Low-pressure self-expandable luminal shield system: mechanical stabilization of high-risk coronary atherosclerotic lesions

The mechanical disruption of a thin-cap fibroatheroma by the use of balloon-expandable stents may potentially lead to the development of adverse periprocedural (no-reflow phenomenon) and long-term (stent thrombosis) clinical adverse events. It has been hypothesized that for this type of high-risk lesion, the use of ‘low radial force’ self-expandable stents specifically designed to provide suitable outward forces enabling proper vessel wall apposition and controlled luminal gain over time could be beneficial. In addition, it is believed that due to their intrinsic mechanical properties, the amount of injury elicited by the implantation of the device may be decreased, thus potentially reducing the amount of neointimal proliferation. In the setting of nonruptured lesions (so-called ‘vulnerable plaques’), necrotic core remodeling could be achieved resulting in thickening of the fibrous cap by a newly formed neointima (so-called ‘neo-cap’), thus potentially stabilizing a thin-cap fibroatheroma from future rupture. In this article, we describe the recent developments of a specific low-pressure self-expandable luminal shield (vProtect™; Prescient Medicals, Inc., PA, USA) designed to achieve these goals.

KEYWORDS: luminal shield, percutaneous coronary intervention, stent, thin-cap fibroatheroma, vulnerable plaque

Balloon-expandable stents have been established as the most common therapeutic alternative for the interventional treatment of obstructive coronary artery disease [1,2]. These devices provide high dilating forces, thus overcoming the different mechanical resistances encountered in almost any type of atherosclerotic lesion (e.g., calcified lesions) [3]. However, this mechanism of deployment imposes an unpredictable degree of mechanical stress on the vessel wall, which in some occasions results in restenosis. Although the development of drug-eluting stents has dramatically reduced the incidence of this condition, uncontrolled vascular injury may be particularly relevant in the setting of high-risk atherosclerotic lesions, such as thin-cap fibroatheroma (TCFA) [4–7]. TCFAs (unruptured or ruptured with or without the presence of thrombus) are usually bulky and contain a large amount of necrotic tissue [8]. It has been suggested that the mechanical disruption of this type of lesion may lead to the development of adverse periprocedural (embolization with slow or no-reflow phenomenon) and long-term clinical (stent thrombosis) events [9]. In addition, it has been proposed that for these high-risk lesions, the development of specially designed vascular scaffolding providing suitable outward forces, enabling proper vessel wall apposition and controlled luminal gain, may be ideal. In addition, it has been hypothesized that the resulting decrease in vascular injury at the time of implantation of the device may potentially result in less neointimal formation. In the setting of nonruptured lesions (so-called ‘vulnerable plaques’), necrotic core remodeling could be achieved, resulting in thickening of the fibrous cap by a newly formed neointima (so-called ‘neo-cap’), thus potentially stabilizing a TCFA from future rupture.

In this article, we aim to describe the vProtect™ luminal shield (Prescient Medical Inc., PA, USA), a low-pressure self-expandable coronary system designed to achieve these goals. We provide a brief technical description of the device and current information about the experimental and clinical experience acquired to date.

Device description
The vProtect luminal shield is a self-expandable nitinol-based stent designed to achieve the mechanical stabilization of nonobstructive, TCFAs in the coronary territory (Figure 1). Its main engineering goals are to reduce mechanical injury to the vessel wall, reshape the lumen, reinforce the fibrous cap and remodel the necrotic core of the treated atherosclerotic lesion. In order to be able to achieve this goal, computational modeling and in vivo models were used to calculate and validate the biomechanical properties of this device. The
biomechanical behavior of the device displays lower chronic outward forces compared with previously designed self-expandable stents while maintaining stable radial resistance forces (crush resistance) compared with balloon-expandable stents. Even though there seems to be additional expansion over time, the calculated chronic outward force appears to be half or less than that of earlier generations of self-expandable coronary stents (Figure 2).

The vProtect™ luminal shield system consists of a self-expanding vascular shield and a rapid exchange delivery system. The delivery system is compatible with 0.014” guidewires and 6-Fr guide catheters. The usable length is 135 cm with a rapid exchange guidewire lumen length of 25 cm. The delivery system consists of a distal outer sheath that houses the luminal shield and an inner body containing radiopaque markers at the distal and proximal ends of the luminal shield. The luminal shield is constructed from a nickel–titanium alloy with an austenitic finish temperature between 20 and 25°C (temperature at which the device achieves its full radial force). The luminal shield has a wall thickness of less than 57 µm and has been designed with the objective to match the elastic properties of the TCFA. The luminal shield has a vessel surface area coverage from 13 to 15% when deployed in 2.5–3.0-mm vessels [10]. Potential limitations of this technology include previously reported issues related to self-expanding stents including potential for achieving lower lumen gains in highly calcified lesions and lack of cell deformability at the time of side-branch crossing and dilatation.

Experimental data

Rabbit studies

Several studies were conducted using the rabbit model of iliac restenosis in order to establish the optimal luminal shield design, radial force and mechanical properties observed at bench testing of several luminal shield versions. These studies also aimed to determine the impact of radial force on vascular injury and endothelialization of the vessels treated with different luminal
In the first rabbit study, a total of 24 luminal shields (eight of three different designs) were implanted in 24 iliacs of 12 rabbits using the iliac denudation model. All animals were sacrificed at 7 days and stents were sent for histological and electron microscopy evaluation. In this study, complete prosthesis apposition was achieved in all cases. Injury and inflammatory scores were minimal in all three groups, reflecting the nature of implantation of the device. Neointimal growth was minimal (<6%), which may be attributed to the time (7 days) in which the tissue was harvested. Endothelial cell coverage above the struts ranged from 39 to 52% and varied in a design-dependent fashion (Figure 3). A second study used longer follow-up time points and aimed to evaluate differences among the two luminal shield designs that had the highest endothelialization rates in the 7-day study. Using the same rabbit model, a total of 12 luminal shields were implanted in 12 iliac arteries. All animals were sacrificed at 14 days and tissues were harvested for histology, electron and confocal microscopy to assess expression of inflammatory markers (CD31, PECAM-1, thrombomodulin and TOTO-3). In this study, there was equivalent endothelial coverage via scanning electron microscopy (>92% coverage for both designs). Surface coverage was composed of more mature endothelial cells, as evidenced by confocal imaging (CD31+ cells). The main findings of these two studies revealed particularly low levels of injury (scores ranged from 0.04 to a maximum of 0.13, depending on the design) with wide-open lumen and no incidents of luminal shield malapposition at day 7. Near-complete device endothelialization (>90%) above the struts was noted in all devices at 14 days.

**Porcine coronary studies**

After selection of the optimal luminal shield design based on the rabbit iliac studies, acute and 28-day studies were performed in the coronary porcine model to evaluate feasibility of device deployment, anchoring and patterns of vascular healing at 28 days. In the acute study, the deployment of coronary luminal shields was feasible and following delivery, all devices were safely anchored to the target segment without evidence of migration. Luminal shield evaluation using optical coherence tomography (OCT) imaging demonstrated complete wall apposition and device conformability to the vessel morphology and diameters. A safety evaluation study was performed using the overstretch model of restenosis. A total of ten luminal shields were deployed and compared with both the Xience (n = 10) and Vision stents (n = 10; Abbott Vascular, CA, USA). After 28 days, the restenosis rate in the shield group assessed by quantitative coronary angiography (QCA) was 20.70% and did not differ between the vProtect luminal shield and the control stents (25.50% in the Vision bare-metal stent and 17.40% in the Xience stent group; p = not significant). Histological analysis demonstrated lower injury scores in the vProtect luminal shields and a comparable percentage of area of stenosis among the studied stents (Figure 4).

**Clinical experience**

**First-in-human study**

The first clinical experience with this device was designed with the objective of testing the safety and feasibility of the vProtect luminal shield (research carried out at Corbic Research Institute, Envigado, Colombia). In February 2009, a total of 29 patients were successfully enrolled. The mean age of all patients was 59 years, of whom 57% were male. More than half of the study population was diagnosed with two- or three-vessel coronary artery disease. A total of 37% of patients were diabetic. The main inclusion criteria were: symptomatic coronary artery disease in patients undergoing percutaneous coronary intervention (PCI) of a single de novo lesion with percentage diameter stenosis of 50% or greater. The average reference
diameter of the target segment had to be in the range of 2.75–3.5 mm. Intravascular ultrasound (IVUS) imaging was carried out before intervention to exclude excessive calcifications of the treated artery. The main exclusion criteria were as follows: known allergy or sensitivity to niti-
nol, contraindication to anticoagulants, planned major surgery within 30 days, severe calcifica-
tion assessed by IVUS and unsuitable coronary anatomy. The primary end points of the study were defined as the postprocedural percentage of diameter stenosis (%DS) less than 30%, IVUS mean lumen area of 4 mm² or greater and an in-hospital and 30-day major adverse cardiac event (MACE). Secondary end points included 9-month angiographic restenosis rate, target lesion revascularization, target vessel revascu-
larization, target vessel failure and a MACE. All treated lesions were predilated with a 2.5-mm balloon in a stepwise fashion until complete dilatation was achieved. The vProtect diameter was then selected based on the QCA and IVUS measurements. Postdilatation was allowed if %DS measured after vProtect implantation was 30% or greater. When two post-vProtect balloon inflations failed to reduce %DS below 30%, bail-
out stenting was indicated. At the end of the procedure, the final IVUS imaging was performed. The mean baseline vessel diameter was 3.05 mm and baseline %DS was 59.4%. It decreased to 35.9% after vProtect luminal shield implantation and further decreased to 9.23% after final balloon postdilatation. In all patients, %DS less than 30% was achieved. Procedural success was 96.6% and there was only one case of technical failure of the device (3.4%) with no periproce-
dural complications. No patient required bailout stenting. Interim IVUS analysis of 11 patients revealed a 21% increase of lumen volume after vProtect luminal shield implantation and a final mean lumen area of 4.7 ± 0.98 mm². There were no incidents of MACEs at 30- and 90-day follow-up. Interim IVUS analysis demonstrated a 14% increase of stent diameter at 9-month follow-up representing positive remodeling of the vessel and continued luminal shield expansion in the artery [11]. Angiographic follow-up has been completed in all enrolled patients (Figure 5).

**SECRITT I trial**
The Shield Evaluated at Cardiac Hospital in Rotterdam for Investigation and Treatment of Thin-Cap Fibroatheroma (SECRITT) I trial was designed as a prospective and randomized study to evaluate preventive treatment of poten-
tially life threatening vulnerable plaques. In 2008, the first European vProtect luminal shield was successfully implanted in the left anterior descending coronary artery of a 63-year-old man at Erasmus Medical Center in Rotterdam, The Netherlands [12]. The trial was designed to include 15 patients in the vProtect group and 15 in the control group (receiving medical therapy only). All-comers with stable or unstable angina underwent QCA analysis of the target lesion. In patients with lesions classified as intermedi-
ate (40–50%), the fractional flow reserve (FFR) examination was performed to further classify the lesion. If the result of the FFR was greater than 0.75, the patient was randomly assigned to either receive the vProtect or to the control group. All patients included in the study received standard statin therapy. Patients also underwent OCT, IVUS virtual histology (IVUS-VH) and palpography examinations to further characterize the plaque. The IVUS-VH technique was used to identify the TCFA, using the following criteria analyzed in the three consecutive image
frames: plaque burden greater than 40% and confluent necrotic core (>10%) in direct contact with the lumen. OCT was applied to accurately measure fibrous cap thickness, increasing accuracy of detecting TCFAs and allowing identification of plaque rupture. In addition, palpography was used to detect high-strain spots in the plaque, which have been proven to be TCFAs-associated [13,14]. All patients with stenosis greater than 50% and patients with intermediate lesions where the FFR result was lower than 0.75 underwent stent implantation to treat the culprit lesion. Of more than 80 patients screened so far (data presented in December 2009) [15], 20 patients met the FFR/IVUS-VH criteria. Of these patients, 12 were included in the vProtect group and eight in the control group. One patient crossed over from the control to the vProtect arm owing to unstable angina presentation. All patients randomized to the study (including control group) were planned to have 6-month follow-up with angiographic, IVUS-VH and OCT examination to observe the progress of the lesion and to assess whether the cap had thickened or remained the same. All patients who underwent luminal shield placement received dual antiplatelet therapy (aspirin and clopidogrel) for 12 months. Patients in the control group were administered aspirin for life and 12 months of clopidogrel therapy if they had a drug-eluting stent implanted in another (not target) vessel. The mean age of the first 20 analyzed patients was 69 years, of whom 75% were male. As many as 17 patients presented symptoms of stable (class II) and three of unstable angina (including one patient with non-ST-segment elevation myocardial infarction). More than 50% of patients had two or three coronary vessel diseases and 25% of patients suffered from diabetes mellitus. A total of 17 patients enrolled in the study in whom baseline QCA analysis was performed had noncalcified lesions with the mean baseline percentage diameter stenosis of $33.2 \pm 13.5\%$ and postprocedural stenosis reduced to $21.0 \pm 10.7\%$ (analysis performed in seven patients so far). At 6-month follow-up, this parameter was further reduced to $18.7 \pm 16.9\%$. The average baseline minimal lumen diameter was $2.01 \pm 0.39$ mm and at 6-month follow-up it increased to $2.19 \pm 0.33$ mm. The mean lesion length was 14 mm and most of the target lesions were localized in the right coronary artery (58%). The rate of procedural success reached 100%. OCT analysis of the images acquired at 6 months from the first five analyzed patients revealed that average cap thickness increased by 174 µm and mean lumen area increased by 1.56 mm². The last change represents positive remodeling and continued luminal shield expansion in the artery. Neointimal thickness was similar to that noted with drug-eluting stents and the FFR results remained greater than 0.75 in all patients [15]. There were no device-related adverse events in any of the patients enrolled in the study at 6-month follow-up. Recently presented OCT data revealed that the mean late lumen loss assessed in nine patients at 6-month follow-up was 0.13 mm and mean stent area increased by 9% [16].

**Conclusion**

Experimental studies have demonstrated the biological advantages of low-pressure self-expandable vascular scaffolding (vProtect luminal shield). First-in-human experience suggests that the luminal shield can be safely...
and accurately implanted in the target segment of coronary arteries. This device maintains its mechanical integrity following implantation and is capable of resisting plaque compression forces (maintaining luminal gain). In addition, this device appears to induce progressive vascular remodeling over time but far less compared with what had been originally reported with first-generation self-expandable stents. In addition, preliminary midterm (6- and 9-month) clinical results have demonstrated promising clinical outcomes. Owing to its intrinsic mechanical properties, this device may improve the outcomes of PCI by inducing less injury at the time of implantation. Thus, this device could be indicated in specific patient subsets, such as acute coronary syndromes, if long-term data in a larger population subset are obtained.

**Future perspective**
In the future, effective treatment of coronary artery disease must rely on a specific and purposefully selected choice of local therapy solutions based on the morphology and type of each individual lesion. The long-term results of ongoing clinical trials will confirm whether the ‘low radial force’ vProtect luminal shield can improve the effectiveness of treatment among patients presenting with high-risk coronary atherosclerotic lesions. Based on the present experimental and clinical data of the vProtect luminal shield studies, it appears that the idea of specific and selective treatment of coronary lesions may be an approach to adopt in the future. In addition, in the fast developing era of imaging techniques, it will be easy to identify the specific lesion morphology and the optimal type of local therapy.

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**Financial & competing interests disclosure**
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No writing assistance was utilized in the production of this manuscript.
In the current article, we aimed to describe the vProtect™ luminal shield and provide a brief technical description of the device and current information about the experimental and clinical experience acquired to date. This device is intended for use mainly in the setting of nonobstructive, thin-cap fibroatheromas in the coronary territory. This reference is of particular importance in order to acquire a complete knowledge of these clinical settings.


