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Deep Learning Detection, Phenotyping, and LVOT Gradient Estimation in Hypertrophic Cardiomyopathy Using Echocardiography

Multi-institutional cohort with international external validation

Fawaz Alenezi, MD, FAHA, FACC, FASE
Associate Professor of Medicine
Duke Heart Center
Duke University Medical Center

DukeHealth

Disclosures

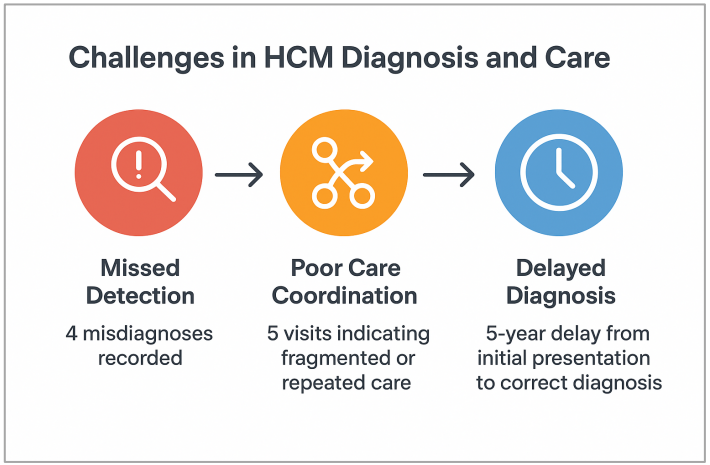
PRESENTER DISCLOSURES

- **Research funding (unrelated to this project)**
  National Institutes of Health (NIH); American Heart Association (AHA) Career Development Award; United Therapeutics.

- **Relationship to this study**
  None of the above sources funded or supported this specific project.

- **Study-specific funding and conflicts**
  This study received no external funding. Technology partner Us2.ai (Singapore) contributed model development and preprocessing infrastructure. No other relevant financial relationships to disclose.

HCM is often missed on routine echocardiography



1. **Subtle imaging features**
   Some HCM patterns may be missed or overlaps with HTN, athletic remodeling, amyloidosis.
2. **Operator-dependent interpretation**
   Recognition varies between readers (sensitivity 37–59% across readers).
3. **Genetic testing isn't universal**
   Diagnosis often remains clinically and imaging based.
4. **Cardiac MRI is not widely available**
   Access to confirmatory imaging may be limited.

Clinical need: A scalable, operator-independent tool to detect HCM and distinguish it from LVH phenocopies.

Study objectives

Can a fully automated deep-learning model detect and phenotype HCM from routine echocardiography?

Four pre-specified objectives:

1 Detect

Develop and internally validate the model against clinically diagnosed HCM.

2 Differentiate pheno- & subtypes

Distinguish HCM from cardiac amyloidosis, aortic stenosis, hypertensive heart disease & HCM subtypes.

3 Validate

Externally validate HCM detection at an independent U.S. academic center.

4 Sensitivity to gradient severity

Automate LVOT gradient estimation and identify obstructive physiology.

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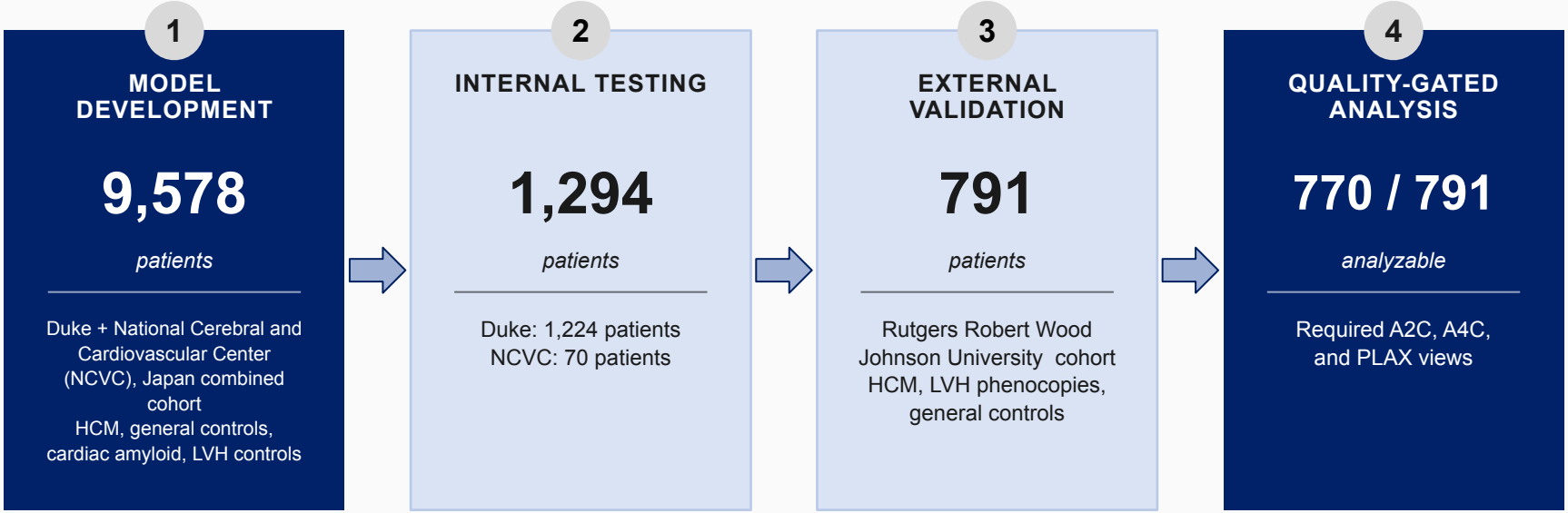
4 Quantify obstruction

Automate LVOT gradient estimation and detect obstructive physiology.

HCM detection cohorts: development, internal testing, and external validation



We trained and internally tested the HCM detection model using Duke and NCVC cohorts, then tested generalizability in an independent Rutgers cohort enriched with both HCM and LVH phenocopies.

Can the model detect HCM from routine echo views?

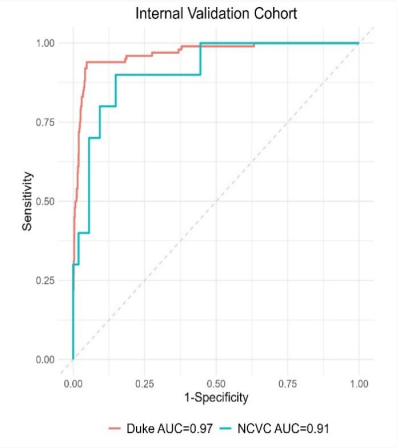
Duke + NCVC cohorts, patient-level, 80:10:10 split at the patient level

Overall Internal Validation AUC	Overall Internal Test AUC	Test Accuracy
0.96	**0.97**	**93.8%**

SENSITIVITY	SPECIFICITY	PPV AT 0.5% PREVALENCE	NPV AT 0.5% PREVALENCE
92.6%	**94.0%**	**7.2%**	**100%**
(86.1–96.2%)	(92.3–95.3%)	(5.7–9.0%)	(99.9–100%)

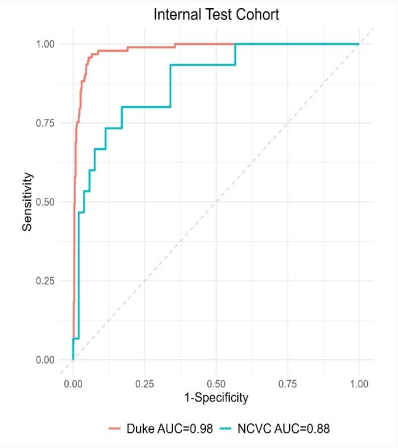
n = 1,119 classified (100 TP, 8 FN, 950 TN, 61 FP)

Internal Validation Cohort



Duke AUC=0.97 — NCVC AUC=0.91

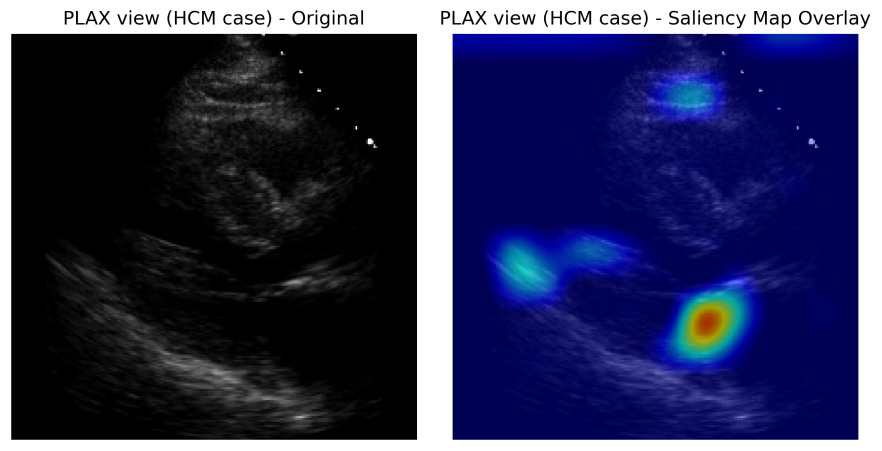
Internal Test Cohort



Duke AUC=0.98 — NCVC AUC=0.88

Interpretation: Accuracy 93.8%, with performance consistent across internal validation and test cohorts.

Model attention maps to anatomically plausible HCM features



Grad-CAM saliency overlays (red-yellow = higher activation), representative HCM cases

Routine echo clips → preprocessing → AI analysis → one HCM probability per patient.

Finding: PLAX activation concentrates at the mitral–septal contact zone and interventricular septum; A4C activation centers on the mitral leaflets and septum, regions anatomically consistent with HCM diagnosis.

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Distinguish HCM from cardiac amyloidosis, aortic stenosis, and hypertensive heart disease & HCM subtypes.

3 **Generalize**

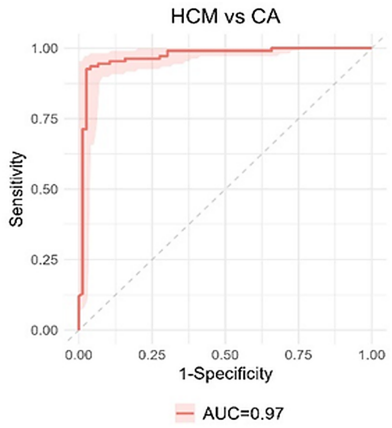
Externally validate detection performance at an independent U.S. academic center.

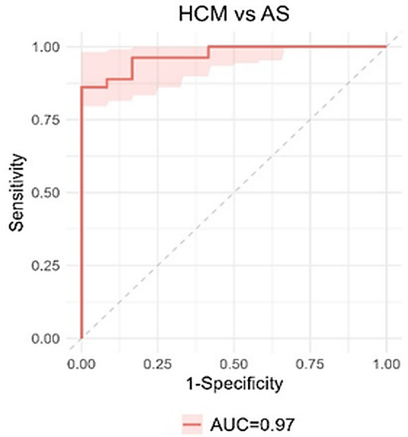
4 **Quantify obstruction**

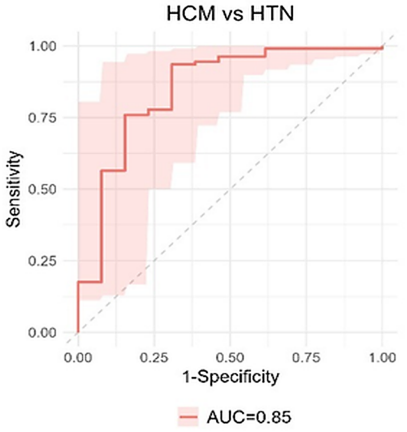
Automate LVOT gradient estimation and detect obstructive physiology.

The model separates HCM from LVH phenocopies

HCM vs Cardiac amyloidosis	HCM vs Aortic stenosis	HCM vs Hypertensive heart disease
AUC **0.97**	AUC **0.97**	AUC **0.85**
n = 184 · Duke + NCVC CA	*n = 120 · NCVC AS*	*n = 121 · NCVC HTN*







Discrimination is excellent against cardiac amyloidosis and aortic stenosis. Hypertensive heart disease remains the most morphologically similar and therefore the hardest to separate (AUC 0.85).

Discrimination remained strong across morphologic HCM subtypes

Exploratory internal-test subgroup analysis · detection vs. controls within each morphologic subtype

Basal sigmoid HCM	Concentric HCM	Apical HCM
AUC	AUC	AUC
0.98	**0.99**	**0.92**
n = 72 · sensitivity 95.8%	*n = 14 · sensitivity 100%*	*n = 5 · sensitivity 80%*

Discrimination remained strong across all three morphologic subtypes (AUC 0.92–0.99), including subtypes not explicitly represented during training.

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Performance is preserved in an independent cohort

HCM vs General population controls	HCM vs LVH controls
AUC **0.96**	AUC **0.93**
n = 644 · Sens 87.4% · Spec 95.2%	n = 162 · Sens 87.4% · Spec 89.3%

SUBTYPE BREAKDOWN

Obstructive HCM

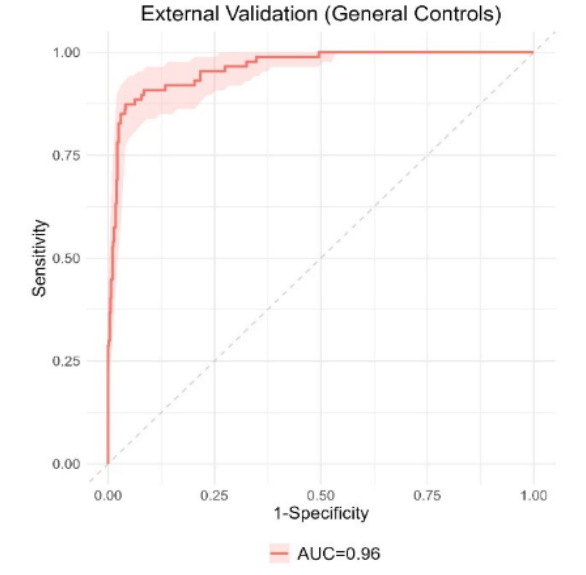
AUC 0.97 *sensitivity 91.1%*

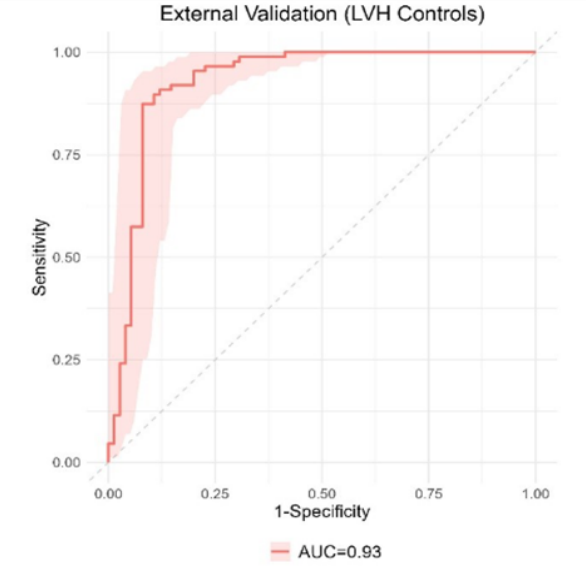
Non-obstructive HCM

AUC 0.95 *sensitivity 82.9%*

Interpretation: Discrimination remains strong against both general and LVH controls with no institutional overlap; sensitivity is consistently higher for obstructive HCM.

Performance is preserved in an independent cohort





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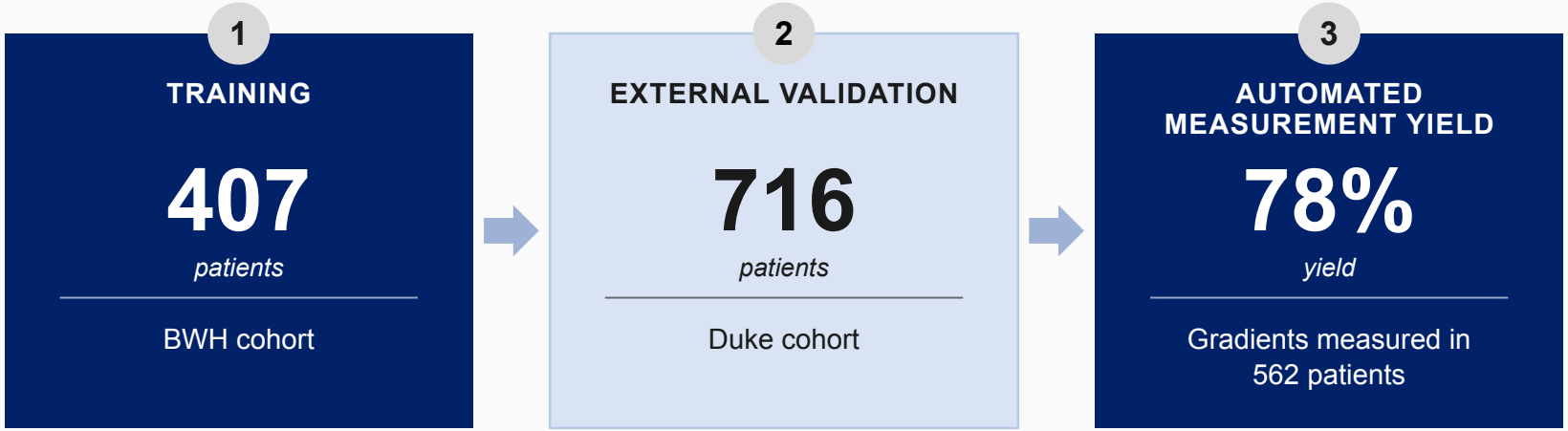
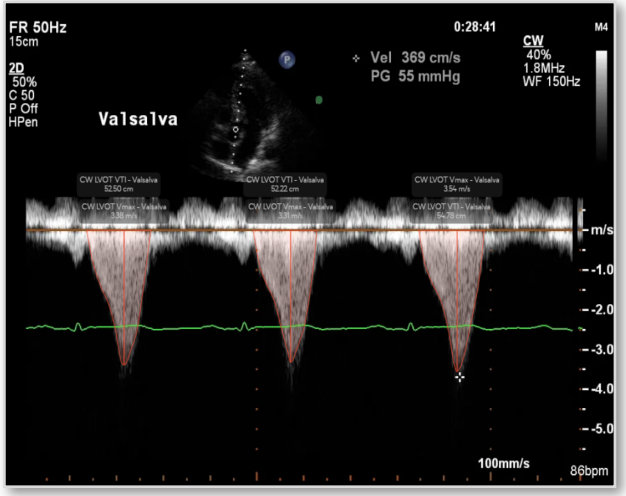
LVOT gradient cohort: automated LVOT gradient quantification



For obstruction assessment, the LVOT gradient model was trained at BWH and externally validated at Duke, with automated gradient measurement achieved in 78% of patients.

LVOT gradient: from Doppler signal to obstruction gradient

1. **View identification**
   CW Doppler view identified (LVOT, apical, or mid-ventricular)
2. **AI segmentation**
   U-Net++ (EfficientNet-B0) segments the VTI envelope
3. **Gradient calculation**
   Bernoulli equation converts peak velocity to pressure gradient
4. **Patient-level reporting**
   Maximum gradient across all views reported per patient



Peak LVOT gradient (mmHg) at rest and with Valsalva, fully automated with no manual VTI tracing or Doppler measurement, the model segments the Doppler envelope and directly calculates the gradient.

Automated Doppler gradients identify obstructive physiology

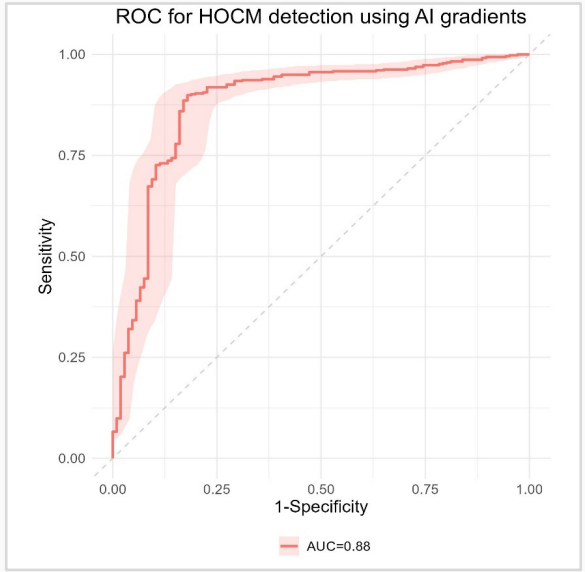
External validation · 716 HCM patients, Duke University Medical Center

AUROC

0.88

SENSITIVITY
90%
at ≥30 mmHg threshold

SPECIFICITY
81%
at ≥30 mmHg threshold



AGREEMENT WITH CLINICAL MEASUREMENT

Overall	Rest	Valsalva
ICC 0.77 MAE 17.6 mmHg	ICC 0.74 MAE 15.9 mmHg	ICC 0.72 MAE 20.0 mmHg

LIMITATIONS

1. Single-center external validation.
Rutgers was the only external site; prospective, multi-national validation is still needed.

2. No universal genetic confirmation.
HCM was adjudicated clinically and by imaging, not genetically in all cases; some controls may harbor subclinical HCM.

3. CMR available in a subset only.
Limits full morphologic subtyping and may bias subtype-specific performance estimates.

4. Doppler view classification limits gradient yield.
Overlapping CW envelopes (LVOT vs. AV vs. MR) capped gradient yield at 78%; detection-model yield remained 91–93%.

KEY FINDINGS

1. A fully automated pipeline detects HCM from routine echo views.

No manual tracing, Doppler measurement, or specialized operator input; AUC 0.97 internally, 0.96 externally.

2. It reliably separates HCM from its hardest mimics.

AUC 0.97 vs. cardiac amyloidosis and aortic stenosis; 0.85 vs. hypertensive heart disease.

3. Performance generalizes to an independent cohort.

AUC 0.96 (general controls) and 0.93 (LVH controls) at Rutgers, with no institutional overlap.

4. A second model automates obstruction assessment.

AI-derived LVOT gradients identify obstructive HCM with 90% sensitivity, AUROC 0.88.

AUTHORS

Fawaz Alenezi[1], Ankush D. Jamthikar[2], Naveena Yanamala[2], Takeshi Kitai[3], Jonathan W. Cunningham[4], Hicham Skali[4], Xiaowen Wang[4], Sze Chi Lim[5], Matthew Frost[5], Carolyn S.P. Lam[6], Svati Shah[1], Deepa Upadhyaya[1], Partho P. Sengupta[2], Sabahat Bokhari[2], Andrew Wang[1], Sreekanth Vemulapalli[1]

Underlined = corresponding author

AFFILIATIONS

1 Duke University Medical Center, Durham, NC, USA
2 Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, USA
3 National Cerebral and Cardiovascular Center, Osaka, Japan
4 Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
5 Us2.ai, Singapore
6 National Heart Centre Singapore & Duke-NUS Medical School, Singapore

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Questions?

Email: fawaz.enezi@dm.duke.edu