[1] Laboratorio de procesado de imagen
Universidad de Valladolid

[2] Instituto de ciencias del corazón
Hospital clínico universitario

[3] Division of imaging sciences and biomedical engineering,
King's College London

An Automated Tensorial Classification Procedure for Left Ventricular Hypertrophic Cardiomyopathy

S. Sanz-Estébanez[1], J. Royuela-del-Val[1], S. Merino-Caviedes[1], A. Revilla-Orodea[2], T. Sevilla[2], L. Cordero-Grande[3], M. Martín-Fernández[1] and C. Alberola-López[1]

4th International Work-Conference on Bioinformatics and Biomedical Engineering April 20-22, 2016. Granada.

Introduction

- Cardiomyopathies are complex heart muscle diseases caused by multiple etiologies and heterogeneous phenotypic expressions.
- Functional tensorial descriptors from MR-Tagging (HARP) provide quantitative analysis of cardiac function and its anomalies.
- Multi-stage scheme for hypertrophic cardiomyopathies classification composed by different machine learning methods.

Introduction: State of the art

References	Modalities	Methodology	Contributions
Cordero-Grande, 2013	MR-Cine and LE-MR	Non-rigid registration	Mechanical characterization of fibrotic tissue
Gopalakrishnan, 2014	MR-Cine	Global biomarker extraction	Sequential classification of pediatric cardiomyopathies
Piella, 2010	MR-Tagging	Non-rigid registration	Segmental strain tensor analysis in athletes, healthy and HCM patients
Rahman, 2015	ECG	Signals heartbeat features	Identification of pathologic behaviors on heartbeats
Shimon, 2000	Echocard.	Block-matching	GLS correlated with global presence of fibrosis
Richard,2003	ECG, blood, echo.	Genetic analyses	Distribution of disease genes in HCM-genotype

- We propose a multi-stage pipeline to classify heterogeneous groups of HCM according to the characteristics of the different pathologies.

Materials: Subjects

Hypertrophic patients were previously diagnosed according clinical history and MR information (47 cases).

- 23 were diagnosed as primary HCM (16 male and 8 female, aged 57.1±17 years).
- 10 were diagnosed with secondary forms of hypertrophy, such as hypertensive heart disease or aortic stenosis (6 male and 4 female, aged 69.5±10.2 years).
- 14 were healthy non-athletes controls (8 male and 6 female, aged 47.3±21.4 years).

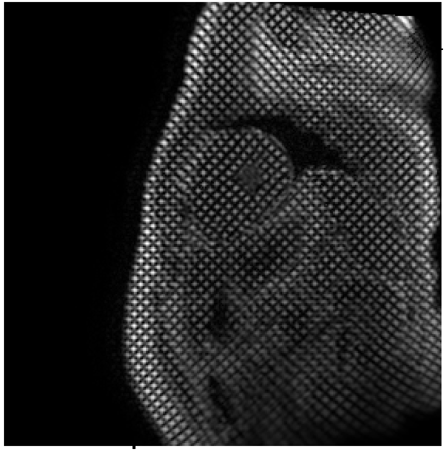
Materials: Acquisition

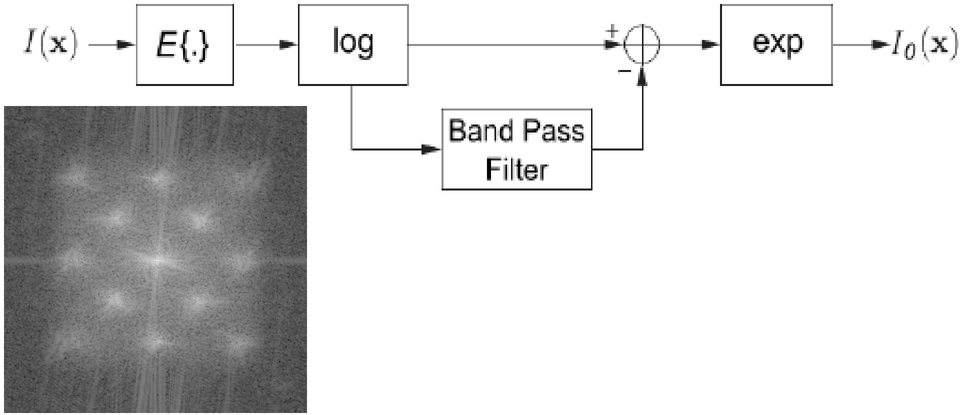
Sequence	MR-Tagging SA	MR-Tagging LA	MR-Cine SA	MR-Cine LA
Δ_p	1.21-1.32	1.21-1.34	0.96-1.18	0.98-1.25
Δ_l	10	10	8-10	8-10
N_t	16-25	15-27	30	30
N_l	10-15	1-3	10-15	1-3
N_p	256-432	240-340	240-320	256-448
T_R	2.798-6.154	2.903-4.507	2.902-3.9178	2.858-3.529
T_E	1.046-3.575	1.097-2.897	1.454-2.222	1.251-2.132
α	7-25	45	10-45	45

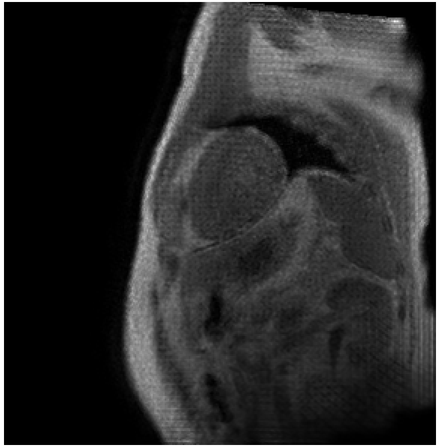
Table 2. *Detailed sequences.* Δp*: Pixel resolution (mm).* Δl*: Slice Thickness (mm).* Nt*: Temporal phases.* Nl*: Number of slices.* Np*: Number of pixels.* TR*: Repetition Time (ms).* TE*: Echo Time (ms).* α*: Flip Angle (degrees).*

Methods: Alignment

- MR-Cine manual segmentations mapped onto the MR-Tagging sequence by affine registration.
- MR-Tagging sequence detagged for suitable performance.
- The anatomical image shows a low variability (low pass signal), allowing suppressing the tag pattern by means of a notch filter.







Methods: LAD Reconstruction

- Redundant information when using SA and LA. HARP 3D requires 3 wave vectors.
  - 4 wave vectors K with their correspondent phase images Y(x) available.

$$\mathbf{Y}(\mathbf{x}) = \left[\frac{\partial^* \phi_{1,SA}}{\partial \mathbf{x}^T}(\mathbf{x}), \frac{\partial^* \phi_{2,SA}}{\partial \mathbf{x}^T}(\mathbf{x}), \frac{\partial^* \phi_{1,LA}}{\partial \mathbf{x}^T}(\mathbf{x}), \frac{\partial^* \phi_{2,LA}}{\partial \mathbf{x}^T}(\mathbf{x})\right]^T$$

- Material deformation gradient tensor F(x) obtained as:

$$\mathbf{K} = \mathbf{Y}(\mathbf{x})\mathbf{F}(\mathbf{x}).$$

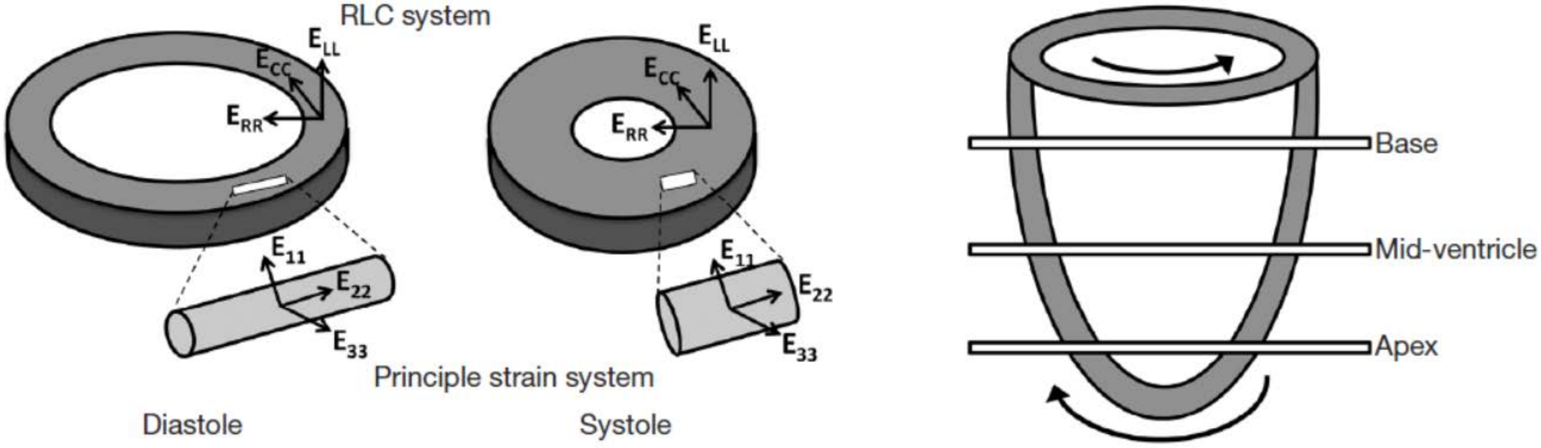
- Phase interferences, mainly near boundaries, give rise to multiple outliers.
- Least Absolute Deviation method (LAD) is suitable due to its robustness.
  - Solved by Iterative Re-Weighted Least Squares (l_1 norm minimization).

$$\mathbf{F}_{l+1}(\mathbf{x}) = (\mathbf{Y}^T(\mathbf{x})\mathbf{W}_l(\mathbf{x})\mathbf{Y}(\mathbf{x}))^{-1}\mathbf{Y}^T(\mathbf{x})\mathbf{W}_l(\mathbf{x})\mathbf{K},$$

Methods: Classification

Tensorial mechanical descriptors useful for HCM classification:

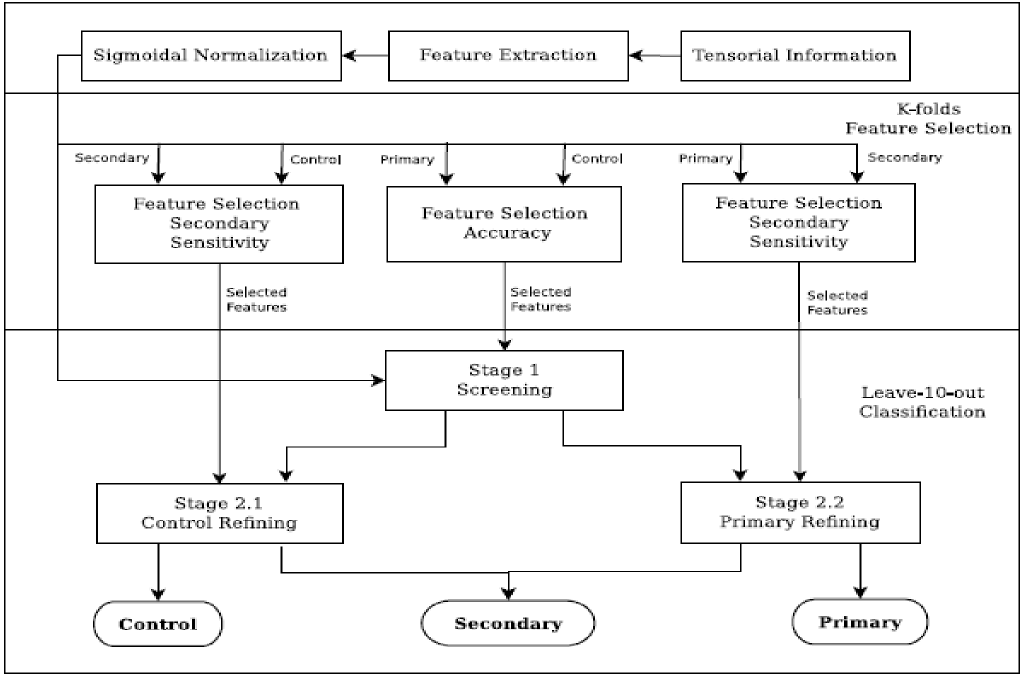
- Projected components of the strain tensor on the RLC space (polar coordinates).
- Rotation/Torsion as difference of curl or twist between apical and basal slices.
- Location of the zero crossing for rotation-related components.



Jiang and Yu. Quantitative Imaging in Medicine and Surgery, 2014

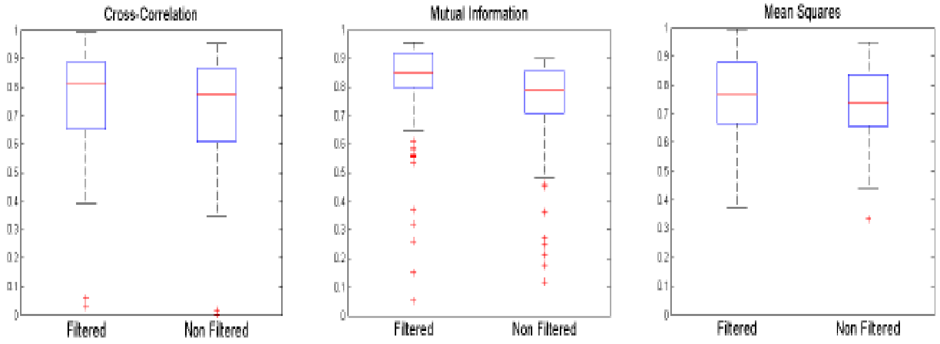
Methods: Classification

- Sigmoidal Normalization for outlier suppression.
- Fuzzy c-Means and SVM with quadratic and Gaussian kernels tested at every stage.
- Randomized Leave-10-out cross validation. Population rate unaltered along trials.

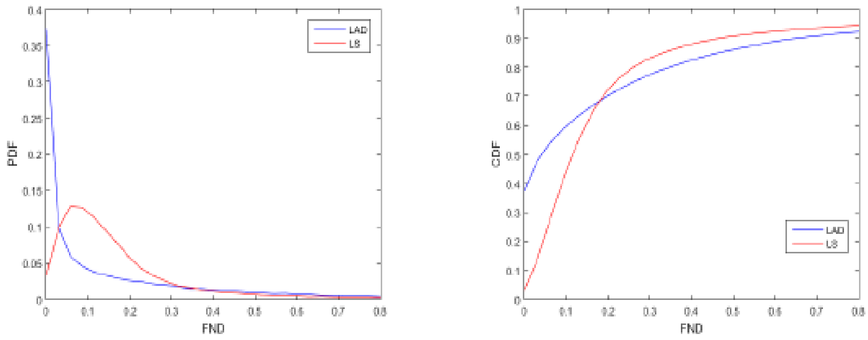


Results

- Affine registration methods tested with/without filtering.
- Improved performance in terms of Dice coefficient independently from metric.



- 3D tensors calculated using LS and LAD reconstruction methods.
- Error (FND) distribution between the 2D components and tensor from SA images.
- LAD estimator better behaves in presence of phase inconsistencies. CDF is left skewed despite of heavier tails.



Results: Confusion matrix

- Accurate multi-stage methodology for classifying HCM patients.
- Better sensitivity for control and primary HCM with respect to the secondary patients.
- No primaries are classified as controls and vice versa. Good performance as an screening tool.

	FCM			SVMq			SVMg			Mixed		
	Con	Sec	Pri	Con	Sec	Pri	Con	Sec	Pri	Con	Sec	Pri
Con	0.245	0.055	0	0.225	0.072	0.003	0.215	0.085	0	0.239	0.061	0
Sec	0.051	0.125	0.024	0.063	0.136	0.001	0.08	0.119	0.001	0.036	0.147	0.017
Pri	0.012	0.016	0.472	0	0.148	0.352	0.004	0.069	0.427	0	0.034	0.466

Table 3. *Confusion matrixes. *Mixed approach consists of Fuzzy C-Means in stages 1 and 2.2 and SVM with Gaussian kernel in stage 2.1.*

Conclusions

- Robust 3D tensor estimation technique from SA and LA MR-Tagging with a novel homomorphic filtering preprocessing step leading to multimodal schemes.
- Phase interferences have proven to be a major issue in HARP analysis. LAD estimator improves robustness for overdetermined reconstruction.
- Different machine learning methods tested. A mixed approach takes advantage of each method improving performance with respect to homogeneous classifiers.
- Although the classifier is stablished for HCM, other cardiovascular diseases can be classified even with biomarkers extracted from different technologies.