

the fat attenuation index of perivascular tissue (FAI_{PVAT}), is positively associated with the presence of coronary artery disease (CAD) and the volume of fibrous plaque in the proximal RCA independently of the presence of coronary calcium. As part of the same study, the present inventors also showed that FAI_{PVAT} changes in a dynamic way in response to local rupture of a culprit lesion in patients with acute MI and can distinguish culprit from non-culprit lesions. These observations supported the inventors' hypothesis that FAI_{PVAT} could function as a dynamic biomarker of vascular inflammation and cardiovascular risk and offer diagnostic and prognostic information beyond that of traditional biomarkers, such as coronary calcium.

However, there remains an urgent need for the identification and development of functional biomarkers that will describe vascular inflammation, rather than structural and non-reversible changes in the vascular wall, and diagnostic tools to aid non-invasive detection of vascular inflammation and enable stratification of patients who are at risk of suffering serious cardiac events.

Summary

According to a first aspect, the present disclosure is directed to a method for determining the perivascular water index (PVWi) of a blood vessel, comprising

- (i) using data gathered from a computer tomography scan along a length of the vessel to determine the total volume of voxels of water within an attenuation window around the attenuation of water within the perivascular space a pre-determined distance from the outer wall of the vessel, and
- (ii) correcting the total volume of the voxels of water for the volume of the vessel by dividing the total volume of voxels of water determined in step (i) by the total perivascular volume.

As described herein, the present disclosure provides a method for determining the perivascular water index (PVWi) of a blood vessel, comprising (i) using data gathered from a computer tomography scan along a length of the vessel to determine the total volume of voxels of water within an attenuation window around the attenuation of water within the perivascular space a pre-determined

distance from the outer wall of the vessel, and (ii) correcting the total volume of the voxels of water for the size of the vessel by dividing the total volume of voxels of water determined in step (i) by the total perivascular volume.

- 5 According to a second aspect, the present disclosure is directed to the use of perivascular water index (PVWi), as defined according to the method of the first aspect of the disclosure, as a functional biomarker of vascular inflammation. According to this aspect, PVWi can be used alone, or in combination with one or more other biomarkers, to predict all-cause or cardiac mortality risk in a patient.
- 10 In particular, PVWi can be used in combination with one or more of calcium index, fibrous plaque index, fat attenuation index of the perivascular adipose tissue, volumetric perivascular characterisation index, fat attenuation index and total volume of the epicardial adipose tissue to predict all-cause or cardiac mortality risk in a patient.

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According to a third aspect, the present disclosure is directed to a method for predicting the mortality risk or risk of a patient suffering a cardiovascular event, said method comprising:

- (a) using data gathered from a computer tomography (CT) scan along a length
20 of a blood vessel to determine:

- (i) calcium index (Calcium-i); and/or
- (ii) fibrous plaque index (FPI);

and at least one of

- (iii) fat attenuation index of the perivascular adipose tissue (FAI_{PVAT});
- 25 (iv) perivascular water index (PVWi); and/or
- (v) fat attenuation index of the epicardial adipose tissue (FAI_{EPAT}); and

(b) comparing each of the values determined in (a) to a pre-determined cut-off value or using the absolute value of each variable in order to generate an output value that indicates the patient's risk of suffering a cardiovascular event.

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Further described herein, is a method for predicting the risk of a patient suffering a cardiovascular event, said method comprising:

(a) using data gathered from a computer tomography scan along a length of a blood vessel to determine:

- (i) calcium index (Calcium-i); and/or
- (ii) fibrous plaque index (FPI);

5 and at least one of

(iii) fat attenuation index of the perivascular adipose tissue (FAI_{PVAT}); and/or

(iv) perivascular water index ($PVWi$); and

10 with the possible addition of any of the following:

(v) volumetric perivascular characterisation index (VPCI)

(vi) total epicardial adipose tissue volume ($EpAT-vol$);

(vii) fat attenuation index (FAI) of epicardial adipose tissue (FAI_{EpAT});

15 (b) comparing each of the values determined in (a) to a pre-determined cut-off value or using the absolute value of each variable in order to generate an output value that indicates the patient's risk of suffering a cardiovascular event.

20 According to a fourth aspect, the present disclosure is directed to use of the method according to the third aspect for non-invasive monitoring of aortic aneurysms and/or carotid plaques, wherein said method does not include determining $EpAT$ volume or FAI_{EpAT} .

25 In a preferred example of the method of the third aspect of the disclosure, both FAI_{PVAT} and $PVWi$ are determined in step (a) of the method.

In one example, the method according to the third aspect of the disclosure further comprises determining one or more of (vi) fat attenuation index of total
30 volume of the epicardial adipose tissue ($EpAT-vol$), (vii) the epicardial adipose tissue (FAI_{EpAT}), (viii) age and (ix) gender of the patient.

In certain examples, the method according to the third aspect of the disclosure can be used for non-invasive monitoring of aortic aneurysms and/or carotid
5 plaques.

Description of the Drawings

The invention is described with reference to the following Figures, in which:

10 **Figure 1** provides a definition of perivascular adipose tissue (PVAT) indices. (A) Coronary CT angiography images were reconstructed in 3 dimensions. The right coronary artery was tracked and the proximal 10-50mm of its course were selected on curved multiplanar reconstruction images. The inner and outer walls of the vessel were manually optimized and the perivascular area (up to 20mm
15 distal to the outer vessel wall) was analysed based on the respective tissue attenuation. A Hounsfield Unit range of -15 to +15 was used to detect perivascular water, whereas a range of -190 to -30 was applied for detection of adipose tissue. (B) The perivascular area was then split in 20 concentric cylindrical layers of 1mm thickness and fat attenuation index (FAI), defined as
20 the mean attenuation of adipose tissue within the pre-defined range, was then calculated in each layer and plotted against the distance from the vessel wall. PVAT was defined as AT within a radial distance equal to the diameter of the vessel, whereas AT in the most distal layer was defined as non-PVAT. The volumetric perivascular characterization index (VPCI) was then defined as the
25 percent change from FAI_{PVAT} to $FAI_{non-PVAT}$. Further analysis by tertiles of fibrous plaque index (FPI, fibrous plaque volume divided by the total volume of the vessel) revealed a positive association between fibrous plaque burden and FAI of the adipose tissue in the perivascular area. Perivascular Water Index (PVWi) was defined as the total volume of voxels of water within an attenuation window
30 around the attenuation of water (-15 to +15 HU) within the perivascular space a pre-determined distance from the outer wall of the vessel (e.g. a radial distance equal to the diameter of the vessel) divided by the total perivascular volume.