

## 'Fused-Gold' vs. 'Bare' stainless steel NIRflex stents of the same geometric design in diseased native coronary arteries. Long-term results from the NIR TOP Study

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### KEYWORDS

Stents, restenosis, gold-coating

### Abstract

**Objectives:** We evaluated the long-term clinical and angiographic results of 'fused-gold' (NIRFlex Royal) and 'bare' (NIRFlex) stainless steel stents in patients undergoing percutaneous coronary intervention (PCI).

**Background:** Recent studies have shown high clinical and angiographic restenosis rates following the intracoronary implantation of 'gold-coated' stainless steel stents. The new 'fused-gold' stent, with improved surface characteristics and flexibility, was developed to improve procedural and long-term results, while maintaining enhanced radiopacity.

**Methods:** A total of 305 patients (358 lesions) with symptomatic native coronary artery disease (CAD) undergoing native vessel PCI were randomised to receive a 'fused-gold' (n=147) or 'bare' (n=158) stent. Primary endpoint was minimal luminal diameter (MLD) at 6 months angiographic follow-up. Secondary endpoints included technical and procedural success, major adverse cardiac events (MACE), target vessel failure (TVF), angiographic binary restenosis rates, and additional angiographic comparisons.

**Results:** There were no major differences in the baseline angiographic variables or patient characteristics between the two groups, however there was a trend towards a higher risk in the 'fused-gold' stent group. Clinical and angiographic follow-up was 100% and 87% respectively. MLD at 6 months follow-up was smaller in the 'fused-gold' stent group compared to the 'bare' stent group (1.61±0.65 vs. 1.81±0.60 mm, respectively); Therefore, the null hypothesis of non-inferiority cannot be rejected (p=0.49); equivalency cannot be claimed for the two stent types. The 'fused-gold' stents were also associated with a higher angiographic binary and clinical restenosis rates (33 vs. 18%; p=0.002 & 26.9 vs. 20.3%; p<0.001, respectively).

**Conclusion:** The 'bare' NIRflex stent was associated with excellent long-term clinical and angiographic results. Taking into account the equivalence margin, the null hypothesis of non-equivalence between the 'fused-gold' NIRflex Royal stent and the 'bare' NIRflex stent cannot be rejected (p=0.49), so equivalence cannot be claimed for the two stent types.

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## Abbreviations and acronyms

CAD: coronary artery disease  
CABG: coronary artery bypass surgery  
CK: creatine kinase  
IVUS: intravascular ultrasound  
LVEF: left ventricular ejection fraction  
MLD: minimal lumen diameter  
MACE: major adverse cardiac events  
PCI: percutaneous coronary revascularisation  
QCA: quantitative coronary angiography  
SAT: sub-acute stent thrombosis

## Introduction

The majority of intra-coronary stents in clinical use today are constructed from stainless steel. Stainless steel is relatively radiolucent compared to other stent materials, such as tantalum or cobalt-chromium alloy. Radio-opaque stents offer the potential clinical advantage of facilitating more accurate stent positioning within the target lesion during PCI<sup>1,2</sup>. The radio-opacity of stainless steel stents can be enhanced either by increasing strut thickness or coating stents with a more radio-opaque metal. Increasing strut thickness results in an undesirable decrease in stent flexibility. Gold has been used to enhance stent radio-opacity, as it is biologically inert<sup>3-5</sup>. Gold-coated stainless steel stents have been shown to be associated with reduced neointimal proliferation compared to other stent coatings in animal studies, and with decreased platelet activation and thrombus formation *in vitro*<sup>3,6-8</sup>. However, recent studies have shown an increased rate of restenosis with gold-coated stents<sup>9-12</sup>. This prospective randomised trial sought to assess the long-term clinical and angiographic results of new 'fused-gold' (NIRFlex Royal) and 'bare' stainless steel stents (NIRflex) of the same geometric design (both Medinol Ltd., Israel) in symptomatic patients undergoing PCI of native coronary arteries.

## Methods

### Study population

Patients were eligible if they had symptomatic CAD, with one or more *de novo* or non-stented restenotic lesions of the native coronary circulation suitable for stent implantation. The visually estimated reference vessel diameter was 2.5-4.0 mm, and lesion length < 30 mm. Exclusion criteria were recent CABG or PCI within 2 weeks, acute myocardial infarction within 3 days, LVEF of < 25%, or patients unable or unwilling to undergo repeat coronary angiography. Angiographic exclusion criteria were excessive vessel tortuosity likely to prevent insertion of an intracoronary stent, unprotected left main disease, ostial or bifurcation lesions, chronic total occlusions, intra-luminal thrombus, in-stent restenosis, or any contraindication to emergency coronary artery bypass surgery. The local ethics committees approved the study protocol. Written, informed consent was obtained from all patients. Patients also gave written, informed

consent before undergoing follow-up angiography at 6 months, performed in accordance with institutional guidelines. A subset of patients underwent intravascular ultrasound (IVUS) imaging immediately post-procedure and at follow-up.

### Stent implantation

Patients were randomised to receive either a 'fused-gold' (NIRFlex Royal) or a 'bare' (NIRflex) stainless steel stent of the same geometric design (Medinol Ltd., Tel Aviv, Israel). Randomisation took place after angiographic confirmation of lesion suitability. All patients received combination anti-platelet therapy, consisting of aspirin > 100 mg per day for an indefinite duration and clopidogrel 300 mg pre-procedure and 75 mg once daily for 30 days post-procedure, or ticlopidine 250 mg twice daily 1 day pre- and for 14 days post-procedure. Heparin was administered to achieve an activated clotting time of > 250 seconds. A glycoprotein IIb/IIIa inhibitor was used at the discretion of the operator. Target vessel angiography was performed after the administration of intra-coronary nitroglycerin (100-200 µg) to ensure maximal vasodilatation. Stent length and diameter were determined by visual estimation or quantitative coronary angiography (QCA) with a stent to distal reference vessel ratio of between 1:1 to 1.1:1.0. Direct stenting (without balloon predilatation) was performed at the discretion of the operator. Stents were post-dilated, when necessary, using high-pressure balloon inflations to obtain optimal stent expansion.

### QCA / IVUS imaging

QCA was performed at pre- and post-procedure and at 6 months follow-up. The 6 months follow-up angiography was performed in the same technique as above, with same angiographic angles that were taken pre- and post- stent implantation. IVUS was performed at 6 months follow-up using one of two commercially available systems (CVIS/Boston Scientific Corp., San Jose, CA, USA or JOMED, Sweden) with mechanical pullback of the IVUS catheters (3.0 Fr 'Atlantis' or 2.9 Fr 'AVNAR') at 0.5 mm/sec. IVUS images were recorded on Super-VHS.

### Off-line quantitative coronary angiography and IVUS

Off-line QCA and quantitative IVUS were performed by an independent core laboratory (Cardialysis BV, Rotterdam, The Netherlands) according to established methodology<sup>13,14</sup>. In-stent restenosis at follow-up was classified using the Mehran classification<sup>15</sup>. IVUS analysis presented in this paper was performed within the stented segment. QCA was performed both within the stented segment and the total analysis segment.

### Definition of end points and follow-up

Primary endpoint was in-stent MLD at 6 months angiographic follow-up. Secondary endpoints were technical and procedural success, occurrence of MACE (death, myocardial infarction, and repeat target lesion revascularisation), target vessel failure (TVF), angiographic binary restenosis rates, acute gain and late loss at six months follow-up. IVUS measurements (in-stent neointimal and

percentage obstruction volumes) were also reported. Death was defined to include all-cause mortality. Myocardial infarction was defined as new pathological Q waves or by an increase in the creatine kinase (CK), or its CK-MB iso-enzyme, of more than or equal to twice the upper limit of normal. CK was determined pre-procedure and at least twice at the following intervals: 6-8, 8-16 and 20-24 hours post-procedure. Angiographic restenosis was defined as  $\geq 50\%$  diameter stenosis by QCA within the stented segment. Target vessel revascularisation was defined as a repeat percutaneous or surgical revascularisation involving the original target vessel within 6 months of the index procedure.

## Statistics

Power calculations were performed based on the results a previous study using the 'bare' NIR (Boston Scientific, San Jose, CA, USA/Medinol, Tel Aviv, Israel) with an expected MLD of  $1.88 \text{ mm} \pm 0.63^{16}$ . Two group, one-sided t-test ( $\alpha=0.05$ ) will have a 90% power to reject the null hypothesis that the two stents are not equivalent with 171 patients in each group undergoing follow-up angiography. All data expressed as the mean value  $\pm$  SD. The analysis was performed on the actual stent received. Differences in normally distributed continuous variables were tested by the unpaired Student's t-test. Categorical data were assessed by Fisher's exact test. A p-value  $< 0.05$  was considered statistically significant.

## Results

### Patient and procedural characteristics

Three hundred and five patients (358 lesions) undergoing native vessel PCI were randomised to receive a 'fused-gold' ( $n=147$ ) or 'bare' ( $n=158$ ) stent. There were no major differences in the baseline patient characteristics between the two groups, however there was a trend towards a higher risk in the 'fused-gold' stent group (Table 1). Baseline qualitative angiographic variables were comparable between the two groups (Table 2). The maximum balloon size and pressure used in the 'fused-gold' and 'bare' stent groups were similar at  $3.3 \pm 0.4$  vs.  $3.3 \pm 0.5$  mm ( $p=0.84$ ) and  $15.3 \pm 4.7$  vs.  $15.5 \pm 3.1$  atms ( $p=0.73$ ) respectively.

### Clinical follow-up

All 305 patients were available for one month clinical follow-up. Six month clinical follow-up was available for 304 patients (Table 3). No deaths were observed during the study. Technical success in the 'bare-stent' group was 100%, in the 'fused-gold' group 96% ( $p=0.028$ ). Procedural success for both groups was 97 and 94% ( $p=0.28$ ). A small percentage of patients experienced a myocardial infarction, either peri-operatively or within the first 30 days, in both groups (1.4 vs. 2.5% in the fused-gold' and 'bare' stents respectively:  $p=0.69$ ). There were no incidences of SAT in either stent at 270 days follow-up. Clinical restenosis was more frequent in the 'fused-gold' stent group (Table 3). In the 'fused-gold' stent group 83% of patients remained MACE-free at 270 days, compared to 88% in the 'bare' stent group ( $p=0.25$ ). The majority of these events were repeat revascularisation via PCI (14.3 vs. 8.9%

**Table 1. Clinical characteristics of the study patients.**

	NIRflex Royal	NIRflex	p-value
No. of patients	147	158	
Age (yrs)	60 $\pm$ 11	60 $\pm$ 11	0.93
Male gender (%)	78	82	0.40
Risk factors/Medical history (%)			
Diabetes mellitus	27	19	0.10
Smoking history	64	60	0.56
Hypertension	54	55	0.82
Family history	44	34	0.08
Dyslipidaemia	76	73	0.60
Stroke	5	4	0.59
Peripheral vascular disease	10	2.5	0.008
Previous MI	47	38	0.13
Previous CABG	10	4	0.07
Previous PTCA	4	3	0.76
Angina status (%)			
Unstable angina	48	46	0.73
Stable angina	42	46	0.49
Silent ischaemia	11	10	0.85
Vessel disease (%)			
Single	52	53	0.82
Double	29	30	0.80
Triple	20	17	0.46

Data are expressed as mean  $\pm$  SD or percentage of patients.

**Table 2. Baseline qualitative angiographic lesion characteristics.**

	NIRflex Royal	NIRflex	p-value
No. of lesions	167	191	
Target vessel(s) (%)			
LAD	34	37	0.58
RCA	41	42	1.0
LCX	25		0.37
LM	0	1	1.0
TIMI flow			
(Grades 0/1/2/3) (%)	0/1/16/83	1/2/14/84	
ACC/AHA lesion type (%)			
A	7	9	0.57
B1	26	25	0.90
B2	64	63	1.0
C	3	2	0.74
Lesion length (%)			
Discrete (< 10 mm)	68	71	0.64
Tubular (10-20 mm)	29	27	0.72
Diffuse (> 20 mm)	2	2	0.71
Calcification (%)	28	26	0.81
Thrombus (%)	4	5	0.80
Concentric (%)	13	13	1.0
Major side branch involvement (%)	12	7	0.10

Data are expressed as mean  $\pm$  SD or percentage of patients.

LAD = left anterior descending artery; RCA = right coronary artery; LCX = left circumflex artery; TIMI = thrombolysis in myocardial infarction trial; ACC/AHA = American College of Cardiology/American Heart Association

**Table 3. Clinical outcomes at 6 months follow-up.**

	NIRflex Royal	NIRflex	p-value
No. of patients	147	158	
MACE (%)	5.4	7.0	0.64
Death (%)	0	0	
Myocardial infarction (%)	2.7	3.2	1.0
Q-wave	0.7	0	0.48
Non Q-wave	2.0	3.2	0.72
Target lesion revascularisation (%)			
CABG	0	0.6	1.0
Repeat PCI	2.7	4.4	0.54
TVR (non-target lesion) (%)	0	2.5	0.12
Stent thrombosis (%)	0	0	
Bleeding (%)			
Major	0	0	
Minor	0	1.3	0.50
Recurrent angina (%)	26.9	20.3	<0.001

Data are expressed as mean±SD or percentage of patients. MACE = major adverse cardiac events; TVR = target vessel revascularisation; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention. Recurrent angina: stable or unstable angina at 6 months follow-up. In case of a re-intervention before 6 months follow-up the adjudication of the Clinical Event Committee is taken.

respectively:  $p=0.15$ ). In the patients who underwent repeat PCI, symptomatic or documented ischaemia was documented to be present based on clinical symptoms, prior to repeat angiography, in 74% ( $n=14/19$ ; no information for 2 additional patients) of those who received 'fused-gold' stents, compared to 50% ( $n=6/12$ ; no information for 2 additional patients) with 'bare' stents ( $p=0.26$ ).

### Angiographic analysis

There was a trend towards a larger MLD and a lower percentage diameter stenosis in the 'fused-gold' stent immediately post-procedure (Table 4). At 6 months 265 patients (311 lesions) underwent follow-up angiography. The 'fused-gold' stent was associated with a lower MLD, greater late loss and a higher binary restenosis rate at follow-up compared to the 'bare' stent group (Table 4). Taking into account the equivalence margin for MLD at follow-up, the null hypothesis of non-equivalence cannot be rejected ( $p=0.49$ ), so equivalence cannot be claimed for the two stent types. Patterns of in-stent restenosis were similar with both stents (focal: - 45 vs. 63%,  $p=0.16$ ; in-stent: - 28 vs. 10%,  $p=0.09$ ; proliferative: - 21 vs. 23%,  $p=1.0$ ; & total occlusions: - 6 vs. 3%,  $p=1.0$ ; 'fused-gold' vs. 'bare' stents respectively). In the IVUS sub-group, QCA at follow-up suggested no significant differences between the 'bare' and 'fused-gold' stent group (Table 5).

### IVUS analysis

Table 6 summarises the quantitative 3-D data at follow-up in the IVUS sub-group. Of the vessels that underwent follow-up IVUS imaging, in-stent lumen, neointimal and percentage obstructive volumes were similar in the two stents.

**Table 4. Quantitative angiographic analysis.**

	NIRflex Royal	NIRflex	p-value
No. of lesions	167	191	
Reference vessel diameter (mm)			
Pre-procedure	2.75±0.55	2.74±0.52	0.80
Post-procedure	2.91±0.50	2.85±0.48	0.26
Follow-up	2.73±0.55	2.68±0.52	0.46
Diameter stenosis (%)			
Pre-procedure	62±9	63±9	0.62
Post-procedure	12±7	14±8	0.06
Follow-up	41±21	33±17	<0.001
MLD (mm)			
Pre-procedure	1.03±0.31	1.02±0.31	0.69
Post-procedure	2.56±0.47	2.46±0.44	0.06
Follow-up	1.61±0.65	1.81±0.60	0.49*
Lumen gain (mm)	1.52±0.43	1.44±0.40	0.07
Late loss in-stent (mm)	0.95±0.54	0.65±0.47	<0.001
Absolute net gain			
In-stent (mm)	0.56±0.62	0.78±0.55	0.001
Late loss index in-stent (mm)	0.66±0.41	0.46±0.37	<0.001
Binary restenosis rate (%)	33	18	0.002
Lesion length (mm)	10.84±4.38	10.31±4.47	0.27

Data are expressed as mean±SD or percentage of patients.

\* P value from Equivalence test.

**Table 5. Quantitative angiographic analysis for the IVUS subgroup.**

	NIRflex Royal	NIRflex	p-value
No. of lesions	30	43	
Reference vessel diameter (mm)			
Pre-procedure	2.57±0.43	2.61±0.52	0.75
Post-procedure	2.76±0.40	2.78±0.48	0.82
Follow-up	2.54±0.37	2.48±0.46	0.54
Diameter stenosis (%)			
Pre-procedure	59±7	61±9	0.19
Post-procedure	9±7	13±7	0.05
Follow-up	32±19	31±14	0.77
MLD (mm)			
Pre-procedure	1.05±0.19	1.01±0.29	0.50
Post-procedure	2.49±0.38	2.42±0.45	0.51
Follow-up	1.72±0.49	1.72±0.47	0.98
Lumen gain (mm)	1.44±0.41	1.41±0.35	0.75
Late loss in-stent (mm)	0.77±0.47	0.71±0.40	0.53
Absolute net gain in-stent (mm)	0.67±0.52	0.70±0.39	0.74
Late loss index in-stent (mm)	0.54±0.35	0.49±0.32	0.51
Binary restenosis rate (%)	13	12	1.00
Lesion length (mm)	9.83±3.90	9.08±3.83	0.42

Data are expressed as mean±SD or percentage of patients.

### Discussion

This prospective randomised study did not demonstrate equivalence in the long-term results of the 'fused-gold' NIRflex Royal and 'bare' NIRflex stainless steel stents. The results of the 'bare' NIRflex stent were excellent, with low angiographic binary restenosis rate and low late loss. The NIRflex Royal stent was associated with greater angiographic late loss, reduced MLD and higher angiographic and clinical

**Table 6. Six month follow-up quantitative intravascular ultrasound analysis.**

	n=	NIRflex Royal	n=	NIRflex	p-value
<b>Vessel area (mm<sup>2</sup>)</b>					
Post-procedure	33	15.6±4.1	40	15.6±4.8	0.97
Follow-up	26	16.9±4.3	41	16.8±5.9	0.99
<b>Vessel volume (mm<sup>3</sup>)</b>					
Post-procedure	33	204.4±101.1	40	212.0±118.3	0.77
Follow-up	26	210.0±89.1	41	219.8±126.8	0.73
<b>Mean stent area (mm<sup>2</sup>)</b>					
Post-procedure	38	7.4±1.7	46	8.0±2.1	0.17
Follow-up	30	7.8±1.8	43	8.1±2.3	0.62
<b>Stent volume (mm<sup>3</sup>)</b>					
Post-procedure	38	100.2±51.6	46	102.6±52.3	0.83
Follow-up	30	98.5±35.7	43	104.3±52.7	0.58
<b>Mean lumen area (mm<sup>2</sup>)</b>					
Post-procedure	38	7.4±1.7	46	8.0±2.1	0.160
Follow-up	30	5.4±2.0	43	5.9±2.5	0.38
<b>Lumen volume (mm<sup>3</sup>)</b>					
Post-procedure	38	99.7±49.9	46	102.5±52.4	0.81
Follow-up	30	69.8±37.8	43	76.7±49.7	0.52
<b>Minimal lumen area (mm<sup>2</sup>)</b>					
Post-procedure	38	6.2±1.7	46	6.8±2.1	0.20
Follow-up	30	4.1±1.5	43	4.5±2.2	0.37
<b>Minimal lumen diameter (mm)</b>					
Post-procedure	38	2.6±0.4	46	2.6±0.4	0.30
Follow-up	30	2.0±0.4	43	2.1±0.5	0.42
<b>In-stent neointimal volume (mm<sup>3</sup>)</b>					
Post-procedure	30	28.8±19.9	43	27.6±19.0	0.80
<b>In-stent volume obstruction (%)</b>					
Post-procedure	30	31.3±19.0	43	27.6±15.8	0.36

Data are expressed as mean±SD.

restenosis rates at follow-up compared with the NIRflex stent. However, MACE and target vessel revascularisation rates at 6 months were similar, with no incidences of SAT with either stent. The IVUS sub-study was included to address concerns over the possible methodological difficulties with current QCA algorithms in the evaluation of the radio-opaque NIRflex Royal stent, as has been previously recognised with other highly radio-opaque stents<sup>17,18</sup>. Such difficulties may, in part, explain the observed trend towards a higher post-procedure MLD with the NIRflex Royal stent seen in this study despite similar baseline lesion characteristics and stent implantation technique. IVUS also allowed a blind analysis of the radio-opaque and radiolucent stents. In this sub-study, in contrast to the clinical and angiographic restenosis results and in agreement with the similar MACE, IVUS demonstrated similar in-stent neointimal and percentage obstruction volumes in the two stents. However, the QCA results at follow-up (MLD, percentage diameter stenosis and late loss) in this subgroup were also similar, indicating that these patients were either not typical of the entire study population, or that they were subject to IVUS-guided therapy (Figure 1).

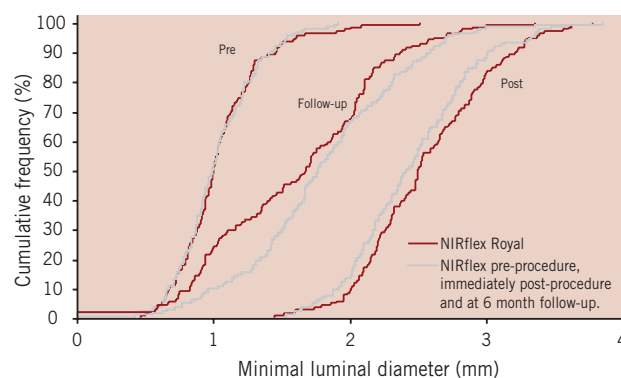


Figure 1. Cumulative frequency distribution curve of minimal lumen diameter.

The baseline angiographic characteristics of the patients enrolled in this study were remarkably similar to those enrolled in recent drug-eluting stents trials, with a reference vessel diameter of around 2.75 mm and total lesion length of < 15 mm. The 6 month angiographic results of the 'bare' NIRflex stent in this study are intermediate between those reported with paclitaxel- and sirolimus-eluting stents and other 'bare' metal stents, although this requires confirmation in a 'head-to-head' randomised trial<sup>16,19-28</sup>.

Despite the previous evidence that gold is bio-compatible, the non-equivalent clinical and angiographic results of the NIRflex Royal in this study are similar to those of previous studies using gold-coated stents<sup>9,12</sup>. It appears that post-plating thermal processing of the gold coating on the NIRflex Royal stent, in an attempt to negate the adverse tissue response, is insufficient when deployed in human native coronary arteries, although incompatibility with current QCA algorithms cannot be excluded<sup>3</sup>.

### Study limitations

The radio-opacity of the 'fused-gold' NIRflex Royal prevented a double-blinded comparison of the two stents. Although IVUS imaging did allow blinded analysis, only a small number of patients were entered into this subgroup. Follow-up IVUS measurements only included vessels which underwent repeat IVUS imaging. The clinical symptomatic status at follow-up was not collaborated with non-invasive testing in the majority of patients.

### References

1. Cremonesi A, Benit E, Carlier M, Colombo A, Piva R, Probst P, Wirtzfeld, Pico-Bourdonnec C. Multicentre registry to evaluate the efficacy of the NIROYAL stent in *de novo* or restenotic coronary stenoses. *J Invas Cardiol*. 2000;12(5):225-232.
2. Fischell T. All the glitters...is it gold? *J Invas Cardiol*. 2000;12:233-235.
3. Edelman E, Seifert P, Groothuis A, Morss A, Bornstein D, Rogers C. Gold-coated NIR stents in porcine coronary arteries. *Circulation*. 2001;103:429-434.
4. Zitter H, Plenck H Jr. The electrochemical behavior of metallic implant materials as an indicator of their biocompatibility. *J Biomed Mater Res*. 1987;21:881-896.

5. Ignatius MJ, Sawhney N, Gupta A, Thibadeau BM, Monteiro OR, Brown IG. Bioactive surface coatings for nanoscale instruments: effects on CNS neurons. *J Biomed Mater Res*. 1998;40:264-274.
6. Tanigawa N, Sawada S, Kobayashi M. Reaction of the aortic wall to six metallic stent materials. *Acad Radiol*. 1995;2:379-384.
7. Alt E, Schömig A. The Inflow coronary stent. In: Serruys PW, Kutryk MJB, eds. *Handbook of Coronary Stents*. London, UK: Martin Dunitz; 1998:265-273.
8. Hehrlein C, Zimmermann M, Metz J, Ensinger W, Kubler W. Influence of surface texture and charge on the biocompatibility of endovascular stents. *Coron Artery Dis*. 1995;6:581-586.
9. Kastrati A, Schomig A, Dirschinger J, Mehili J, von Welsch N, Pache J, Schulen H, Schilling T, Schmitt C, Neumann FJ. Increased risk of restenosis after placement of gold-coated stents: results of a randomized trial comparing gold-coated with uncoated steel stents in patients with coronary artery disease. *Circulation*. 2000;101:2478-2483.
10. Silber S, Reifart N, Morice MC, vom Dahl J, Benit E, Hauptmann KE, Sousa JE, Webb JG, Kaul U, Chan C. The NUGGET Trial (NIR ultimate gold-gilded equivalency trial): 6 months post-procedure safety and efficacy results. *Circulation*. 2001;104:(suppl II) 623 (abstract).
11. vom Dahl J, Haager P, Grube E, Gross M, Beythien C, Kromer EP, Cattelaens N, Hamm CW, Hoffmann R, Reineke T, Klues HG. Effects of gold coating of coronary stents on neointimal proliferation following stent implantation. *Am J Cardiol*. 2002;89:801-805.
12. Park SJ, Lee CW, Hong MK, Kim JJ, Park SW, Tahk SJ, Jang YS, Seung KB, Yang JY, Jeong MH. Comparison of gold-coated NIR stents with uncoated NIR stents in patients with coronary artery disease. *Am J Cardiol*. 2002;89:872-875.
13. Serruys P, Foley DP, de Feyter PJ. *Quantitative Coronary Angiography in Clinical practice*, Dordrecht, the Netherlands: Kluwer Academic; 1994.
14. Hamers R, Bruining N, Knook M. A novel approach to quantitative analysis of intravascular ultrasound images. *Comp Cardiol*. 2001;28:589-592.
15. Mehran R, Dangas G, Abizaid AS, Mintz GS, Lansky AJ, Salter LF, Pichard AD, Kent KM, Stone GW, Leon MB. Angiographic patterns of in-stent restenosis. *Circulation*. 1999;100:1872-1878.
16. Baim DS, Cutlip DE, O'Shaughnessy CD, Hermiller JB, Kereiakes DJ, Giambartolomei A, Katz S, Lansky AJ, Fitzpatrick M, Popma JJ, Ho KK, Leon MB, Kuntz RE; NIRVANA Investigators. *Am J Cardiol*. 2001 Jan 15;87:152-6.
17. Strauss BH, Rensing BJ, den Boer A, van der Giessen WJ, Reiber JH, Serruys PW. Do stents interfere with the densitometric assessment of a coronary artery lesion? *Cath Cardiovasc Diagn*. 1991;24:259-64.
18. Ozaki Y, Keane D, Nobuyoshi M, Hamasaki N, Popma JJ, Serruys PW. Coronary lumen at six-month follow-up of a new radiopaque Cordis tantalum stent using quantitative angiography and intracoronary ultrasound. *Am J Cardiol*. 1995;76(16):1135-43.
19. Kereiakes DJ, Midei M, Hermiller J, O'Shaughnessy C, Schlofmitz R, Yakubov S, Fink S, Hu F, Nishimura N, Sievers M, Valentine ME, Broderick T, Lansky A, Moses J. Procedural and late outcomes following Multi-link Duet coronary stent deployment. *Am J Cardiol*. 1999;84:1385-1390.
20. Moses JW, Buller CE, Nukta ED, Aluka AO, Farhat N, Barbeau G, Popma J, Moussa I, Feit F. The first clinical trial comparing a coated versus a non-coated coronary stent: the Biocompatibles bioDivYsio stent in randomized control trial (Distinct). *Circulation*. 2000;101:11-664 (abstract).
21. Baim DS, Cutlip DE, Midie M, Linnemeier TJ, Schreiber T, Cox D, Kereiakes D, Popma JJ, Robertson L, Prince R, Lansky AJ, Ho KKL, Kuntz RE. Final results of a randomized trial comparing the Multi-link stent with the Palmaz-Schatz stent for narrowings in native coronary arteries. *Am J Cardiol*. 2001;87:157-162.
22. Kastrati A, Mehili J, Dirschinger J, Dotzer F, Schühlen H, Neumann FJ, Fleckenstein M, Pfafferoth C, Seyfarth M, Schomig A. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO) trial. *Circulation*. 2001;103:2816-2821.
23. Pache J, Kastrati A, Mehili J, Schühlen H, Dotzer F, Hausleiter J, Fleckenstein M, Neumann FJ, Sattelberger U, Schmitt C, Müller M, Dirschinger J, Schomig A. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO-2) trial. *J Am Coll Cardiol*. 2003;41(8):1289-1292.
24. Regar E, Serruys PW, Bode C, Holubarsch C, Guermontprez JL, Wijns W, Bartorelli A, Constantini C, Degertekin M, Tanabe K, Disco C, Wuelfert E, Morice MC. Angiographic findings of the multicenter randomized study With the sirolimus-eluting BX velocity balloon-expandable stent (RAVEL): sirolimus-eluting stents inhibit restenosis irrespective of the vessel size. *Circulation*. 2002;106(15):1949-56.
25. Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, Caputo RP, Kereiakes DJ, Williams DO, Teirstein PS, Jaeger JL, Kuntz RE. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med*. 2003;349: 1315-1323.
26. Colombo A, Drzewiecki J, Banning A, Grube E, Hauptmann K, Silber S, Dudek D, Fort S, Schiele F, Zmudka K, Guagliumi G, Russell ME. Randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for coronary artery lesions. *Circulation*. 2003;108:788-794.
27. Schofer J, Schuler M, Gershlick AH, Wijns W, Garcia E, Schampaert E, Breithardt G. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). *Lancet*. 2003;362:1093-1099.
28. Schampaert E, Cohen EA, Schuler M, Reeves F, Traboulsi M, Title L, Kuntz RE, Popma JJ. The Canadian study of the sirolimus-eluting stent in the treatment of patients with long *de novo* lesion in small coronary arteries (C-SIRIUS). *J Am Coll Cardiol*. 2004;43(6):1110-1115.