A Comparison of Angiography Versus Intravascular Ultrasound In The Treatment Of Peripheral Arterial Disease

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A COMPARISON OF ANGIOGRAPHY VERSUS INTRAVASCULAR ULTRASOUND IN THE TREATMENT OF PERIPHERAL ARTERIAL DISEASE

By

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Submitted in Partial Fulfillment of the Requirements for Graduation with Honors from the South Carolina Honors College

May, 2014

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# TABLE OF CONTENTS

THESIS SUMMARY ........................................................................... 2

INTRODUCTION ............................................................................... 5

TREATMENT ..................................................................................... 5

IMAGING MODALITIES ................................................................. 6

STENOSIS ....................................................................................... 9

VESSEL WALL MORPHOLOGY ....................................................... 11

PLAQUE SHAPE ............................................................................. 12

PLAQUE MORPHOLOGY ................................................................. 13

VIRTUAL-HISTOLOGY IVUS (VH-IVUS) ........................................... 14

PLAQUE CALCIFICATION ............................................................... 16

TECHNICAL GUIDANCE ................................................................. 17

COMPLICATIONS ........................................................................... 21

LIMITATIONS ................................................................................ 23

CONCLUSION ................................................................................ 24

REFERENCES ................................................................................. 25
Thesis Summary

Peripheral Arterial Disease is a growing epidemic throughout the United States. It is estimated that 8 to 12 million Americans currently suffer from PAD, a disease of the circulatory system that limits blood flow to your hands and feet. This limited blood flow is due to the narrowing of the arteries that supply blood throughout your body and can disrupt the balance of the nerves and tissues that make up your extremities. If left untreated, it can cause irreparable, life-threatening damage that may result in amputation of the diseased limb. Although the mechanism of PAD is known and well understood, different treatment options are still being researched and evaluated in order to fully understand which is the most effective and efficient for each clinical presentation.

The least invasive treatment options are lifestyle changes, including the implementation of exercise regimes or medical therapy in an effort to control the primary causes of PAD. However, these may be met with limited success, and greater more invasive intervention may be necessary. Surgical treatment options usually include the use of a long wire to reach the obstructed region of the blood vessel and remove the plaque. In rare cases, it may be necessary to use a man-made artery in order to create an alternate route for blood to flow around the occluded segment. All of these surgical interventions require the use of an imaging technique in order to both navigate through the arteries to the obstructed segment and view the plaque accumulation inside the vessel.
Angiography has long been considered to be the best method for navigating through the different arteries of the leg, even though its ability to view the accumulated plaque is adequate at best. In recent years, intravascular ultrasound has shown to be capable of providing more accurate details regarding the vessel lumen, plaque shape, and composition as compared to angiography. A greater understanding of these components aids in both the diagnostic and treatment process. Intervening physicians are able to gain a greater understanding of where the obstruction is located and how bad it is, which allows them to better decide if intervention is necessary. In addition, in the event that intervention is warranted, greater knowledge regarding the plaque shape and composition allows them to choose the interventional technique that will produce the best outcome for the patient.

The solution to the current lack of information most likely comes in the form of using IVUS in adjunct with angiography during interventional procedures. This would allow the intervening physician to both navigate to the right location and view the extent of the plaque accumulation. IVUS, however, is currently limited by its cost of implementation, which can range anywhere from $70,000-$120,000 for a basic system, in addition to a $600 disposable catheter tip per patient. As research continues to develop, new solutions and technological advancements may help lower the costs of the existing technology.
Introduction

Peripheral arterial disease (PAD) is a disease of the circulatory system classified by the narrowing and hardening of the arterial wall due to the buildup of fatty deposits called plaque. PAD affects at least 8 to 12 million Americans, and one in every three people 70-years of age or older has PAD. As plaque fills the arterial wall, blood flow distal to the obstructed region is reduced. If the blood volume provided to the distal vasculature is not sufficient to keep up with the tissue’s oxygen demands, damage to the nerves or tissue may occur. There are many risk factors – conditions that increase the risk of disease or infection – associated with PAD, including: smoking, old age, diabetes, hyperlipidemia, hypertension, and renal insufficiencies. These risk factors may also lead to other co-morbidities such as Coronary Artery Disease and heart attacks or strokes. If left untreated, PAD can progress into a Critical Limb Ischemia, a more serious form of PAD that can result in chronic pain and/or numbness in the feet or toes, nonhealing wounds or ulcers, tissue necrosis (gangrene), and even amputation of the affected limb. PAD is also likely to be a sign of widespread accumulation of fatty deposits within the arteries of other areas of your body.

When diagnosing patients suspected of PAD, physicians utilize a sliding scale of diagnostic tests ranging from least invasive to most invasive. Although each patient’s presentation will ultimately determine his or her treatment, the general procedure is as follows. After collecting their medical and family history, the physician usually conducts a physical exam that checks blood flow for weak
or absent pulses and compares blood pressure between the left and right side of the circulatory system (measured at the brachial artery of each arm). Then, further non-invasive testing is conducted in order to determine the general progression of atherosclerosis. The Ankle-Brachial Index compares blood pressure in your ankle to blood pressure in your arms, with a normal reading ranging from 0.9 to 0.13. The Segmental Leg Pressures test leg pressures at the ankle, below the knee, above the knee, mid-thigh, wrist, below the elbow, above the elbow, and mid upper arm. By identifying the location with the greatest drop in blood pressure, it is possible to narrow down the location of the possible arterial occlusion to a certain segment.

**Treatment**

Treatment begins with lifestyle changes that minimize the risk factors for PAD, such as the implementation of exercise regimes or smoking cessation. In addition, medical therapy and pharmaceutical options may be undertaken in an effort to lower cholesterol, prevent blood clots, or minimize pain. Surgical treatments are only considered if the previously mentioned treatment options fail. Angioplasty and stenting procedures utilize a system of guide wires and catheters with a balloon at the tip. The tip is inserted into the artery and inflated, pushing the plaque outward into the arterial wall. A small mesh tube is then placed in the artery to help maintain the patency of the vessel. Atherectomy is a similar procedure in which the balloon tip of the catheter is replaced by a small cutting device that is inserted into the artery and used to remove the plaque
burden. Finally, the most invasive option, a bypass graft, uses a blood vessel from another part of the body or a man-made tube to bypass the occluded arterial segment. Amputation of the diseased leg is reserved as a last resort in the event that the patient’s life is in danger. Treatment decisions are ultimately dependent upon the characteristics of the stenosis as well as the symptoms and co-morbidities of the patient.

Imaging Modalities

Vascular surgeons, cardiologists, and radiologists alike rely heavily on imaging modalities for both diagnostic and procedural assistance when treating patients with PAD. Angiography has long been considered the “gold standard” for investigating the vessel lumen, defining peripheral vasculature, and providing arterial navigation during percutaneous procedures. Typically, cardiologists use a system of guide wires and catheters to inject a contrasting agent into the femoral artery. They can then use X-ray imaging to view the dye, which shows up by absorbing the X-rays, as it passes through the blood vessel of interest.

Angiography is capable of depicting characteristics of both the lumen and lumen-border interface, allowing for evaluation of atherosclerotic plaque burden and morphology. Image accuracy is limited by arterial wall motion artifact, vessel tortuosity, overlying structures, or overlapping vessels, which may reduce accurate interpretation regarding the extent of the plaque burden, although this can be overcome to some degree with multiplanar imaging. To produce multiplanar images, the arm of the X-ray machine is rotated to provide different
visual planes of the arterial lumen. Angiography depicts the contour of the lumen, but cannot quantitatively evaluate the level of atherosclerotic plaque buildup, often resulting in misleading interpretations of stenosis.\textsuperscript{5-6} In addition, luminal stenosis from angiography may not be in agreement with more accurate quantitative measurements by intravascular ultrasound or histological analysis.\textsuperscript{6} These discrepant results may make the need for endovascular intervention difficult to determine.

When treating patients suffering from PAD, the inability to objectively evaluate plaque burden, composition, morphology, and vessel wall architecture through angiography has led to underestimated arterial dimensions and degrees of stenoses, which further limits thorough evaluation of the various interventional options, let alone whether or not intervention is necessary.\textsuperscript{3-7} As a result, angiography may contribute to reduced long-term procedural success rates during endovascular interventions as compared to IVUS, resulting in increased rates of restenosis, thrombosis, and other post-procedural complications. Although the intervening physicians are dependent on angiography for arterial navigation, intravascular ultrasound (IVUS) has shown potential to assist in both diagnostic and interventional procedures by providing intraluminal cross-sectional images with higher image resolution than angiography.

Similar to angiography, IVUS utilizes a system of guide wires and catheters in order to collect information; however, IVUS deploys a miniature ultrasound device on the distal end of the catheter that allows the operator to see
through the surrounding blood column and visualize the inner wall of blood vessels from inside the vessel itself. Percutaneous IVUS catheters capture cross-sectional images that enable 360°-intraluminal visualization of peripheral vasculature. A revolving transducer on the catheter tip emits ultrasound waves during pullback of the probe through the vessel segment of interest. The axial scan uses a grey scale to differentiate amplitudes of reflecting ultrasound waves from different tissue types, enabling the categorization of different plaque types according to their composition. Calcified plaque reflects brightly because it impedes ultrasound waves, appearing white, while thrombus is much more hypoechoic and reflects dark grey. The close proximity of the probe allows for a higher frequency ultrasound to be used, which in turn provides higher image resolution and magnification compared to other imaging techniques. This enables more accurate assessment of vessel or lesion diameters and lengths, plaque shape, length, volume, composition, and concentricity, as well as the completeness of treatment after intervention. IVUS is also capable of stacking consecutive images in order to create a 3-D image of the plaque. These detailed images and cross-sectional measurements, when used in adjunct with angiography, can increase the capability and accuracy of diagnostic and interventional procedures for patients with PAD. Each image has the potential to uncover critical information that can be utilized to increase technical success and long-term outcomes.
Stenosis

Angiography details the continuity of the peripheral vasculature through representation of the vessel lumen. Evidence of stenoses can be measured through decreases in the luminal area; theoretically, as plaque begins to accumulate along the vessel wall the cross-sectional area should decrease and limit distal blood flow. However, histological analysis has shown that the elasticity of the external elastic membrane (EEM) allows the arterial walls to expand centrifugally in order to accommodate the accumulating plaque. Because of this positive remodeling of the EEM, the lumen area may remain unchanged until 40% of the cross-sectional area is filled with atheroma deposits. Only after full expansion of the arterial wall does further atheroma deposits begin to encroach into the lumen. Even with multiple projections, angiographic evidence of stenoses to support intervention is usually undetectable until the plaque covers 40-50% of the total cross-sectional area of the artery.

Kashyap et al. researched the effects of positive remodeling in minimally diseased arteries with apparent stenosis <30%. Both linear and area stenosis levels of popliteal artery segments were evaluated using angiography and histological analysis of the internal elastic lamina (IEL). They determined that their angiographic scoring of atherosclerotic burden (18.5%) consistently underestimated the level of atherosclerosis when compared with the histological findings (34.9%). Because angiography uses luminal diameter measurements to calculate geometric dimensions, both IEL and vessel area stenosis
measurements produced increasingly discrepant results compared to angiography, 39.2 (p<0.0001) and 60.9 (p<0.0001) respectively.³

While angiography repeatedly underestimates stenoses when compared with histological analysis, IVUS is capable of providing accurate luminal dimensions to monitor plaque progression, in addition to offering additional information on the arterial wall.⁴¹⁰ IVUS correlates as high as 95% with angiography when calculating luminal diameters, but is capable of determining true vessel wall dimensions in both diseased and normal arteries. These more accurate measurements account for positive remodeling and any plaque burden not identified by angiography, increasing the accuracy when computing stenosis area.¹¹ Using true arterial dimensions to compute the maximal percent area stenosis, IVUS determined a 10% degree of stenosis was unaccounted for by angiography, most likely because luminal diameter measurements do not account for positive remodeling.⁴

In addition to greater accuracy, IVUS is capable of surveying blood flow within the lumen when using frequencies greater than 30MHz. This information can replace subjective angiographic assessment of stenoses area with quantitative measurements, enabling more accurate evaluation of stenoses while still compensating for vascular remodeling.⁴⁸ The discrepancy between actual and inferred stenoses levels imposes severe limitations when evaluating the need for endovascular intervention.
Vessel Wall Morphology

Information on the interaction between plaque and the vessel wall is essential when investigating peripheral atherosclerosis. The cross-sectional diameter of the lumen is calculated with angiography by using the lumen diameter dimensions. However, this method is best suited for concentric lesions, as accuracy tends to decrease as the level of ellipticity increases. Angiography is unable to provide this information accurately because of its limited ability when defining dimensions of obstructed or irregular vessel segments. Angiography overestimates the true lumen cross-sectional diameter compared with IVUS for non-elliptical or irregular lumens because vessel wall architecture cannot be accurately determined. This can result in an underestimation of lesion stenosis in diagnostic studies or overestimation in the beneficial results of intervention.

Analysis of the high-resolution images captured by IVUS may provide insight into morphological characteristics of the vessel wall, plaque identification, and location of lesions. This additional information can be used to analyze mechanisms of plaque progression or recession and vessel-plaque interaction. In addition, the accurate measurements of maximum and minimum lumen diameters enable calculation of the ellipticity index for each IVUS image. The ellipticity index is the ratio of the maximum luminal diameter to the minimum luminal diameter and defines the ellipticity for individual images. As the index increases, the imaged lumen becomes more elliptic. Compared to angiography, IVUS images and their morphological analysis produce more detailed information...
regarding the location, eccentricity, and cross-sectional area of the lumen.\textsuperscript{12} Accurate interrogation of vessel wall morphology may also be beneficial for determining plaque characteristics, branch vessel location, and the extent of disease involvement.\textsuperscript{14}

**Plaque Shape**

Atherosclerotic plaque can accumulate in many different shapes and lengths depending on spatial location and composition, but lesions are generally classified as concentric or eccentric along with their fiber composition if it is known. The shape in which atherosclerotic plaque accumulates is largely determined by the curvature and elasticity of the inner arterial wall because atherosclerotic plaque components tend to coagulate in areas of low shear stress.\textsuperscript{2} Angiographic methods misrepresent plaque shape and volume because of limitations for determining true arterial dimensions and compensating positive or negative remodeling.\textsuperscript{7} While the operator can determine if stenosis is present, detailed anatomical characteristics are unreliable even with multiple projections of the diseased segment. On the other hand, the axial images IVUS produces allows for evaluation of both lumen and true arterial diameters. By comparing the true and luminal diameter measurements, it is possible to recreate the diseased segment in order to accurately identify plaque architecture and volume.

Arthurs et al. documented the disassociation of plaque shape between the two imaging modalities when they analyzed 93 patients with peripheral arterial disease. Their angiographic data showed a shorter length of stenosis at 14.3mm,
which underestimated the IVUS findings of 17.3mm by 3mm (20%). When examining lesion concentricity, their IVUS results produced over twice as many concentric lesions (60%) as compared to their angiographic results (28%), showing that the angiographic operators were much more likely to overestimate the ellipticity index for target lesions. In further evaluation of the findings from Arthurs et al., Kashyap et al. compared concentricity data from angiographic and histological plaque evaluations. Angiography underestimated plaque concentricity finding 23 of 59 (39%) plaque evaluations were concentric compared to 35 of 65 (54%) concentric plaque evaluations from the histological analysis. Because most atherosclerotic lesions are eccentrically located within the vessel, it would be necessary to use multiplanar angiographic views to adequately evaluate the degree of stenosis for a specific lesion. It is plausible to conclude that the increased accuracy for computed measurements and the more accurate concentricity findings are the result of the more accurate geometric data analysis from IVUS over other imaging modalities when determining both true and diseased diameters.

**Plaque Morphology**

When evaluating therapeutic options for PAD patients, plaque morphology and target lesion information are helpful in predicting success rates of different endovascular treatments. The information IVUS provides can help predict how the target lesion will respond to therapeutic procedures and predict its interaction
with blood flow and the vessel wall; these events will determine if the plaque will resist recoil and balloon/stent deployment or be liable to embolization, dissection, and/or perforation. Histological analysis can be used to analyze plaque characteristics and determine composition, but this cannot be done in vivo because the necessary tissue samples can only be obtained at autopsy.

Advancements in IVUS modalities, such as virtual histology IVUS (VH-IVUS) and integrated backscatter IVUS (IB-IVUS) have facilitated the collection of the necessary structural information in situ as well as the ability to assess plaque morphology.

**Virtual Histology IVUS (VH-IVUS)**

VH-IVUS is capable of providing valuable histological data for plaque by analyzing the frequency and amplitude of backscattered radiofrequency (RF) data and comparing the acquired information to RF spectral profiles based on the echogenicity of different tissue types. The reflecting signals are combined through a process known as synthetic aperture to recreate the image. When recreating the image, VH-IVUS uses the RF spectral profiles to classify lesions in situ into color-coded categories based on four different histological components of plaque: dark green: fibrous; yellow-green: fibro-fatty; white: calcified; and red: necrotic lipid core.

Although peripheral applications are still being researched, VH-IVUS in the coronary has proved to be fairly accurate when compared with histological analysis. Diethrich et al. compared thirty carotid plaque samples with their true
histological results and recorded high correlations between the two histologies, ranging from 72.4% (calcified fibroatheroma) to 99.4% (thin-cap fibroatheroma). The results showed a strong correlation between VH-IVUS and histological plaque characterization, especially in vulnerable plaque types, providing support to the diagnostic accuracy of VH-IVUS. For comparison, IVUS correctly identified calcium in 100% of the histopathology samples containing calcium, while angiography identified only 54% and gray-scale IVUS missed one lesion. The accuracy levels for defining plaque morphology depicted instill confidence for using VH-IVUS to track progression of atherosclerotic plaque volume and changes to plaque composition.

The ability to accurately analyze the morphology, spatial arrangement, and geometric dimensions of vulnerable or calcified plaque types aides in the evaluation of endovascular interventions and the selection of the appropriate therapy. Other imaging methods are limited by reproducibility from the operator’s ability to adjust intensity, frame average, and power level. Spectral analysis of the pure RF backscatter data signals to determine lumen and vessel area as well as plaque burden and composition has shown to have high correlation coefficients (<0.90) and reproducibility rates similar to tradition IVUS measurements. The reproducibility of VH-IVUS enables the quantitative spectral measurements to act as a definitive standard when evaluating plaque composition. The ability to accurately determine the different histological
constituents of targeted plaque lesions in situ will be beneficial to facilitating further understanding of different mechanisms related to PAD.

**Plaque Calcification**

Identifying plaque histology in situ is particularly helpful in identifying the presence of calcified plaque. Calcified plaque is much harder compared to fibrous plaque and can have many implications for patients with PAD, especially regarding therapeutic options because of the decreased elasticity of the diseased vessel segment. The specific shape, volume, and location of the calcified plaque are essential factors when determining which interventional procedure is most applicable, as more complex plaque and rapid plaque growth by area has been associated with risk of stroke and heart attack. For example, during balloon angioplasty, higher levels of plaque calcification will require increased balloon inflation pressures compared to soft atherosclerotic plaque. The correct balloon pressure is essential in order to prevent adverse effects or vessel disruption from over-inflation. Contrarily, the softer, more fibrous lesions have greater elasticity and may be treated with additional stenting and/or atherectomy to prevent negative remodeling.¹⁰

Kashyap et al. quantified the limits of angiography in determining plaque calcification by comparing angiographic evaluations to true histological results. Angiographic evidence was used to differentiate plaque calcification into four groups: none, minimal, moderate, and severe. Their results showed angiography underestimated plaque calcification, with 15% of scores recording no calcification
compared to 0% of histology. In addition, angiographic evidence identified 15% of the samples as severe calcification, compared to 34% by histology. Angiography’s inability to produce quantifiable plaque calcification data leads to subjective interpretation, which appears to be the primary cause for the discordant results. This conclusion was further supported by the relatively low intraobserver reliability reported from the study (0.3985). These results not only speak to the limits of angiography, but also to the need for a definitive standard for quantifying calcified plaque in situ.

Calcified plaque can be identified through the bright white locations depicted on IVUS images, providing interventionalists a better understanding of lesion morphology, shape, and location. During atherectomy procedures, the location of calcified plaque is directly related to the methodology used during treatment. For example, high-speed rotational atherectomy is best suited for superficial plaque close to the lumen surface. However, if the calcified plaque is deep within the vessel wall in contact with the media, directional atherectomy may be more appropriate. For these reasons, objective measurements on specific plaque morphologies using IVUS are more valuable than the subjective angiographic representation when selecting the appropriate therapy and predicting results of the different interventions.

**Technical Guidance**

IVUS has a wide variety of clinical applications because of the numerous data points that can be computed pre-, during, and post-therapeutic intervention.
IVUS can provide assistance through accurate evaluation of the diseased and true vessel dimensions, cross-sectional area, arterial wall architecture, lesion dimensions, plaque morphology, concentricity, and virtual histology. From conventional stenting to balloon angioplasty to atherectomy, IVUS imaging results can be easily interpreted to provide essential information that adds real-time technical guidance to intravascular procedures.

IVUS’ ability to image entire vessel segments, including the lumen, wall, and lesions, facilitates diagnosis and intervention in patients with PAD. True arterial dimensions that include angiographically silent stenosis and vascular remodeling can be compared to lumen measurements to determine lesion morphology and the need for intervention. In diseased segments, IVUS obtains reference data for specific vessel locations both proximal and distal to the target lesion. These reference points define target areas for the interventional procedure and allow for more accurate vessel and lesion analysis. Accurate reference segments and vessel dimensions are equally beneficial for determining correct device sizing so that all secondary plaque distal and proximal to the stenosis will be treated. Many recent studies have recorded the positive effects of IVUS on long-term clinical outcomes, some of which suggest that fewer post-operative complications reduce the need for re-intervention, potentially offsetting the original invested procedural costs.

Interventional cardiologists often use intravascular stents in adjunct with balloon angioplasty to improve patient outcomes by compressing plaque outward
against the inner arterial wall in order to maintain patency of the arterial lumen.\textsuperscript{14} Non-stented lesions treated with angioplasty alone have shown restenosis from negative remodeling and elastic recoil of the treated vessel.\textsuperscript{11} Both immediate and long-term patency of stented lesions appears to be directly related to proper stent deployment, as determined by three factors: full stent expansion, complete apposition to the vessel wall, and full lesion coverage during stent placement.\textsuperscript{10} Angiography provides luminal rather than true vessel measurements – that include the plaque accumulation – when determining the appropriate stent size, relying on subjective interpretation compared to the objective measurements of IVUS.\textsuperscript{4} In addition to the precise measurements that enable more accurate stent sizing, IVUS images showing the lesion and the stent-wall interface facilitate more accurate stent positioning and expansion.\textsuperscript{9}

Before stent deployment, IVUS can accurately assess the correct size to which a vessel should be dilated. If the stent is not fully apposed to the vessel wall, platelets, fibrin, and thrombus can accumulate between the stent and arterial wall, forming a lesion that may serve as the starting point for restenosis.\textsuperscript{11} On the other hand, stent oversizing or overexpansion severely increases rates of ischemic complications such as perforated or ruptured vessels.\textsuperscript{11} After device implantation, IVUS can evaluate device placement, ensuring full device expansion with complete stent-vessel wall apposition and no prolapsed plaque.\textsuperscript{10} The confirmation IVUS images provide may reduce complications - such as
missing the lesion location, stent malapposition, or dislodged stents during implantation – that are associated with in-stent restenosis.\textsuperscript{11}

Arko et al. documented vessel diameters in 25 of 40 lesions (62\%) were underestimated when using angiography as compared to IVUS analysis. As a result, 16 of 40 (40\%) stented lesions were under-deployed by IVUS evaluation, but appeared adequately expanded through angiography. They concluded arteriography was of limited value for evaluating adequate stent expansion.\textsuperscript{10} In further support, Clifford et al. documented 20 of 49 (41\%) stents were determined to be under-deployed by IVUS evaluation, even though angiography had depicted adequate expansion.\textsuperscript{14}

In addition to assisting in stenting and balloon angioplasty, true vessel analysis has proven to be beneficial for atherectomy procedures. The ability to quantify plaque volume in a vessel segment has enabled in-depth evaluation of plaque removal techniques. Limitations on data analysis from angiographic images allow for interpretation of changes in lumen space. As a result, angiography has limited ability when attempting to differentiate between plaque removal and vessel wall expansion because both mechanisms increase lumen diameter. If vessel wall expansion were present, compensatory stretching would increase lumen diameters, resulting in misleading angiographic evidence of plaque removal. IVUS images offer definitive results due to the quantitative data available from true vessel evaluation.\textsuperscript{6} IVUS may also offer further technical guidance during atherectomy through proper blade orientation with respect to the
target lesion, maximizing plaque removal while reducing inadequate debulking and vessel perforation.\textsuperscript{5}

**Complications**

Although angiography and other imaging modalities have facilitated successful advancement of endovascular interventions, many procedures are still plagued by immediate or long-term complications. During intervention, vessel morphology is distorted making it difficult to analyze and quantify procedural success from comparing post-operative results to pre-operative evaluations.\textsuperscript{6} In addition, many interventional procedures are complex with multiple mechanisms that can cause complications such as excess residual stenosis, restenosis, stent malapposition, or stent thrombus. Accurate images are necessary to help reduce the possibility of post-procedural complications and assess the completion of treatment. IVUS analysis provides the information required to increase interventional success rates and ensure thorough treatment.

Aside from malapposition or stent thrombus, other complications such as restenoses or occlusions can result from the loss of arterial patency following angioplasty or stenting. Residual stenosis data can quantify initial procedural success and depict immediate changes in lumen area. Angiographic interpretation following directional atherectomy has shown to underestimate residual stenosis, identifying 21\% residual plaque volume compared to the 48\% from IVUS evaluation.\textsuperscript{5}
Moderate to long-term procedural success is determined through evaluation of the vessel lumen patency. Late obstructions to blood flow can result from restenosis, occlusions, or stent failure. Clifford et al. researched the influence of IVUS in addition to angiography compared with angiography alone on the long-term patency of arterial lesions treated with balloon angioplasty and primary stenting. After treating 49 limbs using IVUS and angiography, there were no restenoses or occlusions recorded. The five-year patency rate was 100% and no limbs needed additional treatment or evaluation because of suspected restenoses or occlusions. However, after treating 22 limbs using angiography alone, early restenosis or occlusion of stented lesions occurred in 4 limbs (18%). The five-year patency rate was 82% and two cases of each severe stenoses and occlusions were documented. In all four cases, subsequent IVUS evaluation found under-deployed stents and additional intervention was needed. Including two late failures from the angiography alone group, secondary procedures were performed on 5 out of the 22 limbs evaluated (23%). They concluded IVUS significantly improved long-term patency by correctly defining the optimal angioplasty diameter endpoint and adequacy of stent deployment during the initial procedure.\textsuperscript{14}

A similar study by Frank et al. documented long-term patency data from IVUS and angiographic analysis of 52 patients after balloon angioplasty and stenting of atherosclerotic aortoiliac occlusive lesions. While none of the 36 IVUS-assisted patients had restenoses or occlusions, 4 of the 16 (25%) patients
assisted by angiography alone developed restenoses or occlusions. All four were found to have under-deployed stents and were subsequently treated with adequate stent redeployment using IVUS criteria. These lesions remained patent and continued to do so at the time the study was concluded four years later. In the IVUS-assisted group, IVUS found 40% of the stents were under-deployed, even though they appeared adequately expanded on angiography. They concluded IVUS is possibly the best imaging method for assessing adequacy of arterial stent deployment, which may then improve long-term clinical outcomes of balloon angioplasty and stented aortoiliac occlusive lesions.

Limitations

Even with all of the benefits IVUS has to offer during endovascular interventions, there are some limitations to the technology, especially its implementation. The biggest inhibitor of widespread integration of IVUS systems is the associated costs of operation. Each disposable catheter-delivered transducer costs approximately $500. The IVUS systems themselves can cost between $70,000-$120,000 and require a trained technician to operate. On average, the additional cost-per-case is approximately $1,000. However, although there is a substantial upfront cost, investing in IVUS pays dividends once the increased diagnostic abilities, technical guidance, and success rates are factored in. Each failed endovascular procedure can costs around $12,000-$15,000 to salvage. The increased success rate will allow catheterization labs to recover their initial investment in lieu of the operational costs for reinterventions.
During the study performed by Clifford et al., if IVUS had salvaged the four failures from the arteriography alone group during the initial treatment, the money saved from not performing the four reconstructions would have paid for its use in all 52 patients.¹⁴

Other limitations of IVUS are associated with its clinical applications or analysis. Using a manual pullback system has the potential to cause inconsistent retraction rates of the transducer, which could result in incorrectly stacked images or poor image quality.⁸ IVUS also mandates additional time, equipment, and personnel. In addition, there is no standard present between manufacturers, so IVUS catheters cannot be interchanged.⁴ However, in experienced hands, using an integrated IVUS system adds only a few minutes to procedural time. The information is both information, necessary, and easy to interpret because of the analysis software and color-coded maps of VH-IVUS.

**Conclusion**

Angiography is adequate for viewing luminal characteristics, but has repeatedly been shown to provide inaccurate measurements without providing insight into the vessel or plaque morphology. As geometric measurements become more complex, evaluating stenosis areas, concentricity, and treatment analysis with angiography has shown to produce increasingly discrepant results when compared to IVUS. IVUS imaging and analysis software is capable of filling the gaps with objective, quantifiable data that provides accurate analysis and evaluation of the diseased and true lumen, lesions, and vessel walls. This is
particularly true in significantly diseased vessels, in which IVUS can provide more
accurate evaluation of vessel wall and lumen morphology as well as plaque
distribution.\textsuperscript{12}

In addition, IVUS has many clinical applications during interventional
procedures and has demonstrated positive effects on technical guidance,
treatment analysis, and long-term patency rates. With continuing advances in
therapeutic options, the success of interventional procedures may be directly
related to the capabilities of the accompanying guidance system. However, it is
important to note that angiography may still play a role in preliminary diagnosis
and peripheral navigation of the arterial vasculature. Ideally, IVUS should be
used in conjunction with angiography in order to incorporate the beneficial
aspects of both imaging modalities.

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