OTHER

CRT-605

Multimodality Imaging Demonstrating Liposomes Preferentially Home to Regions of Myocardial Injury

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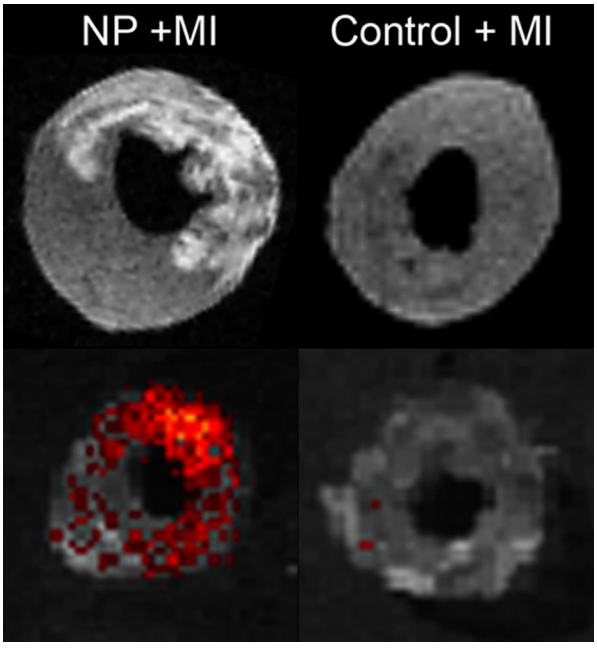
INTRODUCTION Nanoparticles may serve as a promising means to deliver novel therapeutics to the myocardium following myocardial infarction. We assessed whether lipid-based liposomal nanoparticles specifically target injured myocardium following intravenous injection.

METHODS CD1 male mice that underwent LAD ligation surgery with 45 minutes of ischemia followed by reperfusion (I/R) and then received tail-vein injection 24 hours following surgery with either Gd-DTPA labeled, fluorescent NBD-labeled liposomes (n=7) or a saline vehicle control (n=7). The hearts were harvested 24 hours later and underwent T1 and T2-weighted ex vivo MR imaging using a 7 Tesla Bruker magnet. The hearts were the sectioned for immunohistochemistry and also optical fluorescent imaging using an IVIS imaging system.

RESULTS The mean size of the liposomes was 100 nm by dynamic light scattering. T1-weighted imaging demonstrated a significant increase in signal intensity in the LAD territory vs the posterior wall with liposomes compared with control (41 ±10% vs 9± 2%, p=0.009). Optical imaging demonstrated significant increase in the LAD territory vs the posterior wall for animals that received liposomes compared with those that received control (163±31% vs 13±14%, p=0.001). The Figure shows T1-weighted MR images and optical images below. Fluorescent microscopy demonstrated the presence of green fluorescence consistent with NBD-labeled liposomes within the infarct area of hearts from mice that received liposomes while there was no green fluorescence in the hearts of mice that received injection of saline control.

CONCLUSIONS Following a murine model of MI, liposomes traffic to the heart and preferentially home to regions of myocardial injury. These liposomes can be loaded with therapeutic agents to deliver novel agents directly to regions of myocardial injury.



TECHNOLOGY

BIODEGRADABLE POLYMERS

CRT-700

Endovascular AAA Bioabsorbable Graft–A Pilot Study Demonstrating A Confluent Endothelium And Neotissue Formation In Swine

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BACKGROUND A confluent endothelium is needed to reduce thrombosis in vascular grafts, including EVAR stent-grafts. A pilot study was designed to assess the tissue formation and cellular response to an endovascular stent-graft containing a bioabsorbable graft material designed to treat aneurysms through endovascular tissue regeneration. The objective of the study was to determine the in vivo response of the graft material in an AAA model.

METHODS A peritoneal patch was used to form an AAA in swine for 2 weeks then treated with the bioabsorbable stent-graft (n=7). The stent-graft consisted of a synthetic polymer graft material sutured to a stent (Megalink, Guidant, USA). The stent-graft was delivered endovascularly using an 11F sheath with a dilation catheter (Powerflex P3, Cordis, USA). After treatment for 28 days, the animals were sacrificed and the tissue was examined through both gross and microscopic histology to determine the presence of endothelial cells (CD-31 antibody), smooth muscle cells (SM a-actin antibody), collagen (Masson's Trichrome) and any adverse tissue responses (H&E). Physical attachment of the graft to the vessel and gross appearance of the lumen surface were also noted.

RESULTS The stent-grafts placed endovascularly demonstrated no evidence of blood flow into the aneurysmal sac upon deployment, based on angiography and ultrasound imaging. During the course of the study, no endoleaks were observed in the treated animals. Upon gross examination after sacrifice at 28 days, the graft material appeared well adhered to the aorta with a shiny, white appearance on the lumen surface. No evidence of thrombi was noted. The graft demonstrated a confluent endothelial lining as evidenced by histologic staining for CD-31 antibody which positively stained a single layer of cells on the lumen surface. The new endothelium was supported by a thin neointima consisting of collagen. In addition, the SM a-actin antibody stain indicated the presence of smooth muscle cells on the abluminal portion of the graft with cells penetrating the porous graft material. No significant adverse tissue response was noted. The graft material was integrated with the vessel wall and grossly intact without any defects or degradation.

CONCLUSIONS A stent-graft containing a bioabsorbable graft material was successfully deployed endovascularly in a surgical swine model. The results of our pilot study suggest that aneurysms may be treated using an appropriate bioabsorbable material for endovascular tissue regeneration.

BIODEGRADABLE SCAFFOLDS

CRT-701

Clinical Outcomes Of Overlapping Absorb BVS For The Treatment Of Long Coronary Lesions: Data From The Italian RAI Multicenter Registry

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AIMS BMS and DES overlap is associated with impaired clinical outcomes at long-term follow-up, whereas data on the impact of overlap with overlapping everolimus-eluting bioresorbable vascular scaffold (Absorb BVS) are scant. We report the procedural and mid-term clinical outcomes in a cohort of patients having at least one vessel treated with ≥2 overlapped Absorb BVS.

METHODS AND RESULTS Patients included in a multicenter registry at 5 centers in Italy were systematically followed for major adverse cardiac events (MACE). Clinical data were obtained for 92 patients (mean age 57.1 years, 74.0% males) with a total of 95 lesions treated with overlapping Absorb BVS. Fifty-seven (61.9%) patients underwent scaffold implantation due to acute coronary syndrome. Diabetic patients were 17.3%. Multivessel disease was present in 63.0% of patients. Treated lesions were type B1 (21.3%), type B2 (23.0%), and type C (55.7%). Mean length covered by overlapping BVS was 48.0 ±16 mm. The mean number of implanted Absorb BVS was 2.25 scaffolds per lesion and 2.63 scaffolds per patient. Angiographic and procedural success occurred in all patients. At a median follow up of 10 months (interquartile range, 5-14.75 months), cumulative occurrence of MACE was 4.34%. Adverse events were: 1 possible late scaffold thrombosis (unexplained cardiac death occurring two months after elective revascularization), 2 TLR due to BVS restenosis (documented BVS recoil in 1 case), 1 TVR due to restenosis of drug eluting stent proximal to two overlapped scaffolds.

CONCLUSIONS Our findings suggest that treatment of long lesions by means of overlapped Absorb BVS appears to be safe at mid-term follow up.

DRUG ELUTING STENTS

CRT-702

Composite Outcomes In 2.25-mm Drug Eluting Stents: A Meta-analysis And Systematic Review

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BACKGROUND Percutaneous coronary intervention (PCI) of small vessels is associated with a high restenosis rate. Drug-eluting stents (DES) reduce restenosis in coronary arteries, but the role of DES in small coronary vessels has not been well defined. In our systematic review, we aim to summarize all known angiographic and clinical outcome of 2.25-mm DES, to highlight the need for specific outcome data in this cohort.

METHODS A systematic literature search of 394 relevant citations from PubMed, EMBASE, Web of Science and the Cochrane Central Register of Controlled Trials yielded 8 eligible studies studying FDA approved 2.25-mm DES. Angiographic and clinical outcome data were extracted and compared between each type of DES. Subgroup analysis comparing clinical outcome between sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) was done using a random effects model.

RESULTS Of the 8 studies included in the analysis, 6 were non-randomized and 2 were randomized against bare-metal stents (BMS). A total of 1,037 patients were studied, with follow-up ranging from 1 month to 5 years. PES, SES and everolimus-eluting stents (EES) were studied. Myocardial infarction at one year was highest in PES vs. SES and EES: 4.2% vs. 3.4% and 1.5%. Target vessel revascularization at one year was highest in PES vs. SES and EES: 13.8% vs. 5.7% and 8.8%. Death rate was highest in PES at 4.2% vs. SES and EES (3.4% and 1.5%). Mean late lumen loss for PES, SES, and EES was 0.28±0.11 mm, 0.15±0.11 mm, and 0.16±0.41 mm at 9 months to 1 year. Mean diameter stenosis for PES, SES and EES was 34.7±4.2%, 29.5±6.2%, and 20.9±22.5%. Mean binary stenosis for PES, SES and EES was 26.9±7.8%, 10.4±6.7%, and 9.6% respectively. No 2.25 mm specific data was available for zotarolimus eluting stents, which was reported in combination with larger stent sizes.

CONCLUSION Our composite data suggest that 2.25-mm SES and EES have superior clinical and angiographic outcomes compared with 2.25-mm PES, which has been shown to be superior to BMS in a randomized controlled study. Given the unique theoretical challenges posed by small vessel PCI, the overall lack of randomized data in this cohort needs to be addressed with future studies evaluating 2.25 mm stents in next-generation DES.

CRT-703

Comparison of Biolimus A9-eluting Stent and Platinum Chromium Alloy Everolimus-eluting Stent in Patients with De Novo Coronary Artery Lesion: A Propensity Score-Matched Analysis

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BACKGROUND There have been limited data comparing efficacy and safety of Biolimus-eluting Stents (BES, Biomatrix™, Biosensors and Nobori™, Terumo) with Platinum Chromium Everolimus-eluting Stent (PtCr-EES, Promus Element™, Boston Scientific) in a series of Asian population in real world clinical practice.

METHODS A total of 626 patients (pts) receiving BES or PtCr-EES were pooled from our prospective percutaneous coronary intervention (PCI) registry from March 2008 to May 2013. To adjust potential confounders, a propensity score matched (PSM) analysis was performed using the logistic regression model, and clinical outcomes were compared between the two groups up to 12 months.

RESULTS After PSM analysis, 2 propensity-matched groups (149 pairs, n = 298 pts, C-statistic=0.793) were generated and the baseline characteristics of the two groups were balanced. Six to 9-month angiographic outcomes showed that the incidence of binary in-stent restenosis was higher in the BES group than PtCr-EES (18.9% vs. 7.0%, p=0.034). This adverse angiographic outcomes were translated into worse 12-month clinical outcomes; the incidence of target lesion revascularizations (TLR: HR; 3.879, C.I; 1.06-14.2, p=0.041) and TLR-MACE (HR; 3.465, C.I; 1.103-10.88, p=0.033) BA9 were significantly higher than PtCr-EES despite of similar incidence of mortality and myocardial infarction.

CONCLUSIONS As compared with PtCr-EES, BES seem to be associated with higher rate of TLR and TLR MACE up to 12-month in a series of Asian population in real world clinical practice.

Table. Mid-term angiographic and 12-month Clinical Outcomes after propensity score matched analysis

Variables, N (%)	Total (n=145)	BES (n=74)	EES-PtCr (n=71)	p Value
Six to 9 month angiographic outcomes				
Binary In-Stent restenosis (>50%)	19 (13.1)	14 (18.9)	5 (7.0)	0.034
Variables, N (%)	**Total (n=298)**	**BES (n=149)**	**EES-PtCr (n=149)**	**p Value**
One-year clinical outcomes				
Total death	9 (3.0)	5 (3.3)	4 (2.6)	ns
Cardiac death	4 (1.3)	2 (1.3)	2 (1.3)	ns
Myocardial infarction: MI	5 (1.6)	3 (2)	2 (1.3)	ns
ST segment elevation MI	1 (0.3)	1 (0.6)	0 (0.0)	0.316
Revascularizations	26 (8.7)	16 (10.7)	10 (6.7)	0.218
Target lesion: TLR	14 (4.6)	11 (7.3)	3 (2.0)	0.029
Target vessel: TVR	18 (6.0)	12 (8.0)	6 (4.0)	0.145
Non-Target vessel: NTVR	8 (2.6)	4 (2.6)	4 (2.6)	ns
Stent thrombosis	4 (1.3)	2 (1.3)	2 (1.3)	ns
Acute	1 (0.3)	0 (0.0)	1 (0.6)	
Subacute	1 (0.3)	0 (0.0)	1 (0.6)	
Late	2 (0.6)	2 (1.3)	0 (0.0)	
Total MACE	34 (11.4)	21 (14.0)	13 (8.7)	0.145
TLR MACE	17 (5.7)	13 (8.7)	4 (2.6)	0.025
TVR MACE	26 (8.7)	17 (11.4)	9 (6.0)	0.101

*BES; Biolimus-eluting stent, EES; Everolimus-eluting stent, PtCr; Platinum chromium

CRT-704

Ultra-Hydrophilic Stents Promote Early Healing and Minimize Late Tissue Response: A Potential Alternative to Second-Generation Drug Eluting Stents

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BACKGROUND Clinical trials and meta-analyses demonstrate the low restenosis and stent thrombosis risks of next generation drug eluting stents (DES). Co-evolution of device, delivery technique, and drug-related factors all contribute, yet relative advantages are difficult to surmise. On a background of optimized contemporary bare metal stents (BMS), we asked if locally eluted drugs are still as useful or if simple design changes might obviate need for drug, further enhancing performance, manufacturability, and cost.

METHODS We hypothesized that thin, bare metal cobalt chromium or platinum chromium stents modified with an ultra-hydrophilic surface (UHS) treatment could reduce late intimal hyperplasia (IH) as with second-generation DES, yet maintain fast healing akin to bare metal stents (BMS). To test this, commercially available, FDA-approved DES and BMS were compared with UHS in A) porcine coronary models to assess IH and late thrombosis; and B) a rabbit iliac model to assess early healing and subacute thrombosis.

RESULTS *In vitro* tests demonstrated similar to faster endothelialization with reduced platelet adhesion (97% reduction, p<0.001) compared with untreated BMS. Hydrophilic treatment reduced IH in porcine coronary arteries relative to 3 corresponding BMS and DES platforms (2-3-fold reduction in 30-day angiographic restenosis; p<0.03). In contrast to early healing of UHS and BMS (porcine 30-day endothelialization score uniformly 4.0 of 4.0; confirmed in rabbit), DES trended to delayed healing at one month (range 2.67 to 4.0 out of 4.0) that resolved by 3 months, correlating with computed drug-receptor saturation. Elevation in thrombotic indices correlated with reduced endothelialization (p<0.0002) and occurred most often with DES, never with UHS (Poisson probability=0.135).

CONCLUSION Ultra-hydrophilic surface treatment of contemporary stents conferred excellent healing while moderating neointimal and thrombotic responses. With