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A new definition of left ventricular compaction/ noncompaction - the new gold-standard?

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Background

Abundant, abnormal myocardial trabeculae define left ventricular noncompaction (LVNC) but measurement is difficult and at least 5 techniques are described. We hypothesized that part of the reason for difficulties was that LV trabeculae were fractal in nature and beyond the simple geometry of 1 or 2 dimensional (2D) measurement. We designed and validated a new, rapid, clinically applicable method of measuring LV trabeculae based on fractal analysis.

Methods

We developed a fractal analysis technique for measuring LV trabeculation using CMR volume stack images.

With no gold-standard for LV trabeculae, we validated the method on the actual compaction process itself

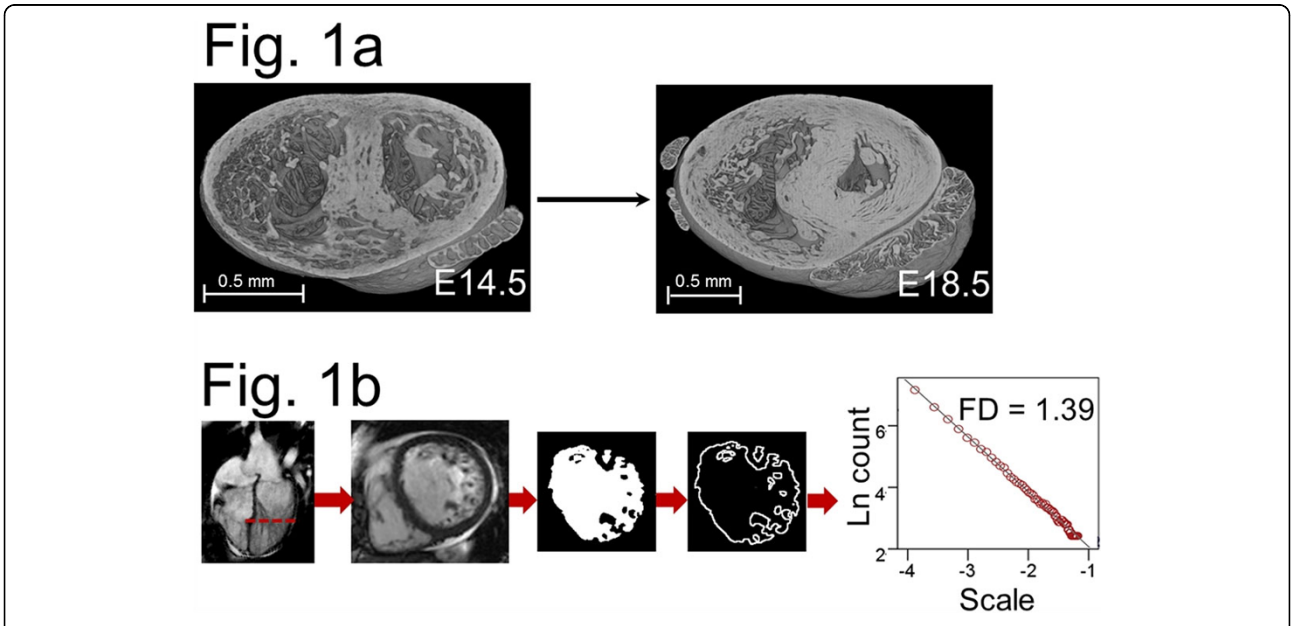

Figure 1 (a) Maturation of the murine heart as seen with HREM (E14.5 to E18.5). (b) Image processing sequence of human CMR data. Each slice from within the LV cine stack undergoes binarization, edge-detection and fractal analysis (illustrative LVNC heart shown). HREM indicates high-resolution episcopic microscopy; E, embryonic day; CMR, cardiovascular magnetic resonance; LV, left ventricle; LVNC, left ventricular noncompaction; Ln, logarithm.

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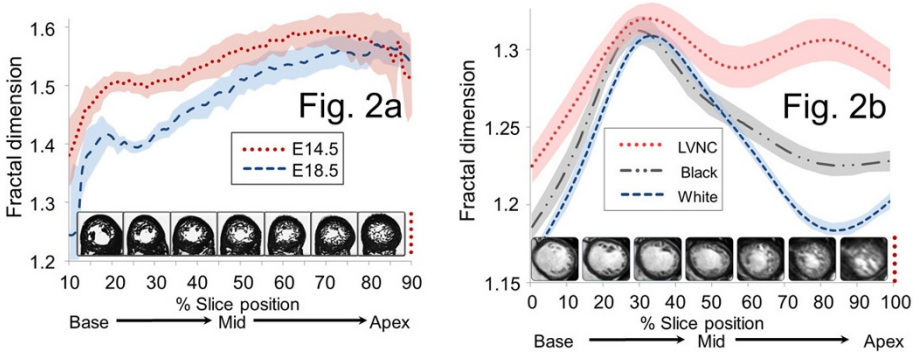

Figure 2 (a) In embryonic mice, transformation from trabeculated to more compacted myocardium is accompanied by a fall in FDs across the left ventricle from base to apex (shaded areas represent mean ± 95% CI). (b) In humans studied by CMR, FDs change in a characteristic pattern across the left ventricle in LVNC, healthy black and healthy white volunteers (shaded areas represent s.e.m.). FD indicates fractal dimension; CI, confidence intervals; s.e.m., standard error of mean. Other abbreviations as in Figure 1.

using 3D images of the compacting embryonic murine heart (between day 14.5 and 18.5) during cardiomorphogenesis (Figure-1a). We studied 24 mouse embryos, each with 1,000-1,200 ventricular slices in a 3D isotropic dataset (resolution 3 microns). In humans, hearts were analyzed for slice-by-slice fractal gradients (Figure-1b). Here we compared health to overt disease (LVNC) and compared the trabeculae of black and white healthy volunteers. Intra and inter-observer reproducibility of 60 fractal readings was analyzed and compared with 2 other CMR approaches (Petersen and Jacquier). In humans we studied a total of 135 subjects: LVNC cases, n=30; healthy blacks, n=30; healthy whites, n=75.

Results

The fractal approach could measure embryonic compaction revealing a fall in FD with cardiac development as the heart compacts (E14.5 to E18.5, P<0.0001)(Figure-2a).

All 135 human hearts were analyzable (average analysis time: 5.3±0.4 minutes per subject). The FDs of whole human hearts were: LVNC, 1.29±0.007; healthy black, 1.25 ±0.006; healthy white, 1.23±0.003, P value <0.001 for trend and pairwise comparisons. Across the heart there was a characteristic base-to-apex FD gradient. This was lost in LVNC (Figure-2b) so the maximal difference was noted in the apical third (maximal apical FD: LVNC, 1.391±0.010; black volunteers, 1.253±0.005; white volunteers, 1.235 ±0.004; P<0.0001). A maximal apical FD cut-off of ≥1.30, predicted LVNC with a high degree of accuracy, AUC 1.0. Normal reference ranges were created for black and white populations. Reproducibility analysis showed the fractal technique to be substantially more reproducible than other CMR methods.

Conclusions

A fractal-based approach to measuring LV trabeculae is mathematically sound, reproducible, clinically feasible and for the first time, validated against embryonic myocardial compaction. It describes trabeculation as a novel continuous variable, distinguishing health from disease but also detecting more subtle inter-ethnic differences.

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