

## Novel imaging techniques to identify unstable atherosclerotic plaques

Disruption of atherosclerotic plaques is the main cause for acute ischaemic syndromes. Up to now, the prediction of plaque rupture is challenging, since imaging techniques fail to precisely detect key characteristics of vulnerable atherosclerotic plaques such as microcalcification, a large necrotic core, or positive remodelling. The development of modern functional molecular imaging techniques represent a novel approach to detect such unstable plaques *in vivo*, and therefore allows to identify patients at risk for cardiovascular events. There is increasing evidence for a potential role of PET-CT imaging in the diagnosis of cardiovascular disease. However the current gold standard, using  $^{18}\text{F}$ -fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) as a tracer does not allow for differentiation of plaque vulnerability, also  $^{18}\text{F}$ -FDG metabolically interferes with high blood glucose levels and therefore is not well applicable in patients with diabetes.

Joshi et al. investigated  $^{18}\text{F}$ -sodium fluoride ( $^{18}\text{F}$ -NaF) as a new tracer for PET-CT imaging and its role in identifying vulnerable atherosclerotic plaques in a prospective clinical trial on 80 patients with cardiovascular disease [1]. In detail, 40 patients with acute myocardial infarction (AMI) and 40 patients with stable angina pectoris underwent PET-CT as well as invasive coronary angiography. As tracer,  $^{18}\text{F}$ -sodium fluoride ( $^{18}\text{F}$ -NaF) and  $^{18}\text{F}$ -fluorodeoxyglucose ( $^{18}\text{F}$ -FDG), the current gold standard, were used. The tissue-to-background ratio as the uptake of  $^{18}\text{F}$ -NaF in culprit and non-culprit lesions in AMI patients served as primary end-point. Secondary endpoints were comparative analysis of  $^{18}\text{F}$ -NaF positive and negative atherosclerotic plaques with intravascular ultrasound imaging in patients with stable angina, and characterization of histological samples in symptomatic carotid artery disease.

The study found the highest  $^{18}\text{F}$ -NaF uptake in culprit lesions of 37 (93%) patients with AMI (median max. tissue-to-background ratio: culprit 1.66 [1.40–2.25] vs. highest non-culprit 1.24 [1.06–1.38];  $p < 0.0001$ ). However, standard PET-CT by use of  $^{18}\text{F}$ -FDG did not discriminate

between vulnerable and non-vulnerable plaques (1.71 [1.40–2.13] vs. 1.58 [1.28–2.01];  $p = 0.34$ ). In stable angina, significant  $^{18}\text{F}$ -NaF uptake occurred in 18 (45%) patients. Further correlation with intravascular ultrasound showed more high-risk features in the  $^{18}\text{F}$ -NaF marked lesions compared to those without: e.g. higher remodelling index (1.12 [1.09–1.19] vs. 1.01 [0.94–1.06];  $p = 0.0004$ ), more microcalcification (73% vs. 21%;  $p = 0.002$ ), or necrotic core (25% vs. 18%;  $p = 0.001$ ).

In summary, the use of non-invasive imaging techniques to detect ruptured or unstable atherosclerotic plaques would represent a seminal opportunity to identify patients at high risk for imminent cardiovascular events with further impact on treatment strategy. Looking at current literature, Adamson et al. assess PET-CT assisted plaque prediction favourably [2]. As a new tracer  $^{18}\text{F}$ -NaF does allow for detection of high-risk plaques and may overcome some of the major drawbacks of the current standard method, using  $^{18}\text{F}$ -FDG in terms of metabolic interaction. However, the method needs to be proven in a larger, non-selected patient cohort to give evidence for its broad applicability and predictive validity.

### References

1. Joshi N V et al.  $^{18}\text{F}$ -fluoride positron emission tomography for identification of ruptured and high-risk coronary atherosclerotic plaques: a prospective clinical trial. *Lancet*. 2014; 383: 705–13.
2. Adamson P et al. Translational Coronary Atherosclerosis Imaging with PET. *Cardiol Clin* 2016;34: 179–86.

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