to detect small vessel calibres (~40 μm vs. 200 μm using a conventional X-ray device) and quantify regional differences in resistance vessels of interest, even under conditions of high heart rate (>500 bpm).

Experiments were conducted at the Japanese Synchrotron, SPring-8, using anaesthetised Sprague–Dawley rats three weeks after treatment with vehicle (control) or streptozotocin (diabetic, 65 mg/kg i.p.). The right carotid artery was cannulated and angiograms of the coronary vasculature were recorded. Using cine-radiograms we investigated endothelium-dependent and -independent vasodilatory responses in individual coronary vessels, in vivo. Change is from baseline.

Diabetic animals had elevated blood glucose concentration ($p < 0.001$) and reduced final body weight ($p < 0.001$) and mean arterial pressure ($p < 0.05$). Vessel recruitment was lower in diabetics during acetylcholine (ACh, $p < 0.05$), while nitric oxide synthase (NOS) and cyclooxygenase (COX) blockade, resulted in a strong trend towards loss of visible microvessels ($p = 0.059$). Diabetic animals displayed numerous focal stenoses during NOS/COX blockade which persisted and increased after ACh infusion. Segmental constriction was also noted in diabetic rats during NOS/COX blockade which remained following ACh infusion. Diabetes was further associated with smaller vessel calibre in the 101–200 μm vessels during NOS/COX blockade ($p < 0.05$).

Synchrotron imaging provides a novel method to investigate coronary microvascular function in disease models, in vivo, and this study indicates that the early diabetic state is associated with localised and systemic impairment in coronary endothelial function in the diabetic microvasculature.

doi:10.1016/j.hlc.2011.05.033

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Effect of Adenosine on Pulmonary Vascular Resistance in Patients with Pulmonary Hypertension due to Left Heart Disease and Scleroderma

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Introduction: Functional assessment of the pulmonary vasculature is an important tool in the diagnosis of pulmonary hypertension. The effect of adenosine on pulmonary haemodynamics in left heart disease is not well understood

Methods: Right heart catheterisation was performed in eight subjects with mean PA pressure (mPAP) >25 mm Hg. In four subjects this was due to scleroderma (SCL) whilst four patients had heart failure with normal ejection fraction (HFNEF) defined by a pulmonary capillary wedge pressure (PCWP, mm Hg) >18 mm Hg and an ejection fraction >50%. Invasive haemodynamic measures were obtained before and during an adenosine infusion (140 mcg/kg/mins)

Results: Four SCL patients had a mean age of 58 ± 13 years, all were female and none were on pulmonary vasodilator therapy. Four HFNEF patients had a mean age of 62 ± 8 years, all were female and were receiving systemic antihypertensive therapy. The four patients with HFNEF all had LV end diastolic pressure >18 mm Hg (mean 21.5 ± 4.2 mm Hg). The effect of adenosine on pulmonary haemodynamics is summarised in the table: in patients with SCL, adenosine infusion resulted in a significant decrease in PVR in both groups, and an increase in CO in HFNEF patients. Despite the reduction in PVR, there was a trend to increased mPAP in HFNEF patients

Conclusions: Adenosine is an effective pulmonary vasodilator. Further study is required to elucidate whether the effect on pulmonary arterial and wedge pressures may vary with the etiology of pulmonary hypertension.

	SCL pre	SCL adenosine	HFNEF pre	HFNEF adenosine
mPAP	47.5 ± 12.9	45.3 ± 10.2	27.8 ± 5.9	30.3 ± 3.7
PCWP	15.3 ± 6.6	16.8 ± 6.6	18.2 ± 6.2	20.0 ± 5.0
CO	5.9 ± 1.7	8.1 ± 4.4	6.2 ± 1.5	10.1 ± 2.3†
PVR	5.8 ± 2.3	4.2 ± 2.3†	1.6 ± 0.6	1.1 ± 0.4*

* $p < 0.05$ for paired *t*-test comparison with pre adenosine.

† $p < 0.01$ for paired *t*-test comparison with pre adenosine.

doi:10.1016/j.hlc.2011.05.034

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Gender Differences in Internal Mammary Artery Vasoconstrictor Responses

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Background: Women have poorer in-hospital outcomes following coronary artery bypass grafting compared with men although the reasons are unclear. Gender-mediated differences in the vascular reactivity of the arterial conduit may contribute to these differential outcomes. This study investigated gender-dependent differences in the vasoconstrictor responses of the internal mammary artery used for coronary artery bypass grafting.

Methods: Internal mammary artery segments were obtained from patients undergoing coronary artery bypass grafting and subjected to vascular myography. Following assessment of endothelial function, concentration-response curves were determined to noradrenaline, phenylephrine, seotonin, U46619 (thromboxane analogue) and endothelin. The EC50 values for each vasoconstrictor are summarised in the table below, expressed as mean ± SEM (*significant difference between males and females, $p < 0.05$).

	Males ($n = 13$)	Females ($n = 7$)
Noradrenaline	0.73 ± 0.25 μM	0.23 ± 0.40 μM
Phenylephrine	3.36 ± 0.29 μM	0.36 ± 0.22 μM*
U46619	11.29 ± 0.12 nM	2.32 ± 0.41 nM*
Serotonin	4.08 ± 0.27 μM	0.16 μM ± 0.10 μM*
Endothelin	9.36 ± 1.05 nM	7.65 ± 1.49 nM

Conclusion: The internal mammary arteries of women are more sensitive to constriction by thromboxane, phenylephrine and serotonin, compared with men. Ongoing studies are evaluating the molecular mechanisms responsible for these differences.

doi:10.1016/j.hlc.2011.05.035

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Heme Oxygenase-1 is Necessary for Ischaemia-mediated Neovascularisation

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Due to confidentiality reasons, the text of this abstract has been withheld from publication.

doi:10.1016/j.hlc.2011.05.036

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Left Atrial Specific Endothelial Dysfunction and Inflammation in Atrial Fibrillation

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Introduction: Atrial fibrillation (AF) is associated with a prothrombotic state, with thrombus formation frequently occurring within the left atria (LA). We have previously shown that platelet reactivity is increased within the left atria in patients with AF. However little is known about endothelial function and inflammation within the LA.

Methods: Fifteen AF patients and 16 left sided accessory pathway (REF) undergoing radiofrequency ablation were studied. Following transseptal puncture and prior to the administration of heparin a blood sample (20 mL) was collected from the LA. Markers of endothelial dysfunction (von Willebrand factor [vWF]), and inflammation (intracellular adhesion molecule [ICAM-1] and vascular adhesion molecule [VCAM-1]) were measured using enzyme linked immunosorbent assay.

Results: AF patients had significantly higher levels of vWF within the LA compared to the LA of REF patients, indicating endothelial dysfunction. ICAM-1 and VCAM-1 were raised in the LA of AF patients when compared to REF (see table).

Conclusion: AF is associated with left atrial specific endothelial dysfunction and inflammation. This data suggests that LA endothelial dysfunction and inflammation are important contributing factors in the prothrombotic risk associated with AF.

	REF left atria	AF left atria	*P* value
vWF (mU/mL)	571 ± 132	1669 ± 223	<0.0001
ICAM-1 (ng/mL)	121 ± 76	200 ± 98	0.05
VACM-1 (ng/mL)	386 ± 190	499 ± 246	0.21

doi:10.1016/j.hlc.2011.05.037

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Lipid-free Apolipoprotein A-I Enhances Endothelium generation from Human Blood Monocytes

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We have recently reported that human blood monocytes are capable of rapidly transforming into endothelial-like cells after adhering to preexisting endothelium. This indicates that blood monocytes are a potential source for the repair/maintenance of intact endothelial layers. In this study, we investigated the effect of lipid-free apolipoprotein (apo) A-I, the main apolipoprotein in HDL, on endothelium generation from endothelial-adherent blood monocytes. Peripheral blood mononuclear cells (PBMCs) obtained from healthy HLA-A2+ donors were co-cultured with HLA-A2− human umbilical vein endothelial cells (HUVECs), thus allowing the PBMC-derived cells to be tracked by their HLA-A2 expression. The co-cultures were exposed to lipid-free apoA-I at final concentrations of 0.5 and 2.0 mg/ml. The cell layers were analysed by immunofluorescence and dual-color flow cytometry at serial time points. After 24 hours of co-culture, the proportion of monocyte-derived endothelial-like cells (M-ELCs) in the controls (no apoA-I) was 17 ± 0.9% while the proportion of M-ELC in co-cultures containing 0.5 mg/ml and 2.0 mg/ml of apoA-I were increased to 33 ± 1.4 and 35.8 ± 1.7% (both $P < 0.01$ compared to control). At an earlier two hour time point, at which potential M-ELC proliferation is minimal, a similar two-fold increase in the proportion of M-ELC was also observed. Endothelial transformation of the adherent blood monocytes was characterised by the acquisition of CD105, CD144, and eNOS expression. This was not affected by exposure to apoA-I. In conclusion, a physiologically relevant concentration of apoA-I enhances the generation of endothelium from endothelial-adherent blood monocyte by increasing monocyte recruitment.

doi:10.1016/j.hlc.2011.05.038