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Review article

Advances in Imaging Methods to Detect Vulnerable Plaque: A Review

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Abstract

Acute coronary syndromes (ACS) are anticipated to remain the important cause of mortality and morbidity now a days. ACS are mostly caused by plaque rupture.

This review paper focuses on the prognostic value of different *in vivo* determination modalities of vulnerable lesions in coronary artery by OCT, IVUS-VH, intravascular ultrasound (IVUS), intravascular magnetic resonance, Roman and near-infrared spectroscopy, and non-invasive multidetector computed tomography, Positron Emission Tomography (PET) scan, Single Photon Emission Computerized Tomography (SPECT) scan, Magnetic Resonance Imaging (MRI) and their different combinations in patients undergoing coronary angiography.

Coronary angiography is considered the standard modality to estimation of the coronary artery disease but the difference in expression of the opacified vascular lumen is too high. By coronary angioscopy, the plaque surface and intraluminal structures can be visualized directly with the utility of intracoronary angioscopy (CAS). The plaque color variation can enlighten plaque complications, such as ulceration, fissures, rupture, intimal breaks and thrombosis with a higher sensitivity than angiography. For intracoronary imaging, IVUS is being used as a "gold standard" which is used to evaluate the positive vessel remodeling. In addition to real-time, high-resolution images of the plaque, but IVUS method is also capable of determining the borders and vessel lumen. Despite amplitude resemblance, the power and frequency of the signal usually vary among different tissues. OCT is found with higher sensitivity, specificity and capacity for description of coronary plaques as compared with other imaging modalities. For identification of fibrous and lipid-rich tissue by measuring differential water diffusion, MR spectroscopy can be used. 18F-FDG PET is normally done for the estimation of myocardial consumption of glucose. SPECT is particularly being used to target high-risk lesions with atherosclerosis.

It is concluded that every technique has its own significance and specificity in detection of particular feature of vulnerable plaque. Until now, we are unable to define a single modality in order to detect *in vivo* vulnerable plaques accurately. A varying combination of above given techniques can help the physicians and medical expertise to increase the predictive value of prognostication. It is highly desired to device such combination of different diagnostic techniques to improve accuracy in early detection of vulnerable plaque.

Keywords: Acute coronary syndromes (ACS), intravascular ultrasound, Magnetic Resonance Imaging (MRI), coronary angiography, prognostication.

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Introduction

Acute coronary syndromes (ACS) are anticipated to remain an important cause of morbidity and mortality nowadays[1]. Patients with cardiovascular problems are more prone to ACS and it is proven by post-mortem studies that thin-cap fibroatheroma (TCFA) lesions are the major cause of it[2]. Furthermore the progress in prognostication and best choice of treatment in detection of coronary lesions may be highly relevant as they are highly vulnerable to rupture. But, the detection of these high-risk lesions is also not possible by the angiography of coronary artery[3].

Intravascular ultrasound (IVUS) radiofrequency analyses, also called IVUS virtual histology, permit recognition of plaques which are prone to rupture and discrimination of different plaque phenotypes[4]. The plaque vulnerability cannot yet be definitively evaluated. However, several reports particular for the vulnerable plaques regarding numerous morphologic and immunologic determinants have been published[5]. Recently, we came to know that a highly developed atherosclerotic plaque is defined by a superimposed fibrous cap rich in collagen composition with a core of extracellular lipid. The occurrence of acute ACS is produced in most cases by ulceration or fissuring of the fibrous cap with resultant generation of thrombus and conversion of an intact coronary lesion into highly complex sort of atherosclerotic plaque. A fraction of myocardial

infarction (MI) occurs in vulnerable plaques with fairly thicker caps which ulcerate or may be a high-risk plaque which has a physiologically stable cap but undergoes an intra-plaque hemorrhage that results in abrupt intra-luminal thrombus formation and subsequent blockage. Histological features of highly vulnerable lesion like a bulky lipid-core and high plaque macrophage burden are associated with positive remodeling in culprit lesions, as have been shown by postmortem studies[6].

Acute coronary syndrome (ACS) can also arise from the sudden worsening of coronary plaque with barely mild-to-moderate luminal stenosis[7]. Based on this clinical standpoint, a number of groups have tried to illuminate the characteristics of high-risk lesions of coronary artery by the use of multimodal techniques like IVUS, angioscopy, virtual histology-IVUS, intravascular-OCT' non-invasive multidetector computed tomography, PET scan, SPECT scan, MRI and their different combinations[8].

Aim of Study

Ruptured plaques are the main reason for the development of acute coronary syndromes (ACS). This review was intended to enhance the prognostic values of *in vivo* evaluation in high-risk coronary plaques by intravascular ultrasound (IVUS), IVUS-VH, OCT, thermography, intravascular magnetic resonance, Roman and near-infrared spectroscopy, and non-invasive multidetector computed tomography, PET scan, SPECT scan, MRI and their different combinations in patients undergoing coronary angiography.

Coronary artery angiography

Coronary artery angiography is the major technique for evaluation of the diseases related to coronary artery tree but there is still a huge difference in manifestation of the opaque lumen of vessels and the real degree of atherosclerotic burden **(Figure 1)**. Furthermore, the degree of narrowing of lumen does not present trustworthy data about further occurrence of a MI event leading to high a mortality rate [9]. Many trials for lipid reduction on clinical and angiographic evaluation have revealed very little or no progress of angiographic luminal diameter, but highly remarkable decrease in myocardial infarction[10]. Luminogram is actually not capable of providing details about the wall constitution of coronary artery and consequently it fails in making differentiation in stable and high-risk lesions.

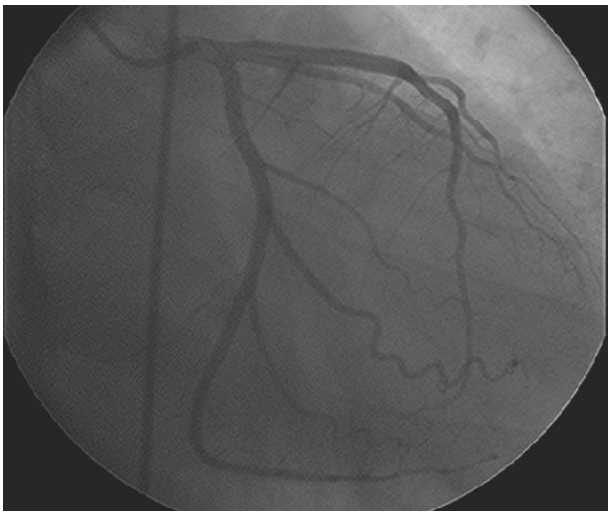

Figure 1: Image of coronary artery angiography showing left coronary tree

Angioscopic imaging of coronary artery

The plaque surface and intraluminal structures can be visualized directly with the utility of intracoronary angioscopy (CAS). It gives evaluation for the color of lesion (white, red or yellow), which also enlighten complications of lesions, such as ulceration, fissures, intimal breaks and thrombosis with improved detection capability as compared to angiographic analysis[11]. By angioscopic analysis, intact portions of coronary artery are visualized as glossy white, while lesions with high plaque burden are classified depending upon color acquisition by angioscopy from white to yellow. Thrombus with high platelet count at plaque rupture area with coarse white substance and erythrocyte/fibrin-rich thrombus as an asymmetrical, bulging-out red mass in the lumen. Thrombus formation and acute coronary syndrome are associated with yellow colored lesions[12]. The major shortcoming of angioscopic analysis is its requirement of area without blood during image attainment that is only achievable either by absolute vessel blockage or by uninterrupted washing with saline, during angioscopic analysis. Finally, vessel intramural changes which are reflected on luminal surface being captured by angioscopy, may not be sensitive enough to find out future changes in lesion constitution or plaque load[13].

Plaque analysis intravascular ultrasound

Recently, IVUS is thought to be the gold standard for intracoronary imaging. IVUS not only to examine the lumen and vessel borders but also provide real-time, high-resolution images of the plaque **(Figure 2)**. Visual evaluation echogenicity of plaque gives semi-

quantitative tissue depiction, and calcification can be recognized with about 90% sensitivity and specificity[14]. Deposition of lipids, illustrated as an echo-lucent area, and can be recognized with 78–95% sensitivity and with 30% specificity[15]. For the imaging purpose of vasa vasorum thickness, a strong marker for plaque vulnerability in which micro bubble contrast enhanced IVUS can be used to evaluate lesions with enhanced metabolic activity in inflamed lesions[16]. Intravascular ultrasound (IVUS) is capable of providing valuable information regarding plaque burden and remodeling of vessel. These unique IVUS techniques have been formed to illustrate the rigidity of culprit lesion and identification of the existence of necrosis in fibro-fatty tissue[4].

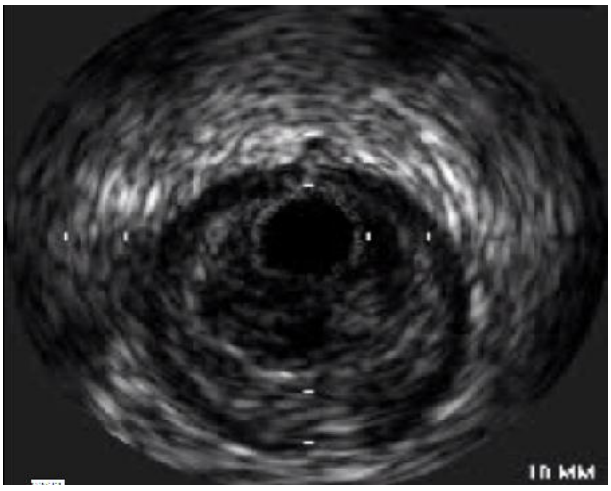

Figure 2: IVUS Image of coronary artery showing atherosclerotic burden

Intravascular ultrasound virtual histology

A technique called IVUS gray-scale imaging, developed by the amplitude of the signals by radiofrequency, in which a significant amount of information lying below and between the peaks of the signal is removed. The rate and power of the signaling among tissues, without considering likelihood in the amplitude. Four types of tissue maps i.e. fibrolipidic, necrotic, calcium and fibrous are constructed by the use of IVUS-virtual histology. Each type of tissue map is coded with different color, such as, white is assigned to calcified, green to fibrous, greenish-yellow for fibrolipidic and red to necrotic core.[17] The sensitivity and specificity of IVUS-VH is 50 and 98.9% for dense calcium, 79.3 and 100% for fibrous tissue, 67.3 and 92.9% for necrotic core and 86 and 90.5% for fibrofatty, respectively.

Palpography

Local mechanical tissue properties are evaluated by this technique. Specified pressure gradient, among high lipid containing pliable tissue constituents will distort at higher degree as compared to calcified and fibrous tissues which possess high rigidity.[18] Data obtained with comparison of radiofrequency at various pressure grades is used to assess the distortion of local tissue. At a cardiac rhythm of 60 bpm, 1.0 mm/s pullback speed and 1.0mm longitudinal resolution palpograms are obtained using a 20-MHz phased array IVUS catheter (Eagle Eye).[19] *In vitro* assessment of high-risk lesion by palpography has high sensitivity and specificity which is 88% and 89%, respectively.[18]

Optical coherence tomography

An optical analogue of ultrasound called optical coherence tomography (OCT) in which an image is generated by using light rather than sound waves. Low coherence, near-infrared (NIR) light with about 1300nm wavelength range, which reduces energy absorption by water, protein, lipids and hemoglobin for imaging by OCT. A better *in vivo* as well as *in vitro* resolution up to 10–20μm is provided by OTC which is far better resolution level as compared to IVUS technique i.e. 100–150μm. Fibrous plaques have 71–79% and 97–98%, whilst fibrocalcific plaques have 95–96% and 97%, and 90–94% and lipid-rich plaques have 90–92% sensitivity and specificity, respectively. [20] [21] On the other hand, latest studies showed a comparison between OCT and histopathology, and found least sensitivity for plaque constituents, and mal-classification was observed in lesions (41%), mainly because of combined effect of inadequate traveling distance into the arterial wall and least capacity to discriminate Ca^{++} deposits from lipid components.[22]

Low penetration depth only up to 2mm in tissue is the major drawback of OCT, which dampers imaging of the entire artery wall in larger vessels and presence of blood which absorb light needs to be improved by running a saline gush and balloon tamponade. By this way, it can reduce the effectiveness in the process of assessment of long and proximal segments of the coronary artery, which is the major demerit for clinical practice of this modality.

Coronary artery SPECT scan

Radiotracers labeled with Technetium-99m (99mTc) i.e. 99mTc-sestamibi and 99mTc-tetrofosmin are common in clinical use to evaluate the perfusion of cardiac myocytes and their normal metabolic

function. New 99mTc-labelled tracers with new iodine-123 tracers are under development process for SPECT imaging in perfusion of cardiac cells which effectively reveal high cardiac utility and enhanced imaging of cardiac cells,[23] although further clinical trials are required to prove their diagnostic significance. SPECT with 99mTc-labelled tracers are trailed to target high-risk atherosclerotic lesions specifically to identify such changes.

A study was conducted by Johnson, *et al.*[24] in a swine model for *in vivo* detection of atherosclerotic lesions. Plaque imaging was performed by using 99mTc-labeled with Annexin A5. Histopathologic analysis revealed that the coronary lesions in general were at an early stage and were mostly featured by smooth muscle cells. Focal uptake of 99mTc Annexin A5 was observed in 13 out of 22 coronary vessels *in vivo*. The results showed the feasibility for *in vivo* identification of cell death in atherosclerotic plaque in the coronary artery with equal effectiveness in human model. Although results from studies on animal models are showing satisfactory outcomes, still the significant application in cardiac nuclear imaging relies on the utility of PET to image high-risk coronary lesion as SPECT is restricted for the imaging of coronary artery plaques.

Intravascular magnetic resonance

Magnetic resonance (MR) is a non-ionizing diagnostic technique exploiting the spins of the nuclear protons in a heavy magnetic field. Two types of methods are used for intravascular imaging for diagnostic purpose. This technique is to illustrate coronary anatomical structure by a device having a coil fixed in a wire or catheter associated with an external magnet (MR imaging [MRI]). Although this method proves to be highly efficient in providing composition and structural details of vessel wall and coronary lesions, still this technique is not applicable in catheterization of cardiac lesions.

Clinical feasibility of Catheter-based, self-contained IVMR spectroscopy has been recently demonstrated for patients programmed to carry out cardiac angiography.[25] IVMR spectroscopy might precisely distinguish various parts such as smooth muscle cells, fresh thrombus, organizing thrombus, fibrous cap, edema, calcium and lipid having 84 to 100% sensitivity and specificity, respectively. Some shortcomings such as inadequate field of view, the catheter size, the requirement of direct vessel wall contact and the time duration need for acquisition.[26]

Coronary plaques imaging by targeted-Nanoparticles

Recent advances in nanotechnology have opened new horizon of inventions to improve a variety imaging techniques for coronary plaques by using targeted-nanoparticles as contrast agents. This accomplishment can also be helpful in identification and evaluation of the vulnerable atherosclerotic plaques. In fact, a number of studies have revealed that imaging by targeted-nanoparticles made it possible to enhance the sensitivity and specificity in comparison with the techniques being used in routine .[27]

A number of studies for imaging at molecular level for biomarkers related to atherosclerosis were conducted by using nanoparticles of iron oxide and their results were interpreted by using magnetic resonance imaging.[28] Nanoparticles made up of Iron oxide are proved to be compatible with biological tissues and is a substance that has been extensively utilized as a MRI contrast agent to detect atherosclerotic plaques in clinical practice. Although, iron oxide nanoparticles are accepted for clinical use as a MRI contrast agent, still dextran is required to coat the iron oxide particles to make dextran-coated iron oxide (DIO) which is biocompatible and biodegradable, to make it appropriate in clinical use. This DIO nanoparticle is frequently used for contrast-enhanced T1 and T2-weighted MRI scans. However, new synthetic method by sulfating DIO with sulfur trioxide pyridine complex is trailed to produce sulfated DIO (SDIO) nanoparticles because of complexity of DIO in clinical applications.[29] SDIO have proved higher contrast enhancing quality due to its higher affinity to be mustered at the area with atherosclerotic lesion, experimentally. Nanoparticles made up of polymers of radio-labeled zirconium-89 dextra nanoparticles (DNP) ware also being use in integrated PET/MRI to image atherosclerotic lesions [38].

This *in vivo* molecular imaging technique possibly aid in detection of these high-risk coronary lesions, their evaluation and results of medication. By using all these information about integrated imaging modality, Nahrendorf et al have effectively devised a new tri-modality nanoparticle contrast medium that can precisely identify the increased influx of macrophages in atherosclerotic lesions.[30] Such captivating innovation could be of immense value for being used in PET/CT and PET/MR scans, and consequently several molecular imaging-based outcomes on early recognition of vulnerable

atherosclerotic lesions are anticipated to be discovered in the future.

Raman and near-infrared spectroscopy

Many types of spectroscopic intravascular imaging modalities have been devised in recent era and are still under the process of development and investigation.[31] Modalities such as spectroscopy can provide details and chemical composition of vulnerable plaque with high sensitivity and specificity. Laser light with wavelength in range of 750–850nm can variate in wavelength (generation of Raman effect) by tissue molecules excitation, which disperse light at a diverse wavelength. This Raman effect is dependent upon chemical constitution of the tissue [32] which results in quantitative values of molecules.[33] *In vitro,* Raman spectroscopy has found adequate relationship in comparison with histology (r = 0.68 for cholesterol and r = 0.71 calcification) and with IVUS.[34] In near-infrared spectroscopy, it is demonstrated how various substances absorb and scatter NIR light to various degrees at different wavelengths.

Postmortem studies of aortic and coronary artery demonstrated that the ability of the this modality to detect lipid-rich TCFAs.[35] A system with catheter has been established to deal with the problems to approach the coronary vessel, blood, motion and the scanning requirement, which must be dealt in use for patients. Further studies are still needed to confirm the ability of this modality to discover lipid-rich coronary artery plaques and eventually link chemical features with subsequent rate of an ACS.[36]

Laser Speckle Imaging

Laser Speckle Imaging (LSI) evaluates the biomechanical characteristics of atherosclerotic lesions by demonstrating time-varying laser speckle patterns. When a scattering medium such as tissue is visualized utilizing temporally laser coherent light, a granular pattern of multiple bright and dark spots, named as speckle, becomes evident in the image with resultant photons bouncing back interference from various parts of tissue molecules. In tissue, endogenous light dispersion particle's Brownian motion results in scatter pathways and optical path lengths to dynamic changes, causing in time-dependent intensity modulations of the laser speckle. The frequency of laser speckle modulation is completely dependent on the motion of endogenous scatterers, which is effected by the medium visco-elasticity.[37] By means of these principles, a study carried out on *in vitro* vasculature has shown that the calculation of the time constant de-correlation intensity modulations of time-varying laser speckle patterns establishes a technique for characterizing atherosclerotic lesions and for evaluating unstable necrotic core plaques with 100% sensitivity and 93% specificity.[38]

The combination of spatial and temporal data analysis from laser speckle patterns has been shown that LSI may also provide a measure of plaque fibrous cap thickness.[39] A new study has demonstrated that LSI can be performed through minute diameter optical fiber bundles, allowing the opportunity to perform intra-coronary LSI through miniaturized intravascular catheters.[40] Recently, however, a clinically feasible LSI system has yet to be constructed and evaluated, although active research and development in this area is advancing rapidly. If effectively translated into the clinical research, the intracoronary LSI technique provides the opportunity of achieving a measure of the biomechanical characteristics of coronary plaques, a characteristic that is presently not measured with other intravascular optical imaging techniques.

PET imaging of coronary plaques

Radiopharmaceutical-fluorodeoxyglucose PET

In cardiology, 18F-FDG PET is regularly conducted to evaluate glucose utility in cardiac cells at risk, uptake of FDG indicates viability and possible positive response to myocardial revascularization.[41] In addition to the extensive application of 18F-FDG PET for screening and staging of tumors, 18F-FDG PET is the highly reliable technique to detect inflamed lesion, as 18F-FDG shows buildup in inflammatory cells in which glucose metabolism is at its active form. Arterial imaging by using 18F-FDG PET has extensively been utilized as a biomarker to explore the metabolic state of atherosclerosis.[42] Wykrzykowska, *et al*.[43] demonstrated the potential value of 18F-FDG PET to image inflammation in coronary arteries by conducting coronary catheterization, after particular dietary intervention reducing uptake of glucose in cardiac cells. One or more coronary segments with atherosclerosis showed uptake of 18F-FDG in invasive coronary angiography.

Radiopharmaceuticals in cardiac PET

Even though 18F-FDG is a suitable and extensively utilized radiopharmaceutical, exploration of more highly specific targeting mediums for the recognition of inflamed plaque and recognition of break in plaque has been providing very promising information in new studies.[44] 18F-labeled mannose (2-deoxy-2-

[18F] fluoro-D-mannose, 18F-FDM) demonstrates a subset of macrophages and it may present a suitable to locate the inflamed vasculature with the use of properly labeled 18F-FDM. Tahara, *et al*.[45] in their new study data have analyzed and compared the uptake of 18F-FDM with 18F-FDG in experiments on animal models, and their results demonstrated relatively high specific uptake of both tracers in the aortic arches and abdominal aortas in animal models having atherosclerotic lesions both in both *in vivo* and *in vitro* images.

Quantification Ca^{++} load on coronary wall with cardiac CT scan has been extensively adopted as a trustworthy non-invasive modality for screening risk of subsequent cardiac events.[46] Even though clinical worth to assess subsequent cardiac events, cardiac CT does not precisely evaluate plaque inflammatory status and the degree of molecular calcification which represents plaque stability.[47] 18F-sodium fluoride (18F-NaF) is a innovative radiopharmaceutical that can be anticipated to predict the precision in evaluating the mechanism of vascular calcification.[48] Initial investigations have illustrated precise association in the risk factor cardiac events and the level of calcification in aorta and heart,[48] further information about plaque physiology with use of 18F-NaF, even though more prospective investigations are required to validate the above given conclusions.

Apart from the aforementioned radiopharmaceuticals, a number of tracers have been studied and evaluated to image vulnerable lesions such as 11C-choline,[49] 18F-galacto-RGD,[50]11C-acetate,[51] and 11C-PK11195.[52] Since 11C-PK11195 exclusively targets translocator proteins extensively expressed on the surface of metabolically active macrophages, it may show more specificity to image atherosclerosis than 18F-FDG. In spite of promising results have been shown in many studies, patients investigations in clinic are required to establish their clinical efficacy to image atherosclerosis. The potential power of PET scanning depends upon its outstanding sensitivity, effective penetration, and quantitative characteristics.[53] Nevertheless, there are some drawbacks that must be addressed in PET scanning of vulnerable lesions: the tiny area in atherosclerotic plaque with proximity of blood, and the uninterrupted cardiac and respiratory motions in image acquisition.[54] Moreover, the association in different PET scannings of vulnerable plaques, their pathological features and clinical confirmation of verse cardiac effects, is deficient.

Integrated PET/CT imaging

The nuclear medicine combined with multi-slice CT such as PET/CT and SPECT/CT gives a distinctive prospect to outline cardiovascular diseases and their physiological events together. To evaluate the patient which are identified or supposed to have coronary vessel complication, it provides assessment and quantitative analysis of coronary lesion components, vessel reactivity, endothelial health, detection of flow-limiting coronary plaques, estimation of myocardial perfusion and viability.[55] The probability of using PET/CT in the recognition of soft plaque in the coronary artery was established in a case report.[56] Fusion of PET/CT images recognized and localized areas of enhanced FDG uptake in the proximal portion of the left coronary artery with non-calcified lesion, which was linked to inflamed atherosclerotic plaques. The more clinical availability of PET/CT scanners makes, non-invasive determination of vulnerable atherosclerotic plaques, possible.

Even though 18F-FDG is valuable and important marker of inflammatory process of vessels, 18F-FDG PET may not be capable of evaluating the plaque rupture due to complex assembly of variety of cell types that are implicated in the vulnerable plaque. Thus, it is highly desirable to invent some other tracers that can preferentially target plaques with high inflammatory activities and they are capable of detecting an atherosclerotic lesion at risk for rupture, therefore making it possible to detect and intervene as early as possible to get better outcomes.

18F-NaF-PET/CT imaging is thought to be a valuable technique in identifying calcification at molecular level in the beginning of the atherosclerotic process as micro-calcification has been involved in plaque rupture.[48, 57] A study conducted in 2014, researchers sophisticatedly established that 18F-NaFPET/CT provides the first non-invasive imaging approach to recognize pinpoint lesion fissuring and vulnerable lesions as compared to 18F-FDG.[58] On the contrary, coronary 18F-FDG uptake was fundamentally interchangeable at confined built up of agent in myocardium and enhanced uptake was observed in the diseased arteries[59]. This finding illustrates that ruptured plaque or plaque vulnerable to rupture can be detected by non-invasive imaging technique, thus 18F-NaFPET/CT has the capacity to modify management and resuscitation of patients with stable and unstable cardiac events.

Nahrendorf, *et al*. illustrated their data in animal model by using cell adhesion molecule (VCAM)-1 by integrated PET/CT scanning in atherosclerosis and

plaques at high-risk to rupture, which have high expression of VCAM-1 on the surface of macrophages, smooth muscle cells and endothelial cells. Their findings reveal a significant progress in molecular imaging of vascular inflammation that facilitate a further step closer to the reality of PET/CT imaging in humans.[60]

Integrated PET/MRI imaging

The accessibility of PET/MRI systems might spectacularly assist the transformation of capable clinical application of PET scanning for atherosclerotic lesions due to the pliable component of lesion with better contrast ability of MRI.[61] By utilizing the combination of PET/MRI to estimate variations in the vulnerable lesion with high inflammatory activity with use of 18F-FDG PET provides greater sensitivity than contrast-enhanced MRI to identify earlier variations in plaque inflammation.[73] Even though CT scan is capable of generating high-resolution anatomical images during PET/CT scanners, misaligning of PET and CT information is frequent because the both imaging technique are not obtained at same time. In newly constructed PET/MRI scanning devices, PET and MR data can be obtained at the same time that's why information mustered with MRI can be utilized to enhance data the analysis of PET images.

Velocity improved PET/MRI which was anticipated to settle the misalignment issues occurred in PET/CT since all PET data are reconstructed within the same reference phase, which provides precise spatial registration between PET and MR data.[62] This modality has been proven to enhance illustration and identification of coronary lesions. Multi-modal imaging of plaques such as PET/MRI might be an ultimate application since combination of the imaging techniques functions synergistically to maximize diagnostic effectiveness of each imaging technique and strengthens the recognition and quantification of calcified and non-calcified plaques load, quantification of vascular reactivity and endothelial health, detection of flow-limiting coronary narrowing, and possible recognition of vulnerable coronary tree lesions.[63] At present, PET/MRI is not efficient in preclinical cardiac imaging in animal models, therefore, further trails with additional advancements in modalities are anticipated to establish its medical significance in vulnerable plaque imaging.

Conclusion

Studies on imaging of vulnerable plaques preferentially are being focused on myocardial perfusion imaging and morphological analysis. However, the most problematic barrier is achieving precise detection of unstable from stable plaques prone to rupture before clinical symptoms appear (due to narrowing or thrombus formation in the coronary tree) to reduce high mortality rate of ACS. It is concluded that every technique has its own significance and specificity in detection of particular feature of vulnerable plaque. Until now, we are unable to define a single modality in order to detect *in vivo* vulnerable plaques accurately. A varying combination of above given techniques can help the physicians and medical expertise to increase the predictive value of prognostication. It is highly desired to device such combination of different diagnostic techniques to improve accuracy in early detection of vulnerable plaque.

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