Atherosclerotic cardiovascular disease, including myocardial infarction and stroke, remains a common cause of death and disability.

Vascular imaging using PET scan is now a well established non-invasive technique in detecting the vulnerable plaques at different vascular levels, as well as the process of neo-angiogenesis.
PET imaging of Angiogenesis

Angiogenesis is a physiological process by which new capillaries are formed from pre-existing vessels.

Formation of new vessels networks can assist in restoring the perfusion to cardiac tissue exposed to hypoxic conditions and potentially prevent the onset of tissue necrosis.

Angiogenesis is regulated through multiple angiogenic factors, cells, and the extracellular matrix, and can be stimulated by various conditions associated with cardiovascular disease, such as ischemia, hypoxia, inflammation, and alterations in vascular shear stress.

The process usually started by the initial activation of endothelial cells that leads to increased their proliferation.

Hossam Sherif. JNM, 2013

**Imaging of Angiogenesis in Cardiology**

<table>
<thead>
<tr>
<th>Integrin subtype</th>
<th>ECM ligand</th>
<th>Expression in quiescent vessels</th>
<th>Angiogenic activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>αvβ3</td>
<td>RGD sequence</td>
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<td>+</td>
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<td></td>
<td>Vitronectin</td>
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<td>Thrombospondin, etc.</td>
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<td></td>
<td>Thrombospondin</td>
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Radiotracers for myocardial angiogenesis imaging

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<tr>
<th>Biological target</th>
<th>Tracer</th>
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<tbody>
<tr>
<td>$\alpha_v\beta_3$ integrin</td>
<td>$^{99m}$Tc-NC100692</td>
<td>SPECT</td>
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<tr>
<td>$^{99m}$Tc-RAFT-RGD</td>
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<td>$^{111}$In-RP748</td>
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<td>$^{125}$I-gluco-RGD</td>
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<td>$^{18}$F-AIF-NOTA-PRGD2</td>
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<td>CD13</td>
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<td>VEGF receptor</td>
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<tr>
<td>CD105</td>
<td>$^{64}$Cu-NOTA-TRC105</td>
<td>PET</td>
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</table>


Imaging of angiogenesis targeting $\alpha_v\beta_3$ integrin expression in a patient post-MI

2 weeks post-MI

Makowski MR. Eur Heart J. 2008
LV Remodeling & Angiogenesis

Myocardial infarction, and subsequent LV remodeling, is the most frequent cause for the development of chronic heart failure.

Post-MI, myocardial tissue undergoes a healing process associated with inflammation, angiogenesis, fibroblast proliferation, and collagen deposition resulting in scar formation.

Dissoki S. Mol Imaging Biol., 2015

Early αvβ3 Integrin Expression using 18F galacto-RGD PET
Predicts long-term LV Remodeling post-MI in small animal model

Hossam Sherif. JNM, 2013
Integrin $\alpha v\beta 3$ Expression in the Infarcted Myocardium is Related to the Clinical Outcome?

18F-RGD PET uptake was increased in the follow up of the infarcted myocardium with better outcome


PET imaging of Coronary Artery Vulnerable Plaques
Certain coronary atheromatous plaques are more susceptible to rupture and erosion. Termed ‘vulnerable plaques,’ these atheromata are histologically defined by a large lipid-rich core and thin overlying fibrous cap.

Many modalities presently developed to identify vulnerable coronary plaques are invasive in nature; IVUS and OCT (optical coherence tomography)

Non-invasive PET/CT has been used to identify high-risk plaques; using the tissue / background ratio uptake (TBR) for the culprit plaques and the non-culprit plaques

Marchesseau S, Journal of Nuclear Cardiology, 2017
Lee JM. Circ Cardiovasc Imaging. 2017

Hybrid PET/CT and PET/MRI Imaging of Vulnerable Coronary Plaque using 18F-NaF in STEMI

CT calcium scoring images in the axial view where the LAD and 2 ROIs have been segmented.

Stephanie Marchesseau, Journal of Nuclear Cardiology, 2017
Imaging of Ruptured Coronary Atherosclerotic Plaque Using 18F-FDG PET/CT

FDG-PET-CT demonstrated intense FDG

Koiwaya H. JACC: Cardiovascular Interventions, 2016

18F-NaF PET has been recently introduced as a potential noninvasive imaging tool to identify and localize plaque with high-risk characteristics in patients with CAD.

Its activity is localized in coronary plaque suggesting early stage of vascular inflammation.

Group 1 (non-risk plaque) by both IVUS and OCT,
Group 2 (low-risk plaque) only in 1 imaging tool, and
Group 3 (high-risk plaque) by both tools.
Group 3 showed the highest 18F-NaF TBR value and proportion of positive lesions.

Lee JM. Circ Cardiovasc Imaging, 2017
Dual Motion Correction of 18F-NaF PET for Imaging Coronary Atherosclerotic Plaques

3-D PET-CT images without correction (left) and with (right)
It reduces image noise, and increases TBR.
Increased uptake is seen in RCA, LAD, and LCX.

Coronary Plaque Imaging using Simultaneous PET-MR

Mathieu Rubeaux, J Nucl Med 2016;

Carotid artery stenosis is a well-established risk factor of ischemic stroke, contributing to up to 20% of strokes or TIA.

PET/CT can be used now to risk stratify these patients on how vulnerable the plaque is to rupture, resulting in ischemic stroke.

PET/CT is an effective technique to identify active inflammation or presence of lipid-rich necrotic core within the plaque.

Brinjikji W. J Neurosurg, 2015
Sun ZH. Journal of Geriatric Cardiology, 2014
Criteria of the American Heart Association (AHA) for histological classification of the carotid atherosclerotic plaque

Brinjikji W. J Neurosurg, 2015

High-risk plaque detected in non-stenotic carotid plaques of patients with ischemic stroke using 18F-FDG PET/MR imaging

Non-stenotic 40% (NASCET criteria) vulnerable plaque with 18F-FDG PET/MRI of Lt. internal carotid artery ipsilateral to the territory of stroke. But also increased in Rt. carotid artery contralateral to the stroke; with large non-stenotic vulnerable atherosclerotic plaque.

The high-risk vulnerable plaques are prone to rupture and develop intra-plaque hemorrhage in comparison to stable plaques.

Thus, the ability to **non-invasively** detect and analyse these plaques at early stages, especially in asymptomatic and low-risk patients, would improve risk stratification without the need for more invasive procedures.

Thank You
For Your
Attention

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