Reviewer's report

Title: Assessment of Plaque Evolution in Coronary Bifurcations Located Beyond Everolimus Eluting Scaffolds: Serial Intravascular Ultrasound Virtual Histology Study

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Reviewer: Kenichi Tsujita

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The paper by Lee et al. describes an interesting study that examined the atherosclerotic evolution in coronary bifurcations located proximally and distally to a bioresorbable vascular scaffold (BVS) with the use of intravascular ultrasound (IVUS). When examining separately the bifurcations located proximally and distally to the BVS, no changes were found at the distal bifurcations, while at the proximal bifurcations there was a statistical significant decrease in the plaque burden (36.67±13.33% at baseline vs. 35.06±13.20% at 2 years follow-up, p=0.04). Taken these findings into consideration, the authors speculated that the results may potentially be due to the effect of the downstream drug delivery on vessel wall physiology. Although these IVUS findings are of potential interest, additional discussion is strongly recommended to promote our better understanding of the atherosclerotic evolution in coronary bifurcations.

Major comments

1. In each bifurcation, the frames portraying the proximal rim, in-bifurcation, and distal rim of the ostium of the side branch were analyzed. The geometric parameters and plaque types were then evaluated at baseline and 2-years follow-up. However, there were no significant differences in the geometrical parameters such as lumen, vessel and plaque areas as well as in the composition of the atheroma between baseline and 2-years follow-up. Underlying this negative data, there may be methodological problem. As the authors described in the Discussion section, at the distal rim of the ostium of the side branch and in particular at the outer side of the flow divider low or oscillating shear stress have been detected and these segments appear to be susceptible to atherosclerosis, in-depth analysis (e.g. IVUS image acquisition both from main branch and side branch as shown in a paper by Oviedo et al. [Circ Cardiovasc Interv 2010;3;105-112]) was required to elucidate the atherosclerotic evolution in coronary bifurcations. The authors had better mention about the methodological limitation.

2. The authors analyzed separately bifurcations located proximally and distally to the BVS, and found plaque regression at the proximal group and no changes in the plaque at the distal group. They explained that this may potentially be due to the effect of the downstream drug delivery on vessel wall physiology. In view of the small number of the study patients, the credibility of the results is questioned,
and the study itself is hypothesis-generating. Figure 4 seems to lead misunderstanding to the readers, because serial change of the plaque burden was quite similar between proximal and distal bifurcation. Please remake the graph, and clarify the difference between the groups.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

No conflict of interest to declare.