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ARTICLES

Intracoronary Heparin Delivery in Humans

Acute Feasibility and Long-term Results

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Abstract

Background Inefficacy of systemic drug administration for restenosis prevention may partially relate to insufficient local drug concentration. This study aimed to evaluate the acute feasibility and long-term outcome of using an infusion-perfusion coil balloon, Dispatch.

Methods and Results In 22 patients after balloon angioplasty, the coil balloon was studied for (1) feasibility of local heparin delivery, (2) symptoms and signs of ischemia during prolonged deployment compared with angioplasty balloon occlusion, (3) coronary pressure and flow distal to the inflated device, and (4) long-term clinical and angiographic results. During prolonged intracoronary deployment of the coil balloon (29±8 minutes), 5 of 22 patients developed mild chest pain versus 20 of 22 during angioplasty (275±283 seconds). Neither hemodynamic nor vectorcardiographic signs of ischemia were detected, in contrast to angioplasty balloon occlusion. Baseline flow across the coil balloon was 44±31 mL/min, increasing by a factor of 1.8±0.7 during pharmacologically induced hyperemia. A mean volume of 14.2±6.1 mL containing 1416±608 IU of heparin was infused locally at a pressure of 122±54 mm Hg. At 7±1-month follow-up, 1 asymptomatic patient had died, and of the remaining 21, 17 (81%) were asymptomatic. Angiographic follow-up was obtained in 15 of 21 patients (71%), including all 4 symptomatic patients. Mean minimal luminal diameter after the procedure was 2.16±0.49 mm and at follow-up, 1.89±0.45 mm, which corresponds to a restenosis rate (diameter stenosis ≥50%) of 7% (1/15).

Conclusions Intracoronary use of the coil balloon after balloon angioplasty proved to be feasible and subjectively as well as objectively well tolerated during prolonged deployment by virtue of its perfusion properties. High volumes of heparin solution can be infused locally at very low pressure. No unfavorable clinical or angiographic long-term effects were observed.

angioplasty heparin restenosis hemodynamics perfusion

The main unresolved issue after PTCA is coronary restenosis, which occurs in 35% to 50% of the patients.[1 2] A device-oriented approach to reduce restenosis rate has led to the development of a variety of revascularization systems.[3] However, the incidence of restenosis has not, as yet, been reduced dramatically by any new angioplasty device or biological agent. The advent of the intracoronary stent implant may have provided the first real breakthrough in reducing the restenosis rate, but at the cost of increased bleeding complications linked to a prolonged anticoagulation regimen.[4 5] A pharmacological approach to reduce restenosis has led to the systemic administration of many different drug classes during or after PTCA.[6 7 8 9] Failure of

systemic administration has been attributed partially to insufficient drug concentration at the site of angioplasty to suppress neointimal proliferation, which is thought to be the cornerstone of restenosis.[10 11 12] Local delivery has been reported to achieve higher concentrations of chemical compounds at the site of angioplasty in experimental studies. The first local drug delivery device for coronary application was the porous balloon,[13] consisting of an angioplasty balloon with laser-made perforations around its circumference. This catheter, however, caused jet-stream lesions to the vessel wall because of the high local infusion pressure.[14] Other infusion methods and a variety of infusion catheters have been designed to overcome this limitation, such as controlled low-pressure infusion,[15] microporous balloon,[14] dual balloon,[16] multichannel balloon,[17] drug delivery sleeve,[18] or iontophoretic balloon.[19] However, all devices have the drawback of not allowing simultaneous distal arterial perfusion. The duration of infusion and amount of drug administered are thereby limited. The potential hazards of local arterial damage and of absence of coronary perfusion while the drug is being delivered have, until recently, confined the use of these devices to the animal experimental laboratory.[16]

A new local drug-infusion catheter (Dispatch Scimed Systems Inc) has been designed to overcome these limitations by combining infusion and perfusion characteristics.

The aim of this study was to assess in humans the following aspects of this new drug-delivery device: (1) acute feasibility of prolonged local deployment with simultaneous infusion of a heparin solution after balloon angioplasty, (2) signs of myocardial ischemia during prolonged intracoronary deployment compared with temporary balloon occlusion during angioplasty, (3) coronary hemodynamics distal to the inflated device, and (4) chronic effects of prolonged local coil balloon deployment and simultaneous infusion of a heparin solution after balloon angioplasty.

Methods

Drug-Delivery Device

The local drug delivery device (Dispatch Scimed Systems Inc) is depicted and described in Fig 1⇓. By design, the coil balloon is a nondilatational catheter. When the coil balloon is inflated, a nonporous polyurethane sheath wrapped around the coils forms a cylindrical, hollow structure that allows both coronary perfusion through the central conduit and drug infusion over the external surface between the coils (drug compartments). The system is designed to be used after percutaneous revascularization procedures.

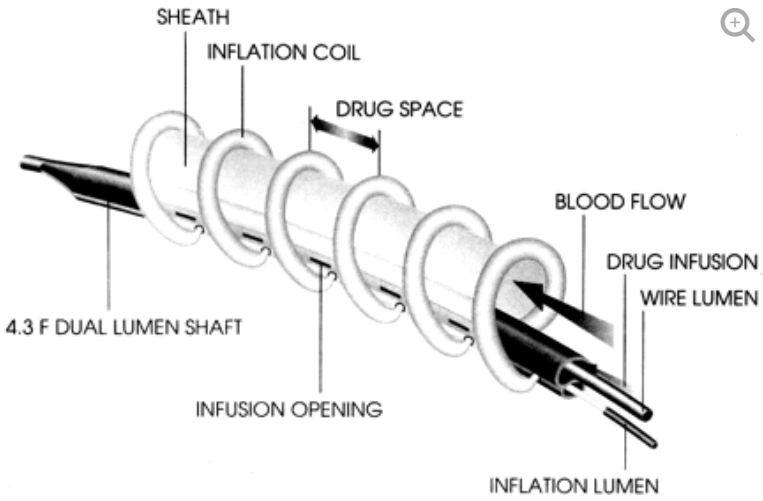

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Figure 1.

Diagram of the drug delivery device (Dispatch), an over-the-wire catheter consisting of a 160-cm-long, 4.4F shaft containing three separate channels: (1) for guide-wire insertion, (2) for coil balloon inflation, and (3) for drug infusion. The 20-mm-long nondilatational coil balloon consists of six single coils of polyolefin copolymer (POC-6) wrapped around a nonporous polyurethane sheath. The coil balloon is available in sizes of 3.0, 3.5, and 4.0 mm (nominal pressure, 6 atm), corresponding to a wrapped profile of 0.063, 0.065, and 0.070 in., respectively. When inflated, the coil balloon deploys a central conduit allowing blood perfusion. Calculated inner lumen diameters (surfaces) of the conduit are 1.5 mm (1.77 mm^2), 2.0 mm (3.14 mm^2), and 2.5 mm (4.9 mm^2) according to the device size (diameter of inflated single coil, 0.75 mm at 6 atm). Drug solution infusion is delivered over the external surface between the coils (drug compartments) through isolated slits in the catheter shaft.

Study Population

The clinical and angiographic characteristics of the 22 patients included in the study are summarized in Table 1⇓. The study period consisted of two consecutive evaluation phases, each of which included 11 patients, each with a recruitment period of 25 days (cohort 1) and 53 days (cohort 2), respectively. The selected study populations represented 23% (11/48) and 11% (11/103), respectively, of the population treated by balloon angioplasty over the same time period at our institution. Inclusion criteria were stable or unstable angina pectoris, one- or two-vessel disease, and normal or hypokinetic left ventricular wall motion in the territory supplied by the vessel to be treated, with a global ejection fraction of >50%. In the second cohort, patients with a target vessel supplying either the anterior wall (LAD, n=6) or the inferior wall (RCA, n=3, and dominant circumflex artery, n=2) were selected. Except for vessel size (reference diameter ≥2.5 mm), no specific lesion type precluded initial enrollment. Exclusion criteria were age <18 years or >80 years, evolving myocardial infarction in the territory supplied by the vessel to be treated (<7 days old), left bundle-branch block or bifascicular block, life expectancy <6 months, and factors making follow-up difficult. Written informed consent was obtained from all patients before inclusion.

Table 1.

Clinical and Angiographic Characteristics of 22 Patients Treated With Local Heparin by Means of the Coil Balloon (Dispatch) After Angioplasty

Age, y (mean±SD)	57±9
Sex (male/female), n	13/9
Anginal syndrome	
Stable	
CCS 1-2	1
CCS 3-4	8
Unstable	13
Previous myocardial infarct, n	11
Ejection fraction (n=19), %	63±9

No. of vessels diseased, n	
1	18
2	4
Treated vessel	
LAD	14
LCx	3
RCA	5
Lesion type	
A	11
B1	3
B2	8
C	0
Lesion length, mm	7.28±2.80
Interpolated reference diameter, mm	2.8±0.55
Minimal luminal diameter, mm	1.07±0.40
Eccentricity index	0.62 ±0.29

Balloon Angioplasty and Local Heparin Delivery Procedure

After an intravenous bolus injection of heparin 10 000 IU, aspirin 250 mg, and diazepam 5 mg, a conventional balloon angioplasty was performed. After an optimal angioplasty result was achieved, as assessed visually, the nondilatational coil balloon was inserted through an 8F guiding catheter and deployed at the angioplasty site. A 30-minute-long deployment was attempted unless subjective symptomatic intolerance or ECG signs (1 of 3 leads) of ischemia occurred. A solution with commercially available heparin (100 IU/mL in NaCl 0.9%) was infused at 12 to 36 mL/h. In the first 11 patients, the infusion rate was increased in a stepwise manner by 12 mL/h every 10 minutes up to 36 mL/h to detect potential detrimental effects of augmenting volume administration. In the second 11 patients, the infusion rate was 36 mL/h from the onset.

Signs of Myocardial Ischemia: Angioplasty Balloon Versus Coil Balloon

Symptoms. Angina was scored as described earlier[20 21] on a subjective scale from 1 to 10 during angioplasty balloon occlusion and coil balloon deployment. Use of analgesic was restricted as much as possible, and it was never administered before drug delivery device insertion.

Left ventricular hemodynamics. An 8F pigtail high-fidelity tip manometer (Sentron, Cordis Europe NV) was inserted via the contralateral femoral artery into the left ventricle to monitor pressure changes throughout the procedure. Pressure and derived indexes were calculated and displayed on-line with an updated version of a system previously described.[22 23 24 25] Monitored left ventricular hemodynamic changes included the following contraction parameters: peak LVP, peak positive dP/dt, and maximal velocity of contraction (V_{max}), as well as diastolic and relaxation parameters: EDP, peak negative dP/dt, and time constant of relaxation (T). Time constant of LVP fall, T (ms), was determined with the semilogarithmic model of relaxation: $P(t)=P_0\, e^{-t/T}$, where P is pressure, t is time, and P_0 is equivalent to P_b (P begin) defined as pressure at the point at which dP/dt is minimal (maximal negative dP/dt).[24] In the biexponential fitting model of pressure fall, T for the first 40 ms is defined as T_1 and that after 40 ms as T_2. Ischemia during coronary occlusion by conventional balloon was evaluated by use of a baseline value ≤5 minutes before angioplasty and a value at the end of PTCA. For evaluation of ischemia during coil balloon deployment, a baseline value ≤5 minutes before inflation, a value every 5 minutes up to 30 minutes, the last value before deflation, and the value at the end of coil balloon inflation were selected. End values for conventional balloon and coil balloon were defined as mean of the last value before deflation and first value after deflation.

Vectorcardiography. Vectorcardiographic analysis (MIDA, Ortivus Medical AB) was performed continuously during the procedure as previously reported.[26] Vectorcardiographic changes were assessed as changes in QRS VD as well as ST VM and were calculated as described earlier[27] and depicted as a continuous trend. Clinically relevant QRS VD and ST VM changes were defined as changes ≥15 μVs and ≥0.1 mV, respectively. Baseline values were defined as the mean values over a 5-minute period before conventional balloon inflation and coil balloon deployment, respectively. Values during conventional balloon and coil balloon deployment were represented as averaged value over the whole inflation period. In cases of multiple inflations, the longest inflation period was selected.

Ventriculography. Ventriculography (one projection at a 30° right anterior oblique angle at 25 frames per second) was performed before PTCA and during coil balloon deployment by injection of 0.75 mL/kg of nonionic contrast medium (Iopamiro 370, Bracco). Ventriculograms were assessed off-line by automated contour detection (CESAR system version 86) and analyzed according to the model of Slager et al[28] : Segmental end-systolic and end-diastolic volume changes were calculated along a system of 20 coordinates: segmental contribution to total ejection fraction was used to quantify regional wall motion and regrouped in five regions of interest (anterobasal, anterolateral, posterobasal, posteroapical, and apical). According to the vessel treated, the corresponding regional wall motion change, defined as difference before PTCA versus during coil balloon deployment, was calculated.

Enzymes. CPK was determined 6 and 12 hours after the procedure. CPK-MB was measured whenever the values of CPK were elevated.

Coronary Hemodynamics

During coil balloon deployment, after removal of the guide wire, mean fluid-mediated pressure gradient across the device was measured through the wire port. A 15-MHz 0.014-in. Doppler guide wire (Flowire, Cardiometrics) was then inserted through the guide-wire port. Coronary flow velocity was measured 1.5 to 2 cm distal to the device in basal conditions and after intracoronary injection of papaverine (left coronary artery, 12.5 mg; RCA, 8 mg) or adenosine (left coronary artery, 18 μg; RCA, 12 μg).[29] The change in protocol from papaverine to adenosine was due to one episode of ventricular fibrillation secondary to intracoronary injection of papaverine. Angiography was performed with the Doppler wire at the site of volume sampling. Blood flow through the device was calculated as the product of time-averaged peak flow velocity and cross-sectional area determined by QCA at the site of Doppler volume sampling (Fig 2⇓). Flow measurements obtained by this method have been validated with electromagnetic flow probes in open-chest experimental animals.[30]

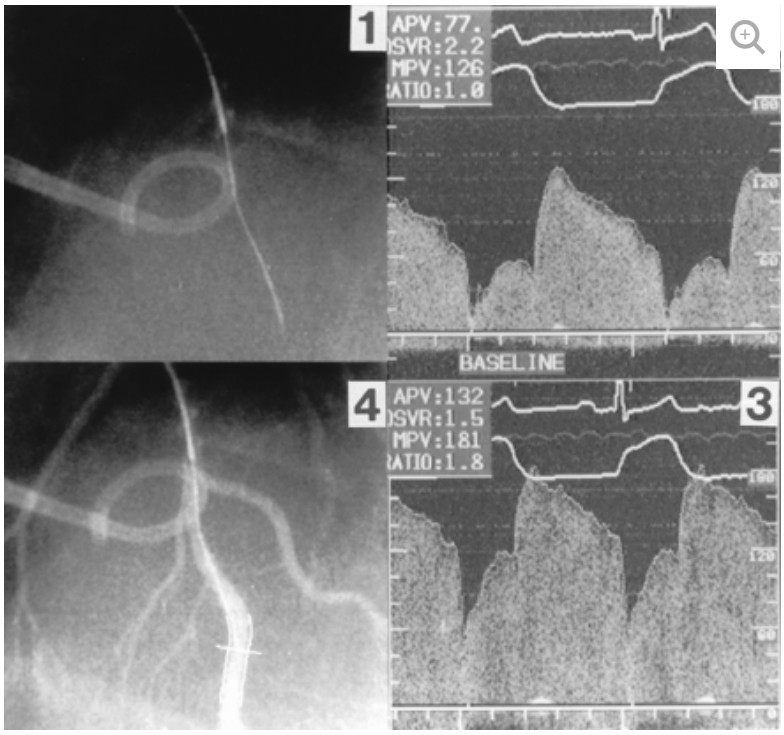

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Figure 2.

Doppler study consisting of (1) Doppler guide wire tip positioned 1.5 to 2 cm distal to the end of the device of the intracoronary inflated coil balloon; (2) coronary flow velocity measurement at baseline; (3) after pharmacologically induced hyperemia; and (4) QCA analysis at the site of Doppler volume sampling to allow calculation of flow.

Inventory of Analyzed Ischemia and Perfusion Parameters per Patient

Left ventricular tip manometry monitoring was not carried out in 4 of the 22 patients because of recent stroke, aortic stenosis, or a severe peripheral arteriopathy. Vectorcardiographic monitoring was performed in the first cohort of patients (patients 1 through 11), whereas ventriculography before PTCA as well as during coil balloon deployment was performed in the second cohort of patients (10 of 11; patients 13 through 22). In one case, ventriculography was not performed because of severe peripheral arteriopathy.

Trans–coil balloon pressure gradient measurement and Doppler study (baseline) were performed in 17 patients. In 5 patients, flow velocity evaluation distal to the deployed coil balloon was not performed because of a second significant lesion distal to the treated one (n=2), angiographically visible collaterals in a total occlusion (n=2), and technical failure (n=1).

Acute Feasibility and Long-term Evaluation

Acute feasibility evaluation included technical, angiographic, and clinical adverse events during and after coil balloon procedure.

Long-term evaluation was scheduled after 6 months and consisted of an interview, a physical examination, and angiographic follow-up. In case of refusal of angiographic follow-up, a perfusion scintigram was requested.

Recorded clinical events were the following: death, cerebrovascular accident, myocardial infarction, bypass surgery, or a second percutaneous intervention involving the previously treated lesion between the time of the initial procedure and the follow-up angiography (7±1 months) as well as an unplanned stent implantation after balloon angioplasty. According to our institutional practice, stenting was planned after angioplasty if a dissection type B, C, or D was longer than 10 mm without compulsory flow impairment or in case of a dissection type E or F. All cerebrovascular accidents were considered, regardless of their cause. Myocardial infarction was diagnosed if there were new pathological Q waves according to the Minnesota Code[31] or if there was an increase in serum creatine kinase to more than the normal value, together with a pathological increase in myocardial isoenzymes. Coronary artery bypass graft surgery was defined to include emergency or elective surgery involving the previously treated segment.

Angiographic Analysis

Before the procedure, the lesion type was classified according to the modified AHA classification.[32] After PTCA as well as after local heparin administration, the lesion was evaluated qualitatively and by QCA. QCA was performed off-line with an automated computer-assisted edge-detection system (Cardiovascular Angiography Analysis System II [CAAS II], Pie Medical).[33 34]

Acute and long-term angiographic results were evaluated with the same matched “working” projection before the procedure, after PTCA and coil balloon deployment, and at follow-up.[35]

Statistics

Continuous variables are expressed as mean±SD. Hemodynamic, vectorcardiographic, and ventriculographic characteristics during conventional balloon and coil balloon deployment were compared by repeated-measures ANOVA. Predefined comparisons were performed by paired *t* test using Bonferroni correction. Differences were considered significant if the null hypothesis could be rejected at the .05 probability level.

Discrete variables are expressed as counts and percentages.

Results

Acute Feasibility

The drug-delivery device could be placed and inflated at the lesion site in all cases. No acute complications occurred during intracoronary coil balloon insertion, prolonged deployment, or retrieval in the guiding catheter.

Angiographically, in 22 patients, the MLD of the treated lesions was 1.07±0.40 mm at diagnostic angiography. After PTCA, with balloon nominal values ranging between 2.5 and 3.5 mm and with a mean inflation pressure of 8.6±2.9 atm (range, 4 to 14 atm) and a mean inflation time of 274±270 seconds (range, 60 to 1200 seconds), MLD increased to 1.92±0.36 mm. After coil balloon (balloon size ranging from 3.0 to 4.0 mm nominal size at mean inflation pressure of 6.9±1 atm and a mean inflation time of 29±8 minutes), MLD increased nonsignificantly to 1.98±0.41 mm. In 14 of 22 patients (64%), the diameter after coil balloon was greater than or equal to the diameter after PTCA. The diameter size of the drug-delivery device matched (n=19) or was 0.5 mm larger than (n=3) the largest balloon used for the conventional dilatation.

Dissections were observed in 7 patients after PTCA (1 type A, 2 type B, 2 type C, 2 type D). Of these 7 dissections, 4 fulfilled the criteria for stenting before local drug delivery (Fig 3⇓). One type B dissection (8.2 mm long) was successfully treated by prolonged deployment of the coil balloon device. Among the 6 remaining dissections, a type A dissection after PTCA was evaluated as type B (5.5 mm long) after coil balloon deployment. A type D dissection (34 mm long) became a type F dissection after coil balloon deployment at two sites for 15 and 18 minutes and was successfully treated by a bailout stent implantation. Three further dissections (types B, C, and D) were stented after coil balloon deployment according to the institutional clinical practice (>10 mm long). Their dissection lengths after heparin solution infusion did not change significantly (B, 10.5 versus 11.1 mm; C, 24.5 versus 19.4 mm; and D, 24.5 versus 26.1 mm). A last type C dissection (<10 mm long) did not change significantly in length after heparin infusion (5.6 versus 6.3 mm) (Fig 3⇓).

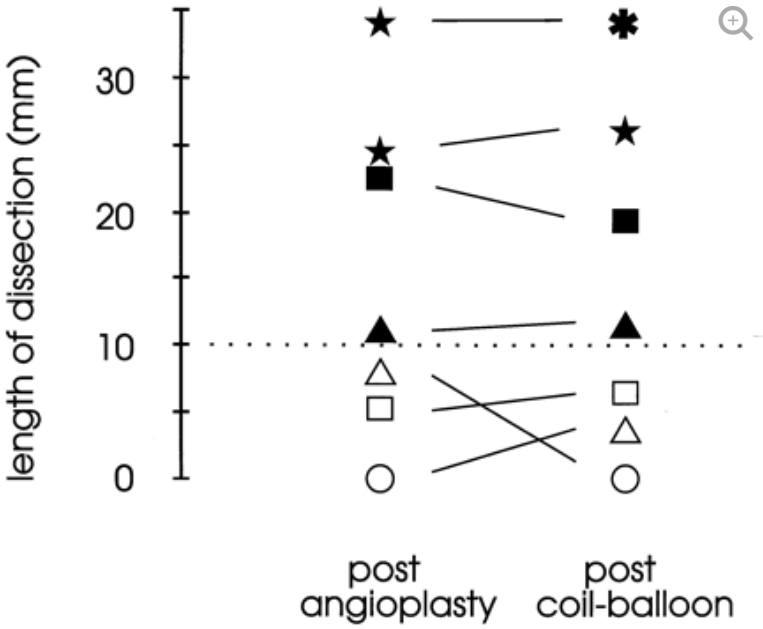

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Figure 3.

Graph showing influence of coil balloon deployment on dissections caused by balloon angioplasty. According to our institutional practice, stenting was planned after angioplasty if a dissection type B (triangle), C (solid square), or D (star) was longer than 10 mm without compulsory flow impairment or in case of dissection type E or F (asterisk). According to this predefined criterion, no unplanned stent deployment occurred after coil balloon inflation. However, of four planned stent deployments (1 type B, 1 type C, 2 type D), a 34-mm-long dissection type D needed a bail-out stent deployment for an acute occlusion after coil balloon inflation (type F dissection). Closed symbols indicate planned stenting after angioplasty; open symbols, no stenting planned after angioplasty.

Signs of Ischemia: Angioplasty Balloon Versus Coil Balloon

Symptoms. Of 22 patients, 18 (82%) suffered angina grade 3 to 10 (mean, 8±3) during inflation of the conventional PTCA balloon. Of 22 patients, 5 (23%) developed grade 2 to 7 (mean, 4±2) symptoms during coil balloon deployment. Of these 5 patients, 3 described anginal symptoms of grade 2 to 3 and 2 patients, symptoms of grade 6 to 7, one of whom had a lesion at a major bifurcation point (coil balloon covering first marginal branch) and the second a subocclusive dissection of the first diagonal branch occurring during the introduction of the Doppler wire. After coil balloon removal and intracoronary nitrate administration, flow was restored and symptoms abated rapidly in both cases.

Left ventricular hemodynamics. Left ventricular hemodynamic parameters during conventional balloon as well as coil balloon inflation are summarized in Table 2⇓. No significant hemodynamic changes were observed during coil balloon deployment. During conventional balloon occlusion, T_1, T_2, negative dP/dt, and EDP changed significantly compared with the baseline value (Fig 4⇓).

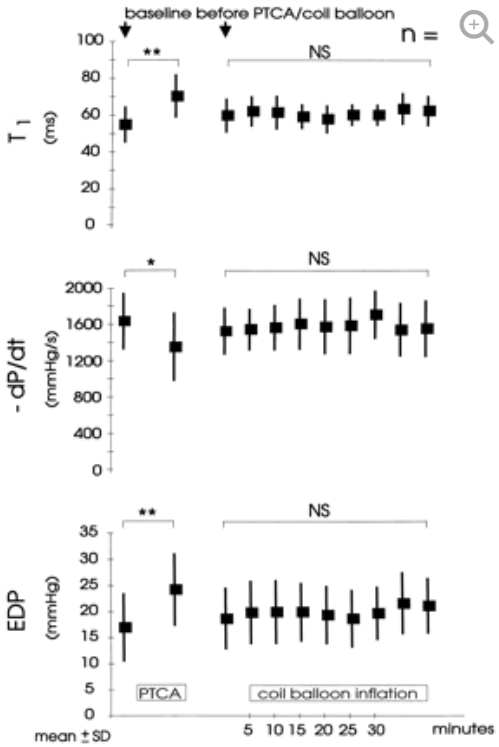

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Figure 4.

Graphs showing time constant of relaxation (T_1), negative dP/dt, and EDP during conventional angioplasty balloon inflation compared with coil balloon deployment. The following values are depicted during angioplasty: 1, baseline value; 2, at end of procedure and during coil balloon inflation; 3, baseline value; 4 through 9, every 5 minutes up to 30 minutes; 10, final value defined as just before coil balloon deflation; and 11, at end of procedure. End-of-procedure values are defined as the mean value just before and just after angioplasty and coil balloon deflation, respectively. *P<.05; **P<.01.

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Table 2.

Hemodynamic Parameters in 18 Patients During Conventional Balloon Inflation and Coil-Balloon Inflation at Baseline and at the End of Procedure[1]

	PTCA			D-3				
	Baseline	End	*P* by *t* test[2]	Baseline	End	*P* by *t* test[2]	*P* by *t* test[3]	*P* by ANOVA[4]
HR, bpm	63±9	61 ±13	NS	60±11	60 ±12	NS	NS	NS
Peak LVP, mm Hg	128 ±15	128±23	NS	126±16	136 ±25	NS	NS	.03

	PTCA			D-3			*P* by *t* test	*P* by ANOVA
	Baseline	End	*P* by *t* test	Baseline	End	*P* by *t* test		
Peak+dP/dt, mm Hg/s	1313 ±195	1277±281	NS	1247±218	1332±342	NS	NS	NS
V_{max}, s^{-1}	52±8	54 ±10	NS	50±8	51±9	NS	NS	.04
T_1, ms	55±10	70 ±12	.0001	60±9	62 ±8	NS	.0013	.0001
T_2, ms	48±8	62±10	.0002	55±8	54 ±7	NS	.0024	.0001
Peak−dP/dt, mm Hg/s	1634±309	1350±374	.0064	1522±256	1548 ±309	NS	.0046	.0001
EDP, mm Hg	17 ±7	24±7	.0001	19±6	21±5	NS	NS	.0001

HR indicates heart rate; V_{max}, maximal velocity of contraction; and T_1 and T_2, time constant of relaxation for the first 40 ms and after 40 ms, respectively.

1 Defined as mean value just before and just after device deflation.

2 Paired *t* test baseline vs end;

3 paired *t* test end PTCA vs end D-3.

4 ANOVA indicates univariate analysis of variance.

Vectorcardiography. Vectorcardiographic monitoring did not reveal any significant ST-VM changes during conventional balloon inflation and coil balloon deployment compared with baseline values (94.6±68.5 versus 125±84.4 mV and 91.5±59.2 versus 90.5±50.8 mV, respectively). QRS VD showed an ischemia-induced increase during conventional balloon angioplasty, but no changes were observed during coil balloon deployment (6.6±4.6 versus 16.8±5.3 μVs [*P*<.01] and 9.1±4.1 versus 9.0±2.8 μVs [NS]) (Fig 5⇓).

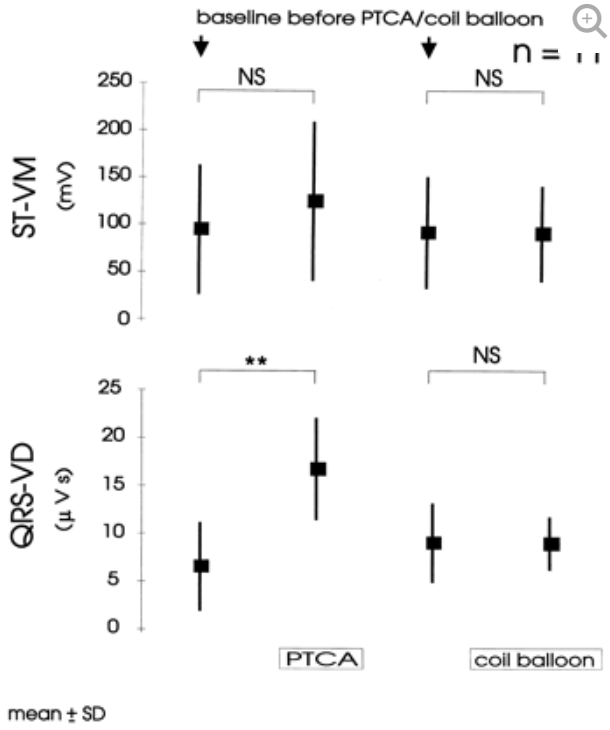

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Figure 5.

Vectorcardiographic changes were assessed as ST VM and QRS VD. The following four monitoring values are depicted: baseline values before angioplasty and before coil balloon inflation and values during angioplasty and coil balloon inflation. The baseline value was defined as the mean value over a 5-minute period before the procedure, and the value during the procedure was defined as the mean value over the entire inflation period. ***P*<.1.

Ventriculography. As summarized in Table 3⇓, during coil balloon deployment, ventricular function remained unchanged with respect to ejection fraction (baseline value during diagnostic procedure versus value during coil balloon inflation). Similarly, regional left ventricular wall motion in the targeted region seemed not to be affected by prolonged coil balloon deployment.

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Table 3.

Left Ventricular Parameters During Diagnostic Ventriculography and During Ventriculography With Simultaneous Coil-Balloon Inflation

	Diagnostic	**Coil Balloon**
Ejection fraction, % (n=10)	64±8	66±8
CI, L · min^{-1} · m^{-2} (n=10)	2.4±0.63	2.69±0.77

	Diagnostic	Coil Balloon
Regional wall motion according to treated vessel		
LAD (n=6)		
Anterobasal (NV, 14.5-22.8)	20.3±2.7	17.9±5
Anterolateral (NV, 7.4-13.2)	11.1±3.3	12.2±0.9
Apical (NV, 2.1-5.0)	3.6±1.3	4.8±1.5
LCx (n=2)		
Posterobasal (NV, 12.5-23.3)	9.9±1.6	9.4±1.5
Posteroapical (NV, 10.3-17.3)	10.5±1.4	12.2±7.1
Apical (NV, 2.1-5.0)	3.7±0.6	5.3±3.2
RCA (n=2)		
Posterobasal (NV, 12.5-23.3)	16.2±2.1	15.5±3.0
Posteroapical (NV, 10.3-17.3)	8.8±1.9	9.2±3.7

CI indicates cardiac index; NV, normal values.

CPK. No CPK rise was observed at 7±1 and 14±4 hours (71±10 and 40±16 IU/L [normal values up to 110 IU/L]), with the exception of one stented patient (CPK, 406 IU/L) at 7 hours after the procedure. In this patient, however, CPK-MB was <6% (6 IU/L), and CPK rise was attributed to soft-tissue compression secondary to the use of an external mechanical compression device for local hemostasis after sheath removal.

Coronary Hemodynamics

Coronary hemodynamic findings are reported with respect to the diameter of the device.

Mean pressure gradients across the device were 32±13 (n=12), 22±13 (n=4), and 4 (n=1) mm Hg for device sizes of 3.0, 3.5, and 4.0 mm, respectively. The influence of drug infusion flow (12 to 36 mL/h) on pressure gradient was negligible. Flow velocities and flow measurements are summarized in Table 4⇓.

Table 4.

Intracoronary Flow Velocities and Flow at Baseline and After Pharmacologically Induced Hyperemia Distal to the Inflated Coil Balloon

Coil Balloon Size, mm	Basal n	APV, cm/s	MPV, cm/s	Flow, mL/min	Hyperemic n	APV, cm/s	MPV, cm/s	Flow, mL/min	Ratio APV_h/A
3.0	12	27.5±19.8	44.7±29	36.9 ±26.9	11	43.3±33	64.1±44.6	59±44.9	1.6 ±0.4
3.5	4	21.9±6.7	39.4±9.8	70.5 ±34.6	4	39.5±11.6	61±21.6	135.7±68.1	2±1
4.0	1	13.1	25.9	22.7	1	35.9	64.2	62.2	2.7

APV indicates time-averaged peak velocity; MPV, maximal peak velocity; h, hyperemic; and b, basal.

Long-term Results

Clinical follow-up was available in all 22 patients. One 78-year-old asymptomatic patient with aortic stenosis (gradient, 50 mm Hg) and suffering from a reactivation of an ulcerative colitis died of sustained acute heart failure 52 days after the procedure after two blood transfusions.

At 7±1 months, no patient presented with a myocardial infarction or a revascularization of the treated segment. Of 21 eligible for follow-up, 4 (19%) were symptomatic. Two complained of atypical angina and 2 of stable effort angina, CCS stage 2.[36] Follow-up angiography was performed in 15 of 21 patients (71%) and included the 4 symptomatic patients. Of the 6 asymptomatic refusal patients, 3 had a thallium perfusion scintigraphy and 3 refused any further investigation.

Of the 4 symptomatic patients, the 2 suffering from stable effort angina presented with a progression of previously insignificant lesions. One of the 2 patients presenting with atypical angina had a negative exercise test and no significant lesions. The second presented with restenosis of a lesion dilated during the drug-delivery procedure but treated solely by conventional angioplasty.

The 3 asymptomatic patients who underwent a sesta-MIBI myocardial perfusion scintigraphy did not show any signs of redistribution, which presumably excluded a silent ischemia.

Postprocedure angiography (15 patients: coil balloon, n=12; coil balloon and stent, n=3) showed an MLD of 2.16±0.49 mm and at follow-up an MLD of 1.89±0.45 mm, corresponding to an absolute loss of 0.27±0.51 mm (Table 5⇓). If we compare the 12 lesions treated only with coil balloon and the 3 lesions also stented, MLD after the procedure was 2.01±0.39 versus 2.78±0.39 mm, and at follow-up, 1.83±0.41 versus 2.13±0.62 mm, corresponding to a loss of 0.18±0.43 versus 0.65±0.71 ±13% (range, 17% to 59%). One patient of 15 (7%) had a diameter stenosis >50%.

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Table 5.

Angiographic Data of the Patients With Angiographic Follow-up

Discussion

Acute Feasibility

The coil balloon (Dispatch) is a drug-delivery device combining infusion and perfusion characteristics. In all 22 patients, the wrapped coil balloon could be advanced and deployed at the angioplasty site and retrieved in the guiding catheter after deflation.

By design, the coil balloon is a nondilatational device and is not apt to develop a high mechanical force against the vessel wall (at nominal coil inflation pressure [6 atm], the pressure against the wall is <2 atm; Scimed data on file). However, it is able to exert a low uninterrupted pressure for a long time period because of its perfusion properties.

In our series, prolonged deployment (29±8 minutes; 30 minutes per protocol) of the coil balloon after angioplasty slightly increased the mean MLD (MLD, 1.98±0.41 versus 1.92±0.36 mm), and a case-by-case analysis showed an unchanged or improved MLD in 14 of 22 patients (64%) and deterioration in 8 of 22 (36%). No coronary spasms were observed after prolonged deployment.

Dissections not longer than the device (20 mm) were not substantially affected by local infusion of the heparinized solution (Fig 3⇑). In one patient with a type A dissection after PTCA, local infusion of heparin revealed a dissection flap (type B dissection), presumably by dissolving the mural thrombus and rendering the flap angiographically visible or worsening a mural dissection (length, 5.5 mm). Of the 3 patients with a dissection length greater than the device after balloon angioplasty, one patient (34 mm, type D dissection) developed an occlusive dissection (type F), necessitating a subsequent bailout stent implantation after two prolonged deployments of the coil balloon (first proximal, then distal). The potential hazard of worsening a preexisting dissection by fluid infusion has to be borne in mind when a dissection cannot be entirely covered by the device.

The driving mechanisms of drug solution transfer by the coil balloon are pressure and flow. Pressure in the drug compartment can theoretically be modified in two different manners: (1) by regulation of flow rate and (2) by variation of inflation pressure in the compliant polyolefin copolymer coils.[37] In our study, pressures inside the drug compartment did not vary significantly in respect to the infusion rate used (12 mL/h, 114±12 mm Hg [n=4]; 24 mL/h, 114±45 mm Hg [n=5]; and 36 mL/h, 127±66 mm Hg [n=13]). This may be due to infusion fluid leakage at the proximal and distal ends of the coil, maintaining infusion pressure within the above-mentioned limits, and provides the system by its design and 6-atm inflation pressure with an infusion pressure control. Variations of inflation pressure were not specifically studied because of the recommended nominal inflation pressure of 6 atm by the manufacturer. As used in this study, heparin was driven by low pressure (117±54 mm Hg=0.15±0.07 atm) and by flow (12 to 36 mL/h) at the site of delivery. A volume of 14.2±6 mL (corresponding to 140 to 2220 IU of heparin) was infused at the site of angioplasty.

Theoretical disadvantages related to the design of the device could be an uneven delivery of drug to the endothelial surface due to the contact of the spiral coil with the vessel wall and jet-stream lesions produced at the level of the infusion slits. At the infusion rates used, however, only weeping could be observed at the distal end of the coil balloon. In normal porcine coronary arteries, infusions of Evans blue dye using a coil-balloon catheter showed macroscopically a spiral-shaped distribution of the dye on the vessel surface. Histological examination revealed minimal endothelial damage, without jet-stream lesions.[38]

Signs of Ischemia

The perfusion properties of the coil balloon catheter were indirectly evaluated in the clinical setting by assessment of signs of myocardial ischemia. The subjective tolerance to prolonged deployment observed in these patients was encouraging. Hemodynamic parameters of relaxation and of diastolic function (T_1 and T_2, negative dP/dt, and EDP; Table 2⇑ and Fig 4⇑) did not reveal any significant changes during prolonged coil balloon deployment compared with respective baseline values. These variables were the most discriminatory hemodynamic parameters of ischemia, as demonstrated during conventional balloon inflation, confirming earlier reports.[25] Vectorcardiographic analysis did not show any significant changes during coil balloon deployment either. Even QRS VD, which is more sensitive than ST VM in detecting ischemia (Fig 5⇑),[27] did not change significantly from baseline. Ventriculographic analysis of regional wall motion during intracoronary deployment of the coil balloon (Table 3⇑) did not detect any significant changes compared with diagnostic ventriculography using the “regional contribution to ejection fraction” method.[25 39]

Limitations in Assessment of Signs of Ischemia

Sequence of procedures. A limitation in the methodological evaluation of signs of ischemia might be that conventional balloon inflation systematically preceded the coil balloon deployment and thereby enhanced collateral recruitment[40] and preconditioned the myocardium to ischemia.[41] Of the 22 patients, 8 (36%) had multiple conventional balloon inflations (range, 2 to 4) before coil balloon insertion. To avoid this potential bias, a randomized sequence of inflation might have been incorporated. However, the coil balloon cannot be used directly for angioplasty because by design, this balloon is not intended primarily for dilatations of stenotic lesions.

In a previous study evaluating the Stack perfusion balloon,[21] a final conventional balloon inflation was performed after perfusion balloon inflation, which was preceded by a conventional balloon inflation. In that study, although inflation time was 30% longer (107±55 versus 139±71 seconds) and pain score slightly lower (6.1±2.1 versus 5.2±3.1), ECG changes remained similar, indicating that the two preceding inflations (conventional balloon, 107±55 seconds and perfusion balloon, 513±333 seconds) did not alter objectively appreciable changes. These findings were consistent with previously reported data[42 43] in which occlusion pressure measured distal to the stenosis during balloon inflation did not change after serial occlusions.

The time elapsed between the last conventional balloon inflation and coil balloon deployment was 16±6 minutes. Since metabolic disturbances after conventional balloon inflations are reported to be short-lasting[44] and totally reversible within 5 minutes,[41] it might be inferred that complete recovery had been achieved in our patients, allowing a return to metabolic baseline before coil balloon deployment.

Left ventricular hemodynamics. The alteration of left ventricular relaxation reflects an asynchrony of contraction-relaxation of the left ventricle. These parameters are maximally altered within 15 seconds of ischemia,[25] and although they have a tendency to regress partially, synchrony remains altered throughout the entire duration of occlusion.[45] Therefore, the absence of abnormalities throughout the total duration of coil deployment is indicative of an adequate coronary perfusion.

Ventriculography. It could be argued that localized wall motion abnormalities were missed because a single projection (right anterior oblique 30°) was performed. This may be of particular concern for the territories supplied by the LCx and, to a lesser extent, for the RCA.[46] However, even the subanalysis of the 6 cases supplied by the LAD did not reveal any left ventricular wall motion abnormality during prolonged coil balloon deployment (Table 3⇑).

Perfusion Properties

Autoperfusion properties of the coil balloon catheter measured directly in vitro (38% glycerol at room temperature and 100 mm Hg continuous perfusion pressure) have indicated that flow is a function of device size (mean of 15 consecutive measurements: 54±3, 74±1, and 80±2 mL/min for the 3.0-, 3.5-, and 4.0-mm devices, respectively; data on file, Scimed). These data have been confirmed by our in vivo Doppler guide wire studies (Table 4⇑) evaluating the 3.0- and 3.5-mm devices (37±27 and 70±35 mL/min). For the 4.0-mm device, only one set of measurements in an RCA (segment 2) is available, precluding any conclusive statement. These autoperfusion properties were also confirmed by a preserved pharmacologically induced hyperemic response during intracoronary deployment of the coil balloon (Table 4⇑).

Previous data on the most extensively evaluated perfusion balloon (Stack perfusion catheter, Advanced Cardiovascular Systems) reported in vitro flows of 60 mL/min with glycerol 38% at room temperature and a continuous pressure gradient of 80 mm Hg, irrespective of the balloon inflation pressure.[47] With fresh human citrate blood (43.6% at 37°C), measured flow was 55 mL/min with a driving pressure of 80 mm Hg.[48] In the clinical setting, calculated flow was 55±23 mL/min (n=7), derived from flow-velocity measurements using a Doppler-tipped guide wire alongside the balloon and angiographic cross-sectional area.[49] Despite apparently similar perfusion data (coil balloon versus Stack balloon), inflation times longer than 20 minutes were rarely performed in evaluations of the Stack balloon.[21 50 51] Furthermore, Quigley et al[21] reported indirect signs of ischemia as assessed by ECG in more than 30% of patients before reaching the target inflation time of 10 minutes, and maximal chest pain score was more than half the value of that sustained with conventional balloon inflation (3.2±3.5 versus 6.1±2.1). These data suggest that the previously reported perfusion rates through the Stack perfusion catheter may have been overestimated.

Long-term Results

One asymptomatic patient with aortic stenosis died 52 days after PTCA of acute congestive heart failure after blood transfusions for active ulcerative colitis. Postmortem examination was not performed. Clinical outcome at 7±1 months of this first cohort of patients treated by local low-pressure heparin infusion after balloon angioplasty (4 of 21 patients treated with coil balloon followed by stent deployment) showed that 81% (17/21) of the patients were asymptomatic. In this cohort of 21 patients, no myocardial infarction or revascularization procedure occurred. Angiographic follow-up was obtained in 15 of 21 (71%) of the patients. Angiography did not show any aneurysmatic dilatation or an excessive restenosis rate of the site treated with the coil balloon. Restenosis rate, according to the categorical criterion diameter stenosis >50%, was 7% (1/15) at follow-up. The patient presenting an angiographic diameter stenosis of 59% on the proximal LAD was clinically asymptomatic, with a negative exercise test.

A cautious comparison to an angioplasty series with similar “vessel size” (reference diameter size at diagnostic angiography) shows an expected angiographic restenosis rate (% diameter stenosis >50%) at 6 months of 33.3% to 37.3% compared with 7% in our series.[52] The late loss observed in the comparative series for a reference diameter of 2.75±0.04 and 2.92±0.06 mm was far superior to that observed in this series (0.28±0.45 to 0.26±0.46 versus 0.18±0.43 mm) (Table 5⇑). This preliminary result has prompted us to undertake a multicenter open study to confirm whether this result can be achieved in a larger cohort of patients.

Conclusions

In conclusion, the coil balloon does not induce significant ischemia during prolonged intracoronary deployment by virtue of its perfusion properties. In situ infusion of high volumes of heparinized solution after balloon angioplasty is feasible. The use of the device seems, however, not recommendable in case of dissections longer than 20 mm because of the potential risk of aggravating dissections. Long-term effects of local heparin administration did not show any deterioration of the treated site. On the basis of these preliminary results, data collection in an open multicenter registry appears indicated.

Selected Abbreviations and Acronyms

CCS	=	Canadian Cardiovascular Society
CPK	=	creatine phosphokinase
EDP	=	left ventricular end-diastolic pressure
LAD	=	left anterior descending coronary artery
LCx	=	left circumflex artery
LVEDP	=	left ventricular end-diastolic pressure
LVP	=	left ventricular pressure
MLD	=	minimal luminal diameter
PTCA	=	percutaneous transluminal coronary angioplasty
QCA	=	quantitative coronary angiography
RCA	=	right coronary artery
VD	=	vector difference

VM	=	vector magnitude

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