# Ultrathin-Strut Stents

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Studies have shown a lower risk of very late stent thrombosis with developing second-generation DESs with biocompatible and biodegradable polymers or without polymers altogether. In addition, research has indicated that thinner struts are associated with a reduced risk of intrastent restenosis and angiographic and clinical results. A drug-eluting stents (DES) with ultrathin struts (strut thickness of 70 µm) is more flexible, facilitates better tracking, and is more crossable than a conventional second-generation DES. The question is whether ultrathin eluting drug stents suit all kinds of lesions.

Keywords: eluting drug stents ; ultrathin-strut eluting stents ; stent thrombosis ; stent restenosis ; calcified coronary lesions ; neointimal hyperplasia

## 1. Introduction: From Coronary Balloon Angioplasty to Drug-Eluting Stent Interventions

Atherosclerotic plaques are responsible for developing coronary artery disease (CAD), which remains a leading cause of morbidity and mortality. A metallic drug-eluting stent (DES), inserted after balloon angioplasty on top of medical treatment, is frequently used to treat unstable or clinically significant coronary artery disease [1]. Andreas Gruentzig performed the first coronary angioplasty in 1977 [2]. In the early days of angioplasty, when stents were unavailable, their effectiveness was reduced by acute closure or re-stenosis. Sigwart and Puel were the first to implant a coronary stent in 1986 [3] (Palmaz-Schatz®; Johnson & Johnson, New Brunswick, NJ, USA). Initially, coronary stents were used to treat failures in balloon angioplasty treatment, such as acute vessel closure due to dissection or restenosis due to elastic recoil. Many other stents have become available since the beginning of 1990, including Wiktor® (Medtronic, Minneapolis, MN, USA), Micro® (Applied Vascular Engineering, Twickenham, UK), Cordis® (Cordis, Santa Clara, CA, USA), and MULTI-LINK® (Advanced Cardiovascular Systems, Santa Clara, CA, USA) [4]. There was a reduced incidence of acute vessel closure and early elastic recoil using bare metal stents (BMSs).

However, a revolutionary paradigm was born. There was a significant risk of in-stent restenosis primarily because vascular smooth muscle cells proliferated and migrated within the device [5]. Until two landmark trials changed the trajectory of coronary PCI (percutaneous coronary interventions), stents were reserved for acute or threatened closures or restenosis following balloon angioplasty. Although there is evidence to support the superiority of BMSs over balloon angioplasty [6][7] in the Belgium Netherlands Stent Arterial Revascularization Therapies Study (BENESTENT) [8] and the North American Stent Restenosis Study (STRESS) [9], it remains that 20–30% of patients experienced in-stent restenosis (ISR).

A polymer coating was used to improve the performance of coronary stents further. Compared with coronary stents without an antiproliferative drug coating, drug-eluting stents (DES) reduce neointimal hyperplasia, reducing the need for repeat revascularizations [10]. The first sirolimus-eluting stent was implanted in 1999 by Eduardo Sousa and became clinically available in 2002 as CYPHER (Cordis). Compared with BMSs, CYPHER demonstrated a significant reduction in in-stent restenosis and target vessel revascularization (TVR). Although a great step up in the evolution of PCI, it has been found that early-generation DESs are associated with an increased risk of very late stent thrombosis, probably as a result of a delayed endothelialization response to anti-restenotic drugs or a delayed hypersensitivity reaction to the polymer [11] [12][13]. There has been a significant development in the design of second-generation DESs with biocompatible and biodegradable polymers, or even without polymers altogether, to reduce the risk of very late stent thrombosis. Stent thrombosis is induced by the antiproliferative effect of the DES, which delays the re-endothelialization of synthetic materials. When oral antiplatelet therapy is discontinued, the exposed scaffold surface can activate platelets, resulting in late restenosis or thrombosis [14]. Restenosis caused by neointimal hyperplasia generally occurs gradually, while thrombosis caused by stents develops abruptly and can escalate to life-threatening complications. Despite its low incidence, it is associated with a high mortality rate [15].

The development of third-generation drug-eluting stents containing biodegradable rather than durable polymers was prompted by the potential for late and very late stent thrombosis and the necessity for prolonged dual antiplatelet therapy associated with the durable polymer coating of first- and second-generation drug-eluting stents. Apart from being made from bio-degradable polymers, most of these new stents are also made from cobalt–chromium or platinum–chromium platforms, especially in ultrathin struts, and a few have abluminal polymers.

## 2. The Advantages of Ultrathin-Strut Stents in Early Vessel Healing

Due to the antiproliferative drugs used in first-generation DESs, fewer patients had neointimal hyperplasia, but vascular healing was impaired, leading to late and incomplete endothelialization. On top of that, there may be a delay in recovery due to hypersensitivity reactions caused by permanent polymers. As a result, the blood flow is exposed to thrombogenic struts, which can lead to stent thrombosis [16].

In a rabbit denudation model presented by Soucy et al., strut coverage at day 14 was as high as 95% in the thinnest struts (81 µm) and lower with thicker struts: 88% in stents with 97 µm struts and 77% with 132 µm struts [17]. Based on an in vivo optical coherence tomography (OCT) study in a porcine model, the thinnest strut stent (61 µm) achieved faster and better strut coverage [18]. Endothelialization may be delayed, and the risk of restenosis increases with thicker struts due to the larger surface taking longer to endothelial. Moreover, thicker struts may contribute to more significant vessel injury and inflammation in adjacent tissue due to the penetrating struts' traumatic disruption of the internal elastic lamina. As a result of increased intimal inflammation, neo-intimal growth and hyperplasia lead to restenosis.

The ISAR-STEREO trial demonstrated that strut thickness affects ISR rates [19]. There were 651 patients randomized to receive either a thin-strut stent (50 µm) or a comparable stent with a strut thickness of 140 µm, without a polymer or antiproliferative agent. There was almost twice as much angiographic restenosis (defined as >50% stenosis at 6-month follow-up angiography) in the thick-strut group compared with the thin-strut group (15.0% versus 25.8%, respectively).

Rittersma et al. also suggested that thinner struts are associated with a decreased risk of ISR and a reduced risk of angiographic and clinical restenosis [20].

## 3. The Advantages of Ultrathin-Strut Stents in Deliverability of Drug-Eluting Stents

Data on mechanical behavior during delivery of the stent is limited, even though there are numerous studies on deployment and especially in vivo function. Many different delivery systems are available for stent placement, and the deliverability is determined by pushability, trackability, and crossability [21].

Compared with conventional second-generation DESs, ultrathin struts may be more flexible, improve trackability, and have a lower profile, improving crossability [22].

## 4. A Negative Influence of Ultrathin Struts on the Mechanical Properties of Drug-Eluting Stents

Coronary stents should have an excellent radial force to maintain lumen patency to resist high external pressures. Generally, this pressure is around 200 mmHg in a healthy coronary artery and much more significant in a calcified lesion. It is possible to develop ISR due to failure to resist (chronic) external pressure [23]. Bonin et al. suggested that a stent's resistance to external forces is determined by its radial stiffness, which occurs when uniform external radial forces are applied, and its radial strength, which is determined by the pressure that permanently deforms the stent [21]. As a result of its higher elastic modulus and tensile strength, cobalt–chromium has a higher radial strength than stainless steel, thereby allowing thinner struts to be used without sacrificing radial strength.

The majority of contemporary stents are modular, consisting of undulated rings. These rings are connected by connectors, which provide longitudinal support to the stent. In coronary stent design, the number and orientation of connectors between rings play a critical role in determining mechanical properties. Compared with an open-cell structure, closed-cell designs (more connectors) provide better vessel wall coverage and are likely to prevent plaque prolapse [24]. Several authors reported that improved coverage with less thrombus protrusion reduced the risk of distal embolization in patients with ST-elevation myocardial infarction (STEMI) [25].

Open-cell designs, however, are more flexible, deliverable, and conformable than closed-cell designs. A further advantage of these devices is that they facilitate more accessible access to side branches in cases of bifurcation lesions.

There is a possibility that a stent may recoil due to low radial strength. Acute stent recoil leads to residual stenosis and repeated artery revascularization [26][27][28]. According to an observational study conducted on 128 patients who underwent PCI for chronic total occlusions (CTOs), the ultrathin-strut Orsiro stent was associated with higher absolute (measured in millimeters) and relative (measured in percent) recoil than the Resolute Onyx zotarolimus-eluting stent with 81 µm struts (Medtronic Cardiovascular, Santa Rosa, CA, USA) [27].

Teeuwen et al. demonstrated in the randomized PRISON IV trial, which compared the Orsiro stent with the Xience stent in CTO patients, that the Orsiro ultrathin stent failed to prove non-inferiority in terms of in-segment late lumen loss and did show statistically higher rates of restenosis [29].

Overall, radial strength is determined by the type of metal used, the strut's thickness, and the stent's design. While cobalt–chromium and platinum–chromium alloy struts have comparable radial strength to stainless steel struts, some clinical data indicate that the radial strength of ultrathin-strut stents may not be sufficient to treat CTO lesions and may result in a more significant stent recoil than conventional second-generation DESs. Different manufacturers are developing ultrathin-strut stents. **Table 1** reviews the most commonly used features [22].

**Table 1.** A brief research of mainly used ultrathin-strut stents.

| Stent Name | Orsiro | Biomime | CoroFlex IsarNeo | Supraflex | Evermine 50 | MiStent |
|---|---|---|---|---|---|---|
| Company | Biotronik | Merril | B.Braun | SMT | Meril | Micell |
| Material | Cobalt-chromium | Cobalt-chromium | Cobalt-chromium | Cobalt-chromium | Cobalt-chromium | Cobalt-chromium |
| Strut thickness (µm) | 60 | 65 | 55 | 60 | 50 | 64 |
| Coating distribution | Circumferential | Circumferential | - | Circumferential | Circumferential | Circumferential |
| Polymer | Biodegradable | Biodegradable | Polymer free | Biodegradable | Biodegradable | Biodegradable |
| Eluting drug | Sirolimus | Sirolimus | Sirolimus | Sirolimus | Everolimus | Sirolimus |
| Drug dose | 1.4 µg/mm$^2$ | 1.25 µg/mm$^2$ | 1.2 µg/mm$^2$ | 1.4 µg/mm$^2$ | 1.25 µg/mm$^2$ | 2.4 µg/mm$^2$ |
| Drug release | 50% by 1 month 80% by 3 months | 30–40 days | 80% by 28 days 100% by 90 days | 70% by 1 week 100% by 3–4 months | 30–40 days | 9 months |

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