Intravascular Ultrasound Analysis of Polymer-Based Paclitaxel-Eluting Stents

With great interest I read the report by Weissman et al. (1) regarding intravascular ultrasound (IVUS) analysis of polymer-based paclitaxel-eluting stents. The investigators stated in the text that “positive remodeling assessed as the absolute increase in the paclitaxel-eluting stents. The investigators stated in the text that “positive remodeling assessed as the absolute increase in the internal elastic membrane volume over time tended to be slightly more prominent with the TAXUS stent (7.66 ± 48.64 mm³ vs. –12.29 ± 36.05 mm³, respectively, p = 0.064).” Also Figure 1 suggested positive remodeling in the TAXUS stent. However, Table 2 of their article (1) shows an inconsistent result, that is, decrease of external elastic membrane volume in the TAXUS-stent group (283 ± 91 mm³ at postimplantation vs. 280 ± 89 mm³ at nine-month follow-up). Because a previous IVUS analysis has also suggested positive remodeling in the TAXUS stent (2), it may be of great importance to better clarify this result.

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REPLY

We appreciate Dr. Kaneda’s astute observation about the data contained in our report (1) on the intravascular ultrasound (IVUS) results from TAXUS-IV. It is indeed true that there was a trend for the vessel receiving a TAXUS stent to demonstrate positive remodeling, similar to prior drug-eluting stent (DES) reports. The analysis for remodeling used only TAXUS and non-TAXUS patients with complete volumetric IVUS data of the external elastic membrane (EEM) throughout the stent length at both the time of stent implantation and at follow-up. As it states in the Methods section, “Volumes were calculated only if the vascular interface was visualized every millimeter throughout the stent” (i.e., we did not extrapolate the EEM border for images in which it was not visualized). Thus, not all patients with EEM volume data at stent implantation had EEM volume data at follow-up, and vice-versa. Table 2 of the study (1) reports all the volume data at one time point (postimplantation or follow-up) and the statistical analysis for change (and Figure 1 of the report [1] displaying change over time) used only patients that had paired postimplantation and follow-up EEM volume data. Hence, the results of a trend toward positive remodeling in the TAXUS stent are indeed accurate and in concordance with other DES studies.

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Restenosis, Statistics, and Reasonable Inferences

We appreciate the accompanying editorial (1) to our recent report entitled “Relationship Between Angiographic Late Loss and Target Lesion Revascularization After Coronary Stent Implantation: Analysis From the TAXUS-IV Trial” (2) but we wish to clarify several apparent misconceptions. Our principal messages are that in the era of drug-eluting stents (DES), it is not only the mean value but also the shape of the distribution curve (variance and skewness) that will determine the population target lesion revascularization (TLR), and that with a homogeneous response in-stent late losses up to about 0.75 mm may provide acceptable clinical results (2). That DES may have rightward skewed late loss histograms has been previously reported (3). The fact that the individual patient late loss/TLR relationship is curvilinear with an apparent inflection point, rather than linear, had not been reported and is a novel and unique observation that has since been replicated in several other DES trials (DELiVER, ENDEAVOR-II). Most importantly, given the rightward skew in patient population data seen in all these trials (including the pivotal SIRIUS trial of the sirolimus-eluting stent), a certain lower level or “floor” of TLR may be unavoidable, somewhat independent of the mean late loss.

Moreover, recent data reported at the most recent American College of Cardiology meetings substantiate our findings. The ENDEAVOR-II trial, with a considerably higher mean late loss (0.62 mm) but with rather a homogeneous effect (standard deviation of late loss 0.46), reported a low TLR of 4.6% with the ABT-578-eluting stent. The large-scale REALITY trial, comparing the sirolimus-eluting and paclitaxel-eluting stents, found significantly greater in-stent late loss with the latter (0.09 vs. 0.31 mm, respectively, p < 0.001), but nearly identical eight-month TLR rates (5.0% vs. 5.4%, p = 0.81). Thus, given the patient and lesion complexity studied in the pivotal DES trials to date, an “acceptable” TLR can be achieved with a relatively high in-stent late loss, providing that a homogeneous response is seen.

In addition, other variables beyond angiographic late loss that may affect TLR rates must be considered, including the inaccuracies and variability of quantitative measures of late loss. Variable thresholds of patient angina perception, follow-up ischemia detec-
tion, and practice to refer patients for subsequent repeat catheterization and revascularization procedures will also minimize the practical relevance of any differences in late loss. In the end, probably all would agree that, up to a point, less late loss is better, but the range of late loss that is associated with infrequent clinically driven TLR may be wider than previously believed. Whether this relationship holds in more complex and challenging lesion subsets will be analyzed in the TAXUS-V and -VI studies.

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paclitaxel-eluting stent vs balloon angioplasty for prevention of recur-
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**Table 1.** Randomized Comparative Trials of Cypher Versus Taxus Stents

<table>
<thead>
<tr>
<th>Trial</th>
<th>Late Lumen Loss (mm)</th>
<th>BAR (%)</th>
<th>TLR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cypher</td>
<td>Taxus</td>
<td>Cypher</td>
</tr>
<tr>
<td>ISAR-DIABETES</td>
<td>0.19</td>
<td>0.45</td>
<td>6.9</td>
</tr>
<tr>
<td>SIRTAX</td>
<td>0.13</td>
<td>0.25</td>
<td>6.7</td>
</tr>
<tr>
<td>REALITY</td>
<td>0.09</td>
<td>0.31</td>
<td>9.6</td>
</tr>
<tr>
<td>ISAR-DESIRE</td>
<td>0.10</td>
<td>0.26</td>
<td>14.3</td>
</tr>
</tbody>
</table>

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