($p<0.05$) and mitochondrial respiration assessed by a Seahorse flux analyser decreased by 25% ($p<0.05$).

To determine the effects of mtDNA damage, we studied arterial ageing in mice that overexpressed the mitochondrial helicase Twinkle (Tw^+), or with a mutation in the proof-reading ability of the mitochondrial polymerase gamma (PolG). Twinkle expression restored mtDNA copy number with concurrent improvement in mitochondrial respiration. Twinkle expression delayed all physiological parameters of vascular ageing, associated with decreased collagen and elastin breaks ($p<0.05$). In contrast, PolG mice with increased mtDNA damage showed accelerated vascular ageing compared to controls ($p<0.05$).

Conclusions We have identified multiple, reproducible parameters of arterial ageing in mice that are detected at far earlier time points than previously described; in particular, compliance, distensibility and □SI at 44wk provide the earliest discrimination. Arterial mitochondrial function reduces markedly with age, and accelerates vascular ageing, whereas augmenting mitochondrial function delays ageing, identifying prevention of mtDNA damage and dysfunction as a therapeutic target in ageing.

C HYPERPOLARIZED MAGNETIC RESONANCE IMAGING OF CARDIAC INFLAMMATION AND REPAIR

[1]Andrew JM Lewis*, [3,1]Jack J Miller, [2,3]Oliver J Rider, [3]Robin P Choudhury, [3]Stefan Neubauer, [1]Carolyn A Carr, [1]Damian J Tyler. *[1]Department of Physiology, Anatomy and Genetics, University of Oxford, UK; [2]Department of Physics, Clarendon Laboratory, University of Oxford, UK; [3]Radcliffe Department of Medicine, University of Oxford, UK*

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Myocardial infarction (MI) remains a major killer despite highly optimised systems for the delivery of primary percutaneous coronary intervention (PPCI), highlighting a need for novel therapeutics that could be administered in the days following the event. The healing myocardium undergoes a macrophage driven inflammatory response which is a compelling therapeutic target, though clinical exploration of this process has been limited because conventional imaging techniques cannot assess cellular inflammation in the heart.

We hypothesised that the huge increases in signal-to-noise ratio provided by hyperpolarized MRI could provide a solution to this problem. In rodent models, hyperpolarized [1–13C]pyruvate MRI using a custom designed metabolite mapping sequence *in vivo* demonstrated that experimental MI caused intense [1–13C]lactate signal in healing myocardial segments at both day 3 (paralleling the maximal 'inflammatory' phase of the macrophage response) and also at day 7 ('reparative' phase), compared to sham operated controls. Monocyte/macrophage depletion using clodronate liposomes normalised the [1–13C]lactate signal at both timepoints.

Gene expression analysis of monocytes/macrophages sorted from infarct tissue demonstrated regulation of key enzymes of glycolysis, suggesting that monocyte/macrophage recruitment and metabolic reprogramming of those cells underlies the high lactate signal detected. Hyperpolarized [1–13C]pyruvate MR spectroscopy in macrophage-like cell suspensions confirmed that cellular activation and polarisation almost doubles hyperpolarized lactate label flux rates *in vitro*; blockade of glycolysis with 2-deoxyglucose (2-DG) in activated macrophage-like cells normalised lactate label flux rates and also markedly inhibited production of key pro-inflammatory cytokines at both mRNA and protein level, without major cytotoxicity.

Systemic administration of 2-deoxyglucose following rodent MI normalised hyperpolarized [1–13C]lactate signal in healing myocardial segments and also caused dose dependent improvement in IL-1β expression in infarct tissue, providing proof-of-concept of 'MR visible' immunomodulation. Furthermore, cine MRI demonstrated improvements in myocardial remodelling and systolic function in 2-DG treated rats at 3 months. Finally, we present initial human experience of cardiac hyperpolarized [1–13C]pyruvate MR, demonstrating unprecedented improvements in signal-to-noise ratio and highlighting the potential for rapid clinical translation of these findings.

We conclude that hyperpolarized MRI provides a novel biomarker of cardiac inflammation and repair post-MI by detecting the induction of an immuno-metabolic pathway in cardiac macrophages which controls key inflammatory cytokine production and influences myocardial remodelling. In addition to a role in the development of novel therapeutics to improve remodelling post MI, hyperpolarized MRI may have broad applications in other inflammatory cardiovascular diseases.

D ATHEROSCLEROTIC INFLAMMATION IMAGING USING ^{68}GA-DOTATATE PET VS. ^{18}F-FDG PET: A PROSPECTIVE CLINICAL SUDY WITH MOLECULAR AND HISTOLOGICAL VALIDATION

[1]Jason M Tarkin*, [2]Francis R Joshi, [3]Nicholas R Evans, [4]Mohammed M Chowdhury, [1]Nichola L Figg, [1]Aarti V Shah, [1]Lakshi T Starks, [1]Abel Martin-Garrido, [5]Roido Manavaki, [1]Emma Yu, [6]Rhoda E Kuc, [7]Luigi Grassi, [7]Roman Kreuzhuber, [7]Myrto A Kostadima, [7]Mattia Frontini, [8]Peter J Kirkpatrick, [4]Patrick A Coughlin, [4,9]Deepa Gopalan, [3]Tim D Fryer, [9]John R Buscombe, [10]Ashley M Groves, [7,11]Willem H Ouwehand, [1]Martin R Bennett, [3]Elizabeth A Warburton, [6]Anthony P Davenport, [1]James HF Rudd. *[1]Division of Cardiovascular Medicine, University of Cambridge, UK; [2]Heart Centre, Rigshospitalet, Copenhagen, Denmark; [3]Department of Clinical Neurosciences, University of Cambridge, UK; [4]Department of Vascular and Endovascular Surgery, Addenbrooke's Hospital, UK; [5]Department of Radiology, University of Cambridge, UK; [6]Experimental Medicine and Immunotherapeutics, University of Cambridge, UK; [7]Department of Haematology, University of Cambridge, and NHS Blood and Transport, Cambridge, UK; [8]Division of Neurosurgery, Addenbrooke's Hospital, UK; [9]Department of Radiology, Hammersmith Hospital, UK; [10]Department of Nuclear Medicine, Addenbrooke's Hospital, UK; [11]Institute of Nuclear Medicine, University College London, UK; [12]Department of Human Genetics, Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, UK*

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Background Inflammation drives atherosclerotic plaque rupture underlying most clinical events. While inflammation can be measured using 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET), 18F-FDG lacks cell-specificity and is unreliable for coronary imaging owing to myocardial signal spillover. Up-regulation of somatostatin receptor-2 (SST2) occurs in activated macrophages offering a novel inflammation imaging target.