



## UKE Paper of the Month February 2026

### Deep-learning analysis of 3D microarchitectural remodeling in hypertrophic cardiomyopathy

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#### ABSTRACT:

Hypertrophic cardiomyopathy (HCM), a genetic heart disease defined by unexplained cardiac wall thickening, is a leading cause of sudden death worldwide. However, the three-dimensional organization of cardiac tissue underlying left ventricular hypertrophy remains poorly understood. We developed CaMVIA-3D, a deep-learning volumetric imaging and analysis pipeline to characterize cardiac microarchitecture. Analysis of tissues from HCM hearts revealed genotype-specific differences in cardiomyocyte volume, morphology, and extracellular volume, with pathogenic variants exhibiting greater concentric cellular hypertrophy and disarray and variant-negative cases showing predominant fibrosis. Longitudinal profiling of a pig HCM model revealed early-onset fibrosis preceding cardiomyocyte hypertrophy. Integrating transcriptomic and morphologic changes, we identified genes associated with cellular and extracellular remodeling. These findings define genotype-specific microstructural differences in HCM, offering insights to improve diagnostics and targeted therapies.

#### STATEMENT:

*This is the first study to map genotype-specific microstructural remodeling in human and pig HCM hearts in true 3D at cellular and subcellular resolution, enabling the discovery of genotype-dependent disease signatures. By combining volumetric imaging with deep learning (CaMVIA-3D) and single-nucleus RNA sequencing, we link these remodeling patterns to gene expression programs across disease progression.*

#### BACKGROUND:

This work involved UKE through Martin Beyer (Department of Cardiac Surgery), who is enrolled in the UKE PhD program (Medical Faculty) and contributed to the project during his postdoctoral fellowship in the Department of Genetics at Harvard Medical School in the lab of Christine and Jonathan Seidman. His research focuses on deep learning-based 3D volumetric analysis to understand genotype-specific remodeling processes in cardiac pathologies, with a particular focus on inherited cardiomyopathies. This work was supported by Deutsche Herzstiftung e.V.