AI-enabled cardiac functional quantification

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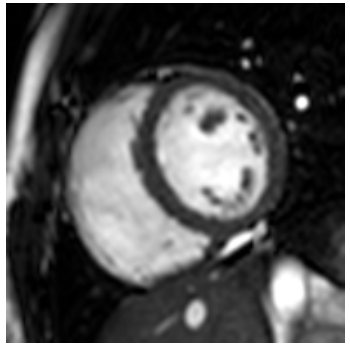
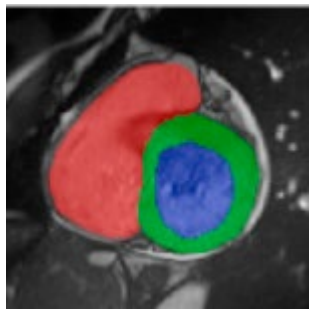
Motivation: cardiac MR workflow

Magnetic resonance (MR)



Segmentation of left ventricle blood pool and myocardium (& right ventricle?)



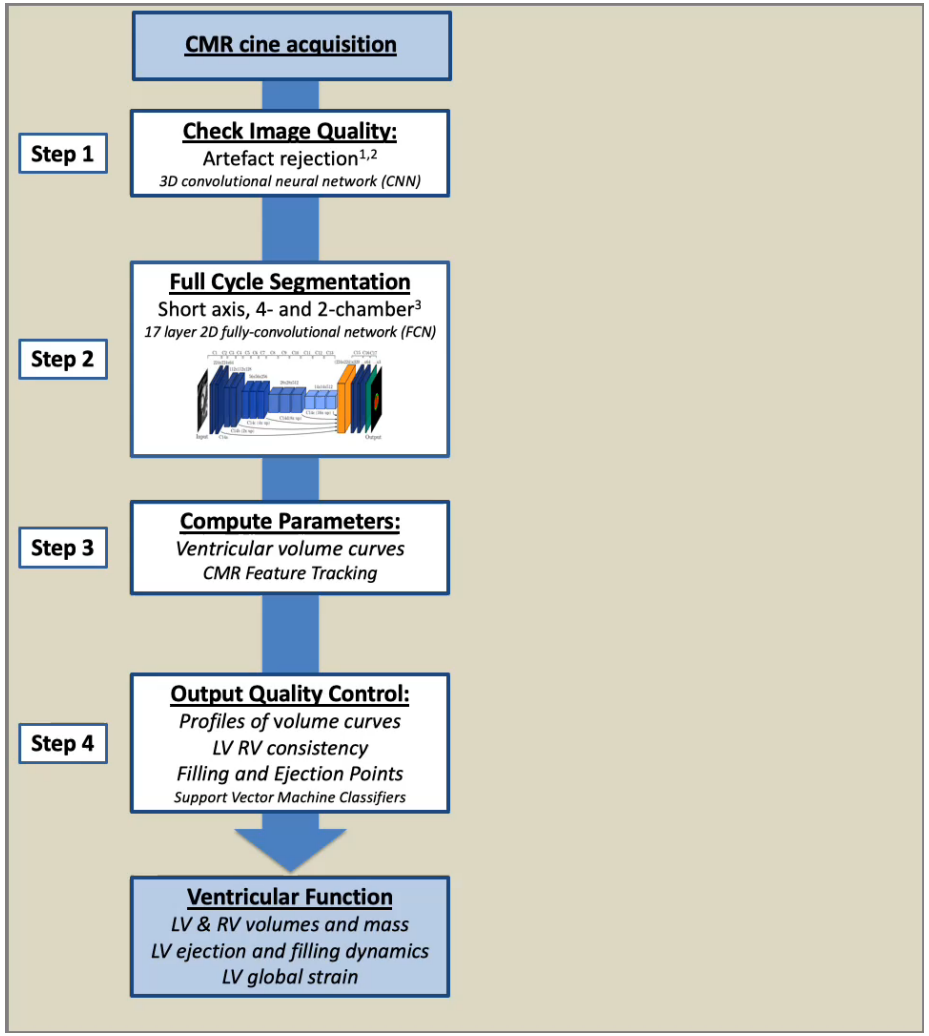
CLINICAL REPORT	
Ejection fraction	
Strain	
Peak rate	
…	

Motivation

Automate calculation of ejection fraction

Enable calculation of other morphological/functional metrics

AI-based quality-controlled automated quantification of cardiac function



CLINICAL REPORT	
Ejection fraction	
Strain	
Peak filling rate	
Peak ejection rate	
EF1	
…	

B. Ruijsink and E. **Puyol-Antón**, et al. (2020) "Fully automated, quality-controlled cardiac analysis from CMR: validation and large-scale application to characterize cardiac function." *JACC: Cardiovascular Imaging*

Domain shift

- Performance of machine learning models depends on training and testing data being from the same *domain* …

- In the case of cardiac MR, domains can be:
  - *Scanner type* (manufacturer, field strength) and scanning protocol
  - *Pathology*
  - Annotation protocol, skill level etc.
  - Patient demographics (disease, age, …)
  - …

- Our AI tool was initially developed and evaluated on the UK Biobank database, i.e. all Siemens 1.5T …

Domain shift in cardiac MR segmentation

Domain Name	Scanner	Pathology Group	No. Subjects
A1	Siemens Aera 1.5 T	Healthy	74
A2	Siemens Aera 1.5 T	DCM, CMP	37
A3	Siemens Aera 1.5 T	HCM	15
B1	Philips Ingenia 1.5 T	Healthy	42
B2	Philips Ingenia 1.5 T	DCM, CMP	14
B3	Philips Ingenia 1.5 T	HCM	9
C1	Philips Achieva 3 T	Healthy	64
C2	Philips Achieva 3 T	DCM, CMP	36
C3	Philips Achieva 3 T	HCM	8

Domain Name	Included Domains
1M	A1 + B1 + C1
2M	A2 + C2
AM	A1 + A2
CM	C1 + C2

DCM: dilated cardiomyopathy

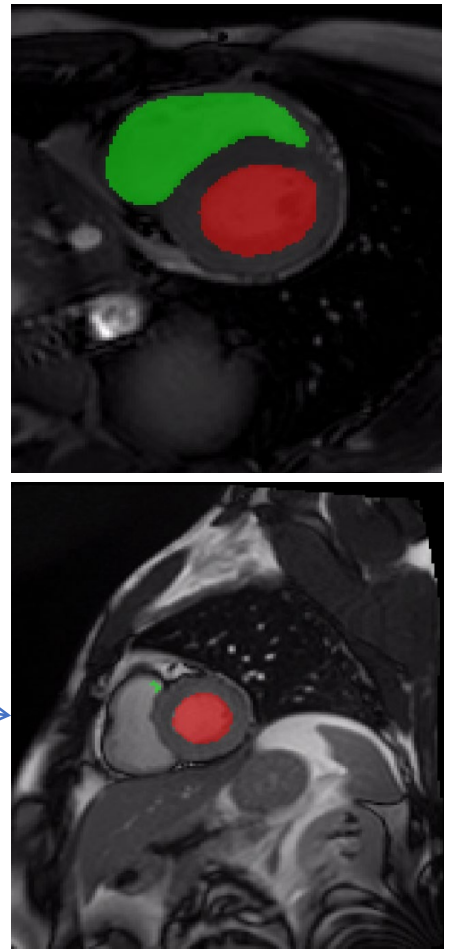
CMP: hypertensive cardiomyopathy

HCM: hypertrophic cardiomyopathy

Ugurlu et al. (2021) “The Impact of Domain Shift on Left and Right Ventricle Segmentation in Short Axis Cardiac MR Images.” *MICCAI STACOM*

Domain shift in cardiac MR segmentation

Train Domain \ Test Domain	A1	B1	C1	A2	C2	B2	A3	B3	C3
A1	0.866	0.859	0.873	0.901	0.872	0.890	0.866	0.843	0.869
B1	0.852	*0.889*	0.870	0.877	0.861	*0.912*	0.858	**0.889**	0.907
C1	0.822	0.875	**0.903**	0.893	**0.910**	0.889	0.828	0.865	*0.920*
A2	**0.881**	0.874	0.884	**0.903**	0.888	0.888	0.867	0.861	0.898
C2	0.677	0.764	*0.900*	0.688	*0.909*	0.794	0.656	0.731	**0.922**
1M	*0.879*	**0.890**	*0.900*	*0.902*	0.907	**0.914**	**0.882**	*0.876*	0.919
2M	0.870	0.879	0.896	0.896	0.907	0.906	0.856	0.871	0.918
AM	0.872	0.870	0.863	0.894	0.875	0.871	*0.871*	0.862	0.866
CM	0.745	0.835	0.899	0.784	0.904	0.849	0.695	0.760	**0.922**



A=Siemens 1.5T
B=Philips 1.5T
C=Philips 3T

1=Healthy
2=DCM/CMP
3=HCM

$$DSC = \frac{2|X \cap Y|}{|X| + |Y|}$$

Cross-domain performance is not symmetric.

Ugurlu et al. (2021) "The Impact of Domain Shift on Left and Right Ventricle Segmentation in Short Axis Cardiac MR Images." *MICCAI STACOM*

Domain shift in cardiac MR segmentation

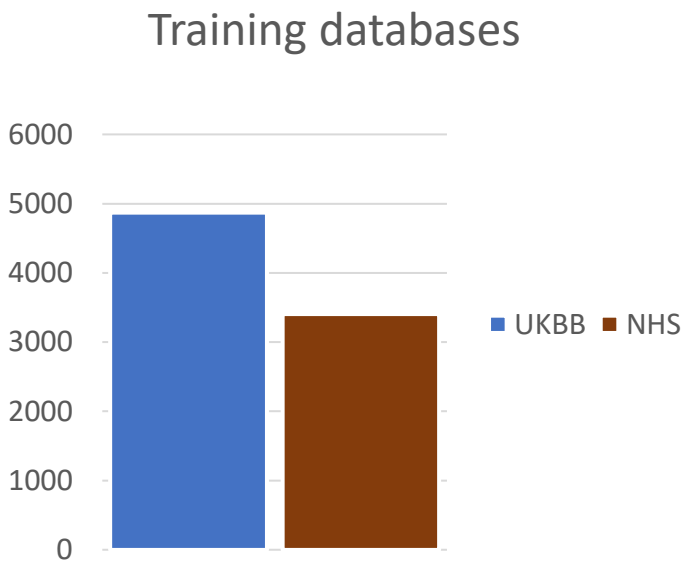
- Intra-scanner performance better than cross-scanner performance for both LV and RV and for both ES and ED frames.
- But not enough evidence to say performance is different for intra-pathology vs cross-pathology groups

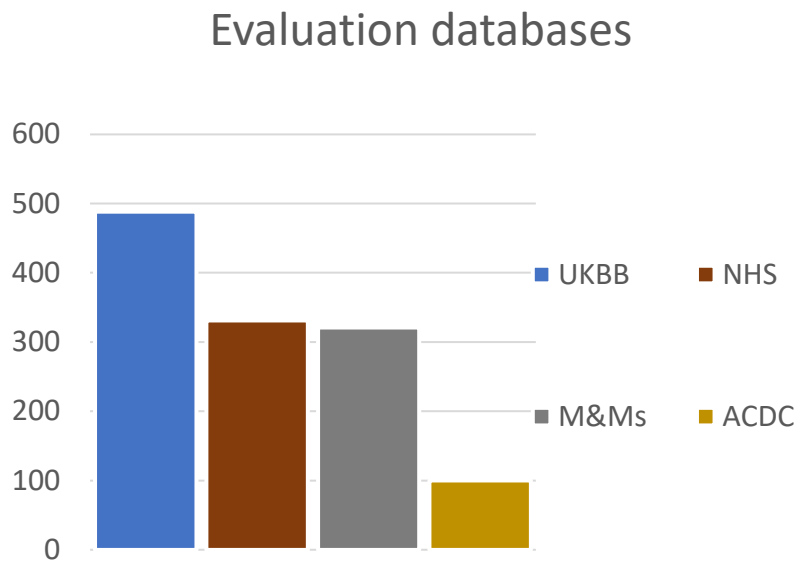
	LV ED	LV ES	RV ED	RV ES
Intra-scanner	0.944 (0.025)	0.887 (0.072)	0.888 (0.057)	0.838 (0.102)
Cross-scanner	0.937 (0.030)	0.873 (0.105)	0.790 (0.214)	0.726 (0.253)
In vs cross-scanner p-val	0.0003	0.0285	0.0000	0.0000
Intra-pathology	0.939 (0.027)	0.880 (0.090)	0.837 (0.137)	0.784 (0.181)
Cross-pathology	0.940 (0.029)	0.877 (0.098)	0.815 (0.208)	0.751 (0.244)
In vs cross-path. p-val	0.2716	0.4126	0.0959	0.4778

Generalising to different scanner domains

- Train using 8000+ CMR scans from UK Biobank and 2 NHS hospitals

- UKBB: Siemens
- NHS: Philips and Siemens
- M&Ms: Canon, GE, Philips, Siemens
- ACDC: Siemens





J. Mariscal-Harana, et al. (2021) "Large-scale, Multi-vendor, Multi-protocol, Quality-controlled Analysis of Clinical Cine CMR Using Artificial Intelligence." *European Heart Journal - Cardiovascular Imaging*

Generalising to different scanner domains

DICE SCORES							
Database	**UKBB**	**NHS**		**ACDC**	**M&Ms**		**Unseen vendors**
Vendor	Siemens (n=488)	Siemens (n=152)	Philips (n=179)	Siemens (n=100)	Siemens (n=96)	Philips (n=125)	GE (n=50)	Canon (n=50)
Left ventricle	0.94 (0.04)	0.95 (0.09)	0.95 (0.06)	0.93 (0.06)	0.90 (0.07)	0.91 (0.06)	0.88 (0.09)	0.91 (0.06)
Myocardium	0.89 (0.03)	0.83 (0.12)	0.85 (0.08)	0.87 (0.03)	0.82 (0.04)	0.87 (0.04)	0.83 (0.06)	0.84 (0.04)
Right ventricle	0.90 (0.06)	0.86 (0.17)	0.90 (0.15)	0.88 (0.07)	0.85 (0.09)	0.88 (0.06)	0.86 (0.06)	0.87 (0.08)

J. Mariscal-Harana, et al. (2021) "Large-scale, Multi-vendor, Multi-protocol, Quality-controlled Analysis of Clinical Cine CMR Using Artificial Intelligence." *European Heart Journal - Cardiovascular Imaging*

Generalising to different scanner domains

CLINICAL MEASURES							
	LVEDV [mL]	LVESV [mL]	LVEF [%]	LVM [g]	RVEDV [mL]	RVESV [mL]	RVEF [%]
Manual	155.7 (52.6)	71.2 (48.0)	56.6 (12.5)	105.7 (40.6)	152.5 (44.7)	71.0 (33.3)	54.4 (10.9)
Proposed	158.4 (53.5)	75.0 (48.9)	54.8 (12.1)	106.2 (37.9)	154.5 (44.2)	73.1 (32.0)	53.4 (10.7)
Absolute bias	2.6	3.8	-1.8	0.4	2.0	2.1	-0.9
Interobserver (mean ± SD)*	6.6 ± 4.1	6.0 ± 4.1	-	5.8 ± 4.3	8.7 ± 5.9	11.3 ± 6.7	-

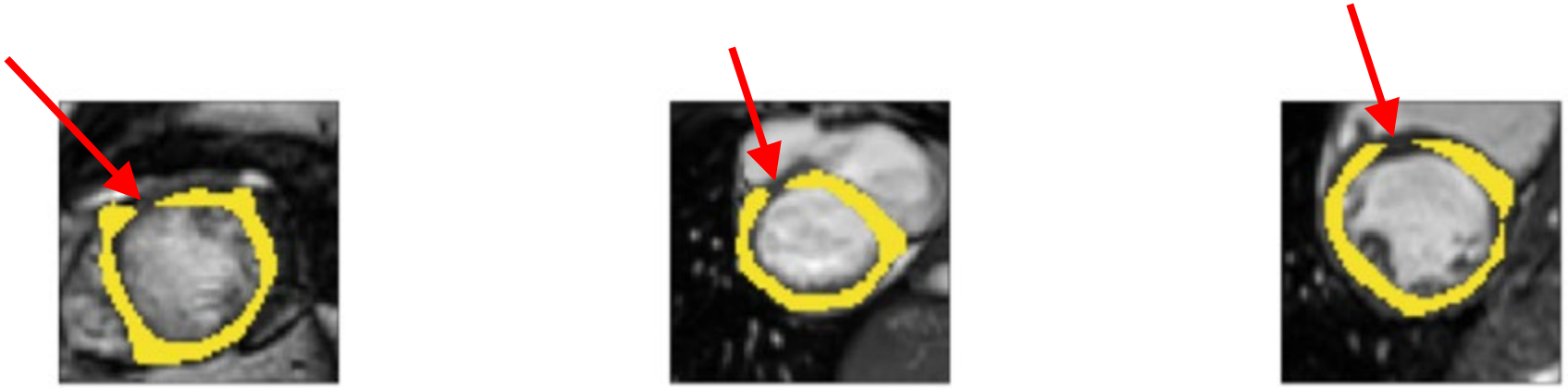
Given a large multi-vendor training set, CNN-based segmentation can generalise to external validation sets and perform at the level of human observers

J. Mariscal-Harana, et al. (2021) "Large-scale, Multi-vendor, Multi-protocol, Quality-controlled Analysis of Clinical Cine CMR Using Artificial Intelligence." *European Heart Journal - Cardiovascular Imaging*

*Bai, W. et al. (2018) "Automated cardiovascular magnetic resonance image analysis with fully convolutional networks." *J Cardiovasc Magn Reson*

Segmentation topology

- CNN-based CMR segmentations are highly accurate but …



- Sometimes they produce nonsensical results that a cardiologist would never produce

- I.e. they are *topologically* incorrect …

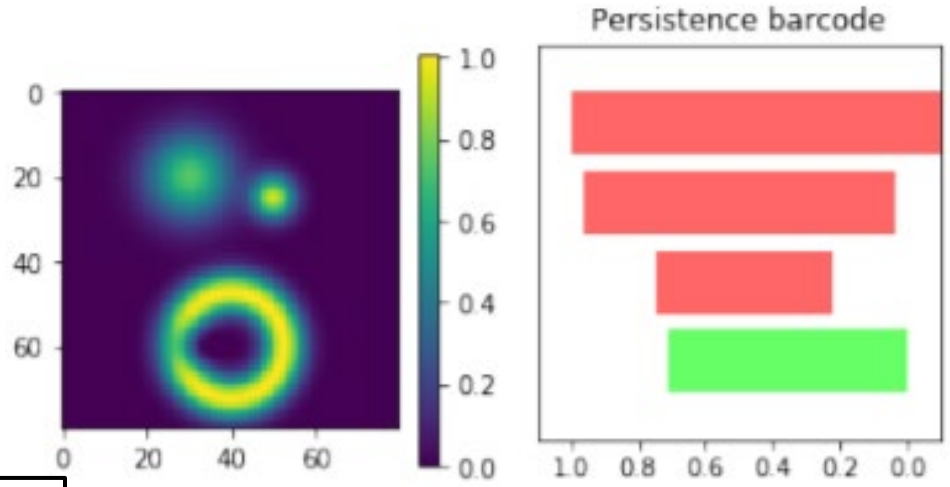
Encoding topology into CNNs

- How can we tell a CNN what the expected *topology* of a structure is, e.g.
  - *LV blood pool* is a single component with no holes
  - *Myocardium* is a single component with a hole
  - Etc.

- Answer: *persistent homology*

$$\mathcal{L}_k(\beta_k^*) = \sum_{\ell=1}^{\beta_k^*}(1 - |b_{k,\ell} - d_{k,\ell}|^2) + \sum_{\ell=\beta_k^*+1}^{\infty} |b_{k,\ell} - d_{k,\ell}|^2$$

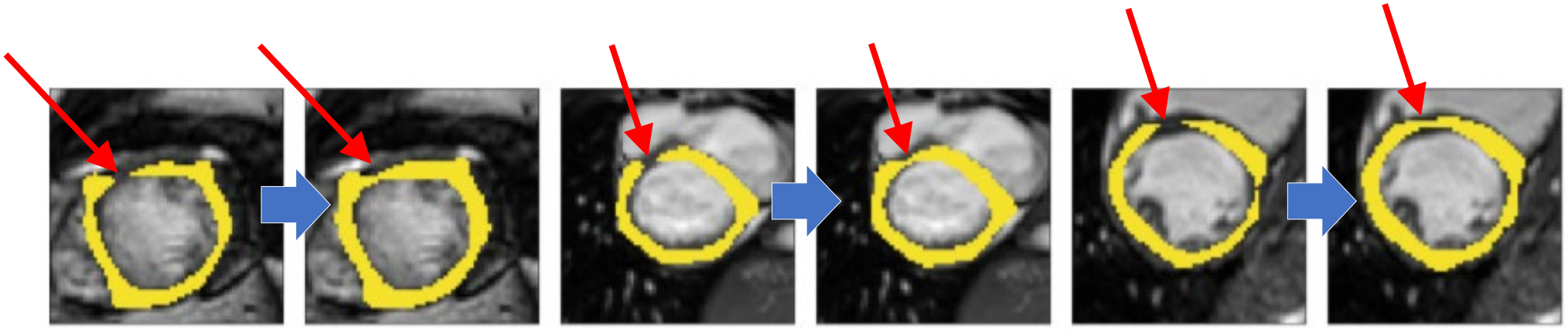
$$\mathcal{L}_{\text{topo}} = \sum_k \mathcal{L}_k(\beta_k^*)$$



β_k^*= Betti numbers (no. topological features of dimension *k*)
$b_{k,l}$ = birth value of l^{th} longest bar of dimension *k*
$d_{k,l}$ = death value of l^{th} longest bar of dimension *k*

Encoding topology into CNNs using persistent homology

- Encoding expected persistence barcodes into a CNN loss function effectively removes nonsensical errors



J. Clough, et al. (2020) "A Topological Loss Function for Deep-Learning based Image Segmentation using Persistent Homology." *IEEE Trans PAMI*

Investigation of sex and race bias in cardiac MR segmentation

- Why?
  - There are known gender/race differences in cardiac structure and function
  - In other applications of AI, training data imbalance has been shown to introduce bias into AI models

Gender Shades: Intersectional Accuracy Disparities in Commercial Gender Classification*

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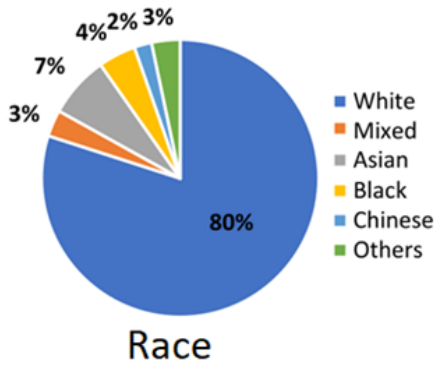
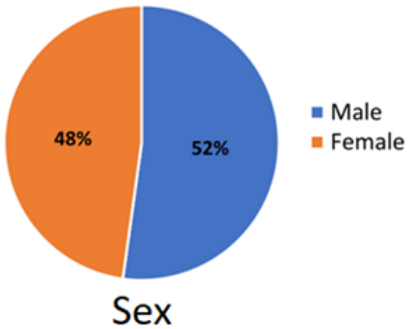
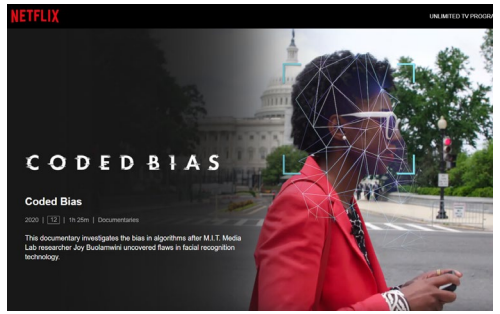
- Question: is there any *bias* in our cardiac MR segmentation models?
- UK Biobank database:



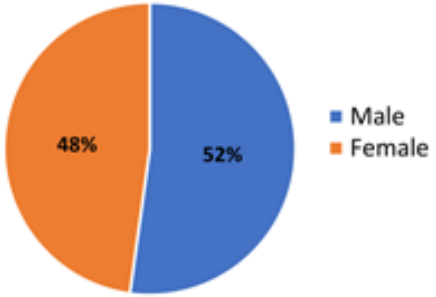




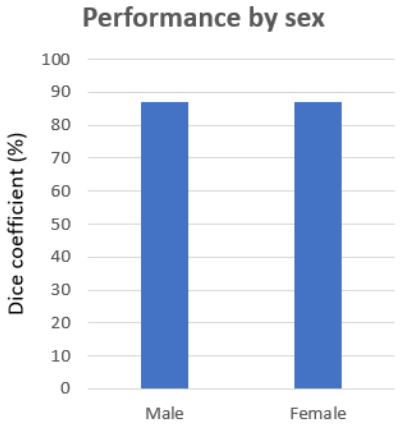
E. Puyol-Antón, et al (2021) "Fairness in Cardiac MR Image Analysis: An Investigation of Bias Due to Data Imbalance in Deep Learning Based Segmentation", *MICCAI*.

Investigation of sex and race bias in cardiac MR segmentation

Sex:

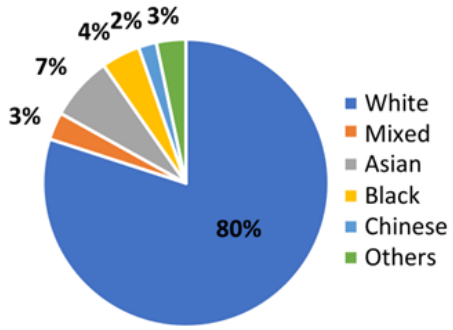


AI

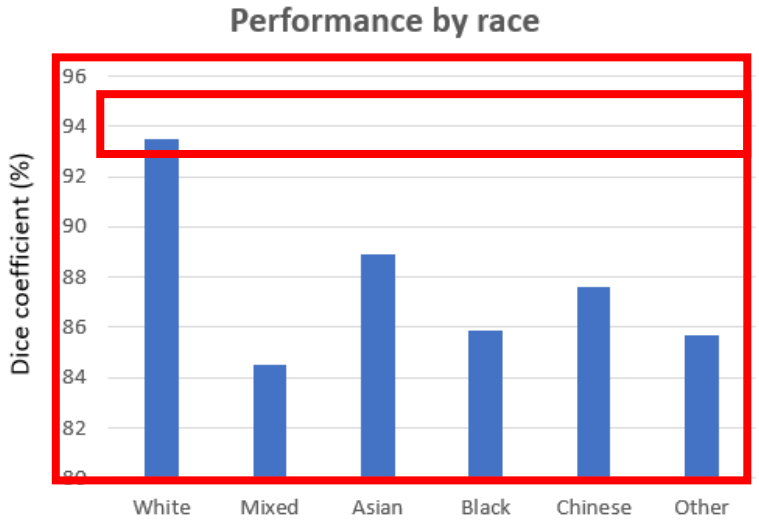


No sex bias

Race:



AI

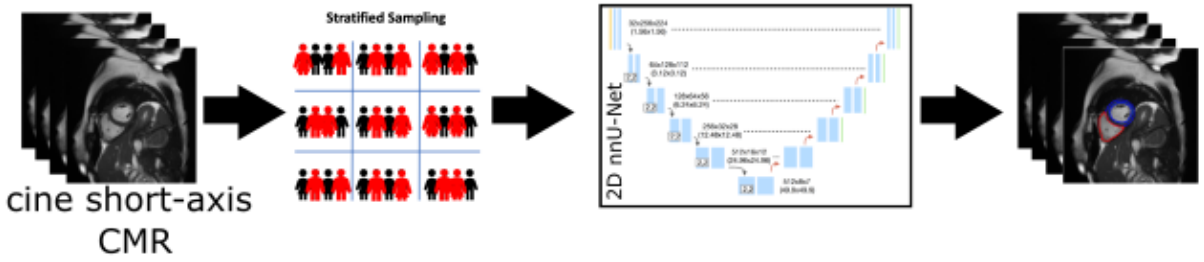


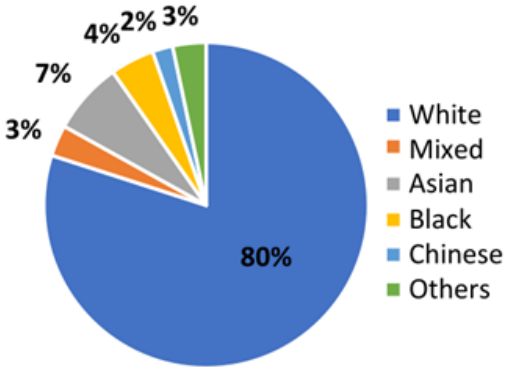
Significant racial bias

E. Puyol-Antón, et al (2021) "Fairness in Cardiac MR Image Analysis: An Investigation of Bias Due to Data Imbalance in Deep Learning Based Segmentation", Proceedings MICCAI.

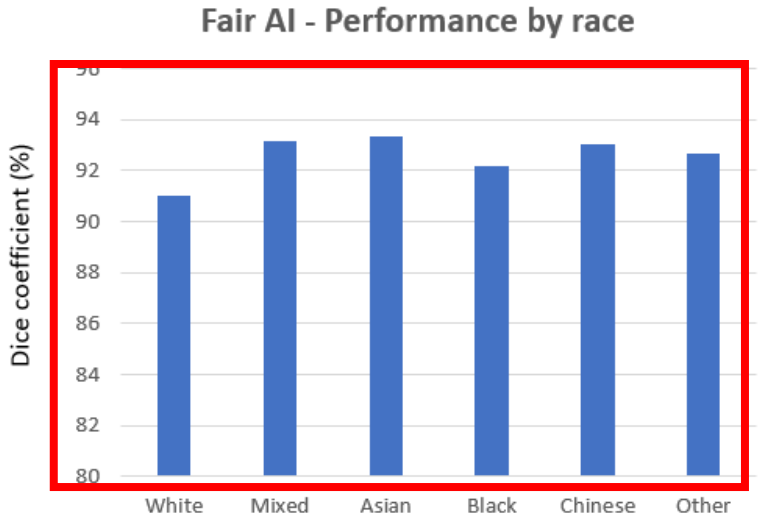
Fair AI for race bias mitigation

- Stratified batch sampling:





Fair AI



No significant racial bias

Summary

- Quality-controlled AI tool for cardiac functional quantification is robust to unseen scanners/domains
  - Trained using >8000 mixed-vendor CMR scans, internal and external validation sets
- Wide range of morphological & diastolic/systolic functional biomarkers estimated to within human observer variability
- Techniques for enforcing correct topology of results
- Identification of racial bias and techniques for debiasing

Impact & clinical translation

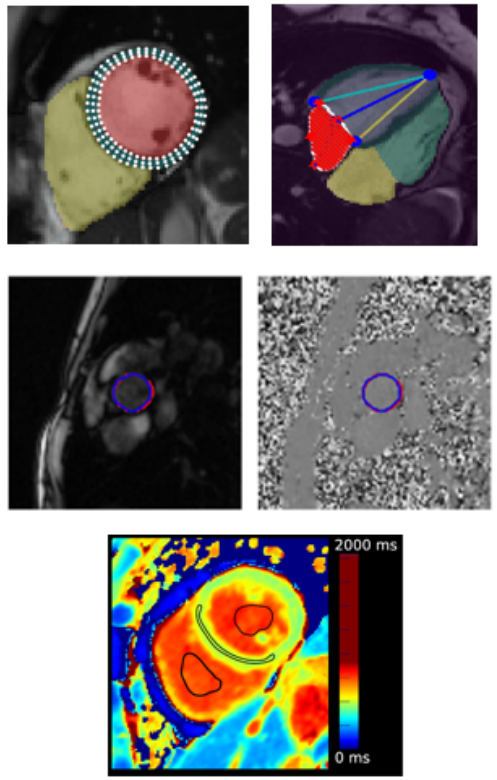
- Software licensing agreement with Perspectum:

Perspectum COVERSCAN STUDY

- *AI-CMR*^{QC} web app currently in use at 3 partner hospitals:

Left ventricle	
LVEDV (mL)	242
LVESV (mL)	90
LVSV (mL)	152
LVEF (%)	63
LV mass (g)	163
LV peak ejection rate (mL/s)	477
LV peak atrial fillinf rate (mL/s)	190
LV atrial contribution (mL)	24
LV cirumferential strain (%)	-29.6
LV radial stran (%)	39.3
LV londitudinal strain (%)	-22.6
MAPSE (%)	15.3
Wall thickness (mm)	11.2
Left atrium	
Max LA volume (mL)	47
LA SV (mL)	42
LAEF (%)	53
LA reservoir (%)	45.2
LA pump (%)	16.3
LA conduit (%)	25.7
T1 mapping	
T1 septum (ms)	961
T1 free wall (ms)	932

Right ventricle	
RVEDV (mL)	245
RVESV (mL)	82
RVSV (mL)	164
RVEF (%)	67
RV peak ejection rate (mL/s)	466
RV peak atrial fillinf rate (mL/s)	403
RV atrial contribution (mL)	38
RV cirumferential strain (%)	-37.3
RV radial stran (%)	33.5
RV longitudinal strain (%)	-28.5
TAPSE (%)	12.4
Right atrium	
Max RA volume (mL)	85
RA SV (mL)	33
RAEF (%)	46
RA reservoir (%)	36.1
RA pump (%)	12.9
RA conduit (%)	20.4
2D Aortic Flow	
Max flow (mL/s)	343
Time to max flow (ms)	137



Thanks …

smartheart

EPSRC
Engineering and Physical Sciences Research Council

Acquisition & reconstruction | Analysis & interpretation | Clinical use

King's College London


Rene Botnar

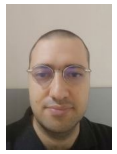

Claudia Prieto


Gastao Lima de Cruz


Julia Schnabel

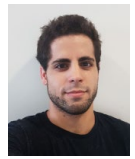

Ilkay Oksuz


James Clough


Devran Ugurlu


Ines Machado


Esther Puyol Anton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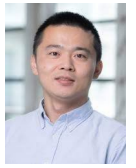
Kerstin Hammernik


Daniel Rueckert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