Possibilities for reducing procedural embolisation in the endovascular treatment of cervical carotid artery stenosis

Ph.D. thesis

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PhD Thesis

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List of original publications cited in the thesis

l. **Szikra P**, Vörös E, Sztriha L, Szólics A, Csikász T. (2005) The force transmission of the distal endings of stent delivery systems. *Hungarian Radiology*, 2005;79 (5):228–233.

ll. **Szikra P**, Vörös E, Sztriha L, Szólics A. (2007) Transcranial Doppler monitoring of distal embolism during carotid stenting. *Hungarian Radiology*, 2007;81 (1–2):46–51.

lll. **Szikra P**, Vörös E, Sztriha L, Szólics A, Palkó A. (2008) Forces exerted on the plaques during in vitro measurements by various carotid stent delivery systems and embolic protection devices. *Hungarian Radiology*, 2008;82 (5–6):202 – 205.

lV. **Szikra P**, Boda K, Rarosi F, Thury A, Barzó P, Németh T, Vörös E, (2016) Aortic arch and common carotid artery plaques with soft components pose a substantial risk of cerebral embolisation during carotid stenting. *Interventional Neuroradiology*, (accepted for publication February 2016.)

List of publications related to the subject of the thesis

l. Szentgyörgyi R, Vörös E, Pócsik A, Makai A, Barzó P, Sztriha L, **Szikra P**, Palkó A. (2003) Stroke prevention: Initial experiences with endovascular treatment of internal carotid artery stenosis. *Hungarian Radiology*, 2003;77:6 – 14.

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V. Szólics A, Vörös E, Sztriha L, **Szikra P**, Szólics M, Palkó A. (2008) Use of covered stents in the endovascular treatment of extracranial stenosis of the internal carotid artery. Hungarian Radiology, 2008;82 (1-2):34–39.

Vl. Szólics A, Sztriha L, **Szikra P**, Szólics M, Palkó A, Vörös E. (2009) The use of covered stents for the endovascular treatment of extracranial internal carotid artery stenosis: a prospective study with a 5-year follow-up. *European Radiology*, DOI 10.1007/s00330-009-1696-8

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List of Abbreviations:

AA aortic arch
ADC apparent diffusion coefficient
BMS bare metal stent
CAS carotid artery stenting
CCA common carotid artery
CEA carotid endartrectomy
CTA computed tomography angiography
DSA digital subtraction angiography
DWI diffusion weighted imaging
ECA external carotid artery
EPD embolic protection device
F French
HITS high intensity transient signals
ICA internal carotid artery
MES microembolic signal
MI myocardial infarction
MRI magnetic resonance imaging
OTW over the wire
POD proximal occlusion device
PTA percutaneous transluminal angioplasty
PTFE poly-tetra-fluor-ethylene
SDS stent delivery system
TCD Transcranial Doppler Ultrasound
TIA transient ischaemic attack

Introduction

Supra-aortic vessels, including the internal carotid artery (ICA) which is one of the main blood supplier of the brain, may be affected by steno-occlusive processes most often atherosclerosis. Embolisation from an atherosclerotic vessel wall or stenosis of critical level may result in transient ischaemic attack (TIA) or ischaemic stroke. Ischaemia is the predominant cause of stroke, causing some 83% of all stroke events [1]. About 40-50,000 people diagnosed with stroke end up in health care institutions a year in Hungary; stroke accounts for 15% of all mortalities in this country and it is also one of the key causes of death worldwide [2,3]. In addition to treatments with medicines and surgical interventions, the treatment of ICA stenosis has become an accepted form of treatment. The endovascular treatment of carotid artery stenosis – carotid artery stenting, (CAS) – is, if performed by an experienced and well-prepared interventional neuroradiologist, equivalent from the aspect of complications in patients, to carotid artery endarterectomy (CEA) performed by an experienced surgeon [1]. Recent clinical comparative studies have found practically equal aggregated morbi-mortality rates in the case of CAS and CEA. While in the case of stenting the risk of periprocedural embolisation is higher, in the case of surgery there are higher risks of acute myocardial infarction (AMI), surgery-related infection and complications associated with anaesthesiology [4,5]. Considering these facts it is obvious that the risks of embolisation of CAS shall be reduced in order to improve success rate of endovascular therapy.

Endovascular catheters and stents used in the treatment of ICA stenosis are variants of devices developed for the haemodynamic reconstruction of peripheral and coronary vessels. Elimination of distal embolisation triggered by the use of catheters was not among the objectives pursued in the development of catheters used in blood flow reconstruction to improve the blood supply of muscle tissues. While in the course of the endovascular treatment of peripheral and coronary artery stenosis a possible embolisation does not result in severe complications thanks to the good collateral network to be found in muscles (resulting from the characteristics of the muscle tissue), in the case of the catheter treatment of an ICA stenosis embolisation resulting from the mechanical manipulation of the plaque-covered vessel may lead to cerebral infarction. Since in the course of the intervention the catheter may come into contact with spontaneously embolising plaques covering the inside of the vessel wall, the force exerted by the catheters and the resistance of embolising plaques to such physical contact may affect the rate of complications resulting from ICA stenting. Knowledge of the dislodging capability of devices used in the intervention and the plaque resistance to mechanical manipulation playing a role in embolisation may help the interventionist in selecting the therapy that is most suitable for the patient concerned.

1. A historical overview

1.1 Evolution of endovascular treatment of ICA

It was on 1 November 1964 that Charles T. Dotter and Melvin P. Judkins successfully carried out dilatation by catheter dilation in a femoral artery, recanalising the vessel by pushing a series of catheters of increasing diameters through the stenotic section, starting thereby what has developed into a highly successful therapy comprising the dilation of blood vessels by catheters [6]. The next major step was taken by Andreas Gruentzig in 1977 by using an inflatable balloon catheter for the dilation of the coronary artery [7]. The dilation of a brachiocephalic vessel with a balloon catheter took place for the first time in the early 1980s; Amir Motarjeme and his team reported on initial results of the dilation of the subclavian artery, the vertebral artery and the common carotid artery (CCA) [8]. One of the pioneers of the catheter dilation of the ICA, Klaus Mathias reported – together with Bockenheimer – of successful case in 1983 [9]. The first direct comparison of the results of ICA balloon dilation to the results of standard surgical intervention showed a higher rate of complications; as a consequence of embolisation, elastic recoil and restenosis occurring during catheter treatment, carotid endarterectomy (CEA) continued to be the gold standard form of treatment [10]. Nevertheless, promising results were achieved thanks to the advancement of technologies and improvements in the intervention itself: it was Krisztina Szász in Hungary who carried out more than 70 successful PTA interventions, while Kachel et al. also reported of good results [11]. It was this period during which the first publications appeared concerning favourable clinical experiences – in comparison to simple balloon inflation – relating to the implantation of stents (metal meshes) in coronary vessels to prevent elastic recoil and in the way of acute treatment of intimal injuries. This technique then revolutionised the catheter therapy [12,13]. It was quite evident therefore that this technique came to be applied in order to reduce complications occurring in the course of ICA dilation and to accomplish the expected more favourable long term results as the first clinical results actually reflected a promising improvement in comparison to dilation by balloon catheters [14]. This was followed by a series of comparative studies focusing on the efficacy of CAS and CEA but neither therapeutic method was found to be absolutely superior relative to the other. It was found that in high risk patients – having at least one other condition accompanying the stenosis resulting in increased risks of surgery – the CEA technique entailed significantly higher cardio-vascular risk than endovascular therapy /SAPPHIRE trial/ [15]. The EVA-3S study however, was prematurely stopped based on considerations of safety,

with reference to failures encountered in the application of the CAS technique. According to results recorded in the treatment of 527 patients the CAS treatment produced twice the rate of complications than did the CEA approach [16]. It should be noted however, that some of the teams performing endovascular intervention were still in the early phases of their learning curves and this fact renders the conclusions drawn from comparison to results produced by experienced vascular surgeons somewhat doubtful. The results of the latest clinical comparative studies indicate similar morbid-mortality rates for CAS and CEA alike. While in the case of stenting higher risks result from the periprocedural embolisation rate, in the case of surgery AMI, infection or complications relating to anaesthesiology entail higher risks [4]. The embologeneity of endovascular treatment may be reduced by increasing knowledge of diagnostic possibilities and the role played by used devices in embolisation.

1.2 Diagnostics in ICA stenosis

In the case of patients with ICA stenosis accurate anamnesis – including knowledge of risk factors or positive family case history – is required for the selection of the most suitable therapy. Even in the phase of the basic general medical examination the bruit – blowing vascular sound with stethoscope – heard over the carotid arteries may be indicative of an ICA stenosis. Ultrasound examination is the most widely applied imaging diagnostic method in the diagnostic of ICA stenosis; it is capable of showing, in addition to the degree of the stenosis, the thickness of the blood vessel, a fundamental differentiation of the plaques and the direction and speed of the blood flow as well. One disadvantage of the ultrasound technique is relative blindness in the case of a distally localised ICA stenosis. Computed tomographic angiography (CTA) – generating more information on the morphology of the stenosis and on the plaque components than an ultrasound examination but entailing a radiation and contrast medium load – may provide an accurate diagnosis. CTA and magnetic resonance angiography (MRA) are suitable for the examination of highly localised stenoses as well as the aortic arch (AA) and the intracranial blood vessel systems. Disadvantages of the MRA technique include its high sensitiveness to movement, the contrast medium load and that it cannot be applied in the case of the presence of a non-MR compatible implant.

Digital subtraction angiography (DSA) is still an indispensable invasive examination method applied in the endovascular treatment of ICA stenosis. This method enables a dynamic

examination of haemodynamic conditions in both the area of the stenosis and the regions supplied with blood by the carotid system. A DSA examination is suitable for establishing the degree of the stenosis and – in the case of an interventional treatment – the optimum sizes of the catheters to be used. Showing only a contrast medium column and the supply of limited information on the plaque and the vessel wall are noted as the disadvantages of this imaging technique, along with the contrast medium load and embolisation resulting from the use of catheters. The disadvantages may be alleviated by carrying out a DSA examination only of the ICA area to be treated, relying on findings of an earlier CTA or MRA examination. The method called Transcranial Doppler examination (TCD) is suitable for generating information on intracranial flow conditions. The method is capable of detecting high intensity transient signals (HITS), indicating the presence of solid and gaseous emboli in the blood stream [17]. The method is also suitable for the detection of embolisation in the course of catheter manipulation [18].

The technique that is suitable for early detection of distal embolisation occurring in the course of a CAS intervention is called diffusion weighted MR imaging (DWI), as it is more sensitive in revealing early ischaemic lesions than other MRI sequences (T2, FLAIR / fluid attenuated inversion recovery/, T1) and CT. In the course of the development of a cytotoxic oedema the diffusion of water molecules can be measured in terms of what is referred to as apparent diffusion coefficient (ADC). Distal embolisation occurring in the course of the treatment can be quantified with the help of the ADC value (which is low in such cases) and the high intensity DWI signal, therefore it is a generally accepted method for the detection of embolisation caused by the dislodging of plaques by the insertion of catheters [19].

1.3 A historical overview of interventional devices used in the endovascular treatment of ICA stenosis

1982 is considered to be the year when the “classic” basic tools of intervention, that are still in use today, including the shapeable guide wire, the guiding catheter and the over the wire (OTW) balloon catheter, were first used in a combination [20]. Carotid angioplasty was carried out first with the help of OTW balloon catheters inserted with a guide wire of 0.035” in diameter through a femoral artery puncture. Instead of using guide wires, in some cases interventionists used diagnostic catheters positioned in the aortic arch through the contralateral femoral artery in performing the control angiographic examination.

Guidewires:

The guidewire – fairly thick by today's standards – available back then together with the balloon catheter inserted with it, did not make it possible to dilate high grade stenosis owing to the limitations on being guided through the stenosis. At that time guidewires were stainless steel core devices with a soft radiopaque loop at the distal end. The "core-to-distal-tip" design of the wire enabled good pushability and great trackability which may be regarded as disadvantageous attributes with a view to the higher likelihood of the dislodging of carotid plaques. To make it more slippery and to prevent the potential settlement of thrombus, the tools were coated with poly-tetra-fluor-ethylene (PTFE). The interventionist could form the most suitable shape at the distal end of the guidewire for catheterising the patient, but the core-to-tip tools did not keep their shapes for very long. An improved technology was what is called "shaping ribbon" where the core did not reach as far as the tip at the distal end; a wire made of a shape-keeping alloy attached to the tip helped maintaining the required form of the tip of the device. This design contributed not only to the durability of the shape but it also equipped the device with a soft atraumatic tip that is crucially important in avoiding the risk of dislodging plaques. The next significant step in the development of atraumatic guidewire tips came in the form of the super-elastic distal catheter tips made of an alloy called Nitinol. Thus the distal end of the wire became very soft and far more resistant to crumpling and breaking than steel tips. (Figure 1).

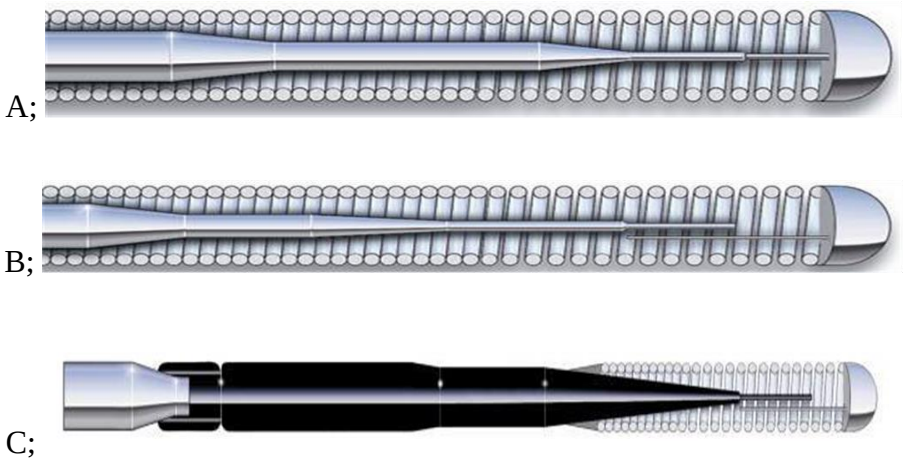


Figure 1: The picture A shows the steel core reaching the distal end of the wire (core-to-tip). The picture B is that of a steel core wire design of a good shape-keeping atraumatic tip (shaping ribbon), while the picture C displays a Nitinol core super-elastic wire design with a shape-keeping tip. (Source http://www.abbottvascular.com/us/products/coronary-intervention)

Further progress was made in the development of guide wires by the application of hydrophilic coatings that are even more slippery than Teflon coating. By binding water molecules hydrophilic fibres can keep blood constituents that are responsible for the forming of thrombus (Figure 2)

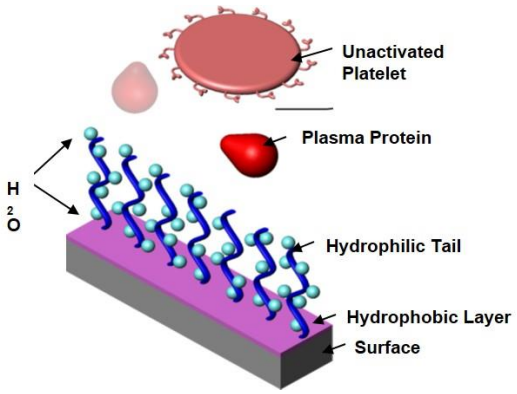


Figure 2: The principle of the operation of hydrophilic coating. (Source Crossroads Institute; Park Lane – Culliganlaan 2B. 1831 Diegem – Belgium: Crossroad Institute Coronary intervention training 2007.)

The polymer technology offering countless possibilities for manipulating the toughness and flexibility of the wire is still being the preferred one among interventionists undertaking carotid interventions, thanks to its low friction contact with plaque and its suitability for being delivered even through very narrow stenosis. A guide wire of a plain polymer surface with a hydrophilic coating requires very cautious manipulation as it easily slides underneath plaques or even through vessel walls (Figure 3)

Figure 3: Polymer-coated guide wire (Source http://www.wikidoc.org/index.php/Guidewire)

The diameters of guide wires used today in carotid interventions have been reduced considerably: with their reduced profile and as a result of progress made in the manufacturing technology 0.014" guide wires can be put through even subtotal occlusions.

Balloon catheters:

Initially, it was the type of balloon catheters used in dilating peripheral vessels that was also applied by interventionists in ICA dilation. Once the balloon was successfully inserted into the

stenosis, the most important requirement to be met by the tool was resistance to bursting under the required dilation force. Primarily sharp plaques with calcified surfaces could rip open catheters pumped up to 18-20 atmospheres and the explosive escape of fluid and gas bubbles present as a consequence of inadequate degassing could cause severe complications. Consequently, interventionists performing carotid angioplasty preferred more highly burst-resistant multi-layer balloon catheters which could be quickly deflated after the dilation of the vessel, in order to cut the time during which blood flow was blocked in the vessel section concerned (Figure 4).

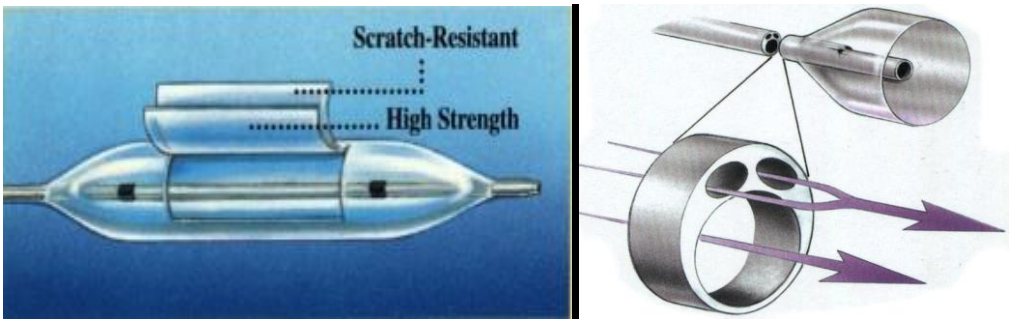


Figure 4: Balloon catheters developed for carotid dilation are protected from bursting by a multi-layer shell. An increased number of in-deflation channels of increased diameters provide for quick deflation.(Source Boston Scientific endovascular training 2002./ Ballybrit Business Park, Ballybrit, Galway, Ireland)

The most recent step in the development of balloon materials has resulted in reduced wall thickness through the integration of the layers, which may be more advantageous from the aspect of embologenity when the catheter is being put through the vessel thanks to its smaller crossing profile and increased trackability (Figure 5).

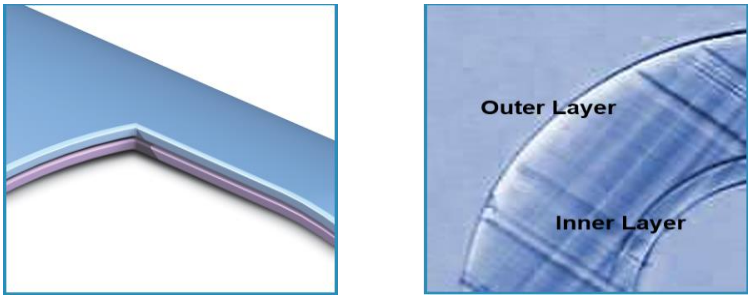


Figure 5: The sandwich structure resulting from the integration of layers in place to provide resistance to bursting and those ensuring resistance to pressure endows the balloon with improved physical parameters with a reduced layer thickness. (Source Abbott Vascular endovascular and coronary intervention training 2010. Cairo, Egypt)

In cases of severe stenosis the catheter's trackability – and thus the likelihood of dislodging of an embolus – is affected by the balloon catheter's diameter before inflation (that is, its crossing profile), the catheter's slipperiness, pushability and the design of the distal tip. Besides the diameters of guide wires those of balloon catheters were also reduced as a result of the advancement of the technologies applied in their manufacture. The hydrophilic coating applied to wires was also applied to balloons to ease crossing stenosis. It is the distal tip's function to bridge the difference between the diameter of the guide wire that has already been put through the stenosis and that of the balloon catheter tip, without dislodging the plaque. The balloon catheters offered today for carotid interventions are a lot more advanced than the comparable earlier devices in this regard as well (Figure 6).

Figure 6: There is a major difference between the distal tips of earlier balloon catheters (black) and modern ones (purple) that can be inflated to the same size. The smooth transition between the balloon tip and the guidewire is an advantage from the aspect of trackability. (Source Abbott Vascular endovascular and coronary intervention training 2010. Cairo, Egypt)

Carotid angioplasty is carried out today with stent implantation together in order to have higher protection from intraprocedural symptoms. Since a sharp-edged calcified plaque is on contact with the stent and not with the balloon, there is a reduced likelihood of bursting during postdilation. In the majority of cases after implantation the stent undergoes on postdilation with the help of a balloon catheter, in which case a hydrophilic coating may be disadvantageous owing to the risk of the balloon's slipping out of the stent while being inflated, which might result in damaging the blood vessel. Today's most cutting edge balloon catheters with hydrophilic coating are recommended only for predilation. Balloon catheters of non-slip materials have been developed for postdilation.

Stents:

The positive experiences gained from the stenting of coronary and peripheral vessel stenosis were promising reasonable application of stents in carotid angioplasty as well, in the 1990s. In the majority of cases cervical internal carotid artery plaques build up at the bifurcation of the common

carotid artery (CCA), affecting both the CCA and the ICA vessels, as a result of turbulences observed at vessel bifurcations [21]. The cervical ICA section is exposed to external impacts (hits) therefore the implant that has been implanted must survive such traumas without getting deformed. This criterion is only met by self-expanding stents; balloon-mounted stents (BMS) collapse under heavy external pressure and a metal mesh not aligned to the internal vessel wall, blocking the flow of blood may cause thrombo-embolic complications (Figure 7).

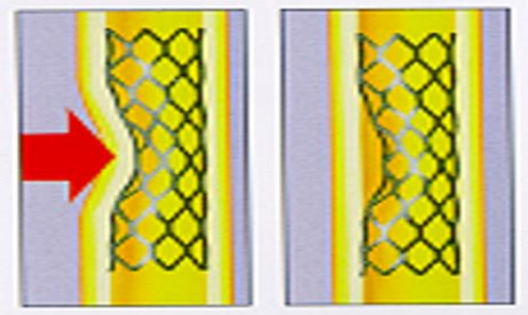


Figure 7: Balloon-mounted stent protruded into the vessel lumen as a consequence of an external impact. (Source Boston Scientific endovascular training 2002. / Ballybrit Business Park, Ballybrit, Galway, Ireland)

Another important reason for choosing self-expanding stents for CAS is that only such stents can bridge the difference between the inside diameter of the CCA and that of the ICA. While the internal CCA diameter tends to fall in the 6-9 mm range, the internal ICA diameter is typically 4-6 mm, resulting in some cases in up to 2 mm differences in size. Accordingly, self-expanding stents were used right from the outset, with the expansive force stemming from the Easy Wallstent's (Boston Scientific, 300 Boston Scientific Way, Marlborough, MA 01752, US) own flexibility as well as the heat-expandable Smart stent (Cordis Corporation, 6500 Paseo Padre Pkwy, Fremont, CA 94555, US) product. Both implants were developed for dilating the arteria iliaca system, inserted with 0.035" guide wires. The device was of a rather robust structure in comparison to today's devices. Experts of neurointervention were quick to realise that atraumatic trackability might be a crucial criterion for the successful treatment of ICA stenosis therefore they started to look around among devices that had been developed by manufacturers for other specific purposes, as no tools developed specifically for the treatment of ICA stenoses were to be found on the market in the late 1990s. A manufacturer came to focus on the Magic Wallstent coronary stent – of a similar structure but with a different delivery system and different parameters – on the basis of which it developed, by introducing some modifications, what came to be known as OTW and

Monorail Carotid Wallstent (Boston Scientific), the latter of which is still one of the most widely applied stents in the treatment of patients with ICA stenoses. The Monorail Carotid Wallstent differs from the Easy Wallstent in terms of both its delivery system (SDS) and its physical parameters. While the OTW delivery system requires a wire channel along the full length of the tool, in the monorail system only the distal section of the catheter accommodates a wire channel, while the wire exiting through the side of the tool runs in parallel in the guide catheter in its proximal section (Figure 8).

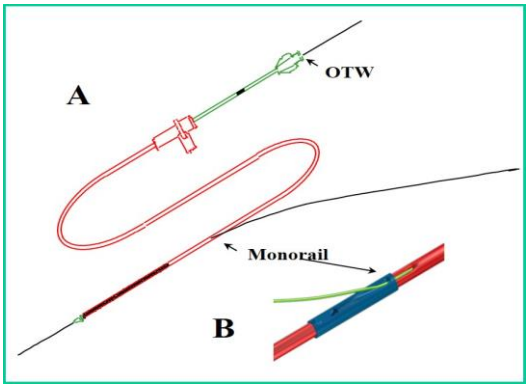


Figure 8: Differences between the over the wire (OTW) and the monorail system. (Source Boston Scientific endovascular training 2002. / Ballybrit Business Park, Ballybrit, Galway, Ireland)

The monorail system enables the use of a shorter, therefore more manageable, guide wire, while the stent delivery system of a smaller diameter makes it possible to put it through high grade stenoses. The stent mesh structure remained unchanged but the angle between the wires was changed, resulting in smaller cells (Figure 9).

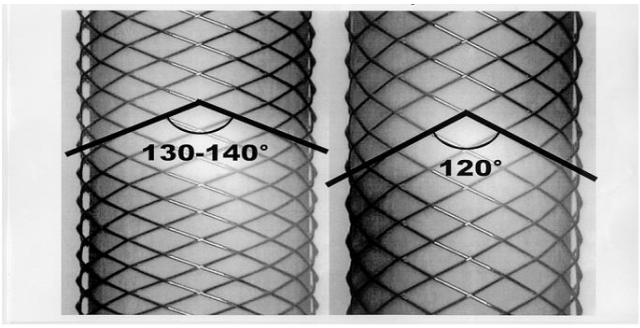


Figure 9: The wider angle between the wires making up the grid produces a denser mesh than the 120 grid structure of the Easy Wallstent. (Source Boston Scientific, endovascular training 2002. /Prague, Czech Republic)

The issue of the stent cell size had already been dealt with in the case of early balloon-mounted stents used in cardiology, in relation to which even a specific technical term, "*unsupported surface area*" was introduced, to denote the size of the area of the vessel wall/plaque that is not propped up by the stent mesh. While in cardiology the cell size is of importance primarily because of the need to keep the side branch open when the bifurcation is stented, in the case of CAS the better plaque coverage capability of the closed cell controls the maximum size and quantity of emboli passing through the stent mesh according to the findings of Bosier et al. [22]. In the development of carotid stents manufacturers are creating designs producing increased coverage rates, where the stent's proximal part – which is attached to the CCA – is of a less dense structure, it is aligned more tightly to the vessel wall, less heavily impeding the blood supply of the external carotid artery (ECA). The mesh making up the middle part or the distal end of the implant – the larger part of the plaque tends to be present in the ICA section – is denser. In the course of the development of self-expanding stents tapered implants were also introduced in order to reduce the stress caused by the diameter difference. It should also be noted however, that advantages or disadvantages of neither the tapered design nor the different cell design have been clinically proven so far (Figure 10).

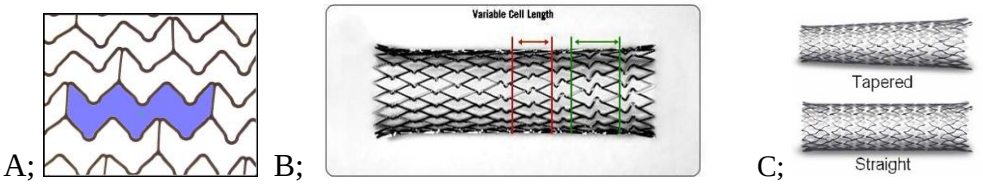


Figure 10: The unsupported surface area (the blue area), that is, the unbroken surface not covered by the stent mesh (A). The shorter cells in the middle of the carotid stent produce a higher mesh density (B). The tapered stent design reduces the stress stemming from the difference between the diameter of the CCA and that of the ICA (C). (Source Crossroads Institute; Crossroad Institute Carotid intervention training 2009)

In our discussion of the history of the evolution of plaque stabilising implants used in carotid angioplasty mention should also be made of some promising results achieved by applying covered stents. The technology applied in this field was originally developed in order to keep in place the soft crumbly embologenic material settling on the narrowed saphenal vein graft wall after coronary bypass operations (Figure 11). Our team has successfully implanted a product called

Symbiot stentgraft (Boston Scientific) in quite a number of patients with plaques limited to the ICA area without affecting the CCA section.

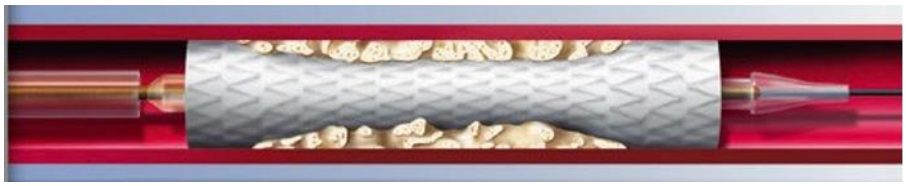


Figure 11: The Symbiot stentgraft excludes the plaque from the circulation. (Source Boston Scientific endovascular training 2002. / Ballybrit Business Park, Ballybrit, Galway, Ireland) (Source Boston Scientific)

In the case of ICA stentgraft implantation that is correctly positioned under TCD control our team found no embolisation either at the time of implantation or during postdilation [23]. The role played by implants applied in carotid angioplasty – studied, analysed and discussed by our team earlier – is not discussed in this paper.

Stents used in cardiological interventions today are increasingly made from – instead of metals – bioabsorbable drug-eluting polymers, making it possible for the foreign material to disappear from the human body through the absorption of the implant, together with all other related favourable consequences [24]. Carotid stents are also expected to be affected by the development of this technology which may add to the benefits of the catheter treatment of ICA stenosis in comparison to other therapies.

Embolic protection devices:

Focusing on the prevention of cerebral embolization during carotid stenting is the first and foremost priority. The first protection device to use was PercuSurge Guardwire, (Medtronic, Minneapolis, MN) but its use was hindered by inability to angiographically visualize the target lesion during stent deployment, the occasional patient intolerance to cessation of cerebral blood flow, and the fact that emboli could still reach the brain through external carotid artery collaterals, or at the completion of procedure due to incomplete aspiration [25]. The appearance of filter-type distal protection devices swiftly replaced the distal occlusion balloon, because did not occlude cerebral blood flow, allowed visualization of the stenosis during stent deployment, and filters being small guidewire-like devices were compatible with the existing conventional CAS instruments. Filters are on the other hand, are only partially protective, allowing particles smaller than their pore size to pass, and by not conforming to the vessel shape accurately the emboli could

pass by the filter. Furthermore these devices could cause severe spasms, occasionally are difficult to retrieve, and the filter can become so filled that spilling debris must be removed separately by aspiration before filter recovery [26,27]. In theory, proximal occlusion devices (POD) should be more effective than filters, as abovementioned shortcomings of filters are absent. A POD device is placed and functioning before the lesion, providing protection without the need of crossing the stenosis itself. On the other hand PODs share the same drawbacks associated with flow occlusion as with distal carotid occlusion devices and the bulkiness of devices is another concern (8-10F).
The lack of proven efficacy of carotid EPDs to reduce clinical events is problematic as there are complications related to their use [28-30] (Figure 12).

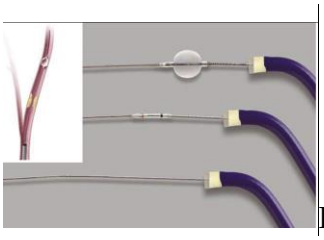
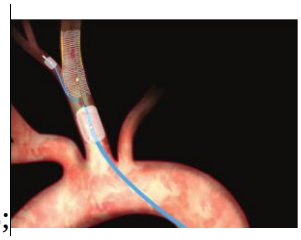
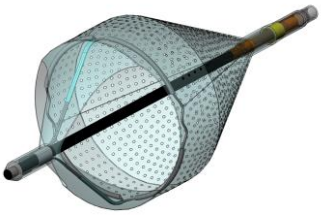
A;  B;  C; 

Figure 12: Distal occlusion balloon (A), proximal occlusion (B) and filter-type distal protection devices(C).(Source A;http://circ.ahajournals.org/content/113/22/2651/F2.expansion.html, B;http://www.endovascularmagazine.eu/articles/2012-09/Mono-Mo-Ma/ C;http://www.abbottvascular.com/us/products/carotid-intervention/nav6.html)

Aims

The specific aims of our investigations were as follows:

- To study of the catheter manipulation steps required for the endovascular treatment of ICA stenosis in order to establish the degree of embolization using TCD monitoring.
- To study the force exerted by the distal conical tips of various SDSs put through the ICA stenosis in order to identify tools with the potentially least embologenic tips.

- To study different embolic protection devices (EPD) and SDSs pushed through ICA stenoses, from the aspect of the force exerted on plaques covering the vessel wall, on ICA models of various angles of curvature and to analyse forces affecting the vessel wall in arteries with curvatures of different angles in order to determine devices and vessel curvature angles of low embologeneity.
- To study the impacts of the AA and CCA plaques on distal embolisation during CAS by plaque components and localisation in order to select patients who are expected to have the lowest embolic complication rate in the course of procedure.

2. Study of TCD monitoring of distal embolism during carotid stenting

2.1 Introduction

In the endovascular treatment of ICA stenosis the various phases of the intervention are carried out using devices of different parameters (including material, diameter, structure, design). The devices of different functions and physical parameters are assumed to entail different risks and likelihoods of embolisation. It is also assumed that real time TCD measurement of the dislodging of plaques by the different tools in the different phases of the intervention may help the interventionist recognise embolisation caused by catheter manipulation, and improve his/her movements that might potentially most directly contribute to the embolising effect.

2.2 Subjects and methods

Intraprocedural TCD examinations were performed between August 2005 and February 2006 during the procedure of stenting ICA lesions at our institute on a total of 50 patients, 33 of whom were men (aged: 46-77, average age: 62 years), and 17 women (age: 50-80, average age: 64 years), see table 1.

Patients	
Population	50 (100%)
Men	33 (66%)
Age	46-80 years
Average age ± SD years	63.2 ± 7.4
70-79 years	15 (30%)
80-89 years	1 (2%)
Comorbidity	
Diabetes Mellitus	15 (30%)
Hypertonia	43 (86%)
Hyperlipidaemia	34 (68%)
Smoking	13 (26%)
Severe cardiac dysfunction (NYHA 3,4)	8 (16%)

Table 1. Patient demography

Endovascular treatment of the ICA stenosis was carried on patients in whom plaques settled in the carotid bifurcation and/or in the internal carotid artery showing stenosis at least at the level of 70%. The severity of the stenosis was established by ultrasound examination before the intervention, complemented when necessary by CTA or MRA. The interventions were directly preceded – in the same time – by diagnostic four-vessel DSA examinations. Each intervention was carried out by the same experienced interventional neuro-radiologist. The interventions were performed on the basis of and in accordance with the relevant international standards [31] and efforts were made to avoid embolisation-related complications by using the lowest profile tools available and by very cautious manipulation. Based on our own experience and in view of manufacturers' recommendations systems of tools best suited to the given circumstances were used, minimising the patients' risk of complications to the best of our knowledge. A treatment of a combined daily dose of 100 mg aspirin and 75 mg was started at least 4 days before each intervention and it was continued for at least 4 weeks after the intervention. During the intervention itself, the patients were administered 5000 international units' of heparin, repeated not more than once, when it was necessary. No EPD were used, predilation was required in 20% of the cases (in 9 out of 50 patients), for which we used balloons, 5 or 6 mm in diameter. In the

rest of the cases direct stenting was carried out. Three different types of suitably-sized self-expanding stents were used: a total of 24 Carotid Wallstent, along with 10 Precise RX stent and 15 Xact stent (Abbott Vascular, 3200 Lakeside Drive. Santa Clara, California 95054-2807, United States). Postdilation was performed in 79.6% of the cases (in 39 patients out of 50). The residual stenosis never exceeded 30%. During each intervention the condition and status of the patient, his/her vital parameters, including heart frequency and rhythm, were continuously monitored by an anaesthesiologist. In the case of bradycardia occurring in the course of balloon-dilation (not more than 2 mg) intravenous atropine was administered, as necessary. Control angiograms were performed after stenting to document the results of stenting and the state of the intracranial branches i.e. to exclude macroembolisation.

The TCD examinations were carried out with a Multi-Dop® T (DWL Elektronische Systeme GmbH) transcranial Doppler ultrasound machine. The ipsilateral a. cerebri media was insonated with a 2 MHz ultrasound head through the temporal window to a depth of 44-58 mm. Emboli were identified on the basis of microembolic signals (MES) in accordance with the relevant international recommendations [17,18,32,33].

Detected MESs were evaluated real-time during the intervention. The results were recorded in a table prepared for this purpose. Signals detected while administering the contrast medium were eliminated from the analysis in accordance with the relevant international recommendations [33].

Clusters of multiple emboli that could not be individually distinguished were referred to as "showers" and taken into account in the evaluation of the data as comprising 15 emboli each.

The embolus detection process lasted from the insertion of the guiding catheter until the completion of the intervention. The endovascular treatment of the ICA was divided into six phases: (1) insertion and entering of the guide catheter, (2) passing the micro-guide wire through the stenosis, (3) predilation, (4) passing the stent delivery system through the stenosis, (5) stent deployment, (6) postdilation.

2.3 Results

49 (98%) of the total of 50 interventions were technically successful; in one case the stent could not be implanted owing to the severity of the stenosis and the atherosclerotic plaque location. The bilateral carotid stenosis of that particular patient was subsequently treated by CEA.

Embolisation was detected in each patient and – in most cases – in each step (Figure 12).

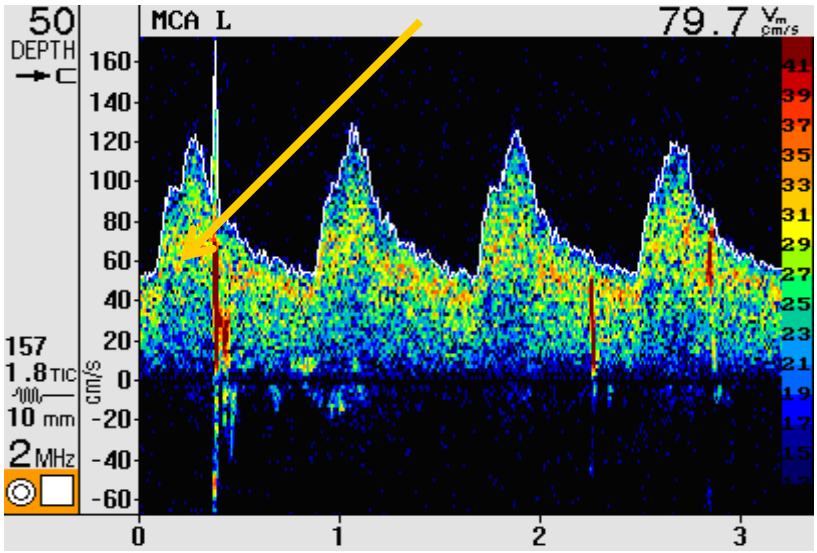


Figure 12 – MES in TCD examination (arrow)

The first step of the intervention – monitored with TCD – comprised the insertion of the guiding catheter through the femoral artery puncture in the common carotid artery of the side concerned. This particular phase of the intervention represented the lowest degree of embolisation (2.6 ± 2.9 MES) was observed. In the next step the .014" micro-guide wire was delivered through the stenosis: successfully in most cases upon the first attempt, though in some case it took minutes for the tip to pass through. The degree of embolisation was proportionate to the time it took to succeed but on the whole it was still modest (3.2 ± 2.3 MES). The most intensive embolisation was observed during predilation (15.9 ± 5.6 MES). The insertion of the stent delivery system (SDS) through the micro-guide wire triggered a 69% higher rate of embolisation than had been observed during the insertion of the micro-guide wire (5.4 ± 2.5 MES). A high rate of microembolic signals was usually observed during the opening of the stent (9.2 ± 4.4 MES), similarly to balloon postdilation (10 ± 6.7 MES). In the case of subtotal occlusions the contrast medium – that has remained static at the proximal end of the occlusion – starting to flow upon the opening of the stent probably obscured some of the signals triggered by true emboli.

A minor stroke was triggered in relation to the periprocedural embolisation in one case. No mortality was recorded within 30 days of the interventions.

2.4 Discussion

From the interventions carried out as part of our study it was concluded that in the course of the endovascular treatment of carotid stenoses some degree of micro-embolisation occurs in practically all cases.

Manipulation with guide catheter and micro-guide wire could cause the dislodging of emboli, the number of which grew with the increase of the time spent performing the intervention.

The number of emboli dislodged by SDS delivery through the stenosis exceeded that of those released by inserting the micro-guide wire, but it was still smaller than those dislodged by the steps relating to dilatation. The plaque is not stabilised by the stent during SDS delivery, therefore the embolic skill of SDS has of great importance.

The intensive embolisation upon the opening of the stent and during the balloon postdilation procedure indicates that the stents' mesh structure does not adequately cover the plaques. The self-expandable stents developed in essence for ensuring the passability are not capable of capturing the atherosclerotic debris underneath their mesh of relatively large (approximately 1-10 mm^2) holes, since by exerting pressure on the vessel wall they practically press the plaque material out of the atherosclerotic segment and this process is then further intensified by postdilation [30]. According to Ackerstaff et al. the embolic load observed during postdilation plays a crucial role in the occurrence of post-intervention cerebrovascular complications [30,34-36]. ICA stenosis treatment using covered stents also confirmed that no embolisation needs to be expected in the case of a properly covered and stabilised plaque even during postdilation. If the plaque is fully covered, no emboli can make it through the covered stent into the blood stream [23]. The effectiveness of the technique is limited by the fact that the contrast medium filling the vessel lumen has radiopacity, but plaque endings are not visible at all cases. Complete plaque stabilization is possible only if the plaque position is well defined. The uncovered part of the plaque may be damaged by the opening of the stent-ends, which, in turn may lead to embolisation. A solution to this problem may be offered by CTA or MRA examinations which can more accurately identify the extension and material of the plaque.

Our examinations have shown that the largest amounts of emboli are dislodged in the course of the stenting of the carotid artery the predilation, the stent opening and the postdilation phases. In the majority of cases the predilation phase and in many cases the postdilation phase may be skipped without jeopardising the success of the intervention [37-38].

At institutes where TCD monitoring – giving off sound signals as well during endarterectomy – has been introduced, the frequency of stroke occurrence has dropped significantly [30,39-41]. The TCD sound signals immediately informed the interventionist of the embologenity of the ongoing catheter manipulation, apparently prompting him or her to proceed even more cautiously. It has been concluded from this observation that the use of TCD with sound signals may be highly beneficial even for those in the process of mastering the technique of carotid stenting, as has also been proven in the case of endarterectomy.

Our experience shows that micro-embolisation that can always be detected in the course of the endovascular treatment of carotid stenoses remain clinically silent in most cases. It is assumed however, that the higher the intensity of the embolisation higher the risk of damage to the eloquent areas and of the development of subsequent neuro-psychological consequences [42,43]. For this very reason, steps towards reducing micro-embolisation definitely produce benefits in terms of mitigating the risk of complications.

2.5 Conclusions

The micro-embolisation that can be detected in most cases in the course of the endovascular treatment of carotid stenosis remains clinically asymptomatic in the majority of cases.

In the endovascular treatment of ICA stenosis every single step of the catheter manipulation (insertion of the guide wire; insertion of the guide catheter; predilation; SDS crossing the stenosis; stent deployment; balloon postdilation) may result embolisation. Three phases with significantly increased MES counts were identified, these were predilation, stent deployment and postdilation. Manipulation with the guide catheter and the micro-guide wire results in the dislodging of increasing numbers of emboli as time passes. The interventionist is immediately informed by the sound signals emitted by the TCD equipment about the embologeneity of the ongoing catheter manipulation.

3. The force transmission of the distal endings of stent delivery systems

3.1 Introduction

Among a number of other potential factors the distal ending of SDSs may play a particularly important role in the dislodging of plaques since during interventions – the overwhelming majority of which are carried out without predilation – they may exert considerable force on plaques. The endings of SDSs vary in terms of diameters and the shapes of the tapered tips. SDSs of diverse sizes and other physical parameters are assumed to have different impacts on the surfaces of plaques, some of which produce even spontaneous embolisation. Our study was aimed at identifying the SDS distal shape entailing the lowest risk of dislodging emboli.

3.2 Subjects and methods

Five different SDSs developed specifically for the endovascular treatment of ICA stenosis were studied with a focus on the diameters and shapes of their distal endings: Precise RX, 8x30 mm (Cordis Corporation) (**a**), Xact carotid stent 9-7x30 mm (Abbott Vascular) (**b**), Carotid Wallstent 8x29 mm (Boston Scientific) (**c**), RX Acculink 8x300 mm (Abbott Vascular) (**d**), Zilver 518, 8x30 mm (Cook Medical, 750 Daniels Way Bloomington, IN 47402-0489, USA) (**e**) (Figure 13).

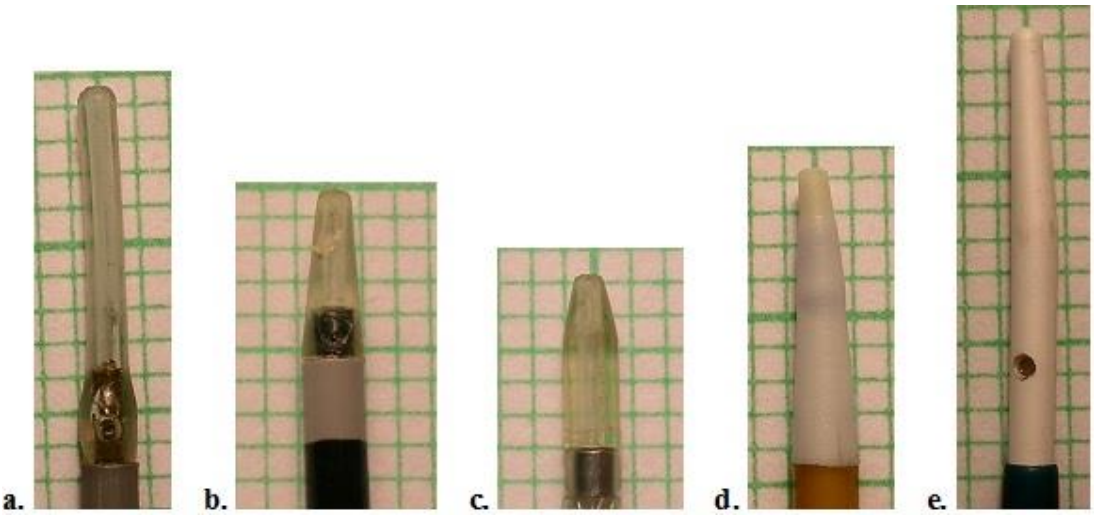


Figure 13: Distal tapered endings of the SDSs involved in the study, photographed against a background of a millimetre grid paper sheet

The 8mmx30mm SDS, the most frequently implanted device in our practice was chosen for the study of each of the above five brands.

The ratio of the largest diameter of each tool to the cross section area of a 5 mm average ICA lumen diameter was calculated – to establish the degree of the stenosis in the case of which mechanical dilatation is always carried out in pushing the tool through a stenosis in a straight section of the vessel – on the basis of the following formula:

$$\frac{(\text{„r”tool})^2 \times \pi}{2.5^2 \times \pi}$$

Each of the SDSs used in our study has a cylindrical body with a tapered ending. The vertical projection (side view) of whose conical tip of which was produced with a digital camera of a 5 megapixel resolution (Nikon Coolpix 5400). A Cartesian coordinate system was placed over the pictures, whose x-axis corresponded to the tool's longitudinal axis with the top in the origin and the cone in the positive half-plane. Measurements were taken at 0.05 mm distances along the line of the cone from the distal tip. The ruler function of the picture editing software (Microsoft Office Picture Manager) was used for taking the measurements on the cone tips superimposed over the mm grid paper. The direction angle of each section of the broken line (a polygon) approximating the shape of the device was calculated from the values measured at the x and x-0.05 spots. The calculations were carried out with the help of the MS Excel ATAN function and the pi=3.14 constant; these did not distort the results over the measurement error. The data were interpreted as indicating that where the cone's angle is below 45º the sideways force is dominant over the forward (dislodging) force (Figure 14).

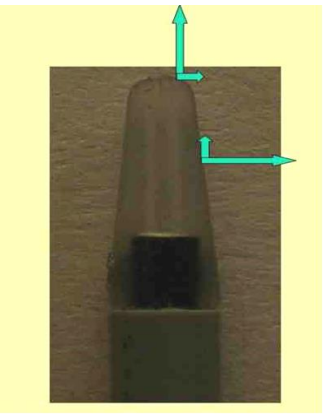


Figure 14: Forward (plaque dislodging) and sideways (plaque stabilising) force vectors on the conical tip surface, indicated by arrows.

3.3Results

The outer diameters of the SDSs involved in our study did not exceed 6 French (F) at the tool tips put through the stenoses.

The diameter of tools **b** and **d** is 6 F, or 2.0 mm, therefore they occupy 16.4% of the lumen of the ICA of an average diameter of 5 mm, accordingly, these delivery tools can be put through stenoses blocking less than 83.6% of the lumen of the same vessel, without mechanically stretching the vessel section affected by stenosis.

The diameter of tools **a**, **c** and **e** is 5 Fr, that is 1.66 mm, taking up 10.8% of the lumen of an ICA of an average diameter of 5 mm when getting pushed through, so they can be inserted through a section affected by a stenosis blocking less than 89.2% of the lumen without mechanically dilating the vessel.

Each of the device ends in a tapered cone tip, showing differences in terms of both sizes and arcs. The point where the sideways force exceeded the forward force, that is from which the cone pushes the plaque more sideways, to the vessel wall, than forwards to dislodge it, was identified relative to the distal tip for each tool. The area of the tools cross section at that particular point was calculated for each tool, specifying the percentage rate of the stenosis in the case of a 5 mm ICA diameter, through which the device can be inserted safely.

Tool **a** reaches the 45º angle where its diameter is 0.9 mm, the area of its cross section at that point is 0.6358 mm^2 which equals 3.24% of the 19.625 mm^2 cross section area of an ICA of the average 5 mm diameter, i.e. it could pass through unblocked through an up to 96.76% stenosis. The cone tip however, meets the shaft in a blunt angle, i.e. the curvature angle increases suddenly to 78.7º at that point. It is where the cone meets the shaft that the tool exerts a low enough force on the vessel wall where the diameter of the tool is such that the stenosis may not block more than 89.76% of the vessel lumen (Diagram 1).

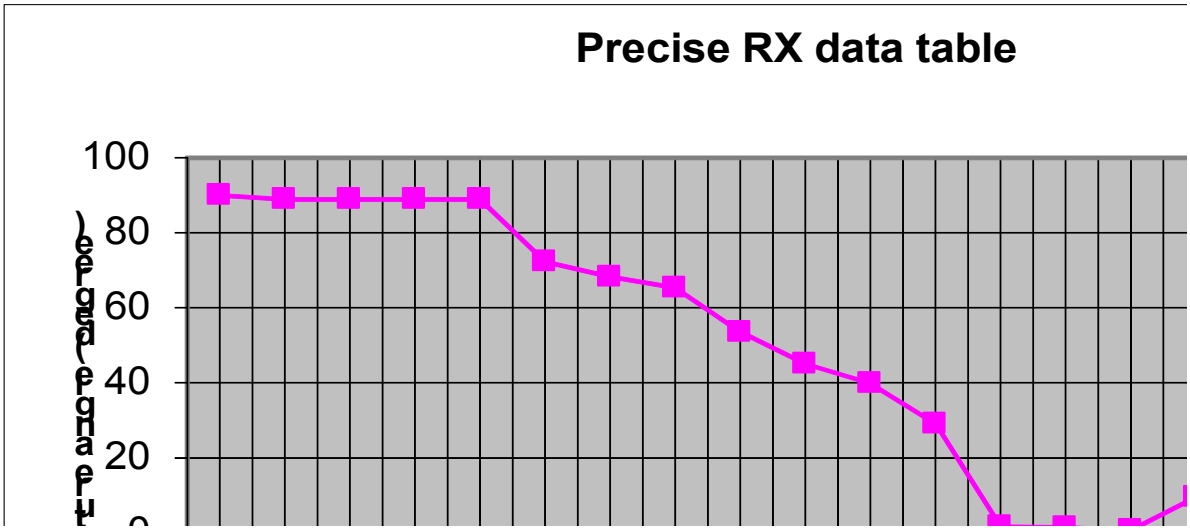


*Diagram 1: The tip of Precise RX SDS marked "**a**" meets the shaft at a sharply increased angle, exceeding the 45% limit value where the radius is 75 mm, where the dislodging force outweighs the force pressing the plaque sideways.*

The tip angle of tool **b** reaches 45º where its diameter is 0.95 mm. The area of its cross section is 0.7084 mm^2 at this point, which is 3.61% of the 19.625 mm^2 cross section of the ICA of the average diameter of 5 mm, consequently this device can be put through a stenosis blocking up to 96.39% of the lumen, with a low risk of dislodging emboli. The conical tip and the shaft are joined by a straight tapering section.

The angle of tapering of tool **c** reaches 45º where its diameter is 0.7 mm, where area of its cross section is 0.3846 mm^2, that is 1.96% of the 19.625 mm^2 cross section of the ICA of the average diameter of 5 mm, consequently this device can be put through a stenosis blocking up to 98.04% of the lumen, with a low risk of dislodging emboli. The conical tip and the shaft are joined by a straight tapering section.

The angle of tapering of tool **d** reaches 45º where its diameter is 0.8 mm, where area of its cross section is 0.5024 mm^2, that is 2.56% of the 19.625 mm^2 cross section of the ICA of the average diameter of 5 mm, consequently this device can be put through a stenosis blocking up to 97.44% of the lumen, with a low risk of dislodging emboli. The conical tip and the shaft are joined by a straight tapering section.

The angle of tapering of tool **e** first reaches 45º where its diameter is 0.8 mm, where area of its cross section is 0.5024 mm^2, that is 2.56% of the 19.625 mm^2 cross section of the ICA of the average diameter of 5 mm. Stenoses up to 97.44% would also be ideal for its insertion however, in

the case of this device the angle of tapering increases to 63.5º where the conical tip meets the shaft owing to the blunt angle in the line of tapering. In the section of transition the angle of tapering returns to 45º where the diameter is 1.48 mm, resulting in a maximum 91.24% stenosis for atraumatic insertion. The conical tip and the shaft are not connected by an evenly tapering section.

3.4 Discussion

The catheters used in endovascular treatment come into contact with the inside of the blood vessel. Where the catheter's diameter exceeds the diameter of the vessel section affected by stenosis, the catheter, when being inserted, mechanically expands and dilates the plaques – of often unstable structure, resulting in an increased risk of embolic complications [31,44]. A significant proportion of the patients with symptoms turn to their doctors because of spontaneously embolised ICA plaques. The often severely embologenic surface of a plaque can be fragmented even under the slightest impacts, causing new ischaemic lesions. Our measurements showed that devices with thicker (6 F or 2 mm) shafts are bound to come into contact with and exert an expanding force on the vessel wall in the case of stenosis of or over 83.6% (assuming an ICA of an average 5 mm diameter). Devices of a diameter of 5 F (1.66 mm) do not touch the plaque below a stenosis of a degree as high as 89.2%, therefore from the aspect of this particular study they pose a potential hazard in a smaller percentage of cases. From this perspective tools marked **a**, **c** and **e** appear to be more favourable than those marked **b** and **d**.

Each of the SDSs ends in a conical tip transmitting the force conveyed along the longitudinal axis of the cone – based on simple physical rules – in different directions and degrees determined by the shape of the given cone to its environment, in this case the structures constituting the vessel lumen's boundaries. The tools to be found in the market end in cones of various shapes. As the instrument is being pushed forward the force transmitted by the cone surface can be broken down into forward and sideways force vectors, where the sideways force is the effective expanding (dilating) force, pressing the plaque into the vessel wall and expecting not to cause embolisation, while the forwards force dislodges plaques, causing potentially embolisation. The relative proportions of the two force vectors (in essence, the cone shape) determines the tool's embologenity.

The conical tips of the delivery systems are characterised by the ratio of the difference between the diameters of the cross sections at the two ends of a given section of the cone to the length of the same section, or in other words, the degree to which the cone widens over a given length.

Any unevenness or a step in the cone end surface profoundly affects the directions and strength of force exerted on the vessel wall. Such modifications to the regular straight line of tapering is to be found in the tools marked **a,** and **e**. Our measurements and calculations alike showed that the tips of the stent delivery systems feature different diameters and shapes therefore they have potential impacts on the rates of embolic complications in the course of the endovascular treatment of ICA stenoses.

Looking at the results of the measurements in our studies the device marked **c** was found to have the most atraumatic end design as the conical tip makes it possible for the device to pass through stenoses up to 98.04% without exerting forwards – that is, embologenic – forces on the vessel wall. It has another advantage in that its largest diameter is 5 F, therefore it produces mechanical dilation only in the case of stenoses over 89.2%.

The device marked **d** also produced good results – it can be safely put through up to 97.44% stenosis. Its largest diameter, however, is 6 F therefore mechanical dilation is to be expected than those specified for the preceding instrument that is already at 83.6% level of stenosis.

The device marked **b** also performed well, as when it is being pushed through a vessel with an occlusion not exceeding 96.39% its lateral force exceeds it's forward pointing force. Its largest diameter is 6 F, therefore it causes mechanical dilation as well in the case of a stenosis exceeding 83.6%.

Though shape of the conical tip of the device marked **e** is safe for insertion through arteries with up to 96.76% occlusions, the cone meets the shaft at an angle below 45º therefore, like in the case of the device marked **e** this tool can also be inserted unhindered only through stenoses not so advanced as those permitted by the cone tip, in other words, it can be safely put through vessel sections with up to 89.76% degree stenoses.

The conical tip of device **a** could permit its insertion through up to 96.76 percent stenosis, but the conical tip meets the shaft at an angle below 45º, consequently, similarly to instrument **e** this tool can also be put through unimpeded only up to 89.76% stenosis (that is, obstacles smaller than those permitted by the cone tip). The ranking order of the instruments discussed above, based on the results of our study, is presented in Table 2.

Stent Delivery System	real diameter * contact limit		** degree of stenosis	diam. step	ranking
Carotid Wallstent (c)	5.0 F	88.85%	98.04%	no	**1**
Acculink (d)	5.9 F	84.32%	97.44%	no	**2**
Xact (b)	5.7 F	85.56%	96.39%	no	**3**
Zilver 518 (e)	5.0 F	88.85%	91.24%	yes	**4**
Precise RX (a)	5.3 F	87.75%	89.76%	yes	**5**

Table 2: Ranking of the tools involved in the study, based on our results.

** Calculated degree of the vessel lumen, SDS is bound to come into contact with the plaque*

*** The highest degree of stenosis through which the SDS can be safely inserted in view the shape of its conical tip*

Limitations:

The practical applicability of our results is limited by the fact that our examinations were carried in regard to stenosis assumed to have developed in straight vessel sections of perfectly circular cross sections, therefore the same devices will not perform quite as well in real circumstances as is indicated by our results; they are bound to form narrowed vessel sections of irregular shapes in accordance with their own shapes, exerting a variety of additional forces. The flexibility of the instruments and their surface friction coefficients are also important factors from the aspect of embologenity, and the mechanical characteristics and attributes of the supplementary devices, including the guide-wires, may have further positive and negative impacts on embologenity, and ultimately all of these together determine embologenity while being put in a closed state through stenosis of various shapes and sizes.

3.5 Conclusions

The conical tips of SDSs differ from one another in terms of the forces exerted on the narrowed sections of blood vessels. All of the devices tested in our study may always be regarded as safe in terms of the forward pointing dislodging force when being pushed through stenosis not exceeding 89.76%. In the case of occlusions exceeding 89.76% the right choice of the stent delivery systems subject to the devices' conical tip shape may also contribute to minimising periprocedural embolisation. Any unevenness on the catheter surface will result in increased dislodging forces as a consequence of which the degree of embolisation entailed by the dislodging of plaques may increase. In the development of devices used in CAS treatments attention must be paid to making sure that there are no edges (steps) in the surface of the tools' conical tips.

4. Forces exerted on plaques during in vitro measurements by various carotid stent delivery systems and embolic protection devices

4.1 Introduction

Our earlier studies showed that SDSs applied in CAS treatment come in a great variety of distal tips and shapes. The history of the evolution of each instrument is also unique, as a consequence of differences in the approaches taken by their respective manufacturers to their development. Carotid stent systems showing major structural differences also differ from one another in terms of their materials and designs. EPDs and SDSs are coaxially structured devices made up of layers including the sheath of the guide wire, the plastic tube carrying the metal parts - stent or EPD basket loop- , made of different materials with different diameters, as well as the plastic sheath covering the device. Each of these layers have different pliability indicators because of their materials and specific thicknesses. Moreover, the friction between the co-axial catheter layers also affects the pliability of the given EPD or SDS. Since the different products are made of different materials, with different material thicknesses and stent or EPD loop designs, they inevitably feature different pliability characteristics. The SDS is the thickest, most robust catheter used in the course of CAS and it exerts force when being put through the stenotic ICA section. The stenosis of the ICA to be treated are located in an arc relative to the distal ending of the guide catheter, so the EPD or SDS has to follow the bend in the blood vessel as it is being inserted. Depending on the curves in the blood vessel and the pliability of the device a force causing pressure and friction on the vessel wall and consequently the plaque as well, having a negative impact on the stability of the plaque – which might even spontaneously embolise even without such intervention – in accordance with certain simple laws of physics.

We found it worthwhile to compare the pliability of EPD devices with those of SDSs, to see the impact on plaques by the additional use of EPD instruments. Our study was aimed at finding the instrument exerting the smallest force on plaques in the case of vessel morphologies with different curvature angles. We wished to identify the vessel curve angle at which the load on the vessel wall increases significantly during the insertion of an EPD and SDS.

4.2 Subjects and methods

Two EPDs and six different SDSs – available on the market, widely used in international practice – were examined: Emboshield PRO, 4-7mm /190 cm; RX Accunet, 4-5mm /190 cm,(ABBOTT Vascular) and four carotid stents: Xact carotid stent, 9-7x30 mm, RX Acculink, 8x30 mm, (ABBOTT Vascular), Carotid Wallstent, 8x29 mm, (Boston Scientific) Precise RX, 8x30 mm, (Cordis Corporation) High Torq Balance micro-guide wire (Abbott Vascular) was used for delivering the SFRs. The measurements were carried out with a device called IDTE 2000 (Machine Solutions Inc. (MSI) 2951 W. Shamrell Blvd. Flagstaff, Arizona 86001 USA) developed for complex catheter tests, with a CE certificate, in Galway /Ireland/. A transparent PVC tube of a 6 mm diameter and a 1.5 mm wall thickness was used as a blood vessel model, narrowing it to a 5 mm inside diameter at the CCA-ICA bifurcation where an amorphous 12 mm long 75-85% occlusion was created in the lumen using a product called Vinilfix (Tetrahidrofurán/PVC powder, manufactured by Ferrokémia, Budapest). The model was created on the basis of Machine Solution's experiences accumulated in the course of cooperation with catheter manufacturer companies.

The insertion range studied using the devices was 12 cm long with a 30 cm/minute rate. The catheters were pushed in automatically by the IDTE 2000 instrument. The tests were carried out on 25º, 50º and 75º angle model settings curved at a distance of 5 cm from the point of entry. A tub filled with 37 ºC tap water was used as medium (Figure 15).

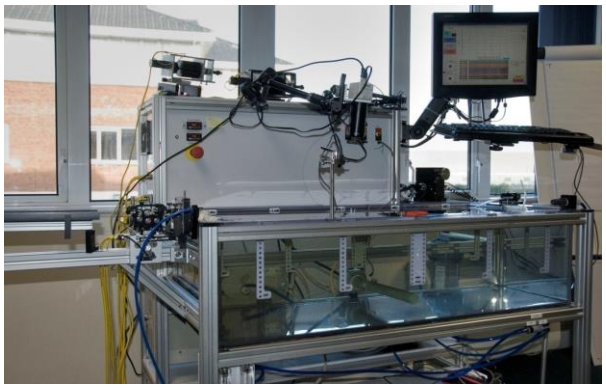


Figure 15: IDTE 2000 measuring system. The measuring zone of the IDTE system in tub filled up with 37 ºC tap water.

Five measurements were taken with each setting, where during the real-time measurements the largest forces exerted by the device on the vessel wall were recorded in a table.

4.3 Results

EPDs and SDSs tested in our study showed a wide range of differences in terms of the forces exerted on the vessel walls. Of the devices concerned the Accunet EPD exerted the weakest force in the case of each angle of curvature, in other words, this device was found to be the most atraumatic of all. The strongest force was exerted on the vessel wall in the case of each angle by the Carotid Wallstent SDS (Table 3)

angle of curvature	Emboshield Pro	Accunet	Xact sds	Acculink sds	Wallstent sds	Precise sds
25°	*24.02*	*15.18*	*77.99*	*46.74*	*157.5*	*30.08*
50°	*21.97*	*9.13*	*79.8*	*53.46*	*151.36*	*90.94*
75°	*33.42*	*19.23*	*261.11*	*227.24*	*821.87*	*294.98*

Table 3: Maximum vessel wall loads (in grams) in the case of different vessel curvatures

The intensity of the force exerted by the devices on the vessel wall increased considerably towards higher degree angles. In the vessel bent at a 75º angles of curvature the instruments exerted pressures many times the intensities measured in the case of the 25º and the 50º angles. The embolic protection devices however, not always exerted increased force on the vessel wall in the case of higher degree angles, e.g. in the case of the 50º angle relative to the 25º angle of curvature. Event the forces measured at 75º did not exceed those measured at 50º by more than 30%.

In terms of relative proportions the total load on the vessel wall resulted – with the increase in the angle of curvature – more from the characteristics of the stent delivery systems than from the embolic protection devices (Diagram 2).

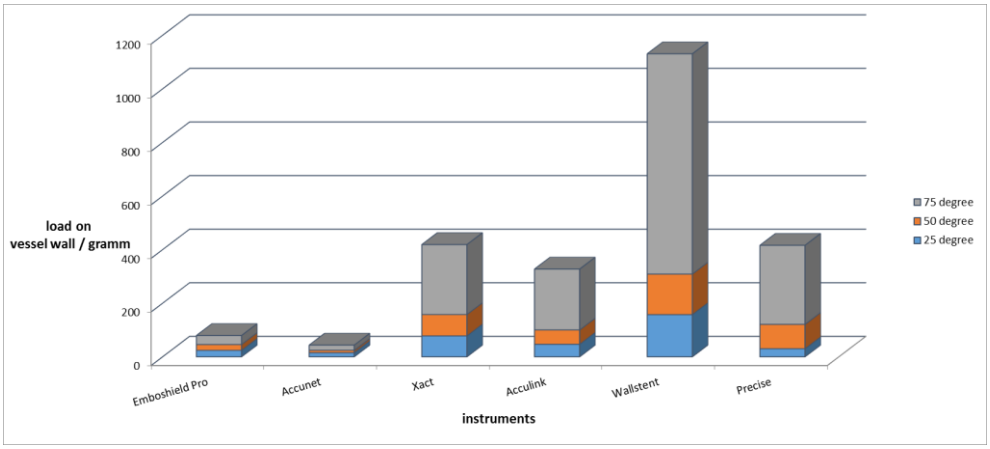


Diagram 2: Sums of the values measured for the various instruments at different angles of curvature

The maximum forces taken in successive measurements on the various tools gradually decreased. The maximum values were always measured during the first trial.

4.4 Discussion

Endovascular catheters have a mechanical impact on plaques – many of which have a fragile structure – while being pushed through stenotic blood vessel sections, potentially resulting in an increase in the risk of embolic complications [31,44]. An EPD or an SDS – even is inserted in a guide catheter – affects the load on plaques on the vessel wall (and thus their embolisation) as a consequence of the shifting of the point where it is contacting the vessel wall and the changes in the forces exerted on it.

Our measurements showed that SDS and EPD instruments exert forces of varying intensity on the vessel wall as they are pushed through stenotic sections. Accordingly, besides a variety of other considerations, this is also very likely to be worth taking into account in selecting the device to be used. The force exerted on the vessel wall is disproportionately higher in tight bends. Embolic protection devices are – in terms of their delivery systems – significantly thinner than are the stent delivery systems (2.9–3.2 F distal diameters, in contrast to 5-6 F distal diameters). It is not surprising therefore, that EPDs exert a smaller force on the vessel wall while being pushed through narrowed vessel sections, than do SDSs. On the whole, the force on the vessel wall increases with the increase in the blood vessel's angle of curvature in the case of the use of EPDs as well, though at a lower rate than in the case of SDSs. The insertion of an EPD however, is an additional impact on plaques in the course of the treatment of the patient, therefore during the endovascular intervention its use entails an additional risk of dislodging of plaques [45-47]. According to our measurements where the narrowed blood vessel section is in a curve of an angle over 50º the alternative of conservative or surgical treatment should be considered in cases where the tools used in the intervention are highly likely to mechanically impact plaques during insertion.

Successive measurements taken by the IDTE system using the same device indicated significant decreases in the forces exerted by the catheters. This phenomenon might be explained by the gradual increase of the temperature of the device from room temperature (21 ºC) at the time of the first measurement to the temperature of the water in the tub (37 ºC) and the resulting softening of the plastics making up the bulk of the materials comprising the catheters (Diagram 3).

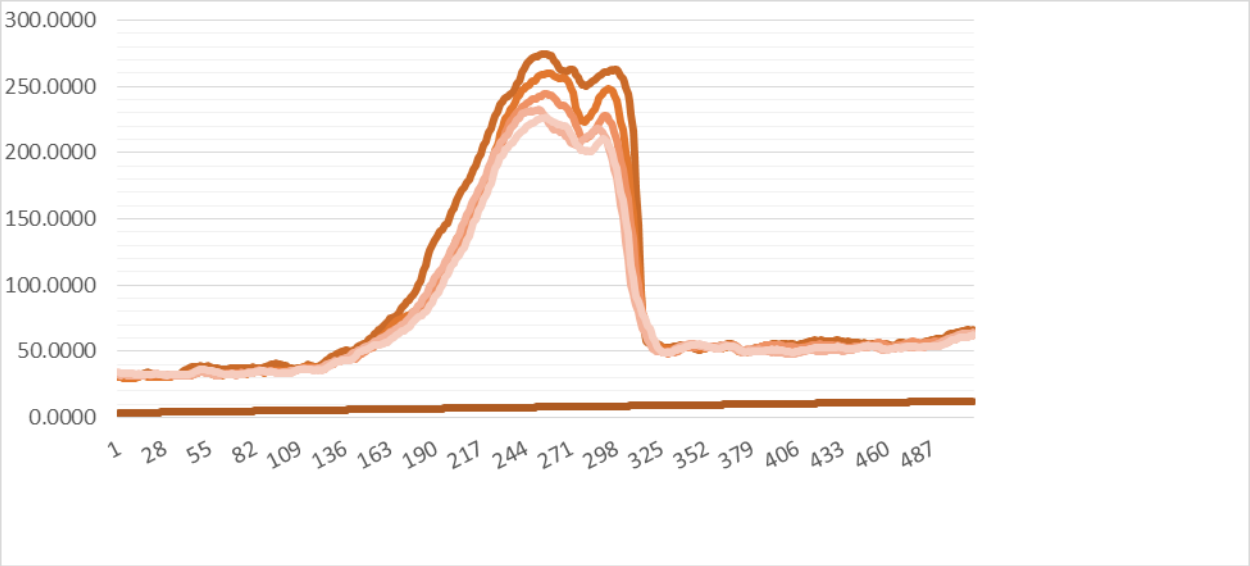


Diagram 3: Successive measurements carried out with the same tool indicated a gradual decrease in the force exerted on the vessel wall. The lighter the colour of the curve the later the measurements were taken. A 21% decrease in the force on the vessel wall was found between the first and the last test in this case.

Another possible explanation might be the expansion of the material as the instrument passed through the bend, growing increasingly marked as the tool was repeatedly pushed through. Consideration should therefore be given to warming up the SDS and EPD instruments to the body temperature before the intervention, along with preoperational shaping of the tools' end similarly to the distal endings of other tools used in neuro-intervention. A slight – up to 15º – bending of the SDS shaft was not found to have any negative impact on the reliable releasability of the stent but the load on the outside arcs of the bends may be reduced by suitably rotating the instrument after leaving the distal ending of the guide catheter so as to enable atraumatic adaptation to the morphology of the vessel. The preoperational shaping of the SDS must not result in breaching the operating instructions. The shaping of the shaft must not affect the region of the distal ending because any opening of the shaft-tip connection might have a negative impact on the dislodging capability of the tool (Figure 18).

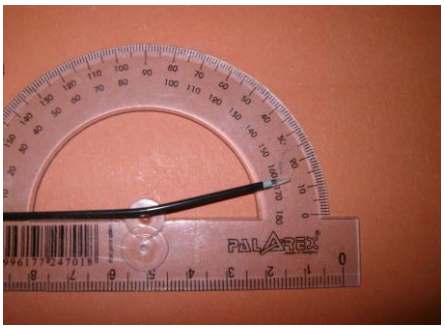
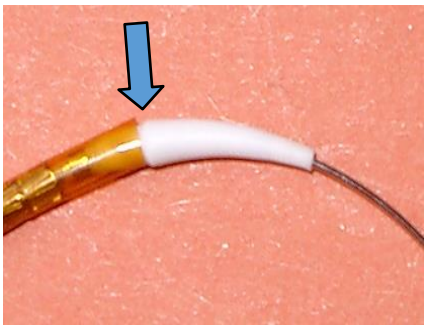
A;  B; 

*Figure 18: A slight bending of the distal end of the SDS did not affect the releasability of the stent (*A*). The joint between the SDS distal tip and the shaft may open up when bent in which case the edge of the shaft forms a chisel-like edge that may damage the plaque upon touching it (*B*).*

The shaft-tip connection should be checked before insertion of the tool and the delivery of the stent, to make sure that the bending of the tool when following the morphology of the patient does not result in the creation of an edge.

4.5 Conclusions

Where CAS instruments need to be inserted in a vessel with bends and curves, the flexibility of the various devices should also be taken into account, to minimise the force exerted on the plaque(s). Where the curve in the vessel to be treated with catheter exceeds 50º consideration must be given to other, alternative therapies for the patient, owing to the increase in the load on the vessel wall and the resulting increase in the risk of dislodging emboli. A catheter of room temperature may grow softer as it reaches the body temperature, exerting a weaker force on the vessel wall passing through a curve of the same angle. The joint between the distal end of the SDS and the sheath may open up in an excessively tight bend, and it increases the risk of dislodging plaques.

5. Aortic arch and common carotid artery plaques with soft components pose a substantial risk of cerebral embolisation during carotid stenting

5.1 Introduction

Frequent observation that after CAS, fresh ischaemic lesions occur not only in areas supplied by the vessel affected by CAS treatment, but also on the contralateral side and in the posterior fossa.

The appearance of these lesions cannot be attributed to the stented plaque [48]. It is known that ulcerated plaques of the AA have an important role in the development of ischaemic stroke as a source of embolization [9]. Therefore, development of fresh ischaemic lesions in the course of CAS is unlikely to be explained by the presence of ICA plaques only, other embolus sources must also be taken into account [48]. Reducing the risk of probably not ICA stenosis related embolisation might increase the endovascular treatment applicability in comparison with CEA.
In this study, we examined whether there are relationships between AA and CCA plaques and the development of fresh ischaemic lesions. We also examined whether the composition of plaques affects the degree of embolisation.

5.2 Subjects and methods

The study was conducted with the approval of the Board of Ethics of University of Szeged, Medical University Centre. All of the patients were fully informed about the study and provided written consent. Between June 2010 and December 2012 a total of 101 consecutive CAS cases involving 92 patients with symptomatic carotid stenosis (40 women; 52 men; mean age: 64.8±8.2 years) were examined retrospectively at our institution (Table 1).

Case number	101	
Patient number	92	
Mean age / Year	64.8 ± 8.2	
Female	40	43.50%
Male	52	56.50%

Table 4: Patient demographics

The length and grade of the stenosis were manually calculated on the basis of digital subtraction angiography according to the North American Symptomatic Carotid Endarterectomy Trial criteria [50]. The CTA procedure was carried out with a 64-slice scanner (GE Light Speed VCT/General Electric Healthcare, Fairfield, CT, USA) in accordance with the following protocol: helical mode, gantry rotation: 0.4 s; collimation: 62 × 0.625 mm; pitch: 0.984:1; section thickness: 0.625 mm; reconstruction interval: 0.5 mm; and acquisition parameters: 120 kV/50–600 mA. The

examination was carried out in the caudocranial direction from the middle of the chest up to the vertex. A volume of 50–70 ml of contrast medium (Omnipaque 350/General Electric Healthcare) was injected through the antecubital vein with an injector at a rate of 2.5–4 mL/s. The test bolus technique was applied to optimise the timing of the CTA. Measurements of stenosis were taken with the Advantage Windows 4.4 (General Electric) workstation using the Advanced Vessel Analysis program, based on a decrease in the cross-sectional area.

CTA images showed the presence or absence of plaques in the AA and CCA – brachiochephalic artery areas. Two groups of were distinguished as plaque analysis: purely calcified and partly or purely soft plaques. In most cases, proper windowing (window width 500–900 HU, window level: 100–250 HU) enabled calcified and soft plaques to be distinguished by visual assessment [51]. When the material of the plaque was in doubt, its density was measured. Plaques of a density over 241 HU were regarded as calcified and those below 240 HU [52,53] were regarded as soft. The density measurements were performed on the source images with the Measure program (Viewer, Display tools) of Advantage Windows 4.4 (General Electric Healthcare).

CAS was carried out under double thrombocyte aggregation protection (aspirin 300 mg/d, clopidogrel 75 mg/d), started at least 3 days before endovascular intervention [54]. At the start of the intervention, 70 U/kg heparin was administered in a bolus. Whenever significant bradycardia or asystolia was noted during the postdilation phase, the required amount of atropine was injected.

Only the vessels that were affected by stenosis were selectively examined with catheter angiography. As a first choice head-hunter 1 type, and in the case of a failed attempt the Simmons 1, 2, or 3 type 4F catheter (Cordis Corporation) was used, introduced by a 035” Standard Glidewire (Terumo, Somerset, NJ, USA) guide wire. In the case of any difficult morphological situation, a 035”×260 Emerald replacement wire (Cordis Corporation) was used. For predilation and postdilation, a 0.014” 4 × 20 mm and 6 × 20 mm Aviator Plus (Cordis Corporation) balloon catheter was used, respectively. No EPD was used in the interventions. Two types of closed-cell stents were implanted: Carotid Wallstent (Boston Scientific) and Xact Carotid Stent (Abbott Vascular).

All stent procedures were done under local anesthesia with monitoring by anesthesiologist. All stenting procedures were performed by the same neuroradiologist, with experience in >800 carotid stenting procedure. Transfemoral arterial approaches were performed in all cases. A diagnostic angiogram of the common carotid artery in question was done to confirm the presence of significant stenosis and to make the final decision for interventional procedure. All stent were postdilated to not less than 90% of the measured diameter of the normal ICA. Finally, angiograms

of the carotid bifurcation and the intracranial circulation were performed to demonstrate the reconstruction of the carotid lumen and to exclude macroembolic complications. After procedure, the patients were monitored in a neurologic intermediate care unit for 24 hours. The period between the first femoral puncture and the end of the first 48 h following revascularisation was regarded as the periprocedural period of the intervention

New ischaemic lesions were detected with DWI and ADC mapping (GE Signa Excite HDxT, 1,5T; General Electric and Advantages Windows 4.4 workstation) within 48 h of the intervention. DWI was acquired with an echo-planar axial sequence as follows: Repetition time 8000 ms; echo time, minimum 97.6 ms; 128 × 128 matrix; FOV, 260 × 260 mm; slice thickness, 5 mm without a gap; and b values of 0 and 1000 s/mm². An ADC map was generated with the Functool program on the Advantage Windows workstation in each case. Areas showing restricted diffusion of a high signal on DWI and a low signal on ADC map were identified as new ischaemic lesions. Depending on localisation, lesions were assigned to three groups: ipsilateral, contralateral, and posterior fossa. The lesions were grouped by size (<10 mm, 10–20 mm, >20 mm). The observer analyzing CTA was blinded to the results of DWI. The CTA, DWI examinations and stenting procedure were always carried out by the same neuroradiologist who is a professional with 20 years of experience (Fig 1).

Statistical methods: Patients with plaques in the AA and CCA were compared with those without such plaques to determine which group had more chance of developing new ischaemic lesions. The relationships between occurrence of plaques and new ischaemic lesions was analysed with the χ^2 test and Fisher's exact test. Logistic regression models were applied for assessing the effect of risk factors. The effect of the composition of plaques in the AA and CCA on the risk of appearance of new ischaemic lesions was measured by odds ratios. Additionally, 95% confidence intervals for the odds ratios were calculated. P values <0.05 were regarded as statistically significant. Statistical analysis was carried out with SPSS 22 software (IBM SPSS Statistics for Windows, Version 22.0).

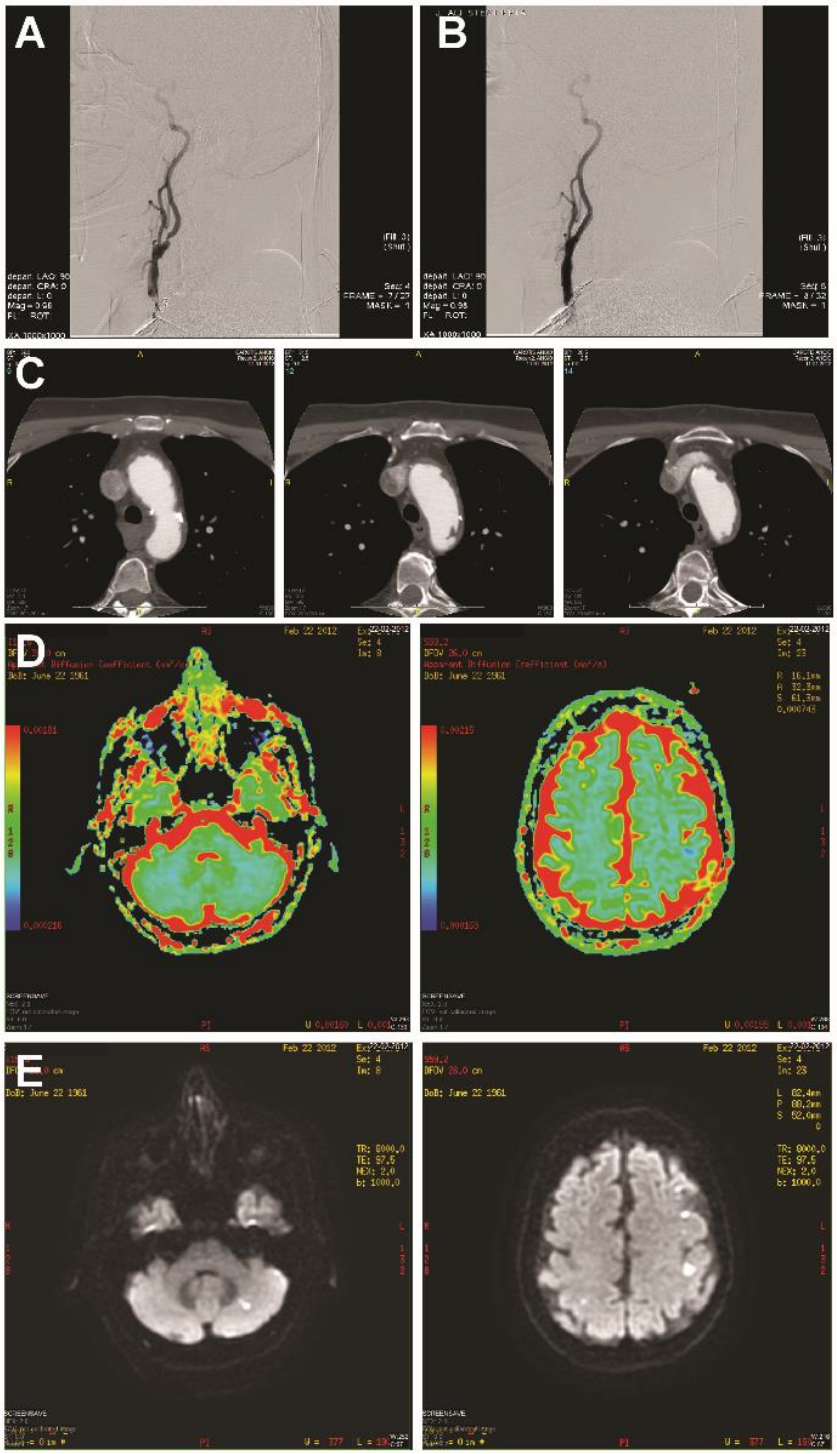


Figure: A 50-year-old female patient had significant ICA stenosis on the right side before (A) and after (B) stenting. Extensive soft plaques with some calcified components were observed on the primary AA slices (C). ADC (D) and DWI (E) images demonstrate several fresh ischemic lesions on the contralateral side. Some new lesions were found on the ipsilateral side (not seen) and posterior fossa.

5.3 Results

All 101 carotid cases were successfully treated with CAS. Two cases developed periprocedural ischaemic stroke (modified Rankin scale 2 and 3). New ischaemic lesions were found in 50% of all cases (50/101). In 19% (19/101) of the cases only one new ischaemic lesion occurred. The sizes of new ischaemic lesions did not exceed 10 mm in 90.8% of cases. Therefore, lesions exceeding 10 mm were not studied as a separate group. The average procedure time was 58.8 (35-115) minutes. The average procedure time of patients without new DWI lesion was shorter (57.2 minutes) while the procedure time of cases with new DWI lesions was numerically longer only (60,32 minute), he difference was not significant. In 12% (12/101) of a failed attempts at entering the first choice diagnostic catheter a second diagnostic catheter was used. New DWI lesions were identified in 75% (9/12) of these cases. A total of 76% (38/50) of these new lesions occured in areas that were supplied by vessels affected by treatment (ipsilateral side). A total of 24% of them (12/50) were not related to the treated stenotic lesion (contralateral side and/or posterior fossa). In 42% (21/50) of cases where new ischaemic lesions were present, embolisation occurred on the ipsilateral side and on the contralateral side and/or the posterior fossa.

The incidence of new ischaemic lesions was statistically not independent of whether the AA was covered by plaques. A significant (P=0.013) relationship was found between the occurence of plaques covering the AA and the incidence of new ischaemic lesions. Where the AA plaque was purely calcified, the occurence of a plaque resulted in a 2.311 times higher risk (odds ratio) of embolisation compared with plaque-free cases, but this increase was not significant (P=0.28, 95% CI 0.505–10.573). For patients with plaques containing soft components, the increase in risk was 5.617 times compared with plaque-free cases (P=0.012, 95% CI 1.453–21.713) (Table 4).

Plaques	**Lesion free cases /%**	**DWI lesion cases /%**	**Total Nr. cases / 100%**	**p-value**	**Odds-ratio**	**95% confidence-interval**
No (ref. category)	13 / 81.3	3 / 18.8	16	0.019	-	-
Calcified	15 / 65.2	8 / 34.8	23	0.28	2.311	0.505 to 10.573
Soft	27 / 43.5	35 / 56.5	62	0.012	5.617	1.453 to 21.714
Total	55 / 54.5	46 / 45.5	101			

Table 4: Confidence intervals and logistic regression analysis of assessment of AA plaque components as risk factors

When comparing cases of purely calcified plaques in the AA with those containing soft components, the odds ratio for the risk of developing new ischaemic lesions was 2.431. However, this result was significant only at a significance level of 10% (P=0.08)

The incidence of new ischaemic lesions was statistically not independent of whether the CCA was covered by plaques. A significant (P=0.004) relationship was found between plaques covering the CCA and the incidence of new lesions. If plaques in the CCA were purely calcified, they did not cause any further increase in risk (odds ratio: 0.812) compared with patients with no plaques (P=0.67, 95% CI 0.3135–2.111). When the CCA plaque contained soft components, the risk of incidence of new ischaemic lesions was 4.411 times higher compared with patients without plaques; (P=0.006, 95% CI 1.517–12.822) (Table 5).

Plaques	**Lesion free cases /%**	**DWI lesion cases /%**	**Total Nr. cases / 100%**	**p-value**	**Odds-ratio**	**95% confidence-interval**
No (ref. category)	26 / 61.9	16 / 38.1	42	0.007	-	-
Calcified	22 / 66.7	11 / 33.3	33	0.67	0.812	0.313 to 2.111
Soft	7 / 26.9	19 / 73.1	26	0.006	4.411	1.517 to 12.822
Total	55 / 54.5	46 / 45.5	101			

Table 5: Confidence intervals and logistic regression analysis of assessment of CCA plaque components as risk factors

When comparing purely calcified plaques in the CCA with those containing soft components, the odds ratio for the risk of developing new ischaemic lesions was 5.429 (P=0.003). When patient represented both AA and CCA plaque contained soft components, the risk of incidence of new ischaemic lesions was 7.037 times higher compared with patients without plaques; (P=0.0003, 95% CI 2.364-20.944).

5.4 Discussion

In the current study, we found new ischaemic lesions in 50% of all CAS cases that we detected. This rate is higher than that in cases of CEA treatment (24–34%), but it is similar to previous results of CAS treatment despite the use of EPD (38–67%) [55,56-59]. We found that not all new ischaemic lesions can be regarded as related to the area of the vessel that has undergone treatment because lesions were also found in 24% of cases on the contralateral side and/or in the posterior fossa. These findings correspond well with those observed in previous clinical studies [60-62].

Yoshimura et al. identified ulcerated plaques in the AA as a source of embolisation that could be related to the development of ischaemic strokes [49]. Kim et al's findings suggest that manoeuvers in the AA during CAS play an important role in the occurrence of new ischaemic lesions in the posterior fossa and contralateral ICA territory [48]. There is a difference between purely calcified plaques and those containing soft components in their potential to produce emboli. Therefore, composition of plaques can be a factor involved in cases of plaques in the AA and CCA [19,63-67]. No embolic protecting device was used in the interventions, at present there is no available level 1 evidence to support the routine use of EPDs [45-47]. While during part of the periprocedural phase an EPD may provide partial protection of the ICA to be treated it does not provide protection against contralateral or posterial fossa embolisation originating from the plaques of the AA on which our study is focused. Unfortunately, at present we have no protecting device restricting embolisation that could provide protection during diagnostic catheter use or the introduction of the thickest endovascular device, a guiding catheter, for both the vessel area that is to be treated and for the areas subject to embolisation by the AA and CCA plaques.

We used CTA to distinguish calcified plaques from soft plaques based on density [52,68-70]. We did not investigate soft plaques further. This is because, according to a study by Wintermark and de Weert et al, the density values of soft components, such as necrotic tissue, other tissues rich in lipids, connective tissue, and plaque haemorrhage, show considerable overlap. Therefore, they are collectively referred to as a "soft plaque" [52,53]. For detecting new ischaemic lesions, we applied the internationally accepted method of DWI [19,42,71]. Most areas of new DWI lesion cause no neurological symptoms (i.e., they are functionally silent ischaemic areas) [48]. In our study, although new ischaemic lesions were detected in 50% of all cases, only 2% of these DWI lesions were found to be symptomatic. However, many studies have shown an association between new asymptomatic ischaemic lesions and worsening results of neuropsychological tests [42,43]. Gensicke et al showed that ischaemic brain lesions discovered on DWI after CAS appear to be a marker of increased risk for recurrent cerebrovascular events therefore, minimising the risk of embolisation should be a priority [43].

In our study, we found that there was a relationship between the presence of AA plaques and development of fresh ischaemic lesions. Embolisation in an area other than that supplied by the stented ICA occurred in 24% of all cases, which is slightly less than the results of a similar study of 32 patients (41%) [48]. However, this finding emphasises the need to further investigate the potential of plaques in the AA to produce emboli.

In our study, not all of the patients who received CAS treatment had plaques in the AA or CCA. In cases where no plaques were present in the AA, we did not encounter any new lesions outside the territory supplied by the vessel in question. This lack of finding confirms our notion of new contralateral and posterior fossa ischaemic lesions originating in the AA. AA and CCA plaques significantly increased the risk of development of new ischaemic lesions compared with cases where AA and CCA plaques were not presented. In cases where the AA plaque was purely calcified, no significant difference in the incidence of new ischaemic lesions was detected. When patients with purely calcified AA plaques were directly compared with those who had plaques with soft components, the risk of developing new ischaemic lesions was not significant (P=0.08). The lack of significance is thought to be due to the moderate sample size. We found a relationship between the presence of CCA plaques and the development of fresh ischaemic lesions. When patients with purely calcified CCA plaques were compared with those with plaques with soft components, the risk of developing new ischaemic lesions was significant. These results suggest that plaques with soft components in the AA and CCA increase the risk of periprocedural embolisation. Use of a smaller, more properly-shaped device in the AA decreases the mobilisation of atheromas [48]. One of the reasons for patients suffering embolism during intervention is related to manipulation of the catheter during the procedure.

The AA and CCA form part of the intervention route that is used in the course of ICA stenting where the guide wires and catheters come into contact with and mechanically insult the vessel walls with plaques on them. Therefore, both of these areas are assumed to increase the rate of complications of embolisation in CAS. While plaques in the AA can also affect the contralateral side and the posterior fossa, plaques in the CCA can only affect the ipsilateral side because of anatomical reasons. It should be noted however, that the use of an inflated flow reversal EPD in a plaque covered CCA with raises questions in view of the results of this study. The CCA plaque definitely deserves to be studied in the case of the most up to date flow reversal devices inserted directly into the common carotid artery (Silkroad system; Silkroad Medical, 735 North Pastoria Avenue, Sunnyvale, CA 94085) when a small incision is performed on the CCA and loop is placed to clamp the artery.

Even when using 4F soft diagnostic catheters, a neurological complication rate of 1.3% should be expected, as shown by a prospective study of diagnostic cerebral angiograms of 2899 patients [72]. Interventionalists navigate instruments by rotating and pushing forward, and withdrawing the guide wire and a 5–8F-diameter catheter towards the ICA stenosis. The catheter always rests on

the inside surface of the vessel wall, where it exerts some force depending on the morphology of the vessel and flexibility of the catheter on the point that supports them. This may result in applying force on the plaque [48]. There are differences between catheters used in ICA stenting in terms of flexibility, and consequently, in terms of the force they exert on the vessel walls. According to results of measurements taken in model experiments, thinner catheters exert a smaller force, while systems carrying thicker devices exert greater force on the vessel wall. The force exerted on the points supporting the catheter increases as a result of changes in the vessel's morphology and a decrease in the radius of bends [73].

New periprocedural ischaemic lesions appearing on the contralateral side or in the posterior fossa are highly likely to be consequences of manipulations of the catheter in the AA therefore, extending CTA mapping to the AA is important. CTA mapping of plaques to decrease complications of embolisation in patients may help make catheter therapy a safer treatment, even if there are plaques in the AA [51].

5.5 Conclusions

In the case of an AA or CCA without plaques or with homogeneous calcified plaques CAS is a form of treatment entailing low risk of embolisation. The presence of soft plaque components in the AA or the CCA results in a significantly higher risk of CAS embolisation in comparison to AA and CCA cases without plaque. In the examination of patients with ICA stenosis mapping the AA and CCA areas using CTA may be highly useful in clarifying the risks of endovascular treatment. Before the application any embolic protection requires incision on CCA or balloon dilatation in CCA an examination of the presence of plaques in the CCA is highly recommended.

6.1 New findings

- In the endovascular treatment of ICA stenosis every single step of the catheter manipulation (insertion of the guide wire; insertion of the guide catheter; predilation, SDS delivery through the stenosis, stent deployment, balloon-dilation) may result in embolisation.
- The interventionist is immediately informed by the sound signals emitted by the TCD equipment about the embologeneity of the ongoing catheter manipulation.
- The conical tips of stent delivery systems differ from one another in terms of the forces exerted on the narrowed sections of blood vessels.
- All of the stent delivery systems tested in our study may always be regarded as safe in terms of the forward pointing dislodging force when being pushed through stenoses not exceeding 89.76%.
- Any edge forming will result in an increase dislodging forces, entailing an increased risk of embolisation when the device comes into contact with the plaque.
- The different stent delivery systems exert forces of different intensities on the vessel walls while passing through the narrowed vessel section.
- The force exerted on the vessel wall increases not proportionally but significantly more than the increase in the angle of the curve in the blood vessel.
- EPDs exert pressure on the vessel wall while being pushed through the angled vessel stenosis but its intensity is smaller than the force exerted by SDSs.
- Over angles of curvature exceeding 50º consideration must be given to other, alternative therapies for the patient, owing to the increase in the load on the vessel wall (plaque) and the resulting increase in the risk of dislodging emboli.
- A catheter of room temperature grows softer as it reaches the body temperature, exerting a weaker force on the vessel wall passing through a curve of the same angle.
- The joint between the distal end of the SDS and the sheath of the stent may open up in an excessively tight bend, and the edge entails a risk of dislodging plaques.
- In the examination of patients with ICA stenosis mapping the AA and CCA areas using CTA may be highly useful in clarifying the risks of endovascular treatment.
- Before the application any kind of POD examination of the presence of plaques in the CCA is highly recommended.

6.2 Practical benefits of the findings

At present there are two invasive solutions for the treatment of neck carotid artery stenoses that may be regarded as more or less equivalent: CEA and CAS. The most significant disadvantage of the CAS – which is otherwise less stressful for the patient – relative to the CEA is its higher risk of embolisation.

The main practical benefit of our work is that our results enable mitigating the embolisation risk of CAS in three different aspects:

As was proven by TCD tests a certain amount of emboli are found to be dislodged in each procedural step of CAS. One obvious solution is therefore the skipping of steps that are not vitally important, such as predilation and in some cases also postdilation. Intraprocedural TCD monitoring may also be useful by emitting sound signals to the interventionists warning him or her of the density of emboli, calling for more cautious manipulation. This may be particularly important during the earlier stages of the learning curve.

The tools available on the market have a variety of advantages and disadvantages in comparison to each other in terms of potential embolisation. Efforts must therefore be made to use the most atraumatic devices. The risk of dislodging plaques can be mitigated by using stent delivery systems with the smallest possible diameters and by choosing tools with smooth elongated conical tips without any edges. The force exerted by the delivery system on plaques in bends in the vessel may be reduced by increasing the pliability of the delivery system. According to our results where the narrowed blood vessel section is in a curve of an angle over 50º the tools used in the intervention are highly likely to mechanically impact plaques during insertion. The plaque stabilising capability of the implant is also crucial; from the aspect of periprocedural embolisation covered stents are a safer choice than metal mesh stents. In the development of the CAS tool kit attention must be paid to improving the physical attributes of relevance to periprocedural embolisation.

Various randomised studies naturally fail to deal with the mitigation of embolisation by choosing suitable patients. In our view this may be highly important in avoiding complications. CTA provides information not only on the position of plaques on the vessel wall but also their structural components, and consequently their embologenity. In addition to the examination of neck’s carotid stenosis this technique is also suitable for examining the AA and CCA at the same time, showing the positions and quantity of potentially embologeneic plaques.

Knowledge of the physical attributes of CAS devices – in view of the embologeneity of the ICA, AA and CCA they need to pass through – may contribute to reducing periprocedural complications in the case of the endovascular treatment of ICA stenosis. With this information in mind it is possible to decide which intervention entails lower risks for the patient.

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