Optical Coherence Tomography after Carotid Stenting: Rate of Stent Malapposition, Plaque Prolapse and Fibrous Cap Rupture According to Stent Design

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WHAT THIS PAPER ADDS
The present study is the first in the literature focussing on the complex interaction between carotid plaques and stents by analysing OCT (optical coherence tomography) findings (stent malapposition, plaque prolapse and cap rupture) according to stent design.
The results of this investigation offer some original and unexpected information, which is available for the first time at such a high definition, and that may influence our future clinical policies in patients with carotid artery disease.

Objectives: This study aims to evaluate the rate of stent malapposition, plaque prolapse and fibrous cap rupture detected by optical coherence tomography (OCT) imaging according to carotid stent design.
Design: It was a prospective single-centre study.
Materials and methods: Forty consecutive patients undergoing protected carotid artery stenting (CAS) and high-definition OCT image acquisition were enrolled in the study. OCT frames were analysed off-line, in a dedicated core laboratory by two independent physicians. Cross-sectional OCT images within the stented segment of the internal carotid artery were evaluated at 1-mm intervals for the presence of strut malapposition, plaque prolapse and fibrous cap rupture according to stent design.
Results: Closed-cell design stents (CC) were used in 17 patients (42.5%), open-cell design stents (OC) in 13 (32.5%) and hybrid design stents (Hyb) in 10 (25%). No procedural or post-procedural neurological complications occurred (stroke/death 0% at 30 days). On OCT analysis the frequencies of malapposed struts were higher with CC compared to OC and Hyb (34.5% vs 15% and 16.3%, respectively; $p < 0.01$). Plaque prolapse was more frequent with OC vs CC (68.6% vs 23.3%; $p < 0.01$) and vs Hyb stents (30.8%; $p < 0.01$). Significant differences were also noted in the rates of fibrous cap rupture between CC and OC (24.2% vs 43.8%; $p < 0.01$), and between CC and Hyb (24.2% vs 39.6%; $p < 0.01$), but not between OC and Hyb stents ($p = 0.4$).
Conclusion: Intravascular OCT after CAS revealed that micro-defects after stent deployment are frequent and are related to the design of implanted stents. Stent malapposition is more frequent with CC stents, while plaque prolapse is more common with OC stents.
It remains, however, unknown whether these figures now detected with OCT are of any clinical and prognostic significance.
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Optical coherence tomography (OCT) is a light-based imaging method that uses newly developed fibre-optic technology. In the cardiovascular field OCT is a catheter-based invasive intravascular imaging system that uses near-infrared light with orders of magnitude higher than those of medical ultrasound signals, providing unprecedented microstructural information on atherosclerotic plaques. OCT is a progressively accepted intravascular modality to study coronary arteries, stent implantation and vessel injury, as it permits accurate measurements of luminal architecture and provides insights into plaque coverage, plaque prolapse, stent apposition, overlap and neo-intimal thickening.[1,2] The superiority of OCT as a modality in the

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setting of coronary stent apposition has been demonstrated;[3] it is due to its ability to resolve small gaps between the stent strut and the vessel wall, which are often missed by intravascular ultrasound (IVUS).

Coronary stent-strut coverage and apposition have been linked to the risk of stent thrombosis,[4] and recent randomised clinical trials have selected these variables detected by OCT as their primary 'end' point,[5] revealing new and unexpected data.

Safety and feasibility of OCT applied to carotid arteries have been recently reported, with both an occlusive and a non-occlusive technique.[6–11]

There is great interest in the possibility to recognise further details regarding the interaction between a carotid plaque and a stent by OCT, considering that plaque prolapse through the cell stent has been suggested as one of the major causes of post-procedural complications following carotid artery stenting (CAS) and that available peri-procedural imaging systems (angiography, IVUS and duplex ultrasound) may not be able to detect such micro-defects.

At present, three designs of carotid stents with distinctive features are available: closed-cell (CC), open-cell (OC) and hybrid (Hyb) cell design, and different rates of neurological events after CAS have been previously reported according to the stent design.

Unfortunately existing intra-procedural imaging systems have not been able to clearly define and provide precise details of the conformability of actual carotid stents to lesion contours and vessel tortuosity after deployment (defined as stent apposition/malapposition) or of the ability of the stent to effectively cover the plaque. High-resolution OCT images might provide more satisfactory results, and this prospective study is the first to investigate the distribution of such micro-defects after CAS according to stent design.

The aim of this study is to evaluate the rate of stent malapposition, plaque prolapse and fibrous cap rupture detected by OCT after CAS according to stent design.

METHODS

This prospective study was performed in a single centre, including 40 consecutive patients undergoing CAS during two interval periods correlated to the availability of the OCT catheters in our Department (first 25 cases from March 2011 to July 2011 and the last 15 cases from January 2012 to March 2012).

The study protocol was approved by our ethics committee, and written informed consent was obtained from all patients. Inclusion criteria were a >80% asymptomatic internal carotid artery (ICA) stenosis or a >70% symptomatic ICA stenosis (NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria[12]) in patients already considered eligible for endovascular treatment.[13]

During the same period 12 patients were excluded from the study because of elevated serum creatinine levels (>1.2 mg dl^{-1}, $n = 6$), a positive history of contrast medium intolerance ($n = 2$) and severe tortuosity of the ICA distal to

the target lesion ($n = 4$) evaluated by the operator as unfit for safe OCT catheter advancement (see 'OCT technique' section).

Demographic variables, clinical figures and intra-operative and follow-up data were prospectively collected by the operating team in a dedicated database.

Lesion characteristics and plaque composition were studied using duplex ultrasound images and classified according to the Gray-Weale classification[14] (Type 1 plaques: dominantly hypoechoic, Type 2 plaques: substantially hypoechoic with small areas of hyperechoicity, Type 3 plaques: dominantly hyperechoic with small areas of hypoechoicity, Type 4 plaques: uniformly hyperechoic and homogeneous). A lesion comprising ≥2 craters of ≥3 mm depth or with poorly defined edges and a hazy appearance was defined as ulcerated.

Echo duplex and independent neurological examinations of all patients were performed before the intervention, at discharge and 30 days after the procedure. All patients underwent a cerebral computed tomography/magnetic resonance imaging (CT/MRI) scan before treatment, whereas a post-procedural cerebral CT/MRI scan was only scheduled in the case of a documented neurological complication.

CAS technique

CAS was performed according to our standard technique, which has been described previously.[15] Briefly, once the common carotid artery is selectively engaged directly using an appropriate 8-F guiding catheter, and a cerebral protection device is deployed in a straight segment of the extracranial portion of the ICA distal to the culprit lesion, the first OCT scan is performed during a non-occlusive flush (see 'OCT technique' section).

Carotid stenting is then carried out using self-expandable stents in all cases. The stent diameter is selected according to the ICA diameter (mean oversize of 1 mm), while stent length is calculated to cover the entire carotid lesion (at least 0.5 cm below and 0.5 cm above the target lesion). In all cases post-dilatation of the stent is performed using short dedicated balloons (maximum size 5.5/20 mm) inflating to nominal pressure, considering ≤30% residual stenosis as acceptable for technical success.

Description of the OCT technique

Carotid OCT images were acquired three times in each of the 40 patients: before stent deployment, immediately after stent placement and following dilatation of the stent.

The optical fibre of the Lightlab FD-OCT system used for the investigation is encapsulated within a rotating torque wire (0.014-inch compatible) built in a rapid-exchange 2.6-F catheter compatible with a 6-F guiding catheter. It acquires 100 frames s^{-1}, scanning a 55-mm artery segment in 2.7 s (pullback speeds up to 20 mm s^{-1}).

Once the cerebral protection device is deployed in a straight portion of the ICA distal to the culprit lesion, the calibrated OCT catheter is advanced over the 0.014-inch

guide wire of the filter and completely passed over the lesion that needed to be scanned.

Pullbacks are started during a non-occlusive flush, mechanically injecting 24 ml of 50% saline diluted contrast medium (Iodinoxanol: Visipaque 320 mg I ml^{-1}; GE Healthcare, Cork, Ireland) at 6 ml s^{-1}, 750 psi, using an automatic injection system (Mark V ProVis; Medrad Inc.) to completely replace blood from the artery. Injections are performed through an 8F guiding catheter with a minimum internal lumen of 2.3 mm, placed just few centimetres proximal to the carotid bifurcation.

Of note, the pullback is started approximately 1.5—2 s after the injection of the diluted contrast medium, when the absence of blood scattering and signal attenuation are noted on the screen of the OCT system (real-time images).

After stent deployment the same OCT manoeuvres are repeated; in particular, two further scans are performed before and after stent dilatation.

Qualitative and quantitative assessment of OCT images

All OCT frames were analysed off-line, in a dedicated core laboratory, by two independent physicians (FS and PS). OCT images were judged of good quality according to a previously reported protocol, based on the accuracy of vessel wall identification.[11]

OCT images after stent deployment and dilatation (third scan) were specifically reviewed and analysed in each patient for the purpose of this investigation according to the design of the implanted stent. In particular cross-sectional OCT images within the stented segment of the ICA were evaluated at 1-mm intervals for the presence of malapposition, plaque prolapse and fibrous cap rupture (Fig. 1).

The term 'malapposition' was used when the distance measured from the surface of the blooming (the inner and outer contours of each strut reflection) to the lumen contour was greater than the total thickness of the stent strut + one-half of the blooming.

Considering that carotid stent struts ranged from 0.106 to 0.186 mm,[16] a strut was classified as 'malapposed' when the distance measured was >200 μm (Fig. 2(a)) and 'well apposed' when the distance measured ranged 10—200 μm (Fig. 2(b)).

Stent struts were further defined as 'embebbed' when burying into the intima for almost the entire size of their thickness (distance measured <10 μm, Fig. 2(c)).

Plaque prolapse after stenting was defined as any appreciable tissue prolapse between the stent struts (Fig. 3(a)), while any discontinuity of the inner layer of the plaque profile was considered as a rupture of the fibrous cap (Fig. 3(b)).

'End' points

The primary 'end' points of the study are the rate of stent malapposition, plaque prolapse and fibrous cap rupture detected by OCT imaging after CAS, according to the design of the implanted stent.
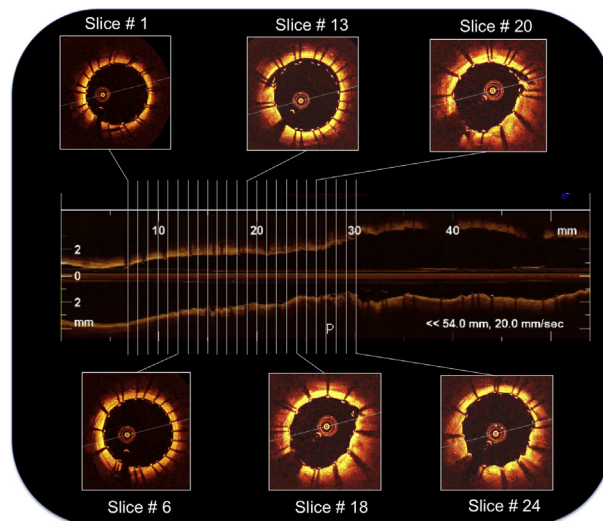

Figure 1. Analysis of cross-sectional OCT images within the stented segment of the internal carotid artery evaluated at 1 mm intervals. Details of slice evaluation for the presence of malapposition, plaque prolapse and fibrous cap rupture are shown in the boxes.

Secondary 'end' points include: stroke or death rate at 30 days and any in-hospital adverse events.

Definition of stent design

The CC design refers to stents in which no regions of the stent are free to move independently from adjacent segments.

The OC design refers to stent designs in which some individual segments of the stent are not attached to adjacent segments and can therefore move independently.

The Hyb design consists of proximal and distal segments with an open-cell design (to maximise conformity) in combination with a central CC segment (for plaque/thrombus coverage).

Statistical analysis

Continuous variables are presented as mean + standard deviation (SD), and Mann—Whitney and Student's *t*-tests were used, as appropriate. Differences in categorical variables were assessed using the χ^2 and Fisher's exact tests.

All statistical analyses were performed using the statistical software package Statistical Package for the Social Sciences (SPSS) v.13 (SPSS Inc., Chicago, IL, USA) and MatLab v.7.0.1 (MathWorks).

RESULTS

Procedural results

CAS with OCT images acquisitions was performed in all 40 patients.

The data of plaque evaluation by OCT are provided in Table 1.

Completion angiograms revealed successful revascularisation and <30% residual stenosis in each case. CC stents were used in 17 procedures (42.5%) (Carotid Wallstent — Boston Scientific Corp, Natick, MA, USA — No.13;
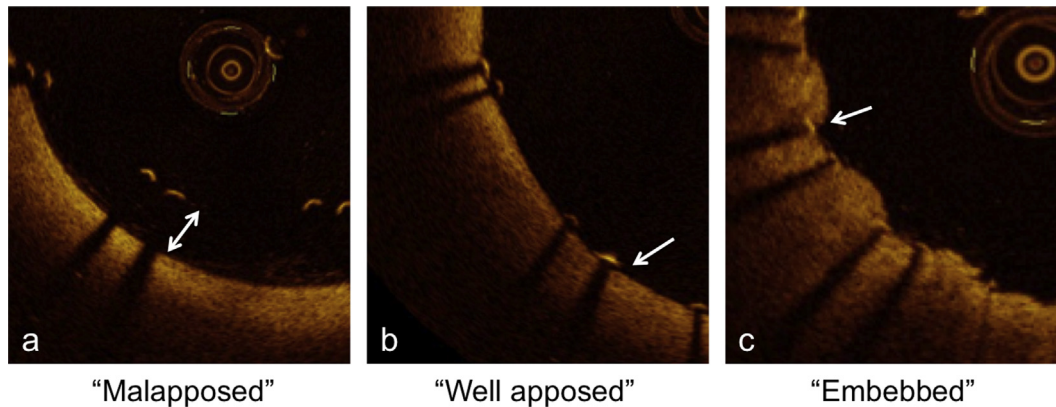
Figure 2. Classification of stent strut apposition. The distance between endoluminal edge of the strut and intima was measured. Based on this value, struts were classified into 3 grades: "malapposed" (>200 µm), "well apposed" (10–200 µm), or "embebbed" (<10 µm).

Adapt — Boston Scientific Corp, Natick, MA, USA — No. 2; X-act — Abbott Vascular, Redwood City, CA, USA — No. 2), OC stents in 13 (32.5%) (Precise — Cordis, Miami Lakes, FL, USA — No. 9; Protégé — ev3, Plymouth, MN, USA — No. 4) and Hyb stents in 10 (25%) (Cristallo Ideale — Medtronic/Invatec, Santa Rosa, CA, USA — No. 10) (Table 2).

Table 3 summarises the patients' demographic data, neurological histories and carotid plaque characteristics according to stent design.

No technical or neurological complications occurred during OCT pullbacks. The mean procedural time was 50 ± 11 min, and the total amount of contrast medium was 85 ± 17 ml/patient (range 60–135).

No major procedural or post-procedural complications occurred in the study population (any stroke/death 0% at 30 days). Two transient ischaemic attacks (TIAs) were recorded in the post-operative period (one in the OC group, one in the Hyb group).

During the hospitalisation period, kidney function was carefully monitored to assess the consequences of the extra amount of contrast media needed for OCT image acquisition. The estimated glomerular filtration rate (eGFR) remained stable in all patients (preoperative value 98 ± 6.5 ml min^{-1} 1.73 m^{-2} vs postoperative 92 ± 7.4 ml min^{-1} 1.73 m^{-2}, $p = 0.9$).

The OCT images acquired after stent deployment and dilatation were judged in all cases to be of appropriate quality to allow the qualitative and quantitative assessment of the primary 'end' points of the study.

OCT analysis

OCT analysis within the stented segment of the ICA at 1-mm intervals produced a mean of 20 ± 5 slices in each patient (Fig. 1). A total of 729 cross-sectional OCT images were analysed to assess the rate for stent apposition, plaque prolapse and fibrous cap rupture.

A mean of 28 ± 2 stent struts were detected in each slice, for a total of 20,412 struts evaluated.

Inter-observer variability was very good for identification of stent apposition ($k = 0.84$), plaque prolapse ($k = 0.85$) and rupture of the fibrous cap ($k = 0.81$). Intra-observer agreement, evaluated asking each observer to assess twice the images within a 7-day interval, was excellent ($k = 0.95$).

The results of stent malapposition, plaque prolapse and rupture of fibrous cap are presented on a slice-based analysis and on a patient-based analysis. Data on stent malapposition are also reported on a strut-based analysis.

In the strut-based analysis (Table 4), an average of 34.5% struts were 'malapposed' in the CC group, compared to 15%
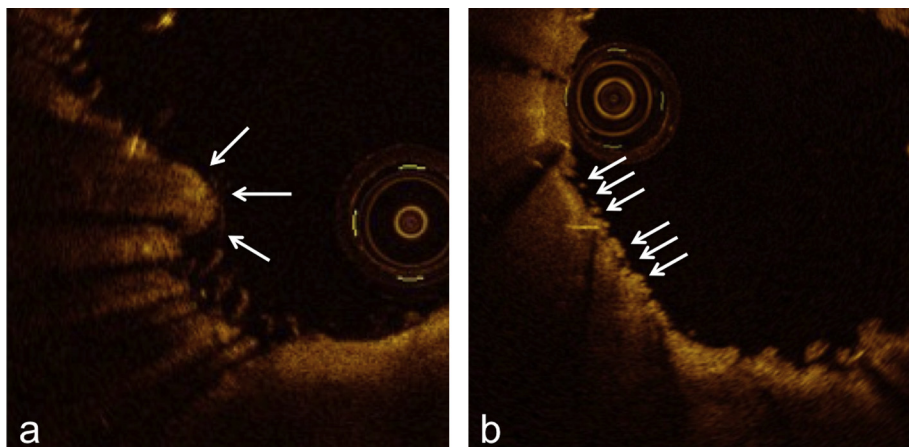

Figure 3. a. Plaque prolapse between the stent struts; b. rupture of the fibrous cap.

Table 1. OCT findings at first pullback.

Diameter stenosis (mean %)	81% ± 4
Calcification[a] (no., %)	18 (45%)
Lipid-Rich Plaque[b] (no., %)	26 (65%)
Ulcerated Plaque[c] (no., %)	11 (27.5%)
Thrombus[d] (no., %)	4 (10%)

[a] Heterogeneous, sharply delineated, signal-poor or signal-rich region, or alternating signal-poor and signal-rich regions.
[b] Homogeneous, diffusely bordered, signal-poor region with an overlying signalrich band corresponding to a fibrous cap.
[c] A cavity with a lacerated superficial intimal layer.
[d] A backscattering protrusion into the carotid lumen with signal-intensity-free shadowing.

in the OC stent and 16.3% in the Hyb stent groups ($p < 0.001$). Stent struts were found to be 'embebbed' into the intima in 9% of the CC stent group, compared to 27% of the OC stent and 25.6% of the Hyb stent groups ($p < 0.001$).

In the slice-based analysis (Table 5), the frequencies of slices with at least five malapposed struts were higher in the CC stents compared to OC and Hyb stents (29.8% vs 13.2% and 14.8%, respectively; $p < 0.01$).

Plaque prolapse was significantly less frequent with the CC (23.3%) and with Hyb (30.8%) compared to the OC stents (68.6%; $p < 0.01$).

Significant differences were also noted in the rates of fibrous cap rupture between CC and OC stents (24.2% vs 43.8%; $p < 0.01$), and between CC and Hyb stents (24.2% vs 39.6%; $p < 0.01$), but not between OC vs Hyb stents ($p = 0.4$).

On a patient-based analysis (Table 6) plaque prolapse was significantly more common with OC (61.5%) compared to CC stents (17.6%; $p = 0.02$), while the rates of fibrous cap rupture were nearly significant between CC and OC stents (17.6% vs 53.8%; $p = 0.05$). A non-significant statistical trend was also noted for the rate of struts malapposition in patients treated by CC compared to those treated by OC (41.6% vs 15.3%, $p = 0.2$).

Table 7 shows an overview of demographic, clinical and procedural data, correlated to the OCT findings in the two patients suffering from TIA after CAS.

DISCUSSION

This is the first study using OCT to assess carotid stent apposition, plaque prolapse and fibrous cap rupture systematically following CAS. To date, limited information

Table 2. Overview of CAS materials.

Stent design	n. (%)
Closed-cell	17 (42.5%)
Wallstent	13
Adapt	2
X-Act	2
Open-cell	13 (32.5%)
Precise Pro Rx	9
Protégé	4
Hybrid	10 (25%)
Cristallo Ideale	10

has been available regarding the complex interaction between carotid plaques and stents, considering that neither angiography nor IVUS has the micro-scale resolution capable of identifying such imperfections. OCT with its high-resolution capability of 10 μm can detect them, and our study has shown that in a relevant number of cases stent strut malapposition, plaque prolapse or rupture of the fibrous cap persists despite technical success detected by angiography.

Regardless of the use of an embolic protection device, percutaneous treatment of carotid pathologies has been correlated with a risk of cerebral ischaemic events related to distal embolisation.[17] Many factors may cause an intra-procedural embolisation (including incorrect endoluminal manoeuvres, complex aortic arch, use of cerebral protection devices, stent deployment and ballooning, etc.),[18] while events occurring in the early postoperative period are contemplated as the consequences of remodelling of the atheroma, which is more or less contained behind the stent struts.

Bosiers et al.[19] reported different neurological rates after CAS with different carotid stent designs. The study focussed on post-procedural events (when the struts of the stent and its scaffolding properties are the only protection against plaque embolisation) and found that the symptomatic population had an event rate highest when an OC type was implanted.

These results opened the debate on the ability of plaque coverage by distinctive stent designs. On the contrary, another investigation[20] has reported that carotid stent cell design is not a determinant of neurologic complications, and periprocedural and early post-procedural complications may occur indifferently from the design of the implanted stent. More recently a randomised controlled trial[21] showed that cerebral embolisation, as detected by transcranial Doppler and diffusion-weighted MRI, occurs with similar frequency after CAS with OC and CC stents.

Actually the precise mechanism for cerebral embolisation after carotid stent implantation is still unknown: it is obvious that plaque prolapse through the stent cell may be responsible for neurological symptoms, but also stent malapposition might play a role. Platelet micro-aggregation can occur behind malapposed stent struts, which may act as a 'lightning rod' for thrombus formation, which might then embolise and cause a cerebrovascular event. Finally the rupture of the fibrous cap, even in a non-prolapsing plaque, may also be the reason for late embolisation.

Our findings confirm that, when interacting with the plaque, all carotid stent designs are susceptible to those micro-defects that are potentially responsible for cerebral embolisation.

Incomplete coronary stent strut apposition has recently received attention with studies suggesting an association with an increased rate of long-term stent thrombosis.[22,23] An OCT-based natural history study[24] has revealed that incomplete stent apposition without stent strut coverage in coronary arteries is significantly associated with the presence of OCT-detected thrombus at follow-up, which may

Table 3. Patient characteristics.

	Total population (n = 40)	Closed-cell design (n = 17)	Open-cell design (n = 13)	Hybrid design (n = 10)	p-value
Male, No. (%)	26 (65%)	11 (64%)	8 (61%)	7 (70%)	ns
Age (yrs)	73 ± 3.8	74 ± 2.6	73 ± 3.1	72 ± 2.9	ns
Neurological symptoms, No. (%)	17 (38%)	11 (64%)	2 (15%)	4 (40%)	CC vs OC $p = 0.01$ CC vs Hyb $p =$ ns OC vs Hyb $p =$ ns
Hypertension, No. (%)	31 (77.5%)	12 (70%)	11 (84%)	8 (80%)	ns
NIDDM, No. (%)	13 (32.5%)	6 (35%)	4 (31%)	3 (30%)	ns
Smoker, No. (%)	18 (45%)	8 (47%)	5 (38%)	5 (50%)	ns
CAD, No. (%)	12 (30%)	6 (35%)	3 (23%)	3 (30%)	ns
Renal function (eGFR; mL/min/1.73 m^2)	98 ± 6.5	99 ± 5.5	102 ± 6.8	96 ± 7.5	ns
Peripheral arterial disease, No. (%)	18 (45%)	8 (47%)	6 (46%)	4 (40%)	ns
Hypercholesterolaemia, No. (%)	25 (62.5%)	11 (64%)	8 (62%)	6 (60%)	ns
Side of carotid lesion (right), No. (%)	21 (52.5%)	9 (53%)	8 (62%)	4 (40%)	ns
Restenosis after CEA, No. (%)	2 (5%)	1 (5%)	1 (8%)	0 (0%)	ns
Carotid plaque composition[a], No. (%)					ns
Type 1	6 (15%)	3 (18%)	1 (8%)	2 (20%)	ns
Type 2	12 (30%)	5 (29%)	4 (31%)	3 (30%)	ns
Type 3	15 (37.5%)	5 (29%)	6 (46%)	4 (40%)	ns
Type 4	7 (17.5%)	1 (5%)	4 (31%)	2 (30%)	ns
Carotid plaque ulceration, No. (%)	8 (20%)	4 (24%)	2 (15%)	2 (20%)	ns

Legends: NIDDM = non-insulin-dependent diabetes mellitus; CAD = coronary artery disease; eGFR = estimated glomerular filtration rate; CEA = carotid endarterectomy.
[a] According to the Gray-Weale classification.[11]

constitute a potent substrate for late stent thrombosis. Additionally the influence of stent design on stent strut apposition has been investigated for coronary intervention,[25] but never for carotid intervention.

It is well known that actual designs of carotid stent have distinctive features: CC stents have better coverage but less conformability; OC stents adapt better to the vessel anatomy but provide less coverage; and Hyb cell stents have intermediate properties.

Surprisingly in our study only <60% of stent struts analysed by OCT were considered 'well apposed' to the arterial wall. CC stent struts were more likely to be malapposed, while OC stent struts were more likely to be embebbed ($p < 0.01$). Moreover, plaque prolapse was more common with OC stents compared to CC stents, but not to Hyb stents, while fibrous cap rupture occurred less frequently in the CC stents compared to the OC or to the Hyb stents ($p < 0.01$).

Of course we cannot exclude that OCT analysis at follow-up might show better stent strut apposition and less prolapse of plaque. In fact we know that the constant radial force of self-expanding stents and the re-endothelisation process might both play a role in this remodelling process of the vessel after CAS.

Except for the rate of symptomatic lesions, which was higher in the CC group ($p = 0.01$), demographic and clinical characteristics of the patients entered into our registry, including age, carotid plaque composition and ulceration, were not significantly different from patients treated by different stent designs (Table 3).

In spite of these apparently similar baseline patient characteristics, we are aware that a number of potential variables in addition to stent design may have influenced the result detected by OCT (see section 'Study limitations'). For example, we may suppose that endovascular treatment

Table 4. Summary of stent apposition to the arterial wall on a stent strut-based analysis (total struts evaluated $n = 20,412$).

	Closed cell (n = 8655)	Open cell (n = 6654)	Hybrid cell (n = 5103)	p-value
Malapposed struts	34.5% (2982)	15% (998)	16.3% (833)	CC vs OC $p < 0.01$ CC vs Hyb $p < 0.01$ OC vs Hyb $p = 0.06$
Embebbed struts	9% (783)	27% (1797)	25.6% (1310)	CC vs OC $p < 0.01$ CC vs Hyb $p < 0.01$ OC vs Hyb $p = 1$
Well apposed struts	56.5% (4890)	58% (3859)	58.1% (2960)	CC vs OC $p = 0.06$ CC vs Hyb $p = 0.08$ OC vs Hyb $p = 1$

Table 5. Summary of OCT images results on a slice-based analysis (total slices evaluated $n = 729$).

	Closed cell ($n = 305$)	Open cell ($n = 242$)	Hybrid cell ($n = 182$)	p-value
Malapposition[a]	29.8%, (91)	13.2%, (32)	14.8%, (27)	CC vs OC $p < 0.01$ CC vs Hyb $p < 0.01$ OC vs Hyb $p = 0.07$
Plaque prolapse	23.3%, (71)	68.6%, (166)	30.8%, (56)	CC vs OC $p < 0.01$ CC vs Hyb $p = 0.08$ OC vs Hyb $p < 0.01$
Rupture of fibrous cap	24.2%, (74)	43.8%, (106)	39.6%, (72)	CC vs OC $p < 0.01$ CC vs Hyb $p < 0.01$ OC vs Hyb $p = 0.4$

[a] At least 5 malapposed struts in a single slice.

of calcified plaque results in more malapposed struts, while soft plaques may generate more plaque prolapse.

Fortunately no major neurological complications occurred in our series. We counted only two TIAs (one in the OC group, one in the Hyb group) that happened in patients with symptomatic plaques. Notably both patients presented at analysis of OCT frames (Table 6) a consistent number of malapposed (15—20%) or embedded struts (25—30%) associated to a high rate of plaque prolapse (55—70%) and fibrous cap rupture (40—45%).

Carotid plaque prolapse through cell stents have been already described in all series of carotid OCT.[6—11] Jones et al.[10] reported one case of OCT demonstration of a large area of tissue prolapse through an OC stent immediately after its implantation. This finding led to the decision to deploy a further stent with a CC design and obtain the resolution of the prolapse.

The main message from our investigation is that an unexpected high number of micro-imperfections after CAS are noticeable with all carotid stent designs. Although these findings might all be potentially responsible for micro-embolisation in the postoperative period with different mechanisms, at the moment we cannot suggest any particular change in the decision-making process after CAS.

In conclusion, it remains unknown whether these figures now detected with OCT are of any clinical and prognostic significance. In fact the absence of clinical events at 30 days suggests that the frequent persistence of these imperfections after CAS remains a benign phenomenon.

Study limitations

This is a single-centre study with a limited number of patients. The 'end' points of the study are a surrogate parameter instead of a clinical event. There are differences in baseline patient data (number of symptomatic lesions) that may have introduced a bias in favour of one specific stent design.

The major limitation of this study is represented by the absence of a multivariate analysis. The events of stent malapposition, plaque prolapse or fibrous cap rupture after CAS are affected by several factors; some are patient-related (age, cardiac disease, neurological status, diabetes, etc.), some are lesion-related (plaque composition, ulceration, etc.), while others are stent-related (design, type, size, etc.) or even procedure-related factors (need for pre-dilatation, maximum dilatation pressure, operator's experience, etc.).

Still there are some cross-relationships between the various independent variables, which call for a multivariate analysis. Unfortunately the small number of cases and the large number of potential determinants made powerful multivariate analysis impossible. Under such circumstances, it was unreasonable to carry out an effective multivariate analysis that should be needed in order to disentangle the various expected effects.

The choice of the stent was made on operator's preference according to a tailored strategy[26] that takes into account plaque type, anatomy at the level of the culprit lesion and patient's symptoms. This may have introduced

Table 6. Summary of OCT images results on a patient-based analysis.

	Closed cell ($n = 17$)	Open cell ($n = 13$)	Hybrid cell ($n = 10$)	p-value
Malapposition[a]	41.1%, (7)	15.3%, (2)	20%, (2)	CC vs OC $p = 0.2$ CC vs Hyb $p = 0.6$ OC vs Hyb $p = 1$
Plaque prolapse[b]	17.6%, (3)	61.5%, (8)	30%, (3)	CC vs OC $p = 0.02$ CC vs Hyb $p = 0.6$ OC vs Hyb $p = 0.2$
Rupture of fibrous cap[c]	17.6%, (3)	53.8%, (7)	40%, (4)	CC vs OC $p = 0.05$ CC vs Hyb $p = 0.3$ OC vs Hyb $p = 0.6$

[a] At least 25% of all the struts defined as malapposed per patient.
[b] At least 10 appreciable tissue prolapses between the stent struts per patient.
[c] At least 10 discontinuities of the inner layer of the plaque profile per patient.

Table 7. Clinical data and OCT findings in the two patients suffering neurological complication after CAS.

	Patient 1	Patient 2
Demographic and clinical data		
Age (years)	74	86
Neurological history	Symptomatic	Symptomatic
Carotid plaque composition	Type 2	Type 2
Carotid plaque ulceration	No	No
Procedural data		
Carotid stent design	Open cell	Hybrid
Carotid stent type	Precise	Cristallo ideale
Carotid stent size	8/40 mm	6—9/40 mm
Size of post-dilatation balloon	5.5 mm	5.5 mm
Maximum dilatation pressure	8 atm	10 atm
Complications		
Type of neurological complication	TIA	TIA
Onset time of complications	1st day (26 h after CAS)	1st day (18 h after CAS)
OCT findings[a]		
Malapposed struts	17% (87/510)	14.9% (79/528)
Embebbed struts	30.6% (156/510)	25.9% (137/528)
Plaque prolapse	Yes (present in 15 out of 21 [71.5%] slices evaluated)	Yes (present in 12 out of 22 [54.6%] slices evaluated)
Fibrous cap rupture	Yes (present in 9 out of 21 [42.8%] slices evaluated)	Yes (present in 10 out of 22 [45.5%] slices evaluated)

TIA = transient ischaemic attack; CAS = carotid artery stenting.
[a] Cross-sectional evaluation at 1 mm intervals within the stented segment of the internal carotid artery.

a bias in the study. A further study randomly allocating a stent design to groups with different histological presentation could be useful to actually verify the potential different behaviour of stent design with intravascular OCT.

Finally, although the analysis of the images post procedure was blinded, due to the unprecedented high-quality assessment of strut apposition and plaque anatomy post stenting, it is reasonable to consider that the two reviewers became aware of the stent type during the images' review process. This may have introduced a bias in the results.

CONCLUSION

Despite technical success detected by angiography, intravascular OCT after CAS revealed that stent malapposition, plaque prolapse and fibrous cap rupture are frequently found and are related to the design of implanted stents.

In particular stent malapposition is more frequent with CC stents, while plaque prolapse is more common with OC stents.

Although the clinical impact of these findings still remains to be determined, the result of this investigation seems to offer some original and unexpected information, which is available for the first time at such high definition. The careful and more detailed analysis of such results may influence our future clinical policies in patients with carotid artery disease.

CONFLICT OF INTEREST/FUNDING

None.

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