achieving adequate depth and circumferential ablation using RF energy; 3) inadequate number and spatial orientation of ablations; and 4) challenges in controlling drug compliance, as well as the addition of antihypertensive medications during the study period (4).

In an important post hoc analysis, Kandzari et al. (4) reported "dose-response" findings with radiofrequency ablation suggesting that inadequate denervation was a root cause of the trial's failure. In this publication, one can see a substantial "dose response" in blood pressure lowering as a function of the number of ablations performed per patient (4). We believe that the SYMPLICITY HTN-3 trial was flawed and should be interpreted not as a global failure of RDN but primarily as a failure to denervate.

In the aftermath of this trial, there has been extensive analysis of the inherent strengths and limitations of the different types of technologies used to perform RDN. It is evident that a successful denervation device must provide predictable, deep, and circumferential nerve inactivation. This is being taken into consideration with current trials of radiofrequency ablation, which are targeting distal ablation in the renal arteries, ablation in the distal branch vessels, and a substantially greater number of thermal ablations than were performed in the SYMPLICITY HTN-3 study. Alternatively, chemical RDN with alcohol, as performed by the Peregrine Catheter (1), may overcome the limitations of radiofrequency-mediated RDN.

In conclusion, much has been learned since the failure of SYMPLICITY HTN-3 about the pathophysiology of RDN. Anatomic, technical, and procedural variables, as well trial execution, must be carefully considered when evaluating RDN clinical trials. We remain optimistic that the refinements in technology will demonstrate the value of RDN for the treatment of difficult to control hypertension, as well as other cardiovascular disorders.

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The Role of Valve Implantation Height

Are We Measuring Depth the Right Way?

We read with great interest the paper by De Torres-Alba (1) on changes in the rate of pacemaker implantation after transition from the SAPIEN XT to the SAPIEN S3 transcatheter aortic valve (Edwards Lifesciences, Irvine, California). The investigators showed, in agreement with other reports, that the rate of pacemaker implantation is almost double with the SAPIEN S3 valve and that depth of implantation is associated with increased rate of permanent pacemaker placement (2–4).

We agree that the deeper the implantation of any device, the higher the risk for complete heart block and need for a pacemaker, given the proximity to the conduction system. This phenomenon seems to be more common with the S3 device, either because of its longer frame or because of its bulkier skirt. However, the accuracy and the magnitude of the association between depth and conduction disturbances as reported are debatable given the methods that were used for depth measurement.

Indeed, there may be flaws in the way implantation depth was estimated before prosthesis deployment and flaws in the way depth was measured after prosthesis deployment. As the investigators describe, 2 angiographic still frames were used to measure implantation depth: 1 pre- and 1 post-implantation. Before the prosthesis is deployed, the aortic annulus is seen in a coaxial projection, with the 3 cusps aligned. This projection is determined either by multislice computed tomography before the procedure or by aortography. The device is then positioned in the annulus, and once the desired depth is achieved, the device is deployed. After deployment, the device is not necessarily coaxial, so the projection is modified to obtain device coaxiality, and this is when final aortography is performed and depth is measured. In this modified projection, however, the aortic annulus is no longer coaxial. Proper localization of the hinge point between the device and sinus

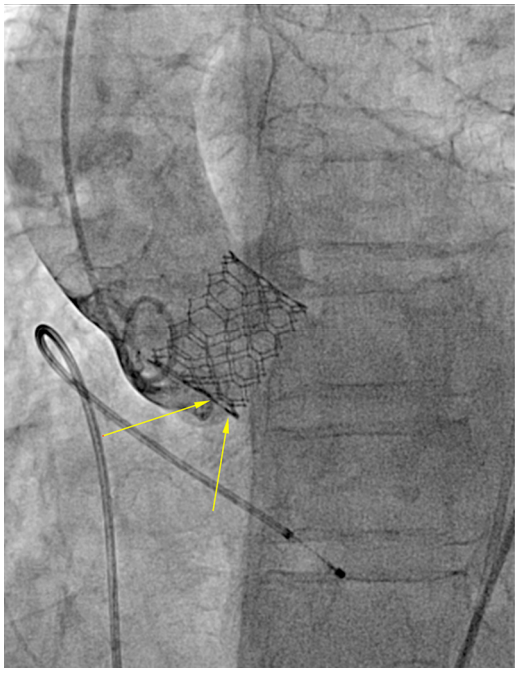
of Valsalva, and therefore proper implantation depth measurement, can be difficult in such circumstances and prone to parallax error (5). If the projection is modified significantly, 2 hinge points can be seen on the same side, making accurate measurements nearly impossible (**Figure 1**).

Another issue is that of difference in orientation between the deployed device and the aortic annulus and root. This is illustrated by the difference in depth on the septal and nonseptal sides of the device. The investigators did not mention how they accounted for this phenomenon: averaging both measurements, recording only the largest measurement, or recording a measurement on only 1 side? The example provided in the figure suggests measurement of depth on the nonseptal side. Whether this is appropriate to assess a complication that arises in the septum seems counterintuitive.

Finally, the unit of measurement of depth, percentage of the prosthesis lying above the annulus, may also induce measurement error. Indeed, with this measurement unit, 2 patients with the same percentage depth of implantation but different device sizes would have different effective device length protruding in the left ventricle. This is because device height is different across sizes. For example, a patient with a 23-mm device with an implantation depth of 66.5% (i.e., the average depth of patients requiring pacemakers) would have 6.03 mm of the device in the left ventricle. Another patient with the same 66.5% implantation depth but a 29-mm device would have 7.54 mm of the device in the left ventricle. Although this 1.51 mm difference may seem trivial, it is actually larger than the difference in effective depth between patients requiring pacemakers and those not. For example, the average effective depth in patients with 29-mm devices requiring pacemakers is 7.54 mm, compared with 6.23 mm in those with the same device size but not requiring pacemakers, with a difference between groups of 1.31 mm on average.

To adequately measure device implantation depth, future studies should rely on post-procedural multislice computed tomography. This would allow measurement of depth all around the annulus, not only on the septal and nonseptal sides. The method described by De Torres-Alba et al. (1) and others could also be validated.

FIGURE 1 Example of Difficult Depth Measurement



In this case, the projection has been modified after implantation, so the device appears coaxial. However, the annulus is no longer coaxial: 2 aortic cusps are seen at different levels on the septal side **(arrows)**, making difficult the localization of the hinge point and therefore the measurement of depth of implantation.

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