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53 **Evaluation of a Novel Slow-Release Paclitaxel-Eluting Stent with a Bioabsorbable Polymeric Surface Coating**

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54 **Initial Assessment of a Novel Radioactive Tin-117m Stent in Porcine Coronary Arteries**

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55 **New Cobalt-Chromium Ultra-Thin Strut Stent: Feasibility, Vascular Compatibility, and Safety Evaluation in Porcine Coronary Arteries**

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Histologic Evaluation of a Novel Fully Biodegradable Salicylate-Based Sirolimus-Eluting Stent

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Background: The concept of fully biodegradable stents has emerged as an attractive alternative to current permanent metalplic stents. We sought to evaluate a novel, fully biodegradable sirolimus-eluting stent (SES) synthesized entirely from salicylate-based polymer, in a clinically relevant animal model.

Methods: Fully biodegradable balloon-expandable stents (n=32) were implanted in pig coronary arteries using quantitative coronary angiography (QCA) and intravascular ultrasound (IVUS) to optimize stent apposition. Dose density of sirolimus was 8.3 μg/mm of stent length with *in-vitro* studies demonstrating elution over 30 days and complete stent degradation in 9-12 months. Animals were terminated at 7, 14, 30, 90, and 180 days for complete histopathologic and histomorphometric analyses.

Results: All stents were deployed successfully without notable mechanical difficulties. At 7 days, stents had thin mural thrombus coverage with scattered leukocyte infiltration. At 14 days, early thrombus organization including invasion with round, spindle-shaped, and stellate cells was seen along with collagen deposition; endothelialization was nearly complete and there was a mild inflammatory reaction. At 30 days, the neointima was increased in size (0.26±0.14mm) and showed a well-healed fibrocellular composition with only minimal residual thrombus components; inflammation was mild to moderate and mostly in the form of multinucleated foreign-body giant cells. At 90 days, healing had progressed so that only rare intramural thrombus was seen, and endothelialization was complete; intimal thickness was 0.4±0.17mm**.** The stent appeared at this time to have undergone considerable absorption mostly in the form of surface erosion, with some cellular infiltration into the stent space. At 180 days, arterial wall incorporation of the absorbable stent involved a highly organized and stable fibrocellular neointima with thickness of 0.31±0.10mm. There was no evidence of any residual thrombus, fibrinoid deposits, or hemorrhage. Inflammatory reaction was minimal and stable, being almost entirely of giant cells. The appearance of the stent profiles suggested further erosion and cellular infiltration compared to 90 days.

Conclusions: This study shows favorable vascular compatibility for a novel fully biodegradable salicylate-based SES. Serial temporal histologic analysis revealed a consistent, gradual process of absorbable vascular prosthesis incorporation into arterial wall tissue, with stable healing and endothelialization.

Evaluation of a Novel Slow-Release Paclitaxel-Eluting Stent with a Bioabsorbable Polymeric Surface Coating

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Objectives: To evaluate a new second-generation drug-eluting stent (DES) comprising a slow-release biodegradable PLGA polymer (polylactide/polyglycolide) and low-dose paclitaxel on a thin-strut cobalt chromium stent platform, in a clinically relevant animal model.

Background: Our previous work demonstrated sub-acute vascular toxicity and necrosis triggering late excess neointima in pig coronaries, with a moderate paclitaxel dose eluted from an erodible polymer. The use of slower-releasing absorbable polymers with lower doses of paclitaxel is expected to minimize such adverse outcomes.

Methods: Three types of stents were implanted in pig coronary arteries using QCA to optimize stent apposition: Bare metal stents (BMS); absorbable, slow-release polymer-coated-only stents (POLY); and absorbable polymer-based paclitaxel-eluting stents (PACL). The dose density of paclitaxel was 0.15 μg/mm² with *in-vitro* studies demonstrating a gradual elution over 12-16 weeks. Animals underwent angiographic restudy and were terminated at one and three months for complete histopathologic and histomorphometric analyses.

Results: At one month, intimal thickness varied significantly according to stent type with the lowest level for the PACL group compared to BMS and POLY (0.06mm±0.02 vs. 0.17mm±0.07, 0.17mm±0.08, respectively, $P<0.001$); histological % area stenosis was 18%±4 for PACL compared to 27%±7 for BMS and 30%±12 for POLY, respectively ($P=0.001$). At three months, PACL showed similar neointimal thickness as BMS and POLY (0.09mm±0.05 vs. 0.13mm±0.10 and 0.11mm±0.03 respectively, $P=0.582$). Histological % area stenosis was 23%±8 for PACL vs. 23%±11 for BMS and 23%±2 for POLY, respectively ($P=1.000$).

Conclusions: This study shows favorable vascular compatibility and efficacy for a novel DES eluting paclitaxel, in porcine coronary arteries. These results support the notion that slowing the release rate and lowering the dose of paclitaxel favorably influences the vascular biological response to DES implant, decreasing early toxicity and promoting stable healing while still suppressing neointima formation.

Initial Assessment of a Novel Radioactive Tin-117m Stent in Porcine Coronary Arteries

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Background: Tin-117m (^{117m}Sn) is a novel conversion electron emitting radioisotope that deposits intense energy in a very short range. It can deliver high doses of radiotherapy to a target while minimizing collateral damage to adjacent normal tissue, and has been used clinically in the management of bone pain associated with osteosarcoma. There are several potential cardiovascular applications of ^{117m}Sn, one being an electroplating on stents; since the coronary media is 0.2-0.3mm thick, no adjacent tissue exposure would result.

Objective: To assess the feasibility and coronary artery effects of an ^{117m}Sn-electroplated stent in a clinically relevant animal model.

Methods: 72 stents of 3 types were implanted in pig coronaries: Bare metal stents (BMS, n=14), Tin-only sham electroplated stents (Tin-only, n=15), and three incremental doses of radioactive ^{117m}Sn electroplated stents (Low 30μCi, n=14; Medium 60μCi, n=14; and High 150μCi, n=15). Pigs were terminated at one month for complete histological analysis.

Results: Intimal thickness varied according to stent type with highest level for the Low, Medium and High radioactive stents compared to BMS and Tin-only (0.43±0.06mm, 0.41±0.06mm, and 0.47±0.07mm, vs. 0.17±0.02mm, and 0.26±0.03mm, respectively, $P<0.001$). % area stenosis was higher for radioactive stents compared to BMS and Tin-only (51±6%, 51±4%, and 55±5%, vs. 27±2% and 35±3%, respectively, $P<0.001$).There was consistently a distinct, discrete, dense collagenous ring of tissue which included a densely cellular outer rim, in the perivascular space at the outer adventitial border ~0.2-0.3mm radially outward from ^{117m}Sn stents. This appears to reflect a unique biological effect or 'signature' of this radioisotope in this application.

Conclusions: This study showed that novel radioactive ^{117m}Sn stents were compatible with porcine coronary artery implant. Although these devices exacerbated rather than inhibited in-stent neointima formation, unique histological effects were observed that support further investigation of ^{117m}Sn effects in the circulatory system to understand the interaction of this unique conversion electron energy with the vascular tissue.

ew Cobalt-Chromium Ultra-Thin Strut Stent: Feasibility, Vascular Compatibility and Safety Evaluation in Porcine Coronary Arteries

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Background: Stent-strut thickness is related to in-stent restenosis. Therefore, modern bare-metal stents (BMS) with lower strut thickness are in development. We sought to evaluate a new 'third-generation' BMS comprising an ultra-thin-strut, cobalt-chromium platform with fixed geometry and uniform cell sizes, in a clinically relevant animal model.
Methods: 36 BMS of two types were implanted in pig coronaries using quantitative coronary angiography (QCA) to optimize stent apposition: a commercially available cobalt alloy thin-strut stent (91μm) as control (n=18), and an ultra-thin-strut (65μm) cobalt-chromium stent (Protea CoCr; n=18). Animals underwent angiographic restudy and termination 1-wk and 1-mo post-implant for coronary artery histology. In addition, 12 overlapping Protea CoCr stents were analyzed at 1-mo.
Results: All stents deployed without difficulties. Thin neointima and mild inflammation was seen in both groups at 1-wk. For 1-mo, QCA % diameter stenosis was significantly less for Protea CoCr (2±5% vs. 17±16%, p=0.032). By histomorphometry, intima thickness (0.11±0.05mm vs. 0.23±0.11mm, p=0.003) and % area stenosis (19±1% vs. 32±11%, respectively, p=0.004) were also significantly lower for Protea CoCr. The strut injury score was low and similar between the two groups. QCA % stenosis; intima thickness; and % area stenosis of overlapping Protea CoCr were 3±3%, 0.13±0.02mm, and 22±4%, respectively. Stable fibrocellular neointimal incorporation of all stents including overlapped Protea CoCr, with complete endothelialization and minimal inflammation, was seen at one month.
Conclusions: Protea CoCr showed favorable arterial response with significant reduction of neointima formation compared to a commercial cobalt alloy BMS, one month post implant in pig coronary arteries. This ultra-thin-strut stent platform therefore appears to be a suitable and attractive alternative to current BMS. Combining the lower levels of neointima formation, fixed geometry, and uniform cell size, the Protea CoCr may be a preferred platform for next-generation drug-eluting stents.