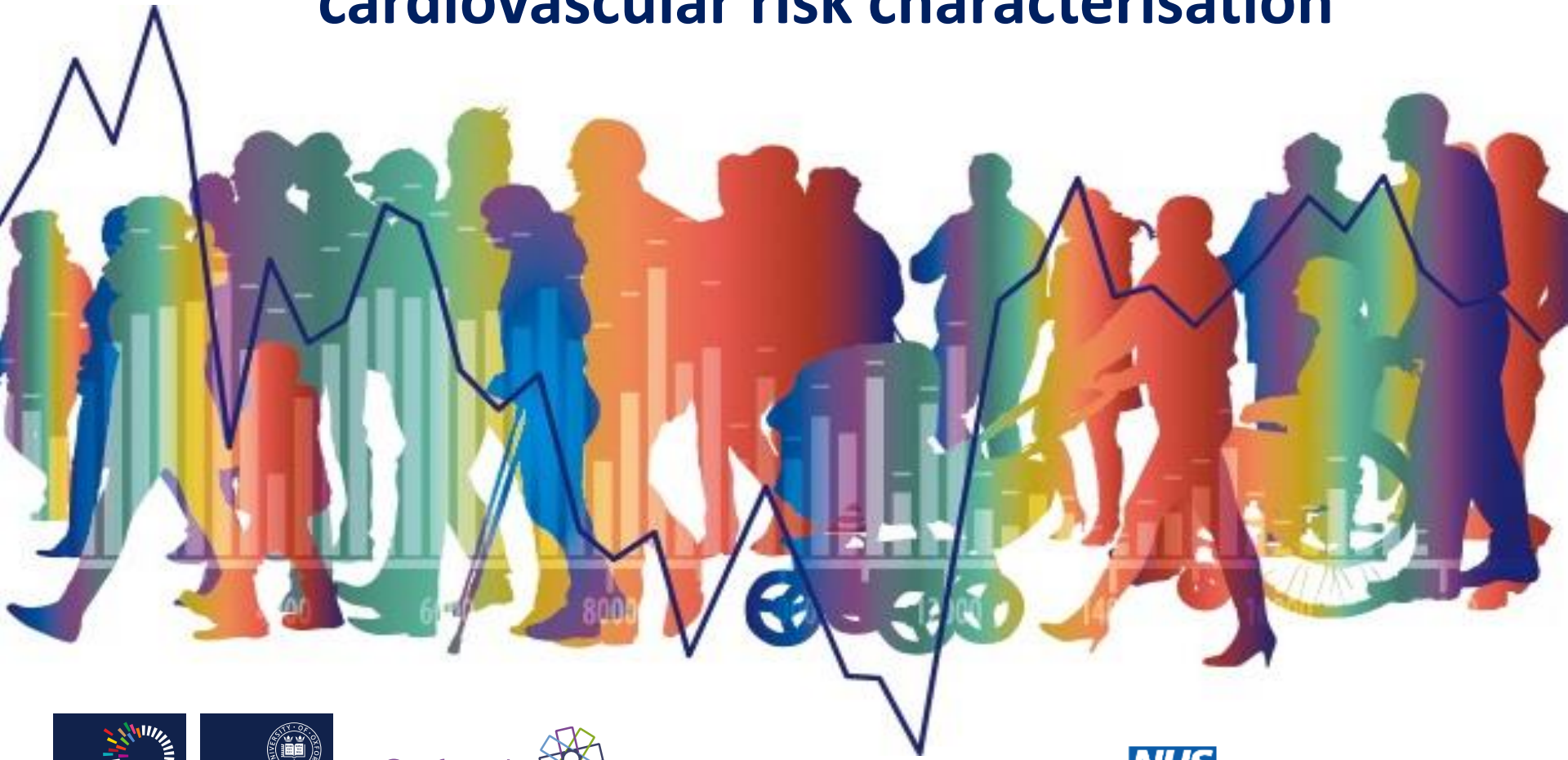
Inflammation quantification for cardiovascular risk characterisation



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Developing an advanced biomarker of Coronary Artery Disease using common CT imaging

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Cardiovascular disease is the #1 killer in industrialised nations

Significant economic burden

£169 billion in EU and **$394 billion** in US per year

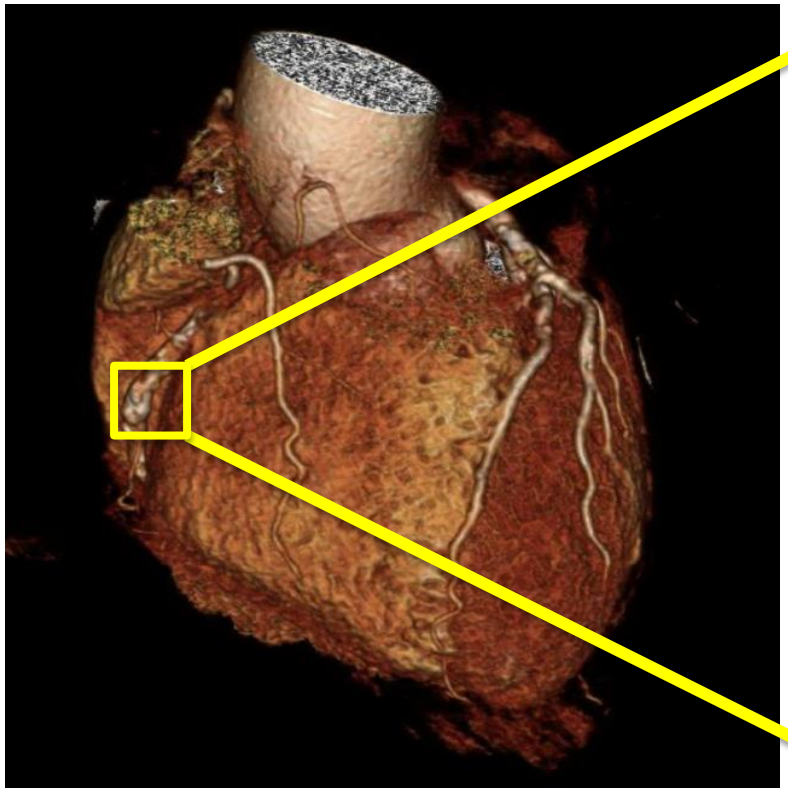
Current diagnostic methods identify **structural changes** in the vascular wall when disease is already **non-reversible**

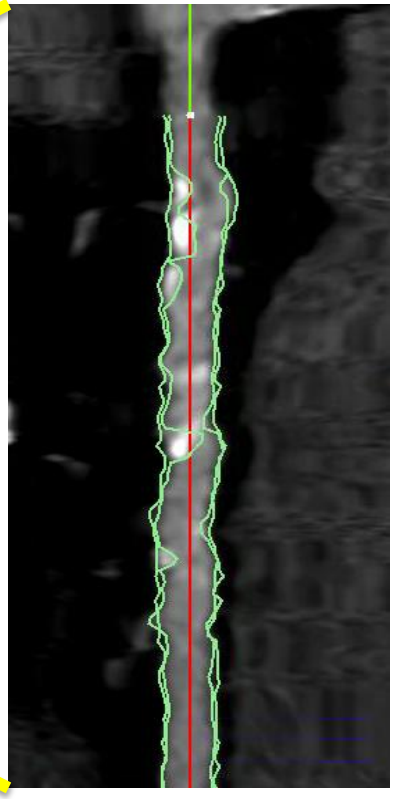
The challenge is to detect CVD early, when it is still **reversible**

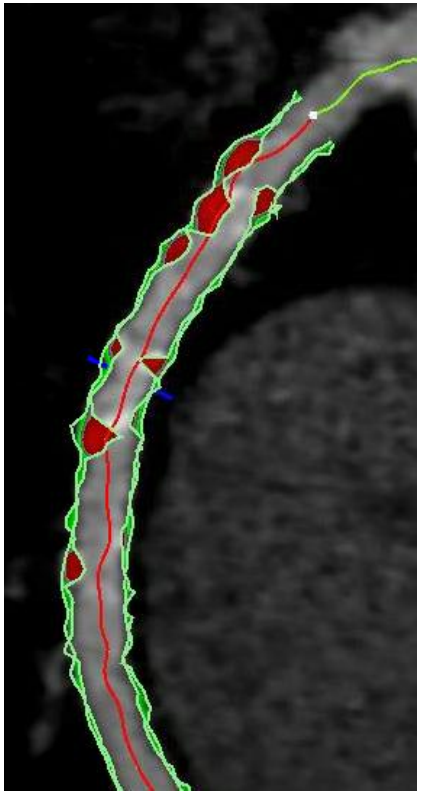
https://www.bhf.org.uk/research/heart-statistics

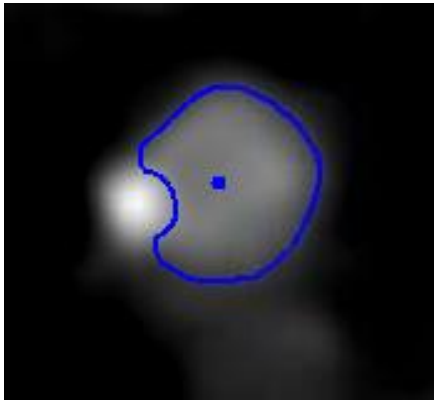
Cardiac CT is a widely used non-invasive imaging technique to assess the coronary vessels

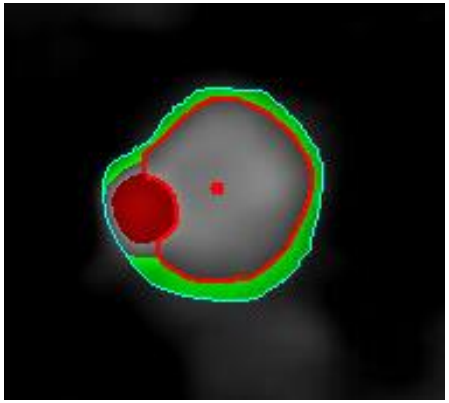
- Acquisition lasts around 20 minutes
- Lower levels of radiation with the newest CT scanners
- Minimal risk to patients
- Easily accessible

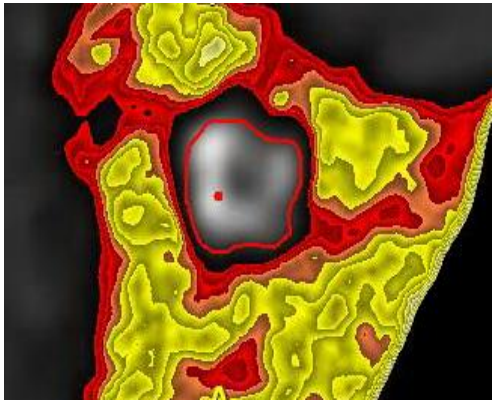












CT angiography is the only non-invasive method that detects coronary artery disease

- Cardiac CT is undertaken to exclude coronary disease, or for risk prediction (Calcium score)

https://www.nice.org.uk/sharedlearning/ct-coronary-angiography

- >95% of cardiac CTs show “non-significant coronary artery disease” and patients are discharged without further management

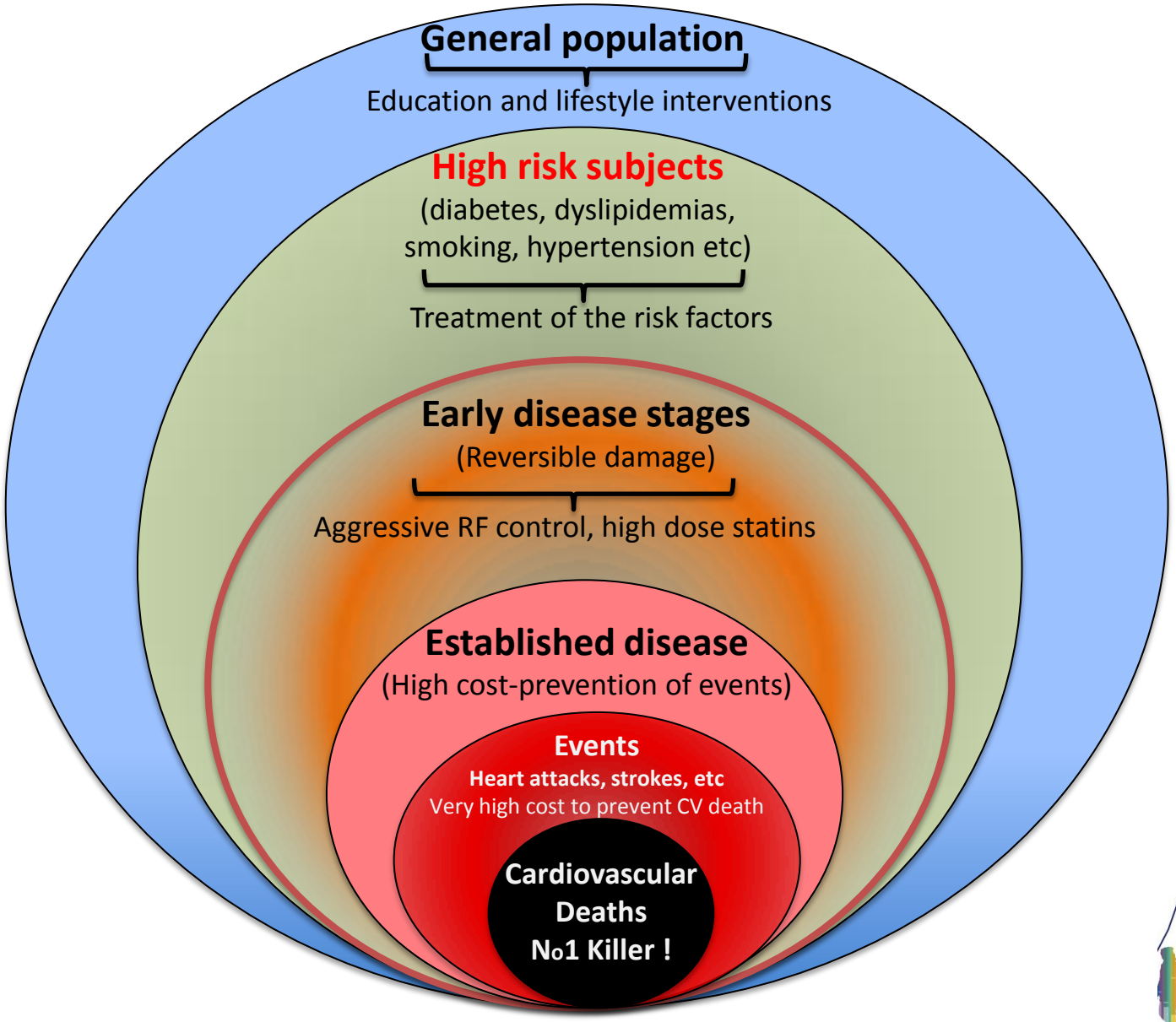
Current clinical practice is unable to correctly identify patients at risk

However…

- **50% of heart attacks** happen in patients with **'NON-SIGNIFICANT'** coronary artery disease, as "minor" **inflamed** plaques rupture

Can we identify these subjects with inflamed coronaries and treat them to prevent disease development and heart attacks?

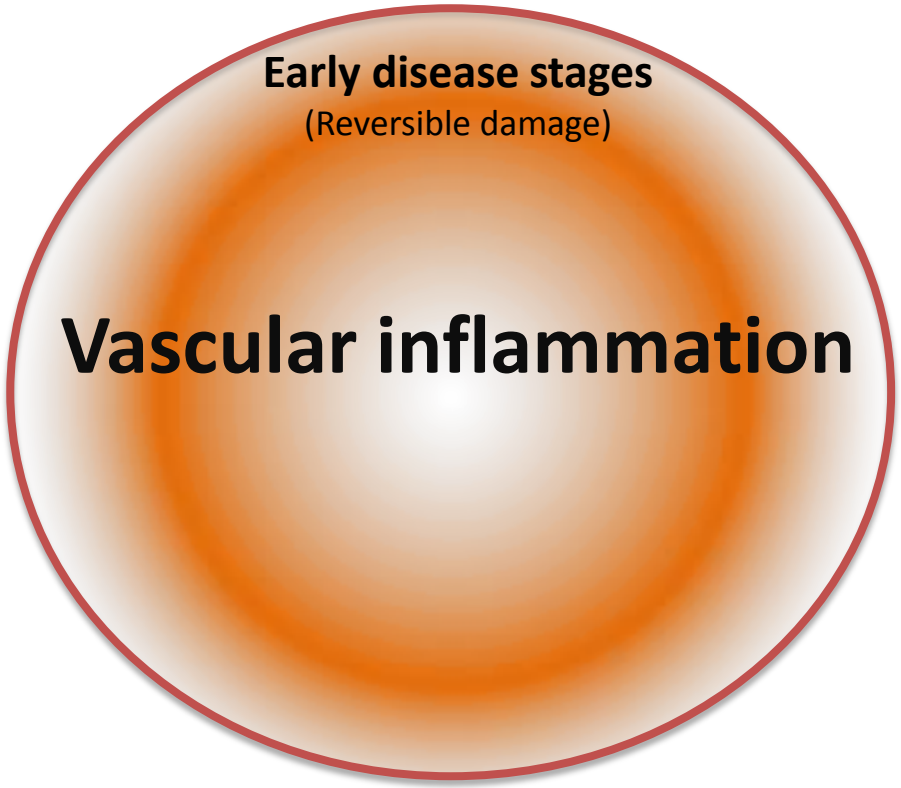
Current management of cardiovascular risk



Current management of cardiovascular risk

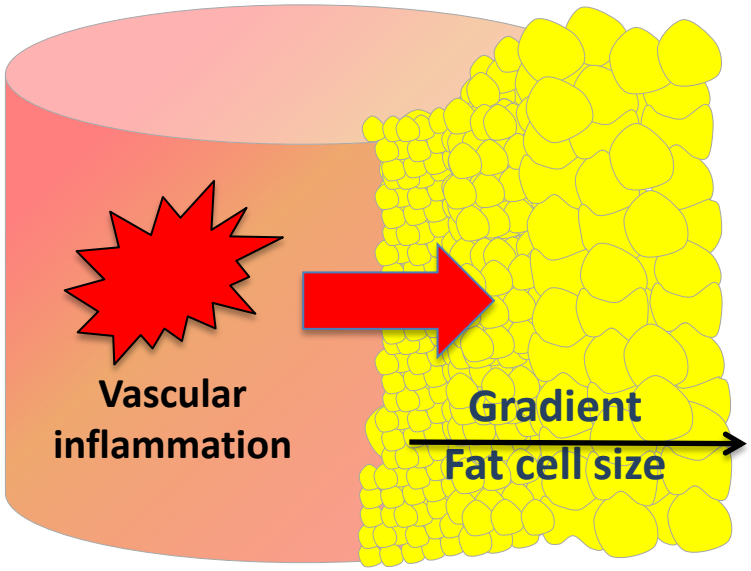
If we detect vascular inflammation, we can treat to prevent:

a) **Disease development**
b) **Disease progression**
c) **CV events and CV death**

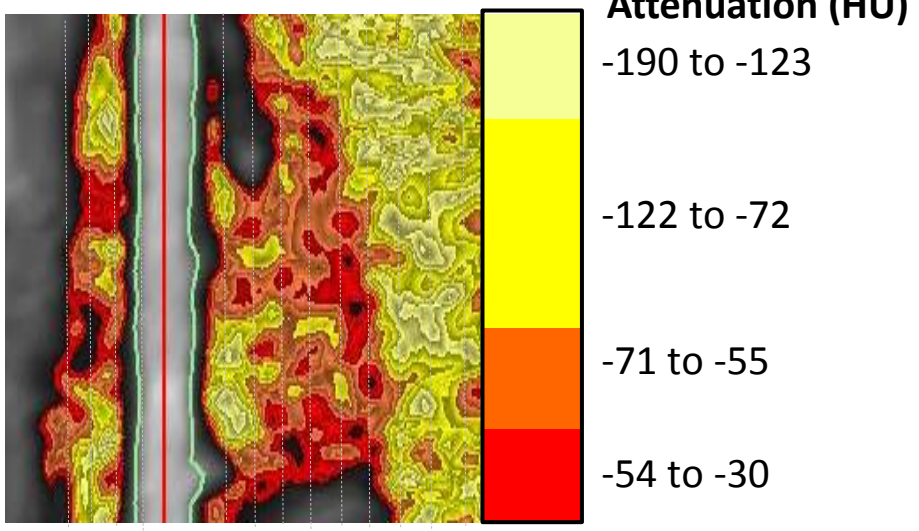


We have developed a **novel method** that quantifies vascular inflammation non-invasively, and **detects the "vulnerable patient"**.

Our scientific breakthrough

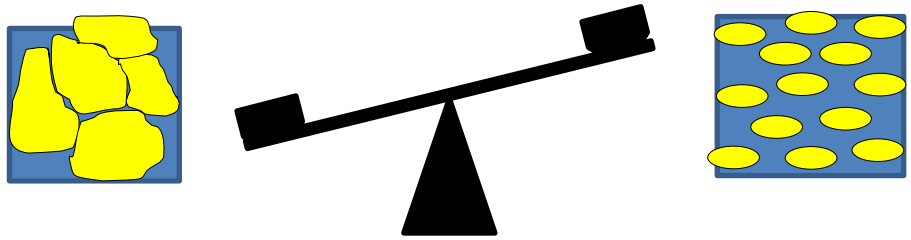


Our novel biomarker:
FAI (Fat Attenuation Index)



So, what is "FAI"?

- **a new index that quantifies fat cell size non-invasively, by quantifying the shift of attenuation related to the balance between the aqueous/lipophilic phases**

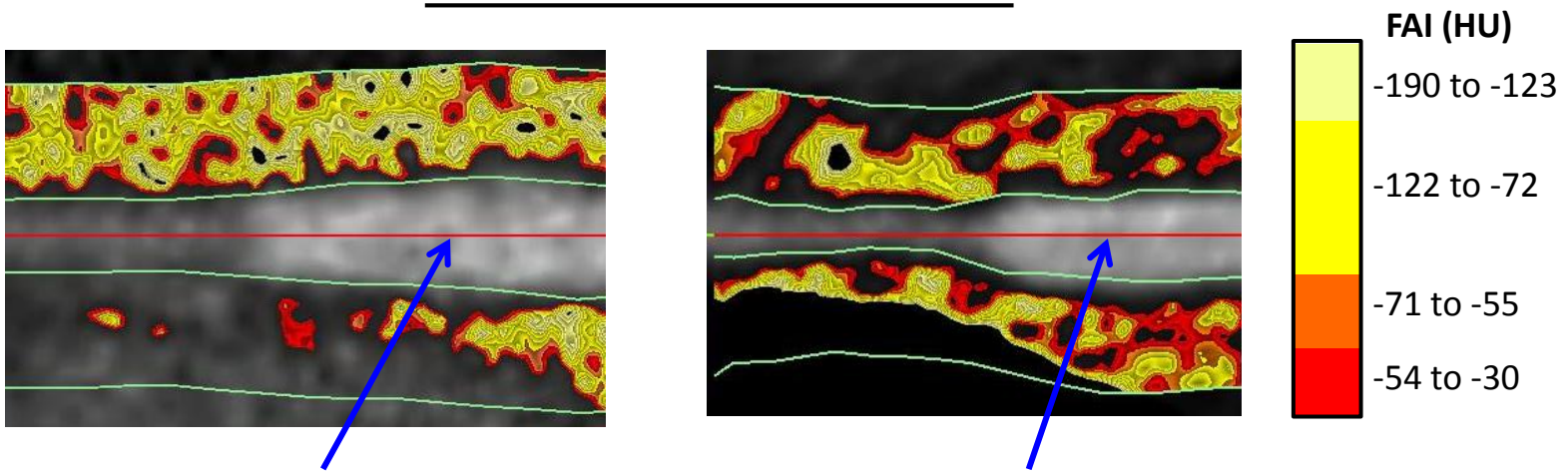


Margaritis et al; Circulation 2013;127(22):2209-21
Antonopoulos A et al Diabetes 2015 64(6):2207-19
Antonopoulos A et al Circ Res 2016; 118(5):842-55

Fat Attenuation Index:
A potential biomarker for 'vulnerable plaques'

- >50% of heart attacks are caused by highly inflamed but anatomically non-significant atherosclerotic plaques
- **Detecting "vulnerable plaques" has been hailed as the 'holy grail' of cardiovascular disease diagnostics**

CT after a heart attack



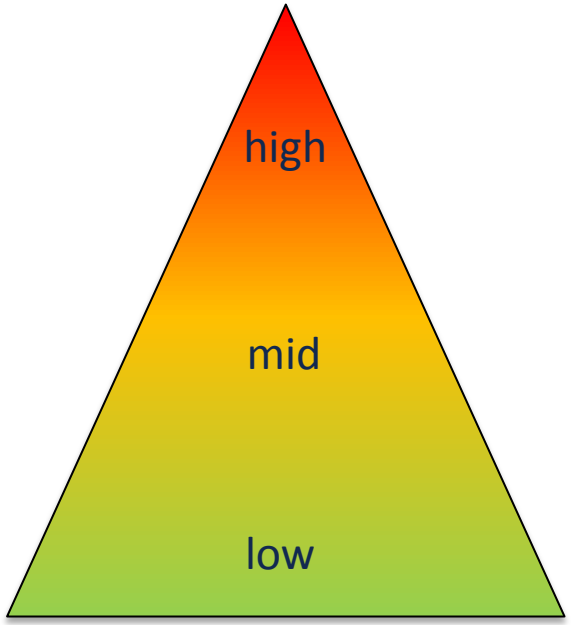
Non-culprit ("stable") lesion **Culprit ("ruptured") lesion**

Fat Attenuation Index:
An advanced biomarker for CVD risk

- Non-invasive biomarker
- Detects vascular inflammation (a reversible condition) at any disease stage
- Detects vulnerable (inflamed) plaques that lead to heart attacks
- Can be applied **retrospectively** to existing scans and **prospectively** into existing care pathways at no additional scanning cost
- Could be a “game changer” in terms of modifying clinical practice

Fat Attenuation Index:
Improving cardiovascular risk stratification

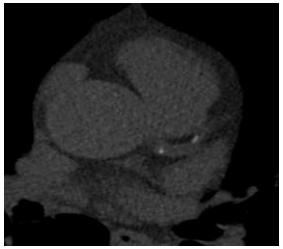
How to stratify cardiovascular risk in a population?



Who should we treat?

Current state-of-the-art

Traditional cardiovascular risk factors



Coronary calcium scoring using cardiac CT

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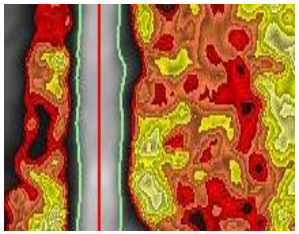
Future addition



Vascular inflammation assessment by FAI

There are multiple opportunities in the cardiovascular diagnostics market

- **10 million** patients received a CT scan in the US last year (10% growth)
- **40 million** patients had an indication for a CT scan in the US last year
- Market for diagnosing/treating vulnerable plaques is expected to reach **$10 billion** over the next decade

Summary

- **Unmet need:** To identify and treat patients with inflamed/vulnerable coronary artery plaques prevent heart attacks
- **Novel biology**: Perivascular fat “senses” vascular inflammation and changes its structure
- **New technology**: Allows non-invasive detection of vascular inflammation, by tracking the changes in perivascular fat.
- **Commercial pull:** Strong - Targets the multi £B market of cardiovascular primary and secondary prevention

Next steps

Currently optimising software design

Implementation in large outcome clinical trials

Assess licensing opportunities of IP
into existing global software applications

Incorporate into clinical care pathways and change clinical practice

Questions