Characterization of interstitial diffuse fibrosis patterns using texture analysis of myocardial native T\textsubscript{1} mapping

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Abstract

Background

The pattern of myocardial fibrosis differs significantly between different cardiomyopathies. Fibrosis in hypertrophic cardiomyopathy (HCM) is characteristically as patchy and regional but in dilated cardiomyopathy (DCM) as diffuse and global. We sought to investigate if texture analyses on myocardial native T\textsubscript{1} mapping can differentiate between fibrosis patterns in patients with HCM and DCM.

Methods

We prospectively acquired native myocardial T\textsubscript{1} mapping images for 321 subjects (55±15 years, 70% male): 65 control, 116 HCM, and 140 DCM patients. To quantify different fibrosis patterns, four sets of texture descriptors were used to extract 152 texture features from native T\textsubscript{1} maps. Seven features were sequentially selected to identify HCM- and DCM-specific patterns in 70% of data (training dataset). Pattern reproducibility and generalizability were tested on the rest of data (testing dataset) using support vector machines (SVM) and regression models.

Results

Pattern-derived texture features were capable to identify subjects in HCM, DCM, and controls cohorts with 202/237 (85.2%) accuracy of all subjects in the training dataset using 10-fold cross-validation on SVM (AUC = 0.93, 0.93, and 0.93 for controls, HCM and DCM, respectively), while pattern-independent global native T\textsubscript{1} mapping was poorly capable to identify those subjects with 121/237 (51.1%) accuracy (AUC = 0.78, 0.51, and 0.74) (P<0.001 for all). The pattern-derived features were reproducible with excellent intra- and inter-observer reliability and generalizable on the testing dataset with 75/84 (89.3%) accuracy.
Conclusion

Texture analysis of myocardial native $T_1$ mapping can characterize fibrosis patterns in HCM and DCM patients and provides additional information beyond average native $T_1$ values.

Introduction

Myocardial tissue characterization via tissue relaxometry has emerged as a powerful cardiovascular magnetic resonance (cardiac MR) imaging tool to investigate myocardial tissue composition[1]. In the presence of interstitial fibrosis, native myocardial $T_1$ time will change and can be measured using $T_1$ mapping sequences. $T_1$ mapping has been used to distinguish between healthy and diseased myocardium in a wide variety of cardiac diseases[2–5], showing elevated native $T_1$ values in patients with hypertrophic cardiomyopathy (HCM)[3,5] and dilated cardiomyopathy (DCM)[6,7] including a strong correlation with extracellular collagen deposition in the latter[6]. Furthermore, recent studies demonstrated the prognostic role of abnormal native $T_1$ values in patients with hypertrophic cardiomyopathy (HCM)[3,5] and dilated cardiomyopathy (DCM)[6,7] including a strong correlation with extracellular collagen deposition in the latter[6]. Furthermore, recent studies demonstrated the prognostic role of abnormal native $T_1$ values in HCM and DCM patients[7–10]. Despite differences in global native $T_1$ values among cohorts with different cardiomyopathies, there is considerable overlap in global $T_1$s [2,4,11] although myocardial fibrosis patterns differ significantly. For example, although myocardial fibrosis in DCM patients is predominantly diffuse[12] and in HCM patients more regional and patchy[13,14], current $T_1$ mapping techniques based on the mean $T_1$ value[8,10] do not capture these differences. Therefore, there is an unmet clinical need for novel imaging biomarkers to better quantify differences in fibrosis patterns.

Cardiac MR images may contain information that is not being extracted by the current standard image analysis workflow. For example, signal variation in cardiac MR images may contain additional information reflecting underlying pathophysiology[12–14] that is not being quantified. Radiomics[15] and texture image analysis have been recently applied to cardiac MR images[16–20] to extract new quantitative features that may provide diagnostic information. That is, radiomics quantitatively extract high-dimensional feature to differentiate images beyond mean signal value such as signal heterogeneity[17]. This process is usually followed by a selection of independent descriptors that best describe the features. Baessler et. al.[18] demonstrates that texture analysis on non-contrast $T_1$-weighted images can detect myocardial tissue alterations in HCM patients with excellent accuracy at differentiating between normal and HCM. Shao et. al.[19] also shows that texture analysis of native $T_1$ maps can differentiate between DCM and control subjects. Similarly, Neisius, et. al. demonstrates that texture analysis can differentiate between HCM and hypertensive heart disease patients where a set of six texture features extracted from cardiac $T_1$ maps can provide an accuracy of 80% in an independent testing dataset using support vector machines classifier[16]. While these studies demonstrate the potential of texture analysis to diagnose different cardiomyopathies, they do not indicate whether texture analysis can be used as an alternative analysis approach to elucidate differences in tissue compositions.

In this study, we propose to characterize fibrosis patterns via texture analysis on native $T_1$ mapping to establish disease-specific features that reflect phenotypic differences of interstitial diffuse fibrosis among HCM, DCM, and control cohorts. We hypothesize that textural analysis of native $T_1$ maps can highlight differences in interstitial diffuse fibrosis patterns between HCM and DCM regardless of their functional or morphological parameters.

Competing interests: The authors have declared that no competing interests exist.

Abbreviations: HCM, Hypertrophic cardiomyopathy; DCM, Dilated cardiomyopathy; Cardiac MR, Cardiovascular magnetic resonance; STONE, Free-breathing multi-slice native myocardial $T_1$ mapping using the slice-interleaved $T_1$; LV, Left ventricular; GLRLM, Gray-level run-length matrix; GLCM, Gray-level co-occurrence matrix; LBP, Local binary patterns; t-SNE, t-distributed stochastic neighbor embedding; SVM, Support vector machines; KNN, K-nearest neighbor; ICC, Intraclass correlation coefficients; ROC, Receiver operating characteristic.
Materials and methods

Study population

We prospectively recruited 321 subjects (55±15 years, 70% male) between July 2014 and March 2018 at Beth Israel Deaconess Medical Center and retrospectively performed radiomic image analyses. The study participants consisted of consecutive patients referred for a clinical cardiac MR exam with suspected or known cardiac disease and healthy volunteers (n = 21) that both meet the criteria described below. The study was approved by the Beth Israel Deaconess Medical Center’s Institutional Review Board (Protocol Number: 2001P-000793). Written consent was obtained. Patients were consented during their CMR scan appointment and research subjects were additionally contacted via advertisement.

The inclusion criteria for the three patient groups were based on established diagnostic criteria and cardiac MR measurements[21–25]. HCM was diagnosed by one of two ways: normal LV cavity size with wall thickness ≥15 mm[21], or a wall thickness above the normal range (≥12 mm for men and ≥11 mm for women[22]) in the presence of high clinical suspicion (i.e. gene carrier and/or HCM family history + LV wall thickness ≥13 mm, etc.), both not explained by loading conditions[21]. DCM was defined as an increase in LV volume (LV end-diastolic volume/body surface area >105 ml/m² for men and >96 ml/m² for women[23]) with coexisting reduction in LV systolic function (LV ejection fraction <53%[25]), and absence of subendocardial-based late gadolinium enhanced (LGE) patterns[24]. Control group subjects (n = 65) had normal cardiac dimensions/volumes, normal cardiac function, and absence of late gadolinium enhancement in common consisted of 21 healthy adult subjects free of cardiovascular disease/intervention and 44 subjects referred for a clinical cardiac MR exam for suspected cardiovascular disease. In the latter group, a review of medical records showed no diagnosis of cardiac disease.

Subjects were excluded from analyses secondary to an established diagnosis of amyloidosis, iron deposition or Anderson-Fabry disease, evidence of inflammatory processes in the myocardium or pericardium, and history of ST-segment elevation myocardial infarction. Part of this dataset (~55%) was previously reported[4,5,16,26,27].

The dataset was randomly divided into two groups: training and testing subsets (237 and 84 subjects with a ratio of ~3:1, respectively). Feature selection and validation were performed on the training dataset, while the testing dataset was used to assess the generalizability of the final selected features for other subjects (Fig 1).

Image acquisition and pre-processing

Imaging was performed on a 1.5T Philips Achieva system (Philips Healthcare, Best, The Netherlands) with a 32-channel cardiac coil. In each subject, T1 maps were acquired at 5 slice locations covering the LV from the base to apex using a free-breathing slice-interleaved T1 (STONE) sequence with the following parameters: TR/TE = 2.7/1.37 ms, FOV = 360×351 mm², acquisition matrix = 172×166, pixel-size = 2.1×2.1 mm², linear ordering, SENSE factor = 1.5, slice thickness = 8 mm, slice gap = 4 mm, bandwidth = 1845 Hz/pixel, diastolic imaging, and flip angle = 70˚. The T1 map of each scan was estimated by pixel-wise curve fitting using a 2-parameter fit model. Motion correction was performed using the Adaptive Registration of Varying Contrast-Weighted Images for Improved Tissue Characterization (ARCTIC) method[28].

Endocardial and epicardial contours were drawn manually on T1 maps of all patients by a single observer (HE with 5 years of experience). To assess intra- and inter-observer variability, the contours were re-drawn by the same observer and an additional observer (UN with 10 years of experience) on a subset of images (84 subjects of the testing dataset) within 6 months from the original drawings. Both observers were blinded to the clinical information and patient data.
For texture feature extraction, the delineated myocardial $T_1$ maps at each slice were transformed to polar coordinates with a standardized rectangular shape of $32 \times 192$ pixels. To maintain the same orientation and starting point of all rectangular maps, a landmark point was manually inserted by the user at the inferior insertion point between the left and right ventricles. The myocardial pixels were resampled into a rectangular form in the clock-wise direction using linear interpolation; such that the bottom left corner of each rectangular map matches the inserted landmark point location on the myocardium. Five rectangular $T_1$ maps at different slice levels were stacked per patient to provide a single map representative of the whole heart (Fig 2A).

A three dimensional (3D) phase-sensitive inversion-recovery (PSIR) sequence with spectral fat saturation pre-pulses during the end-diastolic phase approximately 15 minutes after administration of 0.1 mmol/kg body weight gadobenate dimeglumine (Multihance, Bracco Diagnostics Inc., Monroe Township, New Jersey, US) was used to obtain LV LGE images. For the control group, visual inspection was used to exclude the presence of LGE. For the HCM group, LGE was quantified using an automated LV contour and LGE area quantification algorithm specifically developed for LGE quantification in HCM patients[29]. For the DCM group, LGE was quantified using a five standard deviation approach and CVi42 (Circle Cardiovascular Imaging Inc. Calgary, Canada). For all groups, the assessment was performed by experienced (level 3 trained) reader and blinded to clinical and laboratory data. Accurate measurements were assured by visual review of all contours and corrected when necessary.

**Texture features extraction and selection**

Four sets of texture descriptors were utilized to extract texture features from the rectangular myocardial $T_1$ maps. These descriptors capture spatially-dependent and independent pixel statistics, as well as locally-repeated patterns. Features include: histogram-based features, gray-level run-length matrix (GLRLM)[30,31], gray-level co-occurrence matrix (GLCM)[32], and local binary patterns (LBP)[33] sets of feature descriptors (Table 1). A total number of 152 features were extracted. To reduce redundant information and irrelevant patterns, a feature selection strategy based on the sequential forward selection of the extracted features[34] was employed. In this strategy, features that maximize the characterization of disease-patterns among the different cohorts are iteratively included; where 10-fold cross-validation was utilized to calculate the classification accuracy at each iteration. In this step, 7 features were selected to be most representative of disease-specific patterns in the three cohorts.

**Data analysis**

Selected texture features were combined in one index, the Texture index ($T_x$), using the linear regression equation: $T_x = \beta_0 + \beta_1 x_1 + \ldots + \beta_n x_n$; where $x_1, \ldots x_n$ represents the selected features, and $\beta_0, \ldots, \beta_n$ are regression coefficients calculated from the dataset. The texture index was used to test the capacity of the quantified patterns to identify subjects in binary comparisons (i.e. one-vs-one). The t-distributed stochastic neighbor embedding (t-SNE) method was employed to visualize the ability of the quantified patterns to cluster each cohort on a 2D plane[35].

Four classifiers: linear support vector machine (SVM), radial basis function kernel SVM, k-nearest neighbor (KNN), and ensemble decision trees[36], were utilized to perform multi-class classifications[37] for the quantified patterns among the three cohorts using stratified 10-fold
cross-validation[38]. All feature vectors were normalized by the mean and variance before training the classifiers. Receiver operating characteristic (ROC) curves were calculated to assess the classification performance. Areas under the ROC curves were compared using the DeLong method[39]. Normality of data distribution was determined using the Kolmogorov-Smirnov test and visual inspection of the Q-Q plots. The two-sided Student’s t-test or the Mann-Whitney U-test was conducted as appropriate for comparison of continuous variables between groups. Analysis of variance or Kruskal-Wallis tests were used as appropriate for comparison of several groups. For comparison of categorical data, the Chi-squared test was employed. Significance was declared at two-sided P-values < 0.05. For pairwise comparisons following a three-group inferential test that was significant, a Bonferroni correction was used. Intra- and inter-observer reproducibility of the selected features was tested using intraclass correlation coefficients (ICC) with a two-way mixed-effect model and Bland-Altman analyses.
To test the generalizability of the quantified patterns at identifying subjects from $T_1$ maps, the same analyses were conducted on the testing dataset.

All described methods and statistical analyses in this work including motion correction, image reshaping, texture feature extraction[40], and classifiers, were implemented on Matlab (version 2014b, The MathWorks Inc., Natick, Massachusetts, United States). Patient characteristics and standard cardiac MR parameters (listed in Table 2) were analyzed using SPSS (version 18.0; International Business Machines Corp., Armonk, New York, USA).

### Results

Global native $T_1$ values varied significantly among the control, HCM, and DCM cohorts (1071 $\pm$32 vs. 1096$\pm$38 vs. 1123$\pm$38 ms, respectively; $P<0.001$); however, there was significant overlap among $T_1$ values of subjects from different cohorts (Fig 2B). The number of extracted pattern-derived texture features was optimized to reduce overlap among cohorts since most features were highly correlated. Feature selection reduced the original 152 extracted features to only 7 features: 4 LBP histogram features (at indices 8, 21, 26 and 36), 2 GLRLM features (RLN (135˚), SRHGE(0˚)), and variance of the pixels' histogram. Selected features were found to capture significantly different patterns among cohorts (S1 Table). We visually compared the selected texture features and global native $T_1$ values of the myocardium in all patients, and graphically represented the correlation strength between selected features (Fig 3A and 3B). Box-and-whisker plots show the behavior of 6 selected features to capture specific patterns from different cohorts; each feature either compresses or shifts the data range in one or more cohorts for better identification of fibrosis patterns in each cohort (Fig 3C).

Combining selected features into one index (i.e. Texture index, $T_x$) significantly improved differentiating fibrosis patterns in HCM and DCM subjects of the training and testing datasets (Table 3), relative to pattern-independent global native $T_1$ mapping values ($P<0.001$ for all comparisons) (Fig 4A and 4B).

The performance of the texture analysis to identify fibrosis patterns in a multi-cohort comparison (i.e. one-vs-all) showed the following accuracy: 202/237 (85.23%), 196/237 (82.70%), 193/237 (81.43%), and 192/237 (81.01%) for linear SVM, radial basis function SVM, KNN, and the ensemble tree using 10-fold cross-validation on the training dataset. Based on our preliminary study of different classifiers, linear SVM was used to perform the rest of the comparisons. ROC curves of the texture features showed significant improvement at differentiating fibrosis patterns between cohorts in comparison to pattern-independent global and segmental native $T_1$ values ($P<0.001$).

### Table 1. Summary of the extracted and selected texture features.

| Texture Feature Group                  | All features                                                                 | Total # features | Selected features                                      |
|---------------------------------------|-------------------------------------------------------------------------------|------------------|--------------------------------------------------------|
| Histogram-based features              | Mean, variance, skewness, kurtosis, 5th to 10th high-order central moments    | 10               | Variance                                               |
| Grey-level run-length matrix (GLRM)   | Short Run Emphasis (SRE), Long Run Emphasis (LRE), Grey-Level Non-uniformity (GLN), Run-Length Non-uniformity (RLN), Run Percentage (RP), Low Gray-Level Run Emphasis (LGRE), High Gray-Level Run Emphasis (HGRE), Short Run Low Gray-Level Emphasis (SRLGE), Short Run High Gray-Level Emphasis (SRHGE), Long Run Low Gray-Level Emphasis (LRLGE), and Long Run High Gray-Level Emphasis (LRHGE) in 4 Directions | 44               | Grey-Level Non-uniformity, Short Run High Gray-Level Emphasis |
| Grey-level co-occurrence matrix (GLCM) | Angular Second Moment, Contrast, Homogeneity 2, Entropy, Correlation, Sum of Squares; for 10 displacements in 4 direction | 60               | -                                                      |
| Local Binary Patterns (LBP)           | LBP Histogram features from 1 to 38.                                          | 38               | LBP(8), LBP(36), LBP(26), LBP(21)                      |

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for all) on linear SVM (Fig 4 and Table 4). When only global native T\textsubscript{1} was used, the classifier failed to correctly classify the fibrosis pattern in HCM cases, instead of interpreting them as either control or DCM due to extensive overlap in global T\textsubscript{1} values between control-HCM and HCM-DCM cohorts. Both sensitivity and specificity of the pattern-derived features were higher than global and segmental T\textsubscript{1} at correctly identifying subjects in all cohorts (Table 4).

There were no significant differences between training and testing datasets regarding patient characteristics and relevant measurements with the exception of maximal wall thickness (HCM, 19 [17; 23] vs. 16 [14; 21] mm, P = 0.001; DCM, 11 [9; 14] vs. 9 [8; 11] mm, P<0.001). In the testing dataset, the pattern-derived features were generalizable to accurately identify new subjects based on their T\textsubscript{1} mapping patterns with high sensitivity and specificity values (Fig 5 and Table 4). 2D t-SNE visualization showed the ability of the derived features to separate patients from different cohorts into different clusters with minimal overlap (Fig 5C and 5D). All selected features showed excellent intra- and inter-observer reproducibility (Table 5), and narrow limits of agreement (S1 Fig) except with the exception of T\textsubscript{1} variance (ICC = 0.7)\cite{41}. T\textsubscript{1} variance, however, had the smallest contribution in identifying diseasespecific patterns among the selected features.

To investigate the effect of T\textsubscript{1} map spatial resolution on the texture features, the same texture features were extracted from 2 simulated spatial resolutions; where the myocardium in

Table 2. Cohort characteristics and standard cardiac MR measures of function and anatomy.

|                     | Control (65) | HCM (116) | DCM (140) | P-Value |
|---------------------|-------------|-----------|-----------|---------|
| Age, years          | 53±15       | 55±14     | 55±15     | 0.533   |
| Gender, m (%)       | 36 (55)     | 87 (75)   | 104 (74)  | 0.105   |
| Systolic Blood Pressure, mmHg | 124±15 | 129±16 | 116±18\textsuperscript{15} | <0.001 |
| Diastolic Blood pressure, mmHg | 75±10 | 77±14 | 71±13\textsuperscript{3} | 0.008   |
| Heart Rate, beats/min | 67±11       | 67±10     | 75±16\textsuperscript{16} | <0.001 |
| Height, m           | 1.7±0.13    | 1.72±0.11 | 1.72±0.15 | -       |

New York Heart Association Function Status

|                     | II | III |
|---------------------|----|-----|
| Caucasian, n(%)     | 54 (83) | 3 (5) |
| Hypertension, n(%)  | 25 (38) | 61 (53) |
| Dyslipidemia, n(%)  | 34 (52) | 69 (59) |
| Diabetes Mellitus, n(%) | 3 (5) | 17 (15) |
| LVMI, g/m\textsuperscript{2} | 44 [36; 54] | 71 [57; 90]\textsuperscript{1} | 68 [55; 84]\textsuperscript{1} | <0.001 |
| LVM/LVEDV, g/ml     | 0.60 [0.52; 0.71] | 0.96 [0.80; 1.23]\textsuperscript{1} | 0.52 [0.44; 0.71]\textsuperscript{15} | <0.001 |
| Maximal Wall Thickness, mm | 9 [8; 11] | 19 [16; 22]\textsuperscript{1} | 10 [9; 13]\textsuperscript{15} | <0.001 |
| LVEDV, ml           | 134 [110; 167] | 146 [125; 168] | 267 [220; 317]\textsuperscript{15} | <0.001 |
| LVEF, %             | 62±5 | 65±7\textsuperscript{3} | 32±11\textsuperscript{15} | <0.001 |
| LGE, n(%)           | 0 (0) | 86 (74) | 62 (44) | - |
| LGE/LV mass ratio ′, % | 0±0.0 | 2.0±4.2\textsuperscript{1} | 5.8±5.5\textsuperscript{15} | <0.001 |
| Global Native T\textsubscript{1} time, ms | 1071±32 | 1096±38\textsuperscript{3} | 1123±38\textsuperscript{15} | <0.001 |

LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVM, left ventricular mass; LVMI, left ventricular mass index.

\*When gadolinium quantification was available (n = 78).
\# P<0.001 when compared with control subgroup
\$ P<0.01 when compared with HCM subgroup
\‡ P<0.001 when compared with control subgroup
\|$ P<0.001 when compared with control subgroup
\¶ P<0.01 when compared with HCM subgroup

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Fig 3. Texture features analysis. (a) Visual comparison of the 7 selected texture features and global native T1. Each row represents the feature value for an individual patient. (b) Correlation analysis of the selected texture features. Smaller/lighter-shaded circles indicate lower correlation compared to larger/darker circles. Most of the features have low correlation (i.e. hold independent information). (c) Box-and-whisker plots for the 6 most effective texture features that differentiate disease-specific patterns among 3 cohorts.

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each $T_1$ map was resampled to a rectangular form with resolutions of ($R_{16} = 16 \times 96$ and $R_{64} = 64 \times 384$ pixels per slice) compared to the current resolution ($R_{32} = 32 \times 192$). The selected texture features from the three resolution maps were able to identify subjects in HCM, DCM, and controls cohorts with accuracy of 83.6%, 85.2% and 85.7% for $R_{16}$, $R_{32}$, and $R_{64}$ resolutions, respectively, with 10-fold cross-validation on the training dataset and 86.3%, 89.3% and 87.8% in the testing dataset for $R_{16}$, $R_{32}$, and $R_{64}$, respectively. Reducing the resolution slightly decreased the differential capacity of the features, while increasing the resampled spatial resolution to $64 \times 384$ achieved similar accuracy as the used resolution of $32 \times 192$ pixels.

**Discussion**

We demonstrate that texture analysis of myocardial native $T_1$ maps can elucidate differences in fibrosis patterns between HCM and DCM patients. We extracted several texture features from native $T_1$ maps and subsequently selected independent features that best describe the fibrosis patterns of each cohort in the training dataset. Various classification models were then constructed using the independent information within each feature to improve the differentiation of fibrosis patterns between HCM and DCM.

Standardizing the myocardium in rectangular shape was necessary to allow stacking $T_1$ maps from different slices, performing simultaneous feature extraction from multiple slices, and extracting features that are less affected by myocardial geometry and morphology. However, myocardial reshaping could change the shape of the fibrosis pattern and hence affect the capacity of the extracted features to identify different fibrosis patterns. To further investigate this possibility, we conducted additional experiments using an alternative representation that maintains the original myocardial shape for stacking different slices (S1 File). Application of the same feature extraction and selection processes showed a similar capability to identify fibrosis patterns in different cohorts as the reshaped myocardium. The consistent myocardial reshaping maintains the relative differences among different fibrosis patterns and hence did not affect the differential capacity of the features. In addition, correlation analysis showed a low correlation between extracted texture features from the reshaped myocardium and wall thickness (S1 File) indicating that no extracted texture feature from the reshaped myocardium captures geometrical information induced by the reshaping process.

The size of the rectangular myocardium ($32 \times 192$) was determined based on 6-segments per slice with a segment size of $32 \times 32$ pixels. Although this resampling may introduce consistent stretching in the radial direction, the relative differences of texture elements among different cohorts are maintained and should not affect the discriminatory capacity of the extracted features.

Four texture features from the LBP set demonstrated an excellent potential to capture fibrosis-specific patterns. LBP(8) captures DCM-specific patterns on $T_1$ maps and its high values significantly distinguish DCM from control and HCM subjects. Two LBP features at histogram indices 36 and 21 capture the distinctive local patchy pattern of HCM and shows significantly increased values in HCM subjects relative to control and DCM subjects. Lastly, the LBP(26)
feature had significantly lower values for control T\textsubscript{1} maps, mainly due to its homogeneous intensity profile.

Furthermore, GLRLM features also captured independent information from native T\textsubscript{1} maps. GLN(135˚) and SRHGE(45˚), in particular, added incremental value to identifying different cohorts. GLN(135˚) measures the non-uniformity of T\textsubscript{1} maps and strongly correlated with global native T\textsubscript{1} values ($\rho = 0.98$, $P < 0.001$). Similarly, SRHGE(45˚) measured the joint distribution between run length and the pixel value of native T\textsubscript{1} maps. Despite using GLRLM directional features, the same features calculated at different directions were highly correlated and tended to measure the same pattern.

Similar to LGE scar pattern, texture information of native T\textsubscript{1} mapping could provide differential diagnosis or prognostic information beyond mean T\textsubscript{1} values. The current study was not designed to assess the incremental value of texture analysis for the diagnosis of HCM and DCM. A clinical model that includes baseline clinical characteristics, wall thickness, and LGE pattern can already discriminate between DCM and HCM with high accuracy and it is unlikely that the addition of texture information will provide additional diagnostic information. But rather, we demonstrate that differences in diffuse fibrosis distribution and patterns between the two cohorts reflect on T\textsubscript{1} mapping images and quantifying these fibrosis patterns in form of texture features can differentiate among patients from different cohorts regardless of their functional or geometrical parameters. In addition, differences in interstitial fibrosis pattern may provide additional prognostic information beyond global T\textsubscript{1} values. For example, patients with more heterogeneous scarring and interstitial fibrosis are more susceptible to ventricular hypertrophy.

### Table 4. Sensitivity and specificity of global native T\textsubscript{1} value and pattern-derived texture features to identify subjects in the three cohorts (i.e. control, HCM, and DCM) using multiclass linear SVM.

| Features                      | Control (one-vs-all) | HCM (one-vs-all) | DCM (one-vs-all) |
|-------------------------------|----------------------|------------------|------------------|
| **Global Native T\textsubscript{1}** | Accuracy            | Sensitivity      | Specificity      | AUC (95% CI)     |
|                               | 121/237 (51.1%)      | 0.38             | 0.90             | 0.78 (0.71–0.87) |
| **Segmental Native T\textsubscript{1}** | Accuracy            | Sensitivity      | Specificity      | AUC (95% CI)     |
|                               | 124/237 (52.3%)      | 0.59             | 0.81             | 0.8 (0.74–0.88)  |
| **Pattern-derived Texture Features** | Accuracy            | Sensitivity      | Specificity      | AUC (95% CI)     |
|                               | 202/237 (85.2%)      | 0.79             | 0.95             | 0.93 (0.89–0.98) |
| 10-fold cross-validation on Training Dataset |          |                  |                  |                  |
|                               | 75/84 (89.3%)        | 0.69             | 0.97             | 0.96 (0.92–1.00) |
| Testing Dataset                | Accuracy            | Sensitivity      | Specificity      | AUC (95% CI)     |
|                               | 75/84 (89.3%)        | 0.69             | 0.97             | 0.96 (0.92–1.00) |

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Fig 5. The capacity of the pattern-derived texture features to identify subjects from different cohorts in the testing dataset. (a) the texture index ($T_x$) for patients in HCM and DCM cohorts (i.e. calculated by combining the select features using a linear regression model). Each dot represents the $T_x$ value for one patient. (b) ROC curves for multi-cohort classification performance of selected features to identify subjects in control, HCM and DCM cohorts in the testing dataset by SVM. The t-SNE visualization of the selected features for all cohorts in (c) the testing and (d) training dataset. Each dot represents pattern-derived features of one subject.

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The texture analysis can extract new reproducible imaging markers from myocardial T1 mapping images that have the potential to identify different cardiomyopathies by characterizing disease-specific fibrosis patterns.

Supporting information

S1 Table. Tissue features comparison of healthy, HCM and DCM subjects (median [1st quartile; 3rd quartile]).

(DOCX)

S1 Fig. (a) Bland-Altman plots for the intra-observer variability of the selected texture features to the manual delineation of LV myocardium. Green lines show the bias, while red lines indicate the limits of agreement (±1.96 Standard deviation). (b) Bland-Altman plots for the inter-observer variability of the selected texture features to the manual delineation of LV myocardium. Green lines show the bias, while red lines indicate the limits of agreement (±1.96 Standard deviation)

(TIF)

S2 Fig. Circular myocardium representation. ROI at the myocardium from five slices are stacked from the apex (left) to basal (right) with no reshaping.

(TIF)

S1 File. Additional experiments to study the effect of myocardial reshaping on features.

(DOCX)

S1 Data.

(RAR)
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