Machine Learning Detection of Obstructive Hypertrophic Cardiomyopathy Using a Wearable Biosensor

AHA 2017 Late Breaking Basic Science

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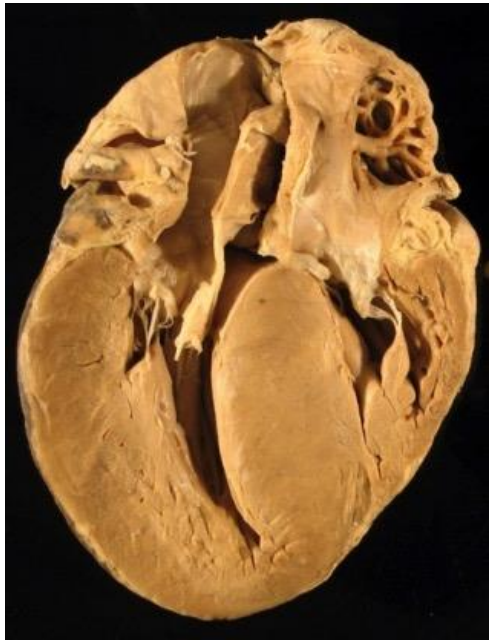
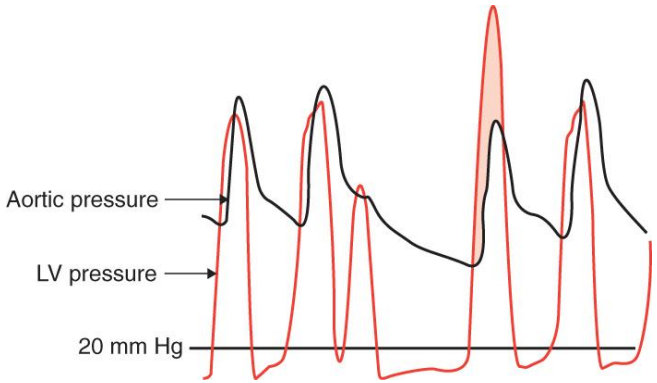
Hypertrophic cardiomyopathy

- Inherited disease of heart muscle characterized by hypertrophy without a systemic etiology
- Characteristic hemodynamic abnormalities related to hypercontractility (with or without LVOT obstruction) and impaired relaxation
- Variable age of onset and disease natural history
- Substantial risk of heart failure, afib/stroke and sudden death





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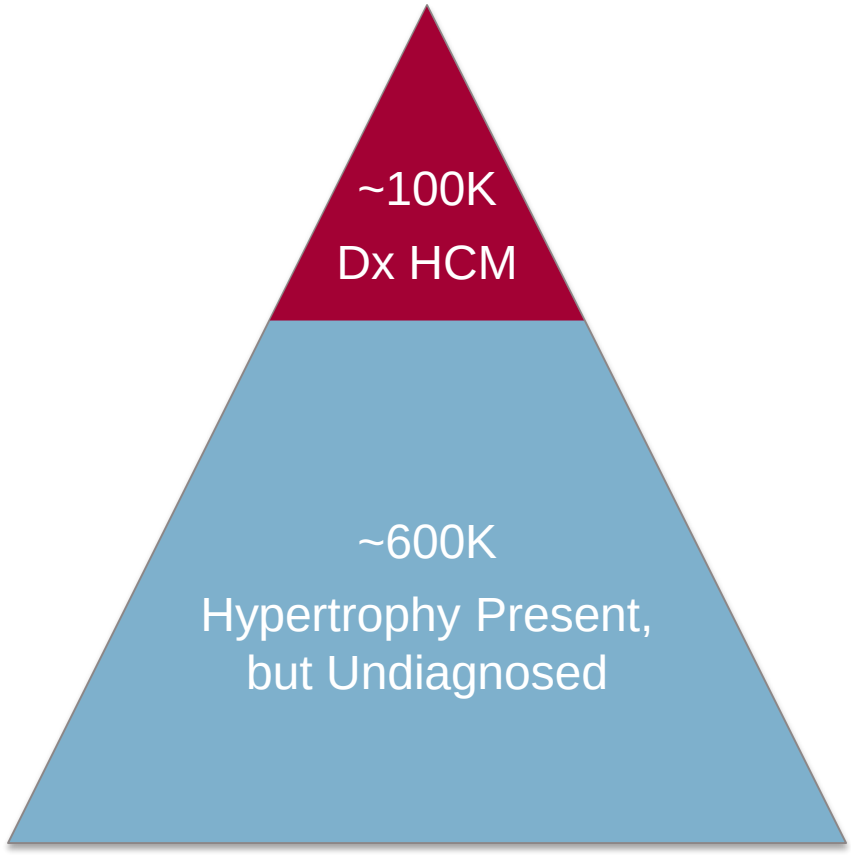
Most Individuals with HCM Are Currently Undiagnosed

- Population studies estimate HCM prevalence at least 1:500
- Medicare claims data show ~100K under care
  - **~16%** diagnosis rate
  - Most patients (~80%) with sudden death and HCM are previously undiagnosed
- Early diagnosis allows for risk stratification for sudden death and other complications
- Diagnosis limited by non-specific symptoms and requirement for expensive, hospital-based testing



Maron, B. J. et al. (1995).. *Circulation*, *92*(4), 785–789.
Maron, M. S. et al. (2016). *The American Journal of Cardiology*, *117*(10), 1651–1654.
Aro, A. L. , et al. (2017). *Circulation*, *136*(17), 1665–1667.

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How can we increase the detection rate for HCM?

Could we develop a method that is non-invasive, does not require a skilled operator and can be widely disseminated?

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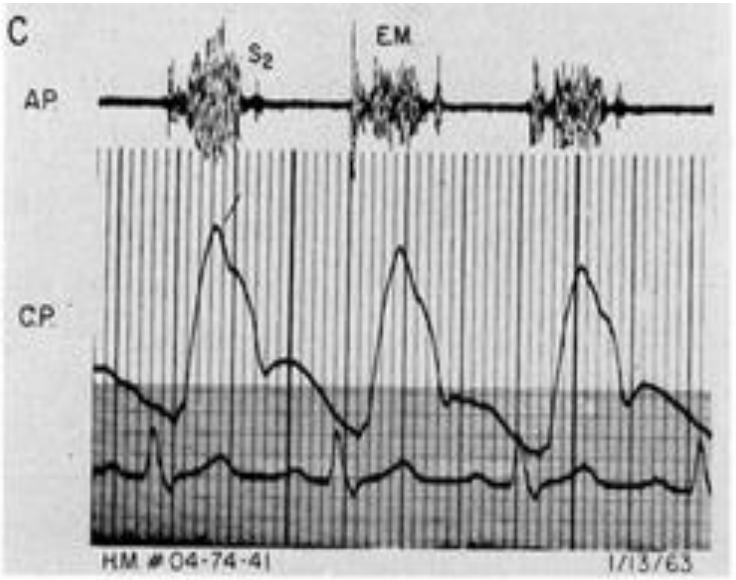
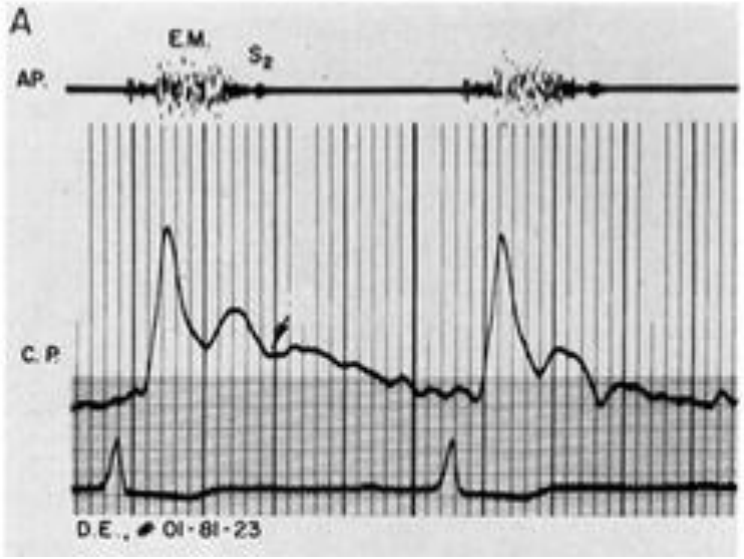
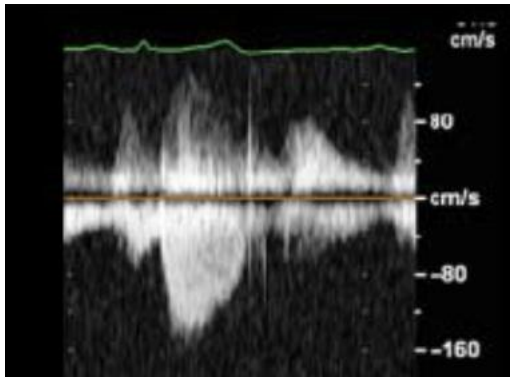
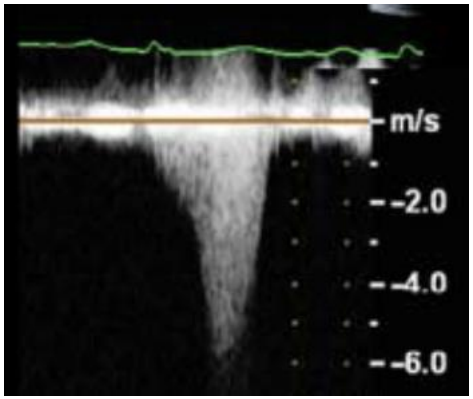
Characteristic Hemodynamics of Obstructive HCM (oHCM)

	Normal	LVOT obstruction
Acoustic phonography		
Carotid pulsations		
Doppler echo		

Frank and Braunwald *Circulation* 1968

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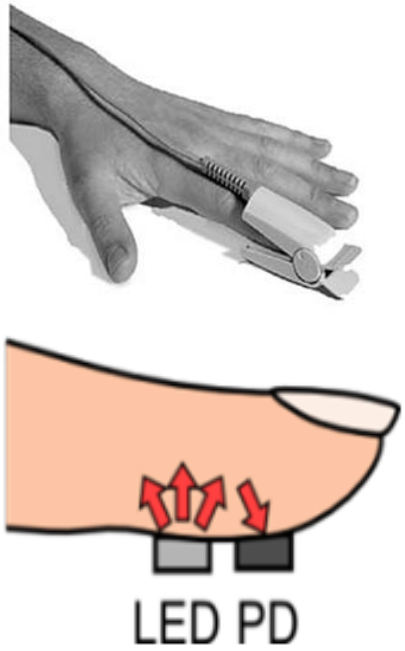
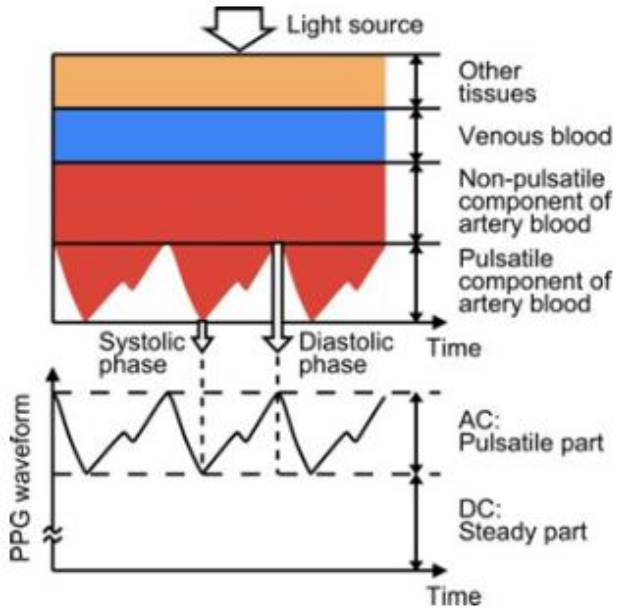
Photoplethysmography Detects Peripheral Bloodflow Patterns

PPG is an non-invasive optical method to detect blood volume changes in the microvascular bed at the skin surface.



Millasseau et al. 2006, Hypertension



Pleth signal

Tamura et al., 2014, Electronics

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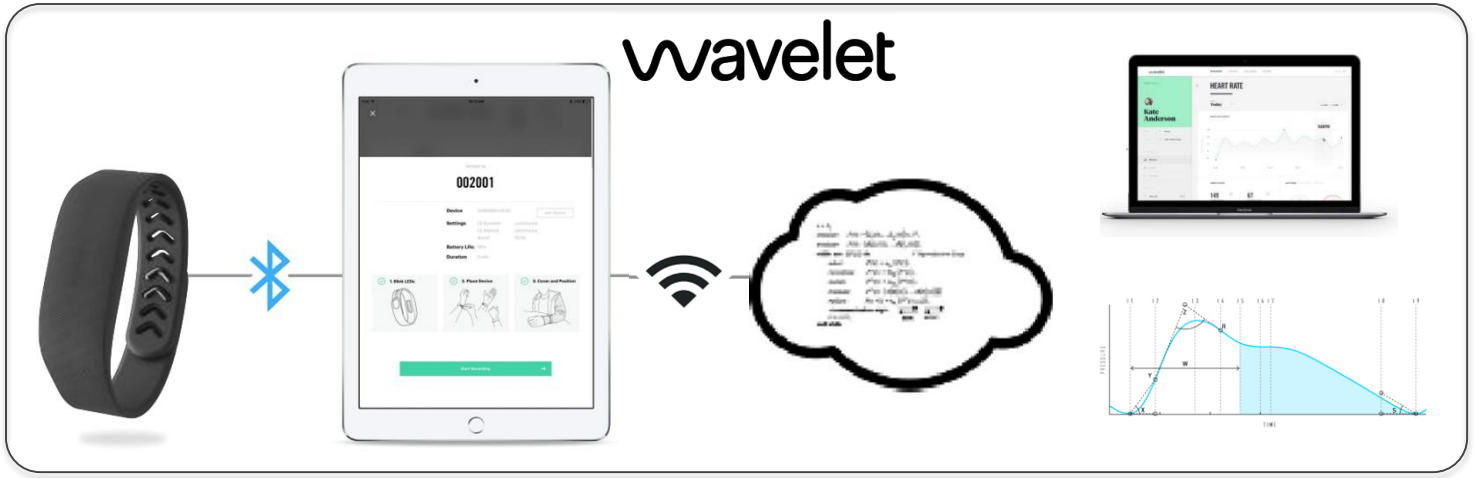
PIONEER-HCM Digital Health Substudy

- *Develop a classifier for oHCM PPG signals prior to treatment*
- Evaluate changes in oHCM PPG signals on treatment

19 oHCM patients

86 controls



5 minute PPG, paired with echo

iPad/mobile apps to collect and transmit data

Train a machine learning classifier for oHCM in a training cohort

Validate oHCM classifier using validation cohort

PIONEER-HCM is an ongoing phase 2 open-label study of multiple doses of mavacamten in patients with oHCM

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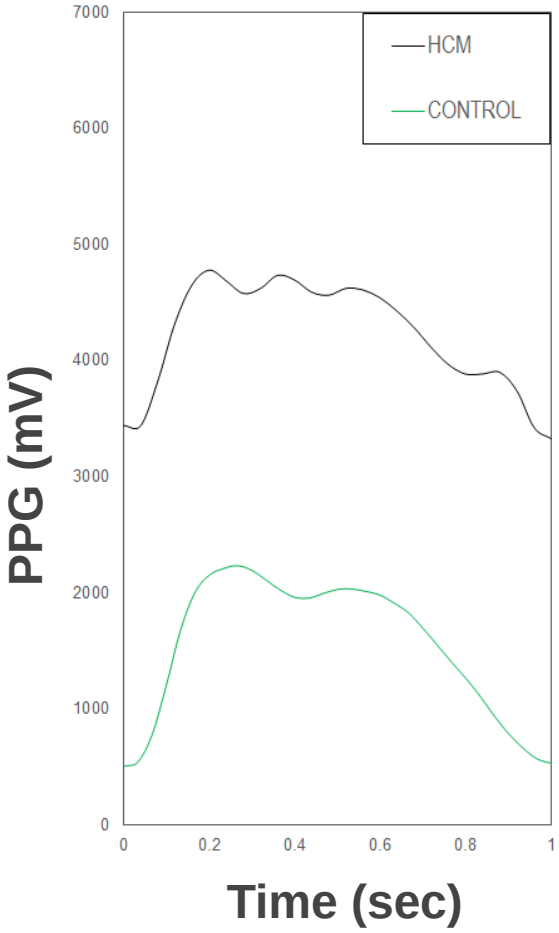
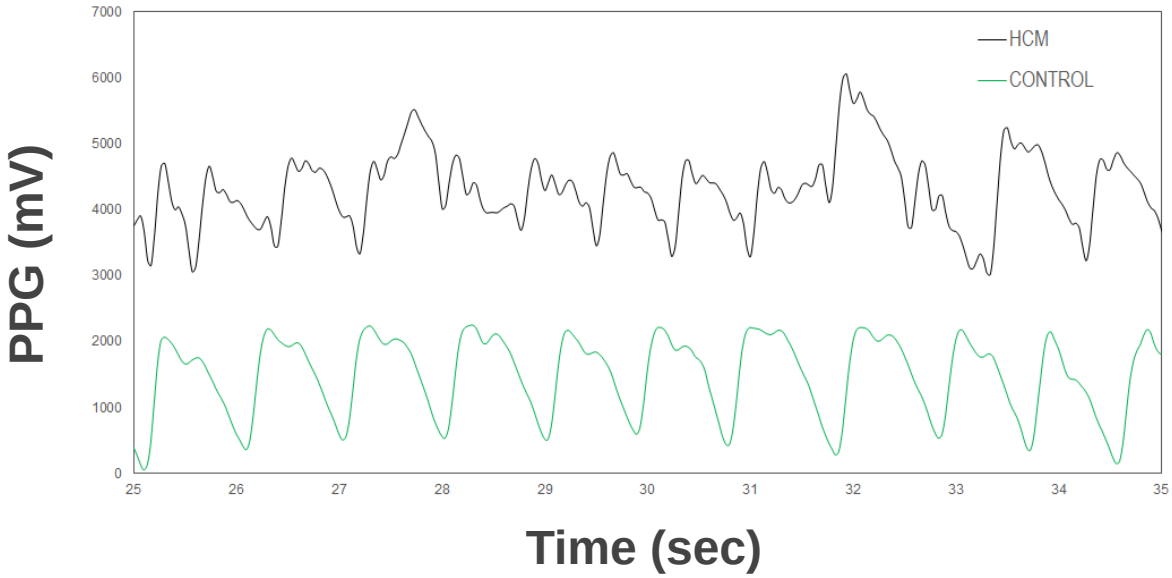
Pulsewave Morphology Differs Between oHCM and Healthy Subjects





Pulsewave morphology in oHCM consistent with turbulent bloodflow and beat-to-beat variability associated with dynamic LVOT obstruction

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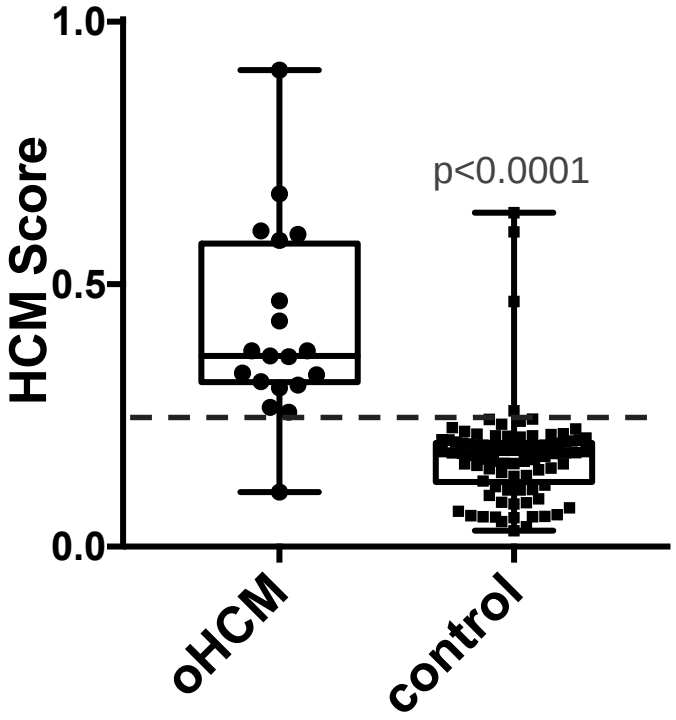
An Accurate Machine Learning Classifier for oHCM



	oHCM	control
Predicted oHCM	18	4
Predicted control	1	82

Overall Accuracy = 0.95
Sensitivity = 0.95
Specificity = 0.95

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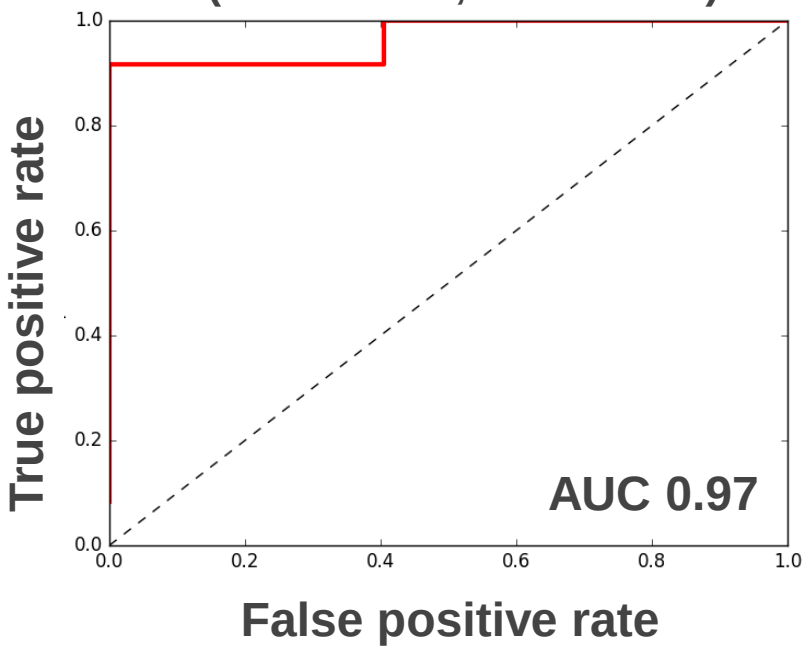
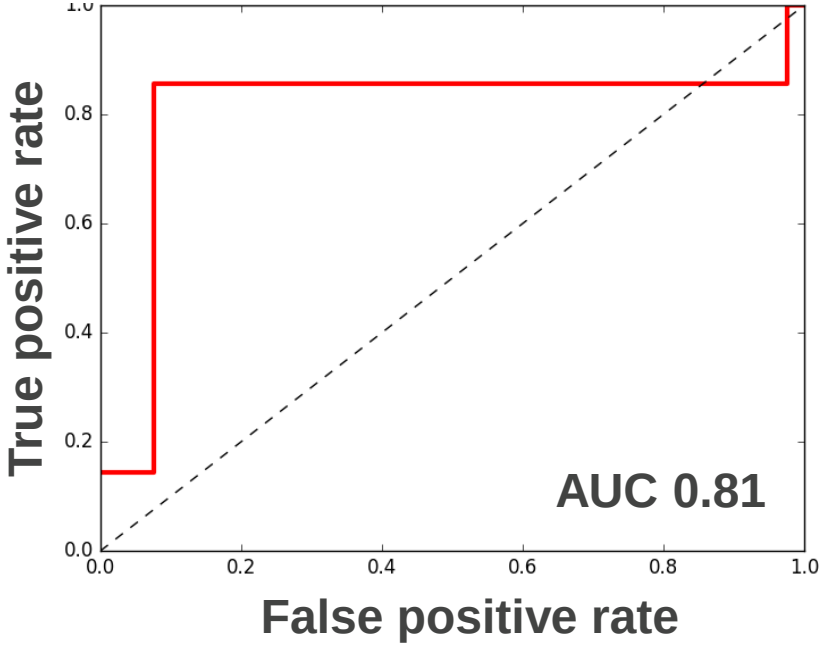
oHCM Classifier Receiver/Operator Characteristics

Training and cross-validation
(n=12 oHCM, 46 controls)



Validation
(N=7 oHCM, 40 controls)



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Summary and Next Steps

Summary

- We demonstrate proof of principle that a wearable biosensor and machine learning algorithm can identify patients with obstructive HCM

Next Steps

- Further validation in large data sets and across hardware platforms
  - Consider combination with other HCM screening modalities such as EKG
- Evaluation of changes in response to mavacamten treatment in PIONEER
- Application to non-obstructive HCM patients
  - Is there an identifiable signature in this population?
- A tool for increased disease understanding
  - Longitudinal measurement to detect dynamic LVOT obstruction in HCM patients outside the clinic, correlate with symptoms, identify stimuli
  - Could identify candidates for SRT or intensified medical therapy based on hemodynamics outside clinic setting

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Future Vision

Sensors

oHCM

afib

Suite of Algorithms

Multiplexed platform for passive disease screening in HCM and beyond

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Acknowledgments

MyoKardia

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