

Original Studies

The NUGGET Study: NIR Ultra Gold-Gilded Equivalency Trial

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This study should clarify whether the gold-coated NIROYAL stent is equivalent to the stainless steel NIR stent. Patients were randomized to either NIR stent (n = 298) or a NIROYAL stent (n = 305). The primary endpoint was the minimum lumen diameter of the target lesion at 6 months postprocedure. Secondary endpoints focused on clinical events. At 30 days, adverse events were similar in both groups. At 6 months, the minimal lumen diameter was 1.83/1.64 mm ($P < 0.001$; 95% CI = 0.08–0.30) and the angiographic restenosis rate was 20.6%/37.7% ($P < 0.001$; 95% CI = –24.7 to –9.3) for NIR/NIROYAL. The 6-month MACE rates were NIR 7.4% and NIROYAL 10.5% (95% CI = –7.7 to 1.4). Compared to stainless steel stent, the NIROYAL stent demonstrated a smaller minimal lumen diameter, a higher late loss (i.e., higher neointimal hyperplasia in spite of a significantly better initial gain), with higher restenosis and similar MACE rates at 6 months. *Catheter Cardiovasc Interv* 2004;62:18–25. © 2004 Wiley-Liss, Inc.

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INTRODUCTION

Since the introduction of the stent in 1986, interventional cardiologists have continued to use stents in progressively more complex lesions and complex therapies. When treating complex lesions (e.g., ostial lesions and long lesions with multiple stents) the need for precise deployment becomes increasingly important. Radio-opacity plays an important role in the ability of the operator to visualize and thus properly place and deploy stents. This was the reason for the development of the NIROYAL stent. A thin layer of gold increases radio-opacity enough to assist with precise deployment but does not inhibit postdeployment evaluation of the lumen inside the stent.

In the past few years, several trials involving gold-coated stents have been conducted and published [1–4]. Two of these studies (one a prospective registry, the other a retrospective analysis) have shown encouraging results with the gold-coated NIR stent. Two other studies (both prospective randomized comparisons using a different gold-coated stent) showed significant disadvantages. Because of the very different clinical outcomes in these studies, some controversy has developed about the

use of gold and the technique of gold coating to improve the radio-opacity of coronary stents. All of the previous

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studies with angiographic endpoints were performed using stents manufactured using a plating technique different from that used in the manufacturing of the NIROYAL stent, which features lower granularity, less surface roughness, higher chemical purity, less trace metals and porosity. It is obvious that even subtle changes in the processing of metal plating can have profound effects on the biocompatibility of a coated device. Therefore, the purpose of this study was to address whether the performance of the gold-coated NIROYAL stent is comparable to that of the stainless steel NIR stent for percutaneous coronary interventions (PCI).

MATERIALS AND METHODS

Study Design

This was a prospective multicenter randomized controlled clinical study involving 21 sites in 14 countries. The primary endpoint was the minimal lumen diameter (MLD) of the target lesion at 6 months postprocedure. Secondary endpoints included procedural success (successful deployment of study device without the use of any additional device, < 30% residual stenosis, no MACE during hospitalization), stent thrombosis (angiographic thrombus or subacute closure within the stent at the time of clinically driven reangiography), target vessel failure (TVF; a composite of procedure failure, clinically driven target lesion revascularization, nonfatal MI, and death), angiographic restenosis ($\geq 50\%$ diameter stenosis), and major cardiac adverse events (MACE, defined as death, Q-wave MI, target lesion revascularization, angiographic stent thrombosis). Clinically driven revascularizations were those in which the patient had a positive functional study, ischemic ECG changes at rest in a distribution consistent with the target vessel, or ischemic symptoms, and an in-lesion diameter stenosis of $\geq 50\%$ by QCA or $\geq 70\%$ in the absence of the above-mentioned ischemic signs or symptoms.

Six centers were chosen to perform IVUS measurements as part of the follow-up examinations. The first 100 patients enrolled in these centers were to have an IVUS examination performed in addition to the angiographic examinations at 6 months. Plaque volume obstruction data collected from these examinations were compared between the study groups.

The study was performed according to the European Standard EN540 ("Clinical Investigation of Medical Devices for Human Subjects") for clinical research, the relevant parts of the ICH Guidelines for Good Clinical Practice ("Clinical Investigation of Medical Devices for Human Subjects"), and any applicable laws or regulations. All study data were monitored and source data verification was performed by qualified monitors inde-

pendent of the investigational sites. All sites received ethical committee approval and all patients gave their informed consent prior to enrollment.

All procedural and follow-up angiograms were analyzed by a central core laboratory (Cardialysis, Rotterdam, The Netherlands) using the previously validated Cardiovascular Angiography Analysis System (CAAS) [5,6]. The 6-month intravascular ultrasound (IVUS) recordings performed as part of the substudy were also analyzed by the same core laboratory.

Patient Population

Patients were considered suitable for the study if they had either angina pectoris or a positive functional ischemia study (ECG exercise test, stress echocardiography, or radionuclear studies), were eligible for coronary revascularization (PTCA and/or CABG), and were willing to comply with the requirements for follow-up evaluations. Specific angiographic inclusion criteria were planned single target lesion PTCA and stenting of a de novo lesion or a single restenotic lesion of a native coronary artery with the target lesion diameter stenosis greater than 50% but less than 100%. Lesions were required to be 30 mm or less in vessels with a reference diameter of greater than 2.5 mm and less than 4.0 mm. The main exclusion criteria were enrollment in other studies where the follow-up period had not been completed for at least 30 days, previous enrollment in this study, left ventricular ejection fraction of less than 25%, myocardial infarction within the past 72 hr, or contraindications to the study medication (aspirin, ticlid, and/or plavix). Additionally, patients with acute or chronic renal impairment, known allergy to gold and/or stainless steel, or other conditions that could limit the patient's ability to participate in the study or comply with follow-up requirements were excluded. Specific angiographic exclusion criteria were unprotected left main coronary artery disease, other lesions in the target vessel requiring treatment, any coronary intervention in the past 2 months, or other coronary lesions in a nontarget vessel requiring treatment within 2 months after the study procedure. Additional exclusion criteria were pretreatment with laser or atherectomy, lesions with intraluminal thrombus, lesions within 3 mm of the ostium of a coronary artery or where a side branch (> 2.0 mm) could have been compromised, bifurcations, severely calcified or angulated lesions, previously stented lesions, lesions located within a graft, or threatening abrupt closure.

Study Procedures

Eligible patients were randomized, via a central telephone service, to one of the two treatment groups. Patients were required to receive either ticlid (250 mg twice per day) or plavix (300 mg) prior to the procedure

TABLE I. Baseline Demographics and Clinical Characteristics

	NIR (n = 298)	NIROYAL (n = 305)	Difference (95% CI)
Age	60.3 ± 9.8	60.9 ± 10.3	-0.6 (-2.3 to 1.0)
Male (%)	75.2%	76.4%	-1.2 (-8.1 to 5.6)
Hypertension (%)	51.5%	53.6%	-2.1 (-10.1 to 5.9)
Current tobacco use (%)	28.7%	27.7%	1.0 (-6.2 to 8.2)
Hypercholesterolemia (%)	65.5%	65.0%	0.5 (-7.1 to 8.1)
Diabetes mellitus (%)	17.2%	18.8%	-1.6 (-7.7 to 4.6)
Angina status			
Stable (%)	57.7%	62.0%	-4.2 (-12.1 to 3.6)
Unstable (%)	33.6%	25.6%	8.0 (0.7-15.2)
Previous MI (%)	40.1%	37.6%	2.4 (-5.4 to 10.2)
Previous PTCA (%)	15.2%	12.2%	3.0 (-2.5 to 8.5)
Previous CABG (%)	3.7%	3.6%	0.1 (-2.9 to 3.1)

(preferably 24 hr prior) followed by 75 mg/d after the procedure; they also were required to receive aspirin (\geq 80 mg per day). During the procedure, heparin was administered according to local protocol. The stenting procedure was performed according to the manufacturer's instructions for use with the exception that no direct stenting was allowed. Patients were required to continue antiplatelet medication for 30 days and aspirin for at least 6 months. All patients were instructed to return for follow-up examination 30 days postprocedure, at which time their angina class was assessed and a 12-lead ECG recorded; details of adverse events and cardiac medication history were also recorded. After 6 months, all patients were instructed to return to the investigational site for further examinations. At this visit, a follow-up angiogram and a 12-lead ECG were performed. Additionally, patients' angina class was assessed and adverse events and cardiac medications were recorded. A subgroup of patients received an IVUS examination during the follow-up angiographic procedure.

Statistical Plan

The expected results of the NIR stainless steel stent were derived from the FINESS 2 trial [7]. The expected MLD was 1.88 mm and the common standard deviation was 0.63 mm. The expected difference in MLD between the NIR and NIROYAL stents was 0 mm. For equivalence testing, using the conservative sample size of 258 in each group, two simultaneous one-sided *t*-tests at the 2.5% level each would have 90% power to reject the null hypothesis that the two types of stents are not equivalent (the difference in means is \pm 0.20 or farther from 0) in favor of the alternative hypothesis that the means of the two groups are equivalent [8]. It was expected that 600 patients needed to be randomized in order to get two groups of at least 258 patients with evaluable QCA follow-up at 6 months. Continuous variables were compared using the Student's *t*-test; categorical variables were com-

pared using the Fishers' exact test. All variables were presented with the significance of 5%. SAS software version 6.12 was used for all analyses.

RESULTS

Between October 1999 and December 2000, 603 patients were randomized into this study (n = 298 for stainless steel NIR, 305 for gold-plated NIROYAL). Baseline patient, lesion, procedural, and stent characteristics are comparable in both groups as shown in Tables I and II. The mean age was 61 years. Nearly 76% of the patients were men, approximately 18% of the patients had a history of diabetes mellitus, and about 28% were current tobacco users. The majority of patients had stable angina, which was similar in both groups (NIR 57.7%, NIROYAL 62.0%). There were significantly more patients in the NIR group with unstable angina (NIR 33.6%, NIROYAL 25.6%; 95% CI = 0.7-15.2). In addition to similar target vessel distribution, lesion characteristics were also similar in both groups with nearly all lesions being type B1 and B2. The procedural success rate was 91.3% (NIR) and 94.1% (NIROYAL). The main reason these rates appear lower than comparative studies is directly related to the study definition of procedural success (< 30% residual stenosis and no use of a second stent).

Angiographic results are shown in Table III and in Figures 1 and 2. The preprocedural reference vessel diameter (NIR 2.79 mm, NIROYAL 2.85 mm), percentage diameter stenosis (DS; NIR 65.7%, NIROYAL 64.9%), and the MLD (NIR 0.95 mm, NIROYAL 0.99 mm) were similar in both groups. In contrast, the post-procedure mean reference vessel diameter of the target vessel (NIR 3.00 mm, NIROYAL 3.12 mm), DS (NIR 16.1%, NIROYAL 14.1%), and in-stent MLD (NIR 2.5 mm, NIROYAL 2.68 mm) were significantly different in the two groups ($P < 0.001$ for all variables). The immediate gain postprocedure (NIR 1.55 mm, NIROYAL 1.68

TABLE II. Baseline Lesion and Procedural Characteristics

	NIR	NIROYAL	Difference (95% CI)
Target vessel			
LAD	43.8%	42.9%	0.9% (−7.1% to 8.8%)
LCx	16.5%	23.1%	−6.6% (−13% to −0.3%)
RCA	39.7%	34.0%	5.7% (−2.0% to 13.4%)
ACC/AHA classification			
A	5.7%	7.0%	−1.3% (−5.2% to 2.6%)
B1	40.2%	34.9%	5.3% (−2.5% to 13.1%)
B2	54.1%	57.7%	−3.7% (−11.6% to 4.3%)
C	0.0%	0.3%	0.3% (−1.0% to 0.3%)
Procedural success	91.3%	94.1%	2.8% (−7.0% to 1.3%)
Stent length (mm)	15.2 ± 5.3	15.1 ± 4.9	0.1 (−0.7 to 0.9)
Number of stents per patient	1.1 ± 0.4	1.0 ± 0.3	0.1 (0.0–0.2)
Final balloon size (mm)	3.5 ± 0.4	3.6 ± 0.6	−0.1 (−0.3 to 0.1)
Maximum balloon pressure (atm)	13.8 ± 3.0	13.2 ± 2.9	0.0 (−0.5 to 0.5)

TABLE III. Quantitative Angiographic Results*

Lesion parameters measured	NIR (n = 298)	NIROYAL (n = 305)	P (95% CI)
Lesion length (mm)	8.84 ± 3.58	8.77 ± 3.49	<i>P</i> = 0.81; 0.07 (−0.52 to 0.66)
Reference vessel diameter (mm)			
Preprocedure	2.79 ± 0.52	2.85 ± 0.52	<i>P</i> = 0.17; −0.06 (−0.15 to 0.−03)
Postprocedure in-stent	3.00 ± 0.45	3.12 ± 0.44	<i>P</i> < 0.001; −0.13 (−0.20 to −0.05)
6-month follow-up in-stent	2.81 ± 0.50	2.88 ± 0.53	<i>P</i> = 0.16; 0.06 (−0.15 to 0.03)
% diameter stenosis			
Preprocedure	65.7 ± 11.7	64.9 ± 9.4	<i>P</i> = 0.37; 0.8 (−0.9 to 2.5)
Postprocedure in-stent	16.1 ± 6.6	14.1 ± 5.7	<i>P</i> < 0.001; 2.0 (1.0–3.0)
6-month follow-up in-stent	35.8 ± 17.5	43.9 ± 17.2	<i>P</i> < 0.001; −8.1 (11.1 to −5.1)
MLD (mm)			
Preprocedure	0.95 ± 0.36	0.99 ± 0.30	<i>P</i> = 0.14; −0.04 (−0.09 to 0.01)
Postprocedure in-stent	2.50 ± 0.40	2.68 ± 0.40	<i>P</i> < 0.001; −0.17 (−0.24 to −0.11)
6-month follow-up in-stent	1.83 ± 0.64	1.64 ± 0.65	<i>P</i> < 0.001; 0.19 (0.08–0.30)
Absolute gain in-stent	1.55 ± 0.44	1.68 ± 0.41	<i>P</i> < 0.001; −0.13 (−0.20 to −0.06)
Change in MLD			
Late loss in-stent (mm)	0.68 ± 0.54	1.04 ± 0.59	<i>P</i> < 0.001; −0.36 (−0.45 to −0.26)
Absolute net gain in-stent (mm)	0.88 ± 0.62	0.64 ± 0.66	<i>P</i> < 0.001; 0.24 (0.13–0.35)
Late loss index in-stent	0.45 ± 0.40	0.64 ± 0.37	<i>P</i> < 0.001; −0.19 (−0.26 to −0.12)
Binary restenosis rate	20.6%	37.7%	<i>P</i> < 0.001; −17 (−24.7 to −9.3)

*Five hundred seventy two lesions treated in 572 patients with follow-up QCA available on 515.

mm) was significantly greater in the NIROYAL group (*P* < 0.001; 95% CI = −0.20 to −0.06).

Although the 30-day MACE rate was not an endpoint of this trial, these data were collected and analyzed. The incidence of any MACE up to 30 days was 1% in both groups. This included death (0% in both groups), Q-wave MI (NIR 0.3%, NIROYAL 0.7%), CABG (0% in both groups), TLR (NIR 0%, NIROYAL 0.3%), and stent thrombosis (NIR 0.7%, NIROYAL 0%).

The 6-month postprocedure in-stent MLD was significantly greater in the NIR group (NIR 1.83 mm, NIROYAL 1.64 mm; *P* < 0.001; 95% CI = 0.08–0.30); this corresponded with the in-stent late loss (NIR 0.68 mm, NIROYAL 1.04 mm; *P* < 0.001; 95% CI = −0.45 to −0.26) and binary restenosis rates

(NIR 20.6%, NIROYAL 37.7%; *P* < 0.001; 95% CI = −24.7 to −9.3).

The TVF (NIR 13.4%, NIROYAL 14.8%), TLR (NIR 6.0%, NIROYAL 8.8%), and overall clinically driven MACE rates (NIR 7.4%, NIROYAL 10.5%) at 6 months postprocedure were similar in both groups (*P* = NS for all above parameters; see Table IV for all events, exact *P* values, and confidence intervals).

In an attempt to understand these study results, the core laboratory retrospectively performed an analysis on the restenotic lesions to determine if there were any differences in the patterns of restenosis between the two groups. The results from this additional analysis (Table V) revealed a significantly higher number of focal lesions (< 10 mm) in the NIR group (*P* = 0.03; 95% CI = 2.0–34.0).

572 Lesions treated in 572 patients with follow-up QCA available on 512.

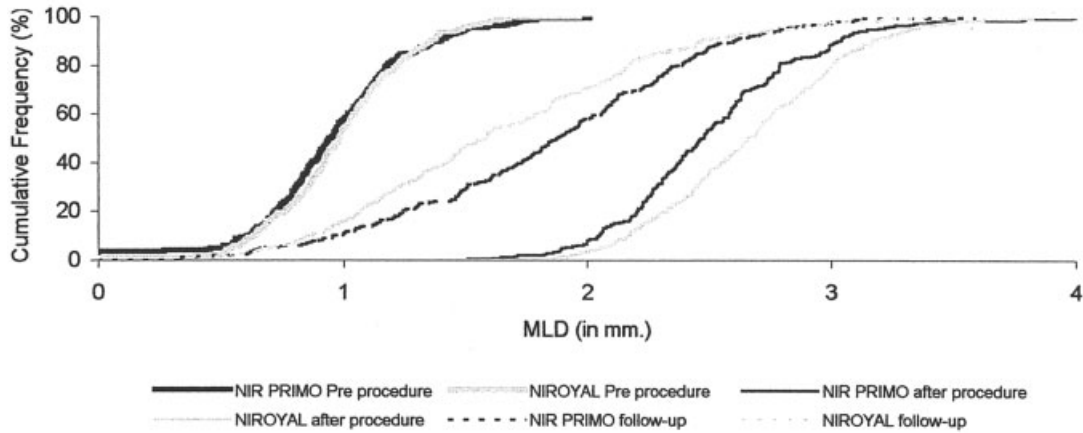


Fig. 1. Cumulative frequency distribution of minimum lumen diameter.

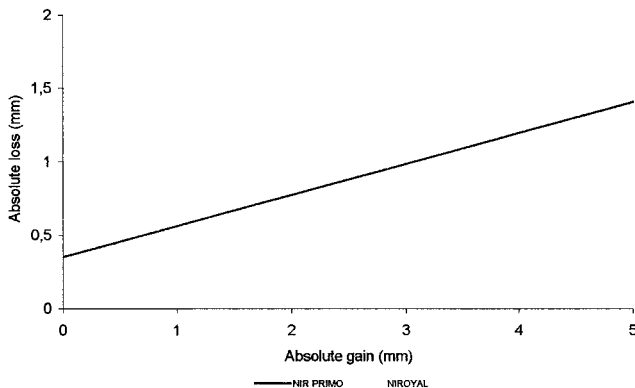


Fig. 2. Univariate linear regression analysis with absolute loss as dependent variable.

A subset of 105 patients in six selected sites underwent an elective IVUS procedure during the scheduled 6-month follow-up visit. The IVUS analysis results are presented in Table VI and Figure 3. No significant differences between the groups were observed for the mean stent area, mean lumen area, stent volume, and neointimal volume as measured by IVUS at 6 months postprocedure. On the other hand, mean lumen volume (NIR 99.21 mm³, NIROYAL 72.87 mm³; $P = 0.007$; 95% CI = 8.1–44.6) and mean area neointimal hyperplasia (NIR 1.99 mm², NIROYAL 2.73 mm²; $P = 0.004$; 95% CI = -1.2 to -0.3) both showed a better outcome in the NIR group. These findings translated into a significantly higher in-stent volume obstruction in the NIROYAL group (25.9% vs. 36.7%; $P = 0.003$; 95% CI = -17.5 to -4.0).

DISCUSSION

Stent radio-opacity plays an ever increasingly important role in accurate implantation and long-term visibility, particularly as the complexity level of coronary interventions continues to rise. Manufacturers have explored many different ways to produce optimal radio-opacity; providing enough radio-opacity for good placement but not preventing assessment of the lumen inside the stent postimplantation or at follow-up. Gold coatings are one method that has been used to increase stent radio-opacity.

Studies have been performed to examine biocompatibility and clinical performance of gold-coated stents in the coronary vasculature [1–4,9,10]. These studies have ranged from retrospective registries to prospective multicenter randomized trials. Some of the studies have shown higher restenosis and target lesion revascularization rates with gold-coated stents than with conventional noncoated stents, thus raising questions about the biocompatibility of this coating [4]. It has been suggested that the different methods of coating (i.e., different granularity, surface roughness, chemical purity, trace metals, and porosity) may be a factor in stent performance, leading to different clinical outcomes with different gold-coated stents [9]. The NIR Ultra Gold-Gilded Equivalency Trial (NUGGET) was therefore conducted to compare the uncoated NIR stent and the gold-coated version of the same stent to address whether the performance of the gold-coated NIROYAL stent (with a gold plating different to those tested in previous studies) is equivalent to that of the stainless steel NIR stent. NUGGET is the

TABLE IV. Principal Effectiveness and Safety Results (n = 603)

Hierarchical complications	NIR (n = 298)	NIROYAL (n = 305)	P (95% CI)
MACE in-hospital ^a	1.0% (3/298)	0.3% (1/305)	<i>P</i> = 0.37; 0.7 (−0.6 to 2.0)
MACE out-hospital at 180 days ^a	6.7% (20/298)	10.2% (31/305)	<i>P</i> = 0.14; −3.5 (−7.9 to 1.0)
MACE at 180 days ^a	7.4% (22/298)	10.5% (32/305)	<i>P</i> = 0.20; −3.1 (−7.7 to 1.4)
Stent thrombosis at 180 days	0.7% (2/298)	0.0% (0/305)	<i>P</i> = 0.49; 0.7 (−0.3 to 1.6)
TVF ^a	13.4 (40/298)	14.8 (45/305)	<i>P</i> = 0.64; −1.3 (−6.9 to 4.2)
TLR (re-PTCA) ^a	4.4% (13/298)	8.5% (26/305)	<i>P</i> = 0.046; −4.2 (−8.1 to −0.3)
TLR (CABG) ^a	1.7% (5/298)	0.3% (1/305)	<i>P</i> = 0.12; 1.3 (−0.2 to 2.9)
TLR (re-PTCA and CABG) ^a	6.0% (18/298)	8.9% (27/305)	<i>P</i> = 0.22; (−7.0 to 1.4)

^aClinically driven (according to protocol).

TABLE V. Classification of In-Stent Restenosis*

Parameters Measured	NIR (n = 50)	NIROYAL (n = 100)	P (95% CI)
Focal ISR (≤ 10 mm)	70.0% (35/50)	52.0% (52/100)	<i>P</i> = 0.037; 18.0% (2.0–34.0%)
Diffuse intrastent (>10 mm ISR)	20.0% (10/50)	32.0% (32/100)	<i>P</i> = 0.18; −12.0% (−26.4% to 2.4%)
Diffuse proliferative (>10 mm extending outside of stent)	6.0% (3/50)	15.0% (15/100)	<i>P</i> = 0.18; −9.0% (−18.6% to 0.6%)
Total occlusion	4.0% (2/50)	1.0% (1/100)	<i>P</i> = 0.26; 3.0% (−2.8% to 8.8%)

*One hundred fifty one patients with restenosis; analysis available in 150. The in-stent restenosis (ISR) pattern was unable to be assessed in one patient.

TABLE VI. IVUS Analysis at Six-Month follow-up*

Lesion parameters measured	NIR (n = 51)	NIROYAL (n = 54)	P (95% CI)
Mean stent area (mm ²)	8.00 ± 1.99	7.86 ± 2.24	<i>P</i> = 0.73; 0.14 (−0.66 to 0.95)
Stent volume (mm ³)	133.15 ± 70.50	113.13 ± 42.39	<i>P</i> = 0.08; 20.02 (−1.92 to 41.97)
Mean lumen area (mm ²)	6.01 ± 2.23	5.13 ± 2.49	<i>P</i> = 0.06; 0.87 (0.02 to 1.77)
Minimal lumen area (mm ²)	4.46 ± 2.23	3.62 ± 2.17	<i>P</i> = 0.054; 0.84 (0.00–1.68)
Lumen volume (mm ³)	99.21 ± 56.42	72.87 ± 38.31	<i>P</i> = 0.007; 26.34 (8.11–44.56)
Minimal luminal diameter (mm)	2.15 ± 0.57	1.92 ± 0.58	<i>P</i> = 0.04; 0.23 (0.01–0.45)
Mean area neointimal hyperplasia (mm ²)	1.99 ± 1.29	2.73 ± 1.25	<i>P</i> = 0.004; −0.73 (−1.22 to −0.25)
Neointimal volume (mm ³)	33.94 ± 28.24	40.25 ± 22.71	<i>P</i> = 0.21; −6.31 (−16.02 to 3.39)
Volume obstruction in-stent (%)	25.9 ± 16.8	36.7 ± 18.7	<i>P</i> = 0.003; −10.8 (−17.5 to −4.0)

*One hundred eleven lesions treated in 111 patients with follow-up IVUS data available on 105.

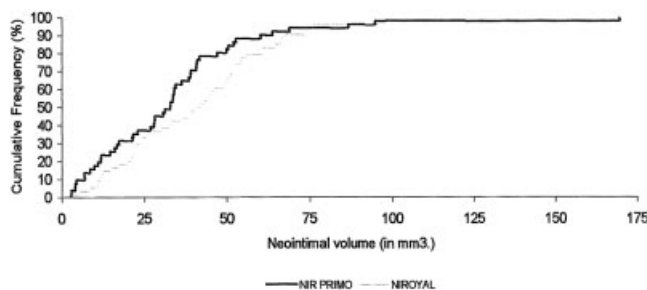


Fig. 3. Cumulative frequency distribution of neointimal volume.

largest prospective randomized multicenter trial to be performed with gold-coated stents. It has shown a significant difference in angiographic and IVUS parameters at 6 months, in favor of the uncoated version of the stent. This is similar to the findings of other studies with gold-coated stents and similar endpoints [3,4].

The performance of the NIR uncoated stent seen in the NUGGET study is comparable to that seen in other

studies performed with the same stent design. The 6-month TLR rate (6%) is at the low end of the range seen in the major studies performed with the NIR stent (TLR in FINESS [11], FINESS 2 [7], and NIRVANA [12] ranged from 5.9% to 11.4%). The TLR rate seen with the Palmaz-Schatz stent in the NIRVANA study was 8.8%. Additionally, the 6-month MACE rate (7.4%) for the NIR stent in the NUGGET study is rather low compared to previous studies (MACE rates for the NIR stent in the above-mentioned studies ranged from 11.5% to 18.4%).

At baseline, differences in reference vessel size, lesion length, balloon size, inflation pressures, risk factors (diabetes) were not seen in the two groups and therefore it is unlikely that they could account for any performance differences between the coated and noncoated stents.

The postimplantation QCA data showed some puzzling results. A highly significant difference (*P* < 0.001) was seen in the postimplantation acute gain, reference vessel diameter, the diameter stenosis, and the minimal

luminal diameter. All were larger in the gold-coated group. We considered the possibility that the high radio-opacity of the gold-coated stent could have in some way interfered with the QCA analysis (angiographic image). This was confirmed by a study involving a radio-opaque tantalum stent in phantom Plexiglas vessels [13], which compared QCA and intracoronary ultrasound (ICUS) measurements in an experimental restenosis model and showed that the reliability of QCA declined in the presence of the radio-opaque stent. The QCA measurements of the reference diameter were significantly different as compared to the IVUS measurements and the actual phantom vessel diameter. This may have been a factor in the postimplantation QCA measurements in the NUGGET study. Due to the fact that no postprocedure IVUS was performed in the NUGGET study, it was not possible to confirm this by comparing the postprocedure IVUS and postprocedure angiographic data. This issue was not encountered when analyzing the 6-month follow-up images due to the normal neointimal growth over the stent struts following stent implantation.

Despite the higher restenosis rates seen in the NIROYAL group, other important clinical outcomes were very favorable when compared to other gold-coated stents. Specifically, the target lesion revascularization rate (8.9%) and 6-month MACE rate (10.5%) were in the lower range of rates seen in all of the other gold-coated studies and comparable to the uncoated stents. One possible explanation for the apparent discrepancy between the angiographic and clinical parameters of stenosis could be related to a biased decision on whether and when to perform a reintervention (based on the high visibility of gold-coated stents). If this were the case, one would expect to see some type of an imbalance in the rate of interventions somewhere close to the 6-month follow-up time point. However, when reviewing the reinterventions that happened after 6 months (210 days), there was no imbalance in the number of reinterventions between the groups.

The NIROYAL differs from previous gold-coated stents in that it features high purity and a two-step plating process to ensure complete coating and to eliminate pores, flakes, and cracks with stent expansion, exposing the underlying metal. However even gold processed to 99.99% purity retains silver, copper, and other base metals and might alter tissue reactions. As suggested by Edelman et al. [9], a thermal treatment of the gold plating could remove imbedded impurities and thus improve biocompatibility and reduce the proliferative response. Alternatively, the use of antirestenosis drug therapy via local elution might help manage this problem. Prospective studies addressing these hypotheses are needed.

Study Limitations

The obvious major limitation to this study was the fact that the investigators as well as the angiographic core laboratory analysts were not able to be blinded to the study treatment. Secondly, difficulties were encountered by the core laboratory in measuring the postprocedure results in the presence of a more radio-opaque stent, which led to an overestimation of the postimplantation reference diameter measurements.

The use of the NIROYAL stent led to significantly higher restenosis rates, late loss (i.e., neointimal hyperplasia), in-stent volume obstruction, and a smaller MLD (as measured by QCA and IVUS) at 6 months when compared to the uncoated control in spite of a significant better initial gain. However, the clinically driven 6-month MACE and TLR rates were not significantly different and were similar to those rates seen in other studies with the NIR and other stents. Nevertheless, gold-coated stents cannot be recommended as a routine implant unless further optimization of gold coating technology (i.e., thermal processing of the stent) has been shown to minimize bioreactivity and improve long-term angiographic and clinical performance as compared to the current version of these stents.

The concept of improved visibility requested by operators should not be abandoned but be combined with other technologies (i.e., drug-eluting coatings, other alloys/metals).

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APPENDIX

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