# Conditional GANs for cardiac aging synthesis using cross-sectional data

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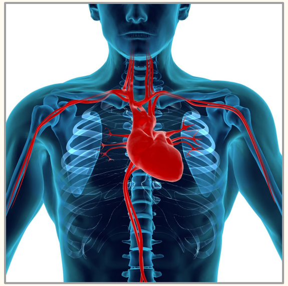
Topological Machine Learning
UB seminar

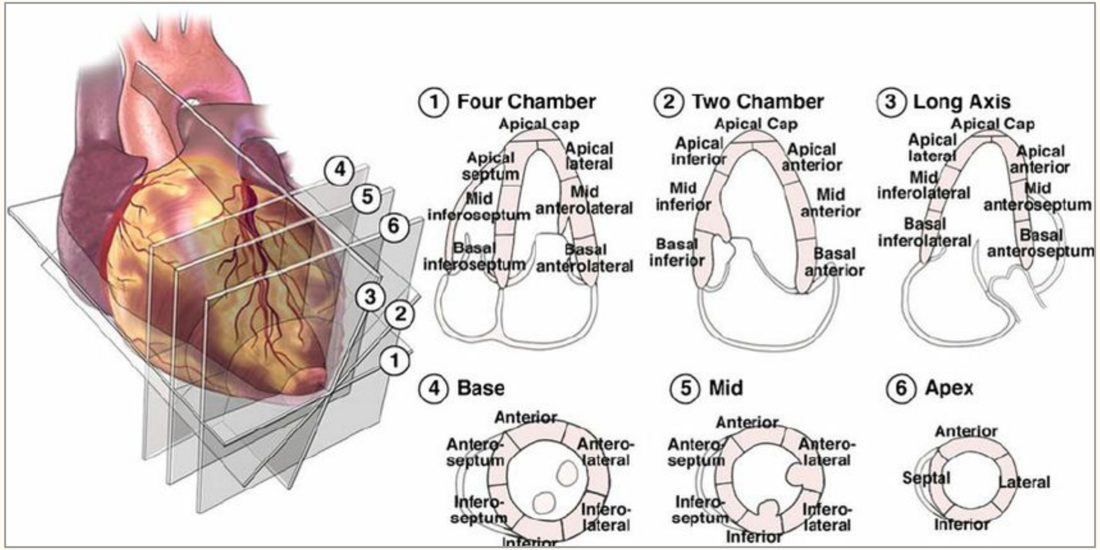
# Outline

1. Cardiac magnetic resonance imaging
2. Generative Adversarial Networks
    - What are GANs?
    - Three architectures
    - One regularization method
3. Modeling aging with cross-sectional data
    - Face aging
    - Brain aging
    - Heart aging

# Cardiac imaging

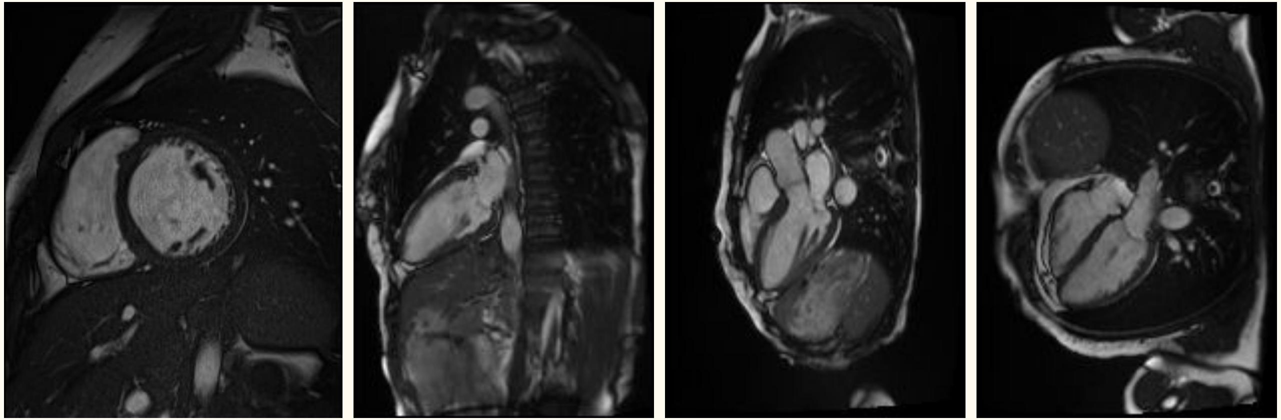
# Cardiac magnetic resonance scan






Source: Shalbaf et al. (2013) (doi: 10.1007/s10278-012-9543-x).

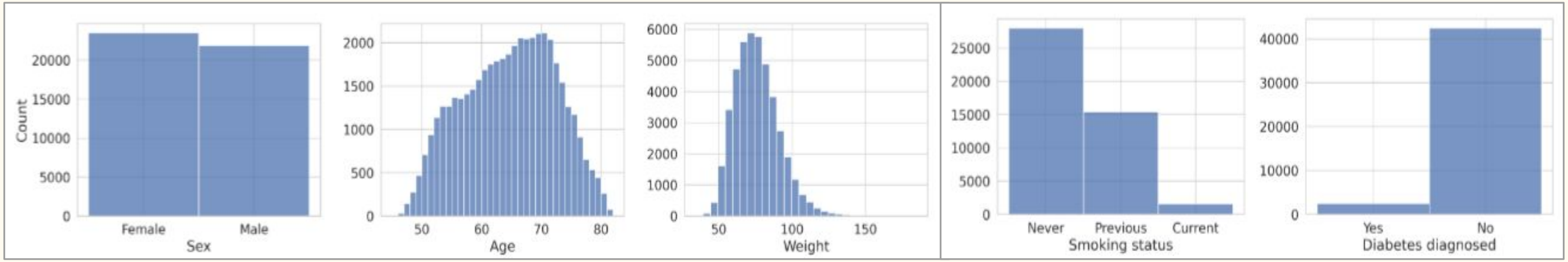
# What does it actually look like?

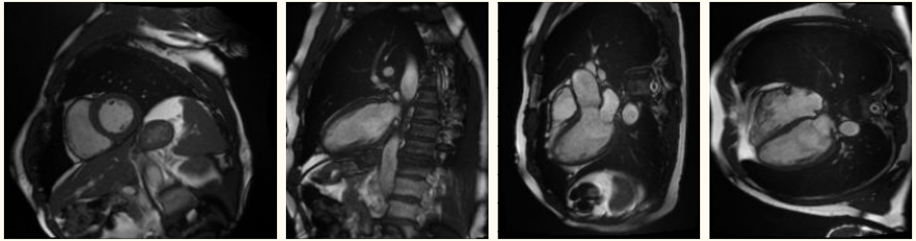


# UK Biobank

Cohort of general population in several cities the UK.

More than 40,000 imaging studies (cine MRI, short and long axes).



# Generative Adversarial Networks (GANs)

# What are GANs?

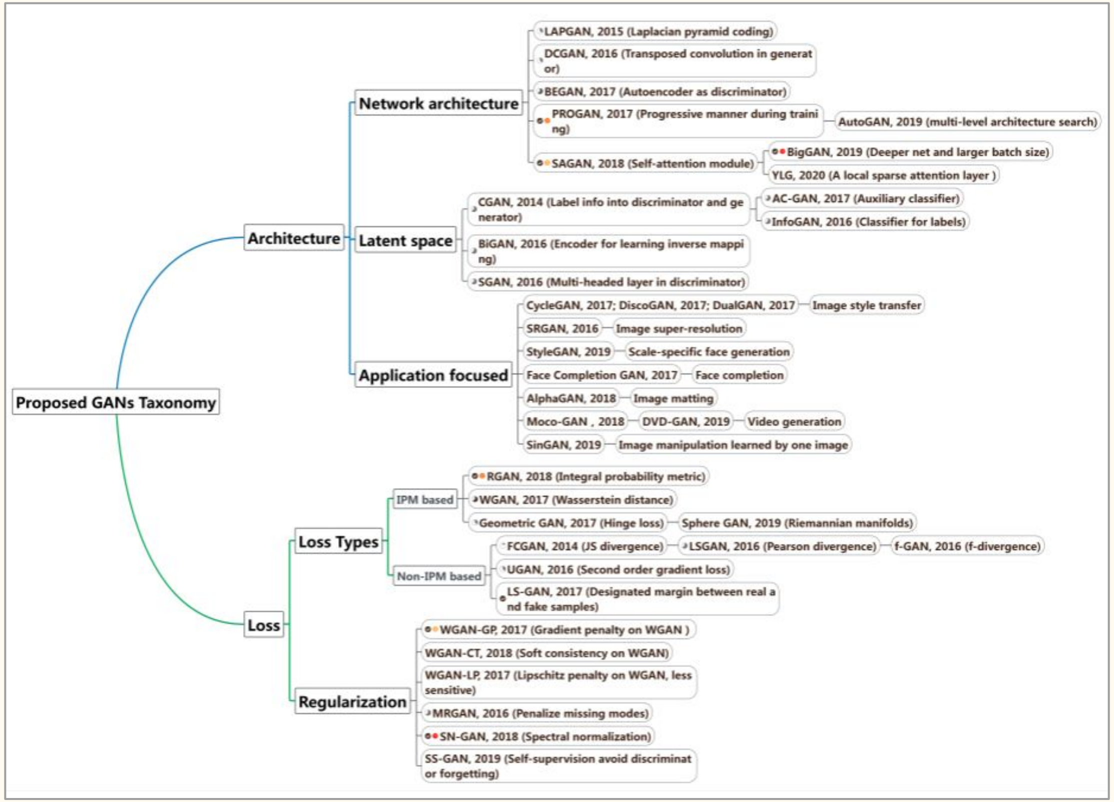
- Models that implicitly learn the data distribution by playing the min-max game with an adversary.

- The target distribution is usually very complex and cannot be approximated using a set of known parametric distributions.

- The fitting process (training) is known to be tricky and unstable.

# What are GANs?

- Recent reviews are proposing a GAN taxonomy in terms of architecture and losses.



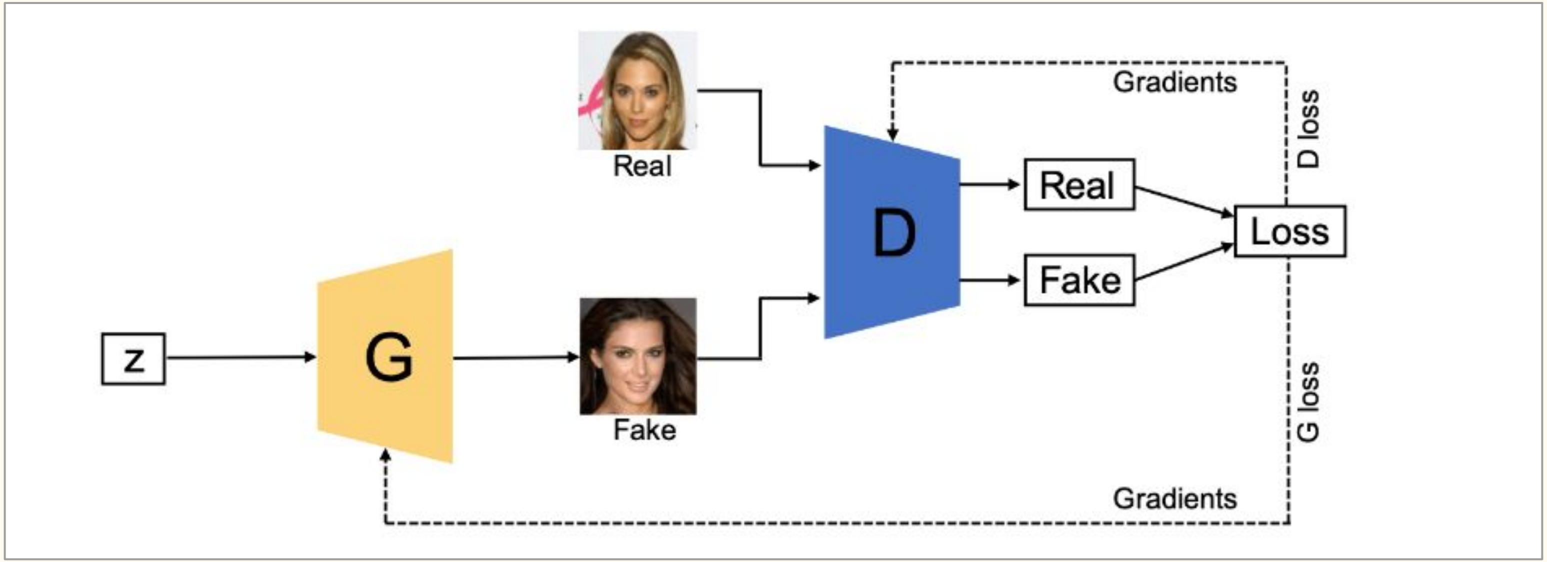

Source: Wang, She and Ward (2019) (arxiv: 1906.01529).

# GANs

Three architectures

- Basic GAN
- Conditional GAN
- CycleGAN

# Basic GAN



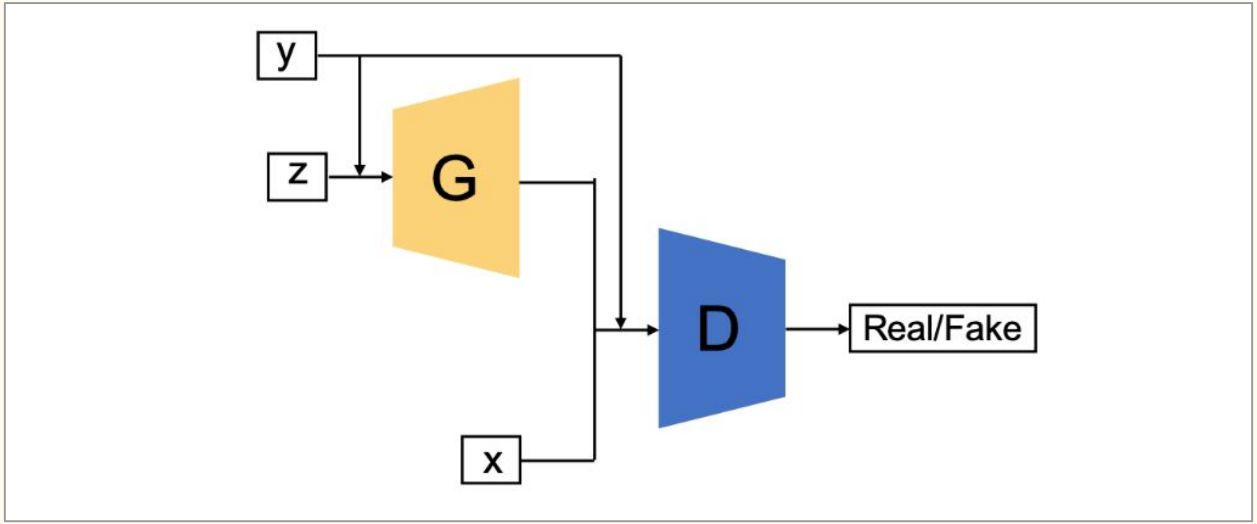

Source: Wang, She and Ward (2019) (arxiv: 1906.01529).

$$\min_G \max_D \mathbb{E}_{\mathbf{x}\sim p_r} \log[D(\mathbf{x})] + \mathbb{E}_{\mathbf{z}\sim p_{\mathbf{z}}} \log\left[1 - D(G(\mathbf{z}))\right]$$

$$JS(\mathbb{P}_r, \mathbb{P}_g) = KL(\mathbb{P}_r \| \mathbb{P}_m) + KL(\mathbb{P}_g \| \mathbb{P}_m)$$

$$KL(p_1 \| p_2) = \mathbb{E}_{\mathbf{x}\sim p_1} \log \frac{p_1}{p_2}$$

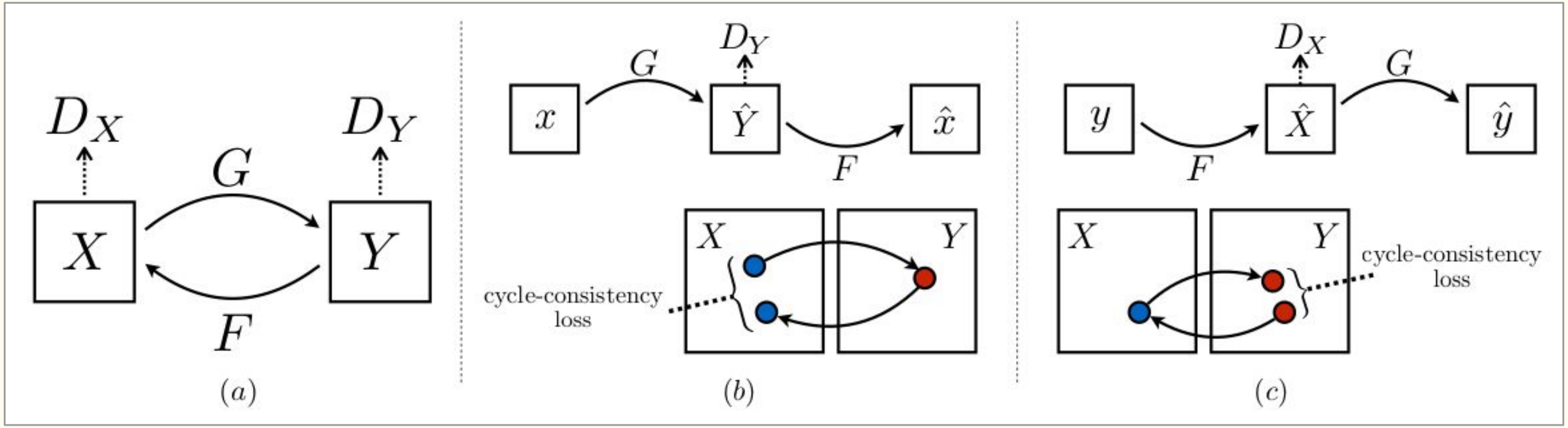
# Conditional GAN



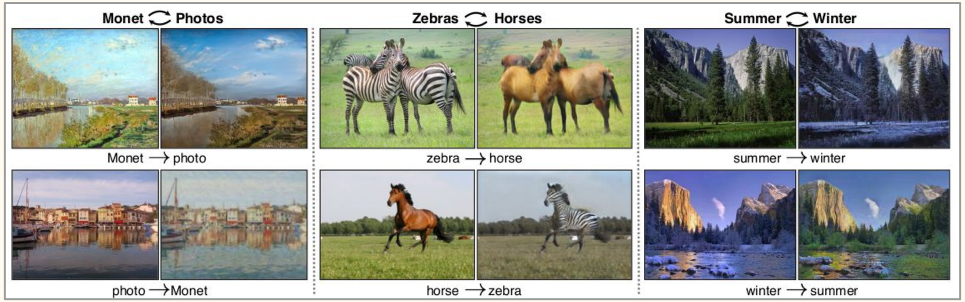

Source: Wang, She and Ward (2019) (arxiv: 1906.01529).

$$\min_G \max_D \mathbb{E}_{\mathbf{x}\sim p_r} \log[D(\mathbf{x}|\mathbf{y})] + \mathbb{E}_{\mathbf{z}\sim p_{\mathbf{z}}} \log\left[1 - D(G(\mathbf{z}|\mathbf{y}))\right]$$

# CycleGAN




Source: Zhang et al. (2017) (arxiv: 1703.10593).



# GANs

Regularization via the loss function

- Wasserstein GAN

# Wasserstein-GAN

$$W(\mathbb{P}_r, \mathbb{P}_g) = \inf_{\gamma \in \Pi(\mathbb{P}_r, \mathbb{P}_g)} \mathbb{E}_{(x,y)\sim\gamma}\big[\, \|x - y\| \,\big]$$

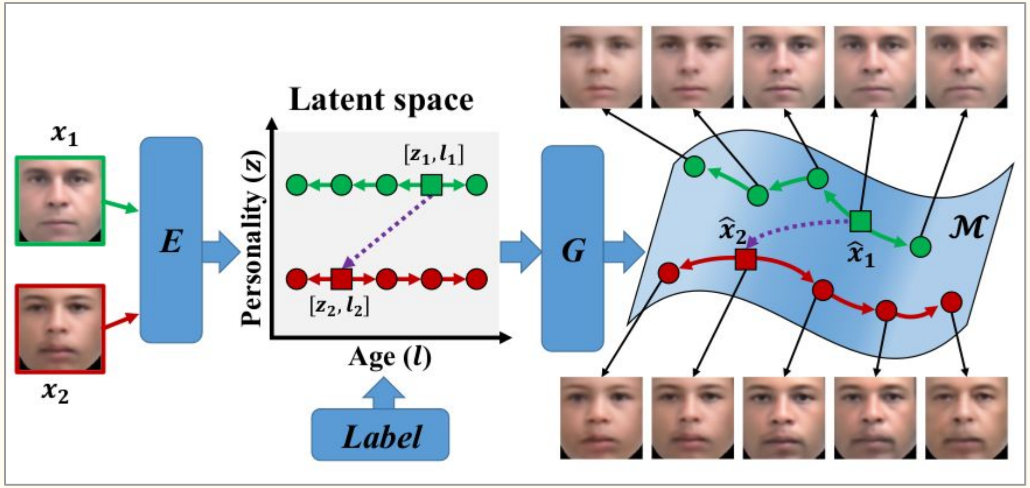
via the Kantorovich-Rubinstein duality

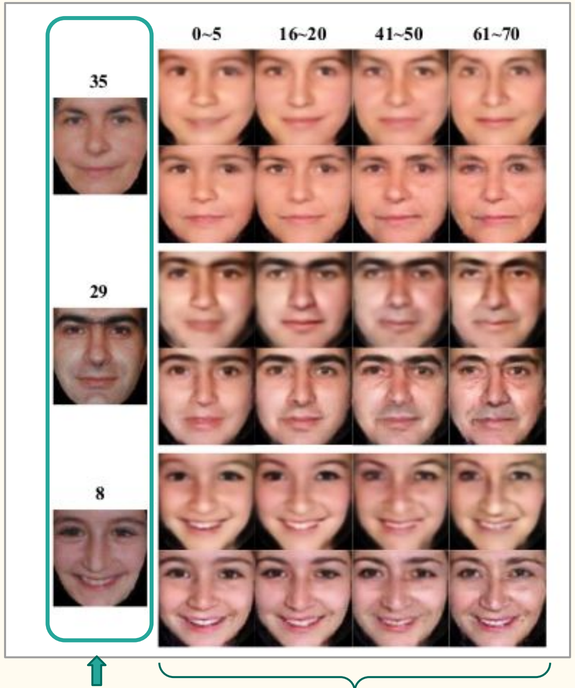
$$W(\mathbb{P}_r, \mathbb{P}_\theta) = \sup_{\|f\|_L \leq 1} \mathbb{E}_{x\sim\mathbb{P}_r}[f(x)] - \mathbb{E}_{x\sim\mathbb{P}_\theta}[f(x)]$$

# Modeling aging

# Face aging

- Zhang et al. (2017) used an autoencoder to build a “manifold of faces” that can be navigated.
- They only used cross-sectional data.



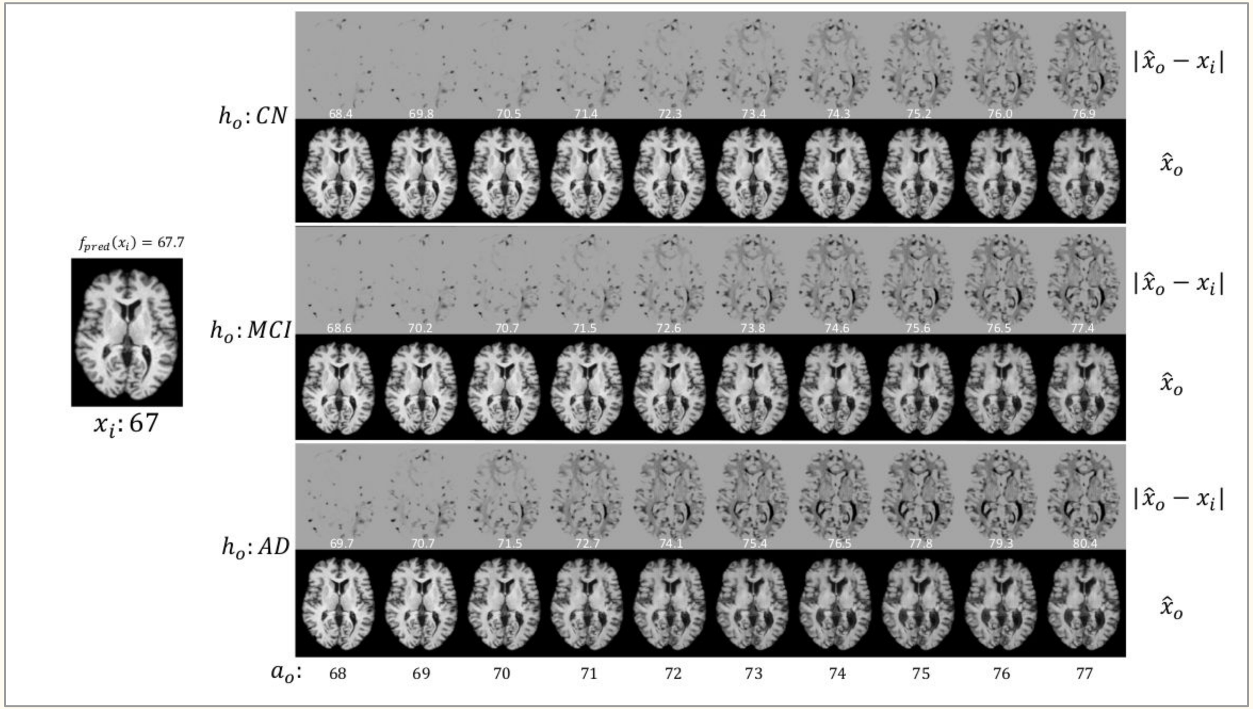




Original

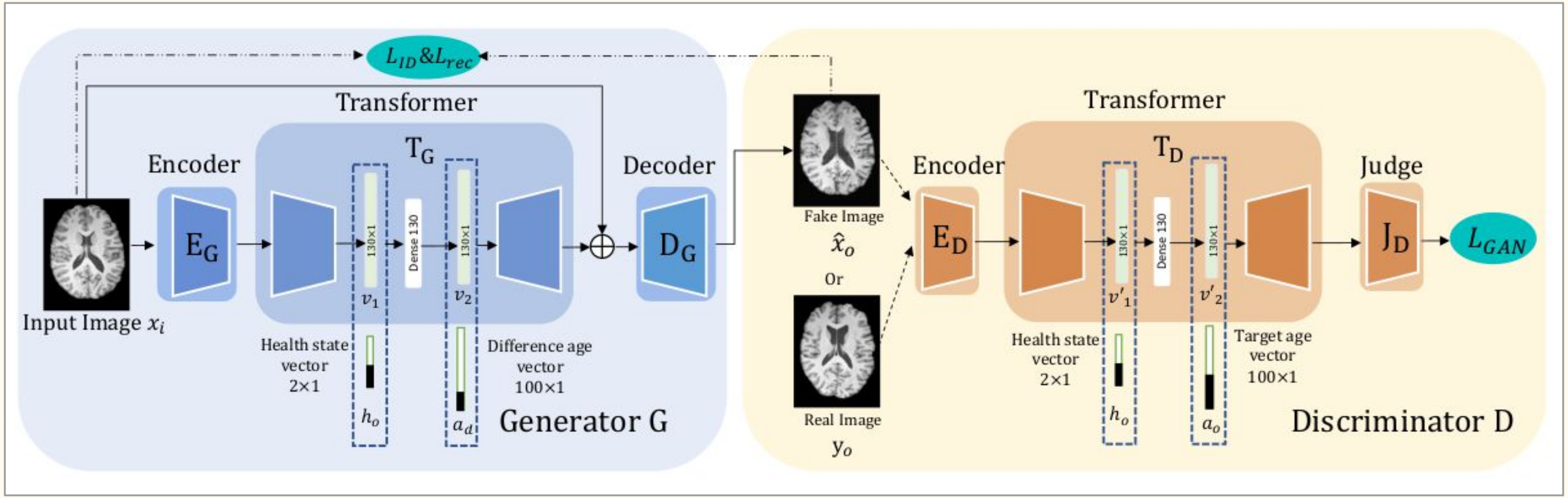
Synthetic

# Brain aging

- Xia et al. (2019) modeled the aging of the brain under different disease statuses.
- Age and disease status were used as covariates.

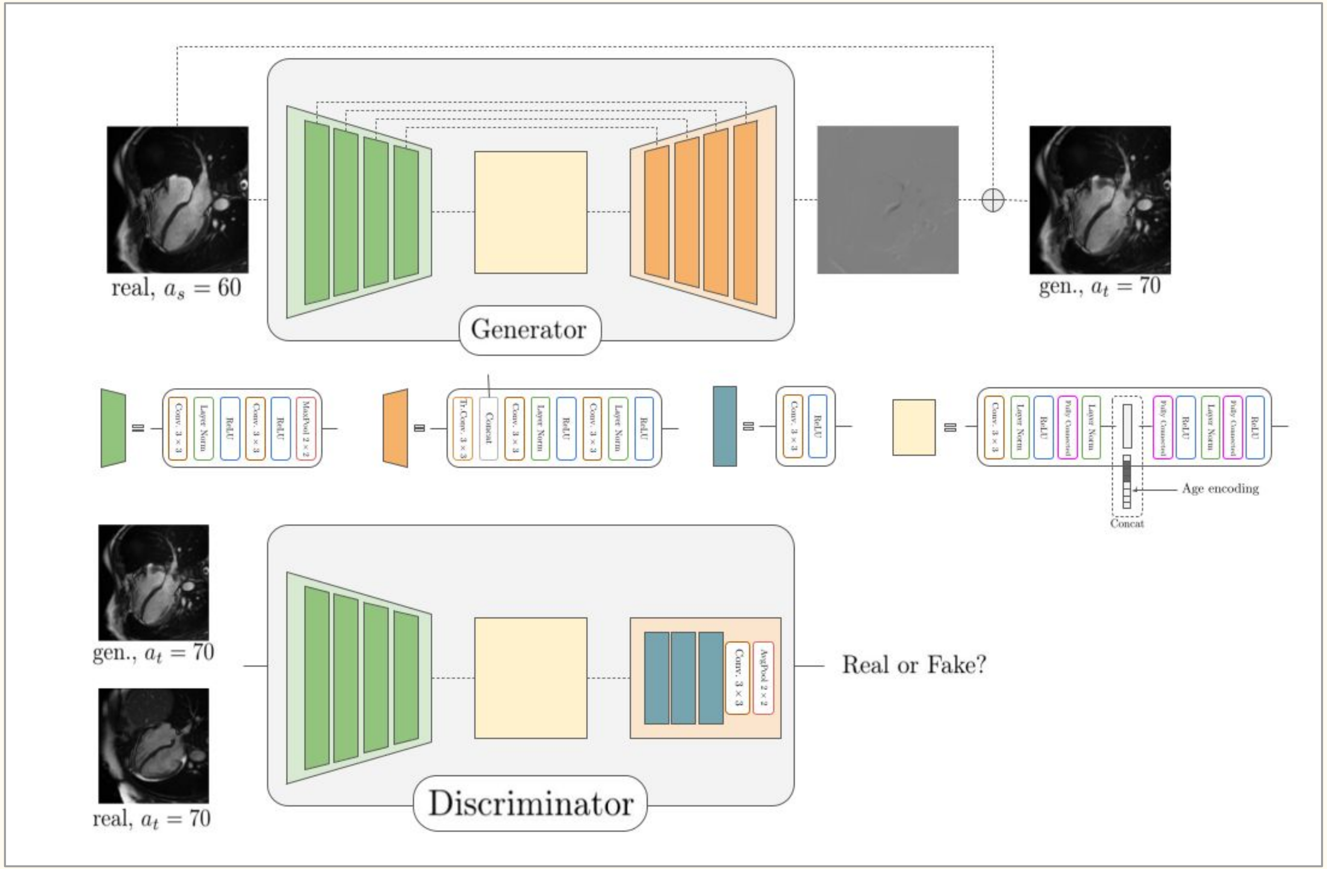


# Brain aging



$L_{ID}$&$L_{rec}$
Transformer
Encoder
$T_G$
Decoder
$E_G$
130×1
Dense 130
130×1
$D_G$
$v_1$
$v_2$
Input Image $x_i$
Health state vector 2×1
Difference age vector 100×1
$h_o$
$a_d$
Generator G
Fake Image
$\hat{x}_o$
Or
Real Image
$y_o$
Transformer
Encoder
$T_D$
Judge
$E_D$
$J_D$
$L_{GAN}$
$v'_1$
$v'_2$
Health state vector 2×1
Target age vector 100×1
$h_o$
$a_o$
Discriminator D

# Heart aging - Method



# Heart aging - Method

$$L = \min_G \max_D \left(\lambda_1 \mathcal{L}_{\text{WGAN-GP}} + \lambda_2 \mathcal{L}_{id} + \lambda_3 \mathcal{L}_{rec} + \lambda_4 \mathcal{L}_{cc}\right)$$

$$\begin{aligned}\mathcal{L}_{\text{WGAN-GP}} = & \mathop{\mathbb{E}}_{\tilde{\mathbf{x}} \sim P_{gen.}} [D(\tilde{\mathbf{x}}, \mathbf{a}_t)] - \mathop{\mathbb{E}}_{\mathbf{x} \sim P_{real}} [D(\mathbf{x}, \mathbf{a}_t)] \\ & + \lambda_{GP} \mathop{\mathbb{E}}_{\hat{\mathbf{x}} \sim P_{\hat{\mathbf{x}}}} [(||\nabla^2_{\hat{\mathbf{x}}} D(\hat{\mathbf{x}}, \mathbf{a}_t)|| - 1)^2],\end{aligned}$$

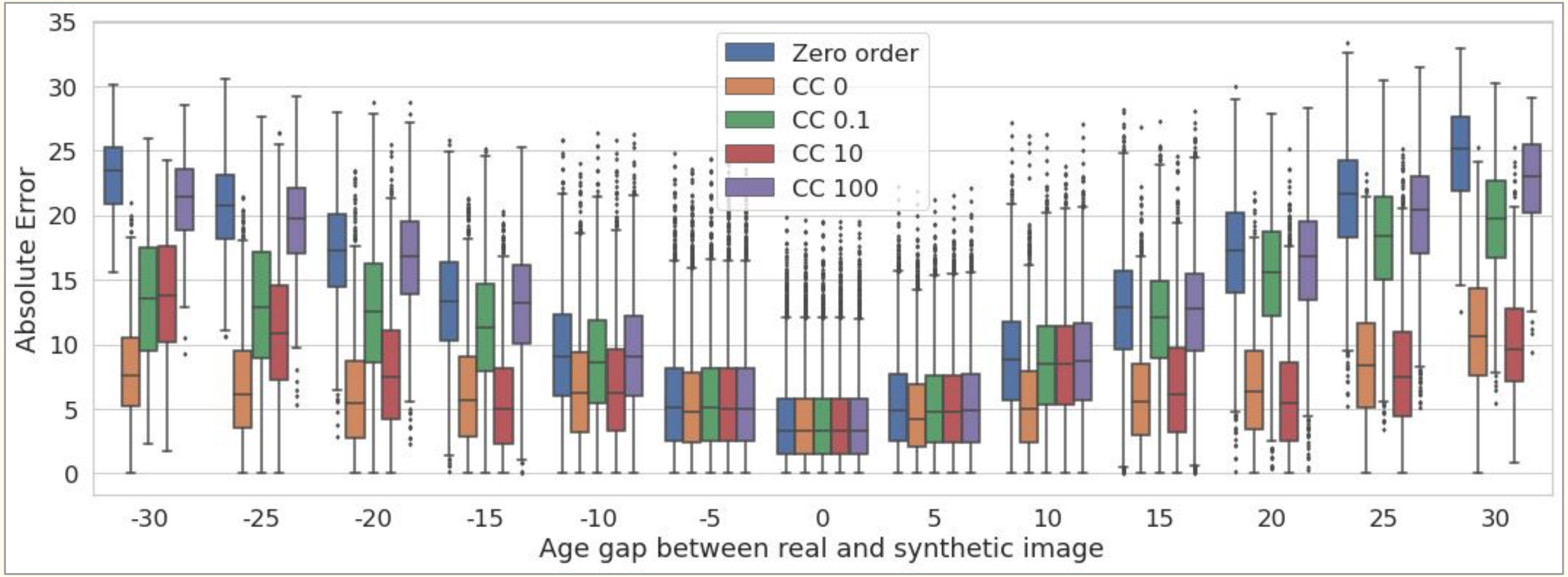
$$\mathcal{L}_{id} = \mathop{\mathbb{E}}_{\mathbf{x} \sim P_{real}} [||\mathbf{x} - G(\mathbf{x}, a)||_1]$$

$$\mathcal{L}_{rec} = \mathop{\mathbb{E}}_{\mathbf{x} \sim P_{real}} [||\mathbf{x} - G(\mathbf{x}, 0)||_1]$$

$$\mathcal{L}_{cc} = \mathop{\mathbb{E}}_{\mathbf{x} \sim P_{real}} [||\mathbf{x} - G(G(\mathbf{x}, \mathbf{a}_d), -\mathbf{a}_d)||_1]$$

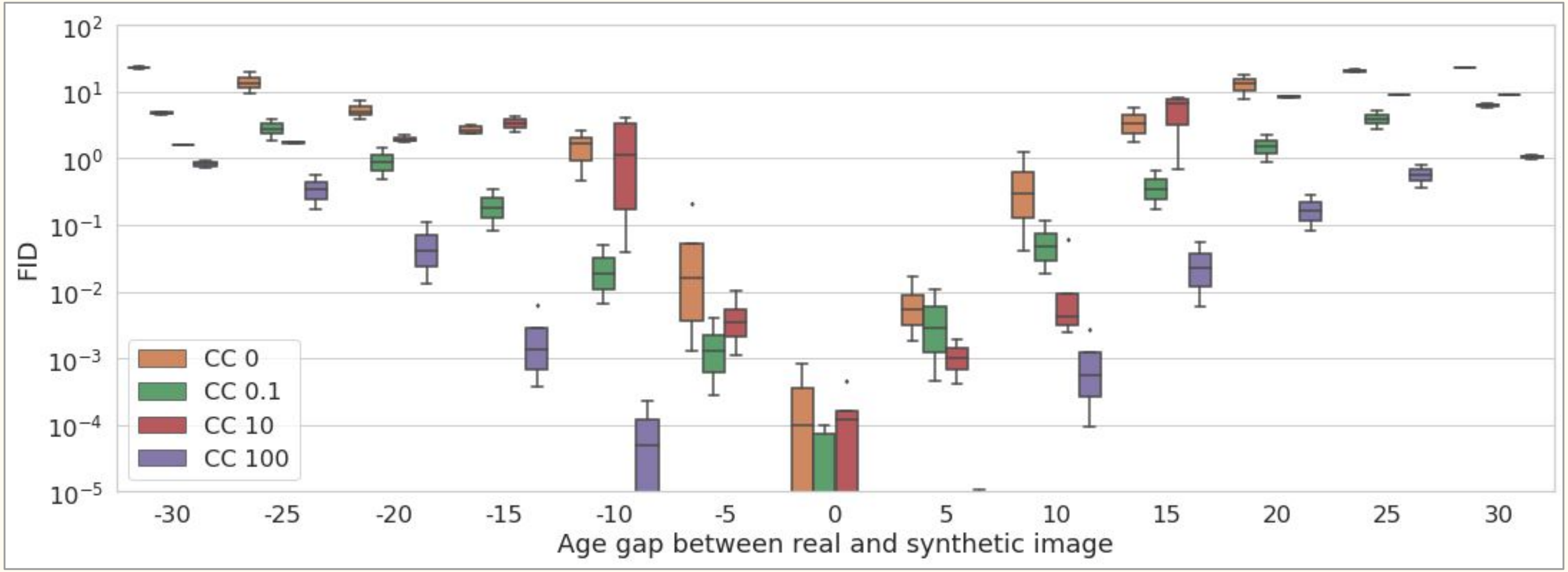
# Heart aging - Results

- Predicted age absolute error of generated images (lower is better):



# Heart aging - Results

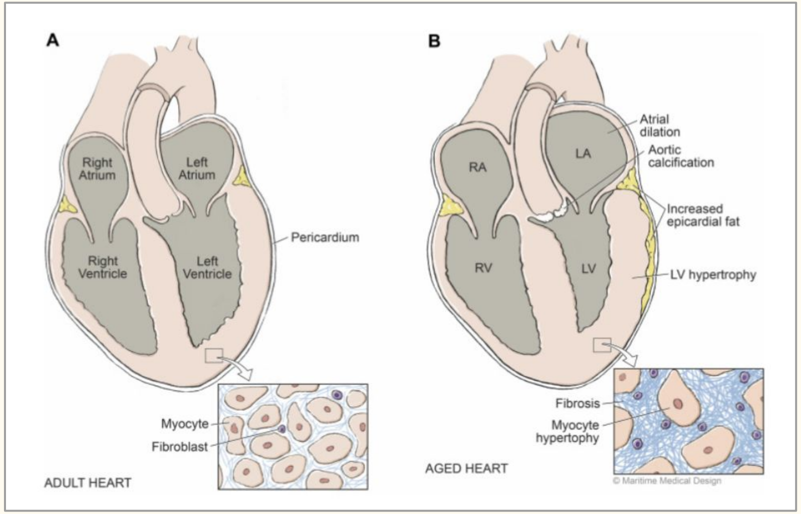
- Fréchet Inception Score (FID) of generated images (lower is better):



# Heart aging - Literature

Structural evolution of the aging heart

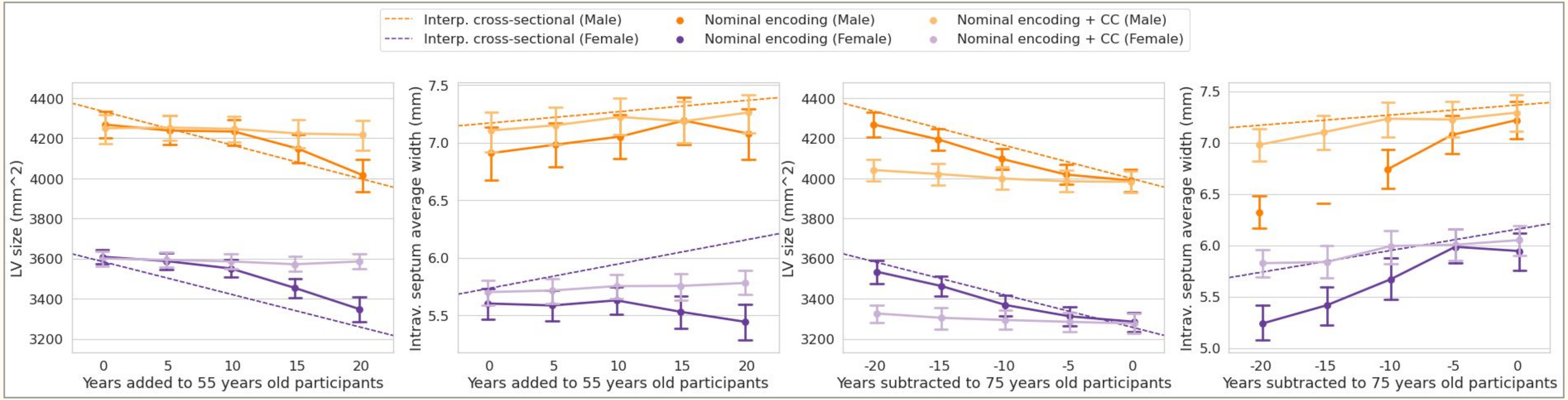
- Age is positively correlated with increased left atrial diameter (LAD).
- LAD increase is greater for higher body mass index (BMI).
- The left ventricle (LV) suffers an increase in wall thickness and a diminuition of LV end-diastolic dimensions.
- Increased fat deposition at pericardium.



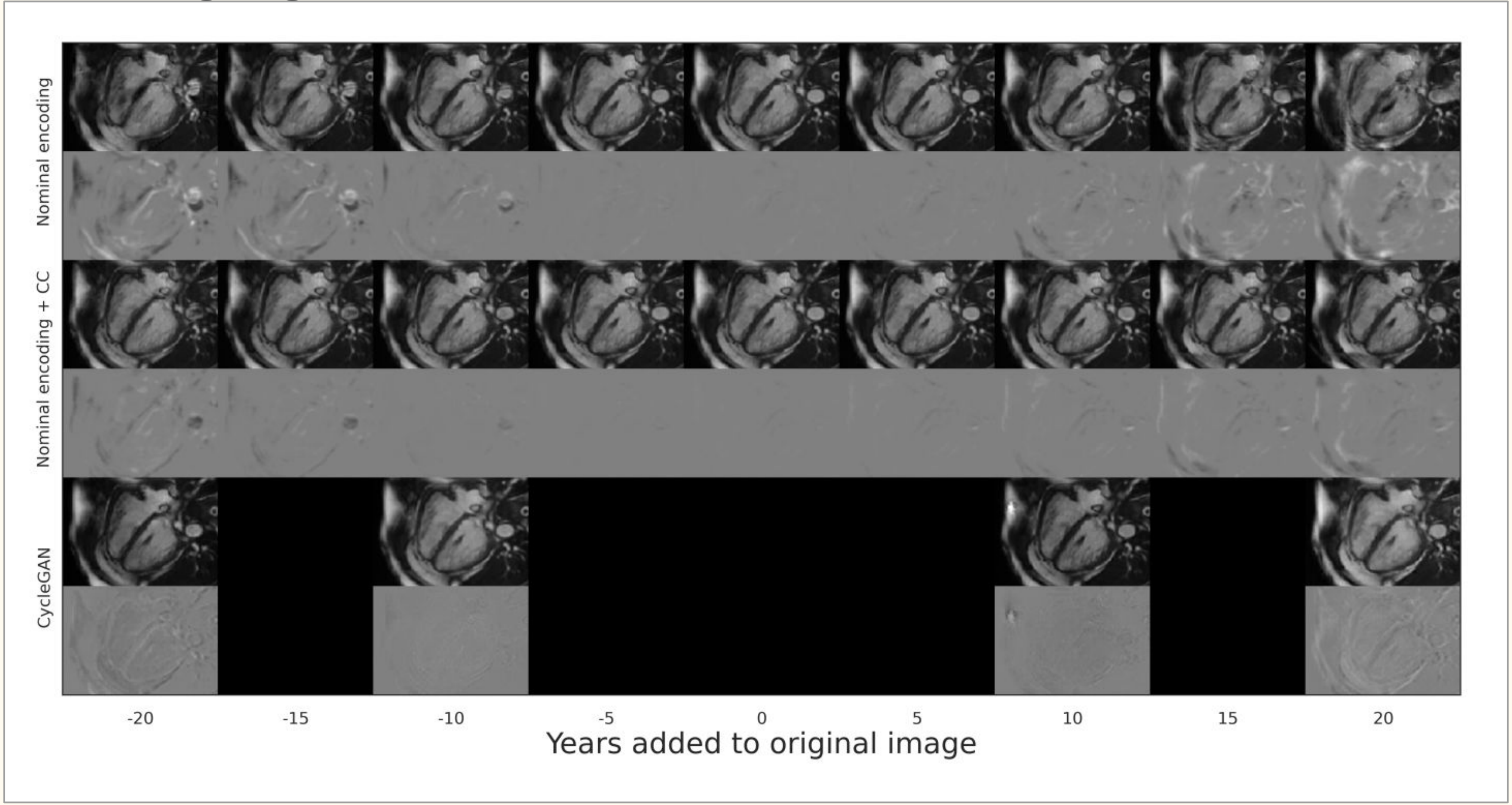

Source: Keller and Howlett (2016)

# Heart aging - Results

- Trajectory of aged and rejuvenated hearts compared to cross-sectional data (dashed lines):



# Heart aging - Results



# Heart aging - Results

Some questions to investigate further are:

- How do other covariates affect the modeling? For example, BMI or smoking status.
- What happens at other timepoints?
- Are the changes really related to age?

# Where can Topology be applied?

- Can we characterize or tell some properties from the high-dimensional manifold implicitly learn by the model?

- Can we better disentangle the latent space (the features at the bottleneck) by enforcing some topological properties?