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## HIGH RESOLUTION SYSTEMATIC DIGITAL HISTOLOGICAL QUANTIFICATION OF CARDIAC FIBROSIS AND ADIPOSE TISSUE IN PHOSPHOLAMBAN MUTATION ASSOCIATED CARDIOMYOPATHY

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**Background:** The p.Arg14del mutation in the phospholamban (PLN) gene is associated with dilated and arrhythmogenic cardiomyopathy. To determine the exact pattern of fibrosis and fatty replacement in PLN mutation positive patients, we developed a novel method for high resolution systematic digital histological quantification.

**Methods:** Transversal mid-ventricular slices were obtained at autopsy or explantation from patients with the PLN p.Arg14del mutation (n=7, mean age 51±15 years; 4 (57%) male). An in-house developed open source MATLAB script was used for digital analysis of Masson's trichrome stained slides. Slides were divided into trabecular, inner and outer compact myocardium. Percentage of connective tissue, cardiomyocytes and fatty tissue was quantified per region.

**Results:** Fibrosis was mainly observed in the left ventricular posterolateral wall (figure top), while adipocytes were more pronounced in the right ventricular myocardium (figure bottom). No difference in distribution pattern of fibrosis and adipocytes was observed between patients with a clinical dilated and arrhythmogenic phenotype.

**Conclusions:** In PLN p.Arg14del mutation associated cardiomyopathy, myocardial fibrosis is predominantly present in the left posterolateral wall, whereas fatty changes are more pronounced in the right ventricle. Systematic digital histological quantification can be used to quantify cardiac fibrosis and fatty tissue in animal models and a broad range of cardiomyopathies.

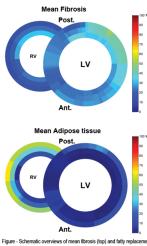


Figure - Schematic overviews of mean fibrosis (top) and fatly replacement (bottom) in combined heart slices of phospholandam p Arg14del mutation carriers (n=7). Epicardial fat is excluded. The results of the mean percentage of fibrosis or adapose lissue are shown using a color scale. LV, left ventricle; RV, right ventricle; Ant., anterior; Post, posterior