Appendix

Intra-dialytic 3T MRI set-up

There were a number of modifications to allow dialysis to be performed in the 3 T MR scanner. To ensure ultrapure water was used (bacterial testing results <0.1 colony-forming unit/ml and <0.03 endotoxin unit/ml), a water treatment unit including a reverse osmosis component was installed in the scan room. Extended and insulated blood lines were used (additional dead volume 66ml) so a standard dialysis machine could be positioned approximately 3m away from the MR scanner, in a field of ~ 5Gauss. Siliconised non-metallic cannulae (Biohole catheter needles, Nipro UK, Quays Reach, Salford, UK) were used.

Cardiac MRI

The detailed MR acquisitions performed in each of scan sessions are listed below:

Global cardiac contractile function: Left ventricular function was assessed using a VCG-gated cine MRI using a multi-slice TFE sequence with slices in a 2CH short axis view with FOV 260 x 209 mm^2, spatial resolution 1.35 x 1.35 mm^2, slice thickness 10 mm, SENSE 2 and Pos factor 2, TE/TR = 2/4 ms, FA (flip angle) 60^o, TFE factor 10, TFE shots 6, 30 heart phases per cardiac cycle. Cine scans were acquired in 6 breath holds with 2 slices acquired per 15-20s breath hold, resulting in a total of 12 slices collected with multiple time points across the cardiac cycle. Analysis was performed using ViewForum software (Philips Medical Systems, Best, NL). The epicardium and the endocardium were first identified by the user, the software then propagates these contours throughout the image time series. This was repeated for each myocardial slice, with the basal slice

chosen for end-diastole and end-systole such that all of the blood volume was surrounded by left ventricle myocardial tissue. The apical slice was defined as the last slice showing intra-cavity blood pool. Cardiac output (CO), stroke volume (SV) and ejection fraction were determined from these measures. CO and SV were BSA corrected to yield cardiac index (CI) and stroke volume index (SVI).

Aortic flow and central venous return: Aorta PC-MRI data were collected with a FOV 280 x 264 mm^2, spatial resolution 0.97 x 0.97 mm^2, slice thickness 10 mm, no SENSE, TE/TR = 2.3/3.7ms, FA = 15^o, TFE factor = 5, TFE shots 25, VENC = 300 cms^{-1}, NSA = 3. Scan time was approximately 1 minute dependent on the patient's heart rate. IVC PC-MRI data were collected with a FOV 280 x 140 mm^2, spatial resolution = 1.2 x 1.2 mm^2, slice thickness 6 mm, SENSE 2 and Pos factor 2, TE/TR = 3.1/5.6 ms, FA = 25^o, TFE factor = 4, TFE shots 13, VENC = 200 cms^{-1}, NSA= 3. Scan time was a 15-20s breath hold. PC-MRI data were analysed using ViewForum software. An ROI was drawn around the walls of the vessel and this ROI was propagated through all time points across the cardiac cycle. From this, waveforms of velocity and cross sectional area, and thus blood flux over the cardiac cycle were derived.

Segmental cardiac function:

2-dimensional (2D) SPAMM tagging datasets of the heart were acquired in the 2CH short axis and long-axis four-chamber (4CH) views. A multishot TFE sequence was collected during an end-expiratory breath-hold with imaging FOV = 320 × 320 mm^2, spatial resolution = 1.33 x 1.33 mm^2, slice thickness 8 mm, SENSE 2 and Pos factor 1.5, TE/TR = 3.5/5.8 ms, FA 10°, 14–16 cardiac phases

and 7 mm tag separation using a grid-tag pattern. Data were analysed using CIM2D software (Auckland Uni Services).

Myocardial fibrosis:

Data were acquired using a MOLLI T_1 mapping sequence with a non-selective inversion thickness of 350 mm. Images were acquired using a bFFE scheme with FOV 288 x 288 mm^2, spatial resolution 3 x 3 mm^2, slice thickness 5 mm, SENSE 2 and Pos factor 2, TE/TR 1.5/3.1 ms, FA 35^o, centric half Fourier acquisition with 12 startup echoes. The MOLLI scheme used trigger delays of 0 – 350 ms in 50 ms steps with three readout pulses following each trigger delay, and an end delay of 3000 ms following the final readouts. Images were first assessed for motion, and discarded if necessary. Data were then fit to compute T_1 measures. This process was performed on a voxel-wise basis to form a map of the myocardium. T_1. These maps were then masked to the myocardium, by drawing an ROI along the epicardium wall, and the mean T_1 value computed. Comparison of myocardium T_1 of dialysis patients to healthy volunteers provides an indication of the degree of myocardial fibrosis, whilst a change in T_1 during dialysis allows for the assessment of the presence of increased water content in the myocardial tissue, due to oedema.

Coronary blood flow: Coronary artery blood flow data were collected using a PC-MRI sequence with FOV 280 x 140 mm^2, spatial resolution = 1.2 x 1.2 mm^2, slice thickness 6 mm, SENSE 2 and Pos factor 2, TE/TR = 3.8/7.5 ms, FA = 25^o, TFE factor = 2, TFE shots 16, VENC = 50 cms^{-1}, NSA= 3. Scan time was approximately per 15-20 s breath hold. PC-MRI data were analysed using

ViewForum software. We were able to visualise and measure flow in the right coronary artery in nine patients.

Myocardial perfusion:

Myocardial perfusion was assessed with Arterial Spin Labelling (ASL), this uses magnetically-labelled water protons as an endogenous tracer (contrast-free). Data were collected using a flow alternating inversion recovery (FAIR) ASL scheme with slice selective thickness of 35mm and non-selective thickness of 350mm, in-plane pre- and post- saturation pulses were applied.

Imaging was performed using a bFFE scheme with FOV 288 x 288 mm^2, spatial resolution 3 x 3 mm^2, slice thickness 5 mm, SENSE 2 and Pos factor 2, TE/TR 1.5/3.1 ms, FA 35^o, centric half Fourier acquisition with 12 startup echoes. For the ASL timings, trigger delays were of 0 – 350 ms in 50 ms steps with three readout pulses collected following each trigger delay, and an end delay of 3000ms after the final readout.

Data were analysed using dedicated software to compute the 2CH short axis perfusion measures of the myocardium, quantified in units of ml/g/min. In this program, images were first assessed for motion and then discarded if necessary. Non-selective and selective data were each fit to a T_1 recovery curve to estimate selective and non-selective T_1 values. Using the Belle model [33] these T_1 values were then used to estimate perfusion of the myocardium. Myocardial perfusion data were obtained for 10 patients across the entire short axis 2CH slice (for two subjects a complete set of data were not collected across all time points).

Supplementary data

Appendix: Detailed MRI methods

Appendix Figure 1: SVI, CI, and EDV and ESV measured using cine-MRI data. These measures show a decrease during dialysis and a return towards baseline at 50min post-dialysis.

Appendix Figure 2: Myocardial T_1 shows no change during and after dialysis treatment. A trend towards increase was seen between -30 and 60min but this did not reach statistical significance. For HD, 5 patients T_1 values increased between -30 and 60 min and for HDF, 8 patients T_1 increased.

Appendix Figure 3: Mean myocardial perfusion and coronary artery flux index pre-, during and after dialysis.