

AI in Medicine: Making impact in Clinical Practice

Never Stand Still

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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

\triangleright Humans + Computers can achieve better performance than either alone

Harvard
Business
Review

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

Al 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."

Convolutional Neural Networks (CNNs)

- A class of deep neural networks suitable for processing 2D/3D data. For e.g., Images and Videos
- \triangleright CNNs can capture high-level representation of images/videos which can be used for endtasks such as classification, object detection, segmentation, etc.
- \triangleright A range of CNNs improving over the years

CNN Architecture

- \triangleright A typical CNN architecture consists of the following layers:
	- \triangleright Convolution layer
	- \triangleright ReLU layer (non-linearity)
	- \triangleright Pooling layer
	- \triangleright Flattening
	- \triangleright Fully-connected layer
	- \triangleright Output layer

 \triangleright There can be multiple steps of convolution followed by pooling, before reaching the fully connected layers.

Vision tasks

- \triangleright Image classification: Assigning a label or class to an image
- \triangleright Object detection: Locate the presence of objects with a bounding box and class of the located objects in an image
- \triangleright Semantic segmentation: Label every pixel (pixel-wise classification)
- \triangleright Instance segmentation: Differentiate instances

(a) Image Classification

(b) Object Detection

Cow

Cow

(c) Semantic Segmentation

(d) Instance Segmentation

Object detection with Faster R-CNN

Determine "what" and "where"

 \triangleright regress the coordinates of object and classify it

- ▶ Region Proposal: R-CNN, Fast R-CNN, Faster R-CNN, Mask R-CNN
	- \triangleright First propose the regions likely to include objects and second classify the regions and regress the BBOX
- R-CNN: Detect RoI by Selective Search (SS) on images, resize the regions to fixed size and let them flow into CNN respectively, and classify them into the classes by SVM

R-CNN: Regions with CNN features

Object detection with Faster R-CNN

- \triangleright R-CNN Issues
	- \triangleright A split between region proposal and classification
	- \triangleright Too slow selective search (can't be used in real-time)
- Fast R-CNN: Do convolution first and then selective search. Adopted RoI pooling to crop fixed vector from the feature map.

\triangleright Fast R-CNN:

- \triangleright RoI Pooling
- \triangleright Speeded up the forward propagation by sharing convolution

Object detection with Faster R-CNN

 \triangleright Fast R-CNN Issues

 \triangleright A split between region proposal and classification was not improved

- \triangleright Selective Search still too slow
- **► Faster R-CNN**
	- Adopted Region Proposal Network (RPN) and abolish Selective Search
	- \triangleright Achieved high performance and high speed

Biomedical Image Segmentation with U-net

- U-net learns segmentation in an end-to-end setting
- Proven to be very powerful segmentation tool in scenarios with limited annotated data
- Doesn't contain any fully connected layers

T2w MRI Volume

Ground truth Segmentation

U-net Architecture

Case Study: Automated Analysis of 4D Fetal Echocardiogram*

\triangleright 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].

Background

- \triangleright Heart is the **first functional organ** that develops in a fetus.
- \triangleright Starts beating by **Week 4**
- \triangleright 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

Background

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

Mitral Valve showing the fibrous annulus ring surrounding the leaflet.

Adult Annulus Segmentation [1]. *Joint work with Philip, Ferrieira, Tomar, Chawla, Welsh, Stevenson

Datasets

Dataset-1

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

\triangleright Dataset-2

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

 \blacktriangleright

Data Preparation

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

1. Annulus Segmentation

- \triangleright 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

- \triangleright For TAPSE measurements, r=0.61 and RMSE=0.14 cm
- \triangleright For MAPSE measurements, r=0.30 and RMSE=0.18 cm
- \triangleright 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.

Annulus Segmentation - Issues

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

Figure : Schematic depicting need for Registration.

2. Whole Heart Segmentation

- \triangleright Instead of identifying just the SEPTUM for orientation-problem redefined to obtain it as a byproduct
- \triangleright The heart is modelled consisting of:
	- \triangleright Left and Right Atrium (LA, RA)
	- Left and Right Ventricles (LV, RV), and
	- \triangleright Tricuspid and Mitral Annulus (TA, MA)
- \triangleright Dataset-1 could not be used
	- \triangleright Whole heart was not in view
	- \triangleright Zoomed in version of the thorax

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

Datasets

\triangleright Dataset-2

- 385 Ultrasound Volumes (Acquired by 1 operator)
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		- ≥ 2 Annotators
		- \geq 30 Volumes (each annotated in triplicates by each annotator)

Issues

\triangleright Inter and Intra observer Variability

Architectures

- \triangleright CNN based models:
	- U-Net
	- V-Net
	- **≻** Res-UNet

- \triangleright Transformer-based models:
	- **▶ TransBTS**
	- Unet-R

Training details

\triangleright Training data:

\triangleright Training Parameters

Whole Heart Segmentation

1. Position Fixing

- \triangleright Manually repositioned to
	- \triangleright Apex down flipping data up/down
	- \triangleright Mitral Annulus visible on the right side – flipping data left/right

2. Localisation (along coronal axis)

 \triangleright SVM classifier trained to classify coronal slices to foreground / background

Flowchart outlining the proposed pipeline.

Segmentation results

- \triangleright No matter the architecture used, clear performance improvement with data enhancement
- \triangleright 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	МA
CNN-Based	U -Net [7]	A	0.60	0.67	0.40	0.69	0.48	0.37
		$\mathbf P$	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
		${\bf P}$	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
		$\mathbf P$	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
		${\bf P}$	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
		$\mathbf P$	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

- \triangleright Physical size constraints reflected in segmentation results
	- Segmentation performance of ventricles > atria > annuli
- \triangleright 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
	- \triangleright TransBTS very similar architecture to U-Net except for the transformer block results very close to U-Net
- Mean DSC improvement after data enhancement:
	- \triangleright U-Net: 0.12
	- \triangleright V-Net: 0.18
	- \triangleright Res-UNet: 0.28
	- \triangleright TransBTS: 0.22
	- \triangleright UNETR: 0.11

3. Automatic segmentation of human placenta in 3D Ultrasound

- \triangleright The placenta is a critical and complex organ that provides oxygen and nutrition to the growing fetus and removes waste from its blood
- \triangleright Fetal health strongly depends on the functionality of the placenta
- \triangleright Any abnormality of the placenta could be harmful to the fetus and the mother
- \triangleright 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
- \triangleright 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
- \triangleright Manual segmentation of the placenta is time-Manual segmentation of the placenta is time-
consuming and have high inter-observer and intra 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 emmerge and birth complications such as PAS, fetal growth restriction, and suspicion of intrauterine fetal demise

Dataset

- \triangleright Total 400 studies having Gray-scale (Bmode) 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:
	- \triangleright use same image in case there is only one annotated (segmented) image
	- \triangleright compute intersection image (i.e., voxelwise logical AND operation) in case there are two annotated (segmented) images
	- \triangleright compute image based on majority voxel-wise voting in case there are three annotated (segmented) images

◎ 巻 ▼ Axial ▼ | 0_thres

Dataset Pre-processing

(a) B-mode Axial

(b) B-mode Coronal

- \triangleright Pre-processing needed to make data suitable for the framework.
- \triangleright Pre-processing:
	- 3D volumes should be of same isotropic size (same size in x, y, z direction)
	- \triangleright data to be provided in numbered format with each sample in folders from 0 to X, where X is the maximum number of studies
- \triangleright All data (B-mode US, Power Doppler US, and annotated masks) were resized to 64 x 64 x 64
- \triangleright B-mode and PD volumes are normalized by rescaling pixel values between range 0 to 255.

Experimental setup

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

Fusion strategies

- \triangleright Early-fusion: concatenates original features at the input level
- Multi-stage or joint-fusion: concatenates extracted features
- \triangleright Late-fusion: aggregates predictions at the decision level

Methodology

Results

Segmentation results comparing U-Net model performance for five folds of the final dataset with each fold having $\#$ train=240, $\#$ validation=80, and $\#$ test=80 3D ultrasound volumes. Results are averaged values over all studies in the test set with \pm standard deviation of metric for that test set.

Segmentation results comparing U-Net $++$ model performance for five folds of the final dataset with each fold having $\#$ train=240, $\#$ validation=80, and $\#$ test=80 3D ultrasound volumes. Results are averaged values over all studies in the test set with \pm standard deviation of metric for that test set.

Results

Segmentation results with and without data augmentation. Results are averaged values over all studies in the test set with \pm standard deviation of metric for that test set.

Segmentation results applying applying early fusion, intermediate fusion, and late fusion for the two modalities, namely, B-mode and Power Doppler 3D ultrasound volumes. Results are averaged values over all studies in the test set with \pm standard deviation of metric for that test set.

Qualitative Results

\triangleright DSC: 0.7135 Jaccard Index: 0.5546 Hausdorff Distance (HD95): 9.4339 MSD: 304.4385

(b) B-mode Coronal

(c) B-mode Sagittal

(d) PD Axial

(e) PD Coronal

(f) PD Sagittal

(g) GT Axial

(j) Predicted Axial

(h) GT Coronal

(k) Predicted Coronal

(i) GT Sagittal

(I) Predicted Sagittal

Singh *et al.*, "Automatic 3D Multi-modal Ultrasound Segmentation of Human Placenta using Fusion strategies and Deep Learning", Ultrasound in Medicine and Biology, 2023 [Submitted] 37

Qualitative Results

 \triangleright DSC: 0.9039 Jaccard Index: 0.8247 Hausdorff Distance (HD95): 3.0000 MSD: 0.7189

(a) B-mode Axial

(b) B-mode Coronal

(c) B-mode Sagittal

(d) PD Axial

(f) PD Sagittal

(g) GT Axial

(e) PD Coronal

(h) GT Coronal

(i) GT Sagittal

(k) Predicted Coronal

(I) Predicted Sagittal

Singh *et al.*, "Automatic 3D Multi-modal Ultrasound Segmentation of Human Placenta using Fusion strategies and Deep Learning", Ultrasound in Medicine and Biology, 2023 [Submitted] 38

Next steps – Whole placenta segmentation

- \triangleright Placenta size grows with the gestation age
- \triangleright 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
- \triangleright The Need Stitching
	- \triangleright The entire placenta can be captured by acquiring, aligning, and stitching multiple 3D US images to get large FOV

39 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

(a) Single US images

 \triangleright Placenta size grows with the gestation age

(b) Multi-view US images

Other Medical Imaging and Informatics projects

Analysis and Enhancement of MR Neuroimages

Q: What is the plane of this MRI? A: Sagittal

(b) Plane category example

Q: The CT scan shows what organ system? A: Spine and contents

(c) Abnormality category example (d) Organ system category example

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*Projects shown are undertaken by PhD, MPhil and Hons Thesis candidates and are supervised by academics in Computer Vision group at UNSW CSE in collaboration with clinical collaborators.

41

Other Medical Imaging and Informatics projects

Vertebral Compression Fracture (VCF) ral Compression Fracture (VCF) **Prostate Segmentation from MR Images** Multimodal Severity Detection for Black in the United Severity Detection for Black Detection for Black in the United Severity Detection for Black in the **Lung Disease Ground Truth** Prediction Comparison mage Trut) UNet (a) (c) **Quantification and Severity Estimation of Automated Segmentation of Coronary Multi-organ and Tumor Segmentation from Abdominal CT images Acute Diverticulitis Arteries** Case#1 Output#1 **TGNet** Case#2 Output#2 Axial CT w/ Contrast (2)

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Concluding Remarks

Computational methods have an increasing role in medical imaging

Challenges

- \triangleright big raw data but limited curated data
- \triangleright combining imaging and non-imaging data
- \triangleright data visualisation
- moving from 2D to 3D
- \triangleright explainable and interpretable models
- \triangleright ethical and legal dilemmas

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Questions?