A novel system for the reconstruction of a coronary artery lumen profile in real time: a preclinical validation

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Departments of 1Biomedical Engineering, 2Surgery, and 3Cellular and Integrative Physiology and 4Pathology, Indiana University-Purdue University Indianapolis (IUPUI), Indianapolis; 5Weldon School of Biomedical Engineering, Purdue University, West Lafayette; 6Department of Cardiology, IUPUI, Indianapolis; and 7St. Vincent Heart Group, Indianapolis, Indiana

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Kassab GS, Choy JS, Svendsen M, Sinha AK, Alloosh M, Sturek M, Huo Y, Sandusky GE, Hermiller J. A novel system for the reconstruction of a coronary artery lumen profile in real time: a preclinical validation. Am J Physiol Heart Circ Physiol 297: H485–H492, 2009. First published May 22, 2009; doi:10.1152/ajpheart.01224.2008.—Accurate sizing of vessel diameter is important for understanding the physiology of blood vessels as well as the treatment of coronary and peripheral artery disease. The objective of this study was to validate a novel catheter-based system [the LumenRECON (LR) system] for the real-time reconstruction of lumen cross-sectional area (CSA) along the length of a vessel segment. A total of 22 swine (20 Yorkshire and 2 atherosclerotic Ossabaw swine) were used to evaluate the accuracy, reproducibility, and safety of the system compared with intravascular ultrasound (IVUS). The CSA of the right coronary artery, left anterior descending coronary artery, and left circumflex artery were determined by IVUS and the LR system over a 3- to 4-cm segment in 12 Yorkshire and 2 atherosclerotic Ossabaw swine and 2 postmortem atherosclerotic human hearts. In eight chronic animals, the effect of the LR catheter on the vessel wall was evaluated at 1 day and 2 wk (4 animals each) after the intervention. A Bland-Altman plot of the LR and IVUS data showed a mean difference between the two measurements of 0.055 mm in diameter, which was not statistically significant from zero, indicating a lack of bias in the comparison of the LR system with IVUS. The root mean square error of the two measurements was 0.45% NaCl). Upon completion of measurements, animals were killed, and vessels were harvested for histological assessment of any chronic remodeling of the endothelium at 1 day and 2 wk (4 animals each) after the intervention.

METHODS

A total of 22 swine was used in the study, with 20 normal (domestic Yorkshire) swine and 2 atherosclerotic (Ossabaw) swine. Twelve of the twenty normal animals were used for acute measurements of the coronary arteries with the LR system and IVUS (6 animals with injections of 1.5% and 0.45% and another 6 animals with 0.9% and 0.45% NaCl). Upon completion of measurements, animals were killed, and vessels were harvested for histological assessment of any acute damage caused by the devices. Two atherosclerotic swine had coronary artery luminal cross-sectional area (CSA) profile in real time. The safety, accuracy, and reproducibility of the LR system were compared with IVUS in a group of normal and atherosclerotic swine and in postmortem human coronary vessels.

sizing; diameter; conductance; interventions; lesion

PERCUTANEOUS CORONARY INTERVENTIONS, such as balloon angioplasty [percutaneous transluminal coronary angioplasty (PTCA)] and stents (bare metal and drug-eluding stents), have revolutionized coronary heart disease treatment in the past three decades. Despite these advances, problems remain with restenosis and late stent thrombosis. The clinical significance of correct sizing of a stent with full deployment of a stent’s strut is well established (3, 7). Inappropriate undersizing of a balloon causes an increase in the restenosis rate, and oversizing may cause dissection or acute vessel closure. The value of optimal balloon sizing during PTCA has been validated in numerous studies using intravascular ultrasound (IVUS). For PTCA, IVUS improves procedural results due to optimal balloon sizing leading to a significant improvement in luminal dimensions (20). Despite the utility of IVUS, it is infrequently used routinely because of the added time, complexity, interpretation of images, cost, and training associated with its usage. Angiography, on the other hand, is used clinically routinely but lacks accuracy for sizing because of spatial resolution and because quantitative coronary angiography uses edge detection, which assumes a circular vessel for noncircular diseased vessels.

The objective of this study was to introduce a catheter that provides lumen size measurements continuous in time (at a spatial point) or continuous in space (average over cardiac cycle) but overcomes some of the limitations with IVUS and angiography for lumen sizing. Accordingly, we have previously introduced a 2.7-Fr conductance catheter that allows the accurate measurement of coronary and peripheral vessels at any point along the vessel (10, 11). Here, we extended the measurements to a time-averaged profile (along the length of a vessel segment) of coronary arteries using the LumenRECON (LR) system. Specifically, the objective of this study was to provide a preclinical validation of the LR system as an accurate method of measuring a coronary artery luminal cross-sectional area (CSA) profile in real time. The safety, accuracy, and reproducibility of the LR system were compared with IVUS in a group of normal and atherosclerotic swine and in postmortem human coronary vessels.
Innovative Methodology

LR Catheter and System

The LR system is composed of a catheter, electrical cable, and console. The catheter is a multilumen, rapid exchange, 2.7-Fr catheter with a main lumen for 0.014-in. wire guide access (the rapid exchange port is 12 cm from the distal tip). The remaining lumens contain electrical leads for measuring electrical impedance with electrodes near the tip, which deliver a very low nonstimulating voltage current (50 μA at 5 kHz) to the lumen of the artery. The catheters are connected to a system console using an electrical cable, where the distal end of the cable connects to the catheter and the proximal end of the cable connects to the console. The system control console contains an end-user system interface, records electrical signals from the catheter, calculates vessel CSA, and displays the graphical representation of the average (peak systolic and diastolic) luminal CSA or diameter profile.

Accuracy Measurements

Phantoms. The accuracy of the LR system was determined in phantoms of known diameters. CSA measurements were performed at room temperature in six Plexiglass tubes of known CSA ranging from 3.1 mm² (2 mm in diameter) to 19.6 mm² (5 mm in diameter). Each of the six tubes was filled with saline solution, and the catheter was placed into the tubes in turn to measure the CSA. The placement of the catheter was intentionally set completely off center (against the wall) to mimic the likely device position in vivo. Similarly, the IVUS was placed against the wall of the tube, and measurements of the CSA were made for each known phantom size.

Animals. Animals were fasted overnight and sedated with telaxol (500 mg), ketamine (250 mg), and xylazine (250 mg) before intubation. All animals were ventilated via a mechanical respirator with general anesthesia maintained via 1–2% isoflurane and oxygen. All animals were monitored, including ECG, blood pressure, and other vital signs. All animal experiments were performed in accordance with national and local ethical guidelines, including Institute of Laboratory Animal Research guidelines, Public Health Service policy, the Animal Welfare Act, and an approved Indiana University-Purdue University Indianapolis Institutional Animal Care and Use Committee protocol regarding the use of animals in research.

Coronary access was made via a standard femoral artery approach where a 7-Fr guide catheter was used to access the coronary ostia and a guidewire was inserted into the selected coronary artery to facilitate device placement. After the guidewire placement, the LR catheter was then advanced distal to the region of interest. The location of the LR catheter was verified via fluoroscopy with an injection of Omnipaque contrast material with an iodine concentration of 350 mg/ml.

The baseline blood conductance was recorded (ratio of electrical current to voltage) in the coronary artery as shown in Fig. 1. Measurements were made using an injection of 1.5% NaCl solution and a 0.45% NaCl solution for each segment reconstruction as detailed in the appendix. A 10-ml syringe containing a 1.5% NaCl solution was attached to the guiding catheter, and up to 10 ml were injected over 2–3 s with the LR system recording the electrical conductance in the lumen of the coronary artery (Fig. 1A).

The saline-induced increase in conductance with the displacement of blood by the solution was obvious, as shown in Fig. 1B. The peak value of conductance was taken for the CSA calculation (appendix). The first syringe was removed, a second solution was attached to the introducing catheter, and an injection of up to 10 ml of 0.45% NaCl was made over 2–3 s while the LR system recorded the change in conductance (Fig. 1B). The decrease in conductance with the 0.45% NaCl solution was apparent, as shown in Fig. 1B. The minimum value of conductance was measured to determine the CSA (appendix).

The LR catheter was then retracted over the length of the vessel segment or lesion, during which the LR system measured return conductance signals from the coronary artery (Fig. 1C). After the catheter had been retracted 3–4 cm within 4–5 s, the two NaCl injections were repeated as previously described using the 0.45% NaCl solution followed by the 1.5% NaCl solution. As with the first injections, the LR system measured return conductance or voltage since a constant current was applied through the excitation electrodes.
The axial profile and corresponding CSA data were recorded and outputted in real time. The 1.5% and 0.45% injections were made in eight animals (6 normal swine and 2 athrosclerotic swine). In another six swine, the method was repeated with 0.9% and 0.45% NaCl (i.e., normal and half-normal saline). The 1.5% NaCl solution has been previously found to produce accurate measurements with the two-injection method (9). Here, the rationale was to determine if 1.5% NaCl can be replaced with normal saline for ease of clinical utility.

Upon completion, the LR catheter was withdrawn and the IVUS (Discovery 40 MHz, Boston Scientific) catheter (model BS, Atlantis SRpro) was advanced to the same distal region previously measured with the LR catheter. The location of the IVUS catheter was verified via fluoroscopy with an injection of contrast material and angiography using branches as markers. Angiography also gave an approximation via fluoroscopy with an injection of contrast material and angiography with the LR catheter. The location of the IVUS catheter was verified with automatic pullbacks with stops at 1-cm intervals along the 3- to 4-cm-long segment.

**Postmortem Human Hearts**

Two athrosclerotic human hearts were obtained from the coroner’s office. Hearts were transported to the laboratory in 4°C Krebs solution within 2 h of harvest. The right coronary artery (RCA) or left anterior descending coronary artery (LAD) was cannulated with a 6-Fr sheath and perfused with saline. A three-way stopcock also connected the RCA or LAD to the two solutions of NaCl (0.5% and 0.9%, respectively). The impedance catheter was inserted through the sheath into the lumen of the artery. Approximately 5 ml of 0.5% NaCl were then infused into the coronary artery, by changing the direction of the stopcock, in a 5-s interval, and the corresponding CSA was measured followed by perfusion of 0.9% NaCl in an identical manner. LR pullback measurements were made for every 1 cm over an 8-cm length. The corresponding points were measured with IVUS.

**Safety**

**ECG and Hemodynamics.** ECG and blood pressure were monitored in the 14 animals that had LR and IVUS lumen CSA measurements. Any electrical changes during the NaCl injections (1.5%, 0.9%, and 0.45%) were noted and monitored postinjection. We made similar observations with contrast injections.

**Histopathology.** Eight chronic normal animals had the LR and IVUS catheters randomly placed into the RCA, LAD, and left circumflex artery (LCX) and then removed to assess safety of the devices. The arterial wall was histologically evaluated 1 day and 2 wk (4 animals each) after the placement of the devices. All acute animals (12 Yorkshire swine and 2 Ossabaw swine) were subjected to the same histopathological assessments of the chronic experiments.

The chest was opened through a midsternal thoracotomy, and an incision was made in the pericardium to reach the heart. Animals were deeply anesthetized followed by an injection of a saturated KCl solution through the jugular vein to arrest the heart. The aorta was clamped to keep air bubbles from entering the coronary arteries, and the heart was excised and placed in a cold saline solution. The coronary arteries of interest were cannulated through the aorta and perfused with 0.9% saline solution to flush out the blood. Vessels were individually perfused at a physiologically distending pressure of 100 mmHg with 6.25% glutaraldehyde solution in 0.1 M sodium cacodylate buffer (total osmolarity of the fixative: 1,100 mosM). Hearts were refrigerated in the fixation solution for at least 24 h before preparation for histological analysis. The main trunks of the coronary arteries were then carefully excised and trimmed of excess tissue.

The main trunks of the coronary arteries were cut perpendicular to their long axes into 3- to 5-mm serial rings from the origin of the coronary artery to where the tip of the LR catheter was placed. Vessel rings were then rinsed three times with a buffer solution, processed by dehydration in increasing concentrations of alcohol (70%, 80%, 95%, and 100%), and embedded in glycol methacrylate (JB-4 solution, Electron Microscopy Sciences). The embedded segments were cut into 3-μm-thick sections using a conventional microtome (HM 340E, Microm), mounted on glass slides, and stained with toluidine blue. The histological sections were then photographed using a Spot Insight Color digital camera (Diagnostic Instruments) attached to a histological microscope (Eclipse E600, Nikon).

**Statistical Analysis**

The relation between the IVUS and LR diameter (D) measurements was expressed as follows: \( D_{\text{LR}} = \alpha D_{\text{IVUS}} + \beta \), where \( \alpha \) and \( \beta \) are empirical constants that were determined with a linear least-squares fit and a corresponding correlation coefficient \( (R^2) \). In a Bland-Altman diagram, we plotted the differences between the two measurements of diameter against their means \( (1) \). In a scatter diagram, the precision and bias of the method can be quantified. We also determined the root mean square (RMS) error to further assess the reliability of the technique. Finally, we assessed the repeatability of the technique by making measurements in duplicates. The duplicates were made with a single insertion, i.e., with the impedance catheter in the same location, two sets of two injections were made to determine duplicate diameters. We calculated the mean and SD of the differences to assess reproducibility.

**RESULTS**

**Accuracy**

**Phantoms.** Figure 2 shows the measurements of accurately drilled phantom dimensions ranging between 2 and 5 mm with both the LR system and IVUS. All LR and IVUS measurements were within 3% and 13% of the actual measurements, respectively. The IVUS measurements always overestimated the actual phantom diameters.

**In vivo.** The CSA measurements from the LR system were made in real time, whereas the IVUS measurements were made offline. Although an infinite number of measurements can be made with the LR system because the CSA profile is determined continuously during the pullback along the vessel, comparisons were made with the respective IVUS measure-
ments only at the 1-cm measurements made with IVUS. The two sets of analyses were compared in a blinded manner.

The objective was to estimate the mean and SD of the difference in diameter as measured by the LR system and IVUS in healthy and Ossabaw pigs. The 1.5% and 0.45% injections resulted in similar measurements as the 0.9% and 0.45% NaCl injections (no statistically significant differences), and hence the data were lumped together, as presented below. A total of 73 IVUS measurements were made in the RCA ($n = 10$), LAD ($n = 41$), and LCx ($n = 22$).

The relation between the LR system and IVUS was expressed by a linear least-squares fit as follows: $D_{IVUS} = 0.82D_{LR} + 0.68$ ($R^2 = 0.809$; Fig. 3A). The limits of agreement for the comparison between the LR system and IVUS, as calculated using the method proposed by Bland and Altman, were −0.67 and 0.78 mm, as shown in Fig. 3B. This result can be interpreted to represent that 95% of the CSA as measured by the LR system will be within approximately ±0.72 mm of the IVUS measurements. Additionally, the mean difference (0.055 ± 0.36 mm) of the CSA was not statistically significant from zero ($P > 0.05$ by the Wilcoxon signed-rank test), indicating a lack of bias in the comparison of the LR system with IVUS.

Figure 4A shows the repeatability of LR measurements made in duplicates. A linear least-squares fit of the relation between the two measurements was expressed as follows: $D_{I2} = 0.90D_{I1} + 0.33$ ($n = 26$, $R^2 = 0.966$), where $D_{I1}$ and $D_{I2}$ are the two LR diameter measurements. The percent difference in the two measurements was plotted against the mean value, as shown in Fig. 4B. The mean percent difference was nearly zero (0.028%), as expected since the same method was used. The SD was found to be 4.5% of the mean of the two measurements, which was defined as the repeatability coefficient.

Figure 5 shows the vessel segment profile (mean over cardiac cycle) measured by the LR system and compared with IVUS measurements at selected points for a normal swine (A and B) and an Ossabaw swine (C). The profile showed either a relatively constant diameter (Fig. 5A) or a more tapered segment (Fig. 5B). The IVUS measurements were superimposed for comparison and showed agreement.

**Atherosclerotic Swine**

The Ossabaw model has been shown to develop atherosclerotic lesions on a high-fat diet (21). In two animals, vessel CSA was measured with the LR system and IVUS. The vessel showed primarily diffuse disease, as shown in Fig. 6C, which reduced the diameter of the proximal LAD significantly ($3$ mm compared with typically $>4$ mm) despite a much larger body weight ($100$-kg Ossabaw swine compared with $60$-kg Yorkshire swine).

**Postmortem Human Hearts**

Figure 6 shows the relation between the histological diameter measurements and both the LR system and IVUS. Although this is a small sample (multiple measurements from 2...
hearts), we can see that there is a better agreement between histology and the LR system than histology and IVUS. IVUS overestimated every measurement, as reflected by the IVUS data always being above the identity line. The variance in the IVUS measurements was also greater, although the data set was too small to make quantitative conclusions.

**Safety**

**Vitals.** Safety was assessed by characterizing the type and frequency of any adverse events. The LR catheter has a soft, tapered tip, similar to the IVUS catheter. Hence, it was confirmed to be of no more risk than the IVUS catheter. The two NaCl solutions (normal and half-normal saline) injected are deemed safe. During some injections, we observed transient changes in the T waves during the duration of injection (2–3 s) and several cardiac cycles after the injection. These T wave changes were transient and were completely restored to baseline morphology several seconds after the injection. These changes were similar to those found with contrast injections. All animals survived all sets of measurements and were euthanized at the conclusion of the study for histological evaluation.

**Histopathology.** The endothelium of all acute experiments that had both LR and IVUS interventions were evaluated and found to be normal. The 1 day and 2 wk postintervention animals were evaluated after placement of the LR catheter and IVUS catheters in different arteries. The insertion of the device resulted in no evidence of mural injury (e.g., no laceration or perforation, etc.), inflammation, thrombosis, hemorrhage, or necrosis. The insertion of the LR system resulted only in minimal intimal hyperplasia and recruitment of inflammatory cells to the endothelial layer similar to the response from IVUS catheter. There were minimal histopathological differences between the acute, subacute, and chronic experiments, and there were no noticeable histopathological differences between the LR and IVUS catheter vessels.

**DISCUSSION**

A stent is a cylinder that can be defined by two dimensions (diameter and length). A simple, accurate, objective, and real-time method to provide the size (proximal and distal diameters) and length of the lesion for stent sizing is important. Despite the utility of IVUS to provide such information, routine use has been hampered by the added time of the procedure, the training required to interpret the images, and the potential inaccuracies in the tomographic measurements. The LR system can provide the proximal and distal dimensions as well as the length of the lesion accurately in real time. The system requires minimal training to operate the simple Windows-based system, and the measurements are direct and objective (i.e., require no interpretation). Furthermore, the reconstruction of lumen CSA can be done both in space (along the length of the vessel) and time (throughout a cardiac cycle), all in real time. The former was validated in this study, whereas the latter is the focus of an ongoing study. Finally, no calibration of the catheter is required by the user, and the device is simply connected to the console and is ready for measurement. The catheter-based sizing system is safe, accurate, reproducible, quantitative, and easy to use, as discussed below.

**Accuracy and Reproducibility**

Phantoms. In phantoms of known diameters, the accuracy of LR measurements are within 3% of actual dimensions (diameter range of 2–5 mm) and the reproducibility is within 2% (data not shown; Ref. 10). IVUS measurements, on the other hand, were in error by as much as 13% of actual diameter (especially for larger dimensions with the catheter off center) for the system used. There has been a report of significant IVUS errors (up to 27% in CSA) depending on the system and catheters used (17).

**In vivo.** Although we found good agreement between LR and IVUS measurements, the scatter in the present study is...
significantly higher (about twice the RMS; Fig. 3) than that previously reported (11). In the previous study, we compared the LR system with B-mode ultrasound at the same time and same spatial point because the LR electrode could be directly visualized using the ultrasound. Accordingly, we found 4.8% RMS in diameter of the LR compared with B-mode ultrasound, while the repeatability of LR diameter measurements was 2.4% (~50% of the values found in the present study). The scatter in that data was larger than that of the previous study as there are several inherent sources of error given the present method of comparison. The underlying assumptions are that the measurements are made 1) at exactly the same point in the vessel, 2) at the same time in the cardiac cycle, and 3) under similar vessel conditions. Although none of these conditions can be strictly met in the validation protocol, as detailed below, we used IVUS as it is considered the “gold standard.”

Since it is inherently required that we make each of the LR and IVUS measurements at the same location, we have to estimate the location of each of the respective catheters and corresponding measurement sensors. This was accomplished with the aid of markings on the catheters and angiographic landmarks (i.e., vessel bifurcations, ribs, and other distinguishable structures). This is clearly an approximation, and, in regions where the vessel tapered, an error can be expected that may account for some of the data scatter. Furthermore, it is estimated that the lumen diameter changes by ~10% through the cardiac cycle in normal vessels. The LR system considers the average (peak systolic and diastolic) dimension of the vessel, and we attempted to match the IVUS measurements accordingly. Several IVUS images were measured through a cardiac cycle to determine a mean value, albeit there is still some inevitable error. Finally, the introduction of any guidewire or catheter (IVUS or LR) has the risk of inducing vasospasm of a normal vessel (especially in the swine model) due to endothelial stimulation. Although we standardized the protocol to give a vasodilator before each of the two respective measurements, some degree of vasospasm may still be present. In two animals, significant vasospasm was observed (>20% difference in diameter), and those measurements were excluded. In the less obviously visible cases, some degree of vasospasm will lead to scatter of data (Fig. 3).

Postmortem Human Hearts

Unlike IVUS, which assumes a certain velocity of sound in the vessel wall, there is no assumption about wall impedance or conductance in the LR system. Although a normal vessel wall is not assumed but is rather calculated in each measurement. Although the atherosclerotic swine has significant intimal hyperplasia and diffuse disease (Fig. 5C, as confirmed histologically), we investigated more severe plaque and calcifications in two postmortem human hearts. The results (Fig. 6) showed better agreement between LR and histology than IVUS. Interestingly, IVUS overestimated all histological measurements. Although it can be argued that histological preparations can cause shrinkage of tissue, we do not believe that to be the case here, for two reasons. First, the vessels were severely calcified, as evident by touch and confirmed histologically. Second, we used a histological fixation and preparation protocol that our group has validated as reliable with no significant shrinkage (2).

Comparison with IVUS

The accuracy of tomographic IVUS measurements is based on some assumptions. An ideal perpendicular angle of incidence of the ultrasound beam to the vessel wall requires a catheter position in the center of the lumen and parallel to the long axis of the vessel (4). A number of factors, such as curvature or tortuosity of vessel, wall irregularities, or dissections, may preclude this condition. The eccentricity of the catheter (near the wall) is the rule rather than the exception. This error is more evident as the diameter of vessel increases (i.e., more potential error for peripheral vessels), as confirmed by the phantom measurements (Fig. 2). Eccentric catheter positions have already been reported as a source of overestimation and distortion of lumen area in IVUS studies of both coronary (8, 15, 16, 18, 19, 22–24) and peripheral vessels (6, 9, 14). Both transducer obliquity and vessel curvature can produce an elliptical image that overestimates the true dimensions (13). Furthermore, significant over- and underestimation of the true CSA have been observed with different catheters and IVUS systems (17). Finally, the interobserver variability is also well known for IVUS and was significantly larger than the 4.5% interobserver variability (Fig. 4) observed for the LR system (5).

The LR system, on the other hand, does not make any such assumptions as the method is based on an electrical impedance principal. The impedance method provides the direct CSA with no assumptions about circularity or shape. The CSA measurements can be made accurately regardless of the geometry of the vessel or lesion geometry. Furthermore, the measurement does not depend on the centricity of catheter or relation to the long axis of the vessel (10). Hence, the measurement can be made accurately even when the catheter is immediately adjacent to the wall and in a curved or tortuous vessel. IVUS does, however, allow the direct visualization of the arterial wall and has been of significant value in the assessment of percutaneous coronary intervention trials and for the evaluation of cardiovascular therapies (12).

Critique of Methods

The major fundamental assumption of the proposed method is to fully displace the blood with the NaCl solution transiently during the injection. This requires good engagement of the introducing catheter to allow a brisk flush, similar to a contrast for an angiogram. It is easy to recognize a good injection as one expects an abrupt upward deflection of conductance with the higher conductivity solution and an abrupt downward deflection of conductance with the lower conductivity solution (Fig. 3, A and B, respectively). Hence, predictable and reliable measurements can be made with good engagement injections. The injections do not cause a significant increase in local pressure, and, hence, the measurements reflect the in vivo distensions (11).

Significance

This is the first report of a novel catheter-based system that provides continuous real-time quantitative measurement of lumen segment CSA in normal and diseased vessels during a standard pullback procedure. Currently, no imaging method
(e.g., angiography or IVUS) has the spatial or temporal resolution to provide the axial contour of the vessel segment and the phasic changes throughout the cardiac cycle in real time. The device and method were found to have good accuracy compared with IVUS and excellent reproducibility. The Bland-Altman analysis showed that the mean differences between the two methods were not statistically significant. The device and method were also found to be safe with no acute or chronic changes in the vessel wall as a result of the interventions. The device and system warrant clinical validation.

**APPENDIX**

The Spatial Reconstruction of a Vessel Segment

The algorithm contained within the LR system for the reconstruction of a vessel segment in real time is outlined below and consists of several sequential steps.

1. **Step 1.** Calculate total conductance \( (G_{\text{total}}; \text{current divided by voltage, or } I/V) \) for two ends (proximal and distal) of a segment.
2. **Step 2.** Calculate the Coeff ratio \( (\text{CSA divided by } G_{\text{total}}) \) at the two ends of the segment.
3. **Step 3.** Linearly interpolate along the length of the pull back for the Coeff ratio, so that the two ends of the segment have the same Coeff values calculated from step 2 above.
4. **Step 4.** Calculate \( G_{\text{total}} \) for the entire length of the pull back (distance between the two ends of the segment).
5. **Step 5.** At each point calculated in the pull back, multiply the \( G_{\text{total}} \) times its respective Coeff value. The product of this calculation is the CSA value.

The diameter of the segment can be found where the two injections are made, and those values may then be used to linearly interpolate across the profile. Once a Coeff value for every point in the pull back is determined, those Coeff values are multiplied by their respective \( G_{\text{total}} \) values to determine the CSA values along the profile, namely:

\[
\text{CSA} = \text{Coeff} \times G_{\text{total}} \quad (A5)
\]

and

\[
\text{Diameter} = \frac{4 \times \text{CSA}}{\pi} \quad (A6)
\]

to determine a cylindrical diameter if desired.

**REFERENCES**


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