

## Cardiac magnetic field map topology quantified by Kullback-Leibler entropy identifies patients with hypertrophic cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is a common primary inherited cardiac muscle disorder, defined clinically by the presence of unexplained left ventricular hypertrophy. The detection of affected patients remains challenging. Genetic testing is limited because only in 50%–60% of all HCM diagnoses an underlying mutation can be found. Furthermore, the disease has a varied clinical course and outcome, with many patients having little or no discernible cardiovascular symptoms, whereas others develop profound exercise limitation and recurrent arrhythmias or sudden cardiac death. Therefore prospective screening of HCM family members is strongly recommended. According to the current guidelines this includes serial echocardiographic and electrocardiographic examinations.

In this study we investigated the capability of cardiac magnetic field mapping (CMFM) to detect patients suffering from HCM. We introduce for the first time a combined diagnostic approach based on map topology quantification using Kullback-Leibler (KL) entropy and regional magnetic field strength parameters. The cardiac magnetic field was recorded over the anterior chest wall using a multichannel-LT-SQUID system. CMFM was calculated based on a regular 36 point grid. We analyzed CMFM in patients with confirmed diagnosis of HCM (HCM,  $n=33$ ,  $43.8\pm 13$  years, 13 women, 20 men), a control group of healthy subjects (NORMAL,  $n=57$ ,  $39.6\pm 8.9$  years; 22 women and 35 men), and patients with confirmed cardiac hypertrophy due to arterial hypertension (HYP,  $n=42$ ,  $49.7\pm 7.9$  years, 15 women and 27 men). A subgroup analysis was performed between HCM patients suffering from the obstructive (HOCM,  $n=19$ ) and nonobstructive (HNCM,  $n=14$ ) form of the disease. KL entropy based map topology quantification alone identified HCM patients with a sensitivity of 78.8% and specificity of 86.9% (overall classification rate 84.8%). The combination of the KL parameters with a regional field strength parameter improved the overall classification rate to 87.9% (sensitivity: 84.8%, specificity: 88.9%, area under ROC curve: 0.94). KL measures applied to discriminate between HOCM and HNCM patients showed a correct classification of 78.8%. The combination of one KL and one regional parameter again improved the overall classification rate to 97%. A preliminary prospective analysis in two HCM families showed the feasibility of this diagnostic approach with a correct diagnosis of all 22 screened family members (1 HOCM, 4 HNCM, 17 normal). In conclusion, Cardiac Magnetic Field Mapping including KL entropy based topology quantifications is a suitable tool for HCM screening.