

repeat-PCI (1% vs 2.7%, $p = 0.005$), need for urgent CABG (0.1% vs 1.3%, $p = 0.03$), seven months MACE (1% vs 3.1%, $p = 0.029$), seven months TVR (11% vs 19.9%, $p = 0.001$), combined MACE/TVR at seven months (14.9% vs 26.9%, $p = 0.001$) and death at seven months (1% vs 3.1%, $p = 0.029$).

Conclusion: Analysis of our large database of bifurcation lesions shows that provisional T stenting is the sole modifiable predictor associated with a reduction in target vessel revascularization as well as MACE and should be the preferred strategy for coronary bifurcation lesion PCI.

11:45 a.m.

878-6

Stenting Under Intravascular Ultrasound Guidance of Coronary Bifurcation Lesions With a New Device Allowing Provisional Side Branch Treatment

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Background: A new stent (MULTI-LINK FRONTIER) was developed for coronary bifurcation lesions. It is an 18 mm stent premounted on a delivery system with 2 balloons. The device is positioned by pushing it up to the carina of the bifurcation. Simultaneous inflation of the balloons deploys the main branch (MB) stent and opens up a portal to the side branch (SB). We studied intravascular ultrasound (IVUS) parameters and their relation to procedural success and 6-month outcome.

Methods: Patients with (un)stable angina pectoris and de novo or restenotic (no previous stent) bifurcation lesion between 2.5 and 4 mm in diameter for the main branch and >2.0 mm for the side branch were eligible. Exclusion criteria were angiographic severe calcification, thrombus or left main lesion. Pre-, post-, and at follow-up IVUS was performed in MB and SB using a 30 MHz catheter and automated pull-back.

Results: 18 patients were included: male 14, age 62 (13) year. The LAD/diag bifurcation was the target lesion in 17/18. After IVUS and mandatory predilatation stent implantation was successful in 16 (89%). Failure to wire the SB or to position the catheter in phase with the SB were the cause. Implantation at the carina succeeded in 12/16 (75%). The cases with "carina failure" had longer segments with calcified plaque proximal to the carina than cases with "carina success" (25 (14) vs 11 (11) mm; $P < 0.05$) as assessed by IVUS. The presence of calcium per se, or its circumferential angle or whether superficial or deep was not associated with carina failure. Carina failure resulted in (partial) overlap of the stent with the ostium of the SB in 75%. Carina failure or SB overlap was not associated with SB restenosis. MLA by IVUS pre-, post-, and at 6 months FU was 2.3 (1.2) mm², 7.3 (2.2) mm², and 4.2 (1.0) mm², resp. ($P < 0.05$). At FU there were no deaths or MIs. Target vessel revascularization occurred in 3 patients (16.6%). Angiographic restenosis (>50% DS) occurred in 18.8% in the Frontier stent MB and in 12.5% in the SB, overall 31.3%.

Conclusion: This bifurcation stent can be implanted in about 90% of lesions, with promising 6 months adverse event rate. Longer proximal calcified segment is associated with less favorable implantation results.

10:45 a.m.

	Baseline (post procedure)	Follow up (9 months)
RVD, mm	2.66±/0.57	2.62±/0.58
MLD, mm	2.07±/0.66	1.61±/0.98
DS, %	23.53±/10.5	38.4±/36.33
In-stent MLD, mm	1.99±/0.56	1.23±/0.76
In-stent DS, %	27.75±/8.48	51.66±/33.2
In-lesion late loss, mm		0.51±/0.99
Binary Restenosis, %		35

880-2

Randomized Comparison of Rotational Atherectomy and Cutting Balloon Angioplasty Followed by Radiation Therapy With a ¹⁸⁸Re-MAG₃-Filled Balloon in the Treatment of Diffuse In-Stent Restenosis

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Background: Randomized comparison of rotablation atherectomy (RA) and cutting balloon angioplasty (CB), followed by beta-radiation for in-stent restenosis (ISR) has not been reported.

Methods: This randomized controlled study was conducted to compare the efficacy of RA (n=58) with CB (n=55) prior to beta-radiation therapy with a rhenium-188-mercaptoacetyltriglycine (¹⁸⁸Re-MAG₃)-filled balloon for diffuse in-stent restenosis (ISR). The radiation dose was 18 Gy at a depth of 1.0 mm into the vessel wall.

Results: The baseline clinical and angiographic characteristics were similar between the 2 groups. The lesion length was 21.0±11.2 mm in the RA group and 20.8±10.2 mm in the CB group ($p=0.77$). Radiation was delivered successfully to all patients. Adverse events including myocardial infarction, death, or stent thrombosis did not occur during the 9-month follow-up period. Six months angiographic follow-up was obtained in 88 patients (78%) and the rates of angiographic restenosis was not statistically different between the RA group (13%, 6/46) and the CB group (12%, 5/42) ($p=0.87$). The risk of a target lesion revascularization or a major adverse cardiac event was similar between two groups (RA group vs CB group: 3.4% vs 3.6%, $p=0.94$) during 9-month follow-up period.

Conclusions: Concomitant treatment of RA or CB with beta-irradiation using a ¹⁸⁸Re-MAG₃-filled balloon for diffuse ISR was safe and had a similarly favorable angiographic and clinical outcomes.

MLD:minimal lumen diameter

	RA group	CB group	P value
Pre MLD (mm)	0.76±0.37	0.84±0.41	0.30
Post MLD (mm)	2.59±0.39	2.69±0.53	0.30
Follow-up MLD (mm)	2.01±0.66	2.22±0.68	0.15
Acute gain (mm)	1.79±0.54	1.85±0.60	0.58
Late loss (mm)	0.35±0.52	0.54±0.60	0.25
Loss index	0.19±0.36	0.29±0.36	0.34

11:00 a.m.

880

Intracoronary Brachytherapy

Wednesday, March 10, 2004, 10:30 a.m.-Noon
Morial Convention Center, Hall E-1

10:30 a.m.

880-1

Repeat Intracoronary Gamma Radiation for Patients With In-Stent Restenosis Who Failed Radiation Therapy: Results From the Re-WRIST Clinical Trial

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Background: Intracoronary radiation (IR) is an effective therapy for preventing the recurrence of in-stent restenosis (ISR). However, nearly 20% of patients enrolled in radiation studies required repeat revascularization to the irradiated site. Re-WRIST is a registry evaluating the safety and efficacy of retreatment with IR.

Methods: Thirty pts (31 lesions) with ISR at the previously irradiated segment and who failed a subsequent angioplasty without radiation were eligible for retreatment with IR. The Checkmate radiation system using Ir-192 seeds was used, and the repeat was prescribed dose was 15 Gy at 2 mm. The antiplatelet regimen post procedure was lifelong aspirin and at least 6 months of clopidogrel.

Results: Pts mean age was 65±7.9 yrs, 67% were males, 52% were diabetic, and 90% had CABG. Lesions were in native coronaries 67.7%, saphenous vein grafts 29.0%, and the left internal mammary 3.3%. Time between radiation treatments was 16.4±8.7 mos and the number of interventions to the target lesion was 5.2±3.5 (range 3-20). The lesion length was 21.74±14.25 mm. At 9 mos, the major adverse cardiac events rate was 36%, target lesion revascularization 32%, MI 0%, and deaths 4%. QCA at 9 months demonstrated a restenosis rate of 35%. There was one late total occlusion and no angiographic complications (evidence of aneurysm, fibrosis, perforation) in any of the pts.

Conclusions: Repeat radiation to the same site using Ir-192 for refractory ISR is safe and should be considered an option in this difficult patient subset.

880-3

Histopathological Characteristics of Edge Restenosis After Intracoronary Brachytherapy for In-Stent Restenosis

Masaharu Okada, Hideo Tamai, Eisho Kyo, Kunihiko Kosuga, Tatsuhiro Hata, Takuji Nakamura, Shinya Fujita, Takafumi Tsuji, Shinsaku Takeda, Nobutoyo Masunaga, Katsuyuki Hasegawa, Seichiro Motohara, Hiromu Uehata, Shiga Medical Center for Adults, Moriyama, Japan

Background: Histopathology of edge restenosis following intracoronary brachytherapy (BT) has not been fully evaluated in humans. The purpose of this study was to clarify the histopathological characteristics of edge restenosis following BT by examining the specimens obtained from directional coronary atherectomy (DCA). **Methods:** Eight edge restenosis lesions which developed in native coronary arteries after BT with the beta-emitting ³²P source wire were obtained by DCA and were compared with the restenosis lesion which developed after ordinary balloon angioplasty without BT (R, 6 lesions). Edge restenosis was defined as a lesion which developed 5 mm proximal or distal to either edge of ³²P source wire. Mean interval from BT to edge restenosis was 242±28 days. Specimens retrieved by DCA were immediately placed in 10% buffered formalin, processed for paraffin embedding and stained with hematoxylin and eosin. To assess the proliferation of myofibroblast, we categorized the severity as grade 0, 1, 2, and 3 by estimating the cell density and analyzed by Mann-Whitney U test. **Results:** 1) Invasion of inflammatory cells and evidence of vasculitis were not apparent in any of the edge restenosis lesions or R lesions. 2) In edge restenosis lesions, myofibroblasts were more scarce and active proliferating.

eration was less evident than R lesions (grade;1.13±0.35 vs 2.17±0.75; P<0.01). 3) In edge restenosis lesions, extracellular matrices were abundant, and they were composed of coarse collagen fiber and abundant mucinous materials. In contrast, the major component of extracellular matrices in the R lesions were finely fibrillar and dense collagen. 4) Thrombi were not apparent in any edge restenosis or R lesions. **Conclusions:** Edge restenosis following BT consisted of weak proliferation of myofibroblasts and abundant deposition of extracellular matrices such as mucinous materials. It was not accompanied by inflammatory reaction or thrombosis. Edge restenosis following BT may be a pathologically distinct entity.

11:15 a.m.

880-4 Intracoronary Brachytherapy Protects Bifurcation Lesions

Karsten Meyer, Ralf Koester, Jan Kaehler, Andreas Schuchert, Horst Thurmann, Manuel Todorovic, Winfried Alberti, Thomas Muenzel, Thomas Meinertz, Andreas Kruell, University of Hamburg, Hamburg, Germany

Background: Intracoronary brachytherapy frequently involves lesions from which side branches originate. These side branches often contain proximal plaques raising the question whether a bifurcation intervention is required. To date it is not clear whether plaque progression at the origin of the side branch is arrested by the brachytherapy of the main branch. In this study we analyzed the plaque progression in side branches of lesions treated with intracoronary brachytherapy.

Methods: One hundred and forty-six patients with in-stent-restenosis >70% in diameter were treated with PTCA followed by intracoronary brachytherapy. Brachytherapy was performed with the Betacath system (Novoste). Thirty-three patients had bifurcation lesions involving a side branch of 1.7±0.4 mm in diameter, originating from the irradiated portion of the LAD (n=20), LCX (n=5) or RCA (n=8). Five lesions in side branches were dilated during bifurcation interventions. Brachytherapy was performed with 18.5±1.5 Gy for 199±35 seconds within the main vessel but not in the side branch. The lumen diameter of the side branch was analyzed by quantitative coronary angiography (QCA) at the time of intervention and at follow-up at 8.6±3.5 months.

Results: There was one asymptomatic side branch occlusion due to the procedure. There were no in-hospital adverse events such as death, myocardial infarction or reintervention. QCA revealed a side branch minimal lumen diameter of 1.3±0.6 mm at the time of intervention and of 1.4±0.7 mm at follow-up corresponding to mean diameter stenoses of 25.2±22.9% and 24.7±23.1% (p>0.05). At follow-up none of the dilated side branch lesions had a binary diameter restenosis (>50%). There was no further side branch occlusion and no adverse clinical event related to the side branch lesion.

Conclusion: Intracoronary brachytherapy appears to have a protective effect on the progression of lesions in side branch origins even if brachytherapy is only performed in the main branch and not in the side branch.

11:30 a.m.

880-5 Optimizing Dosimetry With High Dose Intracoronary Gamma Radiation 21 Gy for Patients With Diffuse In-Stent Restenosis

Ron Waksman, Rebecca Torguson, Ellen Pinnow, Donna J. Whitman, Afework Gebreyesus, Rosanna Chan, Eduard Cheneau, Andrew E. Ajani, Michael Porrazzo, Lowell F. Satler, Augusto D. Pichard, Kenneth M. Kent, Joseph Lindsay, Washington Hospital Center, Washington, DC

Background: The efficacy of coronary gamma radiation in preventing recurrent in-stent restenosis (ISR) is established. Vascular brachytherapy (VBT) may be less effective with the approved dose of 14 Gy. Previously we reported a better outcome with 18 Gy. We sought to examine if escalation of the dose to 21 Gy is safe and improves efficacy.

Methods: 35 pts with diffuse ISR in native coronary arteries and saphenous vein grafts (lesion length 20-80mm) underwent PCI, atherectomy, and/or additional stents. Post-intervention pts were treated with gamma VBT using the Checkmate system (Cordis). A ribbon with 14-23 seeds was positioned to cover the treated segment and adequate margins, with a mean length of 63 ± 8mm. The prescribed dose was 21 Gy at 2mm. All pts were discharged with Clopidogrel for 12 mo. 6-mo clinical outcomes were compared to 120 pts treated with 14 Gy and 120 pts treated with 18 Gy, both groups treated with at least 6 mo of Clopidogrel.

Results: High dose of 21 Gy was associated with prolonged dwell time of 28.6 ± 2.9 min, but with absence of procedural or in-hospital complications, when compared with lower doses. At 6 mo there was significant reduction in the need for repeat target lesion revascularization in the pts treated with 21 Gy (Table)

Conclusions: High dose of 21 Gy for patients undergoing VBT with gamma radiation is associated with less recurrences compared to the approved radiation dose without increase of adverse events. Thus, optimization of the dose should be considered for pts undergoing VBT for ISR.

	14Gy 1M (N=120)	14Gy 6M (N=120)	18Gy 1M (N=120)	18Gy 6M (N=120)	21Gy 1M (N=31)	21Gy 6M (N=12)
Death, %	0	1.7	0	0	0	0
Q-Wave MI, %	0	0.8	0	0.9	0	0
TLR, %	0.8	20.8	2.5	16.5	0	8.3
TVR, %	16.7	25	4.6	22.9	0	25
Late Thrombosis	0.8	1.7	0.9	6.4	0	0

11:45 a.m.

880-6 Three-Year Follow-Up After Intracoronary Gamma Radiation for In-Stent Restenosis in Saphenous Vein Grafts

Seung-Woon Bha, Ron Waksman, Pramod K. Kuchulakanti, Andrew E. Ajani, Larry R. White, Daniel A. Canos, Edouard Cheneau, Verne Mattox, Maureen C. Abbott, Ellen Pinnow, Augusto D. Pichard, Lowell F. Satler, Kenneth M. Kent, Joseph Lindsay, Washington Hospital Center, Washington, DC

Background: The Washington Radiation for In-Stent Restenosis Trial in saphenous vein grafts (SVG WRIST) demonstrated safety and efficacy of intracoronary gamma radiation for the treatment of in-stent restenosis (ISR) in saphenous vein grafts (SVG) at 6 months. The aim of this study was to examine whether the results reported at 6 months continued to be durable at 36 months.

Methods: One hundred and twenty patients (pts) with ISR in SVG underwent PTCA, laser ablation, rotational atherectomy, and/or additional stenting (36% of lesions). Pts were randomized to either ¹⁹²Ir IRT or placebo, with a prescribed dose of 15 Gy or 18 Gy to a 2 mm radial distance from the center of the source. Pts were followed angiographically at 6 months and clinically up to 36 months.

Results: Angiographic restenosis (21 % vs. 44%, p=0.005) and target vessel revascularization [TVR, (18 % vs. 55%, p<0.001)] were dramatically reduced at 6 months in intracoronary radiation therapy (IRT) pts. At 12 months, IRT compared to placebo pts had less target lesion revascularization [TLR, (17% vs.57%, p<0.001)] and TVR (28% vs. 62%, p<0.001). At 36 months clinical follow-up, pts receiving IRT continued to have markedly lower MACE rates when compared with controls (Table).

Conclusions: In SVG WRIST, pts with ISR treated with IRT using ¹⁹²Ir had a marked reduction in the need for repeat target lesion and vessel revascularization at 6 months, with durability of the clinical benefit at three years.

Table. Twelve and 36-Month Clinical Outcomes

	12 Months (%)			36 Months (%)		
Events	Ir-192 (N=60)	Placebo (N=60)	P-Value	Ir-192 (N=60)	Placebo (N=60)	P-Value
Death	7	7	1.0	17	10	0.283
Q-wave MI	2	3	1.0	3	2	0.559
TVR	28	62	<0.001	47	65	0.043
TLR	17	57	<0.001	33	60	0.003
All MACE	23	57	<0.001	38	63	0.006