

Supplemental Material

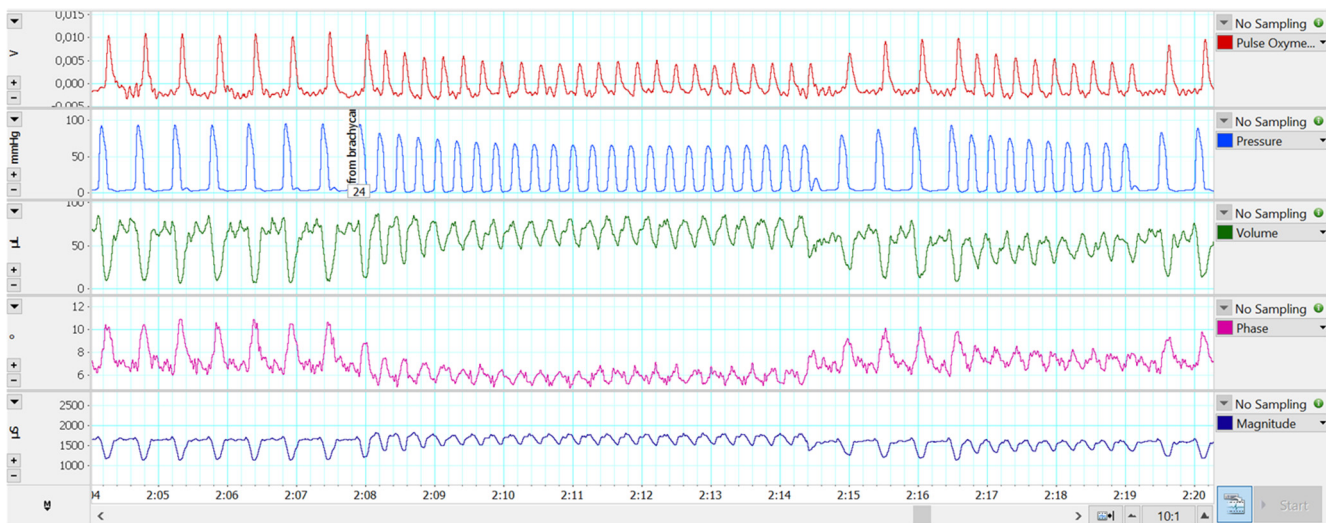


Figure S1. Representative tracings from LabChart Chart View of Animal 7 that was excluded due to arrhythmia.

	PV-loop	Echocardiography	MRI
HR (bpm)	202 ± 17	257 ± 17	230 ± 22
ESV (μl)	99 ± 23	87 ± 20	368 ± 21*
EDV (μl)	325 ± 31	272 ± 30	1000 ± 62*
SV (μl)	225 ± 31	185 ± 11	631 ± 53*
EF(%)	70 ± 7	69 ± 3	63 ± 2
CO (ml/min)	45 ± 7	47 ± 2	150 ± 23*

Table S1. Functional hemodynamic data acquired via PV-loop, Echocardiography and MRI of the same 5 animals.

HR = Heart Rate, ESV = End Systolic Volume, EDV = End Diastolic Volume, SV = Stroke Volume, EF = Ejection Fraction, CO = Cardiac Output

=MRI data significantly different to PV-loop and Echocardiography ($p < 0.05$) Data shown as mean ± SEM (n=5)

	Advantages	Disadvantages
Marmoset	<ul style="list-style-type: none"> - close phylogenetic relationship to humans [62, 63] - relatively rapid reproduction with twin birth [7, 31, 64, 65]; twins exhibit bone marrow chimerism [7, 31, 66-68] - commonly used for various biomedical research fields [7, 8, 69] - relatively easy to handle [7, 8] - least expensive NHP [31] with low zoonotic hazard [8, 31] - used for CV research since the 80s [45, 70-72] - similarities in heart anatomy and relative heart weight [19, 21] - heart size more suitable compared to rats for angiographic investigation [70] - spontaneous development of heart fibrosis, inflammatory cell infiltration and myocardial degeneration [41, 42] - similar age-related changes in microvasculature [73] - mean myocyte volume similar to man [40] - similar age-related changes in cardiovascular system [22, 43], immunology [17] as well as neurological and motor system [74-77] making it suitable for aging research [11, 15, 62, 63, 78] - spontaneous or induced models of obesity and diabetes [14] - similar lipoprotein profile [79-81] - good model to study renin-angiotensin system [82, 83] - possibility for transgenic applications [63, 84] -)similar ECG values(<ul style="list-style-type: none"> - some aspects of the cardiovascular system have been studied (see Advantages), but heart function has never been comprehensively characterized - rhesus macaques closer resemble the human situation [85] - few researchers have experience with marmosets - lower availability than small rodents - relatively expensive/ complicated husbandry and breeding compared to rodents [38, 86] - longer life cycle than rodents - slight differences in cardiac anatomy [37] and myocyte structure [40] compared to human - ethical considerations [36] - heart rate differs from human - difficulties in genetic modification [38] - limited availability of cross-reacting antibodies [39]
Pig	<ul style="list-style-type: none"> - highest analogy of heart and blood vessel sizes [87] - induced lesions more similar to human disease [88] - collateralization enables total infarct by occluding left anterior descending artery [87] - similarity in physiology, metabolism, genomics and proteomics to human [89, 90] 	<ul style="list-style-type: none"> - high cost compared to rodents[38, 88] - difficult handling [88] - few genomic tools [88] - most antibodies for human are not effective in pigs [90]

	<ul style="list-style-type: none"> - availability of various heart disease models and genetically established cardiomyopathy [89] - valid for restenosis studies [88] - genetically modified established model for human atherosclerosis [38] - non-invasive techniques for heart catheterization [91] - availability of monitoring systems in chronic models [91] - availability of imaging-based study techniques [91] 	
Dog	<ul style="list-style-type: none"> - docility and cognitive performance allow non-invasive and non-sedated assessments [92] - shared genetic evolution with humans [92, 93] - left ventricular function and volume similar to human [94] - myosin heavy chain distribution similar to human [94] - comparable electrophysiology [95] - cardiac proteome similar to human [90] - established disease models [96-98] - genetic modifications possible [92] - availability of monitoring systems in chronic models [91] - availability of imaging-based study techniques [91] - naturally occurring cardiomyopathies (summarized in [99]) 	<ul style="list-style-type: none"> - variation in coronary artery supply compared to humans as well as between individual dogs results in a complicated surgery setting for MI [87, 100, 101] - differences in heart anatomy [102] - relatively costly/ complicated housing and breeding [38, 90, 94] - most antibodies for human are not effective in dogs [90] - genetic modification not as easy as in small rodents [38, 103] - complicated operation [38] - ethical considerations due to companion animal status (in Europe)
Mouse	<ul style="list-style-type: none"> - large experience [38, 88] - well-known genome, relative ease of genome manipulation [88] - low cost [88, 94] - short reproductive cycle [38, 88, 91, 94] allows for studies over short time period - useful for noninvasive imaging [88] - rapid development of atherosclerotic plaques in transgenic mice under specific diet [88] - standardized feeding and housing conditions with low variability [38] 	<ul style="list-style-type: none"> - only partial resemblance to humans [88] - heart rate differs significantly from humans [94, 104] - cardiac metabolism differs from human [105] - action potential differs to the human one [94] - different ratio of α- and β-myosin heavy chains [94] - atherosclerosis does not occur spontaneously in mice [106], more atherosclerotic than atherothrombosis model [88] - very high level of blood lipids [88]
Rat	<ul style="list-style-type: none"> - easy to handle, available, low cost [88] - short reproductive cycle [91] 	<ul style="list-style-type: none"> - heart rate differs significantly from humans - do not develop atheroma [88]

	<ul style="list-style-type: none"> - established model of choice for decades in cardiovascular research [107] - useful for restenosis analysis [88] 	<ul style="list-style-type: none"> - modification of hemodynamic conditions in open-thorax models [91]
	Rabbit <ul style="list-style-type: none"> - established disease models [108, 109] - inexpensive, easily available [88, 110] - easy to handle, medium size [88] - short reproductive cycle [111] - mimics alteration of myocardial function observed in end stage failing human myocard [94] - development of fibroatheroma lesion in atherosclerosis model [88] - useful for restenosis models [88] - WHHLMI strain develops myocardial infarction spontaneously [109] 	<ul style="list-style-type: none"> - heart rate differs from humans [104] - few genomic tools [88] - differences in cardiac metabolism [103] - need for high blood cholesterol levels for development of atherosclerosis [88]

Table S2. Selected advantages and disadvantages of different animal models relevant for cardiovascular research.

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