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Myocardial extracellular volume fraction (ECV) assessed by cardiovascular magnetic resonance imaging (CMR) estimates the extent of the myocardial extracellular space relative to its cellular component(1). ECV measured by CMR is increased in a variety of diseases(2)(3) and has been validated against histologically derived myocardial ECV(4). Furthermore, ECV shows promise in prognostication of mortality and morbidity(5)(6). Conventionally, ECV calculation requires knowledge of the patient's haematocrit (Hct). Treibel et al.(7) recently demonstrated that a '*synthetic* ECV' can be accurately calculated by estimating Hct from the longitudinal relaxivity ($R1 = 1/T1$) of blood. This new approach to ECV estimation eliminates the time, cost and inconvenience associated with obtaining a venous Hct sample. So far, *synthetic* ECV has only been described for data acquired with a single vendor (Siemens) and field strength (1.5T). We hypothesised that *synthetic* ECV can also be derived from data acquired with other platforms and acquisition methods, which would further broaden the applicability of this method.

In this single centre cross-sectional study, we analysed the data of 421 patients who had undergone T1 mapping for a mixture of research purposes and clinical indications, 203 of whom underwent CMR scans on 1.5 Tesla (Philips Ingenia) and 218 on 3.0 Tesla (Philips Achieva TX). All clinical patients consented to having their data used for research prior to undergoing CMR examination. All other patients gave informed written consent and were recruited with approval of the local ethics committee. The study was conducted in accordance with the declaration of Helsinki. Patients on both scanners were randomly split into equally sized derivation and validation subgroups. The derivation groups served to enable derivation of linear regression equations for the relationship of Hct and R1 of blood. This equation was used to calculate synthetic ECV and assess its correlation with conventionally calculated ECV in the validation groups. The 1.5 Tesla cohort comprised 47 patients with valvular heart disease and 44 with ST-segment elevation myocardial infarction taking part in research studies and 112 patients referred for CMR for clinical reasons. The 3.0 Tesla cohort comprised 26 healthy controls and 159 rheumatoid arthritis and 33 hypertrophic cardiomyopathy patients undergoing research CMR scans.

Modified Look-Locker Inversion Recovery (MOLLI) sequences were used to produce T1 maps prior to and 15 minutes after administration of either 0.2 mmol/kg

Gadopentate Dimeglucide (Magnevist, Bayer Schering) or 0.15 mmol/kg Gadobutrol (Gadovist, Bayer Schering). T1 values were obtained by drawing a region of interest (ROI) within the interventricular septum and blood pool at mid-ventricular level using post-processing software (CVI 42, Circle Cardiovascular Imaging Calgary, Canada). Scar was included within the interventricular septum ROI when present. Analysis was blinded. Statistical analyses were performed using SPSS version 22 (Chicago, Illinois). All results are presented as mean \pm standard deviation.

There was a broad range of Hct in both 1.5T and 3.0T derivation groups (0.41 ± 0.05 , range 0.27 to 0.53 at 1.5T and 0.42 ± 0.04 , range 0.31 to 0.54 at 3.0T). There was also a broad range of blood T1 in 1.5T and 3.0T derivation groups (1608 ± 105 ms, range 1402 to 1912 ms at 1.5T and 1780 ± 99 ms, range 1457 to 1993 ms at 3.0T). The conventionally calculated ECV in the validation groups was 32 ± 9 % (range 19 to 77%) for 1.5T and 29 ± 5 % (range 20 to 53%) for 3.0T.

The regression lines between Hct and R1 blood were linear at both field strengths (1.5T: $R^2 = 0.50$, $p = <0.001$; 3T: $R^2 = 0.46$, $p = <0.001$), resulting in the following regression equations (Figure 1):

$$1.5T: \text{ Synthetic Hct MOLLI} = (922.6 \cdot [1/T1_{\text{blood}}]) - 0.1668$$

$$3.0T: \text{ Synthetic Hct MOLLI} = (869.7 \cdot [1/T1_{\text{blood}}]) - 0.071$$

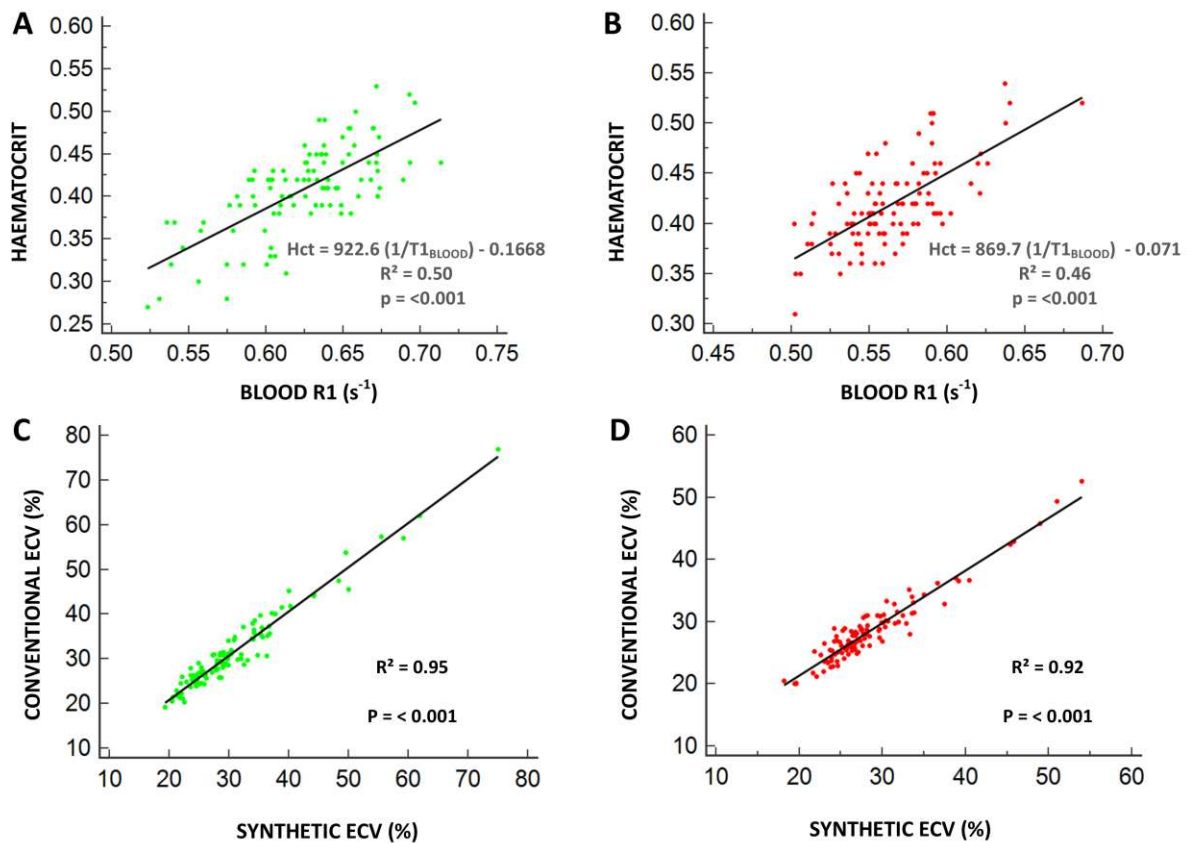
Where Hct is haematocrit (between 0 and 1) and R1blood is 1/T1blood in milliseconds

Using these linear regression equations to calculate synthetic ECV in both validation cohorts, conventional and synthetic ECV were highly correlated (Figure 1) ($R^2 = 0.95$, $p = <0.001$ at 1.5T and $R^2 = 0.92$, $p = <0.01$ at 3.0T).

In the present study we demonstrate that *synthetic* ECV, derived by estimating the Hct from pre-contrast blood T1 values acquired with a MOLLI method on 1.5 and 3T Philips systems, strongly correlates with conventionally calculated ECV. The correlation values we have demonstrated between Hct and R1 blood in the derivation cohort and between conventional and *synthetic* ECV in the validation cohort are very similar to those reported in the Treibel et al. on a Siemens platform using both MOLLI and ShMOLLI pulse sequences. This underscores the accuracy of synthetic ECV and its wide applicability across platforms and field strength. It offers

the potential for use on a routine clinical CMR list, eliminating the need for a venous Hct sample and thereby enabling rapid clinical decision-making.

Figure 1. Panel A shows the linear correlation and regression equation between blood Hct and Blood R1 at 1.5 Tesla. Panel B shows the linear correlation and regression equation between blood Hct and Blood R1 at 3.0 Tesla. Panel C shows the linear correlation between conventional and synthetic ECV at 1.5 Tesla. Panel D shows the linear correlation between conventional and synthetic ECV at 3.0 Tesla.



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