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**804 Angioplasty and Restenosis: Clinical**

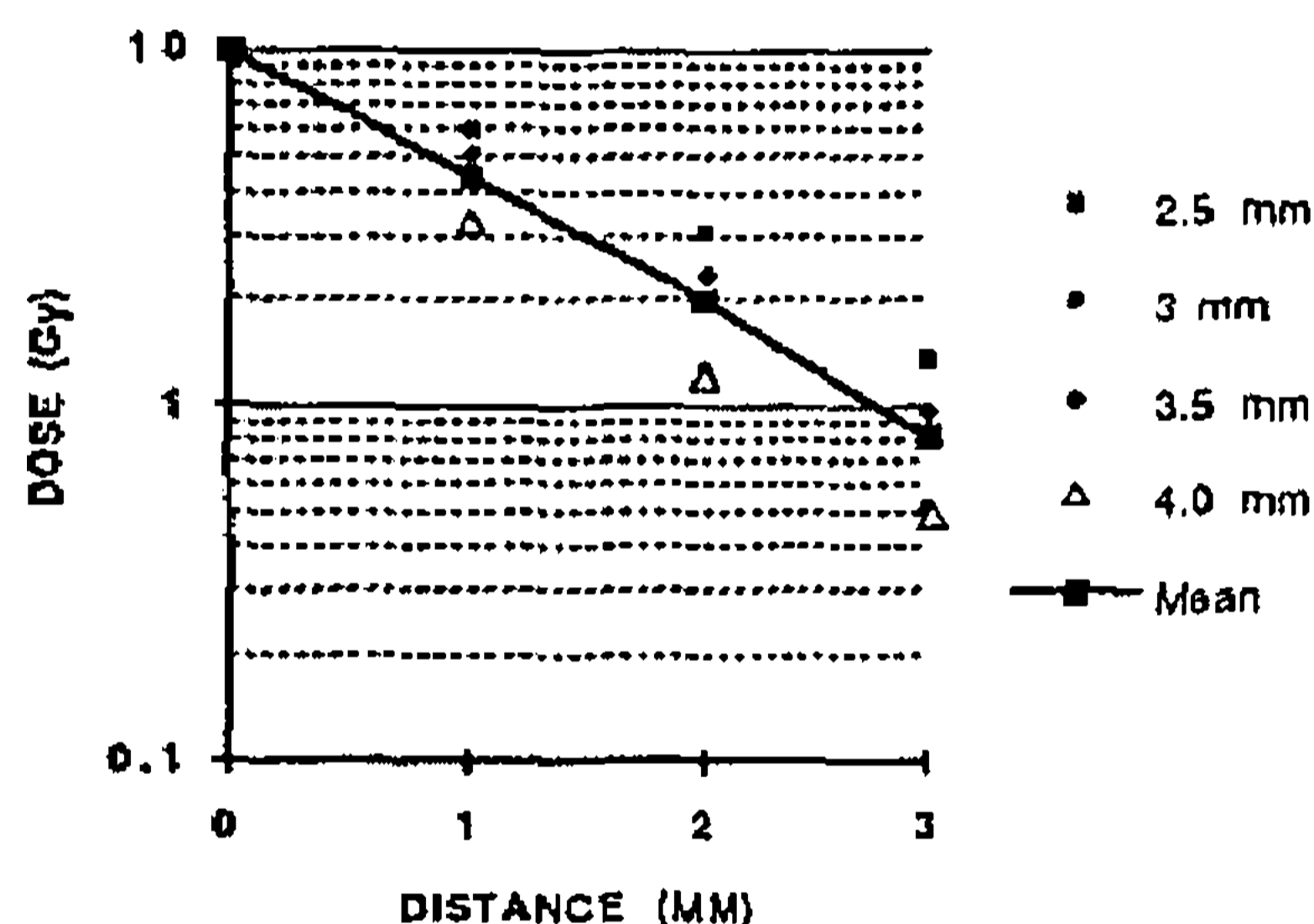
Wednesday, March 27, 1996, 4:00 p.m.-5:00 p.m.  
Orange County Convention Center, Room 209

4:00

**804-1 Yttrium-90, a New Beta Emitter for Prevention of Post Angioplasty Restenosis: Tissue Dosimetry and Importance of Intraarterial Centering**

Vitali Verin, Yuri Popowski, Philip Urban, Phillip Nouet, Michel Rouzaud, Michael Schwager, John M. Kurtz, Wilhelm Rutishauser. *University Hospital, Geneva, Switzerland*

Intraarterial irradiation reduces restenosis following experimental balloon angioplasty. Beta irradiation has the advantages of a markedly steeper dose decrease in tissue and less radioprotection problems, allowing its use in an ordinary catheterization laboratory. We developed a dedicated  $^{90}\text{Y}$  pure beta-emitting source, in the form of a flexible coil (diameter 0.014", length 22 mm) attached to the distal end of a 0.014" thrust wire. A segmented balloon consisting of four interconnected compartments (Schneider-Europe, AG) was developed to allow for intraarterial centering of the  $^{90}\text{Y}$  source. The tissue depth curve and dose variability on the surface of 1) conventional angioplasty balloons and 2) the centering balloon were studied using small thermoluminescent dosimeters. The tissue-depth dose curve for standard 2.5, 3, 3.5 and 4 mm balloons filled with contrast medium (Omnipaque 240) normalized to a surface dose of 10 Gy is presented in the figure. The standard deviations (percents of the mean) for the surface doses of 2.5, 3, 3.5, and 4 mm conventional PTCA balloons were 1.9 (13%), 5.5 (59%), 5.8 (73%), and 6.5 (110%) Gy, respectively. The mean, minimum and maximum doses on the surface of the 3.5 mm centering balloon were 8.4, 7.3, and 9.5 Gy (standard deviation 0.66 Gy, or 8% of the mean).



Conclusions: 1) The tissue dose distribution of  $^{90}\text{Y}$  is well suited to the purpose of selective irradiation of the coronary arterial wall (thickness 0.3-0.8 mm) for prevention of restenosis; 2) Homogeneous intramural dose delivery can be achieved with the help of a specially designed centering balloon.

4:15

**804-2 Imaging of Human Atherosclerotic Lesions With In-111 Z2D3 Antibody Specific for Proliferating Smooth Muscle Cells in Human Atheroma**

Pierluigi Pieri, Ignasi Carrió, Jagat Narula, Giovanni Moscatelli, Lourdes Prat, Luciano Pedrini, Vicens Rimbau, Chris Pak, Francis Chen, Ban-An Khaw. *Bufalini Hospital, Cesena, Italy; Hospital de Sant Pau, Barcelona, Spain; Scotgen, Menlo Park, CA; Northeastern University, Boston, MA*

Radiolabeled mouse/human chimeric antibody Z2D3 specific for an antigen on proliferating smooth muscle cells in human atheroma has been used to noninvasively visualize experimental atherosclerotic lesions in rabbits. Furthermore, negative-charge polymer-modification of Z2D3 allowed enhanced target visualization with very high specific radioactivity and reduced background activity.

To evaluate its usefulness, negative charge-modified Z2D3 F(ab')<sub>2</sub> was administered to 11 patients undergoing carotid endarterectomy. Each patient received 250  $\mu\text{g}$  of Z2D3 labeled with 5 mCi of In-111 i.v. Serial gamma images, blood and urine samples were obtained for 72 H following injection. Carotid endarterectomy was performed within 48 H after the last imaging session. The sites of stenosis seen arteriographically were compared to location of the most intense antibody uptake. Endarterectomy specimens were imaged ex-vivo and then characterized immunohistochemically.

The concentration of the antibody was seen in all patients in the region of the carotid plaques. Uptake was focal and was best seen at 4 H. Intensity of uptake decreased over time. Whole body scans demonstrated localization in the kidneys, liver, and bone marrow which remained essentially unchanged.

No adverse reactions to the antibody were observed. Immunohistochemistry of endarterectomy specimens demonstrated specific localization of Z2D3 in the region of proliferating smooth muscle cells in the intima of the lesion.

The present study demonstrated the feasibility of noninvasive visualization of human atherosclerotic lesions. Further studies will be needed to optimize the imaging technique for potential clinical applications.

4:30

**804-3 What Causes Focal Restenosis at the Margins of Palmaz-Schatz Stents? A Serial Intravascular Ultrasound Study**

Rainer Hoffman, Gary S. Mintz, Jeffrey J. Popma, Augusto D. Pichard, Lowell F. Satler, Kenneth M. Kent, Jennifer Griffin, Theresa Bucher, Rolf Fuessl, Mary K. Kehoe, Donna Hunn, Debra Deforty, Martin B. Leon. *Washington Hospital Center, Washington, DC*

To understand the mechanism of restenosis at the margins of Palmaz-Schatz stents, we compared serial intravascular ultrasound (IVUS) studies post stent implantation and follow-up ( $5.4 \pm 3.8$  months) in 88 lesions and analyzed reference {Ref: arterial, lumen, and plaque areas (in  $\text{mm}^2$ ); plaque burden (plaque/arterial area); remodeling ( $\Delta$  arterial area); tissue growth ( $\Delta$  plaque area); and dissections} and stent margin {stent and intimal hyperplasia (IH) areas}. 29 lesions had focal restenosis involving one or both margins.

	Restenosis	No Restenosis	p
Post-stent Ref arterial area	15.8 $\pm$ 3.8	18.6 $\pm$ 7.5	0.1097
lumen area	8.5 $\pm$ 3.4	10.8 $\pm$ 5.3	0.0686
plaque burden	48 $\pm$ 13	43 $\pm$ 12	0.0868
Ref remodeling	2.2 $\pm$ 1.8	1.2 $\pm$ 2.4	0.0692
Stent area	8.7 $\pm$ 3.6	10.4 $\pm$ 4.4	0.0607
IH area within stent	5.0 $\pm$ 2.7	2.1 $\pm$ 1.8	< 0.0001

Stent margin dissections were uncommon (4/88). There was no significant tissue growth ( $\Delta$  plaque area) at the Ref sites or recoil ( $\Delta$  stent area) of the stent margins. We conclude: Restenosis at the stent margin is common (33%) and is associated with implanting the edge of the stent within smaller, more diseased Ref vessels (smaller arterial, lumen, and stent areas; greater plaque burden). Superimposed Ref segment remodeling and neointimal tissue accumulation within smaller stent margins results in restenosis. These findings underlie the importance of anchoring edges of Palmaz-Schatz stents into healthy vessels with large lumens; this may require more extensive stenting to cover moderate proximal or distal stenoses.

4:45

**804-4 An Open Multicenter Registry to Evaluate Local Heparin Delivery Following Balloon Angioplasty for the Prevention of Restenosis: Preliminary Results**

Edoardo Camenzind, Victor Legrand, Mathias Vrolix, Claude Hanet, William Wijns, Christophe Bauters, Wim Aengevaeren, Peter den Heijer, Tony Gershlick, Eline Montauban van Swijndregt, Peter van der Meer, Rein Melkert, Patrick Serruys, on behalf of the DISPATCH Investigators. *Thoraxcenter, Erasmus University, Rotterdam, The Netherlands*

Although heparin has been shown effective to prevent restenosis in animal studies, previous clinical studies have failed to show any efficacy after systemic administration.

Local, intracoronary heparin delivery (Dispatch™ Scimed; 1783  $\pm$  185 IU during 30  $\pm$  3 min) was successfully performed in 117 patients (79 men, 62  $\pm$  10 years) following balloon angioplasty. No acute cardiac event were observed during hospital stay. Meanwhile 43 patients (32 men, 58  $\pm$  9 years) have been reviewed clinically and angiographically for 6 month follow-up: 10 patients were symptomatic (3 unstable and 7 stable angina). Angiography showed in 10/43 (23%) restenosis (diameter stenosis > 50%). No aneurysmatic dilatation at the site of heparin delivery was observed. MLD measured by quantitative analysis system (CAAS II) in matched projections changed from 1.15  $\pm$  0.36 mm (pre) through 2.03  $\pm$  0.44 mm (post) to 1.75  $\pm$  0.62 mm (at 6 month follow-up).

	Local heparin	Matched group*	p-value
Acute gain (mm)	0.90 $\pm$ 0.46	0.90 $\pm$ 0.46	NS
Late loss (mm)	0.28 $\pm$ 0.58	0.45 $\pm$ 0.58	<0.05

\*matched for vessel size, acute gain and lesion location

Nine patients (21%) required a re-PTCA and 1 patient required surgery (2%) of the treated segment. No myocardial infarction and no death were observed.

Conclusion: Local heparin delivery following balloon angioplasty by means of the coil-balloon may reduce on longterm the incidence of restenosis and decrease the need for re-vascularization.