SELECTED UPDATES FROM THE AI ECHO CORE LAB RESEARCH GROUP

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UBC AI ECHO VGH CORE LAB

Vancouver CoastalHealth

PROJECTS WE LEAD/PARTICIPATE IN:

- AI Echo based projects
- General Echo research lead by our group members
- Site lead for multicenter clinical trials
- Interpretation of echo studies for clinical trials

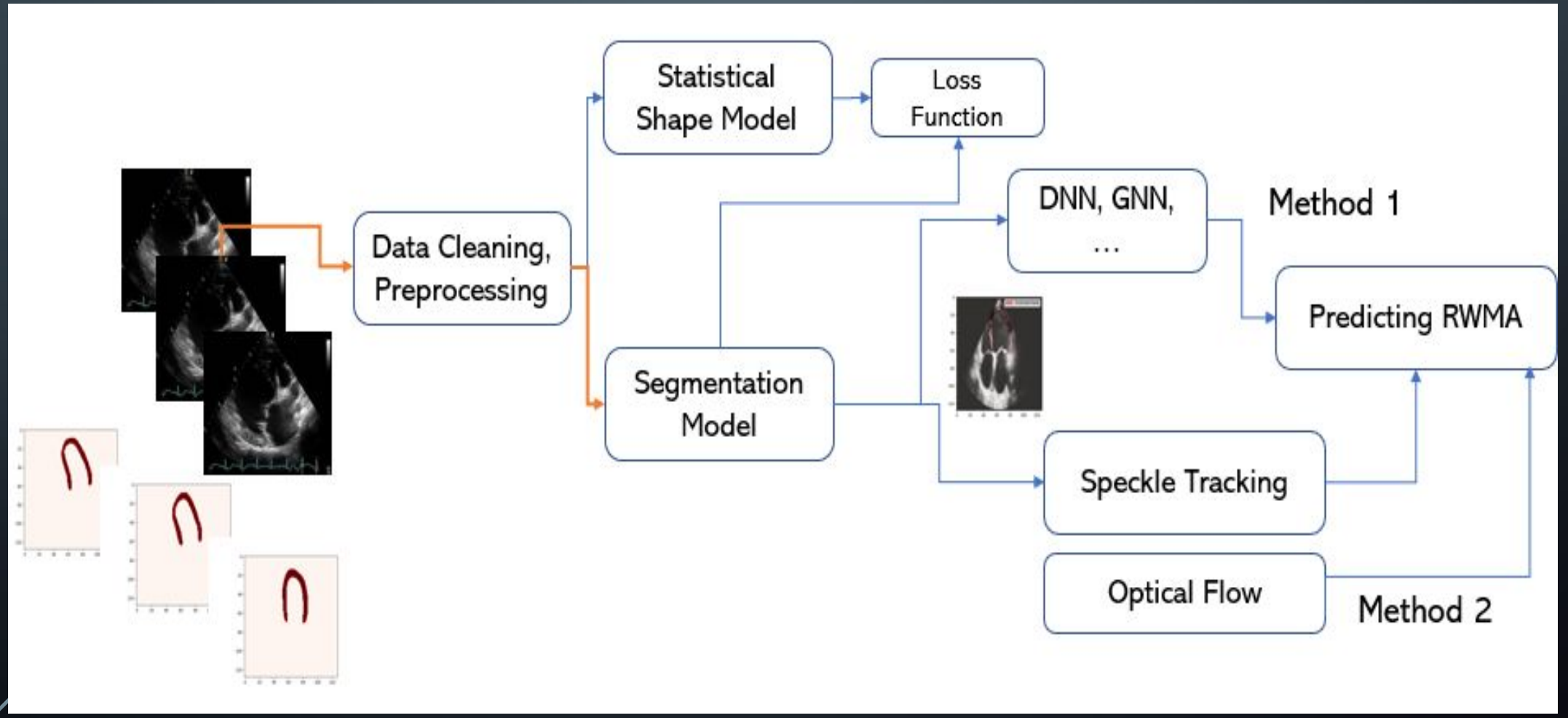
AI ECHO BASED PROJECTS

- CORONARY ARTERY DISEASE
- VALVE DISEASE
- STROKE
- HEART FAILURE
- CARDIOMYOPATHY

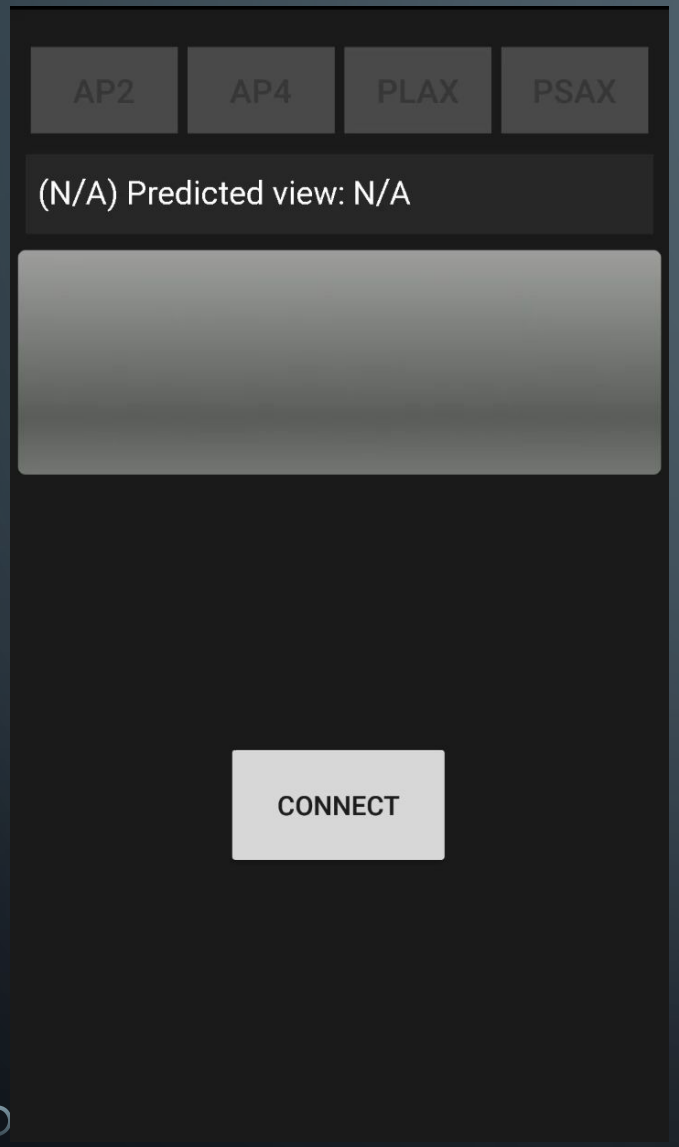
AI MODELS FOR PREDICTION OF ACS OUTCOMES

- Phase 1: Develop and optimize an LV segmentation model for RWMA identification
- Phase 2: Develop a model for prediction of ACS outcomes with echo images/clips and clinical outcome data
- Phase 3: Test the model on a diversity of data sources and potentially fine-tune for specific cohorts

AI MODELS FOR PREDICTION OF ACS OUTCOMES: PHASE 1



Data Cleaning and Preprocessing



- "Real world" unselected data
  - Existing ML view classification model selected AP2, AP3, and AP4 images

Data Cleaning and Preprocessing

Characteristics:

Sex: 25.5% Females

Age: 67±14 years

BMI: 26.3±5.2 kg/m^2

Height: 172±10cm

Weight: 78±18 kg

LVEF: 43±10 %

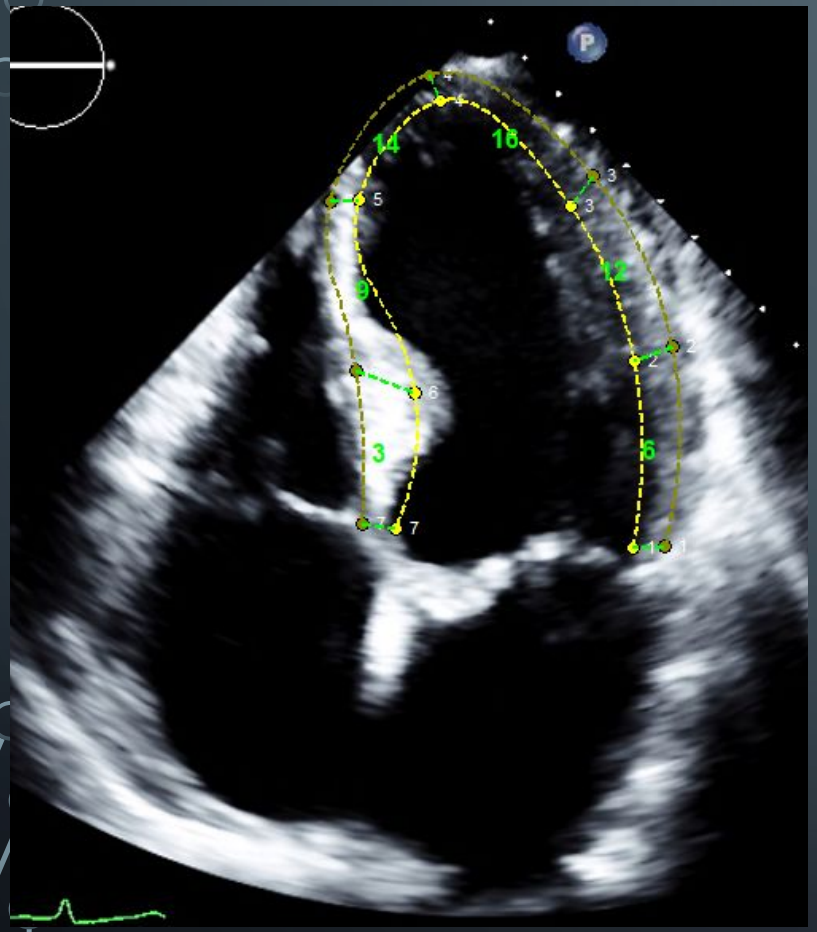
"Real world" unselected data

- Existing ML view classification model selected AP2, AP3, and AP4 images

4,082 videos from 1170 patients

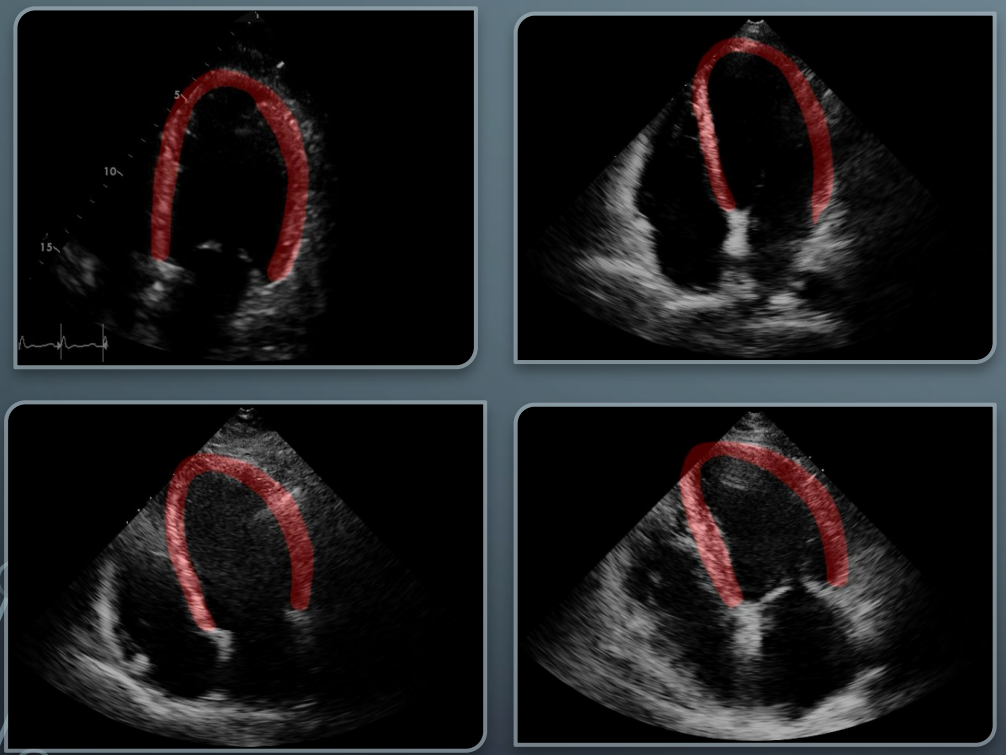
- All samples had LV systolic dysfunction (global or RWMA)
- 33% AP4, 36% AP2, 31% AP3

Data Cleaning and Preprocessing



- "Real world" unselected data
  - Existing ML view classification model selected AP2, AP3, and AP4 images
- 4,082 videos from 1170 patients
  - All samples had LV systolic dysfunction (global or RWMA)
  - 33% AP4, 36% AP2, 31% AP3
- Manual segmentation of the LV myocardium by level III echocardiographer

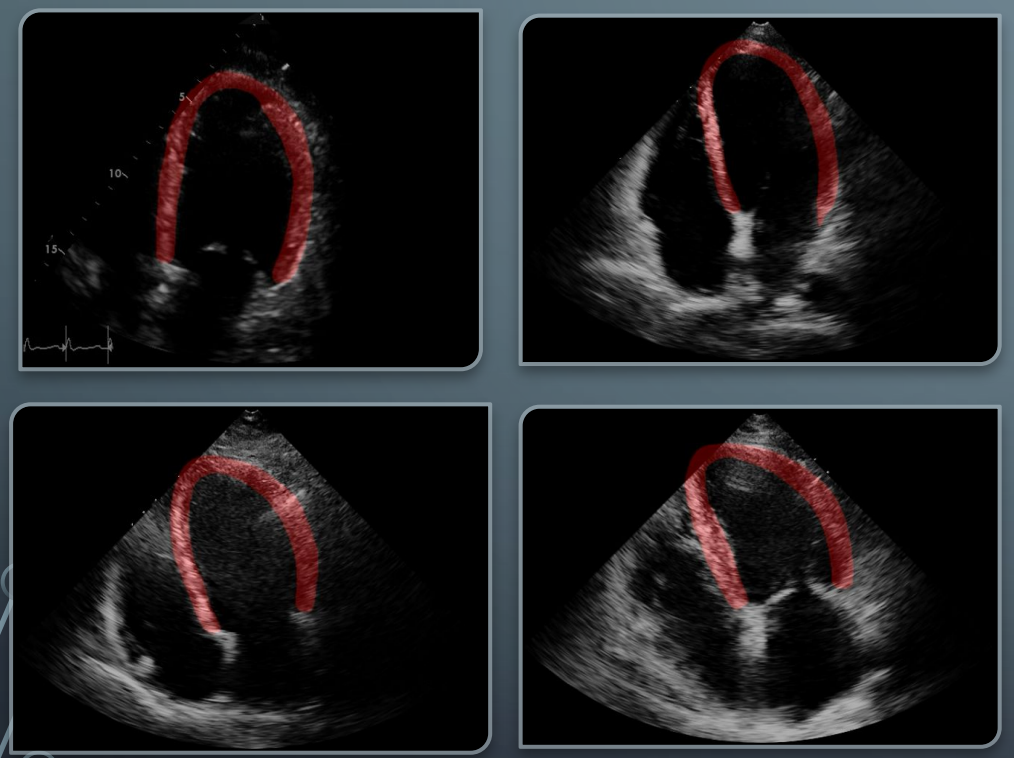
STEP 2: SEGMENTATION MODEL



Current Dice Score for Each view

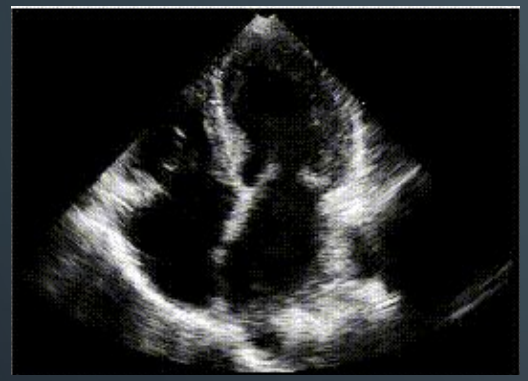
	AP2	AP3	AP4
Supervised/UNET++ (trained separately on each view)	79%	78%	78%
Supervised/UNET++ (trained jointly on all 3 views)	81%	78%	79%

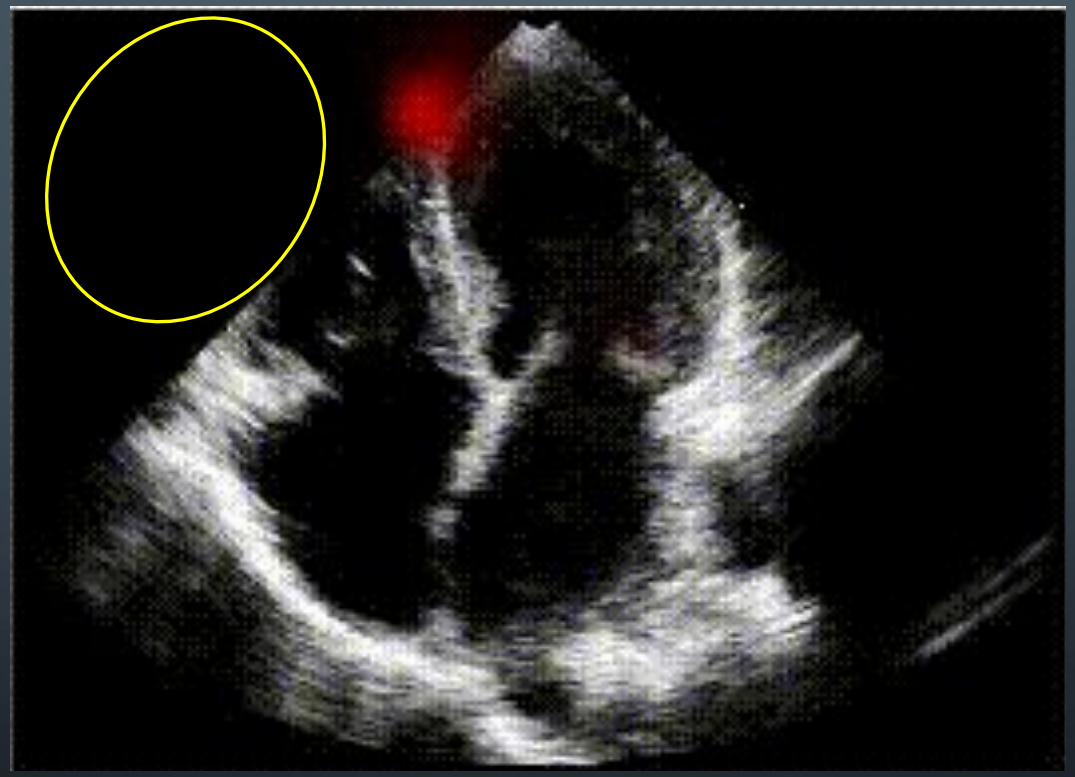
STEP 2: SEGMENTATION MODEL



- RWMA model work is ongoing and will utilize a speckle-tracking approach
  - Uses the speckle pattern of the myocardium to estimate motion of the heart
  - Use motion information to calculate strain
  - L1-SOUL algorithm

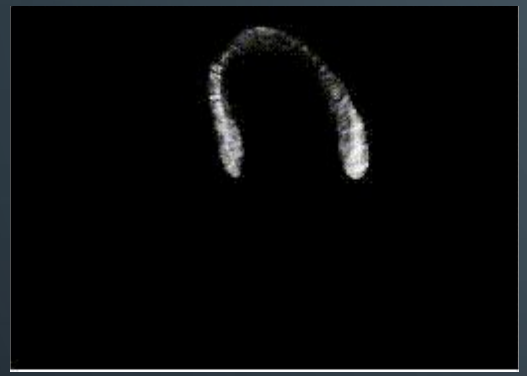
STEP 2: SEGMENTATION MODEL

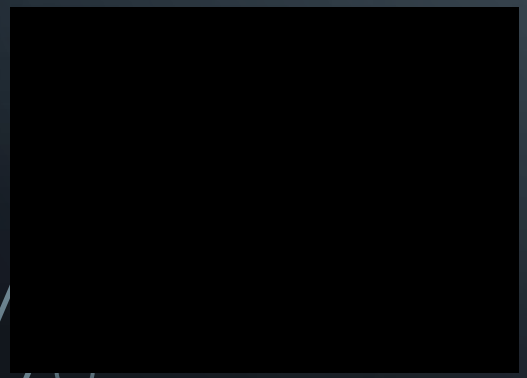


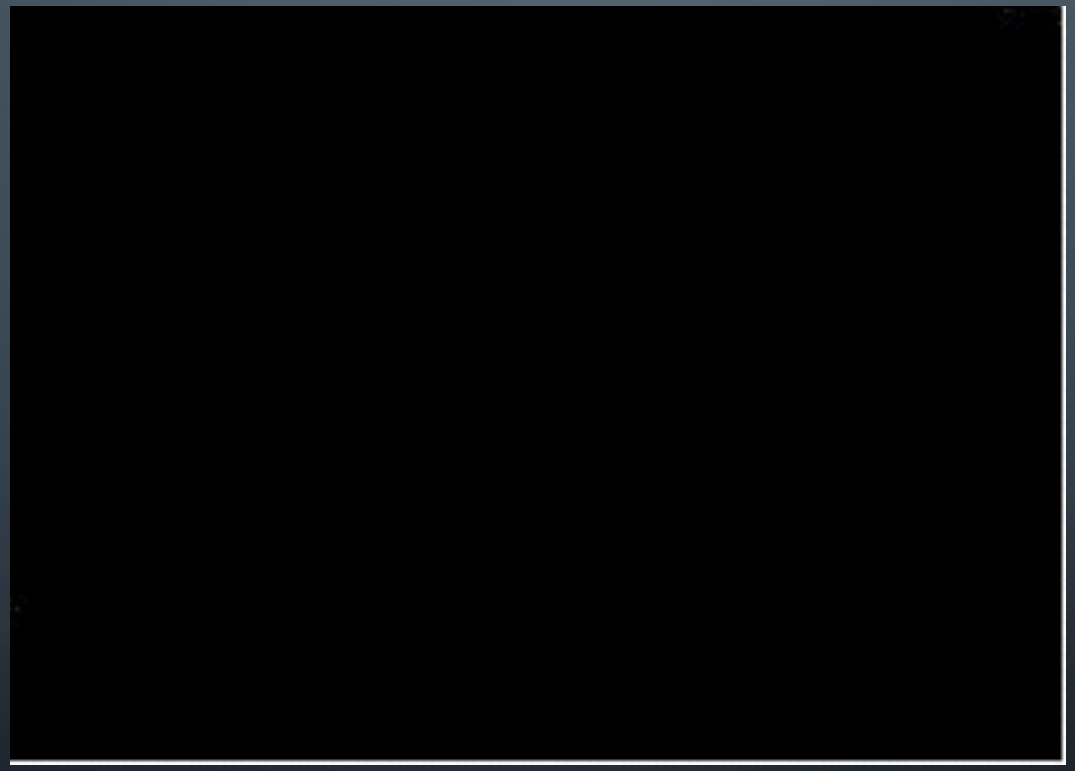


RWMA model work is ongoing and will utilize a speckle-tracking approach

STEP 2: SEGMENTATION MODEL







Add the optimized LV segmentation mask to eliminate signals outside of the region of interest

AI MODELS FOR PREDICTION OF ACS OUTCOMES: PHASE 2

- LV segmentation model will undergo additional training:

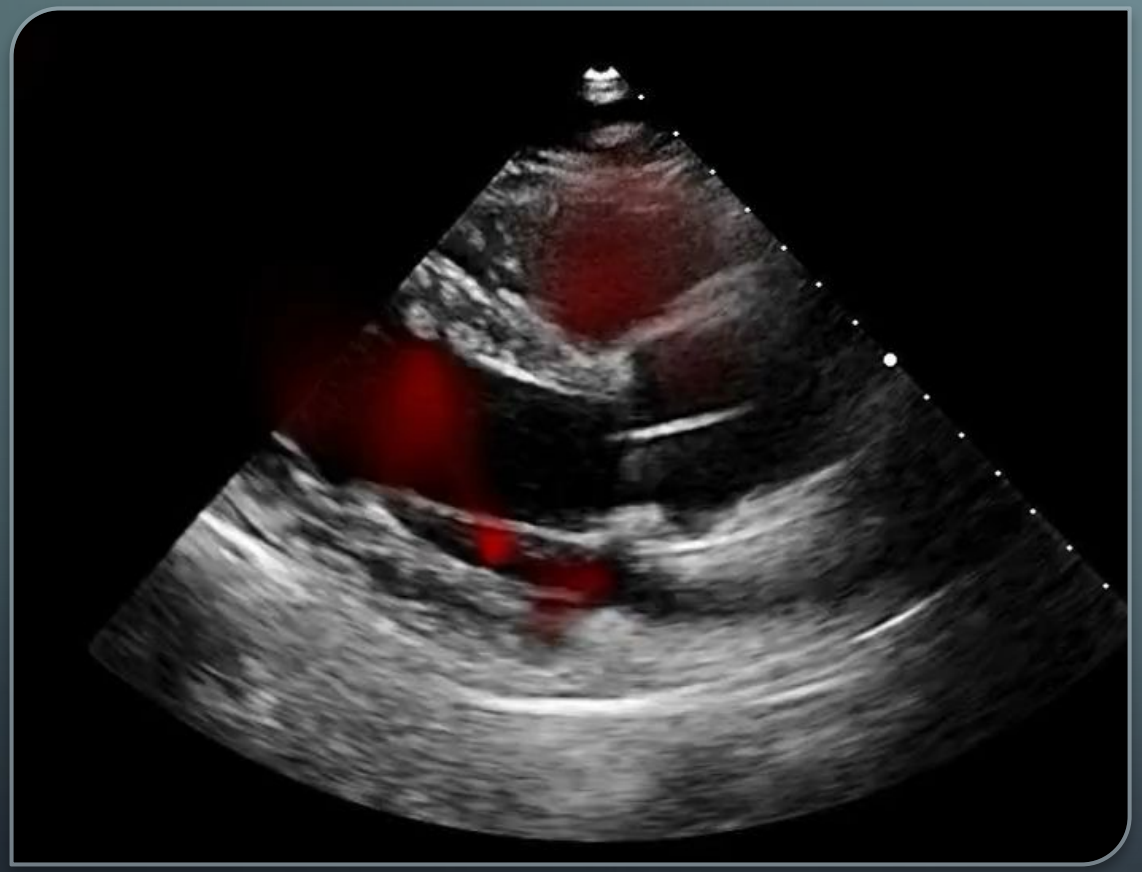
Input: Cardiac ultrasound images in ACS patients

Target outputs :

- Prediction of severe CAD (and distribution)
- Probability of requiring PCI
- Probability of requiring CABG
- Risk of HF and mortality

- Extent of CAD (coronary anatomy in a structured format)
- Death within 30d

MORE AI ECHO BASED RESEARCH



- Automatic Echo Prompts Referral
- Clinical POCUS AI Validation
- AI image quality up-conversion for LVEF assessment

GENERAL ECHO RESEARCH LEAD BY OUR GROUP MEMBERS

- Canadian Longitudinal Study on Aging
- Fabry Disease Screening
- TAVI related:
  - Geographic and sex related differences in treatment of aortic stenosis
  - Left atrial strain and TAVI outcomes
- MITRACURE
- RV dysfunction in Anthracycline-induced cardiotoxicity
- TR and relationship with persistent AF
- Dobutamine stress echo, safety and efficiency of the accelerated protocol

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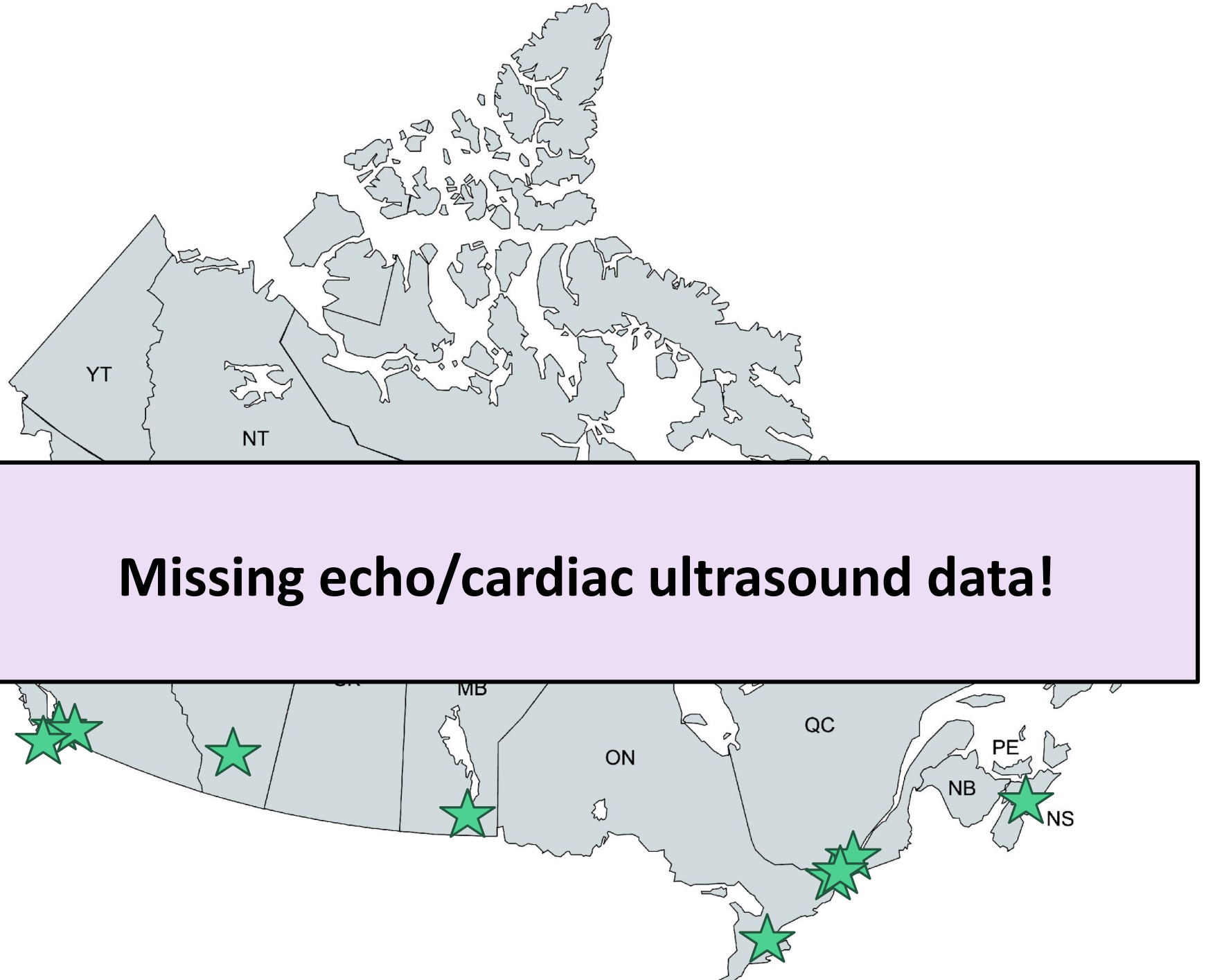

Missing echo/cardiac ultrasound data!

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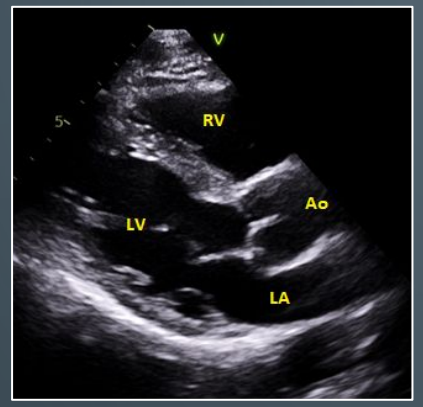
CANADIAN LONGITUDINAL STUDY ON AGING

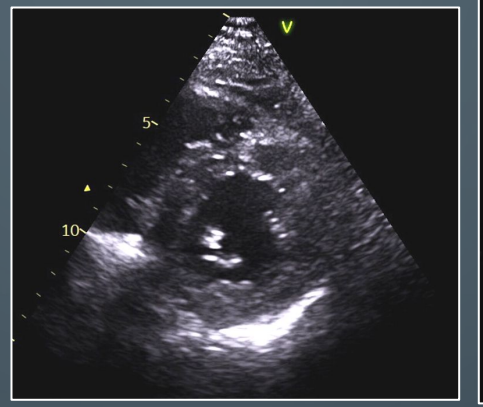
- Our lab has taken on leadership of adding echo as a study parameter and have developed the protocols and will be rolling out the training

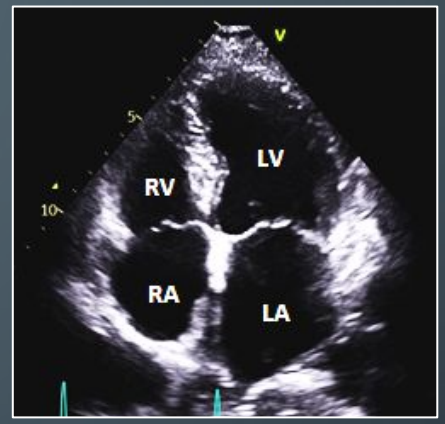
- Images will be acquired by research assistants with a process for transfer of data to the UBC Echo Core Lab for analysis
  - Tentatively: First studies will occur in the Fall of 2024 with completion of rollout in early 2025
  - Planned onsite travel to train personnel
  - Potential for utilizing AI tools to facilitate in scanning

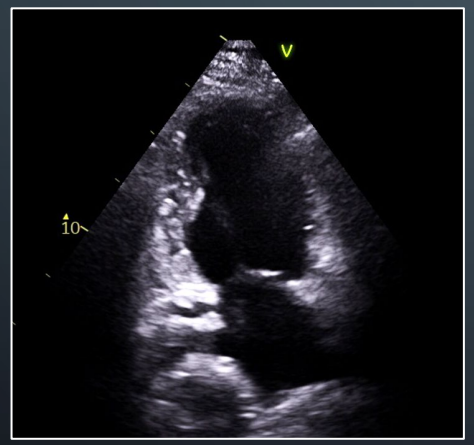
CLSA: ECHO SUBSTUDY

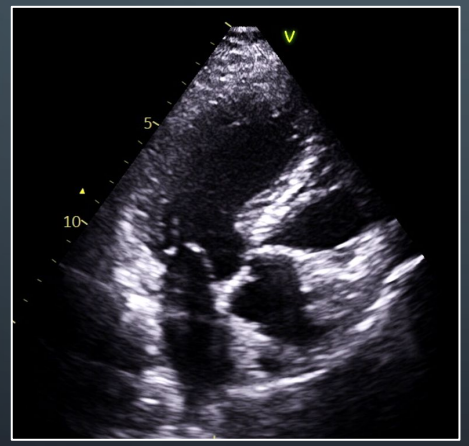
- Target views:

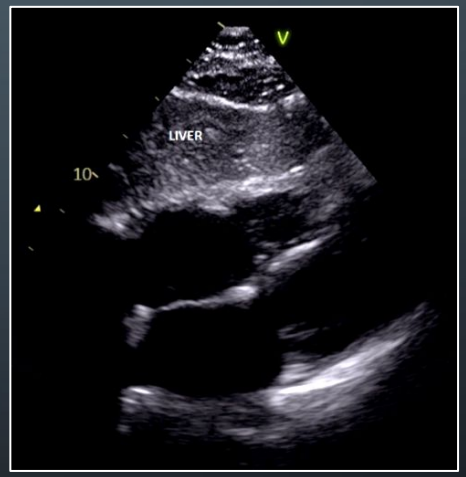


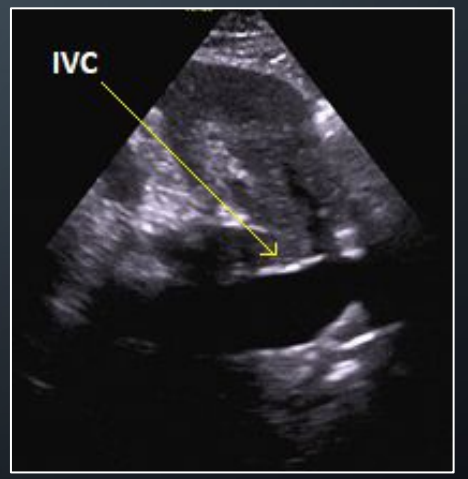












CLSA: ECHO SUBSTUDY OPPORTUNITIES

- Core Lab will be doing the expert reads for all the studies across Canada
  - In Vancouver we expect 3000-5000 studies scanned
- In order for this substudy to be successful we will need image acquisition to be feasible within 10 minutes for non-experts
  - Potential to leverage our ML models to facilitate scanning
  - OR to systematically evaluate a commercially product in a multicenter study
- All data is centralized and can eventually be accessible by all researchers (through an application process) so that further studies can be done
  - This CLSA substudy will produce an invaluable national (novice-scanner) cardiac ultrasound database

INTERPRETATION OF ECHOCARDIOGRAPHIC STUDIES FOR CLINICAL TRIALS

- COMPLETE TAVR

SITE LEAD FOR MULTICENTER CLINICAL TRIALS

- MAPLE-CHF
- EVOID

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EVOID-AS TRIAL:

An Adaptive Phase 2/3 Multicenter, Double-blind, Placebo-controlled, Randomized, Parallel, 3 Arm Study To Evaluate The Efficacy And Safety Of DA-1229 (Evogliptin) In Patient's Calcific Aortic Valve Disease With Mild To Moderate Aortic Stenosis

EVOID-AS TRIAL

- In animal models, endothelial dysfunction in the AV increases DPP-4 expression induced degradation of insulin-like growth factor-1 (IGF-1) osteogenic differentiation of valve interstitial cells
  - DPP-4 inhibitor (sitagliptin) reduced progression of aortic valve calcification

- DPP-4 inhibitors shown to suppress inflammatory cytokine gene expression and myocardial fibrosis therefore proposed for prevention of calcific AS
- Evogliptin is a DPP-4 inhibitor, approved for treatment of DMT2 in South Korea (5mg dose – I think)
  - Animal studies show that distribution of in cardiac tissue is higher than the other 7 DPP-4 inhibitors hence proposed use for a study on AS prevention

EVOID-AS TRIAL

- Purpose: Assess safety and efficacy of Evogliptin compared with placebo in patients with mild-moderate AS
- 45 centres in US and Canada; Target 867 total: 289 per arm, 2022-2026
- 3 arms randomized 1:1:1 to receive study drug or placebo for 104 weeks
  - Drug doses 5 or 10mg daily
- 3 phases:
  1. Screening Period (up to 4 weeks)
  2. Treatment Period (104 weeks)
  3. Follow-Up Period (2-4 weeks)

Total Study Duration is 112 Weeks.

EVOID-AS TRIAL

- Inclusion Criteria:

1. Adult ≥ 35 years of age at time of screening.
2. Subject has calcific aortic valve disease with mild to moderate aortic stenosis as defined by
   - Echo: MG 10-30 mmHg and Aortic Valve Area ≥ 1.2 and ≤ 2.0 cm2 on TTE within 2 weeks prior to randomization and,
   - Cardiac CT test results: aortic valve calcium score (Agatston score) ≥ 200 AU at baseline cardiac CT within 1 month prior to randomization
3. Subject provides written informed consent prior to initiation of any study procedures.
4. Subject understands and agrees to comply with planned study procedures.

EVOID-AS TRIAL

- Exclusion Criteria (lots but basically):
  - ≥ moderate AR, MR, MS, TR, TS
  - LVEF <50% or NYHA III or IV HF
  - Prior AV surgery
  - ALT or AST >2.5x ULN, ESRD,
  - Unable to get cardiac CT
  - Life expectancy <2 y
  - History of pancreatitis
  - On or anticipated to be on: DPP4 inhibitor, Vitamin K, bisphosphonates, chronic use of meds that strongly impact hepatic metabolism
  - History of DPP-4 inhibitor intolerance

EVOID-AS TRIAL

- **Primary Endpoints:**
  - Change in AV calcification in Agatston arbitrary unit (AU) using cardiac CT at 104 weeks
- **Secondary Endpoints:**
  - Change in aortic stenosis severity as measured by mean pressure gradient using echocardiography at week 104 as compared to baseline
  - Change in aortic stenosis severity as measured by aortic valve area (AVA) using echocardiography at week 104 as compared to baseline
  - Time-to-AV intervention to treat aortic stenosis including AV replacement
- **Exploratory Endpoints of note:**
  - Change in serum DPP-4 at week 104 compared to baseline

EVOID-AS TRIAL

- Participant pool identified from echo database (patients with mild-moderate AS from the last 12 months)
- Each potential participant will be screened for the study's inclusion and exclusion criteria and if eligible, they will be approached to assess for their interest
- Visit 1 is a screening visit where they would sign consent and receive a baseline cardiac CT (unless already done within 4 weeks) and echo (unless done within 2 weeks)

EVOID-AS TRIAL: SUMMARY

- Purpose: Assess safety and efficacy of Evogliptin compared with placebo in patients with mild-moderate AS
- Primc
  - Ch CT at
    10

We hope you and your patients will be willing to participate!

- 3 arms randomized in a ratio of 1:1:1 to receive study drug or placebo for 104 weeks
  - Drug doses 5 or 10mg daily

SUMMARY OF PROJECTS

AI CAD	AI Valve disease	AI for stroke prediction	AI for HF prediction	AI cardiomyopathy and diastolic function
Automatic Echo Prompts Referral	Clinical POCUS AI Validation	AI image quality up-conversion for LVEF assessment	Canadian Longitudinal Study on Aging	Fabry Disease Screening
TAVI related: •Geographic and sex related differences in treatment of aortic stenosis •Left atrial strain and TAVI outcomes	MITRACURE	RV dysfunction in Anthracycline-induced cardiotoxicity	TR and relationship with persistent AF	Dobutamine stress echo, safety and efficiency of the accelerated protocol
LA strain for prediction of LV filling pressures	Echo predictors of TTR cardiac amyloidosis	COMPLETE-TAVR echo interpretation	MAPLE-CHF	EVOID