REVIEW

Stent visualization methods to guide percutaneous coronary interventions and assess long-term patency

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Abstract

Evaluation of acute percutaneous coronary intervention (PCI) results and long-term follow-up remains challenging with ongoing stent designs. Several imaging tools have been developed to assess native vessel atherosclerosis and stent expansion, improving overall PCI results and reducing adverse cardiac events. Quantitative coronary analysis has played a crucial role in quantifying the extent of coronary artery disease and stent results. Digital stent enhancement methods have been well validated and improved stent strut visualization. Intravascular imaging remains the gold standard in PCI guidance but adds costs and time to the procedure. With a recent shift towards non-invasive imaging assessment and coronary computed tomography angiography imaging have shown promising results. We hereby review novel stent visualization techniques used to guide PCI and assess stent patency in the modern PCI era.

Key Words: Percutaneous coronary intervention; Stent visualization; Stent underexpansion; Quantitative coronary analysis; Digital stent enhancement; Intravascular ultrasound; Optical coherence tomography; Coronary computed tomography angiography

Core Tip: Evaluation of acute and long-term percutaneous coronary intervention (PCI) results remains challenging. We hereby review current available tools for guiding and assessing PCI results.

INTRODUCTION

Atherosclerosis is a slow-progressing multifocal immunoinflammatory disease of medium and large-sized arteries[1]. Exposure to established risk factors triggers an oxidative response leading to the formation of fatty streaks within the vessel wall. Phagocytosis of these lipid rich proteins by macrophages induces cell apoptosis leading to cellular debris which, along with necrotic endothelial and smooth muscle cells, form the principal constituent of the lipid-rich plaque core. The deposit of calcium and phosphate-rich hydroxyapatite crystals occurs as a macrophage-mediated response to oxidation and endothelial dysfunction[2]. Coronary artery disease (CAD) secondary to atherosclerosis remains the most common cause of death across the globe, imposing a major health and economic burden on nations[3,4]. Despite major technological and therapeutic advances, the prevalence of CAD is expected to continue to rise secondary to an increase in the aging population[5]. Coronary artery angiography (CAG), despite being invasive, remains the gold standard technique to assess significant coronary artery disease and to guide percutaneous coronary intervention (PCI). PCI reduces major cardiac events in acute coronary syndrome events[6] and improves the quality of life in chronic coronary syndrome[7]. The first human cardiac catheterization dates back to 1929 when Dr. Forssmann[8] auto-measured the pressure in his cardiac chambers using a urinary catheter. Cournand *et al*[9] and Nossaman *et al*[10] later developed right heart catheterization with a standard diagnostic tool, and in 1956, along with Dr. Forssmann[8], were awarded the Nobel Prize in Medicine for their work. Dr. Seldinger[11] developed his safe percutaneous catheterization technique in 1953 followed by Dr. Sones[12] who performed the first selective coronary angiogram in 1958. In 1964 the first peripheral angioplasty was performed by Drs. Dotter and Judkins[13]. Since then, PCI has undergone a rapid technological evolution, beginning with Turina *et al*[14] in 1979 who developed the initial coronary balloon angioplasty, later referred to as plain old balloon angioplasty (POBA). POBA was the first step for modern coronary intervention and was limited by the risk of acute thrombosis (3%-8%)[15,16] and early vessel recoil (5%-10%), along with a high rate of restenosis (33%)[17-22]. Nevertheless, POBA paved the way to the first coronary stents that were implanted in 1986 by Sigwart *et al*[23]. Although the recent ISCHEMIA trial did not show evidence of a reduced risk of ischemic cardiovascular events or death for an initial invasive strategy as compared with optimal medical treatment among patients with stable angina and moderate or severe ischemia[7], only 4% of contemporary real-world patients would be eligible for the trial[24]. Using coronary physiology guidance, PCI also decreases cardiac death and myocardial infarction in chronic coronary symptoms[25]. Several trials (BENESTENT, STRESS, CAVEAT) have laid the cornerstone upon which angiographic guidelines have been proposed, and coronary stent implantation after PCI has been shown to improve short- and long-term clinical outcomes[26-28]. However, a coronary stent should meet numerous design criteria in order to fulfill its function, including the fact that the stent platform must be radio-opaque enough to provide the required visibility for correct placement and proper expansion in order to ensure successful stent deployment[29,30]. In addition, a stent must have a narrow profile when collapsed for easy deliverability[31,32]. Strut thickness has been a key element of stent design, with thinner struts associated with greater deliverability. Several studies have also shown a lower rate of restenosis associated with thinner stent' struts[31,33,34]. Consequently, a move towards thinner struts stents has been made, with current stent strut thickness being between 60-100 µm. Initial stents were made of nitinol and were self-expandable. These were later replaced by balloon expandable stents.

Atherosclerosis is an intimal focal disease-causing connective tissue proliferation and lipid accumulation. In order to preserve their lumen, atherosclerotic vessels dilate in a remodeling response and only after reaching the capacity of this response does stenosis occur. These facts imply that an accurate assessment of coronary artery stenosis and reference diameter is of major importance. Lesion severity evaluation by visual estimation remains subjective and has been shown to be inadequate secondary to a high degree of intra-observer and inter-observer variability[35]. In fact, the lumen in eccentric plaques alters in shape and size, and the reference segment (deemed as normal) may be either narrowed or dilated. For decades, PCI guidance and results have been evaluated by visual assessment, nevertheless, angiography alone does not provide sufficient information in several scenarios presenting a major risk factors of stent thrombosis, such as stent fracture, stent malapposition or stent overlap[29,36,37]. To study PCI efficacy and results, several carefully acquired coronary angiographic films need to be interpreted in detail pre- and post-intervention, as well as at follow-up. Alternative imaging techniques have been developed to overcome these

limitations. We hereby review the coronary stent visualization methods currently used for the assessment of PCI results.

QUANTITATIVE CORONARY ANALYSIS

Since visual assessment of lumen diameter and stenosis is scarcely sensitive, quantitative coronary analysis (QCA) was first described for a theoretical objective evaluation of coronary artery stenosis and lumen diameter in clinical settings. Since then, the field has grown substantially, with several methods and algorithms being developed since the late 1970s[38]. The European Society of Cardiology-European Association of Percutaneous Cardiovascular Interventions Task Force on the Evaluation of Coronary Stents in Europe recommended a mandatory assessment by offline QCA core lab analysis in case of comparative studies[39], and QCA was endorsed by the Academic Research Consortium 2[40]. QCA relies on coronary angiography in order to obtain objective parameters and can also be used to assess immediate and long-term PCI results[38]. It is based on the use of dedicated software allowing the precise determination of specific parameters in an operator-independent manner and can serve either a clinical purpose (on-line during a procedure) or a research one (off-line)[41]. With ongoing research, X-ray imaging has significantly progressed, leading to many available computer-integrated applications that allow the quantification of coronary stenosis leading to QCA validation and incorporation in various systems[42]. Multiple validated software are currently available on the market, among which the most widely used are CAAS II (PIE Medical, Maastricht, The Netherlands) and QAngio XA (Medis, Leiden, The Netherlands)[43-45].

QCA requires an optical magnification of the angiographic image. A digital cineangiogram is generated on an image processor after image acquisition. Using an integrated software and analysis system, digital quantification of selected frames can be easily performed with or without magnification. After digitalization, and prior to computer analysis, the images are stored in a specifically designed image processing system.

The real challenge of QCA is the selection of the coronary angiography sequence with a minimal foreshortening and minimal overlap with nearby structures after intracoronary nitroglycerine administration in order to reduce any vasospasm. In addition, the accuracy and reliability of the analysis is improved by increasing the distinction between the contrast-filled coronary artery and the background (best achieved while the patient is in deep inspiration). A frame including a completely contrast-filled catheter is first selected and a central line is hand-drawn along the tip of catheter. Once the image has been acquired and processed, boundary delineation within the area of interest is performed by the computer. QCA usually focuses on one or more coronary segments and is generally carried out in the case of an ambiguous coronary lesion. The area of interest can be identified automatically by the computer software or manually. The operator indicates the window of interest, an approximation of the borders or points along the vessel's central line[46,47]. The software automatically recognizes its margins and performs calibration. In order to derive quantitative information from the analysis, a calibration converts measured pixels to *in vivo* millimeters by using the contrast-filled known catheter diameter as a reference standard or using an automatic calibration obtained from recent systems[48]. By assuming a homogeneous distribution of contrast within the vessel lumen, the errors within the edge definition are minimized in eccentric lesions by densitometry[38]. Then, an appropriate frame that includes the segment of interest is selected during end-diastole when coronaries are least subjected to myocardial contractions. Similar to the calibration procedure, a central line is drawn in order for the software to generate automatic contours. The frames are then automatically transferred to a digital lossless compression file that generates a series of diameters and parameters along the vessel line expressed in millimeters and percentages. This also allows an automatic reconstruction of the vessel lumen and interpolates the diseased segment to the proximal and distal references considered disease-free using an algorithm based on the calculation of mean diameter values at different points along the segment of interest (Figure 1). Edge definition, although more important than quantification, is harder to accomplish[48]. The difference in luminal cross-sectional area can then be compared between normal and diseased segments in addition to the assessment of PCI results. The analysis can also be performed after stent implantation in order to compare several parameters pre- and post-stent implantation. Hence, QCA permits the evaluation of the minimal lumen diameter (MLD, the smallest diameter within the
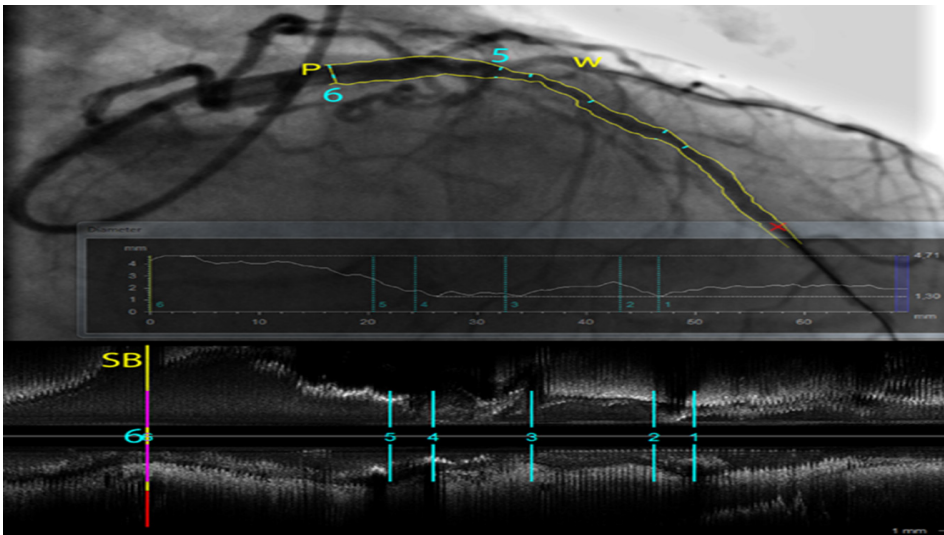
Figure 1 Quantitative coronary analysis analysis (CAAS software, Pie Medical Imaging) of a long stenosis in a left anterior descending artery. The vessel borders are automatically detected and diameters are plotted along the vessel centerline. Different measurements (1-6) are shown on a co-registered intravascular ultrasound (IVUS) pull-back longitudinal view at the bottom. At P (6), the ostium free of disease of a large side branch (first diagonal artery) is better characterized in the 3D volume data from the IVUS pull-back than on the overlapping structures of the angiogram. (W) shows a wire in the second diagonal branch, illustrating the inherent limitations in the interpretation of a coronary angiography that is only a 2D shadow projection of a complex 3D coronary tree filled with contrast that requires multiple views in different projections.

segment studied), the reference vessel diameter (RVD, averaged diameter of the coronary assumed disease-free), the diameter stenosis percentage, the lesion length (LL, measured by two points where the margins change direction), the acute gain (post-procedural MLD-pre-procedural MLD), and late loss (post-procedural MLD-follow-up MLD for example at 6 mo). On-line digital systems and off-line computer processing systems have become widely available. These systems facilitate the accurate clinical analysis of vessel diameter, percent stenosis, stent deployment, and other endovascular interventions. One of the major coronary angiography drawbacks is its two-dimensional luminogram of a three-dimensional structure, as well as vessel overlap and foreshortening during acquisition. Furthermore, QCA is influenced by the frame selection, vessel movement, end-diastolic phase and calibration[49,50].

THREE-DIMENSIONAL QCA

Currently, 2-dimensional QCA remains the most commonly used and validated technique despite its drawbacks. However, as more complex lesions are treated more frequently, 3-dimensional QCA analysis software is a valuable tool. Three-dimensional QCA is based on standard 2-dimensional angiography images obtained in two views at least 30 degrees apart and with as much minimal vessel overlap. Several 3D QCA programs are currently available, among which, the most commonly employed and validated are CAAS 5 (Pie medical Imaging, Maastricht, The Netherlands) and CardiOp-B (Paieon Medical Ltd. Park Afek, Israel)[51-53]. Although these applications defer in their respective calibration methods, nevertheless they allow a better understanding and visualization of coronary anatomy and help the operator find the optimal working angle[54,55]. Three-dimensional QCA software also allows the assessment of bifurcating lesions and helps choose the appropriate treatment strategy [56].

Although 3-dimensional QCA programs are readily available and have already been validated[55,57,58], they fail to improve accuracy by resolving the problem of vessel foreshortening. Several comparative studies between 2-dimensional and 3-dimensional QCA have led to mixed results with regards to the accuracy of this technology[55,57,59-61].

Visual assessment of coronary lesions tends to underestimate < 50% stenoses and to overestimate those > 50%[62,63], while QCA tends more to overestimate lesions < 50% than those between 50% and 75% and underestimate stenoses > 75%[41,64]. QCA may be easily and rapidly employed in everyday clinical practice to objectively, precisely and independently assess coronary lesion severity. Hence, QCA may direct treatment

of a stenosis if a functional assessment is not available. Additionally, QCA instantly assesses objective parameters, such as RVD and lesion length, allowing for a more precise choice of treatment material as well as PCI result assessment. QCA has also played a pivotal role in clinical research through its reproducibility and independence. It has become a fundamental core laboratory tool for the off-line assessment of devices and/or the progression of atherosclerosis following pharmacological therapies[65].

Although QCA has been around for more than 30 years now, it still presents multiple limitations. Nevertheless, it remains an easy-to-use tool, both when used in clinical research and as a complementary tool in practice alongside angiography.

DIGITAL STENT ENHANCEMENT

Stent positioning and deployment is carried out under angiography guidance and hence relies on the radiopaque nature of the material used for visualization. Long-term safety concerns of implanted coronary stents have led to increased research on the improvement of stent technology. It has been stipulated that thinner struts are associated with a better outcome in drug-eluting stents (DES). The ISAR STEREO trials have identified thicker struts thickness to be an independent predictor of in-stent restenosis[33,34,66]. Furthermore, the use of thinner-strut stents has been associated with a significant reduction in myocardial infarction[67]. In addition, inadequate stent deployment and underexpansion has been shown to be a major factor for stent thrombosis associated with a high death rate and non-fatal myocardial infarction[29, 68]. With recent advancements in stent design technology, DES has become the standard-of-care for patients with acute and chronic coronary syndromes. The first DES consisted of a stainless-steel backbone rendering them radiopaque with good visibility on angiography. However, given the inverse relationship between strut thickness and fibrous hyperplasia, newer second-generation DES have switched to cobalt chromium or platinum chromium, along with a trend towards thinner struts decreasing stent radiopacity, all while preserving radial strength. Although the incidence of stent thrombosis has decreased during the first year after implantation as compared to BMS, its rate remains high[69]. Stent architecture assessment is also important in order to assess PCI results and complications. With the trend toward the use of lower X-ray power during procedures at 7.5 frames per second, and despite the use of radiopaque materials in stent construction, the visualization of stents remains challenging and insufficient for stent expansion assessment. Stent visibility is further altered with stent motion within the sequence as well as in larger patients due to X-ray scattering.

Since the early 2000s, a new image processing technique called digital stent enhancement (DSE) has been developed, specifically tailored for stent visualization. In order to produce an enhanced image of an implanted stent, DSE uses a motion-corrected X-ray image sequence making it reliable during the normal workflow during coronary angioplasties[70]. Due to the ease of use of this technique, several manufacturers have become interested in developing and validating new systems.

Although they cannot bring direct information regarding stent apposition onto the vessel wall, DSE systems can provide relevant images for assessing deployment irregularities, lesion treatment, and potentially measuring stent expansion[71]. Several case reports and case series have validated the use of the different DSE systems in different clinical settings. Additionally, a decrease in late loss and binary restenosis, along with a lower incidence of target lesion revascularization at 6 and 12 mo respectively, were found in patients where DSE was used as compared to patients treated without DSE[72].

StentBoost Subtract System® (Philips Healthcare, Best, The Netherlands) is currently the most used technique and is extensively validated[73-77]. StentBoost Subtract System has also been shown to have high enough specificity as compared to intravascular imaging[73,78]. StentViz (GE Healthcare, Milwaukee, WI, United States), StentOptimizer (Paieon, Rosh Haayin, Israel) and ClearStent (Siemens Healthcare, Munich, Germany) have also been studied and validated[79-81]. Nevertheless, these systems all depend on the X-ray angiographic system vendor. StentEnhancer (Pie Medical, Maastricht, The Netherlands) is a recently added DSE with the advantage of being vendor independent.

DSE improves the fluoroscopic image quality by reducing the influence of background noise. It consists of a short X-ray sequence where the stent is moving with each heartbeat and during breathing. This is based on the fact that over a whole sequence, the sum of the images of the stent is displayed with a much higher contrast

to noise ratio. Hence, the DSE algorithm "tracks" the stent motion along the sequence and automatically integrates the value of the stent' pixels along their trajectories. As a result, the overall sum of the pixels is displayed in an enhanced still-image.

After stent deployment, the stent delivery balloon is kept in place deflated and cineacquisition of the stented segment is performed without contrast injection. Stent-motion is detected using the two balloon radiopaque markers[70,82]. Forty-five frames are acquired and automatically transferred to a workstation where software corrects for motion-compensated temporal averaging[83,84]. Immediately after, an enhanced image of the stent is displayed with an improved resolution and a superior signal-to-noise ratio (Figure 2). These steps may be repeated with a post-dilation balloon. A modified DSE technique, aimed at visualizing the stent in relation to the vessel, is also available. This differs from the abovementioned technique by the contrast injection [84]. The resulting image can be used for stent expansion assessment, visually and quantitatively, much like during QCA analysis[85-87]. Its ease-of-use and availability, along with the high-quality stent images delivered, have led to DSE being an important alternative or complement to stent visualization techniques during PCI. DSE systems are rapid, cost-effective, do not require contrast injection and can be used during complex PCI cases, such as ostial or bifurcating lesions[74,88]. However, an increase in radiation exposure has been reported, but this had no significant impact on patient radiation dose[89].

INTRAVASCULAR IMAGING

Coronary angiography only provides a planar, 2-dimensional evaluation of the contrast-filled coronary lumen and fails to evaluate the atherosclerotic plaque located within the arterial wall, hence often underestimating the degree of intraluminal stenosis[35]. The addition of quantitative digital assessment (QCA and DSE) improves the overall coronary assessment but still presents pitfalls. In fact, extensive coronary disease with positive remodeling may appear "normal", leading to a false feeling of reassurance. This is especially apparent with patients presenting with extensive disease on computed tomography angiography but found to have minimal disease on angiography. In order to bypass these limitations, the idea of intravascular imaging emerged in 1971, thanks to Bom *et al*[90] in Rotterdam, and Yock *et al*[91] later recorded the first greyscale transluminal ultrasound images of human arteries. Since then, major breakthroughs have been achieved including intravascular ultrasound (IVUS) radiofrequency tissue characterization and optical coherence tomography (OCT). Intravascular imaging has the advantage of capturing plaques from close proximity. These techniques have been a valuable tool in everyday practice shedding light on whether the plaque is at risk of progression, vessel diameter size, acute PCI results and reasons behind target lesion failure and revascularization.

IVUS

IVUS imaging relies on the properties of ultrasound waves which are produced by the oscillatory movement of a transducer[92]. A piezoelectric crystal inside a transducer, attached to a catheter, produces high frequency sound waves which penetrate tissue, reflect off vascular structures and return to the transducer, which then transmits the information to a dedicated system for processing. These catheters are 3.2 to 3.5 French in size and compatible with 5 French guiding catheters over 0.014 in guidewires.

The first ultrasound imaging catheters, designed by Bom and colleagues, were used for cardiac chamber and valve assessment. It was not until 1988 that the first intracoronary images were recorded[93]. Since then, IVUS has been extensively used and developed, and has been the cornerstone of major interventional trials, from the bare metal stents era to the newer bio-absorbable stents (BVS). In addition, IVUS has allowed a better understanding of CAD progression, vessel reaction to PCI, as well as long- and short-term vessel remodeling after stent implantation.

In order to increase radial resolution, IVUS catheters use higher frequencies than non-invasive echocardiography, typically between 20 and 60 MHz. Resolution increases with increased frequency, however penetration decreases. Currently, 2 types of IVUS catheter designs exist on the market: a solid-state, phased array one and a rotational, mechanical one. Solid-state catheters (Volcano, Philips Healthcare, Best, The Netherlands) consist of multiple transducer elements mounted circumferentially at the tip of the catheter. The phased-array transducers are activated in groups in a rotational
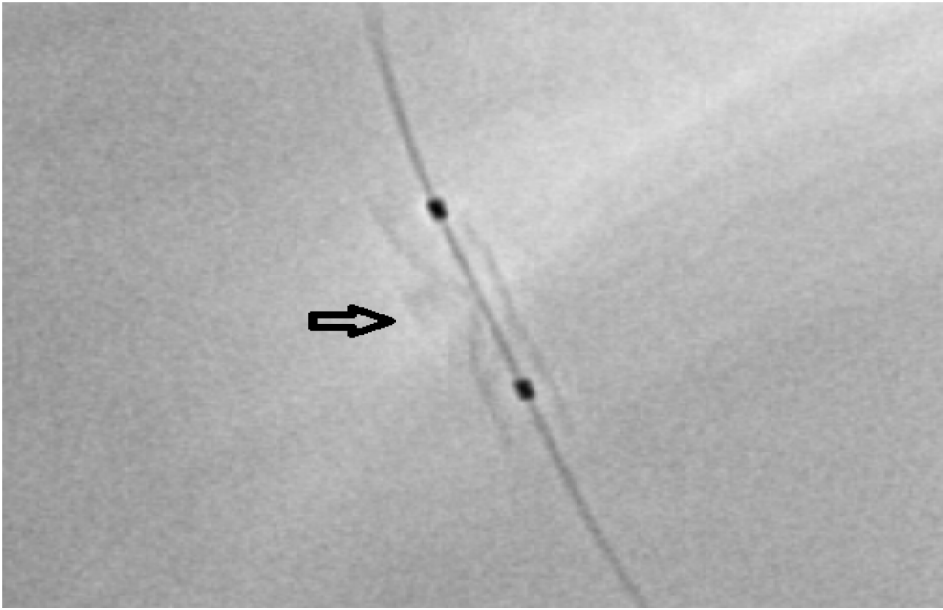
Figure 2 Digital stent enhancement image using StentBoost Subtract System (Philips Healthcare, Best, The Netherlands) showing stent underexpansion. The two balloon markers are visible (two black dots). The calcifications responsible for the underexpansion are clearly visible (arrow).

manner. The collected information is then transferred to a computer system which computes a cross sectional image of the vessel. Volcano catheters also offer kind of virtual histology, (VH-IVUS). The advantage of a solid-state system is its prepackaged ease of setup along with the lack of guidewire artefacts. This is because the catheter is advanced on the wire itself, meaning that there are no non-uniform rotational distortion (NURD) artefacts, which usually result from mechanical binding, as in this case there is no friction on the catheter. On the other hand, solid-state catheters have a low resolution, running at 20 MHz, and a blind spot all around the imaging ring, with a need for masking this "ring down" zone by digital subtraction before acquiring images. Rotational systems (Boston Scientific, Santa Clara, CA, United States; Terumo Corporation, Tokyo, Japan; Philips Healthcare, Best, The Netherlands; Acist Medical Systems Inc., Eden Prairie, MN, United States) use a single transducer element at the tip of the catheter rotated by an external motor drive attached to the catheter. Similar to solid-state systems, a cross sectional image is displayed after gathering echoes while the catheter rotates. Rotational systems have the advantage of having a significantly higher axial resolution with transducers up to 60 MHz with a large bandwidth. Nevertheless, rotational system setup is somewhat more cumbersome with the need to flush the catheter. They use a short monorail with, consequently, an artefact of the wire running along the imaging crystal. However, this offers a more stable automated pull-back of the imaging tip inside a sheath for length measurements of vessel structures. In order to perform imaging, the catheter is advanced beyond the area of interest over a 0.014 in. guidewire after a 100-200 mcg intracoronary nitroglycerin injection in order to minimize vasospasm and to have maximal vasodilation. The catheter is then pulled back in order to obtain the desired images either manually or automatically (motorized) at a standardized speed (up to 10 mm/s). Motorized pull-back has the advantage of providing longitudinal information of the area of interest in order to assess lesion length, while manual pull-back provides a more detailed and prolonged view of the area of interest. Regardless of the system used, proper identification of the three histologic vessel layers is critical for an accurate interpretation (Figure 3). The major advantage of IVUS imaging is its ability to see both intraluminal and extra-luminal elements in the vessel (coronary thrombus, edge dissection after stenting, *etc.*). It also allows for accurate and reproducible measurements of several segments of the vessel. In fact, the proximal and distal reference vessel segments can be identified and measured, along with the minimal lumen area (MLA), minimal and maximal lumen diameter, lumen eccentricity, area stenosis, cross section area (CSA), plaque area and burden, and the remodeling index can be computed. IVUS can also guide PCI, evaluate stent expansion, assess side branch compromise, determine the underlying mechanism of stent thrombosis/underexpansion and evaluate tears of the vessel from coronary dissections[94]. Although IVUS presents many advantages, several pitfalls remain. The displayed image relies on the absorption and reflection of
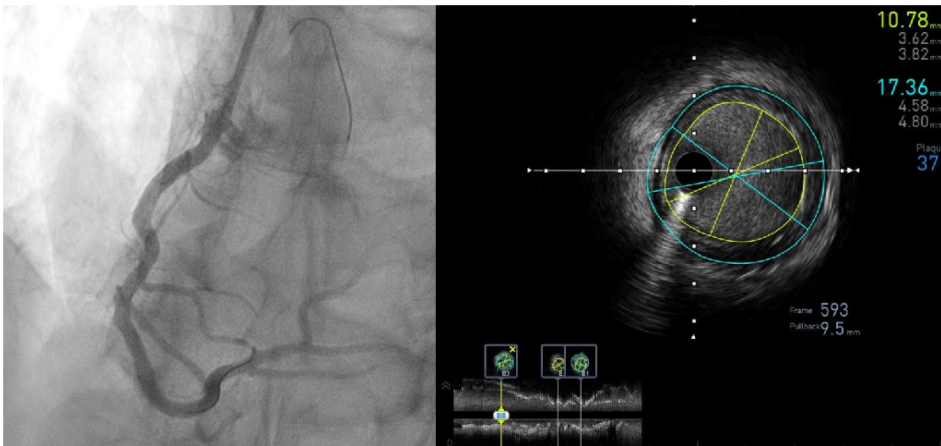
Figure 3 Intravascular ultrasound pull-back of a right coronary artery post stent implantation. Stent expansion is assessed and the minimal lumen area measured in different cross-sections (bottom longitudinal view) while the plaque burden at the distal reference (B3) is shown on the cross sectional frame 593 (lumen area 10.78 mm², vessel area 17.36 mm², plaque burden 37%).

ultrasound waves from tissues and, in the presence of calcium, which is a high reflector, all the ultrasound waves are reflected and do not penetrate beyond the underlying tissue. This reveals reverberation artefacts and shadowing behind the calcium with no possibility to analyze the extent of plaque and vessel structure behind the calcium. A wire artefact during IVUS images analysis may result in shadowing and difficulty seeing beyond the wire. Accurate analysis, especially with longitudinal measurements, can be hindered between systole and diastole secondary to the catheter movement[95]. In addition, blood speckle artefacts increase as blood flow decreases or the transducer frequency increases, hampering the ability to differentiate lumen from tissue, especially in the case of soft plaques and thrombus.

IVUS guided PCI has been shown to increase the choice of balloon and stent size by the PCI operator, increase the length of the stented segment, and increase the minimal lumen diameter and stent CSA at the end of the procedure as compared to angiography alone. Mixed results were found in multiple prospective studies during the bare metal stent era as to whether this increase improved clinical outcome[96-99]. In a meta-analysis, Parise *et al*[100] found a reduced 6-month angiographic binary restenosis with a significant reduction in revascularization rate and major adverse cardiac events in IVUS-guided PCI patients. Several retrospective and prospective studies were conducted during the DES era showing a net benefit of IVUS on overall clinical outcomes[101,102]. Several meta-analyses highlighted the net benefit of IVUS-guided PCI using DES with a significant reduction in major adverse cardiac events, myocardial infarction, target vessel revascularization, target lesion revascularization and stent thrombosis as compared to angiography guided PCI[103-105]. Recently, the 3-year follow-up of the ULTIMATE trial showed a reduction in cardiovascular death, target vessel failure and stent thrombosis in patients who underwent IVUS-guided PCI as compared to patients who underwent angiography-guided PCI alone[106,107]. With the treatment of more complex lesions, IVUS has been shown to improve mortality in left main stenting, probably due to a better stent apposition and lower rate of underexpansion[108-110], as well as in bifurcating lesions in order to predict side branch closure[111]. Moreover, IVUS is currently recommended for evaluating and guiding chronic total occlusion procedures[112,113].

VH-IVUS uses advanced backscatter signal analysis in order to try to characterize plaque composition. VH-IVUS limitations are the lack of thrombus detection and plaque characterization in the presence of calcium shadowing, and a limited resolution.

Despite the introduction of high definition IVUS catheters, the major limitation of IVUS imaging remains its limited spatial resolution, making the assessment of stent-strut tissue coverage challenging.

OCT

OCT is a light-based intravascular imaging technique that provides a high-resolution image of the tissue microstructure by using backscattering and near-infrared light

reflections from a fiber optic wire coupled with an imaging lens while simultaneously being pulled back and rotated. The first OCT clinical application on coronary arteries was reported in 1991 after the addition of transverse scanning[114]. The rapidly evolving technique was named by James Fujimoto and made way to contemporary OCT catheters that use a central light wavelength range of 1300 nm, which limits tissue penetration to 1-3 mm as compared to IVUS. With an axial resolution of 10-15 μm, OCT offers a very detailed picture of the vessel while the imaging optics of the catheter allow for a lateral resolution of 20-40 μm.

The first available OCT systems from LightLab Imaging (Westford, Massachusetts, United States) used an old OCT technology, called time-domain (TD) OCT, based on a broadband light source emitting through a fiberoptic coupler. The main disadvantage of this system was the slow speed of acquisition, which resulted in the need of total vessel flush for a long period. Newer generation OCT systems, termed Fourier-domain OCT (FD-OCT), use a fixed mirror and light is emitted by a "swept laser" source with a variable frequency. This allows for a faster frame acquisition rate (up to 100 frames/s) with only a short vessel flush duration. Continuous flush of contrast fluid is required in order to clear intraluminal blood since blood causes significant signal attenuation. The first FD-OCT was developed by St. Jude Medical (St Jude Medical, St. Paul, Minnesota; United States). It is a 2.5 Fr catheter compatible with 5 Fr guiding catheters. Currently a 2.4 Fr catheter is also available from Terumo (Terumo Corporation, Tokyo, Japan). The OCT catheter is advanced over a 0.014 inch wire to the distal vessel and an automated pull-back is then performed at a rate of up to 20-40 mm/s during short iodinated contrast injection (4 cc/s) in order to clear blood. During pull-back, a long spiral scan is created within less than 3 s in order to map the vessel and create the required frames. The emitted light splits into 2 parts: the first sample arm travels to the patient while the second reference arm travels a predefined distance. The two arms are then collected and an interferometer is used to measure the light reflected (back-scattered) from tissues in order to determine the depth of the tissue (A line). The system then processes the reflected light and computes a very high-resolution image due to the shorter wavelength of light and 3D tissue morphology.

Each image is made up of lines and pixels; the higher the lines/frames ratio is, the finer the image, and the higher the frame rate, the higher the longitudinal resolution. Artefacts associated with OCT include light attenuation from incomplete blood flushing, artefacts secondary to the guidewire, distortion of stent reflections from eccentric wire position (sunflower effect), air bubble artefacts, and stitch artefacts secondary to rapid catheter or wire movements (sew-up effect). These can be minimized through a proper positioning of the guidewire and appropriate contrast injection[115]. Even macrophage accumulation in thin-cap fibroatheroma or small intraluminal thrombi can be seen[116]. Plaque characterization can be achieved by OCT combining backscattering and attenuation measurements[117].

Currently, limited data for OCT-guided vs. angiography-guided interventions are available, while ongoing randomized clinical trials are running. A reduced rate of cardiac death and major adverse cardiac events has been reported in patients who underwent OCT-guided stenting[118], as well as larger final in-stent minimal lumen diameter[119] and a reduction in the number of stents implanted[120]. OCT-guided PCI has also been associated with better clinical outcomes in acute coronary syndrome patients[121,122]. In addition, a better stent coverage at 3 mo was found in OCT-guided PCI chronic CAD patients[123].

OCT delivers high-resolution intravascular images which are used in clinical practice, but mainly in the research field[124,125]. As compared to IVUS, OCT showed comparable stent expansions and comparative efficacy in the ILLUMIEN II and III studies respectively[126,127]. OCT was also shown to have non-inferior clinical outcomes as compared to IVUS in the OPINION[128] study. The latest European Society of Cardiology guidelines have included IVUS and OCT imaging as a class IIa recommendation[129]. Although both imaging modalities share multiple similarities, some controversy remains regarding which modality is to be used in specific cases. The need of contrast injection during OCT imaging tends to be a trigger towards IVUS use in patients with renal failure. The very high resolution of OCT images enables a more detailed evaluation at the endoluminal level and superficial plaques, and better stent implantation short- and long-term results[130]. However, OCT has lower penetration depth as compared to IVUS, which makes larger vessel visualization more challenging, in addition to the external elastic membrane-based approach for vessel sizing. IVUS images are significantly altered by the presence of calcium whereas OCT recognizes calcium plaques as well-demarcated low-intensity structures. The relatively smaller size of OCT may reduce the incidence of coronary spasm, and can identify coronary thrombosis and dissection easily. However, OCT fails to assess aorto-ostial

lesions. Several clinical studies have demonstrated the non-inferiority of OCT imaging as compared to IVUS (OPINION, ILLUMEN III)[127,131].

Co-registration of both OCT and IVUS with angiography has been developed[132] adding to the precision during PCI and reducing the risks of geographic miss[94,115]. An OCT/IVUS hybrid technology (Novasight) has been recently introduced, and further developed by Conavi Medical Inc. (Toronto, Canada), and this was reported in 2018[133]. A second hybrid system is currently under development by Terumo (Terumo, Tokyo, Japan) and is yet to be released.

Intravascular imaging has marked its place during PCI offering multiple benefits over angiography alone. Multiple meta-analyses and registries have proven its improved procedural and clinical outcome. However, intravascular usage rate remains low probably due to the increased cost, time and unfamiliarity of the operators[134]. With increasing PCI complexity, intravascular imaging adds a clinically proven indispensable benefit for successful intervention.

CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY

Coronary computed tomography angiography (CCTA) has recently emerged as a precise non-invasive tool for the detection and evaluation of CAD[135,136]. Computed tomography (CT) technology has advanced significantly since its first use, by Sir Godfrey Hounsfield in 1970, followed by the introduction of electron beam computed tomography by Douglas Boyd improving temporal resolution. A major breakthrough came in the 1990s with the introduction of multidetector computed tomography that has the ability of improving a 360° spatial resolution. CT images depict tissue densities and are the product of X-ray attenuation as they pass through tissue. A CT detector measures and converts the X-ray photons exiting the patient into light. This light is then transformed into an electrical signal by a photodiode and converted into a digital signal by a computer system. The image is an overall estimation of the attenuation of X-rays as they pass through tissues of different densities represented by Hounsfield units.

Currently, multidetector computed tomography scanners include 320-detector rings and two X-ray sources, allowing for the acquisition of submillimeter resolution over large volumes in milliseconds. Improvements in detector characteristics have increased the x, y and z axis spatial resolution, which allows for successful imaging of the coronary arteries while reducing radiation dose[137]. Three steps are required to successfully create a CCTA image: data acquisition, reconstruction and image display. Data acquisition involves scanning portions of the heart with each gantry rotation and requires proper patient selection, preparation, appropriate imaging protocols and contrast injection techniques. Effective heart rate control, proper timing of the scan after contrast injection and minimizing patient movement are all crucial during data acquisition. It is therefore advisable for patients known to have arrhythmias to be deferred from CCTA. CCTA has the advantage of visualizing the entire vessel, and can accurately evaluate stenoses severity and plaque morphology.

Along with CCTA already being established for the detection of CAD and confirming the ability of calcium score in providing a prognostic value in multiple large studies[137-139], it is an excellent diagnostic tool for bypass graft imaging. Moreover, CCTA has been validated and used for the assessment of coronary artery stent with recent technical refinements showing negative predictive values >90% for the exclusion of in-stent restenosis[138,140-142]. However, a blooming effect secondary to the stent struts and beam-hardening artefacts remain a challenge for proper evaluation[143,144]. This is also true for patients known to have excessive coronary calcium, as calcifications may interfere with the accurate interpretation of CCTA. Since coronary stenosis alone does not predict the risk of future cardiovascular events, the coronary artery calcium (CAC) score estimates the overall calcification burden and predicts future ischemic events without contrast use. With the introduction of bioresorbable stents (Figures 4 and 5), this set-back has been overcome[145,146]. Contrary to magnetic resonance imaging (MRI), pacemakers and defibrillators do not preclude the use of CCTA, however it should be noted that their leads may create artefacts.

CCTA has been shown to be a better predictor of obstructive CAD compared to traditional functional testing. The EVINCI study showed the superior accuracy of CCTA for the detection of CAD as compared to single photon emission CT (SPECT), position emission tomography (PET), echocardiography and cardiac MRI[147]. The prognostic value of CCTA was also demonstrated in the PROMISE and SCOT-HEART
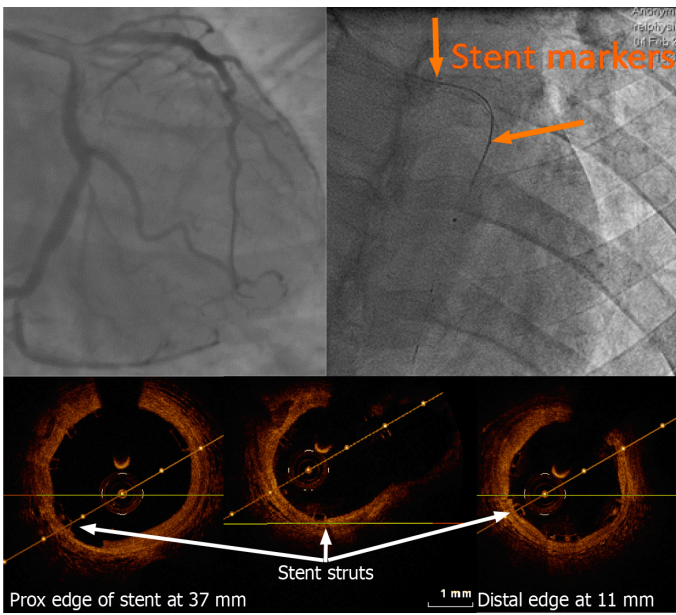
Figure 4 Left anterior descending artery optical coherence tomography pull-back post bioresorbable stent implantation carried out using a 2.7 French imaging catheter with a dedicated workstation (C7 Dragonfly and C7-XR, Lightlab Imaging [Westford, Massachusetts, United States)]. Of note, only the proximal and distal markers are visible. On optical coherence tomography (OCT), the thickness of the stent struts and its good apposition can be assessed without artefact as seen with conventional metallic struts. Stent length could be measured on the OCT pullback with a good agreement with the known stent length.
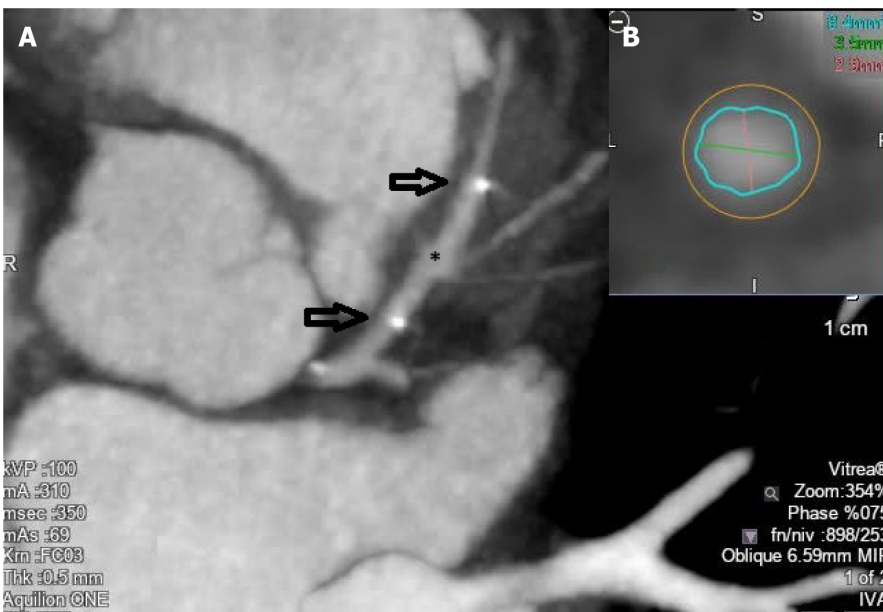
Figure 5 Coronary computed tomography angiography image of a bioresorbable stent (asterisk) implanted at the level of the proximal left anterior descending artery (A) (the two arrows represent the two radiopaque stent markers), and cross sectional cut allowing for lumen measurements (B).

studies which showed high CCTA prediction of cardiovascular events as compared to functional testing and standard care[139,148]. A meta-analysis showed a significant reduction of myocardial infarction as well as an increased incidence of coronary revascularization with no effect on all-cause mortality using CCTA in patients with chronic coronary syndrome as compared to usual care[149].

Observer variability and expertise remain a challenge for CCTA interpretation. Dedicated software programs for increasing automation and identifying high-risk plaques have been validated as well as newer technologies, including fractional flow reserve (FFR) derived from CCTA (FFR$_{CT}$), perivascular fat attenuation index (FAI) and wall shear stress (WSS)[136]. Advances in imaging modalities permitted a 3-

dimensional reconstruction of the coronary artery tree and a decrease in radiation exposure[150]. Myocardial perfusion by CCTA is also possible and allows for the assessment of the physiologic consequences of stenoses[136]. It has evolved as a valuable tool in guiding PCI and assessing lesion characteristics, especially in chronic total occlusion (CTO) lesions using co-registration with angiography[151]. In the acute disease setting, CCTA fails to differentiate between a thrombus and acute plaque hemorrhage.

CCTA technology still has a lot to offer in the future. It has been a useful and promising tool in the assessment and tracking of atheromatous plaques, improving understanding of early atherosclerosis.

CONCLUSION

The success of stent implantation during PCI procedures depends on proper positioning of the stent, expansion and apposition, all of which reduce the rate of major adverse cardiac events. Traditional two-dimensional angiography alone fails to fully assess the result of stent implantation. Pre-procedural measurement of the vessel diameter along with post-procedural evaluation of the strut-level and minimal lumen area and diameter improve clinical outcomes. Despite the substantial technological advances, a growing need for newer and more accurate tools for PCI guidance and assessment has emerged with the increasing number of complex procedures performed worldwide and ongoing stent technology advances.

Quantitative coronary analysis has developed substantially since its early beginnings due to its research and clinical uses both on-line and off-line. Recent 3-dimensional QCA systems have also emerged, providing more reliable assessment of lumen dimensions[152]. The ease-of-use and reproducibility of QCA analysis has made it widely available within PCI centers worldwide. However, several limitations persist and QCA measurements are lower compared with other imaging modalities [153]. Furthermore, QCA measurements are limited for diffuse lesions, as the reference diameter tends to be underestimated[50].

Digital stent enhancement imaging has been thoroughly validated for stent underexpansion. It allows for easy visualization of areas of stent underdeployment for positioning of post-dilation balloons. DSE has been reported to be associated with better angiographic and clinical outcomes[72] as well as stent fracture identification. DSE adds little additional time to the procedure, provides a better image resolution as compared to angiography with no risk of mechanical complications while using less contrast. It has been found to be particularly useful for obese patients, long lesions, in-stent restenosis and bifurcating lesions[77,86,154]. Although the accuracy and resolution of DSE is lower than intravascular imaging, measurement of stent diameters correlated well[71,73,87,153,155]. Its main drawback could be the increased radiation dose, however this does not have a significant impact on the patient[86]. DSE remains a useful and rapid tool that can be used in conjunction with intravascular imaging during PCI.

Intravascular imaging remains the gold standard during PCI and has demonstrated low complication rates. Several randomized controlled trials and observational studies have established the role of intravascular imaging-guided stent implantation during PCI with a reduction in major cardiac events and target vessel revascularization[105]. Compared to angiography, intravascular imaging-guided PCI has been shown to have a relative reduction of cardiovascular death, a lower risk of myocardial infarction, a decreased risk of target vessel revascularization and a reduction in the rate of stent thrombosis[105]. In addition, the greatest benefit of intravascular imaging guidance may be in complex lesions and stent failure patients. The non-inferiority of OCT as compared to IVUS in guiding PCI has been demonstrated in several clinical trials and meta-analyses[128,131,137,153,156]. Clear differences exist between the two technologies. OCT offers a higher resolution along with finer details, whereas IVUS has a better penetration and does not require flushing the lumen with contrast. IVUS and angiography co-registration systems have been tested and validated and provide valuable information. Furthermore, more recently, a 3-dimensional reconstruction of the coronary tree using IVUS co-registration allowed for further detailed information about vessel size, plaque size, shear stress and hemodynamic studies at every position along the vessel[152].

Thus, intracoronary imaging provides an accurate evaluation of coronary anatomy and plaque evaluation during PCI allowing for optimized stent sizing while avoiding stent malaposition, underexpansion and stent edge dissection, all in addition to an

accurate assessment of the stent result. However, its routine use in clinical practice remains low and highly variable, mainly due to the added procedure cost and time. Progress is still ongoing within the field, with further advances on the way using OCT/IVUS hybrid console systems.

With the ongoing paradigm shift towards non-invasive imaging, new reconstruction techniques have significantly improved coronary artery stent imaging by CCTA. The European Society of Cardiology recommends the use of CCTA for the evaluation of CAD for low to intermediate risk patients in the setting of chronic and acute coronary syndromes[157,158]. With its high specificity (97%), CCTA could be used to exclude in-stent restenosis[159]. The CAC score used during CCTA remains an important tool for future cardiovascular ischemic events. Artefacts secondary to the stent struts hinder the accurate evaluation of the stent lumen, however, with higher scan-detector row systems and thinner stent struts, an improved image quality can be achieved using CCTA. In addition, in the PLATFORM trial[160], the introduction of FFR_{CT} reduced the number of patients referred for invasive angiography by 61%. CMR allows the reduction of the contrast dose without compromising image quality. Both CCTA and CMR can easily and accurately assess coronary bypass grafts along with performing myocardial perfusion and a 3-dimensional reconstruction of the vessels. Furthermore, the introduction and on-going progress of newer generation bioresorbable stents have made CCTA an attractive tool for the evaluation of PCI results, as artefacts are greatly decreased[149,161].

In conclusion, invasive angiography remains the gold standard tool for the treatment of CAD and the visual guidance and evaluation of PCI results however, the conjunction and advances of several readily available alternative and complementary tools improve its sensitivity and accuracy.

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