Aneurysm Study of Pipeline in an Observational Registry (ASPIRe). Interventional Neurology. 2016; 5: 89-99. doi: 10.1159/000446503.
24. Liou TM, Liou SN, Chu KL. Intra-aneurysmal flow with helix and mesh stent placement across side-wall aneurysm pore of a straight parent vessel. J Biomech Eng. 2004; 126: 36-43.
25. Kim M, Taulbee DB, Tremmel M, Meng H. Comparison of two stents in modifying cerebral aneurysm hemodynamics. Ann Biomed Eng. 2008; 36: 726-741.
26. Wang C, Tian Z, Liu J, et al. Flow diverter effect of LVIS stent on cerebral aneurysm hemodynamics: a comparison with Enterprise stents and the Pipeline device. Journal of Translational Medicine. 2016; 14: 199. doi: 10.1186/s12967-016-0959-9.
27. Palacios A. The Mass-Energy Equivalence Principle in Fluid Dynamics. Journal of High Energy Physics, Gravitation and Cosmology. 2015; 1: 48-54. doi: 10.4236/jhepgc.2015.11005.
28. Károly Dóra, Kovács Miksa, Terdik Attila, Bognár Eszter. Investigation of metallic surface area of coronary stents. Biomechanica Hungarica. 2013; 6: 1-6. ISSN 2060-0305.
29. Resnick, R. and Halliday, D. (1960), section 18-4, Physics, John Wiley & Sons, Inc.
30. D'Urso P, Lanzino G, Cloft H, Kallmes D. Flow Diversion for Intracranial Aneurysms: A Review. Stroke. 2011; 42: 2363-2368.
31. Byrne JV, Beltechi R, Yarnold JA, Birks J, Kamran M. Early experience in the treatment of intra-cranial aneurysms by endovascular flow diversion: A multicentre prospective study. PLoS One. 2010; 5: e12492.
32. Lubicz B, Collignon L, Raphaeli G, et al. Flow-diverter stent for the endovascular treatment of intracranial aneurysms: A prospective study in 29 patients with 34 aneurysms. Stroke. 2010; 41: 2247-2253.
33. Zanaty M, Chalouhi N, Tjoumakaris SI, et al. Flow-Diversion Panacea or Poison? Frontiers in Neurology. 2014; 5: 21. doi: 10.3389/fneur.2014.00021.
34. Zhou G, Su M, Yin Y, Li M. Complications associated with the use of flow-diverting devices for cerebral aneurysms: a systematic review and meta-analysis. Neurosurgical Focus. 2017; 42: E17.
35. Jinlu Yu, Lei Shi, Yongjie Yuan, Wei Wu. Research progress on complications of intracranial aneurysms with flow-diverting stents Int J Clin Exp Med. 2016; 9: 13340-13350.
36. Lv X, Yang H, Liu P, Li Y. Flow-diverter devices in the treatment of intracranial aneurysms: A meta-analysis and systematic review. The Neuroradiology Journal. 2016; 29: 66-71.
37. Buchanan GL, Basavarajaiah S, Chieffo A. Stent Thrombosis: Incidence, Predictors and New Technologies. Thrombosis 2012; Article ID 956962: 12 pages. doi: 10.1155/2012/956962.
38. Rajah G, Narayanan S, Rangel-castilla L. Update on flow divertors for the endovascular management of cerebral aneurysms. Neurosurgical Focus. 2017; 42: E2.
39. Pyxaras SA, Schmitz T, Naber CK. The stentys self apposing stent. Eurointervention 2015; 11: V147-V148.

Appendix

Supplement Figure 1: Disposition of the stents across the mouth of the aneurysms

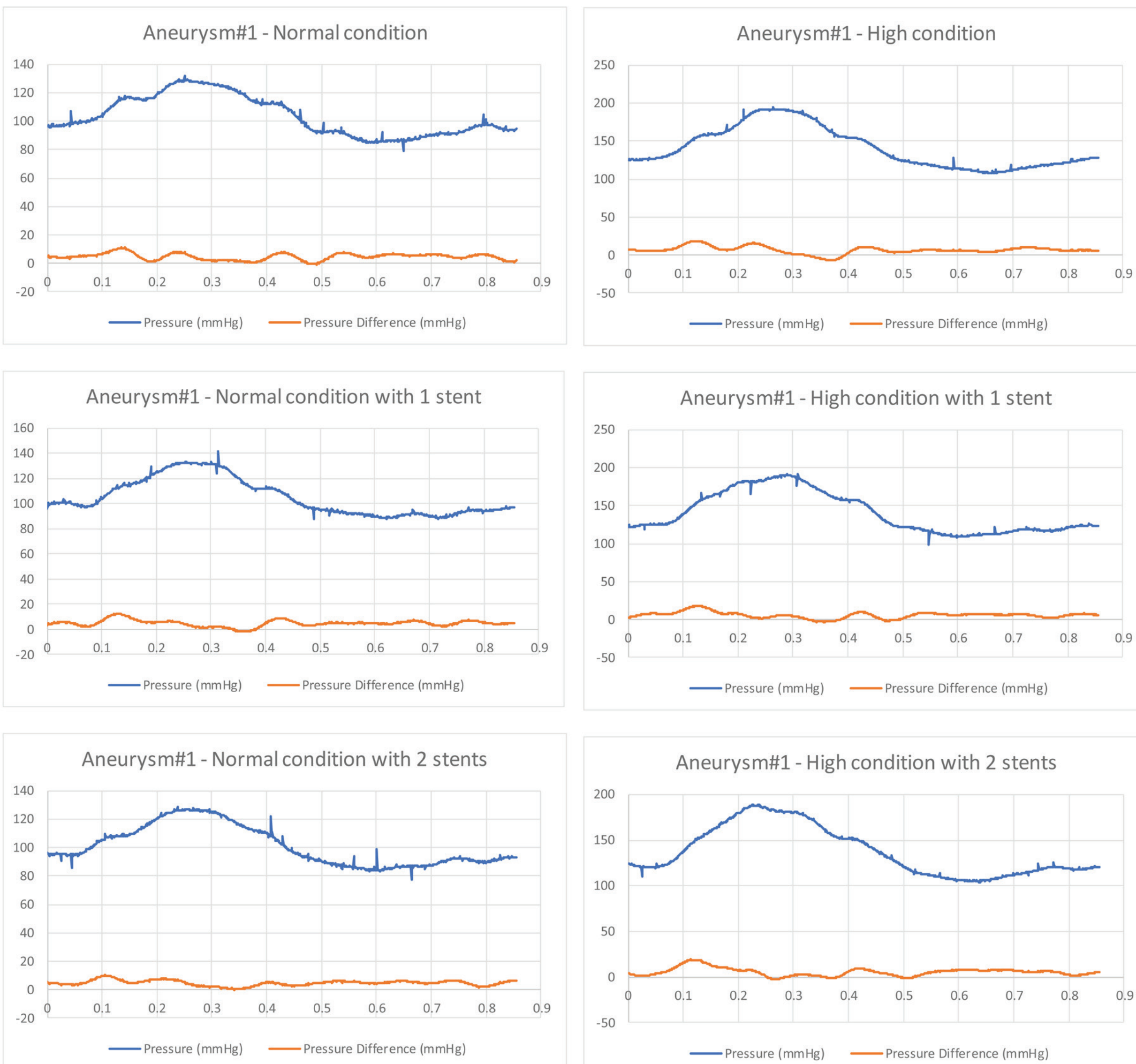


Stent ST4x16 before and after deployment below Aneurysm # 1

Stent RA4x23 before and after deployment below Aneurysm # 1

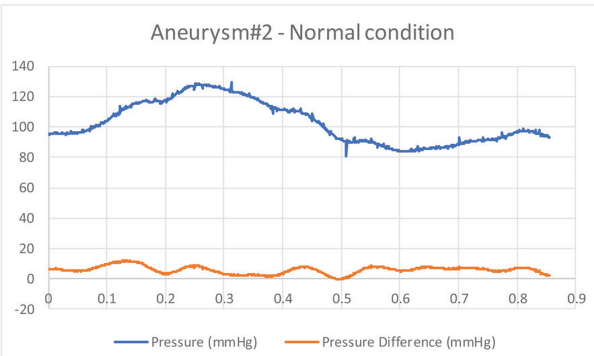
Supplement figure 2: Pressure recordings between the main vessel and the aneurysms – Aneurysm 1

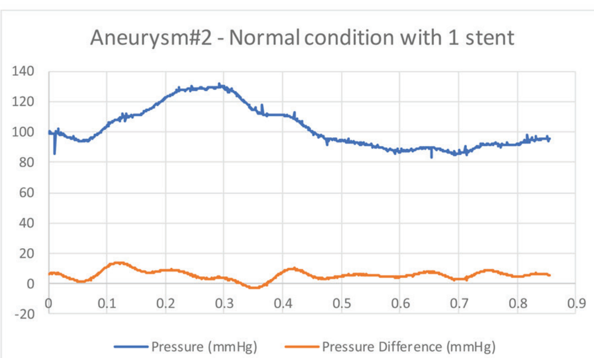
Aneurysm#1 – Normal condition **Aneurysm#1 – High pressure condition**

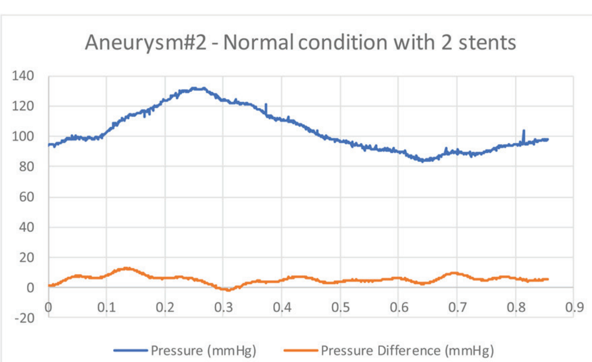


Supplement figure 3: Pressure recordings between the main vessel and the aneurysms – Aneurysm 2

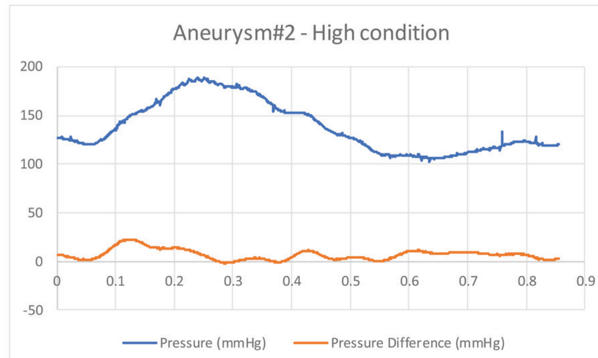
Aneurysm#2 – Normal condition

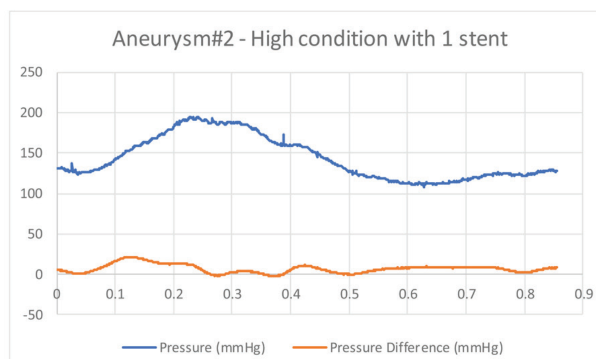


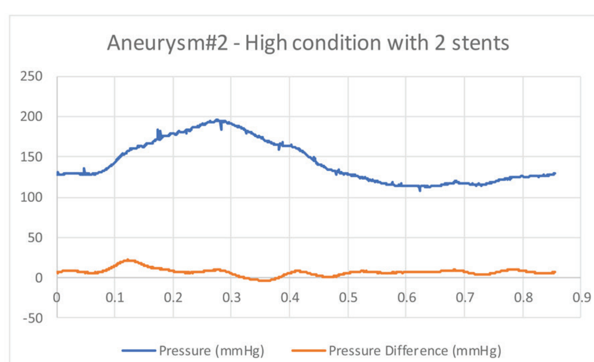




Aneurysm#2 – High pressure condition

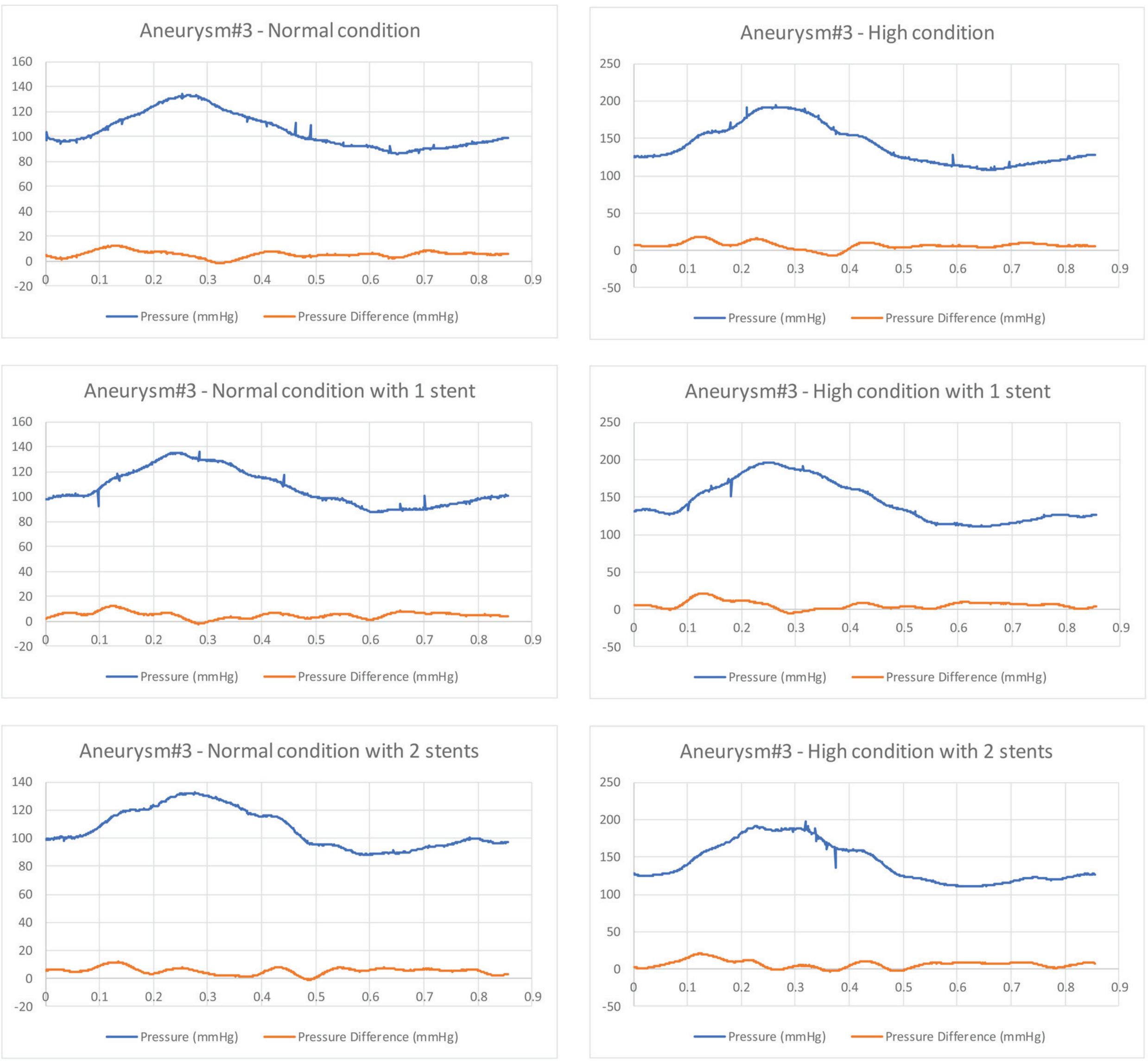






Supplement figure 4: Pressure recordings between the main vessel and the aneurysms – Aneurysm 3

Aneurysm#3 – Normal condition **Aneurysm#3 – High pressure condition**



Gruppo di studio Neuroteoretica

Associazione Alunni Collegio Fratelli Cairoli

Ordine degli Avvocati di Pavia

IRCCS Fondazione Istituto Neurologico Nazionale C. Mondino

UNIVERSITÀ DI PAVIA
Dip. Scienze del Comportamento e Sistema Nervoso e Dip. Giurisprudenza

Camere Penali di Pavia

NEUROSCIENZE, DIRITTI E SOCIETÀ - *V Edizione*

AGGRESSIVITÀ – CARATTERE E TEMPERAMENTO

ORIENTAMENTI BIO-PSICO-SOCIOLOGICI NEL CONTESTO DEL PROCESSO PENALE

Giovedì 16 Maggio 2019 - Ore 14.30 / 18.30

Aula Magna - Collegio Cairoli, P.zza Collegio Cairoli 1 (Pavia)

ORE 14.30: SALUTO AI PARTECIPANTI

Prof. Andrea Zatti, *Rettore del Collegio Fratelli Cairoli - Pavia*
Prof. Enrico Oddone, *Presidente Associazione Alunni Collegio Fratelli Cairoli - Pavia*
Prof. Giuseppe Nappi, *Presidente onorario Gruppo di Studio di Neuroteoretica - Pavia*
Prof. Livio Tronconi, *Direttore generale IRCCS Istituto Neurologico "C. Mondino" - Pavia*
Dr. Annamaria Gatto, *Presidente Tribunale Pavia*
Avv. Roberto Ianco, *Presidente Ordine degli Avvocati Pavia*
Avv. Mariarosa Carisano, *Presidente Camera Penale Pavia*

MODERATORI Avv. Graziano Lissandrin, *Presidente del Gruppo di Studio di Neuroteoretica*
Prof. Franco Maria Avato, *Prof. Ord. a r. Medicina Legale Univ. di Ferrara – Presidente CIRNA*

Dilemmi diagnostici ed esigenze valutative nell'ambito penale
Dott. Mario Venditti, Procuratore della Repubblica Aggiunto Tribunale di Pavia

Dinamiche neuropsichiche nella provocazione e nell'offesa
Dr. Pier Giuseppe Milanesi, Prof. Giorgio Sandrini, Coordinatori scientifici Gruppo di Studio di Neuroteoretica

Discussione e Coffee Break

La predizione dell'aggressività recidiva nella valutazione tecnica della pericolosità sociale
Prof. Cristiano Barbieri, Università degli Studi di Pavia, Dipartimento di Giurisprudenza
Università Cattolica del Sacro Cuore - Sede di Piacenza, Dipartimento Scienze Giuridiche

Le radici sociali del comportamento aggressivo nell'adolescente
Dott. Gianni Schiesaro – Sociologo – Ex direttore Fondazione Adolescere – Voghera (PV)

Discussione finale e chiusura dei lavori

La partecipazione è libera. E' consigliata la preregistrazione e la richiesta va fatta pervenire all'avv.to Luisa Currà (Gruppo di studio di Neuroteoretica) all'indirizzo e-mail: l.curra@avvocatocurra.it. L'evento è accreditato ai fini della formazione continua dell'Ordine degli Avvocati di Pavia e conferisce n. 3 crediti formativi. I crediti verranno assegnati fino al raggiungimento del numero previsto (100 partecipanti) e raggiunto all'atto della registrazione in sede congressuale.
Coordinamento: Fulvia Bianchi, Gruppo di Studio di Neuroteoretica - Pavia
Segreteria: Geom. Vincenzo lista, Centro di Cultura e Partecipazione Civile Città del Sole, Pavia.

Fondazione CIRNA ONLUS

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