Peripheral experiments on animal models from 1977 to 1979, Mathias et al. proposed Carotid percutaneous intervention has a history of more than 25 years. After Carotid Stents Historical View and Structural Characteristics of With our experience in carotid stenting since 1997 (more than 1,900 correct use of specific devices. applicable to all situations. Nevertheless, no data are available regarding the correct use of specific devices.

With our experience in carotid stenting since 1997 (more than 1,900 procedures), we strongly believe that the different devices should be used following pre-defined logical indications, rather than be chosen by chance. As such, an overview of carotid stents and their use in a "tailored" CAS concept, focusing on the new hybrid stent, is presented here.

Overview of Carotid Stents

Historical View and Structural Characteristics of Carotid Stents

Carotid percutaneous intervention has a history of more than 25 years. After experiments on animal models from 1977 to 1979, Mathias et al. proposed the treatment of carotid stenosis using percutaneous angioplasty. The first carotid angioplasty (CA) performed to treat an atherosclerosis stenosis was carried out in 1980, and it soon became an alternative for patients with high surgical risk. The main limitations of CA include the vessel acute elastic recoil after lesion dilatation and the difficulty of dealing with procedure complications, such as artery dissection, luminal flap, acute closure and others.

In fact, the first stent implanted in a carotid artery was performed in 1989 to treat an intimal flap after CA. The initial experience with carotid stents was based on the Palmaz-Schatz balloon-expandable stents and the self-expandable rolling membrane Wallstent. The main limitation of balloon-expandable stents in the carotid district is the susceptibility of these devices to suffering compression by external mechanical forces. The reported compression incidence of the Palmaz stent ranged from 1% to 15% in some series. Other important limitations of balloon-expandable stents are the unsuitable stent length for the carotid district, low conformability to deal with carotid bifurcation anatomy and the risk of arterial damage or dissection by distal/proximal balloon stretch.

After this initial phase, the use of balloon-expandable stents in the carotid district was abandoned and soon substituted by peripheral self-expandable stents, such as the rolling membrane Wallstent (original indication to treat iliac artery lesions) and Magic Wallstent (original indication to treat bypass graft lesions). The clear main advantages of the self-expandable stents when used in the carotid district are their ability to return to their original shape even if suffering external pressures and the possibility of covering very long lesions using a single stent.

From a historical standpoint, the first self-expanding stent dedicated to carotid application was the carotid Wallstent, which was made from cobalt alloy. This braided mesh stent frame is constructed from a single piece of cobalt alloy wire that is woven into a tubular structure to create a highly flexible stent with acceptable radial strength. The braided mesh frame is compressible and can be constrained within a sheath. A spring-like action allows this structure to expand as the sheath is withdrawn during deployment. The experience with this device has been widely described and is still an excellent option when performing CAS.

The second important group of self-expanding carotid stents is represented by nitinol structure stents. Currently, most commercially available carotid stents are obtained from a tube of nitinol (nickel–titanium alloy). The tube is laser-cut to create a meshed frame comprising sequential aligned annular rings, interconnected in a helical fashion. The thermal expansion properties of nitinol characterise these devices. The transition temperature is the temperature at which the nitinol frame
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**Technical Evolution of Carotid Stents**

The nitinol stents were initially proposed for two types of cell (closed cells and opened cells), as well as in two different formats (the cylindrical shape and the tapered shape). The tapered shape allows consideration for the diameter difference between the internal and common carotid arteries, applying a homogeneous radial force. ‘Closed-cell design stents’ are characterised by small, free-cell areas between the metallic struts, compared with ‘open-cell design stents’, which leave larger gaps uncovered.

Recently, the hybrid nitinol carotid stent was introduced into the market. It is composed of both closed and opened cells and is detailed later in this article. Figure 1 shows the different types of stent used in the carotid district.

Some other types of carotid stent were proposed for CAS such as covered self-expandable stents27 (patient population), heparin-coated, balloon-expandable stents (tested in baboon models)28 and membrane stents29 (tested in human carotid cadaveric explants into a pulsatile-flow model), but their use was limited due to the lack of a clear benefit in models or due to higher restenosis rates in humans.

**Self-expanding Carotid Stents – Functional Characteristics**

The differences in material, construction and design between the various self-expanding stents provide each stent with unique functional properties. The functional characteristics of carotid stent frames are the following:

- foreshortening – the difference in stent length before delivery and after deployment;
- conformability or flexibility – the capacity to conform to lesion contours and vessel tortuosity after deployment;
- vessel wall adaptability – the ability of the stent to adjust to the anatomy of the carotid region;
- scaffolding – the amount of support a stent gives to the vessel wall and carotid plaque;
- wall coverage – the ratio between the quantity of stent material and the amount of covered vessel/plaque tissue; and
- outward radial force – the amount of external pressure a stent can withstand without resulting in a permanent reduction of the vessel lumen.

A semi-quantitative comparison of functional differences between braided mesh cobalt alloy and nitinol (open-cell, closed-cell and hybrid design) is reported in Table 1. Because a considerable number of self-expandable carotid stents are produced by different companies, the division of the stents into four big groups gives only an idea of the basic characteristics shared by stents that belong to the same group. According to this division, the basic advantages and disadvantages of each stent group can be summarised generally, as detailed below.

**Cobalto Alloy Braided Mesh Stents**

The advantages include:

- a small and flexible delivery system;
- high scaffolding properties (plaque covering); and
- the ability to accommodate carotid bifurcation.

The disadvantages include:

- potential unpredictable shortening (or lengthening) during deployment;
- a loss of structural flexibility when inserted into vessels; and
- an unpredictable radial force (depending on the angle formed between the braided mesh.

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**Table 1: Functional Characteristics of Carotid Stents**

<table>
<thead>
<tr>
<th>Stent Technical Features</th>
<th>Braided Mesh</th>
<th>Nitinol Open Cells</th>
<th>Nitinol Closed Cells</th>
<th>Nitinol Hybrid Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreshortening</td>
<td>TS</td>
<td>TI</td>
<td>TI</td>
<td>TI</td>
</tr>
<tr>
<td>Conformability/ flexibility</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Vessel wall adaptability</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Scaffolding</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Radial strength</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Radial stiffness</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lesion covering</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

TI = technically insignificant (<15%); TS = technically significant (>15%). Semi-quantitative grading of b, c, d, e, f and g: – = worse than others; + = comparable with others; ++ = better than others.
Peripheral

**Nitinol Open-cell Stents (Either Cylindrical or Tapered)**
The advantages include:

- the absence of shortening during deployment;
- conformability and flexibility;
- high vessel wall adaptability; and
- a predictable radial force.

The disadvantages include:

- moderate scaffolding properties (plaque covering); and
- tent strut malalignment in complex carotid lesions.

**Nitinol Closed-cell Stents (Either Cylindrical or Tapered)**
The advantages include:

- the absence of shortening during deployment;
- high scaffolding (plaque covering); and
- a high predictable radial force.

The disadvantages include:

- significant stiffness of the structure; and
- poor conformability and flexibility.

**Hybrid Nitinol Stent**
The advantages include:

- the absence of shortening during deployment;
- high conformability and flexibility on both extremities;
- high vessel wall adaptability on both extremities;
- high scaffolding at the mid-portion; and
- a predictable radial force.

The disadvantages include:

- the fixed length of the closed-cell portion (10–13mm); and
- lower scaffolding propriety at the closed- and open-cell junction.

**‘Tailored’ Carotid Angioplasty and Stenting Concept**
When planning a CAS strategy, it must be borne in mind that there are no universally accepted rules for device selection. The idea that ‘one device fits all’ is frequently considered the simplest alternative in confronting the lack of clear recommendations for a specific device choice. Different types of carotid stent are demonstrated to be often functionally equivalent if used in the clinical setting of ‘standard’ carotid lesions (stable fibrous plaques, simple supra-aortic anatomy and straight carotid bifurcation), but if we want to widen the CAS indication and treat any kind of carotid lesion, dealing with the above characteristics associated with a tortuous arterial segment (distal and/or proximal), Apart from the technical and functional characteristics, we must also take into account the fact that personal preferences and familiarity with a specific device may legitimately influence the final decision of the operator.

Our group is now using the hybrid stent in short lesions (<20mm), ulcerated lesions, all types of carotid plaque components by echo and in symptomatic patients. The hybrid stent is our first choice when dealing with the above characteristics associated with a tortuous arterial segment (distal and/or proximal). Apart from the technical and functional characteristics, we must also take into account the fact that personal preferences and familiarity with a specific device may legitimately influence the final decision of the operator.

Our group collected, from December 2001 to August 2004, prospective data on 377 consecutive patients to evaluate the feasibility of lesion-related treatment strategies in patients treated for severe CAS under embolic protection devices (EPDs). In this study, the CAS procedure was conducted by using several stents (cobalt alloy frame and nitinol frame) and EPDs (filter wires and proximal endovascular clamping devices) applied to specific lesions and/or anatomies. The primary end-point of this study was to assess the death and stroke rate at discharge. Secondary end-points were to test the feasibility and safety of tailored CAS (angiographic success, any complication between discharge and 30 days and death from any cause at 30 days). The results of the study can be summarised as follows.

- Procedural success was achieved in 377 of 377 patients (100%).
- Adverse events included:
  - during procedure: two transient ischaemic attacks (TIAs) (0.53%);
  - at discharge: one procedure-related death (0.27%), one major stroke (0.27%), two minor strokes (0.53%), four TIAs (1.06%), one intracranial haemorrhage (0.27%); all adverse event rate at discharge: 2.92%; all strokes and death rate at discharge: 1.06%;
  - at 30-day follow-up: one death – not procedure-related (0.27%) – and one minor stroke (0.27%); and
  - overall procedure-related stroke and death rate: 1.33%.

As previously mentioned, the structural and functional features of stents are different and vary between the four groups of self-expandable stents. Based on the stent functional characteristics reported in Table 1, we can try to find a logical relationship between technical features and carotid treatment strategy. Stent applicability should depend primarily on the arterial anatomy and specific details of the lesion being treated. In this functional categorisation, the specific indication for the different groups of stents can be roughly described as follows.

- Cobalt alloy braided mesh and nitinol closed-cell stents are the preferable devices every time reliable plaque covering must be achieved. They exert a long-acting plaque prolapse prevention (soft carotid plaques very prone to distal embolisation and long unhomogeneous lesions).
- Nitinol open-cell stents are chosen when the main technical problem of carotid stenting is represented by the carotid bifurcation and plaque complexity (angled lesions and plaque ulceration/erosion), or when the main goal is to maintain the original anatomy at the lesion site.
- Nitinol closed-cell stents represent a great technical approach when an outward radial force is needed over time when approaching resistant or calcified lesions.
- The self-expanding hybrid nitinol stent offers a hybrid solution using open cells in the distal and proximal segments to enhance flexibility and a closed cell design in the middle segment to provide appropriate scaffolding and prevent plaque prolapse.
An important finding comes from the carotid plaque composition profile in this neurologically complicated subset. At echo-Doppler evaluation, all of the 10 patients with embolic complications presented a pattern of risky soft plaque as confirmation that the best predictor of embolic complications is not the percentage stenosis but the plaque composition.21 Regarding the temporal distribution of embolic events related to CAS, it was also observed that the post-procedural phase (up to 30 days of follow-up) is not complication-free: roughly two-thirds of the neurological complications may occur in this vulnerable time period. Another important finding was that if the procedure was performed in a tailored CAS concept, the procedural embolic complications were limited to TIA.

There is initial evidence regarding the influence of stent design on post-procedural events (level 3–5 scientific evidence). Bosiers et al.22 reported significant benefit in favour of stent scaffolding and wall coverage for reducing post-procedural neurological complications in a retrospectively evaluated symptomatic population (unstable risky plaque). These data are certainly not definitive and require confirmation in other studies, but some points in the experience of Bosiers et al. are notable. Similar to our results, it was reported that the majority of embolic complications (TIs) included occurred in the post-procedural phase when no protection devices are in place and only the carotid plaque and the stent frame are interacting. Also, the varying complication rates among stents seem almost entirely related to the symptomatic status of the population (proportion of unstable risky plaque).

New Hybrid Carotid Stent

Stent Technical Description

The Cristallo Ideale Carotid Stent System is a nitinol self-expanding stent pre-mounted on a 135cm-long, 5-F rapid-exchange-type delivery system compatible with a 0.014-inch guidewire. This device has been designed for permanent implantation in carotid artery bifurcation to maintain the artery luminal diameter and to respect the original anatomy at the lesion site. This implantable device is characterised by a hybrid solution consisting of three segments: a closed cell mid-section (3.24mm2 area) to obtain appropriate carotid plaque scaffolding, and two open-cell portions at both edges (proximal: 15.17mm2 area; distal: 11.78mm2 area) to enhance flexibility and vessel wall adaptability (see Figure 2). One tantalum radiopaque marker is present at each end of the stent. The stent is available in tapered and cylindrical shapes in lengths of 30 or 40mm and diameters ranging between 6 and 10mm.

Multicentre Experience with a New ‘Hybrid’ Carotid Stent

The Cristallo Registry

Our group participated in a prospective multicentre registry, the Cristallo Registry, which evaluated the safety and performance of hybrid carotid stents (Cristallo Ideale, Roncadelle, Italy), recently published in the Journal of Endovascular Therapy.23 Four high-volume centres with physicians who had performed more than 300 CAS as primary operator were involved in this study. The registry was designed to enrol patients for six months and follow them for 30 days after treatment. The study was open to patients with ipsilateral neurological symptoms plausibly related to an angiographically proven ≥60% diameter stenosis or to asymptomatic patients with ≥80% stenosis at the carotid bifurcation or in the proximal internal carotid artery. The primary end-point was the incidence through 30 days of device- or procedure-related major or minor adverse neurological events (MANEs), defined as major or minor stroke and death. Secondary end-points were technical success, defined as the ability to deploy the study stent in the target lesion with residual diameter stenosis of 30%, and procedural success, defined as technical success free of procedural MANEs.

One hundred and twenty-four patients (88 men, mean age 71.8±7.3 years, range 52–87 years) were enrolled in the registry. The demographic, clinical, neurological and angiographic data of the study group are summarised in Table 2. More than half (61.3%) were over 75 years of age, and one-quarter (24.2%) were symptomatic. The average stenosis was 84.1±7.8%. The 124 patients in the study received individual stents measuring 6x9x30mm (n=6), 6x9x40mm (n=22), 7x10x30mm (n=24) and 7x10x40mm (n=72).
Peripheral

Results from the Cristallo Registry

Technical and procedural successes were achieved in all of the enrolled patients (100%). A little more than half of the patients (58.9%) had proximal protection during the procedure, and 51 patients (41.1%) had distal filtration. Visible debris was collected from 71 patients (57.3%). There were no minor or major neurological events during the procedures.

Thirty-day follow-up was available for 119 patients (96%). Two patients (1.6%) were lost to follow-up, and three patients (2.5%) died from non-neurological causes during the study period. An example of a CAS procedure using the Cristallo Ideale stent is shown in Figure 3.

Figure 3: Example of a Carotid Angioplasty and Stenting Procedure Using the Cristallo Ideale Stent

A: Patient with severe ulcerated plaque associated with discrete distal vessel tortuosity. Note the severe lesion (full arrow) and the ulcer (dotted arrow). B: Cristallo Stent positioning. Note the vessel occlusion during stent positioning due to lesion severity. The closed-cell segment (delimited by the circle) was positioned to cover the ulcer and the lesion. The entire stent length is delimited by the square. C: Final result showing no residual stenosis, coverage of the ulcer and maintenance of the original anatomy. D: Stent boost subtraction (Philips Medical Systems Nederland) performed before post-dilatation. The circle delimits the closed-cell segment. E: Stent boost subtraction performed after post-dilatation. F: Final fluoroscopy acquisition. Note the clear difference between closed-cell segment (full line) and open-cell segments (dotted line).

Conclusion from the Cristallo Registry

After analysing those results, it was concluded that the Cristallo Ideale stent, used in conjunction with currently available neuroprotection systems, performed safely and effectively in an unselected study population of predominantly high-risk patients. From this perspective, the results collected in this multicentre registry are very encouraging. No MANEs have been detected and reported, neither during procedure nor in the post-procedural phase up to 30 days follow-up. These results take on more importance when we consider that they were obtained in an unselected population in which any type of carotid lesion and supra-aortic anatomy were accepted. In addition, patients over 75 years of age were in the majority. We also have to take into account that expert operators performed all procedures.

Final Considerations

Based on the scientific evidence emerging both from our studies and from literature data, the following considerations should be taken into account.

- A perfect carotid stent does not exist, and no single stent is applicable to all carotid lesions and anatomies.
- The new stents allow operators to treat more complex lesions and anatomies, thereby widening the indication for CAS.
- Stent design plays a major role in determining its functional behaviour. As the carotid anatomy and the plaque complexity vary from case to case, we should match the stent technical characteristics to the anatomo-pathological variables.
- Available data suggest that the use of new materials/devices matched to specific lesions or anatomies may improve both the procedural and 30-day clinical outcomes.
- ‘Tailored’ CAS was demonstrated to be feasible, but was not without complications.
- The Cristallo Ideale carotid stent is safe and effective in the peri-procedural period. Its newly designed hybrid structure seems to support the rationale of combining adequate plaque scaffolding with high vessel adaptability.