CHEMOTHERAPY-INDUCED CARDIOTOXICITY: COULD A high-resolution microstructural investigation of myocardial histology be performed to identify patients at risk? However in situs inversus totalis (SIT) there is mirror image arrangement of the visceral organs. There are no histological studies assessing how myocardial microstructure is affected in SIT. DT-CMR offers a unique opportunity to evaluate the microstructural abnormalities in SIT.

Methods 12 SIT patients and 12 matched healthy volunteers were scanned in a 3T Siemens Skyra scanner. DT-CMR was performed at peak systole in the short axis at base, mid and apex. 2 people had whole heart tractography. A STEAM sequence with bmain=600 s/mm² and bref=150 s/mm² was used, as previously described. Strain and torsion assessment was performed using DENSE.

Results Patients were age and sex-matched (SIT 39.5 and SS 34.5 years, 3/12 male). Myocyte organisation at base, mid and apex was significantly different in SIT hearts compared to the SS hearts. Figure 1 shows example tractography. In SS, the endocardial positive helix angle (HA) progressed to a negative HA in the epicardium. In SIT hearts this pattern was inverted at the base and approached normal at the apex, with a mid-ventricular transition zone.

Mid-ventricular peak radial and circumferential strain were reduced in SIT (0.4±0.16 vs 0.56±0.16, p=0.02, and −0.16 ±0.02 vs −0.18±0.01 p=0.04 respectively). Peak absolute torsion was reduced in SIT 3.6°[3.5°] vs 8.0°[3.5°].

Conclusion We demonstrate that the SIT heart has an inverted myocyte orientation at the base that approaches normal towards the apex. Peak absolute torsion is reduced. Peak radial and circumferential strain are also reduced at the mid-ventricle. The deranged microstructure in SIT has functional effects, the long-term outcomes of which require further study.

Abstract 18 Figure 1 Tractography of a SIT and SS heart.

REFERENCES
mapping (modified look-locker) to estimate extracellular volume (ECV), T2 mapping (to quantify oedema) and strain analysis. A panel of circulating biomarkers (including inflammatory, ischaemic and fibrosis markers) was performed by multiplex ELISA. Longitudinal histological analysis was performed in the rats and correlated with imaging and biomarker findings.

**Results** Left ventricular function (LVEF) declined steadily during treatment in rats and humans. Persistent LV dysfunction was seen in 23% of patients 12 months after therapy. Peak Troponin I levels correlated with fall in (LVEF) and circulating levels translated well between rat and humans. However, levels did not peak until the final cycle of chemotherapy when significant LV decline had already occurred. There was no significant change in the other circulating biomarkers. ECV did not change significantly during treatment but lower baseline ECV correlated with a greater fall in LVEF. Microscopic changes were seen in the rat myocardium after 6 doses of doxorubicin but electron-microscopy revealed mitochondrial damage after just one dose.

**Conclusions** This translational approach enabled forward and back translation leading to the development of a clinically relevant pre-clinical cardiotoxicity model. Troponin I was the most informative circulating biomarker but peaked at the end of therapy too late to modify treatment and prevent LV decline. The model has the potential to be used to identify earlier biomarkers and evaluate cardioprotective strategies. The imaging findings showed that fibrosis cannot be detected on CMR within one year of chemotherapy but generated a new hypothesis that patients with ‘healthier hearts’ may be a greater risk of drug-induced cardiotoxicity.