Biomedical Letters
2016 | Volume 2 | Issue 2|Pages 119-125

REVIEW ARTICLE OPEN ACCESS

Role of Optic Coherence Tomography (OCT) on Atherosclerotic Plaques in the Carotid Artery and other Vascular Network: A Review

Muhammad Arif Anwar[1], Khawar Ali Shahzad[2], Muhammad Ahmed Javed[3], MD Ruhul Amin[3], Ma Gen Shan*[1]

[1]Department of Cardiology, The Affiliated Zhong Da Hospital of Southeast University, No. 87 Dingjiaqiao, Nanjing, China
[2]Department of Microbiology and Immunology, Medical School, Southeast University, No. 87 Dingjiaqiao, Nanjing, China
[3]School of medicine, Southeast University, No. 87 Dingjiaqiao, Nanjing 210009, China

Abstract
The evaluation of carotid artery lesions as a potential target in order to avoid highly devastating ischemic strokes, which are secondary to a severe carotid artery or thromboembolic events from unstable plaques. Recently, a number of diagnostic modalities are in practice to make an early diagnosis of significant stenosis or vulnerable carotid artery plaques namely ultrasonography(USG), computed tomography(CT), magnetic resonance imaging(MRI). The above mentioned diagnostic tools are effective in their diagnostic spectrum, however, are still unable to give an optimal level of reliable diagnostic results. Optic coherence tomography(OCT) is a relatively new technique which is highly specific in distinguishing stable and unstable coronary artery plaques and additionally provide highly characteristic morphological features of those plaque. There are many studies being conducted to evaluate the ability of OCT in comparison with IVUS study of the carotid artery in patients with symptoms or even without the classic symptoms. OCT is currently allowing unprecedented evaluation of carotid artery plaque morphology in patients. Intravascular OCT assessment of plaque provides a high level of axial resolution. Evidence of increased misdiagnosis in cases of intra-luminal thrombus in the carotid artery due to the utilization of casual techniques, namely duplex ultrasonography, and angiography, has emerged. This has urged researchers and physicians to adopt new techniques with advanced capabilities to identify intravascular thrombus, along with gaining a suitable framework for therapeutic techniques. Plaque vulnerability is a very important feature, determined by the thickness of fibrous cap because plaques with the thin fibrous cap are highly prone to rupture. Hence, OCT is the current emerging technique to evaluate the thickness of the fibrous cap.
Keywords: Carotid artery, ultrasonography, computed tomography, magnetic resonance imaging, intravascular ultrasonography, angiography, atherosclerosis.

Received October 26, 2016; **Revised** December 27, 2016; **Accepted** January 13, 2017
***Correspondence:** Ma Gen Shan **Email** magenshan@hotmail.com, **Contact**: +8613002580569

***To cite this manuscript*:** Anwar MA, Shahzad KA, Javed MA, Amin MDR, Shan MG. The role of optic coherence tomography (OCT) on atherosclerotic plaques in the carotid artery and other vascular network: A review.Biomed Lett 2016; 2(2):119-125.

Introduction

Optic coherence tomography(OCT) is based on light coherence for generating tomographic images of organs in the human body. A novel diagnostic modality with an ultra-high resolution that can demonstrate histological features called optic coherence tomography(OCT) is the technique currently used for three-dimensional and cross-sectional imaging in biological sciences[1, 2]. Huang, et al.[3]first made use of this technique on the biological sciences in 1991 for the assessment of transparent tissues which are mainly found in the eyes[4]. OCT is a unique constellation of diverse techniques including interferometry, biomedical imaging, and fiber optics, clinical practice and *in vivo* and *in-vitro* as well[5]. It has become an emerging modality with its ability to map out pathological changes in the structure of the tissue in the real world (*in-vivo*) and *in-situ*, and it leads to the acquisition of biomedical images[6, 7]. Some medical specialties are being overwhelmed by the use of this emerging technique due to its high axial resolution and power of distinguishing between normal and pathological structural features in the past decade. Recently, it has shown a better application in the evaluation of non-transparent structures present in the gastrointestinal tract and skin, etc.[8, 9].

Optic coherence tomography uses a source of light in place of sound signals; a B-mode ultrasound analog which gives very high-quality images with a greater magnitude as compared to conventional ultrasound. Light intensity being backscattered from tissues into a microstructure and the delay in real echo time is calculated to generate high-quality images by OCT. OCT also serves as an optical biopsy in biomedical sciences. In cardiovascular diseases, intravascular ultrasound (IVUS) optical analog is being used to evaluate coronary artery lesions. Near-infrared light is replacing ultrasound in current use for IVUS analysis, with a 1,300nm wavelength absorbed at relatively low levels by protein, water, red blood cells, and lipids, respectively. IVUS-like tomographic high-quality images with better resolution which possess extraordinary details and cross-sectional information of internal microstructure of tissues. IVUS has the potential advantage of greater penetrating power in tissue but its resolution power is 10-fold less than OCT [10, 11].

Techniques and system of OCT

OCT time-domain (OCT-TD): To evaluate culprit lesions in the vasculature, casual guidewire used in angioplasty is sent beyond the target lesion and is followed by an occlusion balloon. A wire specific for image acquisition is then used to replace the first guidewire. The occlusion balloon is moved in a retrograde direction to the section immediately before the lesion to be examined and is then inflated at a relatively low pressure to stop the flow of blood. Lactated Ringer's or normal saline solution is pushed through to clear the blood field area. It is also reported that lactated Ringer's solution is preferred over normal saline use for the purpose of flushing because ECG findings and symptoms remain constant during this process. This procedure can be onerous as some stenotic lesions are severe, and impede the passing of an occlusion balloon. If such an unusual situation is encountered, the assistance of highly skilled experts is sought to gain access through the severe and complex stenotic lesion, and with the help of an imaging, wire to proximally inflate the occlusion balloon and overcome the situation.

According to a multicenter collection of information for the evaluation of efficacy and safety especially first generation OCT, IVUS was also compared. It was found with vessel obstruction of 48.3± 14.7 sec. On average had no fatal consequences especially MI, dissection of target artery specifically coronary artery, embolic events and alarming rhythm abnormalities (e.g. vent. fibrillation and/or vent. tachycardia). Moreover, OCT is superior to IVUS in visualizing intra-luminal outlines and the evaluation of luminal boundaries with an improved capacity to pass through more than 80% of the severely stenotic lesions that IVUS fails to cross. Nevertheless, IVUS does have particular advantages over OCT because it does not require the use of complex methods like occlusion balloons as has been mentioned above. One new method reported by Katrina et al.[12] and Prati et al.[13]is that a contrast medium or LMW dextran can be used in the guide the catheter for flushing purposes in place of occlusion balloons to get a proper visualization of lesions.

OCT frequency-domain (OCT-FD)

This new modified form of OCT was developed to overcome the drawback encountered in first generation time-domain OCT which was based on moving reference mirror for scanning image pixels with every position of depth in structures being visualized. It reduces the rate of image acquisition with this mechanical process of image scanning. This new OCT frequency domain technique is capable of overcoming this flaw by measuring interferometric data as a function of time and optical wavelength instead of using time function alone. OCT-FD mainly rely on laser light which is tunable as a major source and a fixed, rather than moving reference mirror with a sweep range of 1,250-1,370nm, as a substitute for abroad band light source which was mainly used in OCT-TD for image acquisition. This process of imaging makes it possible to get fast and better image quality with greater speed of pullback. This is a system which is simple and generates a good visualization of the artery by running a viscous contrast media through the guide wire and removes blood. This is considered a non-occlusive method as well [14, 15].

Application of OCT in carotid artery stenosis

Optic coherence tomography(OCT) is the process that has recently been used to detect the carotid artery stenosis, and it can visibly characterize atherosclerotic plaques in the carotid artery, and determine whether the plaque is stable or unstable[16]. The features of carotid plaque are used by the high ruling and non-invasive exterior procedures of OCT. OCT is also a modern technique with the capacity to improve critical patients and delineate whether or not the patient needs a carotid endarterectomy[17, 18]. A new study assesses that OCT is the non-invasive medical process which is able to find the carotid plaque out from the arterial layers (intima, media, and adventitia) in carotid artery[17].

One of the studies which shows the role of OCT in evaluation of classic characteristics related to stenotic changes in the carotid vascular network found that it is quite difficult to figure out the precise detail of the fibrous cap thickness and its plaque burden and fails to fully satisfy the accuracy of defining the vulnerability of the plaque because of reduced amount of penetration from the light rays. This limitation of OCT can be overcome by enhancing the signal-to-noise ratio(SNR), increasing the sample beam's focus depth and with the utilization of dynamic focus tracking modalities[19, 20]. The ratio of signal strength to background noise strength at any given time is defined by SNR. The greater the value of SNR, the more probability of signals to be identified. Utilizing a dynamic focus tracking system enhances the degree of resolution for images generation by OCT special images of the retina[21]. Such a functional principle can also be used for getting better quality carotid lesion characteristics.

When OCT is used for identification of carotid artery stenosis and to evaluate the vulnerability of stenotic lesions, it gives unique features of each type of lesion based on its degree of severity. The vulnerability of the arterial plaque is determined mainly by the thickness of the fibrous cap, plaque burden in the form of lipid contents, and the metabolic activity of the plaques. Therefore, the lipid burden of plaque is characterized by the poor-intensity-signal area surrounding an area of diffusely homogeneous material[22]. If the pool of lipid component is found in ≥2 quadrants in any specific lesion of the carotid artery, then it is referred to as a lipid-rich plaque. Poor-intensity-signal or high-intensity-signal area or with changing regions of poor-intensity-signal or high-intensity-signals which surround the sharply demarcated heterogeneous area is a highly classic indication for calcification[22]. If the images obtained from intra-luminal carotid artery and shower array of signals with backscattering from bulged out mass, it conveys classic features of intra-luminal thrombus[23].When cavities in the smooth endothelial surface are observed, it indicates the superficial laceration of the inner most layer, namely intima respectively, and this is the main characteristic of ulceration in the carotid arterial wall. Micro-channel structures with signal-intensity of zero have no anatomical associations with a main arterial luminal area under investigation and appear in ≥3 consecutive images acquired by OCT study is unique features of, "neovascularization"[24, 25].

A study emphasizing the advantages of OCT over IVUS findings related to carotid artery lesions has shown that clear image acquisition by OCT visualizing tissue components of plaques in the carotid artery. This is relatively safe and effective because it frequently demonstrates neovascularization and thrombus on the luminal surface of the carotid artery. Thrombus on the inner surface of intima was frequently found in patients with clinical symptoms but less frequency for symptomless patients. Recently, proper information related to detailed characteristics of tissue in the human carotid artery is lacking which emphasizes the need for more studies to confirm the reliability of such features[26]. This study also mentioned valuable features and findings related to vulnerable plaque in carotid artery by utilizing OCT in relation to ischemic symptoms [27, 28].

OCT in Acute Coronary Syndrome

In recently conducted studies about ACS, they have shown that patients suffering from this fatal syndrome are at high risk of developing life-threatening complications during their hospital stay and later as well with an approximated rate of death of around 15.85% within the window of 6 months-time [29]. This high risk of death compelled the researchers to explore the detailed morphological features and such type of investigation obtains an underlying mechanism for ACS development and plenty of information. The purpose is to decrease the future risk of ACS development and save patients at risk of developing ACS with better prophylaxis. In this advancing age of medical sciences and technology, many diagnostic modalities have been innovated to assess the characteristics of coronary plaque morphology in patients prone to developing ACS[30]and their resultant significance of prognosis[31]. Evaluation of typical features of plaque morphology found in a coronary artery is made possible with high-quality spatial OCT resolution which is beyond the approach of the once commonly practiced diagnostic techniques. By this modern technique, OCT's ability to identify the pathophysiological features of vulnerable plaque in a coronary artery, new methods of early diagnosis and construction of therapeutic strategies would be natural and more beneficial as compared to before.

OCT-guided Coronary intervention

A group of ACS patients was studied, and criterion about PCI with the use of FD-OCT was proposed. The stenotic lesions with a degree of 40% to 70% stenosis or lesions with haziness are classified as intermediate lesions, so final steps to manage such lesions is based on following features like thrombus identification and minimal luminal cross-sectional area(MLCSA) $<3.5mm^2$ represent plaque vulnerability. OCT has increasingly gained application in assessing the accuracy of stent deployment as well as the assessment of post-dilatation stent apposition to the coronary wall. In certain conditions, it becomes highly significant to use OCT assessment to avoid unacceptable post-operative complications and these conditions are mainly composed of prolapsed extended plaque. On the other hand, significant incomplete stent apposition(ISA), dissection of edges over an area of approximately 200 millimeters, and under-expansion,etc. is one of the greatest approaches in the diagnostic field with good success rates after performing the procedure, and a good clinical outcome[32].Another assessment in patients with stable angina was undertaken by performing OCT in selected cases of PCI[33] and declared clinical findings independently by classifying patients into further small groups with lesions having bifurcations[34]. OCT procedures are being performed in a large number of patients and are revolutionizing the old approaches at a rapid rate. However, post-dilatation with high pressure and dilatation in kissing balloon techniques, and the prevalence of ISA is found at a higher rate after the completion of this procedure, especially in those lesions which harbor high quantity of calcifications, as well as in arterial segments where side-branches take their origin[34].

OCT in Ophthalmic imaging

Developments of better diagnostic tolls in ophthalmology is rapidly being influenced by the use of OCT technique in the recent era of science[35, 36]. OCT can assess choroid and retinal epithelium with high pigments which are richly supplied by blood vessels which give images of scattered structures. The layer of nerve fiber found in retina gives a characteristic pattern of scattered layers originating from the optic disk and continue approaching the fovea centralis with a gradual reduction in their width. In this way, the thickness of retinal nerve fiber and overall retinal thickness can also be measured. OCT has the potential to differentiate minute details within the retina because of its extraordinary high resolution. The retina is unique in containing transparent material and so produces less optical back scattering. Nonetheless, OCT can evaluate and give characteristic features to be seen even with very much feeble optical backscattering due to its high resolution and sensitivity. The feasibility of OCT application is being evaluated in many clinical settings for diagnostic purposes and surveillance variety of retinal pathology especially tumors of choroid, pits in optic disc, membranes of epiretinal, senile degeneration of macula, edema of macula, hole in macula, open angle and closed angle glaucoma and chorioretinopathyetc[37, 38]. OCT is very effective for making diagnosis and observation of progression of disease especially in edematous changes in diabetic macular disease and glaucoma because it is capable of assessing quantitative details related to the pathology of the retina. OCT is unique for having the potential use for early phase detection of changes before clinical features become evident and visual loss becomes irreversible.

OCT in cerebrovascular diseases

There is astounding evidence coming to light that by reassessing information collected from some recently circulating or functional diagnostic techniques in clinical medicine, a huge number of strokes are encountered in symptomless plaque associated with atherosclerosis. They also have increased metabolic activity, and are prone to rupture due to their potential vulnerability and instability. By the matter of fact, to properly assess plaque vulnerability and estimate its chances of a rupture, a detailed understanding of the morphological features and structural constitution of culprit lesions are the main factors for determining acute cerebrovascular accidents (strokes) as compared to the severity or grade of narrowing stenotic lesions alone. Events of acute stroke occur mostly secondary to thrombus formation as a result of sudden rupturing of highly vulnerable asymptomatic plaque which leads to the genesis of new in-situ thrombus and subsequent thromboembolism as well. These unexpected and unpredictable events of cerebrovascular accidents carry a high-rate of morbidity as well as mortality, so it is of great value to map out the major risks of cerebral vascular accidents spectrum which also covers the event of TIA (transient ischemic attack). To reduce the irreversible fatal consequences of cerebrovascular accidents, it is essential to characterize the plaque vulnerability and make new therapeutic strategies to cope with the situation by deploying the stent or endarterectomy of the carotid artery. In patients with stroke, some recent clinically applicable diagnostic techniques including conventional 4-vessels angiography, MRI, CTA, and Doppler scan of the carotid artery are being utilized to stratify the lesion but none of the above-mentioned modality gives adequate morphological and metabolic features of vulnerable plaques. Few new MRI studies and B-type USG are emerging with suitable information in the aspect of plaque vulnerability assessment. Some observations throw light into the ability of B-type USG to evaluate subsequent results in vulnerable stenotic lesions by assessing different features of the plaque[39]. Intramural thrombus, calcified and necrotic material, lipid contents, amount of fibrotic material and hemorrhagic events in plaque are mainly being investigated in current studies. Heterogenic and echo-lucent areas are the main factors for less satisfactory prognostic value on USG assessment in severely stenotic carotid lesion[40, 41]. Being limited in its resolution, ultrasonography also fails to give satisfactory differential features of culprit lesion[42].

OCT in PAD

Peripheral arterial diseases are steadily increasing the burden of disability in patients suffering from this illness which emphasizes the need for adequate and proper therapeutic approach to improve the quality of life. There is a lot of promising techniques of intervention such as intravascular atherectomy, intravascularcryoablation, and angioplasty with a cutting balloon, etc. However, all of the above-mentioned methods can only be more effective if the better constitutional detail of vulnerable lesions is assessed[43]. The baseline pathophysiological changes and characteristics of atherosclerosis in culprit lesions of the peripheral vascular network are similar with differences found is coronary and carotid lesions. So OCT is the best technique available recently as it can also display behavior and characteristics of vulnerable lesions found in the peripheral vascular network. Meissner, et al., evaluated the potential ability of OCT in PAD due to atherosclerotic changes and emphasized that lesion characteristics found in different vascular network namely coronary artery and peripheral vasculature are comparable with each other[43]. This study had shown that OCT findings were in full agreement to histopathological features found in a variety of lesions with atherosclerosis[43]. Limitations of this study were that arterial segments were used instead of real patients and *ex-vivo* arterial study of samples obtained from amputations. Nevertheless, it was one of the first efforts made to assess the potential of OCT in studying PAD and surveillance of deterioration or improvement of arteriosclerosis in real cases[43].

Advantages and limitations of OCT

Good quality images with remarkably fine resolution and very fast image acquisition, decreased cost, portability, and, its great potential for predicting culprit lesion behavior deduced from characteristic plaque morphology, are worth mentioning advantages of recently practicable OCT technique[44].OCT is unique in its potential for visualizing further through lesions with a high amount of calcification and fine assessment of intima, which is also one of its potential advantages[45]. The apparatus used for OCT technique is not very expensive, the guidewire being used for it is not very long, and the transducer is not essential for its catheter[46]. There are some disadvantages of OCT as well, such as hampering of images obtained by OCT due to blood in the area under examination. The quality of images and their interpretation is very much affected by flowing blood in the target area which can even overcome the efficacy of other techniques utilized to keep the area blood-free. An index matching technique has recently been employed to make improve visibility through blood[47]. Tissues with non-transparency offer fewer penetrations by OCT [48]. It can result in an impedance of image qualities in those arteries in which lesion have the significantly high necrotic burden. Recently, encountered drawbacks are being addressed with the introduction of source-sweep OCT and spectral radar in advancing OCT modalities[49]. The temperature of the area under investigation can influence the final result of measurement so such fact should be considered while presenting its interpretation[50]. In a nutshell, OCT is a very productive diagnostic approach which leads to the genesis of unique and valuable information primarily morphological characteristics of lesions which enable effective non-invasive and invasive evaluation and managing naïve and post-intervention carotid and coronary arterial diseases. There has been a gradual surge of advancement in OCT techniques supporting a better understanding of its use augmenting other diagnostic approaches focused on arteriosclerotic lesions.

Conclusion

Optic coherence tomography (OCT), is an emerging diagnostic technique of the recent era with a potential to generate high-quality images, and with well-defined morphological characteristics comparable to histopathological features as well. OCT is capable of *in-vivo* identification of plaque vulnerability. It is a technique that yields a high resolution, better visualization of morphological changes in culprit lesions demonstrated by special histological evaluations. Thus, OCT offers a better assessment of pathophysiological characteristics in the carotid artery and other vascular networks of the human body with great accuracy. A pool of information collected by OCT examination can help to guide us in the development of specific, effective and suitable treatment approaches which would be fully patient-specific. Moreover, further studies are required with a higher number of participants to increase the effectiveness and predictive value of OCT technique. It is predicted that OCT will exert an influential impact on the field of cardiology in the near future.

References

[1] Fujimoto JG, Pitris C, Boppart SA, Brezinski ME. Optical coherence tomography: an emerging technology for biomedical imaging and optical biopsy. Neoplasia. 2000;2:9-25.

[2] Kirtane TS, Wagh MS. Endoscopic optical coherence tomography (OCT): advances in gastrointestinal imaging. Gastroenterology research and practice. 2014;2014.

[3] Huang D, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W, et al. Optical coherence tomography. Science. 1991;254:1178-81.

[4] Swanson EA, Izatt JA, Lin C, Fujimoto J, Schuman J, Hee M, et al. In vivo retinal imaging by optical coherence tomography. Optics letters. 1993;18:1864-6.

[5] Fujimoto JG. Optical coherence tomography for ultrahigh resolution in vivo imaging. Nature biotechnology. 2003;21:1361-7.

[6] Fujimoto JG, Brezinski ME, Tearney GJ, Boppart SA, Bouma B, Hee MR, et al. Optical biopsy and imaging using optical coherence tomography. Nature medicine. 1995;1:970-2.

[7] John R, Adie SG, Chaney EJ, Marjanovic M, Tangella KV, Boppart SA. Three-dimensional optical coherence tomography for optical biopsy of lymph nodes and assessment of metastatic disease. Annals of surgical oncology. 2013;20:3685-93.

[8] Li X, Boppart S, Van Dam J, Mashimo H, Mutinga M, Drexler W, et al. Optical coherence tomography: advanced technology for the endoscopic imaging of Barrett's esophagus. Endoscopy. 2000;32:921-30.

[9] Uno K, Koike T, Shimosegawa T. Recent development of optical coherence tomography for preoperative diagnosis of esophageal malignancies. World journal of gastrointestinal endoscopy. 2015;7:872.

[10] Markis JE, Malagold M, Parker JA, Silverman KJ, Barry WH, Als AV, et al. Myocardial salvage after intracoronary thrombolysis with streptokinase in acute myocardial infarction: assessment by intracoronary thallium-201. New England Journal of Medicine. 1981;305:777-82.

[11] Wijns W, Serruys PW, Reiber J, van den Brand M, Simoons M, Kooijman C, et al. Quantitative angiography of the left anterior descending coronary artery: correlations with pressure gradient and results of exercise thallium scintigraphy. Circulation. 1985;71:273-9.

[12] Prati F, Guagliumi G, Mintz GS, Costa M, Regar E, Akasaka T, et al. Expert review document part 2: methodology, terminology and clinical applications of optical coherence tomography for the assessment of interventional procedures. European heart journal. 2012:ehs095.

[13] Prati F, Cera M, Ramazzotti V, Imola F, Giudice R, Giudice M, et al. From Bench to Bedside A Novel Technique of Acquiring OCT Images. Circulation Journal. 2008;72:839-43.

[14] Prati F, Cera M, Ramazzotti V, Imola F, Giudice R, Albertucci M. Safety and feasibility of a new non-occlusive technique for facilitated intracoronary optical coherence tomography (OCT) acquisition in various clinical and anatomical scenarios. EuroIntervention. 2007;3:365-70.

[15] van der Sijde JN, Karanasos A, van Ditzhuijzen NS, Okamura T, van Geuns R-J, Valgimigli M, et al. Safety of optical coherence tomography in daily practice: a comparison with intravascular ultrasound. Eur Heart J Cardiovasc Imaging. 2016:jew037.

[16] Prati F, Zimarino M, Stabile E, Pizzicannella G, Fouad T, Rabozzi R, et al. Does optical coherence tomography identify arterial healing after stenting? An in vivo comparison with histology, in a rabbit carotid model. Heart. 2008;94:217-21.

[17] Prabhudesai V, Phelan C, Yang Y, Wang RK, Cowling MG. The potential role of optical coherence tomography in the evaluation of vulnerable carotid atheromatous plaques: a pilot study. Cardiovascular and interventional radiology. 2006;29:1039-45.

[18] Libby P. Mechanisms of acute coronary syndromes and their implications for therapy. New England Journal of Medicine. 2013;368:2004-13.

[19] Meemon P, Lee K, Murali S, Kaya I, Thompson K, Rolland J. Sub-cellular resolution imaging with Gabor domain optical coherence microscopy. BiOS: International Society for Optics and Photonics; 2010. p. 75542C-C-9.

[20] Dalimier E, Bruhat A, Grieve K, Harms F, Martins F, Boccara C. High resolution in-vivo imaging of skin with full field optical coherence tomography. SPIE BiOS: International Society for Optics and Photonics; 2014. p. 89260P-P-8.

[21] Stifter D, Leiss-Holzinger E, Major Z, Baumann B, Pircher M, Götzinger E, et al. Dynamic optical studies in materials testing with spectral-domain polarization-sensitive optical coherence tomography. Optics express. 2010;18:25712-25.

[22] Jang I-K, Bouma BE, Kang D-H, Park S-J, Park S-W, Seung K-B, et al. Visualization of coronary atherosclerotic plaques in patients using optical coherence tomography: comparison with intravascular ultrasound. Journal of the American College of Cardiology. 2002;39:604-9.

[23] Kume T, Akasaka T, Kawamoto T, Ogasawara Y, Watanabe N, Toyota E, et al. Assessment of coronary arterial thrombus by optical coherence tomography. The American journal of cardiology. 2006;97:1713-7.

[24] Kitabata H, Tanaka A, Kubo T, Takarada S, Kashiwagi M, Tsujioka H, et al. Relation of microchannel structure identified by optical coherence tomography to plaque vulnerability in patients with coronary artery disease. The American journal of cardiology. 2010;105:1673-8.

[25] Lee T, Murai T, Yonetsu T, Suzuki A, Hishikari K, Kanaji Y, et al. Relationship between subclinical cardiac troponin I elevation and culprit lesion characteristics assessed by optical coherence tomography in patients undergoing elective percutaneous coronary intervention. Circulation: Cardiovascular Interventions. 2015;8:e001727.

[26] Yoshimura S, Kawasaki M, Hattori A, Nishigaki K, Minatoguchi S, Iwama T. Demonstration of intraluminal thrombus in the carotid artery by optical coherence tomography: technical case report. Neurosurgery. 2010;67:onsE305.

[27] Yoshimura S, Kawasaki M, Yamada K, Enomoto Y, Egashira Y, Hattori A, et al. Visualization of internal carotid artery atherosclerotic plaques in symptomatic and asymptomatic patients: a comparison of optical coherence tomography and intravascular ultrasound. American Journal of Neuroradiology. 2012;33:308-13.

[28] Matsumoto H, Rie Y, Masuo O, Hirayama K, Uematsu Y, Nakao N. A Case of In-Stent Neoatherosclerosis 10 Years after Carotid Artery Stent Implantation: Observation with Optical Coherence Tomography and Plaque Histological Findings. Neurologia medico-chirurgica. 2014;54:139.

[29] Fox KA DO, Goldberg RJ, Pieper KS, Eagle KA, Van de WF et al. Prediction, presentation orodamiitsma, observational wacspm, 2006;333:1091. sGBMJ.

[30] Vancraeynest D PA, Roelants V, Gerber BL, Vanoverschelde JL. Imaging, 2011;57:1961–79. tvpJACC.

[31] Stone GW MA, Lansky AJ, de BB, Cristea E, Mintz GS et al. A prospective, 2011;364:226–35. n-hsocaNEJM.

[32] Imola F MM, Ramazzotti V, Manzoli A, Pappalardo A, Di GA et al. Safety, decision afofdocttg, 2010;6: mipciE, 575–81.

[33] Viceconte N CP, Ghilencea L, Lindsay A, Foin N, di Mario C. Frequency, J doctfgocsI, print). CEao.

[34] Viceconte N TP, Ferrante G, Foin N, Chan P, Alegrı´a-Barrero E et al., tomography. Irobsawoc, press). CCIi.

[35] Swanson E.A. IJA, Hee M.R., Huang D., Lin C.P., Schuman J.S., Puliafito C.A., Fujimoto J.G., In vivo, retinal imaging by optical coherence tomography OL, [11] Fercher A.F. HCK, Drexler W.,

Kamp G., Sattmann H., In vivo optical coherence tomography, Am., 113–114. JO.
[36] Spaide RF, Klancnik JM, Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. JAMA ophthalmology. 2015;133:45-50.
[37] Puliafito C.A. HMR, Lin C.P., Reichel E., Schuman J.S., Duker J.S., Izatt J.A., Swanson E.A., Fujimoto J.G.,, Imaging of macular diseases with optical coherence tomography O, [14] Hee M.R. PCA, Wong C., Duker J.S., Reichel E., Schuman J.S., Swanson E.A., Fujimoto J.G., Optical, coherence tomography of macular holes O, [15] Hee M.R. IJA, Swanson E.A., Huang D., Schuman J.S., Lin C.P., Puliafito C.A., Fujimoto J.G., Optical, coherence tomography for ophthalmic imaging: new technique delivers micron-scale resolution IEM, et al.
[38] Jia Y, Bailey ST, Wilson DJ, Tan O, Klein ML, Flaxel CJ, et al. Quantitative optical coherence tomography angiography of choroidal neovascularization in age-related macular degeneration. Ophthalmology. 2014;121:1435-44.
[39] Aburahma A, Thiele, SP, Wulu Jr, JT. Prospective controlled, to sotnhoa, morphology. csatup, 437–442. JVS, 49 Gronholdt M, Nordestgaard, BG, Schroeder, TV,, Vorstrup S, Sillesen, H. Ultrasonic echolucent carotid plaques, et al.
[40] Aburahma A, Thiele, SP, Wulu Jr, JT. Prospective controlled, to sotnhoa, morphology. csatup, 437–442. JVS, 49 Gronholdt M, Nordestgaard, BG, Schroeder, TV,, Vorstrup S, Sillesen, H. Ultrasonic echolucent carotid plaques, et al.
[41] Gupta A, Kesavabhotla K, Baradaran H, Kamel H, Pandya A, Giambrone AE, et al. Plaque echolucency and stroke risk in asymptomatic carotid stenosis a systematic review and meta-analysis. Stroke. 2015;46:91-7.
[42] Eliasziw M, Rankin, RN, Fox, AJ, Haynes, RB, Barnett,, ultrasonography HAapco, North iiscas, Trial ASCE, 1747–1752. NgS.
[43] Meissner O, Rieber, J,Babaryka, G, et al. Intravascular optical, in ctcwh, 69 Octivm, Interv apasJV, 343–349. R.
[44] Tearney G, Brezinski, ME, Bouma, BE, et al. In vivo, tomography. eobwoc, 2037–2039. S.
[45] Jang I, Bouma, BE, Kang, DH, et al. Visualization of, optical capipu, intravascular ctcw, 604–609. uJACC.
[46] Brezinski M, Tearney, GJ, Weissman, NJ, et al. Assessing, of apmc, intravascular octahf, 397–403. uH, 9 Pinto T, Waksman, R. Clinical applications of optical, 566–573. ctJIC.
[47] Kawase Y, Suzuki, Y, Ikeno, F, et al. Comparison of nonuniform, IVUS rdbm, Biol aOuapmUM, 67–73.
[48] Stamper D, Weissman, NJ, Brezinski, M. Plaque characterization, Coll woctJA, C69–C79. C.
[49] Brezinski M, Saunders, K, Jesser, C, Li, X, Fujimoto, J., tomography Imtioc, 1999–2003. itbC.
[50] Van der Meer F, Faber, DJ, Cilesiz, I, van Gemert, MJ,, van Leeuwen TT-dop, by oivwcm, 11: octJBO, 041120.