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International Journal of Cardiology 107 (2006) 247 – 253

International Journal of Cardiology

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Determinants of model of renarrowing after beta radiation for in-stent restenosis☆

Adam Witkowski[a,*], Zbigniew Chmielak[a], Łukasz Kalińczuk[a], Jerzy Pręgowski[a], Cezary Kępka[a], Mariusz Kruk[a], Jakub Przyłuski[a], Jarosław Łyczek[b], Wojciech Bulski[b], Maria Kawczyńska[b], Anna Kulik[b], Jacek Owczarczyk[c], Witold Rużyłło[a]

[a]*Haemodynamics Department, Institute of Cardiology, 42 Alpejska St., 04-628, Warsaw, Poland*
[b]*Maria Skłodowska-Curie Memorial Cancer Center, Warsaw, Poland*
[c]*Compart Medical Systems Ltd., Warsaw, Poland*

Received 4 January 2005; received in revised form 5 March 2005; accepted 12 March 2005
Available online 13 May 2005

Abstract

It is unknown whether model of renarrowing after β-radiation for in-stent restenosis (ISR) is influenced by the type of geographic miss (GM).

Methods: In 166 ISR treated with Galileo, serial quantitative coronary angiographic analysis was done. Minimal lumen diameters and lengths were measured for (1) stent, (2) peri-stent subsegments subjected to angioplasty with/without irradiation, and (3) irradiation margins. GM was defined as: (Type 1) edge injury within the ^{32}P source *dose fall-off*: 2.0 mm inside and outside the source end marker or (Type 2) overt, nonirradiated injury: beyond the outer 2.0-mm long *dose fall-off* zone.

Results: Restenosis rate was 28.3% at 8.9±4.5 months with 60% located exclusively outside the stent. Type 1 GM was present in 24.7% of proximal edges, whereas Type 2 in 18.1%. Respective percentages for distal edges were 23.5% and 15.7%. Regardless of presence and type of GM, significant late lumen loss occurred only outside the stent. However, the biggest late lumen loss at the proximal edge was induced by the Type 1 GM (0.65±0.79, $p<0.001$), while proximal Type 2 GM was not associated with edge renarrowing (−0.04±0.48, p=NS). Both reference lumen diameter and proximal Type 1 GM influenced restenosis independently (OR 0.47; 95%CI 0.24–0.90; $p=0.023$ and OR 2.46; 95%CI 1.12–5.40; $p=0.025$).

Conclusions: Regardless of presence and type of geographic miss, late lumen loss after β-radiation occurs only outside the stent. However, injury within the proximal ^{32}P *dose fall-off* but not overt edge injury is associated with the biggest late lumen loss at the respective edge, triggering recurrent restenosis.

Keywords: Renarrowing; Beta radiation; Restenosis

1. Introduction

Recent reports on the long-term efficacy of drug-eluting stents for treatment of either de novo or in-stent restenosis (ISR) lesions in the 'real life' setting, imply complementary to the newest therapeutic advance and novel applications of vascular brachytherapy [1–4]. The issue of late consequences of presence and type of periprocedural 'geographic miss' phenomenon (GM) after β vascular brachytherapy is still unclear [5]. Therefore, repeated and renewed look at the phenomenon of GM and its impact on occurrence and model of recurrent renarrowing after vascular brachytherapy for ISR treatment is justified. Two types of GM: (1) overt injury within the nonirradiated margin versus (2) edge injury localized within the *dose fall-off* of ^{32}P source, were compared by means of their impact on the overall and edge restenosis after ISR treatment with the Galileo system.

☆ Source of support: State Committee for Scientific Research. Grant NR: 4 P05C 057 15.

* Corresponding author. Tel.: +48 22 812 41 64; fax: +48 22 812 13 46; +48 27 226 45 06.
E-mail address: witkowski@hbz.pl (A. Witkowski).

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doi:10.1016/j.ijcard.2005.03.029

2. Methods

2.1. Study design and population

The study population consisted of 148 consecutive patients (166 ISR lesions) successfully treated with β vascular brachytherapy and with late angiographic follow-up. These patients are part of the prospective registry (198 pts) of irradiation procedures performed in our center between March 2001 and December 2003. Primary end points were defined as binary angiographic restenosis within (1) analyzed segment (the overall restenosis), (2) restenosis located exclusively outside the stented segment (the outer-stent restenosis) and (3) restenosis of either the proximal or distal edge of analyzed segment (edge restenosis). The local council on human research approved the study protocol and patients signed informed consent.

3. Irradiation procedure

Vascular brachytherapy was performed with the Guidant Galileo™ System that uses a ^{32}P beta—radioactive source within a centering balloon catheter enabling accurate positioning of the source in the artery [6]. Initially the fixed length of ^{32}P source was used; encapsulated in the distal 27 mm of nitinol wire that was delivered into the centering balloon of respective length. Then, the system was equipped with the 'stepping source' device, featured by automatic source delivery mechanism for perfectly matched reposition of ^{32}P emitter—allowing precise and uniform dosing during the VBT treatment of long lesions [7–9]. Relocation of the ^{32}P emitter was performed at 20-mm long steps; from the most distal to the most proximal site of either the 32-mm (2 steps) or 52-mm long (3 steps) centering balloons.

After successful (residual stenosis <30%) plain balloon angioplasty, dose of 20 Gy was prescribed at 1 mm beyond

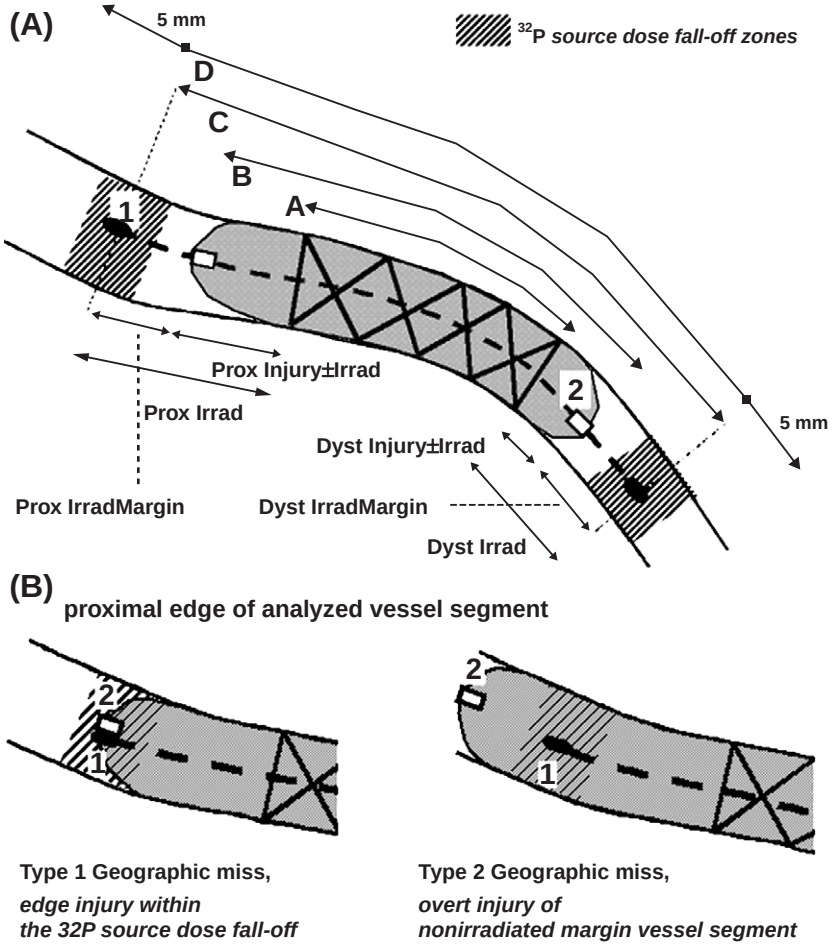

Fig. 1. (A) Serial, quantitative angiographic measurements included lengths of the stented (A), injured (B), irradiated (C) and analyzed (D) segments. Moreover, length and minimal lumen diameter were measured for proximal and distal peri-stent subsegments; subjected to angioplasty with/without irradiation (Injury ± Irrad) and subjected to irradiation but without angioplasty injury—irradiation margins (IrradMargin). Serial measurements of minimal lumen diameter were done at five vessel locations within lengths of stented and distinguished vessel subsegments. Digits: 1—proximal marker of ^{32}P source and 2—distal marker of angioplasty balloon. (B) Shows diagrams of proximal: Type 1 Geographic Miss (GM); defined as presence of edge injury within the proximal ^{32}P *dose fall-off* and Type 2 GM; defined as overt—beyond the outer 2.0-mm of proximal *dose fall-off* zone, injury of non-irradiated margin of analyzed vessel segment.