UNSW
THE UNIVERSITY OF NEW SOUTH WALES

AI in Medicine: Making impact in Clinical Practice

Never Stand Still | Faculty of Engineering | School of Computer Science and Engineering

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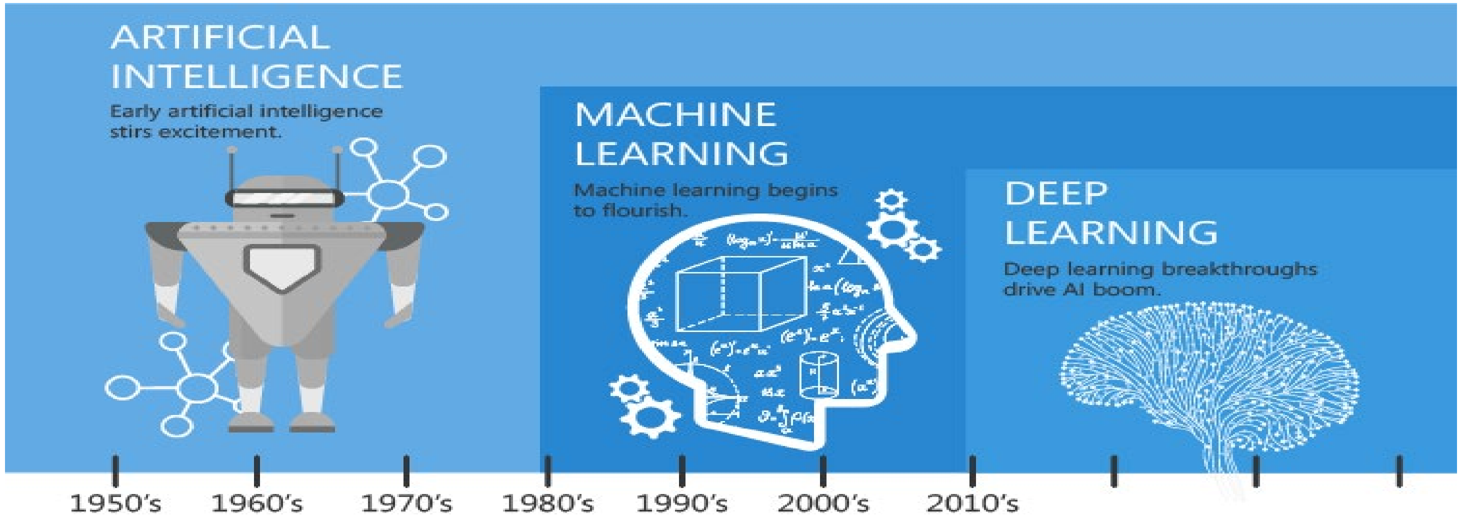
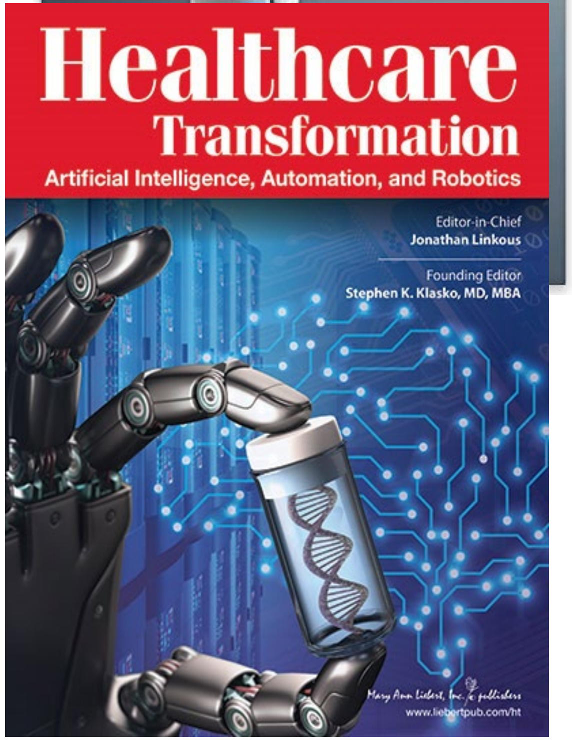
Recent breakthroughs: AI, ML, DL

- Artificial Intelligence (AI): development of smart systems and machines that can carry out tasks that typically require human intelligence
- Machine Learning: creates algorithms that can learn from data and make decisions based on patterns observed. Requires human intervention when decision is incorrect
- Deep Learning: uses complex and deep artificial neural networks to reach accurate conclusions without human intervention. Requires large-scale annotated data to train.





The Need: Augmented Intelligence

- Humans + Computers can achieve better performance than either alone

Harvard Business Review

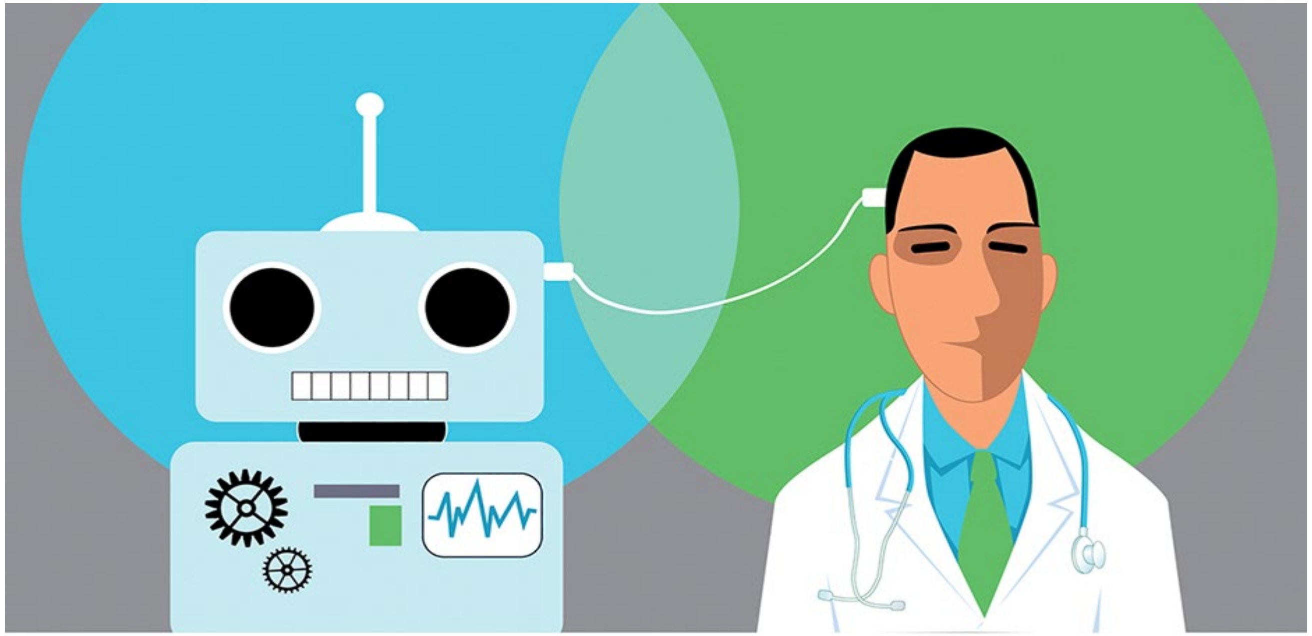
Innovation | AI Will Change Radiology, but It Won’t Replace Radiologists

AI Will Change Radiology, but It Won’t Replace Radiologists

by Thomas H. Davenport and Keith J. Dreyer, DO

March 27, 2018

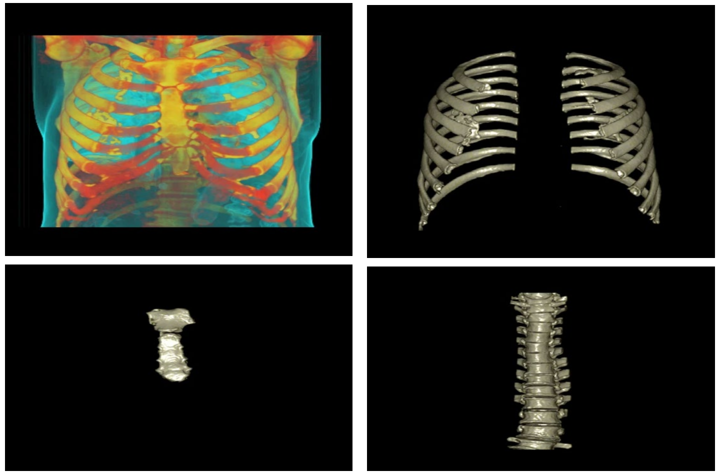
Augmentation or Companionship



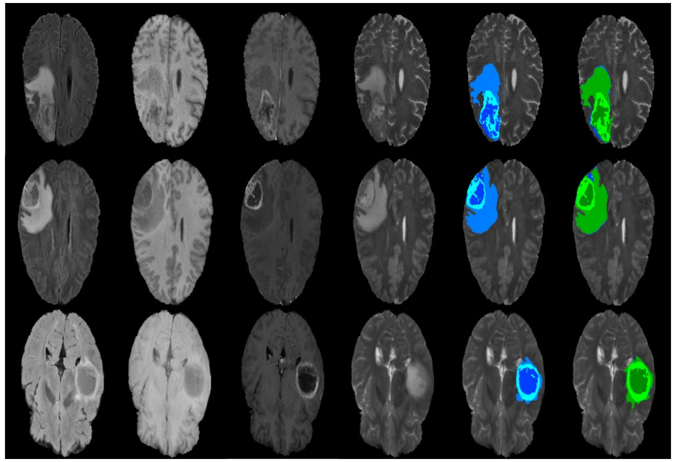
“In contrast to automation, augmentation presumes that smart humans and smart machines can coexist and create better outcomes than either could alone. AI systems may perform some health care tasks with limited human intervention, thereby freeing clinicians to perform higher-level tasks.”

Overview of Medical Imaging and Informatics projects

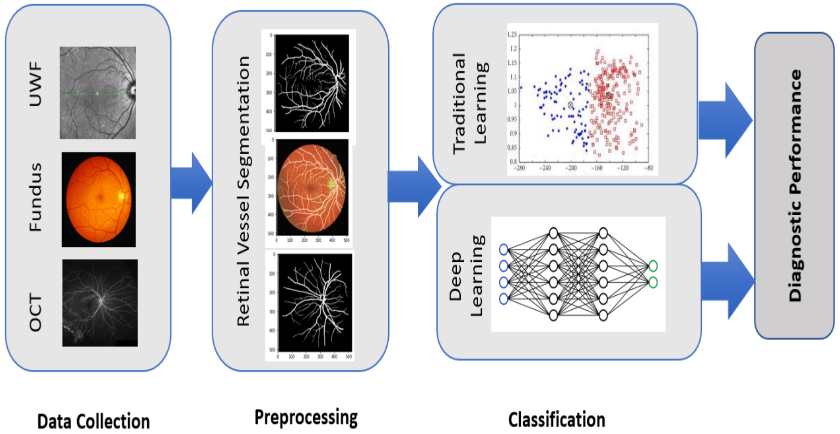
Automated Extraction of ARPD from lung MDCT Images



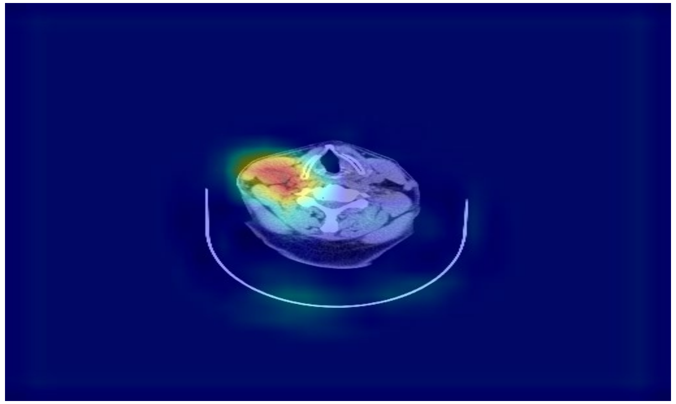
Analysis and Enhancement of MR Neuroimages



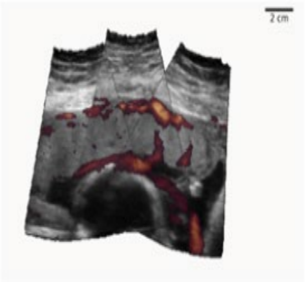
Diagnosis of Neurodegenerative disease using Deep Multimodal Analysis



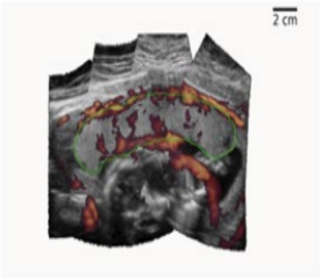
Training Radiomics-based CNNs for Clinical Outcome Prediction



Whole Placenta Volume Stitching and Segmentation from 3D US

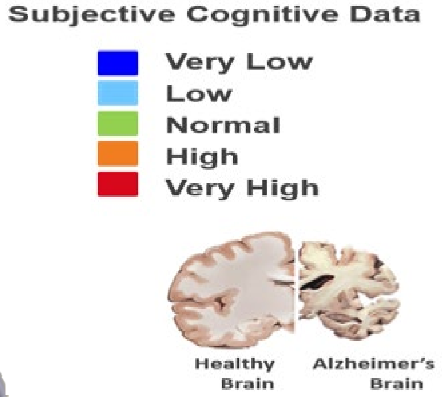


Stitched placental volume



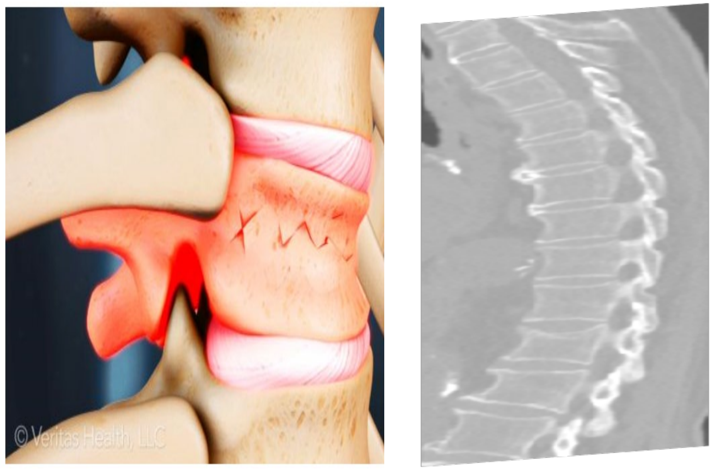
Stitched placental volume with placental shape annotated

Early Detection of Alzheimer's Disease using ML

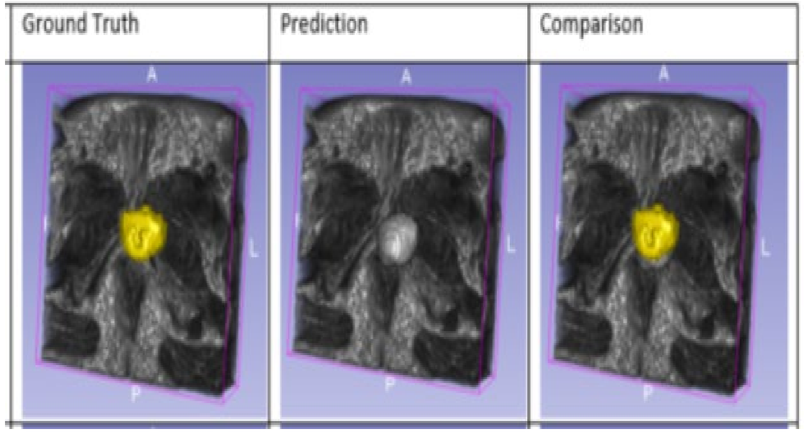


Overview of Medical Imaging and Informatics projects

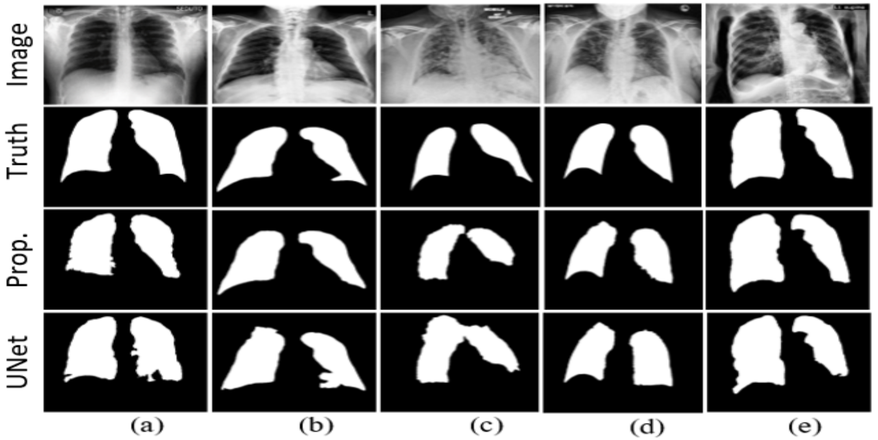
Vertebral Compression Fracture (VCF) Detection in CT images



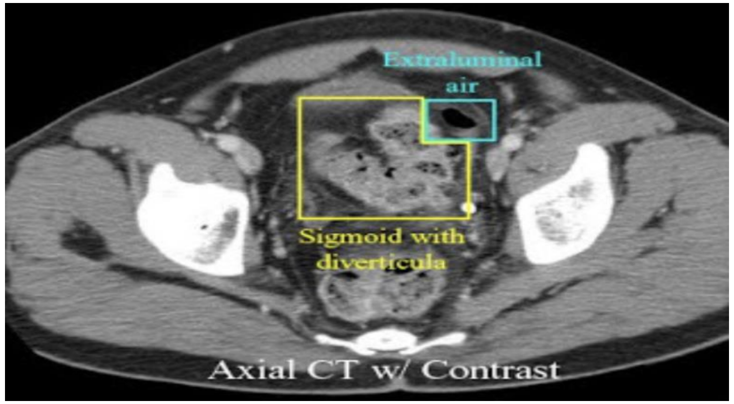
Prostate Segmentation from MR Images



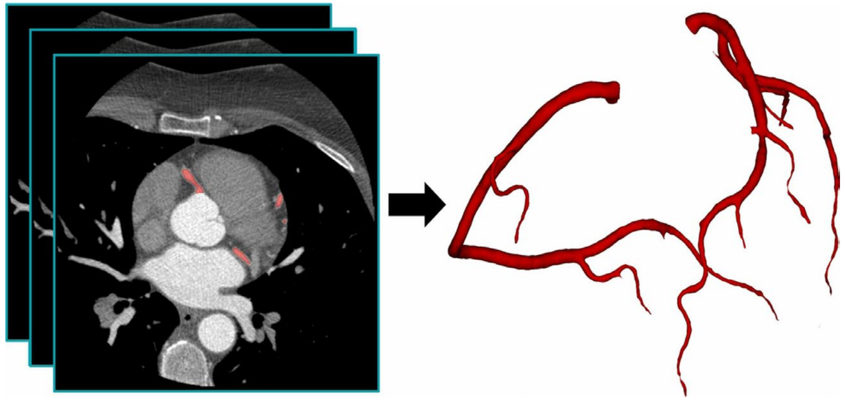
Multimodal Severity Detection for Black Lung Disease



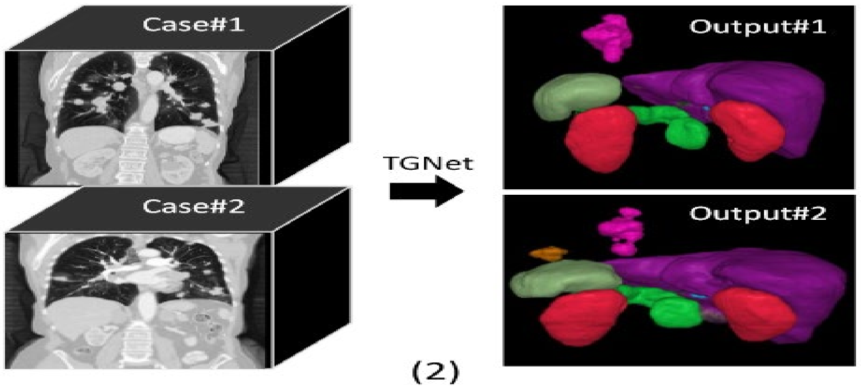
Quantification and Severity Estimation of Acute Diverticulitis



Automated Segmentation of Coronary Arteries



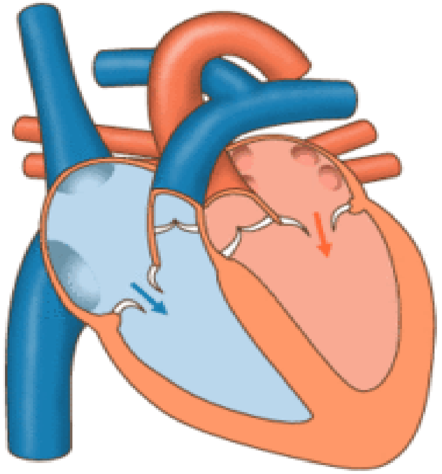
Multi-organ and Tumor Segmentation from Abdominal CT images

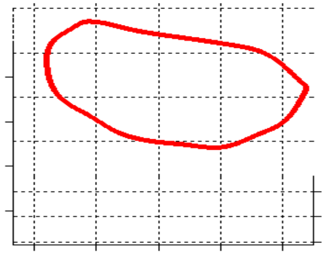


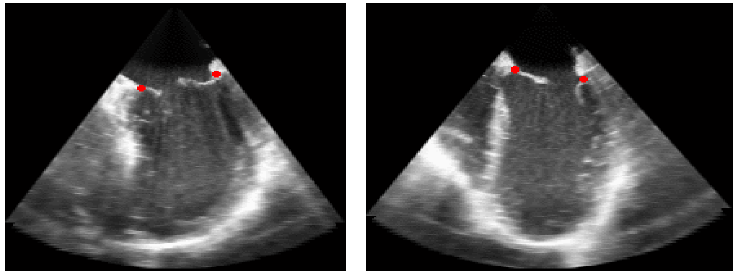
Case Study: Automated Analysis of 4D Fetal Echocardiogram*

- Problem Statement

Given a 4D Fetal echocardiogram, segment the four cardiac chambers and the mitral and tricuspid annulus, creating a 3D model of the fetal heart at End-Diastole. Compute essential biometrics to assess the well-being of the fetus from this model by tracking it over the entire cardiac cycle.







Adult Annulus Segmentation [1].

Image Credit:

*Joint work with Philip, Ferrieira, Tomar, Chawla, Welsh, Stevenson

Background

- Heart is the **first functional organ** that develops in a fetus.
- Starts beating by **Week 4**
- The heart has four chambers, two atria (left and right atrium) and two ventricles (left and right ventricle)
- The fetus has a **parallel circulation** compared to the serial system in adults – because lungs are not functional
- **Mitral (Bicuspid) Valve** (MV): opens during diastole, allows blood to flow down from the LA to the LV and closes during systole to prevent the blood from flowing back to the LA
- **Tricuspid Valve** (TV): opens during diastole, allows blood to flow down from the RA to the RV and closes during systole to prevent the blood from flowing back to the RA

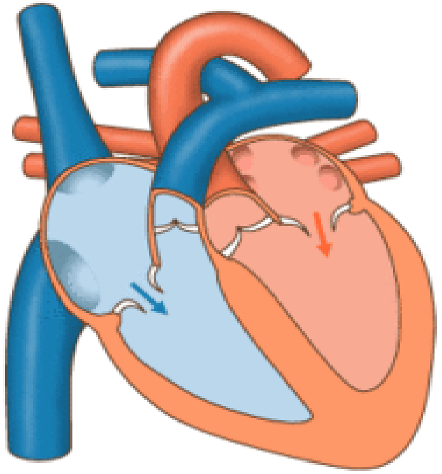
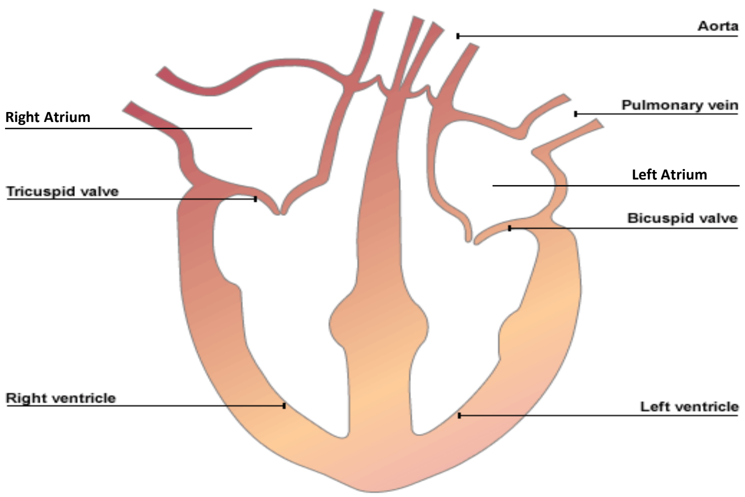


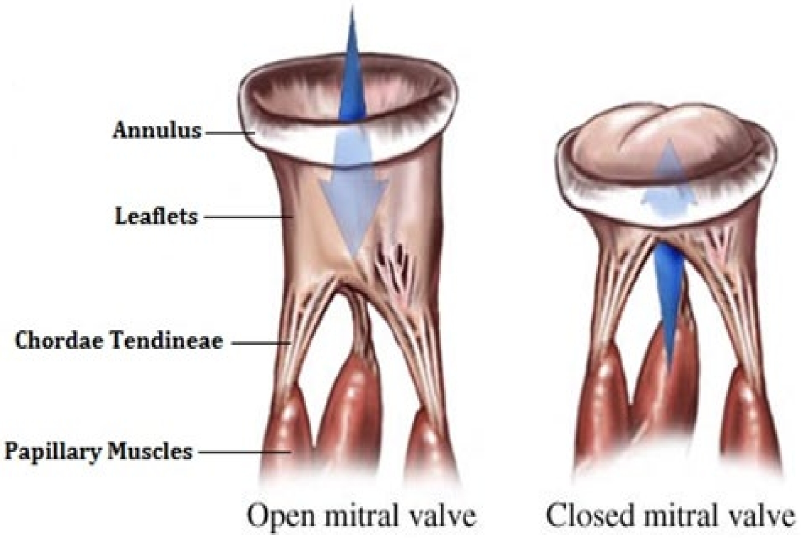
Image Credit:

Background

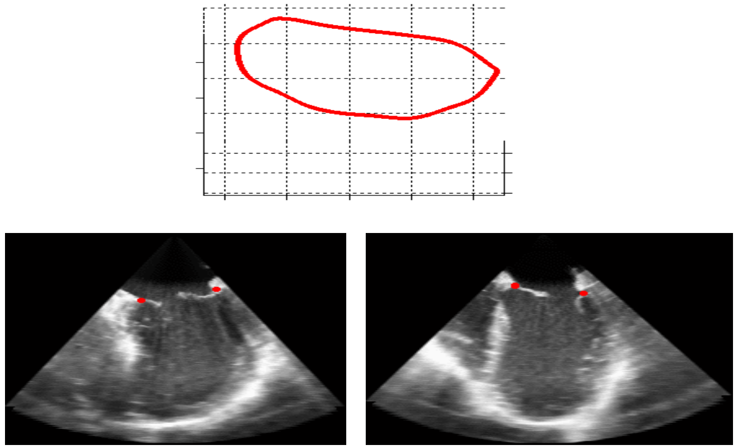
- We are interested in the **Annulus region**, a saddle shaped fibrous ring, which moves up and down during a cardiac cycle.
- The annulus controls the opening and closing of the valves.
- The vertical displacement of the **mitral annulus** is terme **MAPSE**
- The same of the **tricuspid annulus** is terme **TAPSE**



Four chambers of the heart.



Mitral Valve showing the fibrous annulus ring surrounding the leaflet.

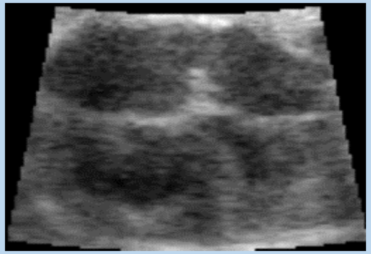


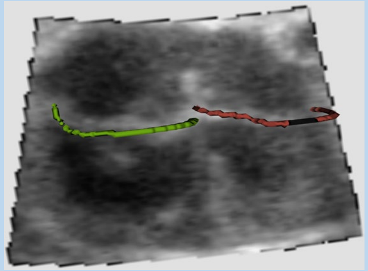
Adult Annulus Segmentation [1].

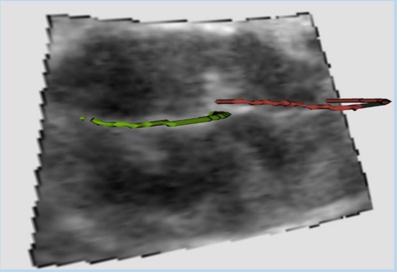
Datasets

➢ Dataset-1

- 295 Ultrasound Volumes (Acquired by 3 operators)
  - 95 foetuses (Gestational Age: 20-37 weeks)
  - **4D** data (3D + time)
  - Annotations available:
    - TAPSE/MAPSE measurements by 3 operators (3 measurements each)
    - Tricuspid/Mitral annuli annotated on 169 * 3D volumes

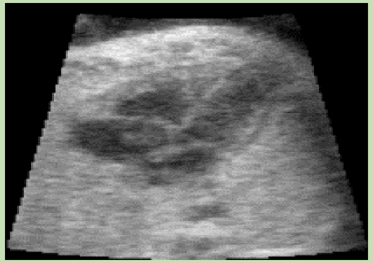


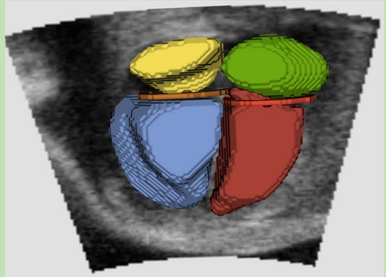


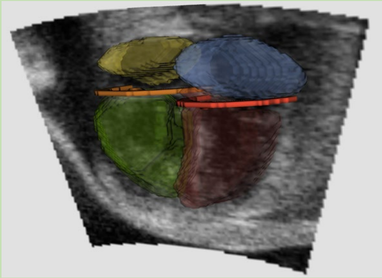


➢ Dataset-2

- 385 Ultrasound Volumes (Acquired by 1 operator)
  - 32 foetuses
  - **4D** data (3D + time)
  - Probe used for data acquisition: E8-STIC, E10-STIC, E10-eSTIC
  - Annotations available:
    - 6 classes: Left Atrium (LA), Left Ventricle (LV), Mitral Annulus (MA), Right Atrium, Right Ventricle, Tricuspid Annulus (TA)
    - 2 Annotators
    - 30 Volumes (each annotated in triplicates by each annotator)



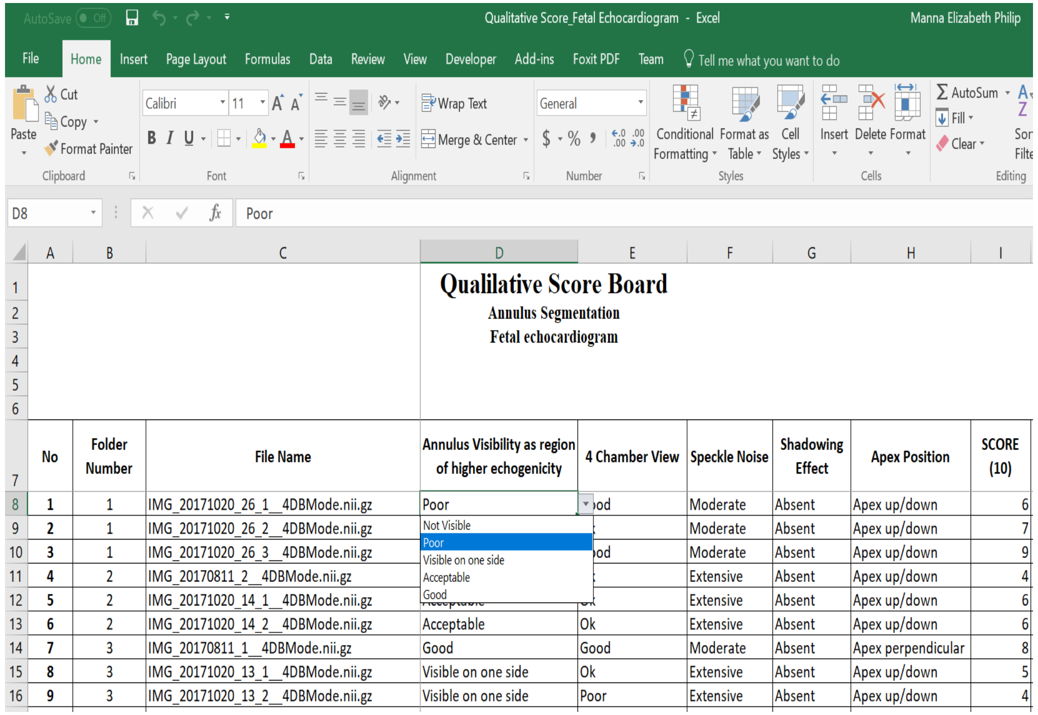




Data Preparation

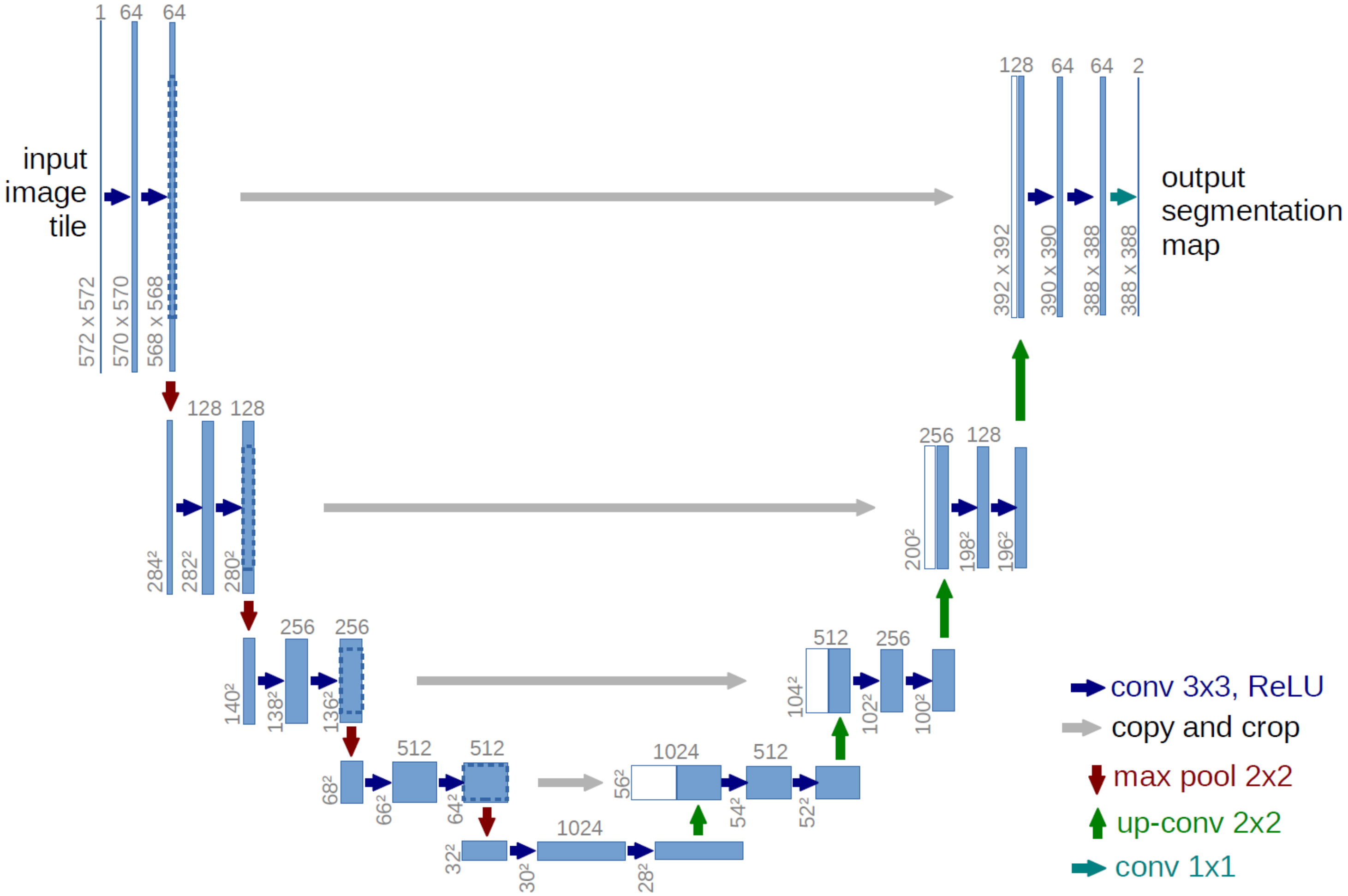
- **Quality Scoring System –** manually evaluated (out of 8)
- Volumes with a score >= 4, selected

Scoring Parameter		Score
Visibility of	4 Chamber View	1
	Aorta	1
	Moderator band	1
	Whole heart	1
Noise level	High/Moderate/Low	1/2/3
Re-orientation required		1
TOTAL		**8**



No	Folder Number	File Name	Annulus Visibility as region of higher echogenicity	4 Chamber View	Speckle Noise	Shadowing Effect	Apex Position	SCORE (10)
1	1	IMG_20171020_26_1__4DBMode.nii.gz	Poor		Moderate	Absent	Apex up/down	6
2	1	IMG_20171020_26_2__4DBMode.nii.gz			Moderate	Absent	Apex up/down	7
3	1	IMG_20171020_26_3__4DBMode.nii.gz			Moderate	Absent	Apex up/down	9
4	2	IMG_20170811_2__4DBMode.nii.gz			Extensive	Absent	Apex up/down	4
5	2	IMG_20171020_14_1__4DBMode.nii.gz			Extensive	Absent	Apex up/down	6
6	2	IMG_20171020_14_2__4DBMode.nii.gz	Acceptable	Ok	Extensive	Absent	Apex up/down	6
7	3	IMG_20170811_1__4DBMode.nii.gz	Good	Good	Moderate	Absent	Apex perpendicular	8
8	3	IMG_20171020_13_1__4DBMode.nii.gz	Visible on one side	Ok	Extensive	Absent	Apex up/down	5
9	3	IMG_20171020_13_2__4DBMode.nii.gz	Visible on one side	Poor	Extensive	Absent	Apex up/down	4

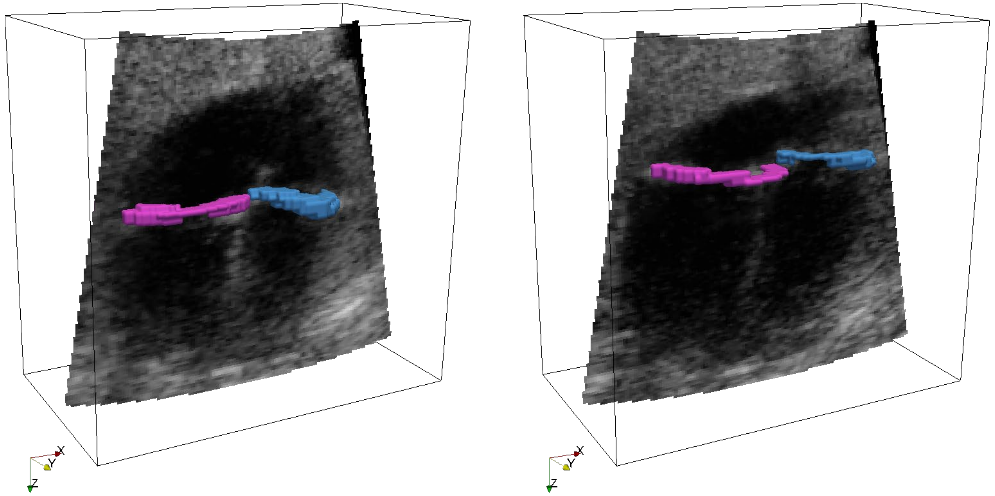
U-net for medical image segmentation

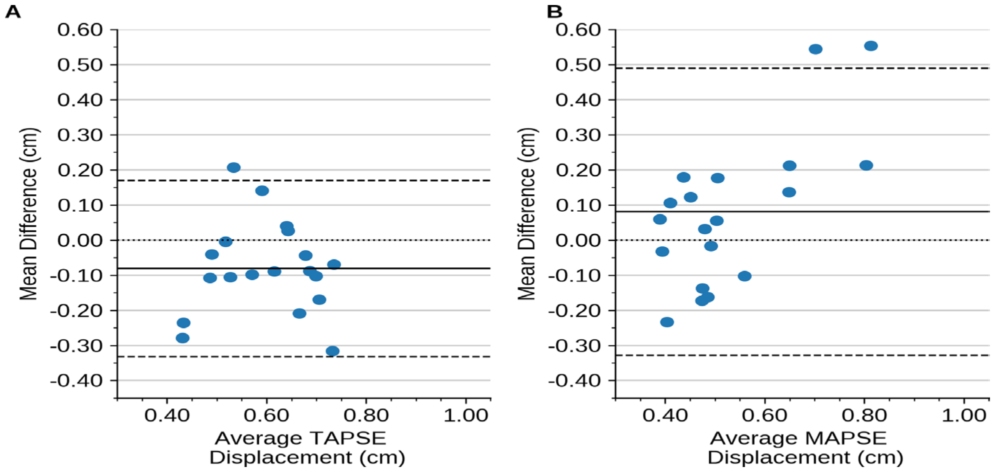


Source: Ronneberger et al. (2015). U-net: Convolutional Networks for Biomedical Image Segmentation. MICCAI 2015.

1. Annulus Segmentation

- U-Net architecture used to segment the tricuspid and mitral annulus
- **Dice Similarity Coefficient** (DSC) values of **0.78** for **Tricuspid Annulus** (TA) segmentation and **0.77** for **Mitral Annulus** (MA) segmentation were achieved.
- TAPSE/MAPSE Measurement
  - For TAPSE measurements, r=0.61 and RMSE=0.14 cm
  - For MAPSE measurements, r=0.30 and RMSE=0.18 cm
- This automated method can provide function cardiac assessment where training is limited and skills lacking
- **Presented @ IEEE ISBI 2019**



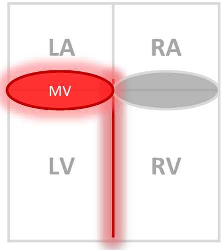


Bland-Altman plots comparing automated TAPSE (A) and MAPSE (B) measurements to average expert measurement.

M. E. Philip, A. Sowmya, H. Avnet, A. Ferreira, G. Stevenson and A. Welsh, "Convolutional Neural Networks for Automated Fetal Cardiac Assessment using 4D B-Mode Ultrasound," *2019 IEEE 16th International Symposium on Biomedical Imaging (ISBI 2019)*, 2019, pp. 824-828, doi: 10.1109/ISBI.2019.8759377.

Annulus Segmentation - Issues

- Change in orientation of the heart due to fetal or probe movement
- Position of the SEPTUM
- Tracking not performed to confirm End-systole and End-diastole



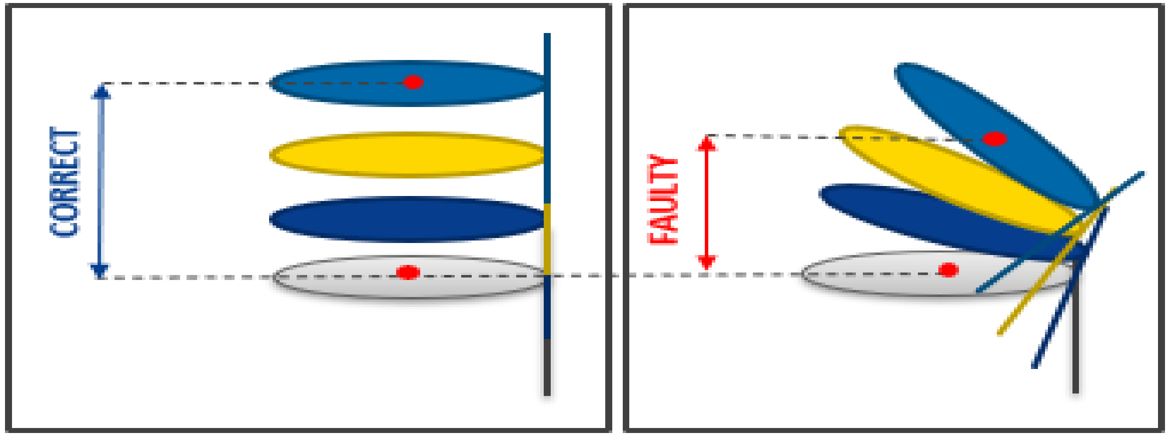
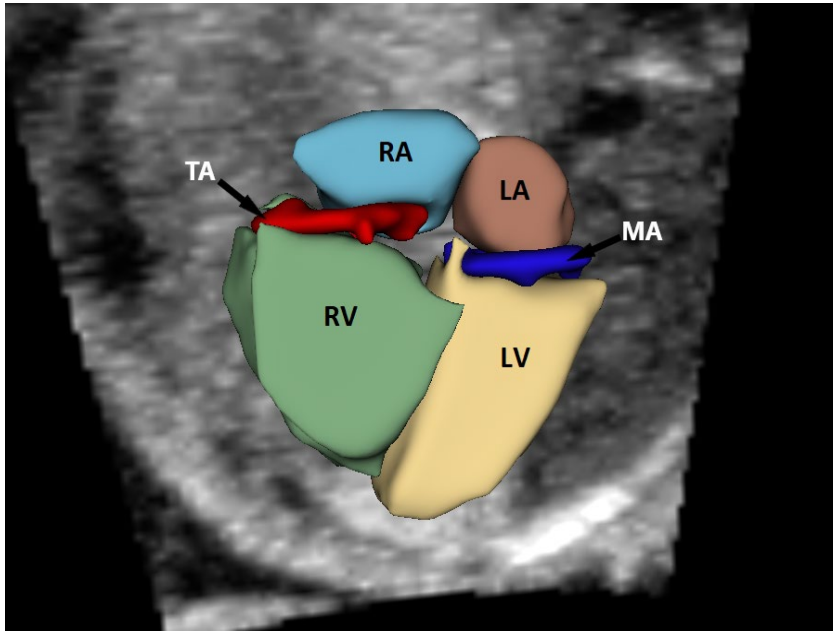


Figure : Schematic depicting need for Registration.

2. Whole Heart Segmentation

- Instead of identifying just the SEPTUM for orientation-problem redefined to obtain it as a by-product
- The heart is modelled consisting of:
  - Left and Right Atrium (LA, RA)
  - Left and Right Ventricles (LV, RV), and
  - Tricuspid and Mitral Annulus (TA, MA)

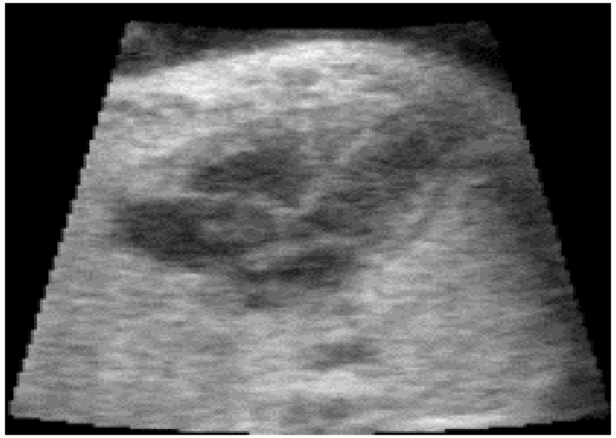


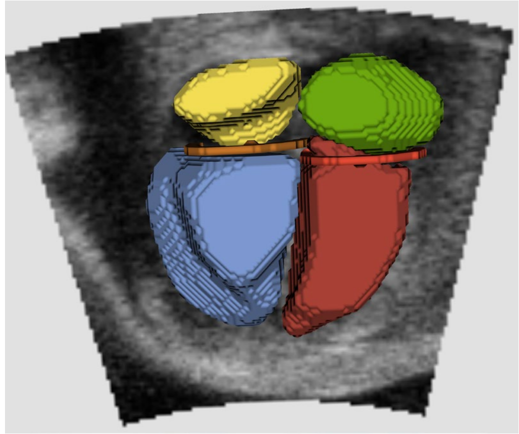
3D render of heart model, showing cardiac chambers and anuuli.

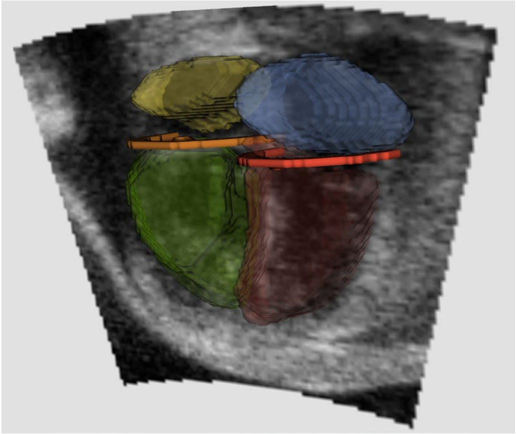
- Dataset-1 could not be used
  - Whole heart was not in view
  - Zoomed in version of the thorax

Datasets

- Dataset-2
- 385 Ultrasound Volumes (Acquired by 1 operator)
  - 32 foetuses
  - **4D** data (3D + time)
  - Probe used for data acquisition: E8-STIC, E10-STIC, E10-eSTIC
  - Annotations available:
    - 6 classes: Left Atrium (LA), Left Ventricle (LV), Mitral Annulus (MA), Right Atrium, Right Ventricle, Tricuspid Annulus (TA)
    - 2 Annotators
    - 30 Volumes (each annotated in triplicates by each annotator)

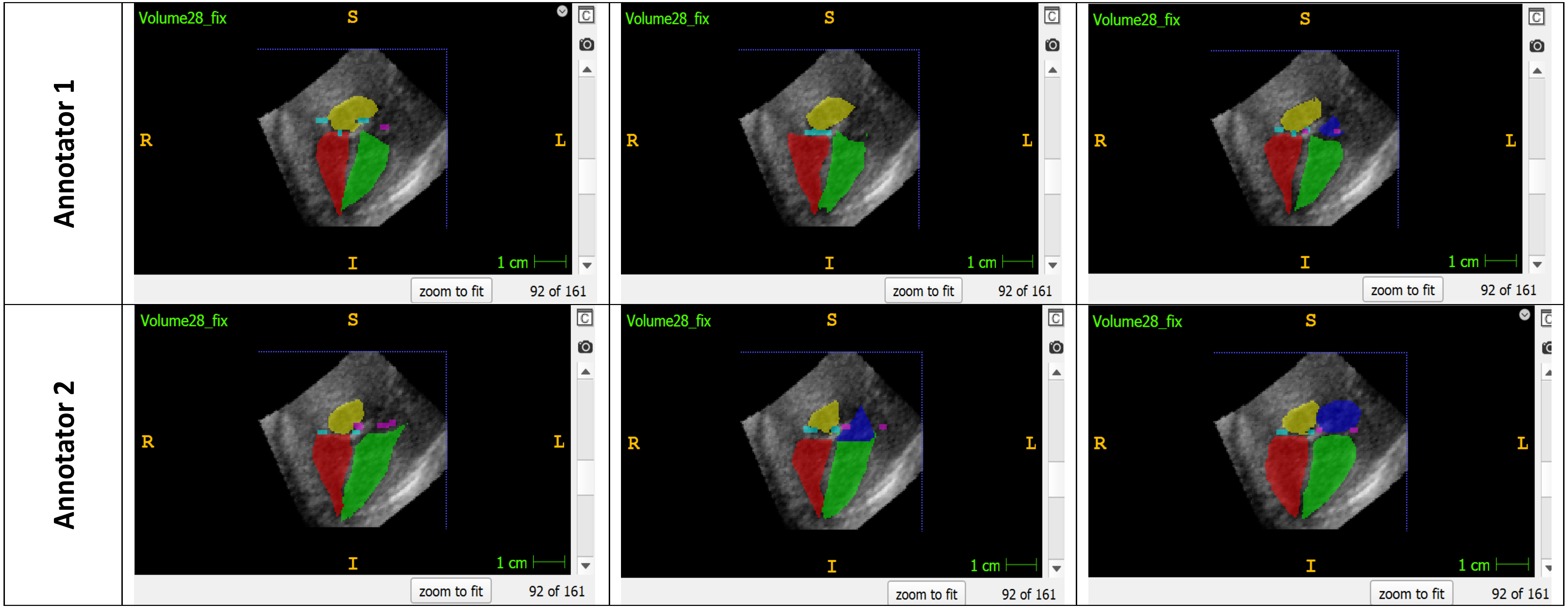






Issues

- Inter and Intra observer Variability



Architectures

- CNN based models:
  - U-Net
  - V-Net
  - Res-UNet

- Transformer-based models:
  - TransBTS
  - Unet-R

Training details

- Training data:

Number of patients	20
Total annotated ED volumes	30
Train volumes	25 (15 patients)
Training Patient IDs	0,2,3,4,5,6,8,9,13,14,24,26,27,28,30,31,35 (Fold 1)
Test volumes	5 (5 patients)
Test Patient IDs	1,7,10,25,32 (Fold 1)

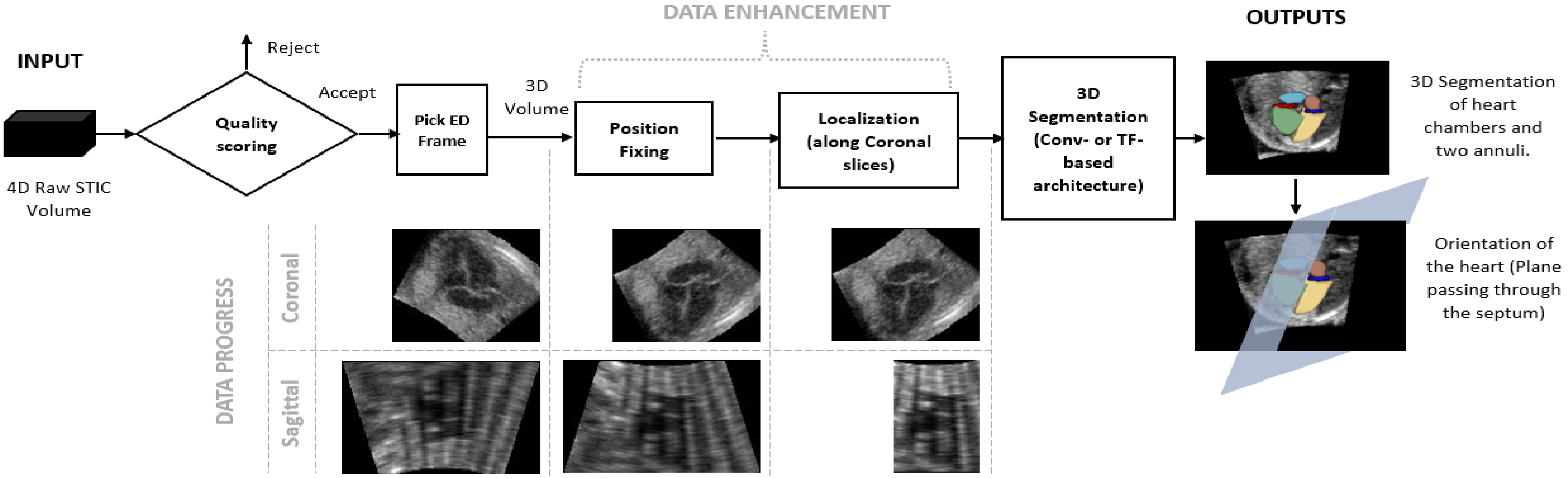
- Training Parameters

Augmentation	Rotation at ±(3,6,9)°, Gaussian noise, Salt and Pepper noise
Training samples after augmentation	2100
Train/ Validation split	90/10
Epochs trained for	100
Optimizer	Adam
Learning rate	1e-4
Batch size	2
Data Size	64 *64 *64

Whole Heart Segmentation

1. **Position Fixing**
   - Manually repositioned to
     - Apex down – flipping data up/down
     - Mitral Annulus visible on the right side – flipping data left/right

2. **Localisation (along coronal axis)**
   - SVM classifier trained to classify coronal slices to foreground / background



Flowchart outlining the proposed pipeline.

M. E. Philip *et al.*, "A Machine Learning Framework for Fully Automatic 3D Fetal Cardiac Ultrasound Evaluation," *2022 IEEE 19th International Symposium on Biomedical Imaging (ISBI)*, 2022, pp. 1-5, doi: 10.1109/ISBI52829.2022.9761613.

Segmentation results

- No matter the architecture used, clear **performance improvement with data enhancement**
- Performance improvement with data enhancement
  - **19%** ↑ in DSC for CNNs and a **16%** ↑ for transformer-based networks

Type	Architecture	Enh.	LV	RV	LA	RA	TA	MA
CNN-Based	U-Net [7]	A	0.60	0.67	0.40	0.69	0.48	0.37
		P	0.76	0.70	0.55	0.74	0.49	0.42
		L	**0.82**	**0.77**	**0.62**	**0.72**	**0.50**	**0.47**
	V-Net [13]	A	0.54	0.52	0.16	0.46	0.32	0.22
		P	0.64	0.65	0.38	**0.66**	**0.42**	**0.39**
		L	**0.74**	**0.73**	**0.44**	0.65	0.39	0.37
	Res U-Net [14]	A	0.36	0.32	0.26	0.48	0.24	0.16
		P	0.63	0.63	0.40	0.71	**0.42**	**0.37**
		L	**0.74**	**0.76**	**0.53**	**0.68**	**0.42**	0.36
TF-Based	TransBTS [15]	A	0.59	0.55	0.26	0.60	0.35	0.21
		P	0.74	0.69	0.59	**0.75**	**0.49**	**0.47**
		L	**0.80**	**0.78**	**0.65**	0.72	0.45	0.46
	U-NetR [16]	A	0.53	0.49	0.26	0.54	0.22	0.16
		P	0.66	0.62	**0.37**	**0.67**	**0.31**	**0.31**
		L	**0.70**	**0.67**	0.35	0.57	0.28	0.26

*Comparison of segmentation performance measured by DSC for multiple deep learning methods. Segmentation was performed using models trained on data using three different enhancements (**A** = Augmentation only; **P** = Augmentation + Position Fixing; **L** = Augmentation + Position Fixing + Localization). Best accuracy for each class is shown in bold*

Results analysis

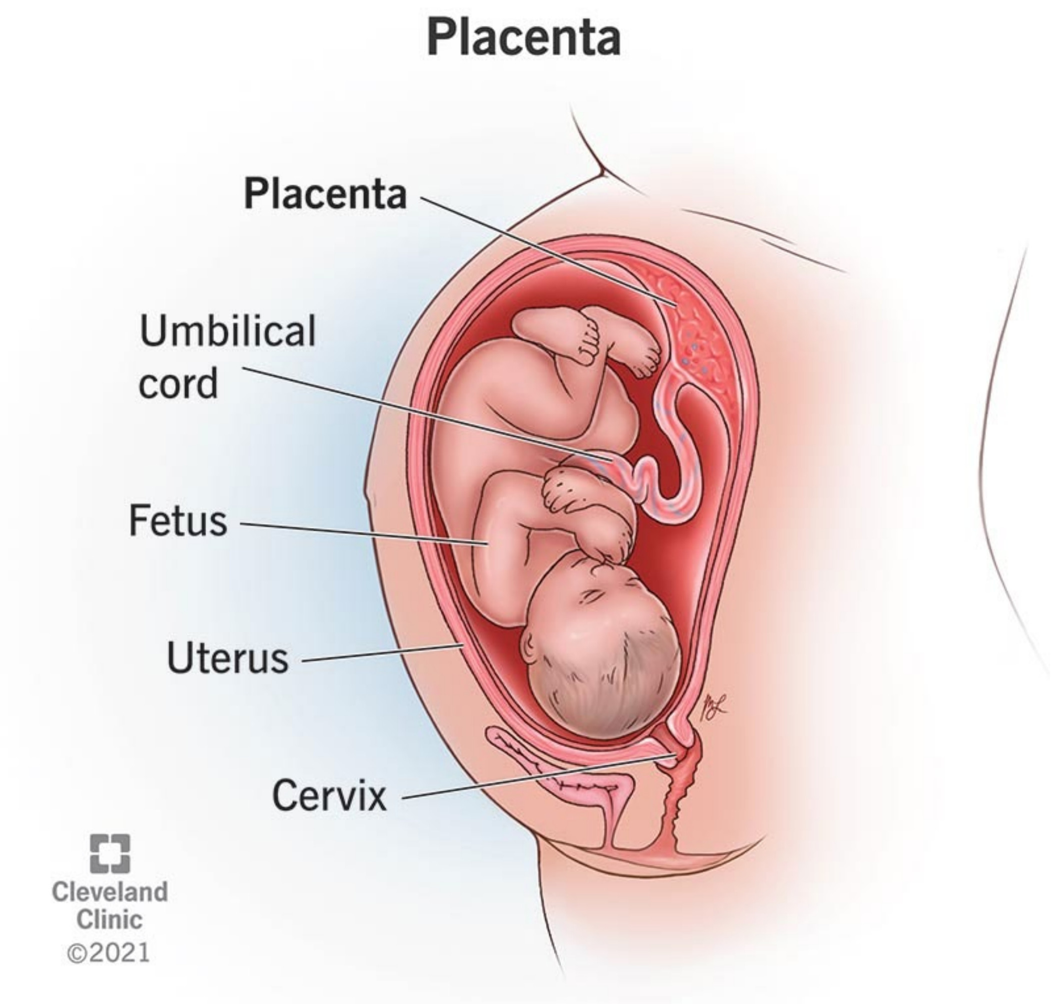
- Physical size constraints reflected in segmentation results
  - Segmentation performance of ventricles > atria > annuli

- U-Net gave the best results
  - V-Net, UNet-R and Res-UNet highly sensitive to noise and fails to learn the general shape of the region
  - TransBTS very similar architecture to U-Net except for the transformer block – results very close to U-Net

- Mean DSC improvement after data enhancement:
  - U-Net: 0.12
  - V-Net: 0.18
  - Res-UNet: 0.28
  - TransBTS: 0.22
  - UNETR: 0.11

3. Automatic segmentation of human placenta in 3D Ultrasound

- The placenta is a critical and complex organ that provides oxygen and nutrition to the growing fetus and removes waste from its blood
- Fetal health strongly depends on the functionality of the placenta
- Any abnormality of the placenta could be harmful to the fetus and the mother
- Assessment of placenta in vivo across gestation is critical to understand placental structure, function, and development



Need for 3D placenta volume segmentation

- 2D US is the standard clinical imaging modality used for accessing placental health and diagnosis of its abnormalities
- In 2D US imaging, physician create 3D model in their mind and subjectively determine volume, location, and features of the placenta – challenging task
- Need – To automatically segment placenta in 3D (voxel-level classification) for qualitative and quantitative analysis
- Manual segmentation of the placenta is time-consuming and have high inter-observer and intra-observer variability
- Automatic 3D placenta segmentation could be used in clinical practice for monitoring conditions that result in pregnancy and birth complications such as PAS, fetal growth restriction, and suspicion of intrauterine fetal demise

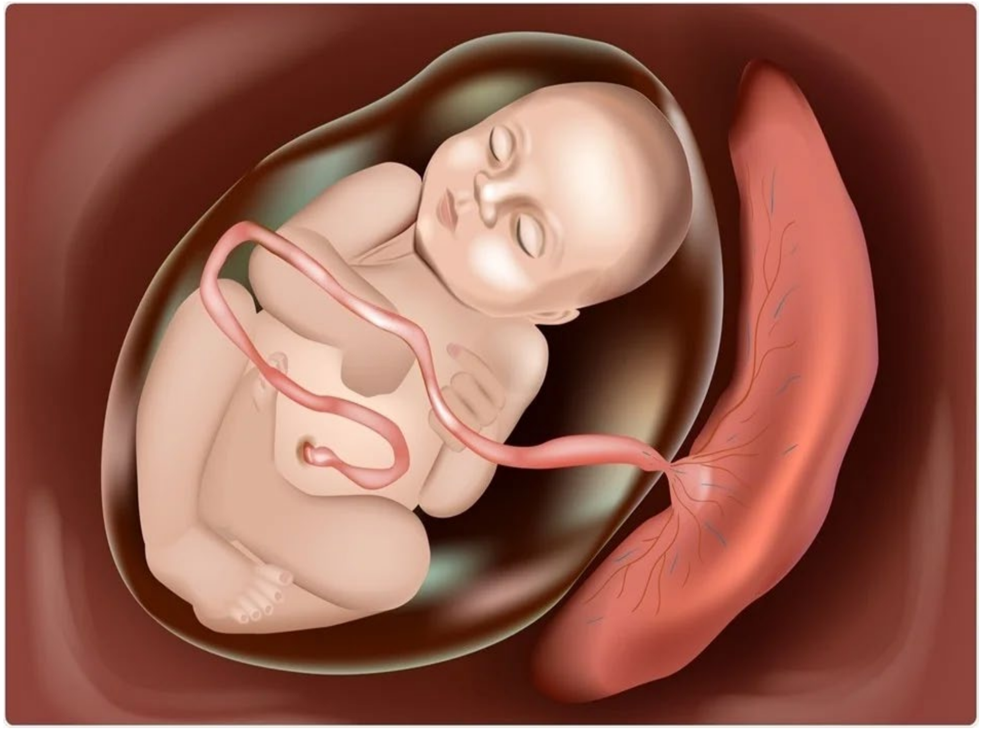
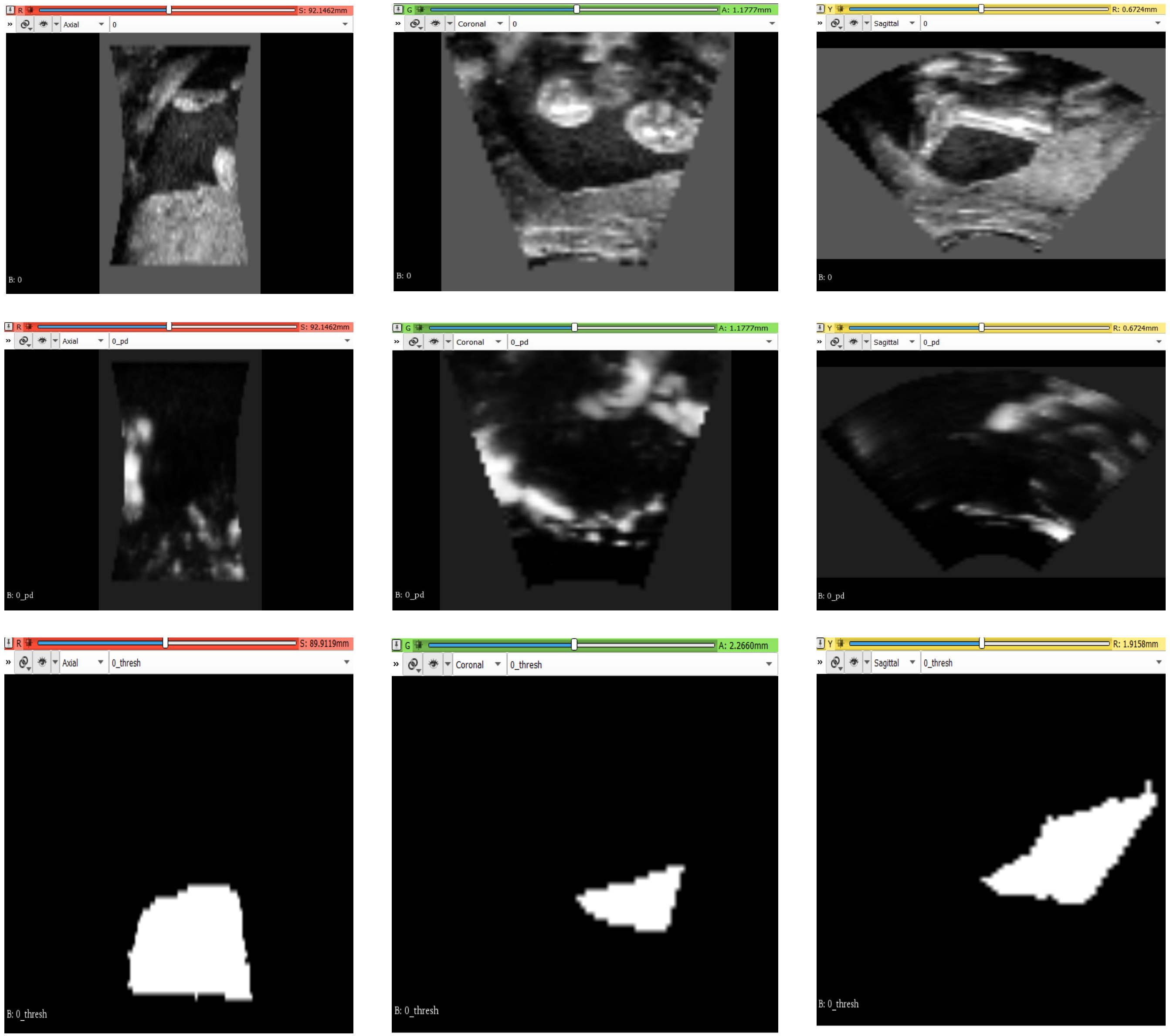


Image Source: Sakurra/Shutterstock.com
https://www.news-medical.net/news/20211116/SARS-CoV-2-replicates-in-human-placenta-with-release-of-infectious-viral-particles.aspx

Dataset

- Total 400 studies having Gray-scale (B-mode) and power doppler (PD) volumes are provided
- For ground-truth (GT) segmentation mask, manual annotation and the best ‘threshold’ images are computed using the following rules:
  - use same image in case there is only one annotated (segmented) image
  - compute intersection image (i.e., voxel-wise logical AND operation) in case there are two annotated (segmented) images
  - compute image based on majority voxel-wise voting in case there are three annotated (segmented) images



Dataset Pre-processing

- Pre-processing needed to make data suitable for the framework.
- Pre-processing:
  - 3D volumes should be of same isotropic size (same size in x, y, z direction)
  - data to be provided in numbered format with each sample in folders from 0 to X, where X is the maximum number of studies

- All data (B-mode US, Power Doppler US, and annotated masks) were resized to 64 x 64 x 64
- B-mode and PD volumes are normalized by rescaling pixel values between range 0 to 255.

Experimental setup

- Data split into training (60%), validation (20%), and testing (20%) without any data leakage (no patient overlap within sets)
- 400 studies divided as below:
  - training -> 240
  - validation -> 80
  - testing -> 80
- Data divided into 5 folds, keeping same ratio in each fold (240 training, 80 validation, and 80 testing)

U-Net results

- Five-fold results (Each fold having 240 training, 80 validation, and 80 testing volumes)
- Results in terms of DSC (Dice Similarity Coefficient), JI (Jaccard Index), HD (Hausdorff distance), and MSD (Mean Surface Distance)
-

Fold# (Dataset)	DSC	Jaccard	HD (mm)	MSD (mm)
1	0.823 ± 0.101	0.708 ± 0.102	8.645 ± 6.322	1.501 ± 0.454
2	0.825 ± 0.058	0.706 ± 0.076	7.920 ± 4.665	1.595 ± 0.631
3	0.823 ± 0.064	0.704 ± 0.082	10.500 ± 6.111	1.664 ± 0.887
4	0.814 ± 0.075	0.692 ± 0.093	7.978 ± 4.839	1.722 ± 0.912
5	0.821 ± 0.045	0.698 ± 0.062	8.262 ± 4.420	1.572 ± 0.408

Fusion of B-mode and PD US

- Given two modalities (B-mode and Power-doppler), we fuse them to improve model performance
- Fusion techniques:
  - Early fusion (at data level)
  - Intermediate-level fusion (at features level)
  - Late fusion (at decision level)
- Using U-Net as baseline

S.No.	Model	Average DSC
1.	Early fusion (U-Net model, w/o data augmentation)	0.830
2.	Intermediate fusion (U-Net model, w/o data augmentation)	0.816
3.	Late fusion (U-Net model, w/o data augmentation)	0.811

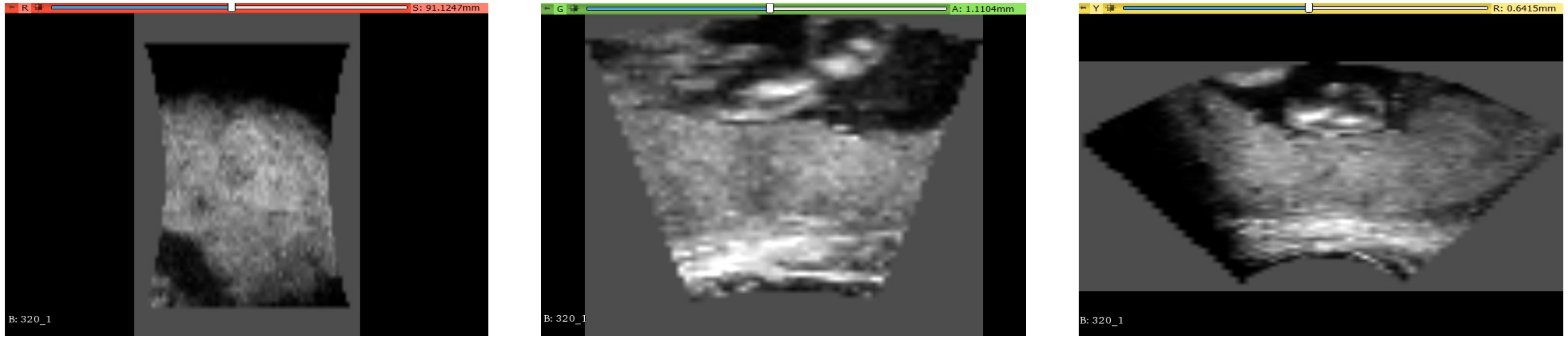
Effect of Data Augmentation and improved variants of U-Net

- Applied Data Augmentation: Rotation, Flipping, etc.
- Using U-Net++ model

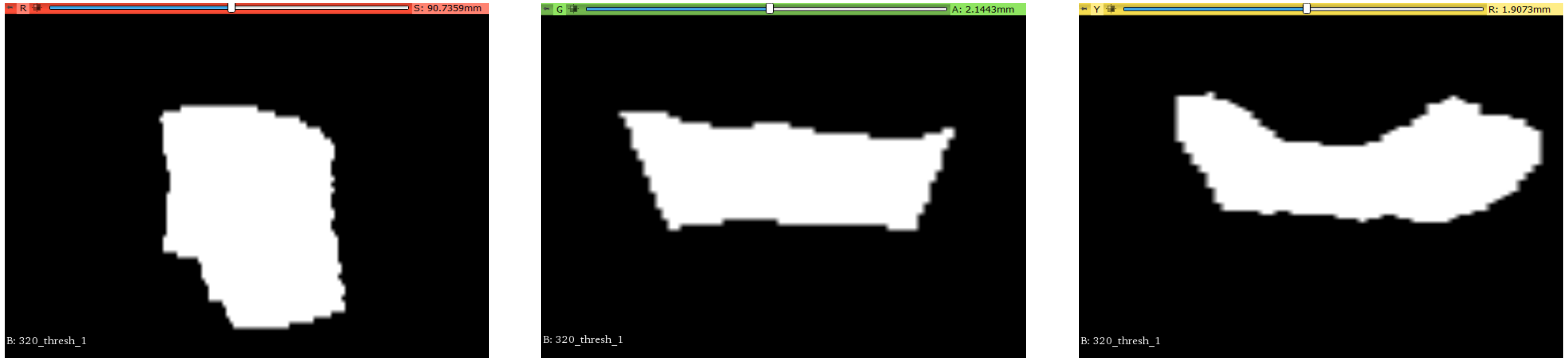
S.No.	Model	Average DSC
1.	U-Net model, w/o data augmentation	0.823
2.	U-Net++ model, w/o data augmentation	0.832
3.	U-Net model, with data augmentation	0.827
4.	U-Net++ model, with data augmentation	0.836

Results – UNet (B-mode) No Augmentation

- DSC: 0.4783
  Jaccard: 0.3143
  Hausdorff: 31.0644
  MSD: 3.2515



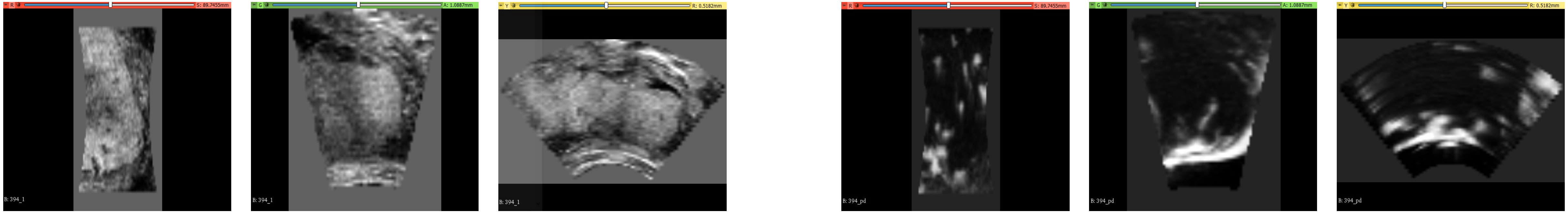
- GT mask



- Predicted Mask

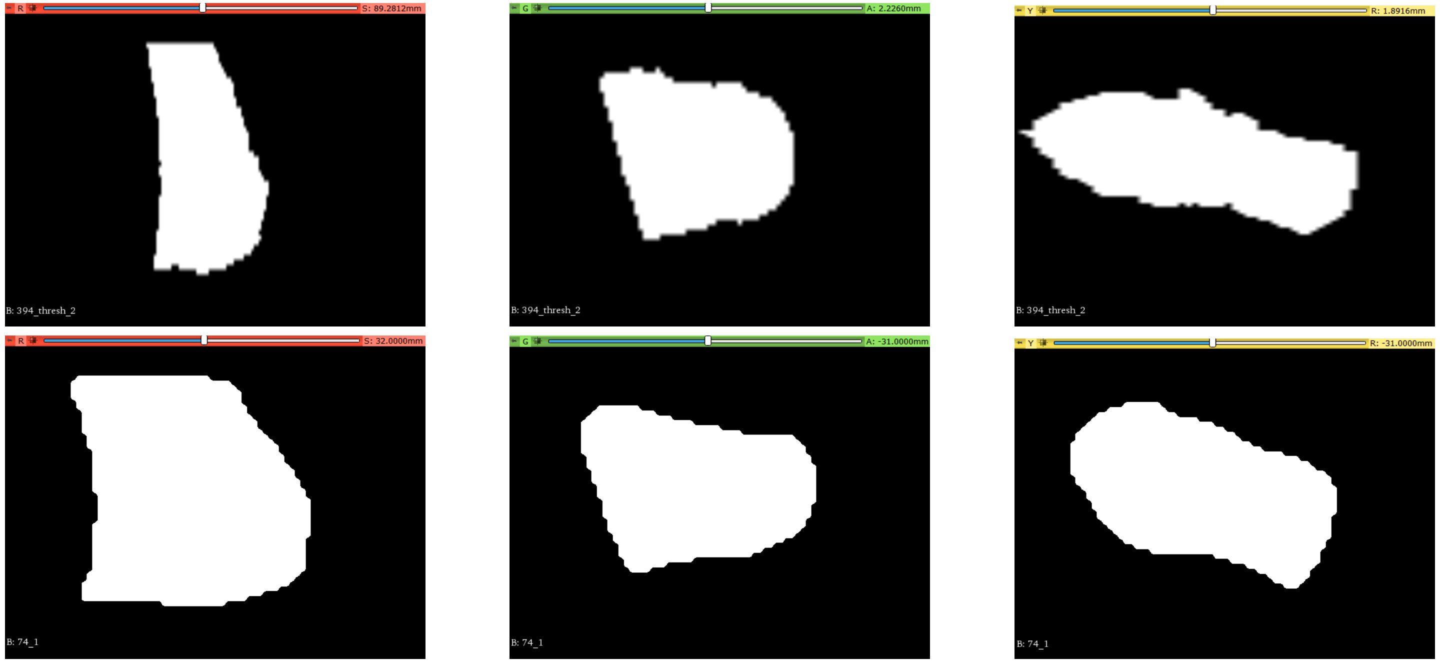
Results- U-Net++ (B-mode + PD) Early Fusion

- DSC: 0.9024; Jaccard: 0.8223 ; Hausdorff: 4.4721 ; MSD: 1.2012



GT mask

Predicted mask

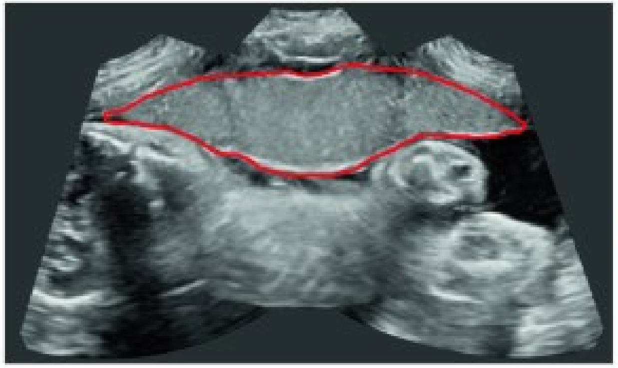


Next steps – Whole placenta segmentation

- Placenta size grows with the gestation age
- It is hard to capture entire placenta at late gestation
  - Limited field-of-view (FOV)
  - A single US probe have too small FOV to capture the whole placenta
- The Need – Stitching
  - The entire placenta can be captured by acquiring, aligning, and stitching multiple 3D US images to get large FOV

Estimated gestational age (weeks)	Mean±SD	
	Placenta thickness (mm)	Estimated fetal weight (g)
15	22.6±2.5	147.0±16.5
16	22.5±1.9	181.5±17.4
17	26.0±0.0	212.5±0.0
18	24.0±0.2	233.3±40.0
19	27.6±2.8	330.5±21.7
20	29.1±5.6	357.8±31.2
21	27.8±4.9	421.7±36.5
22	31.5±5.2	542.5±63.9
23	31.2±3.4	599.8±65.2
24	31.9±3.9	691.5±64.6
25	30.7±2.7	805.3±46.0
26	33.2±3.4	963.5±68.9
27	34.0±3.2	1063.7±66.8
28	34.0±2.2	1235.2±69.2
29	35.5±4.9	1375.9±79.3
30	38.9±5.9	1539.3±211.9
31	36.0±5.3	1617.0±137.0
32	33.5±3.5	1766.6±206.7
33	38.8±6.4	2148.1±202.7
34	39.0±5.3	2348.1±106.1
35	41.4±11.6	2292.4±764.9
36	40.9±7.2	2710.0±275.2
37	40.1±4.8	2884.8±251.6
38	38.5±2.5	3148.4±505.4
39	39.3±4.4	3187.4±305.4
40	39.3±5.7	3304.8±284.6

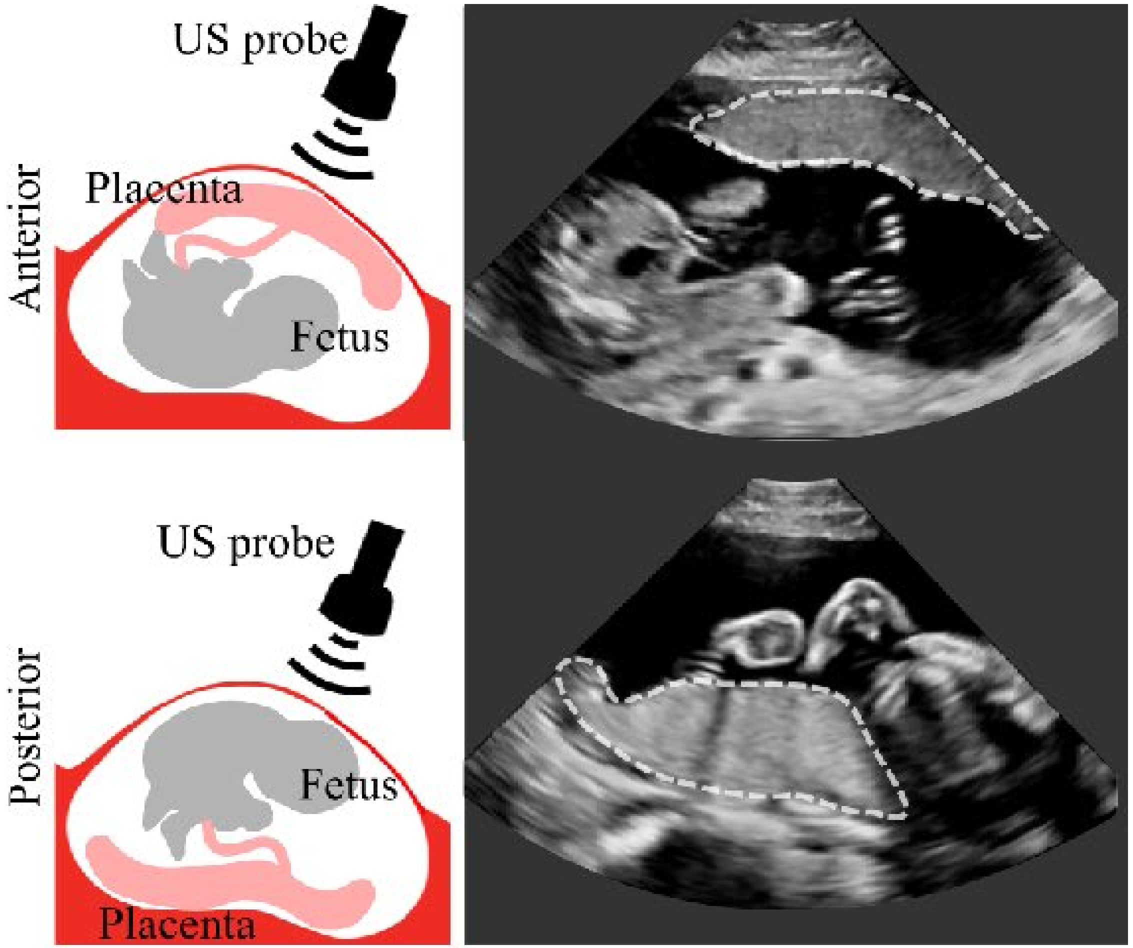
SD: Standard deviation



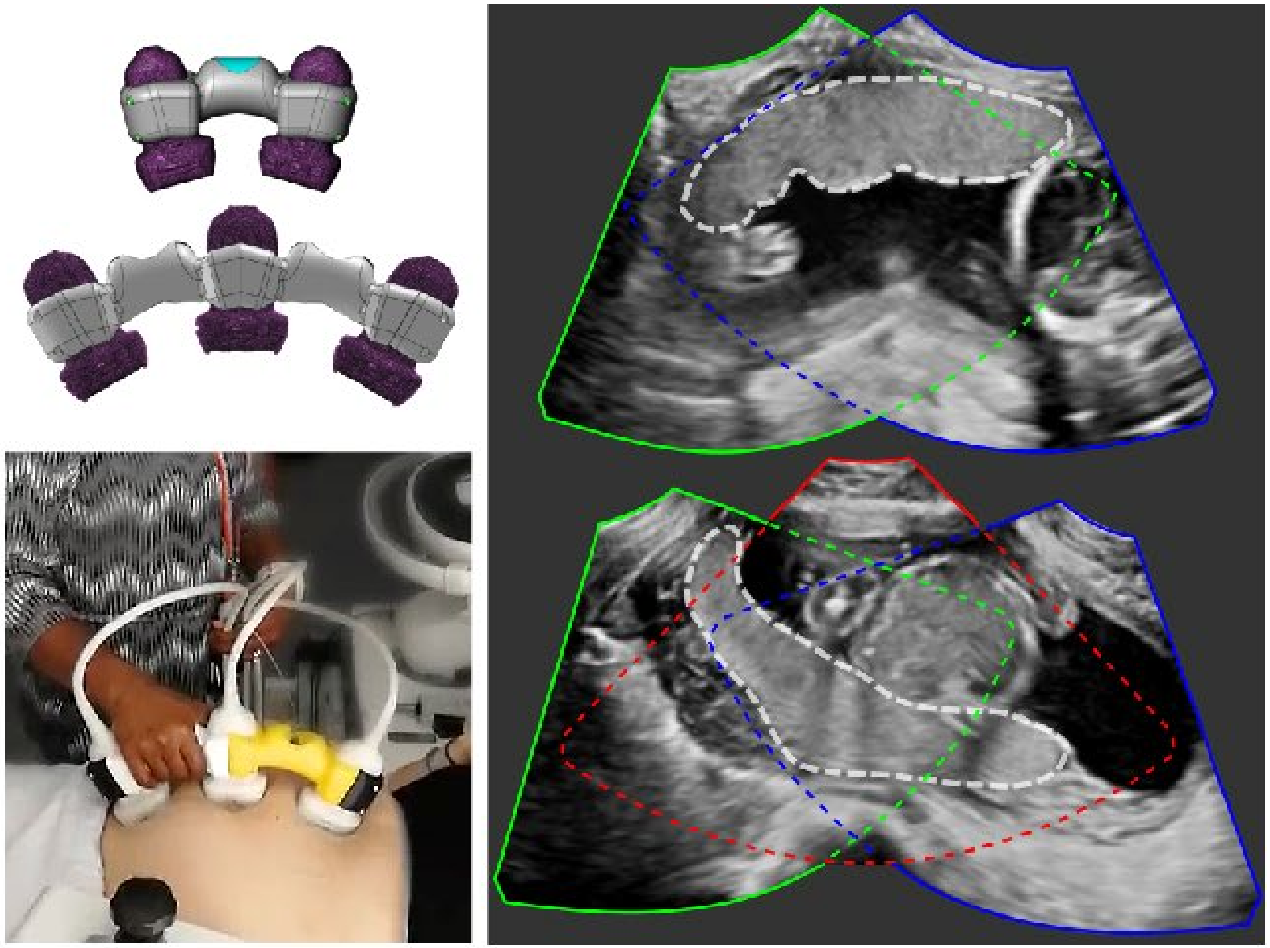
Source: Adeyekun et al. (2015). Relationship between 2-D ultrasound measurement of placental thickness and estimated fetal weight.
Image source: Zimmer et al. (2019). Towards Whole Placenta Segmentation at Late Gestation using multi-view US images. MICCAI.

Whole placenta segmentation

➢ Placenta size grows with the gestation age



(a) Single US images



(b) Multi-view US images

Concluding Remarks

- Computational methods have an increasing role in medical imaging
- **Challenges**
  - big raw data but limited curated data
  - combining imaging and non-imaging data
  - data visualisation
  - moving from 2D to 3D
  - explainable and interpretable models
  - ethical and legal dilemmas
- End-to-end has different connotations, depending on data and application!

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Questions?