Paclitaxel Drug-Coated Balloon Angioplasty Suppresses Progression and Inflammation of Experimental Atherosclerosis in Rabbits

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HIGHLIGHTS

- Restenosis limits the efficacy of PTA or stent treatment of atherosclerosis in peripheral and coronary artery disease.
- Paclitaxel DCBs effectively reduce restenosis; however, recently, their overall safety profile has been called into question.
- In an in vivo molecular-structural imaging study of 25 rabbits with experimental atherosclerosis, DCB-PTA, plain PTA, or sham-PTA was investigated using serial intravascular NIRF-OCT and IVUS.
- DCB-PTA reduced lesion inflammation on NIRF-OCT and halted lesion progression on IVUS, compared with PTA or sham-PTA.
- These findings indicated the potential for DCBs to serve effectively and safely as a regional anti-atherosclerosis therapy.

SUMMARY

Paclitaxel drug-coated balloons (DCBs) reduce restenosis, but their overall safety has recently raised concerns. This study hypothesized that DCBs could lessen inflammation and reduce plaque progression. Using 25 rabbits with cholesterol feeding- and balloon injury-induced lesions, DCB-percutaneous transluminal angioplasty (PTA), plain PTA, or sham-PTA (balloon insertion without inflation) was investigated using serial intravascular near-infrared fluorescence—optical coherence tomography and serial intravascular ultrasound. In these experiments, DCB-PTA reduced inflammation and plaque burden in nonobstructive lesions compared with PTA or sham-PTA. These findings indicated the potential for DCBs to serve safely as regional anti-atherosclerosis therapy. (J Am Coll Cardiol Basic Trans Sci 2020;5:685-95) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Compared with percutaneous transluminal angioplasty (PTA) using standard balloons, paclitaxel (PTX)-eluting, drug-coated balloons (DCBs) have recently shown improved efficacy in treating peripheral arterial disease (PAD)– or coronary artery disease–based restenosis and have become the primary endovascular treatment for femoropopliteal PAD (1–5). However, at present, scant data exist regarding the effects of DCB-PTA on atherosclerosis progression in vivo or the mechanisms by which it may produce its biological effects on atheroma in vivo. A recent meta-analysis of randomized trials demonstrated the potential for paclitaxel DCBs to increase all-cause mortality (6,7); in contrast, several other PTX DCB studies have not shown any differences in overall mortality (8–10). Therefore, additional studies investigating the effects of PTX DCBs on atherosclerosis could provide greater understanding of their vascular safety profile.

This study evaluated the effects of PTX DCB-PTA on inflammation and lesion progression in rabbit atherosclerosis in vivo and compared the results to animals treated with conventional PTA or sham-PTA. In addition to assessing plaque atheroma volume and plaque burden (PB) changes by serial intravascular ultrasound (IVUS), we assessed changes in lesion inflammation using serial intravascular near-infrared fluorescence—optical coherence tomography (NIRF-OCT) molecular–structural imaging of inflammatory protease activity (11,12). To further elucidate mechanisms underlying our in vivo findings, we performed histological and molecular assays of resected lesions and investigated the effects of PTX on human aortic smooth muscle cells in vitro.

**METHODS**

**STUDY DESIGN.** All animal studies were approved by the Institutional Animal Care and Use Committee of Massachusetts General Hospital (Protocol #2013N000015). Figure 1 shows the overview of the in vivo serial imaging study of rabbit atherosclerosis progression and DCB intervention or control subjects.

**EXPERIMENTAL ATHEROSCLEROSIS LESION GENERATION.** Lesions were generated in rabbit aortas using balloon injury in cholesterol-fed animals (Figure 1) as previously performed (13,14). After baseline, 6-week survival intravascular NIRF-OCT, and IVUS imaging, rabbits randomly received 1 of 3 treatments: PTX DCB-PTA (n = 10; IN.PACT Admiral 4.0 \( \times \) 40 mm, Medtronic, Santa Rosa, California; 3.5 \( \mu g/mm^2 \) of drug-coated concentration with urea excipient); conventional PTA (n = 10; INVATEC Admiral Xtreme 4.0 \( \times \) 40 mm, Medtronic); or sham-PTA (n = 5), followed by imaging. Animals were sacrificed 4 weeks later at week 10 (Supplemental Appendix).

In brief, atherosclerosis was induced in the aortas of male and female New Zealand White rabbits (aorta diameter: 3 to 3.5 mm; weight: 3 to 4 kg; Charles River Laboratories; Wilmington, Massachusetts) by local balloon arterial injury and high-cholesterol diet. After a 2-week, lead-in atherogenic diet (1% cholesterol, 5% peanut oil, Research Diets, New Brunswick, New Jersey), the infrarenal abdominal aorta of rabbits underwent balloon injury at week 2, as demonstrated previously (1).

**INTRAVASCULAR IMAGING OF PB AND PLAQUE INFLAMMATION. IVUS.** IVUS images of the abdominal aorta were acquired with a 40-MHz catheter by automated 0.5-mm/s pull back (iLab2, Polaris2 Software Imaging System, Boston Scientific, Marlborough, Massachusetts). Imaging commenced from the abdominal aorta at the level of the lowest renal down to the common iliac artery. IVUS was performed at 6 weeks both pre- and post-angioplasty and at the terminal 10-week imaging session.

**IVUS IMAGING QUANTITATIVE ANALYSIS.** IVUS datasets at 6 and 10 weeks were manually co-registered to each other using fiducial landmarks, including side branches and the known pull back rates of the imaging systems, and then analyzed by manual segmentation (OsiriX, Geneva, Switzerland; and Fiji imaging v2.0.0, National Institute of Health, University of Wisconsin, Madison, Wisconsin) (15), in accordance with expert consensus IVUS recommendations (16). The cross-sectional area (CSA) of the external elastic membrane (EEM) and vessel lumen were measured every 0.4 mm from axial IVUS images for each rabbit at 6 and 10 weeks, across the area that had undergone balloon treatment (total 40 mm length, 200 images per animal [100 images per timepoint]). These measurements permitted calculation of the atheroma CSA and PB for each IVUS slice. All obtained cross-sectional slices were analyzed and included in the image analysis results. On a per-slice basis (every 0.4 mm), atheroma progression was quantified as the change in IVUS PB (\( \Delta \)PB) between 6 and 10 weeks. The Supplemental Appendix section provides the formulas used for NIRF and IVUS quantitative analysis.

**NIRF plaque inflammation measurements.** Twenty-four hours before NIRF-OCT imaging sessions, rabbits received the protease NIRF imaging agent ProSense750 VM110 intravenously (a quenched sensor engineered to generate fluorescence following proteolytic activation by cathepsins B, L, or S; PerkinElmer, Waltham, Massachusetts) (11). Automated reconstruction of dual-modal NIRF-OCT pull backs
was performed, as previously described (17). Quantitative NIRF data were generated using co-registered OCT images to correct the NIRF signal according to the distance between the catheter and the lumen surface, and expressed as both the NIRF concentration (nM) averaged over all the slices that included the plaque and the average NIRF concentration per OCT slice at 0.4 mm intervals (11). The change in NIRF concentration (ΔNIRF, in nM) on a per slice basis was calculated as the difference between the NIRF concentration at 6 and 10 weeks.

Readers (M.M.C., K.S., M.S.A.) were blinded to the group assignment of each animal for all IVUS and NIRF image analyses.

MOLECULAR ANALYSIS. Following sacrifice, rabbit aortas were perfused with cold saline and harvested. Aortas were then processed, measured, and sectioned. Sections were created every 0.5 cm, with selected tissue from 3 regions stored in RNAlater for subsequent RNA analysis. The 3 regions included: 1) the normal aorta (no Fogarty balloon injury); 2) the PTA segment (Fogarty balloon injured and then staged experimental angioplasty 4 weeks later) (Figure 1); and 3) the balloon-injured region (Fogarty balloon injury only). The remaining tissue was snap frozen using dry ice and 2-methylbutane, then placed in optimal cutting temperature compound medium and stored at −80 °C for later sectioning and histopathology.

IN VITRO STUDIES. Primary human smooth muscle cells from healthy donors were purchased from Cell Applications Inc (Cat #354K-05a, San Diego, California). Human smooth muscle cells were incubated with lipopolysaccharide 100 ng/ml in vitro for 24 h and then incubated with graded concentrations of PTX up to $1 \times 10^{-5}$ M for 90 min. Cells then underwent RNA extraction and quantitative polymerase chain reaction analysis as detailed in the Supplemental Appendix.

STATISTICAL ANALYSIS AND REPRODUCIBILITY. Continuous variables were reported mean ± SD,
median (25th, 75th percentiles), or median interquartile range (IQR), as appropriate. Normality was assessed visually using histograms and Q-Q plots, and formally using the Shapiro-Wilk test. The nonparametric Kruskal-Wallis test compared the differences among DCB-PTA, PTA, and sham-PTA groups, and the Mann Whitney U test compared differences between DCB-PTA and PTA groups. Regression analyses using simple and multiple linear regression models were adjusted for baseline (week 6) serum cholesterol, C-reactive protein, minimum lumen area, and the respective plaque parameters (baseline percent atheroma volume [PAV], total atheroma volume [TAV], and PB). For each model, formal statistical tests of the linear regression assumptions were performed. A log-transformation to the ΔNIRF as an outcome variable was performed to improve the model fit. Findings are reported as a percentage change derived from geometric mean ratios. For all regression experiments, sensitivity analyses were performed using serum cholesterol and C-reactive protein levels at endpoint (week 10), instead of baseline. We also examined correlations between ΔNIRF and other IVUS-derived metrics using Pearson’s correlation. For histological and mRNA analyses, comparisons between groups were made using the Kruskal-Wallis H test, with a post hoc analysis using Dunn’s test of multiple comparisons. The p values were
2-sided, and a p value of <0.05 was considered statistically significant. Analyses were performed using Stata/IC version 15.0 (StataCorp, College Station, Texas).

For the purposes of direct statistical analysis, comparative data were analyzed between the DCB-PTA and PTA groups, specifically with reference to regression analyses. Sham-PTA data are available in the Supplemental Appendix.

**RESULTS**

A total of 25 rabbits with aortic lesions (15 male, 10 female) were randomized in the study (Figure 1), with 10 receiving PTX DCB-PTA, 10 receiving uncoated PTA, and 5 rabbits receiving sham-PTA. All animals survived until the planned sacrifice at 10 weeks and entered the analysis.

Serial IVUS images of lesion anatomy and NIRF-OCT images of inflammatory cathepsin protease activity were acquired for all 3 groups, with representative 2-dimensional (2D) NIRF maps, 1D NIRF plots, 2D IVUS images, and 1D IVUS plots (Figure 2). Complete rabbit data showcasing 2D NIRF maps, quantitative 1D plots, and corresponding 1D IVUS PB plots are presented in Supplemental Figures S1 to S3.

**EFFECTS OF DCB-PTA, PTA, OR SHAM-PTA OF ATHEROSCLEROSIS BURDEN AND INFLAMMATION.**

In all rabbits at both 6 and 10 weeks, IVUS frames were analyzed every 0.4 mm over each 40 mm angioplasty balloon length (100 image slices per rabbit per time point; a total of 5,000 IVUS images underwent assessment of lesion plaque area, lumen area, and vessel wall area). The total lesion plaque volume and burden was calculated over the angioplasty region for each rabbit. The baseline 6-week, follow-up 10 week, and change in plaque characteristics, cholesterol, and C-reactive protein measurements are presented in Table 1. At the week 6 baseline, the 3 groups exhibited similar plaque structural measures, including PAV, TAV, and PB (p = 0.348, p = 0.136, and p = 0.179, respectively). Similarly, the 3 groups had comparable baseline NIRF lesion inflammation (Table 1) (p = 0.818). The average percentage area stenosis for each group (DCB-PTA, PTA, and sham-PTA) was 20.8%, 22.1%, and 24.8%, respectively, which indicated the presence of mildly stenotic plaques at baseline 6-week imaging.

At follow-up assessment at 10 weeks (4 weeks after baseline imaging), DCB-PTA induced several benefits on experimental lesions, in comparison to the PTA and sham-PTA groups (Table 1). Analyzing changes in lesion anatomical features, DCB-PTA significantly reduced lesion progression, and moreover, induced lesion regression (DCB-PTA, PTA, sham-PTA, respectively): AV (−19.7 mm³ [4.6], 98.0 mm³ [64.7], 183.6 mm³ [155.5]; p < 0.001); DPAV (−3.0% [4.6], 5.7% [4.1], 9.6% [1.4]; p = 0.001); D average PB (−2.5% [7.6], 5.8% [4.0], 9.8% [1.0]; p = 0.004). DCB-PTA also significantly reduced lesion percent area stenosis by 5.2% (p < 0.001 vs. the other groups). The minimal luminal area also increased over time in all groups. In addition, DCB-PTA significantly reduced the progression of lesion inflammation compared with the PTA group (average NIRF cathepsin activity: 18.3 nM [43.8] vs. 44.6 nM [35.5]; p=0.028) (Supplemental Table 1).
On multivariable analyses adjusted for baseline cholesterol levels, C-reactive protein, minimal lumen area, and baseline IVUS parameters (TAV, PAV, and PB), DCB-PTA remained significantly more effective in reducing TAV, PAV, and PB compared with PTA, in which all 3 measures increased \( (p < 0.006 \text{ for each comparison}) \) (Table 2). Similarly, after adjustment for baseline cholesterol level, C-reactive protein level, minimal lumen area, and baseline NIRF inflammation, treatment with DCB-PTA significantly reduced the average plaque NIRF inflammatory cathepsin activity signal by 48.1% \( (95\% \text{ confidence interval: } -69.45 \text{ to } -12.0; \ p = 0.018) \) (Table 3) compared with the PTA group.

For all regression models, sensitivity analyses using endpoint week 10 levels of C-reactive protein, cholesterol, and minimum lumen area produced the same inference (statistical files in Supplementary Appendix).

**RELATIONSHIP BETWEEN PLAQUE INFLAMMATION AND PB OVER TIME.** To further assess the relationship between changes in lesion inflammation and changes in PB after angioplasty, we examined the association between the change in NIRF concentration and change in IVUS measures of lesion for each slice by pooling data for both angioplasty groups (DCB-PTA plus PTA groups). Across all pooled slices, the ΔNIRF lesion inflammation correlated positively with ΔTAV, ΔPAV, and ΔPB \( (r = 0.50, \ r = 0.49, \text{ and } r = 0.46, \text{ respectively}; \ p = 0.02; \ p = 0.03, \text{ and } p = 0.04, \text{ respectively}) \) (Table 3) from week 6 to week 10.

**EFFECTS OF DCB-PTA, PTA, AND SHAM-PTA ON PLAQUE MACROPHAGE AND SMOOTH MUSCLE CELL CONTENT, AND RNA TRANSCRIPTS IN VIVO AND IN VITRO.** To gain mechanistic insight into the effects of PTX on the artery wall, a subgroup of rabbit lesions from PTX DCB-PTA, PTA, and sham-PTA animals underwent histopathological assessment after the week 10 sacrifice. The presence of lesional macrophages (Figure 3A) supported findings that lesions reproduced a key feature of inflammatory atherosclerosis rather than homogeneous smooth muscle cell–rich neointimal hyperplasia characteristic of typical stent restenosis. Following immunohistochemical staining with the RAM-11 rabbit macrophage marker, and the smooth muscle cell smooth muscle actin marker, DCB-PTA–treated lesion sections displayed significantly lower RAM11+ macrophase and smooth muscle actin marker+ area than PTA- or sham-PTA-treated regions \( (45 \text{ to } 50 \text{ sections analyzed per group for RAM11}; \ p < 0.001 \) \[Figures 3A and 3B\], and 25 to 30 sections analyzed per group for smooth muscle actin; \( p < 0.001 \) \[Figures 3C and 3D\].

To investigate the effects of DCB-PTA on RNA transcripts, a subgroup of resected aortic lesions from every rabbit underwent RNA extraction and quantification of cathepsin subtype \( (B, \ L, \ S) \), along with tumor necrosis factor–\( \alpha \) and interleukin-\( \beta \) gene expression. Lesions treated with DCB-PTA exhibited significantly reduced expression of all measured transcripts \( (p < 0.001) \) compared with lesions from the PTA and sham-PTA groups, which corroborated

### Table 2: Assessment of DCB-PTA Versus PTA on Plaque Progression

<table>
<thead>
<tr>
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<th>DCB-PTA vs. PTA (Unadjusted)</th>
<th>DCB-PTA vs. PTA (Adjusted)</th>
</tr>
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<tbody>
<tr>
<td>Δ Total atheroma volume (mm³)</td>
<td>−1.14.5</td>
<td>−1.14.0</td>
</tr>
<tr>
<td>Δ Percent atheroma volume (%)</td>
<td>−8.5</td>
<td>−8.2</td>
</tr>
<tr>
<td>Δ Average plaque burden (%)</td>
<td>−7.3</td>
<td>−7.0</td>
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Unadjusted and adjusted estimates comparing the changes in total atheroma value, percent atheroma value and plaque burden in DCB-PTA vs. PTA (measured as Δ change) derived from generalized linear regression models with 95% confidence intervals. *Adjusted for baseline cholesterol, C-reactive protein, and minimal lumen area, and corresponding atheroma parameter at baseline (6 weeks). \( tp < 0.001; tp < 0.01 \).

### Table 3: Assessment of DCB-PTA Versus PTA on NIRF Plaque Inflammation, and Relationships Between Plaque NIRF Inflammation and Plaque Progression

<table>
<thead>
<tr>
<th></th>
<th>% Change (95% CI)</th>
<th>( p ) Value</th>
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<tbody>
<tr>
<td>Δ NIRF (unadjusted)</td>
<td>−52.4 (-72.7 to −16.1)</td>
<td>0.0131</td>
</tr>
<tr>
<td>Δ NIRF (‘adj.’)</td>
<td>−48.1 (-69.4 to −12.0)</td>
<td>0.0181</td>
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Pearson Correlation Coefficients for Δ NIRF vs. IVUS-Derived Metrics (measured as Δ):

<table>
<thead>
<tr>
<th></th>
<th>( r_p ) Value</th>
<th>( p ) Value</th>
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<tbody>
<tr>
<td>Δ NIRF vs. Δ TAV</td>
<td>0.50</td>
<td>0.0061</td>
</tr>
<tr>
<td>Δ NIRF vs. Δ PAV</td>
<td>0.49</td>
<td>0.0301</td>
</tr>
<tr>
<td>Δ NIRF vs. Δ PB</td>
<td>0.46</td>
<td>0.0411</td>
</tr>
</tbody>
</table>

\*Adjusted for baseline cholesterol, baseline CRP, baseline minimal lumen area, and corresponding atheroma parameter, at baseline (6 weeks). \( tp < 0.05; tp < 0.01 \). CI = confidence interval; IVUS = intravascular ultrasound; PAV = percent atheroma volume; PB = plaque burden; \( r_p \) = reflecting Pearson; TAV = total atheroma volume; other abbreviations as in Table 1.
in vivo findings that showed dampened inflammation following DCB-PTA (Figure 3E).

**PTX-BASED EFFECTS ON CATHEPSIN PROTEASE TRANSCRIPT EXPRESSION IN VITRO.** To ascertain whether the PTX resident in DCBs could directly exert anti-inflammatory effects relevant to diminished atheroma progression, primary human aortic smooth muscle cells were stimulated with lipopolysaccharide in vitro, and then incubated with graded concentrations of PTX for 90 min. Cells were then processed for mRNA analysis (quantitative polymerase chain reaction; see the Supplemental Appendix). PTX reduced expression of cathepsins B, L, and S mRNA transcripts in aortic smooth muscle cells, in graded fashion ($p < 0.001$) (Figure 3F).

**DISCUSSION**

Treatment with PTX DCB-PTA, but not conventional PTA or sham-PTA, reduced both lesion inflammation and lesion progression in experimental atherosclerosis in rabbits. These findings provided new experimental evidence that PTX-based DCB treatment favorably affected experimental atherosclerosis, which would have implications for the safety of DCBs.
as well as the ability of DCBs to serve as a regional endovascular therapy for atherosclerosis.

Inflammation drives atherosclerosis progression (18), and anti–interleukin-1f mediated suppression of inflammation can reduce cardiovascular events in patients (19). The present serial intravascular in vivo NIRF-OCT molecular imaging study revealed that DCB-PTA significantly reduced inflammatory protease activity implicated in lesion progression compared with PTA or sham-PTA, in experimental atherosclerosis (20). Macrophages and smooth muscle cells and their products, including cathepsin proteases, contribute to the initiation, progression, and complications of atherosclerosis (21). PTX treatment of human primary aortic smooth muscle cells further demonstrated a dose-dependent reduction in cathepsin mRNA transcripts. The present findings indicated that PTX exerted anti-inflammatory effects that underlay the observed favorable PTX DCB-PTA effects on experimental atherosclerosis.

From a lesional volume perspective, PTX DCB therapy induced experimental lesion regression (decreases in TAV, PAV, average PB, and percent area stenosis) (Table 1) in contrast to PTA or sham-PTA treatment. Mechanisms underlying this observation likely include PTX-based anti-inflammatory effects as supported by a moderate correlation between lesion inflammation and lesions progression in these experiments (Table 3). Additional mechanisms might include favorable remodeling effects of the balloon angioplasty itself independent of PTX, because the PTA alone group also exhibited reduced lesion progression compared with the sham-PTA group. For example, treatment of experimental atherosclerosis with bare metal stents stabilized rabbit plaques by reducing macrophage content (22,23).

Although the present rabbit model of atherosclerosis (13,14) included a component of restenosis pathology following endovascular injury, the experimental pathology recapitulated several features of human atherosclerosis, such as the presence of plaque macrophages (Figure 3). Moreover, although other animal endovascular studies of PTX clearly demonstrated inhibition of neointimal proliferation after balloon injury (24–26), the present study provided new insights into the effects of DCBs on experimental lesions with features of atherosclerosis, which demonstrated inhibition of both lesion inflammation and lesion progression.

The ability to image inflammation in coronary and peripheral artery–sized vessels using high-resolution intravascular NIRF molecular imaging offers a translational approach to understanding the mechanisms of clinical atherosclerosis progression and impaired stent healing (11,12,27,28). A recent first-in-human clinical study in patients with coronary artery disease demonstrated the safety and feasibility of intracoronary NIRF-OCT imaging to detect coronary plaque 633-nm–excited NIR autofluorescence, a potential measure of intraplaque hemorrhage or oxidative stress–induced lipid byproducts (29). The present study thus provided a clinical foundation for NIRF inflammation imaging using ProSense VM110 (Perkin Elmer, Waltham, Massachusetts) (VM110 in Detection of Microscopic Tumors: A Phase I Study; NCT03286062) or LUM015 (Lumicell, Inc., Wellesley, Massachusetts), a similar NIR cathepsin protease–sensitive agent (30), which were recently evaluated in patients. Both NIRF-OCT catheter technology and imaging agents are positioned to enable clinical NIRF inflammation imaging trials of patients with atherosclerosis in the near future.

This study provided new experimental evidence that PTX DCB-PTA could mitigate lesion inflammation and progression and could therefore serve safely as a regional strategy for treating atherosclerosis. Potential clinical extensions of DCB-PTA could consider treatment of flanking atheroma around culprit plaques in patients already undergoing coronary or peripheral endovascular treatment. However, before extending the application of PTX-DCBs, the current controversy surrounding PTX-DCBs (6–10) requires resolution; the endovascular community eagerly awaits further analyses and new clinical and experimental data. Recent data on the late mortality signal with DCBs remain inconclusive; however, the long-term risks of these devices need to be balanced against their established and sustained efficacy in improving limb-related outcomes in patient with femoropopliteal PAD.

**STUDY LIMITATIONS.** Balloon injury and severe hyperlipidemia to induce experimental atherosclerosis in rabbits does not fully recapitulate human atherosclerosis complexity but does reproduce some pathological features of human plaques. In addition, the model we used enabled the study of DCBs in atherosclerosis in arteries of a similar caliber to human coronary and peripheral-sized vessels. Furthermore, the investigated experimental lesions induced by balloon injury in this study did not fully recapitulate human atherosclerosis, and therefore, additional DCB studies in clinical subjects are required. A future area of investigation regarding the durability of DCB treatment for preventing atheroma progression in more advanced lesions and for the longer term are questions that exceeded the model and scope of this study. Although the present study required 2 intravascular imaging approaches (NIRF-OCT and...
IVUS), further development of an integrated NIRF-IVUS (28) imaging system might provide a single intravascular imaging approach for future atherosclerosis studies.

CONCLUSIONS

PTX DCB-PTA reduced lesion inflammation and lesion progression in experimental rabbit atherosclerosis in contrast to PTA or sham-PTA. These preclinical findings supported the vascular safety and efficacy of PTX-DCB angioplasty.

ACKNOWLEDGMENT

The authors thank Dr. Amy Mikkola, MGH Comparative Medicine Clinical Pathology Laboratory, for assay of serum cholesterol levels.

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REFERENCES


PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: PTX DCBs reduce peripheral and coronary artery restenosis, but their effects on atherosclerosis have not been fully characterized. There is recent concern regarding their safety profile.

TRANSLATIONAL OUTLOOK 1: PTX DCB-PTA reduces preclinical lesion inflammation and lesion progression in contrast to PTA or sham-PTA, as demonstrated in vivo using translatable intravascular molecular-structural imaging technology.

TRANSLATIONAL OUTLOOK 2: Following resolution of current PTX DCB safety concerns, the present study supports evaluating paclitaxel DCBs as a regional endovascular therapy to stabilize atherosclerosis and improve long-term vascular outcomes in patients with PAD and coronary artery disease.


KEY WORDS atherosclerosis, drug-coated balloon, imaging, inflammation, peripheral arterial disease

APPENDIX For an expanded Methods section and supplemental tables and figures, please see the online version of this paper.