Imperial College London

Title Imaging for experimental cardiovascular science

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Cardiac Myogenesis, Death and Regeneration Group
National Heart and Lung Institute

British Heart Foundation

How to see within

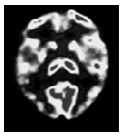
Rembrandt 1632
The Anatomy Lesson of Dr. Nicolaes Tulp

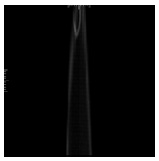
Wilhelm Roentgen 1895
The X-ray

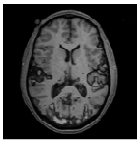
Overview

- *What to image*
- *Animal models for cardiovascular imaging*
- *Overview of modalities*
- *Challenges in cardiac imaging*
- *Advanced MRI methods*
- *Stem cell tracking*

Medical imaging





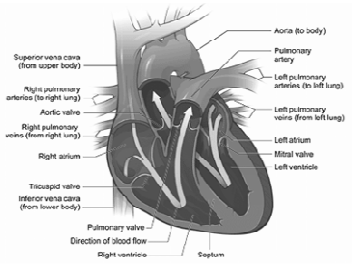


1900 1960 1980 2000

Applications of cardiac imaging

- Diagnosis
- Severity of disease
- Location of pathology
- Response to therapy

- Silent pathology
- Mechanisms of disease
- Location of grafts

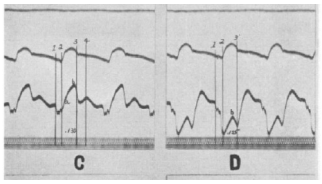


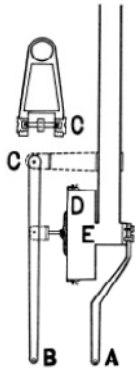
In vivo cardiac imaging modalities

THE EFFECT OF CORONARY OCCLUSION ON MYOCARDIAL CONTRACTION[1]

ROBERT TENNANT[2] AND CARL J. WIGGERS
From the Department of Physiology, Western Reserve University Medical School, Cleveland, O.

Received for publication March 22, 1935





Animal models of CV disease

Myocardial infarction
- Permanent coronary occlusion
- Ischemia - reperfusion
- Cryoinjury

Hypertension and heart failure
- Trans aortic constriction
- Spontaneous hypertension
- Cardiotoxins

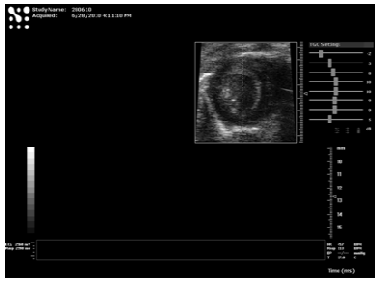
Congenital heart disease – HCM/DCM
- Genetic modification of contractile protein

Myocarditis

US – Ultrasound / echocardiography

Method
- reflection of ultrasonic waves
- 1D, M-Mode imaging

Measure
- Cavity volume
- Contraction

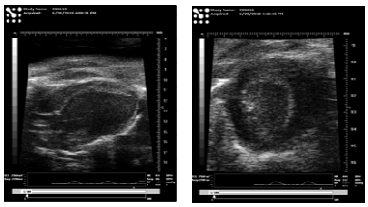


Visualsonics Vevo 770
Hammersmith Hospital
Imperial College

US – Ultrasound / echocardiography

Method
- reflection of ultrasonic waves
- 2D, B-Mode imaging

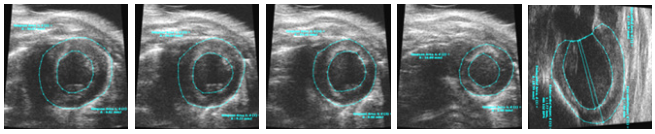
Measure
- Cavity volume
- Contraction



Visualsonics Vevo 770
Biological Imaging Centre
Imperial College

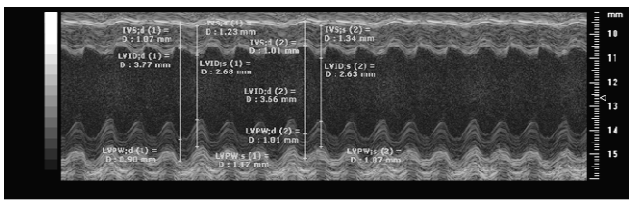
US – Ultrasound / echocardiography

2D B-mode		*mouse*
End diastolic volume EDV	Cavity volume at diastole	70 µl
End systolic volume ESV	Cavity volume at systole	30 µl
Stroke volume SV	EDV-ESV	40 µl
Ejection fraction EF	(EDV-ESV)/EDV	60 %
Cardiac output CO	SV x heart rate	24 ml/min
Wall volume (LV mass)		100 mg

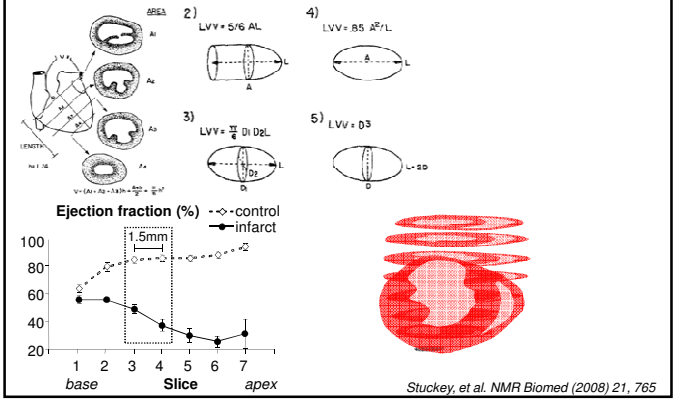


US – Ultrasound / echocardiography

1D M-mode		*mouse*
End diastolic dimension EDD	Cavity diameter at diastole	3.5 mm
End systolic dimension ESD	Cavity diameter at systole	2 mm
Fractional shortening	(EDD-ESD)/EDD	40 %
Wall thickness		1 mm



US – Ultrasound / echocardiography

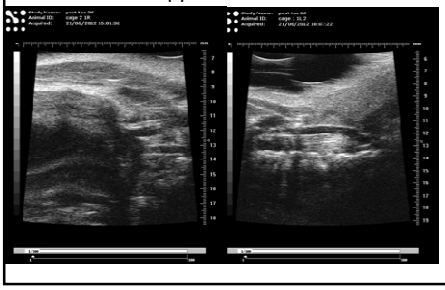


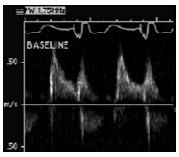
Stuckey, et al. NMR Biomed (2008) 21, 765

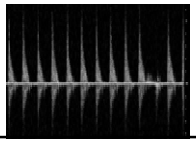
US – Doppler

Method
- Doppler effect on ultrasound
- 1D flow Doppler
- 2D tissue Doppler

Measure
- mitral/aortic flow
- tissue movement



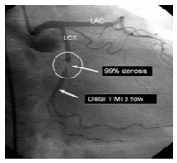




Angiography

Method
- Catheterization + X-ray
- Infusion of Iodine based CA

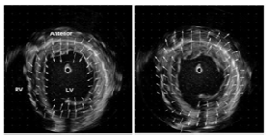
Measure
- Coronary occlusion
- Contraction



US - speckle tracking

Method
- motion of “speckles”
- 2D/3D image processing

Measure
- regional stress/strain



Suffoletto *et al. 2006. Circ* 113: 960

CT – Computed Tomography

Method
- Multiple 2D X-ray
- Iodine based CA
- Resolution 50 um

Measure
- Cavity volume
- Contraction

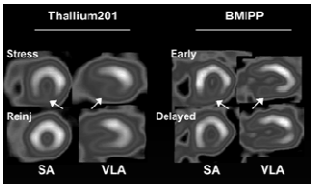
Siemens PET/SPECT/CT
Biological Imaging Centre
Imperial College

Dr W. Gsell, BIC Impérial College London

SPECT – Single Photon Emission Computed Tomography

Method
- Gamma emitting radioisotope
- Directly detected by CCD
- Resolution 2-3 mm

Measure
- Perfusion Technetium-^{99} Thallium-^{201}
- Metabolism BMIPP-I^{123}



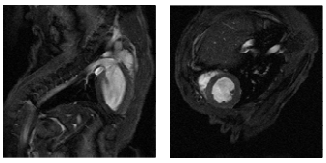
Mimosa *et al.* 2001 *Neuromusc Dis*

MRI – Magnetic Resonance Imaging

Method
- Magnetization of 1H
- Fourier transformed into 2D
- Resolution 100 um

Measure
- Cavity volume
- Contraction
- Myocardial viability
- Myocardial perfusion

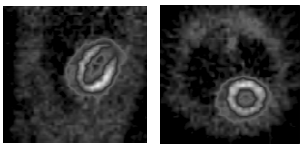
11.7T MR system
CMRG, DPAG
University of Oxford



PET - Positron Emission Tomography

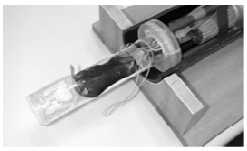
Method
- Positron emitting radioisotope
- Annihilation by e^- collision
- Pair of photons produced
- Resolution 1.5-2 mm

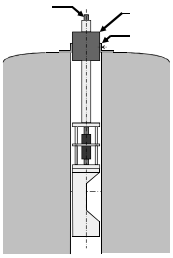
Measure
- Perfusion ^{13}N ammonia ^{15}O water
- Metabolism ^{18}F FDG
- Plaques ^{18}F FDG



Dr W. Gsell, BIC Impérial College London

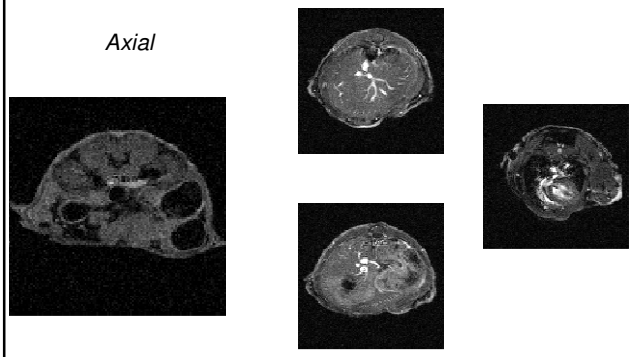
In vivo MRI of heart @11.7T





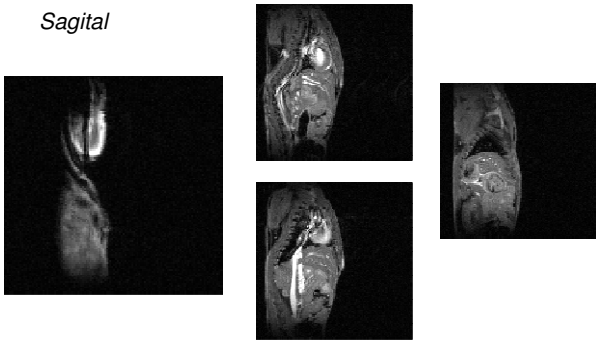
In vivo MRI

Axial



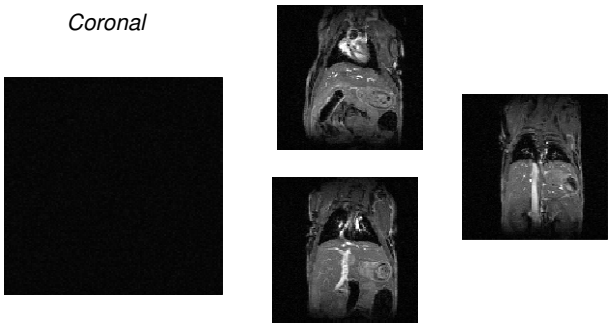
In vivo MRI

Sagital

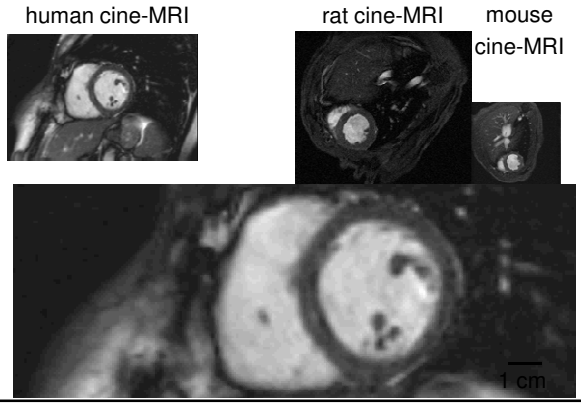


In vivo MRI

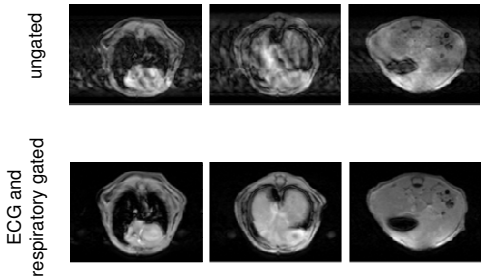
Coronal

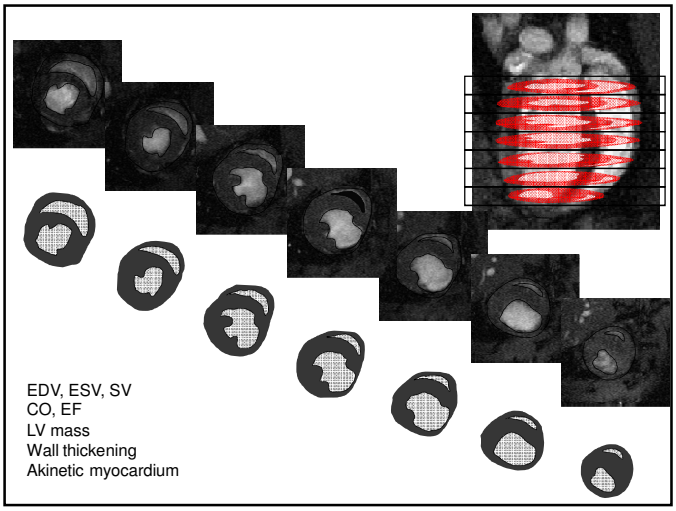


Small animal MRI - size

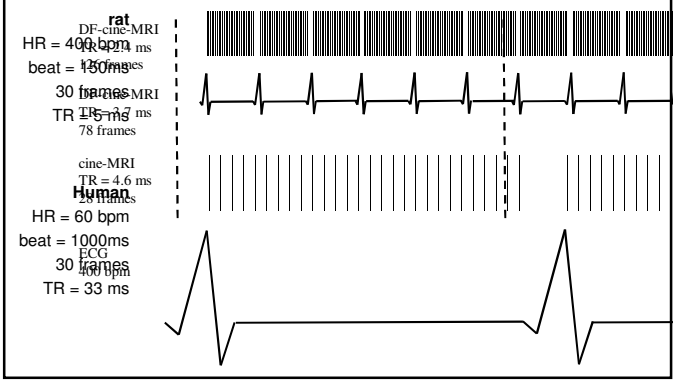


Small animal MRI - motion

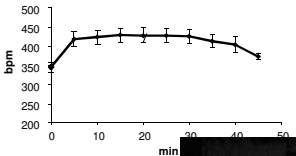


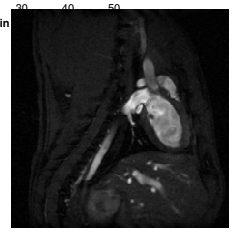


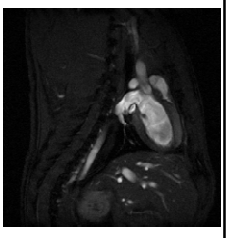
Small animal MRI - heart rates



Dobutamine stress MRI

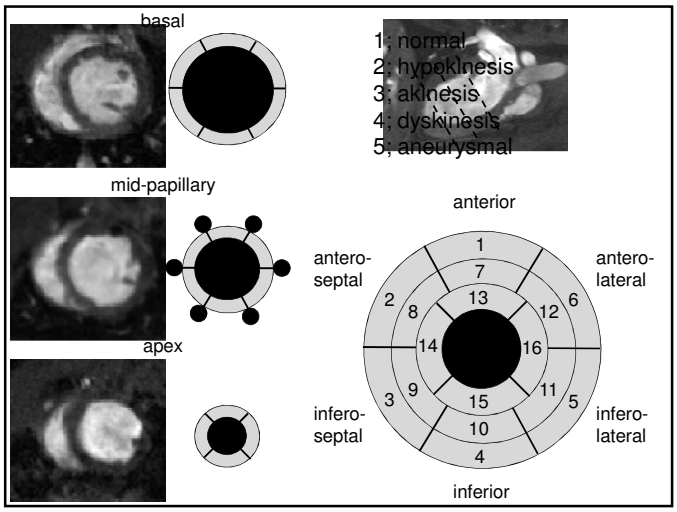




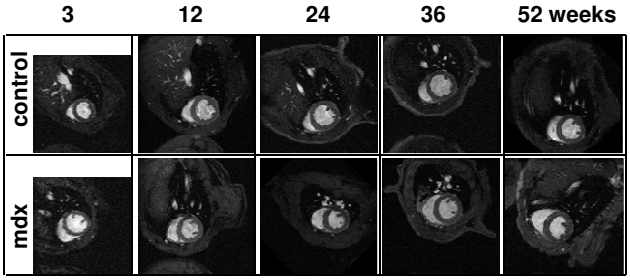


Pre Db (380 bpm)

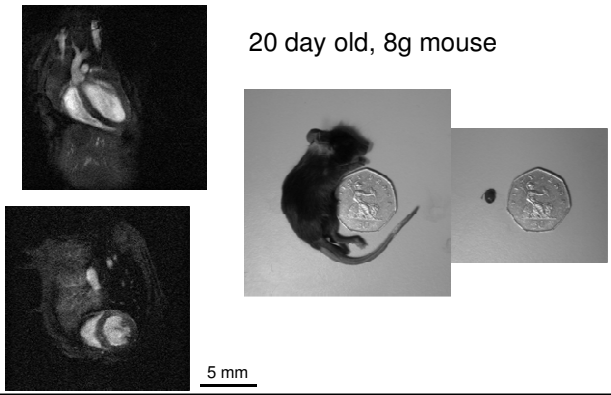
Post Db 460 bpm)



Cardiomyopathy in mdx mice

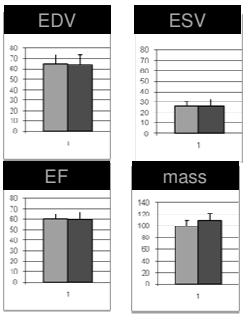


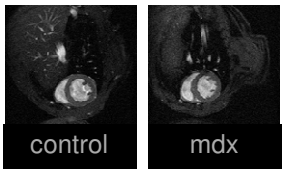
Serial imaging studies



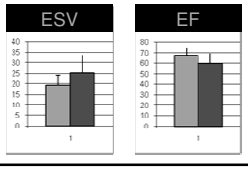
Cardiomyopathy in mdx mice

LV Function at 12 weeks

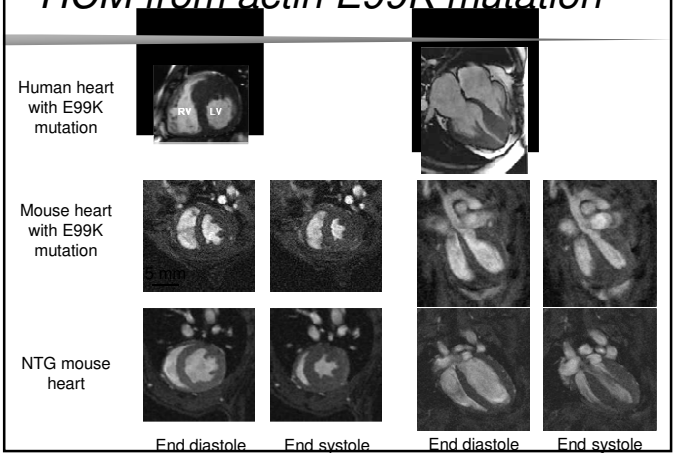




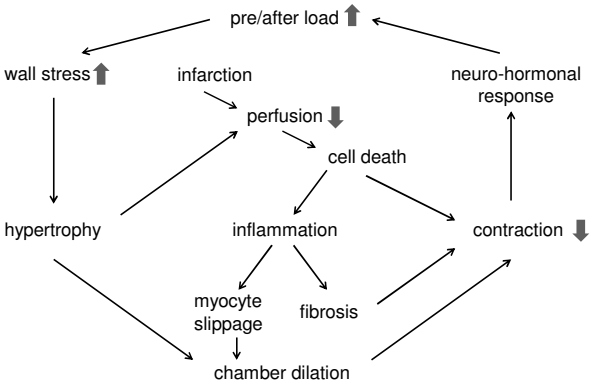
RV Function at 12 weeks



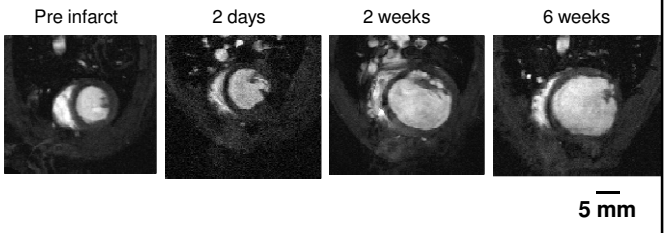
HCM from actin E99K mutation



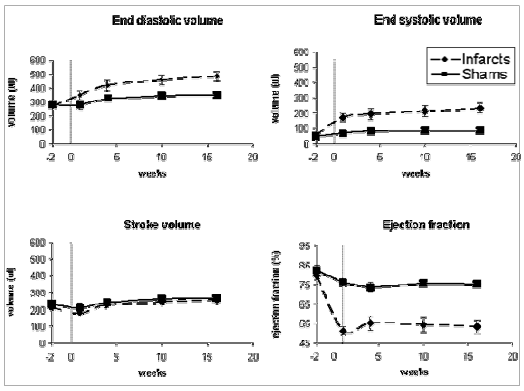
Cardiac remodelling



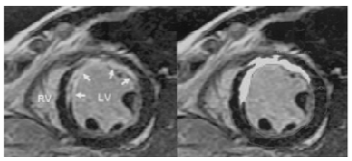
Myocardial infarction in rat

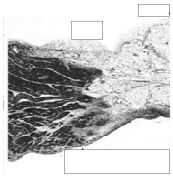


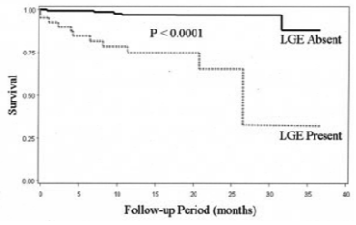
Myocardial infarction in rat



Delayed enhancement MRI (human)

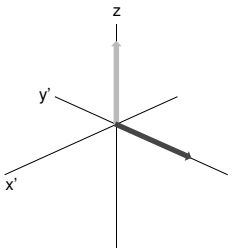






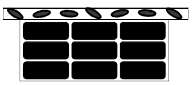
Kwong *et al.* 2006, Circulation

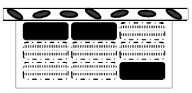
Inversion recovery imaging

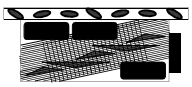


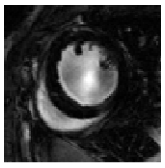
Late Gd enhancement MRI

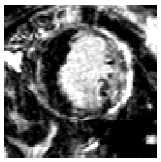
normal myocardium | acute infarction | chronic infarction





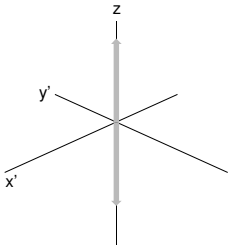




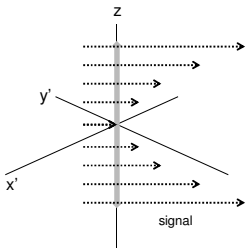


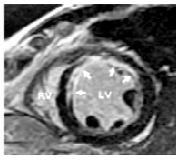
Gd @ 0.5 µmol/g

Inversion recovery imaging

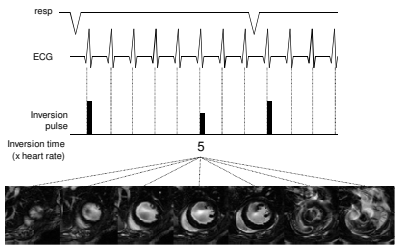


Inversion recovery imaging

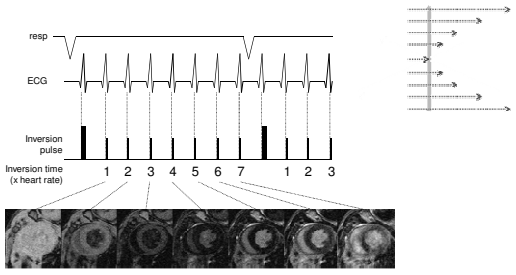




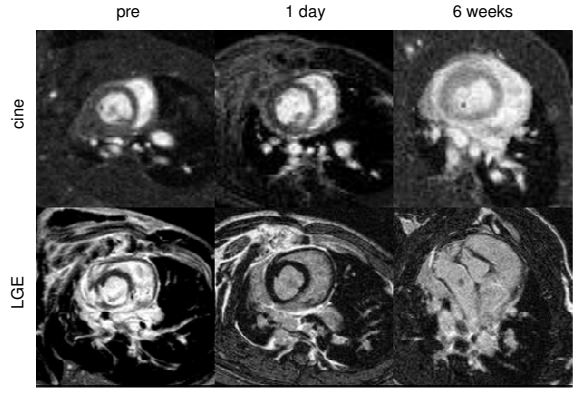
Multi slice inversion recovery imaging



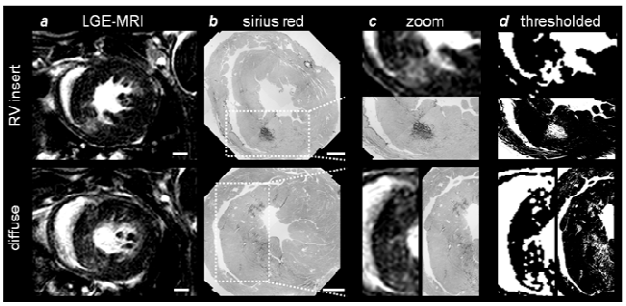
Multi inversion time imaging



Delayed enhancement MRI (infarcted rat)



LGE and picrosirius red staining

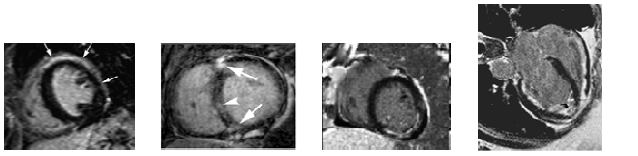


Myocardial fibrosis

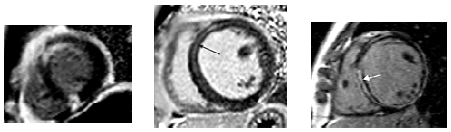
Clinical	***Pre-clinical***
•Replacement Fibrosis	
Infarction	MI
HCM/DCM	IR
Myocarditis	transgenics
•Reactive interstitial (diffuse) fibrosis	
Hypertension	TAC
Diabetes	Gq/MAP4K4
Aging	TNFa
Genetic	Aged mice
Drug induced	Doxorubicin

Diffuse fibrosis quantified from biopsy

LGE in cardiomyopathies



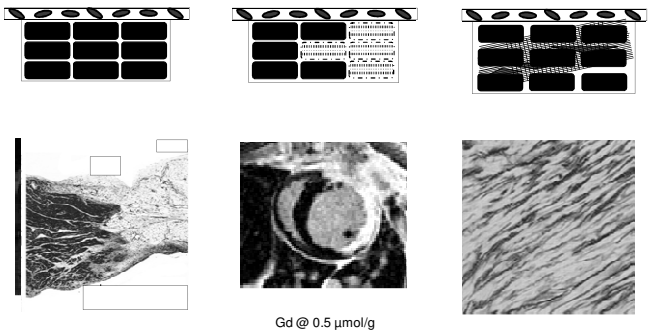
myocarditis sarcoidosis amyloidosis Endomyocardial fibrosis



HCM DCM Muscular dystrophy

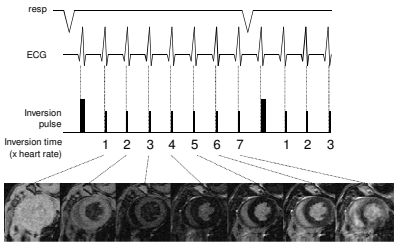
Mechanism of LGE-MRI

normal myocardium | myocardial infarction | hypertension, aortic stenosis



Gd @ 0.5 µmol/g

Quantifying diffuse fibrosis

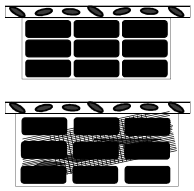


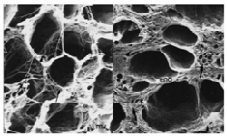
Extracellular volume

When Gd is at equilibrium between blood and myocardium...

$$\frac{ECV_{myo}}{ECV_{blood}} = \frac{[Gd]_{myo}}{[Gd]_{blood}}$$

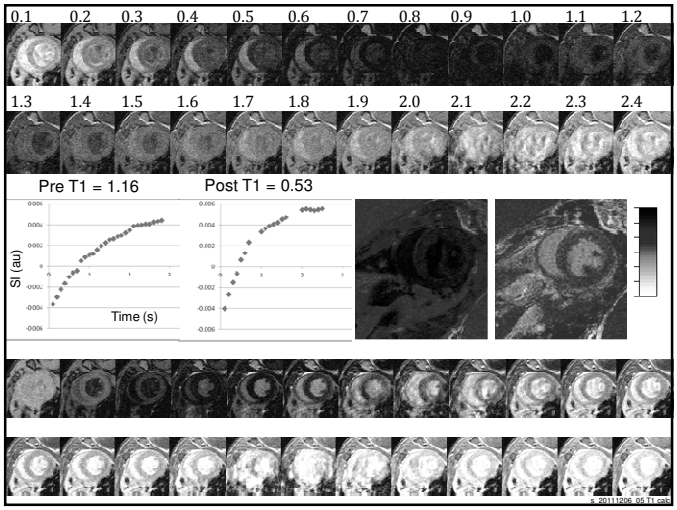
$$ECV_{myo} = (1 - Hct) \times \left(\frac{\Delta R1_{myo}}{\Delta R1_{blood}}\right)$$





Messroghli *et al.* 2011 Circ CVi

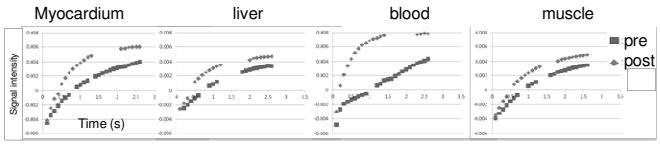
White et al, **Heart** *2012*



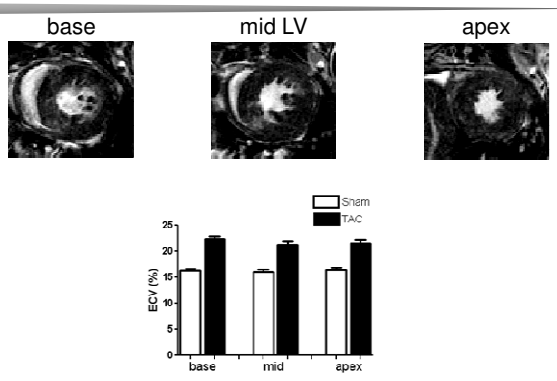
Extracellular volume

$$ECV_{myo} = (1 - Hct) \times \left(\frac{\Delta R1_{myo}}{\Delta R1_{blood}}\right)$$

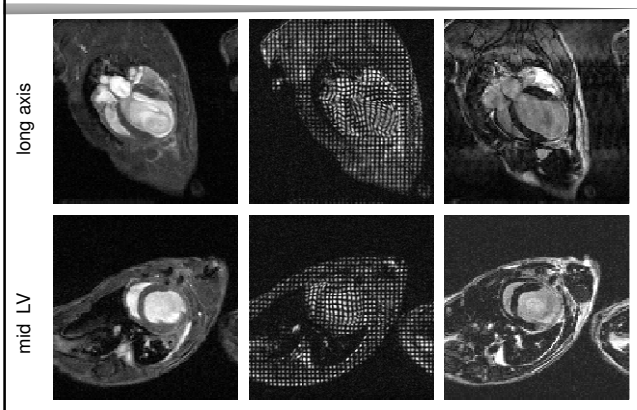
	Pre Gd (s)	Post Gd (s)	ECV (%)
Heart	1.18 ± 0.05	0.61 ± 0.06	17 ± 0.01
Liver	0.91 ± 0.06	0.53 ± 0.06	17 ± 0.02
Blood	1.27 ± 0.15	0.30 ± 0.13	55 ± 0.00
Muscle	1.16 ± 0.10	0.71 ± 0.08	12 ± 0.01



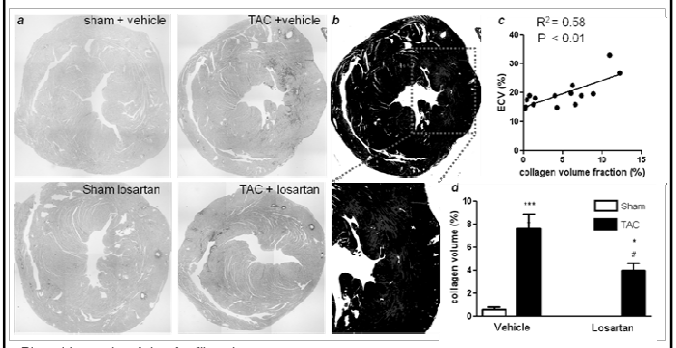
Regional ECV measurements after TAC



Tagged MRI (infarcted mouse)



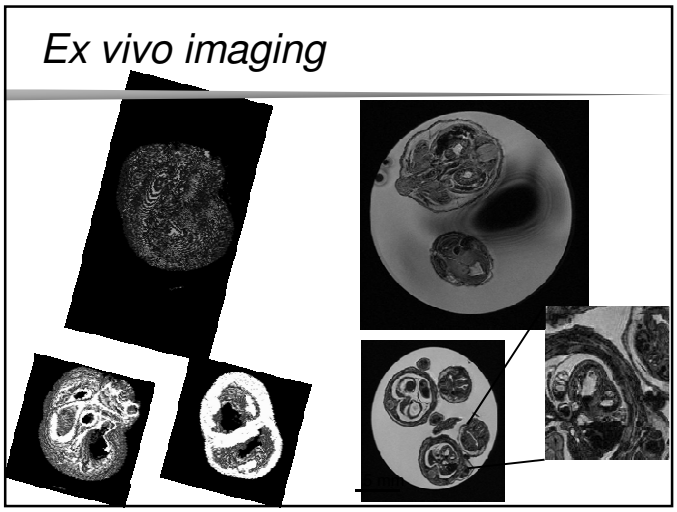
Collagen volume fraction



Picrosirius red staining for fibrosis

Other MR measurements

Arterial spin labelling	*myocardial perfusion*
Dynamic contrast enh	*myocardial perfusion*
T2 weighting	*edema/inflammation*
DTI	*myocardial ultrastructure*
MEMRI	*myocardial viability*
Molecular imaging	*arthrosclerosis*
	inflammation


Ex vivo imaging