Smart learning on Ultrasound Image Features and Quantitative Parameters for Deep Detecting and Classifying the Degree of Soft Tissue Lesions

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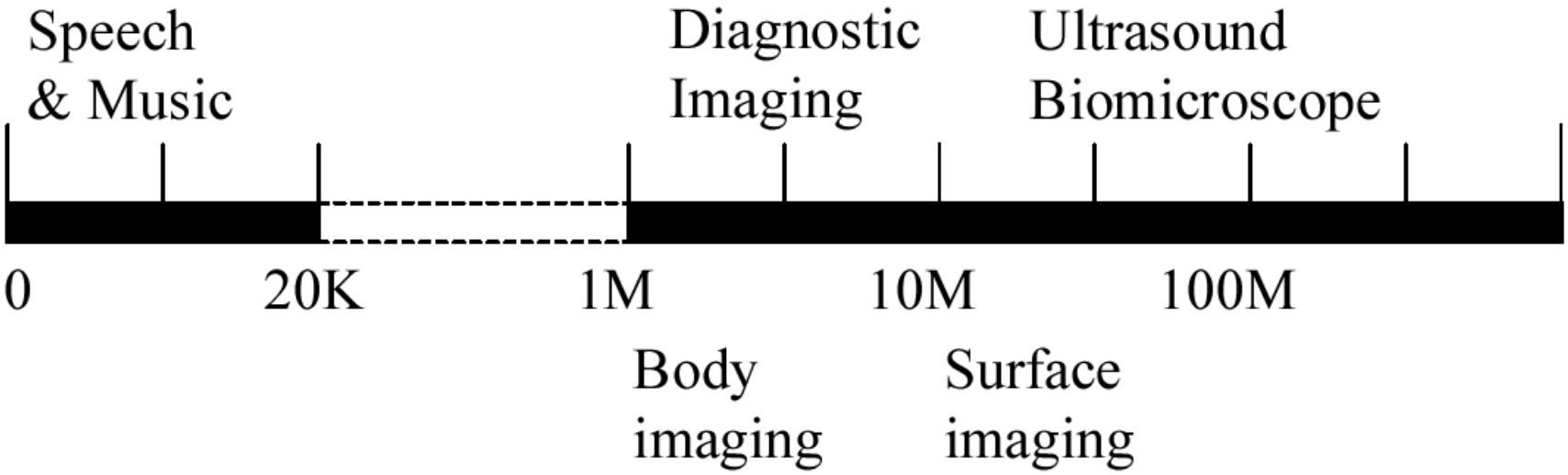
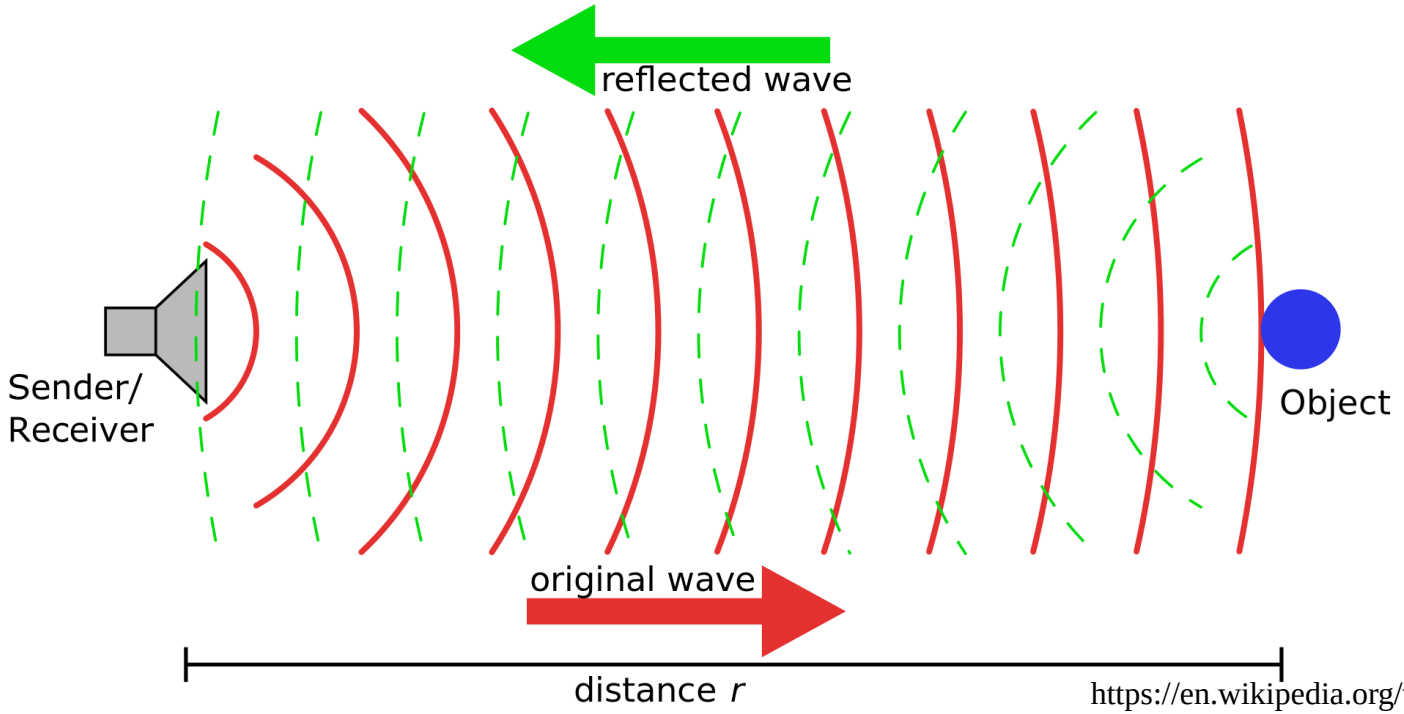
Outline

- Fundamentals of Ultrasound Imaging
- Liver Fibrosis Classification by CNN Models Trained with Ultrasonic Images
- Machine/Deep Learning with Compounding Contrast-Enhanced Ultrasound Image and Quantitative Parameters for Muscle Injury Classification

Fundamentals of Ultrasound Imaging

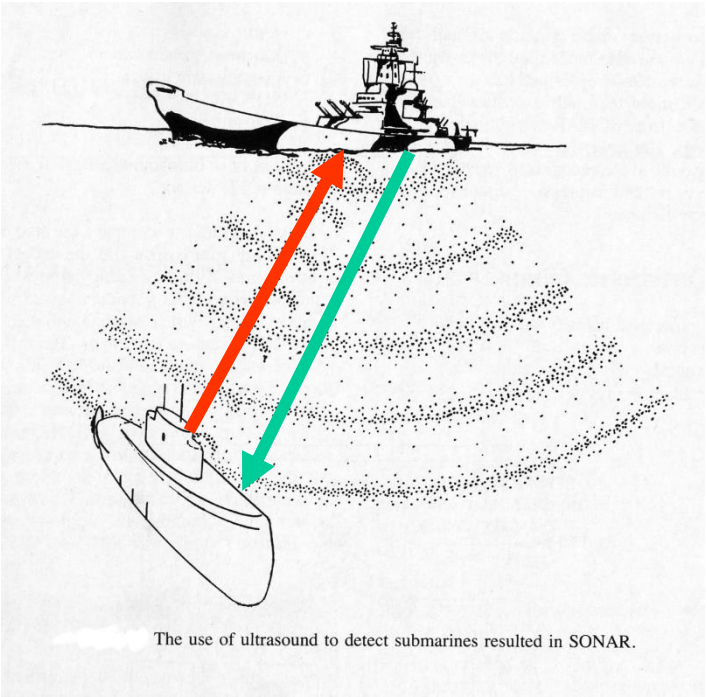
Ultrasound is like the ordinary sound that we hear except it has a frequency higher than 20 KHz





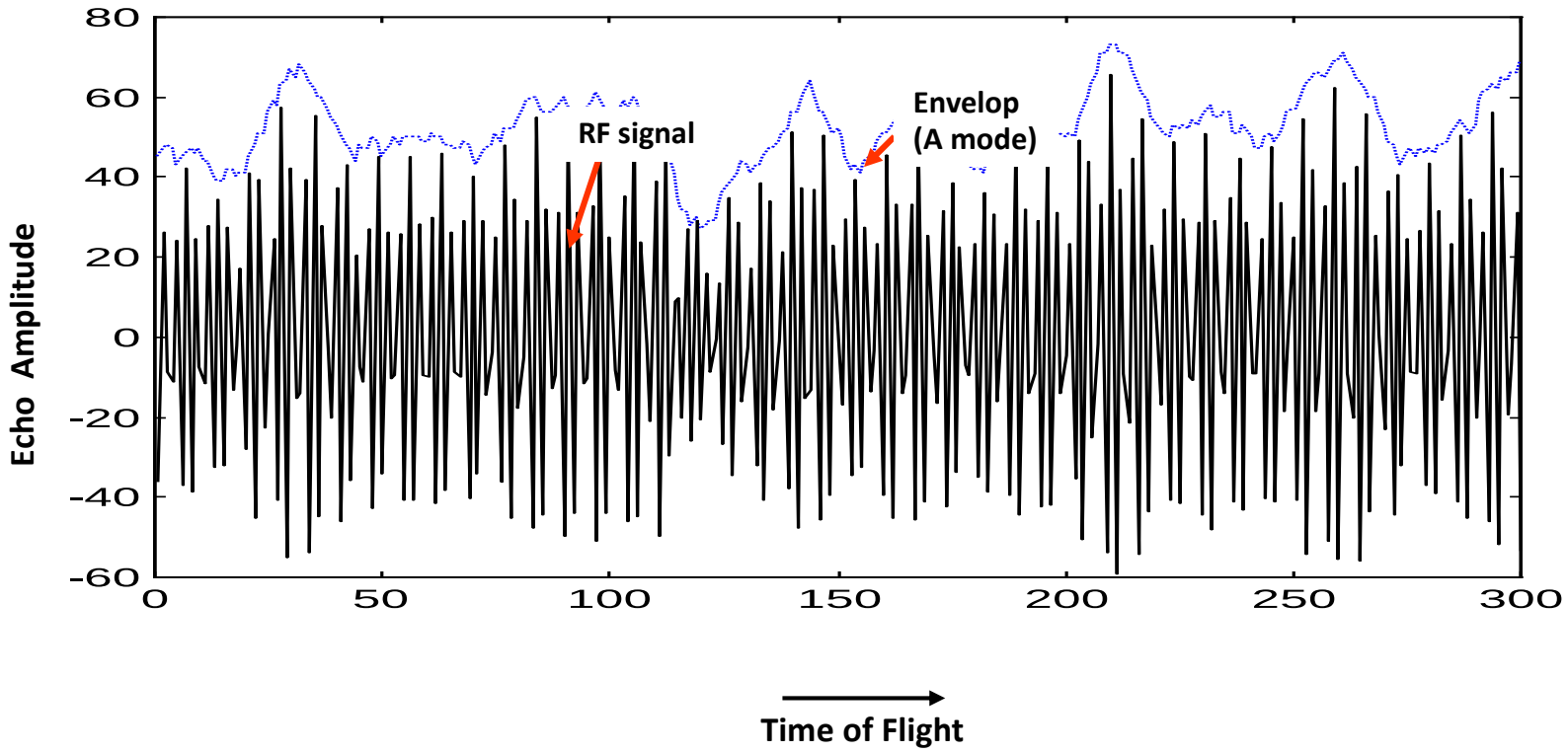
https://en.wikipedia.org/wiki/Ultrasound

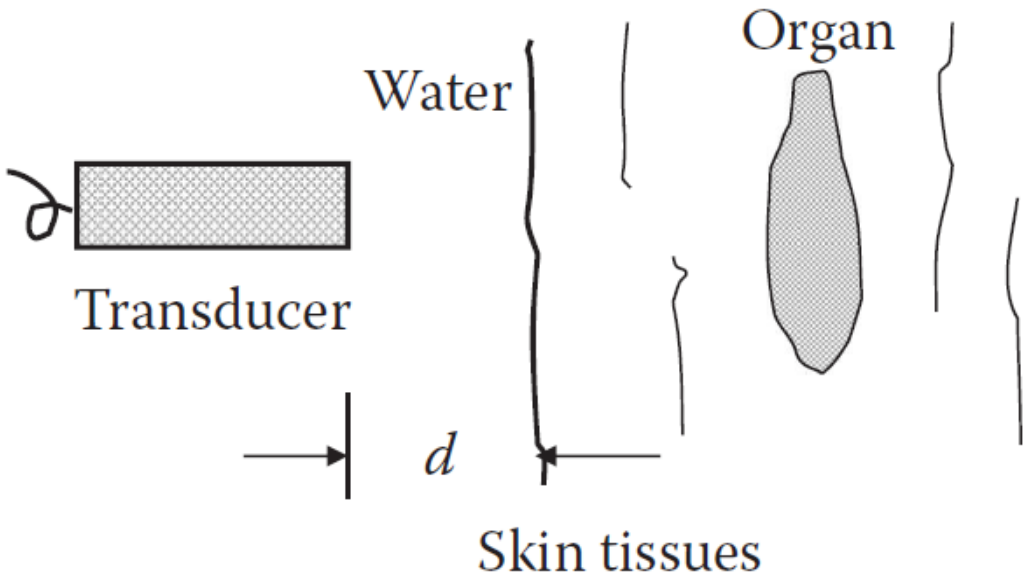
Sonar detection

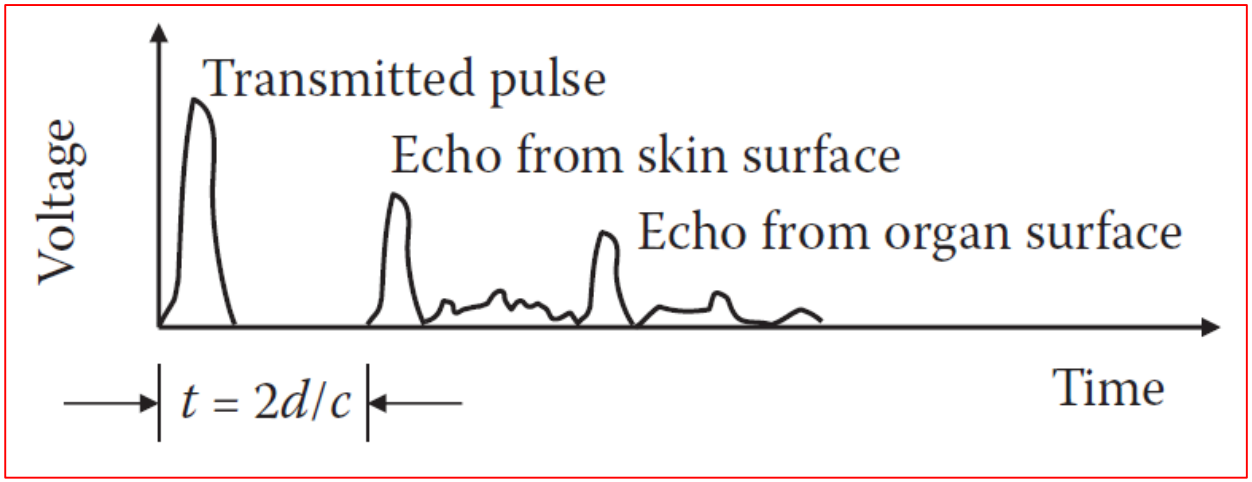


Typical Ultrasound Signal/Imaging Processing

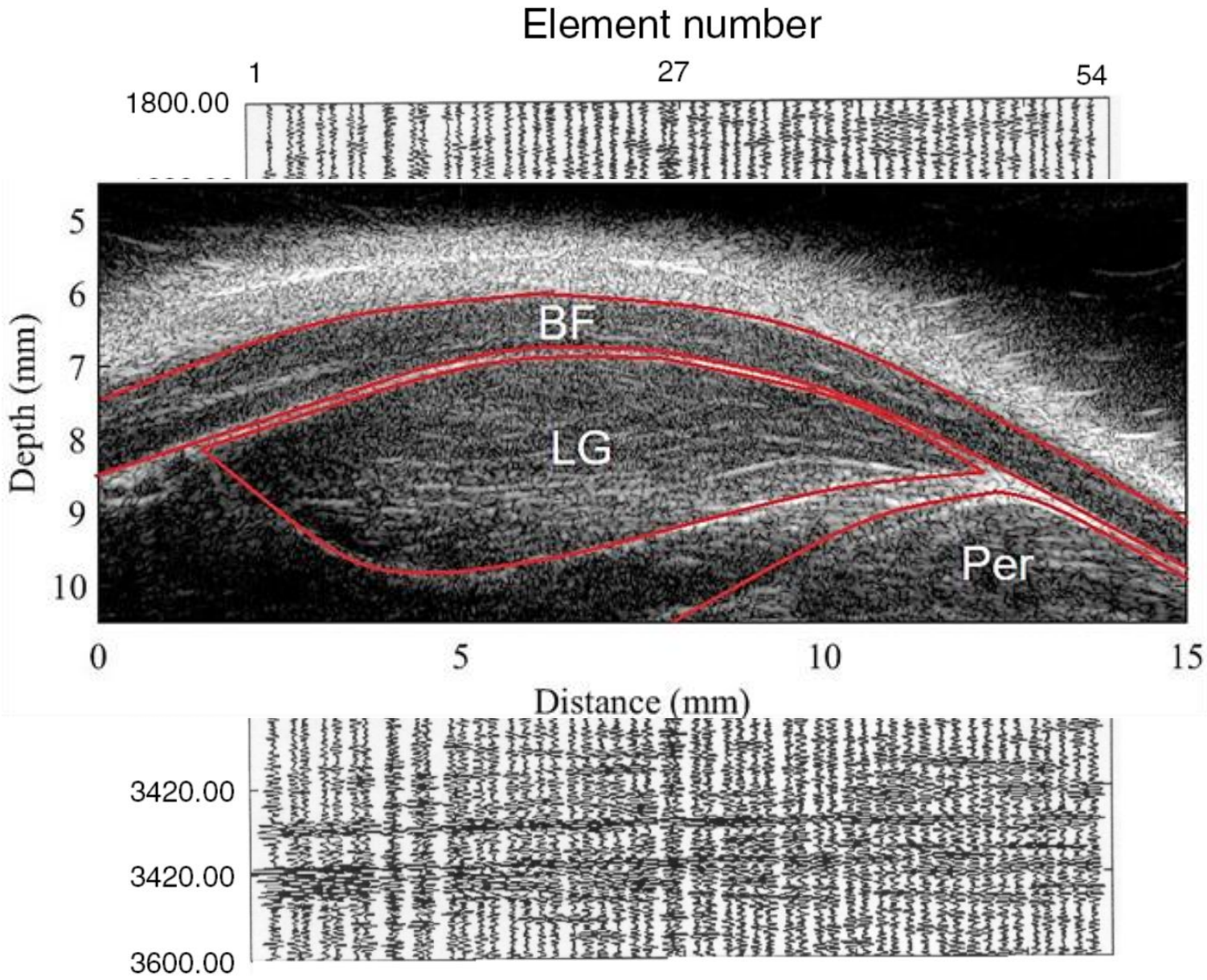
RF signals → Filtering → Envelope Detection → Compression → Scan Conversion

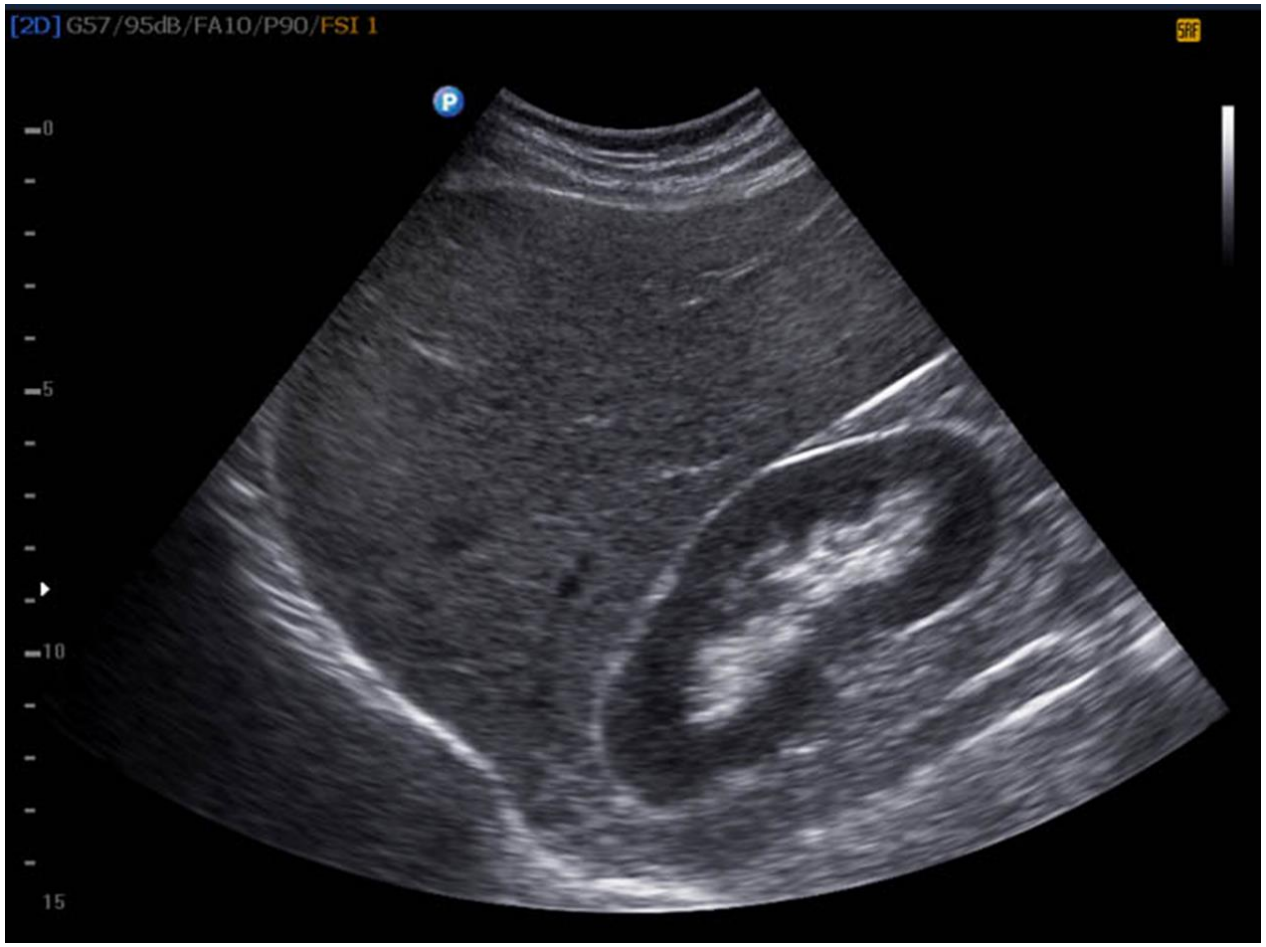



Organ
Water
Transducer
d
Skin tissues


Transmitted pulse
Echo from skin surface
Echo from organ surface
Voltage
t = 2d/c
Time

Ultrasound Scan Lines / Image Formation





- Organ?
- Location?
- Size/volume?
- benign/malignant?
- Phase?
- Severity?

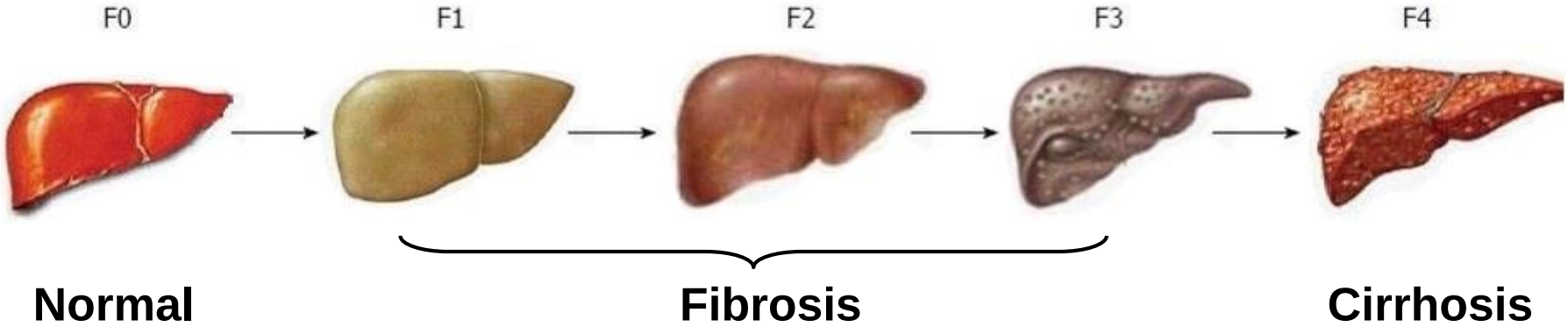
Liver Fibrosis Classification by CNN Models Trained with Ultrasonic Images

Introduction – Liver Fibrosis

- Excessive accumulation of extracellular matrix proteins [1]

WHO [2]	Global Infection	Death each year
Hepatitis B	257 m	887 k
Hepatitis C	71 m	399 k

- **Liver fibrosis stages** [3]

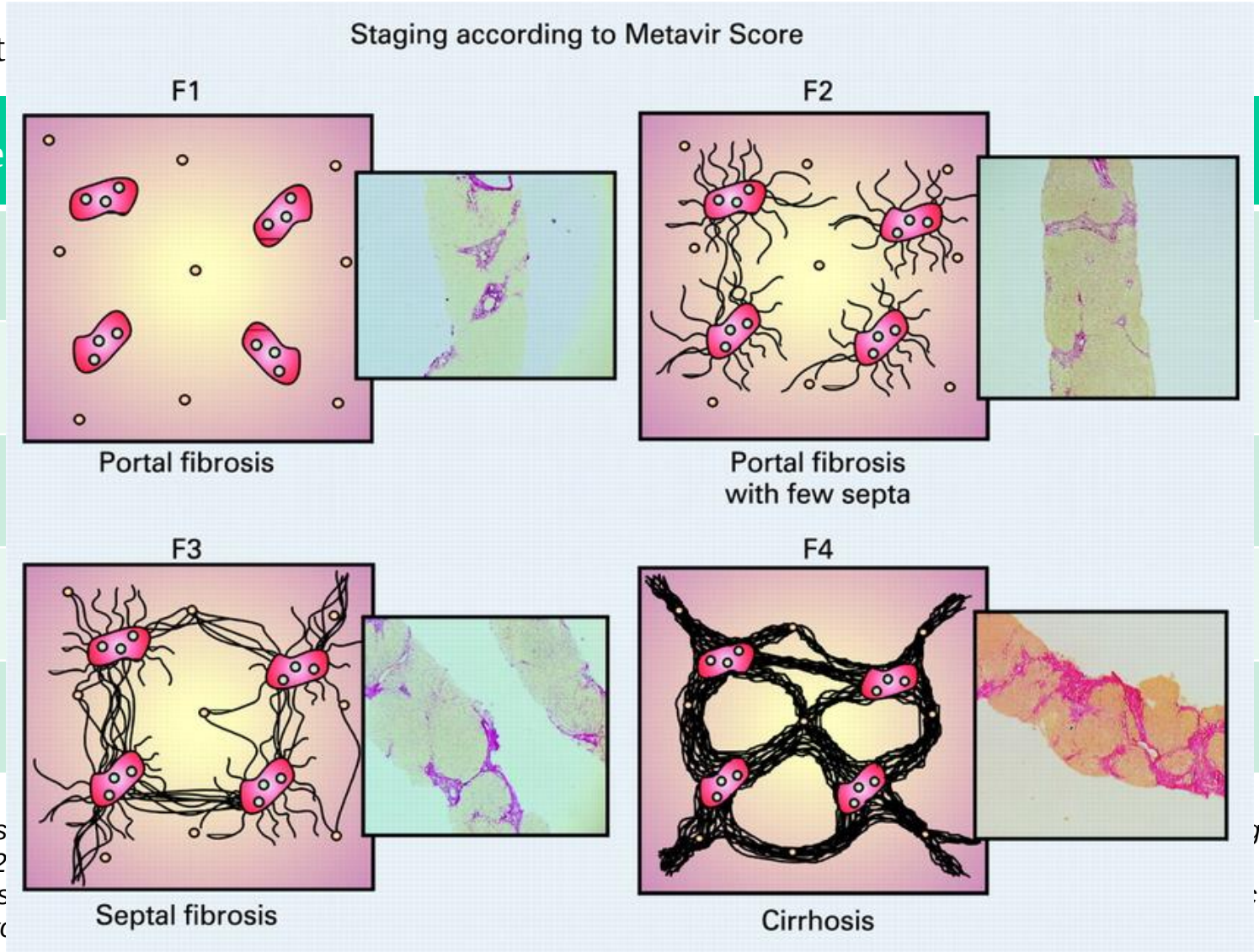


[1] R. Bataller and D. A. Brenner, "Liver fibrosis," Journal of clinical investigation, vol. 115, no. 2, p. 209, 2005.
[2] WHO, "Global hepatitis report, 2017," p. 83, April 2017.
[3] O. Ramos-Lopez, E. Martinez-Lopez, S. Roman, N. A. Fierro, and A. Panduro, "Genetic, metabolic and environmental factors involved in the development of liver cirrhosis in Mexico," World journal of gastroenterology, vol. 21, no. 41, p. 11552, 2015.

Introduction – Liver Fibrosis Stages

- Int

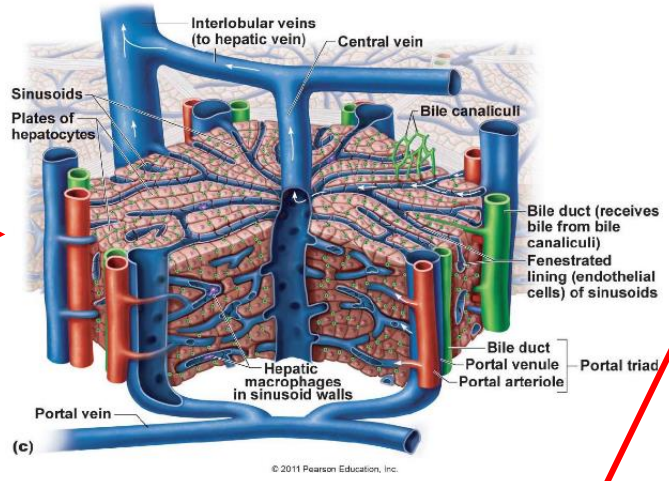
Stage
F0
F1
F2
F3
F4



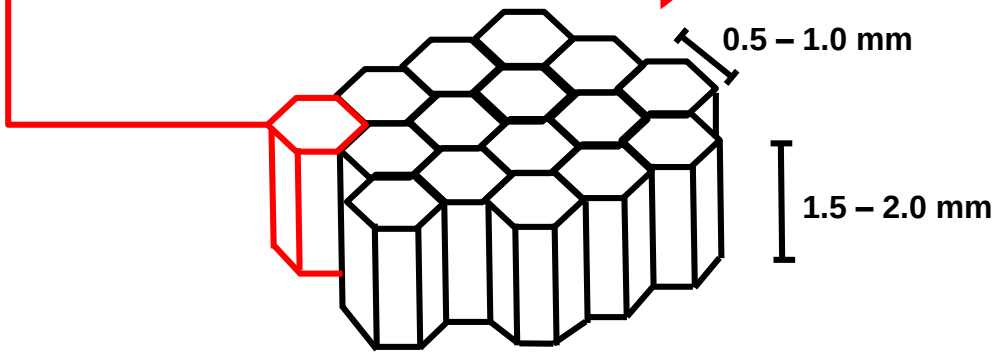
[1] K. P. Batts ... gical pathology, vol. 19, no. 12

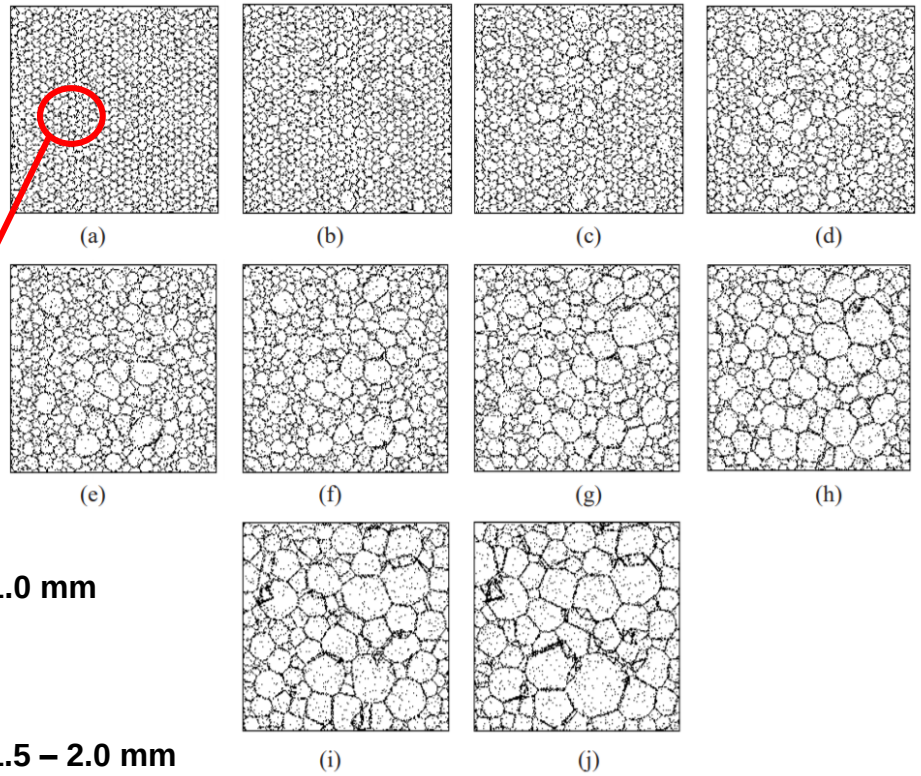
[2] P. Bedos ... hepatitis C," Hepatology, vo

Introduction – Liver Lobule Anatomy



[1]

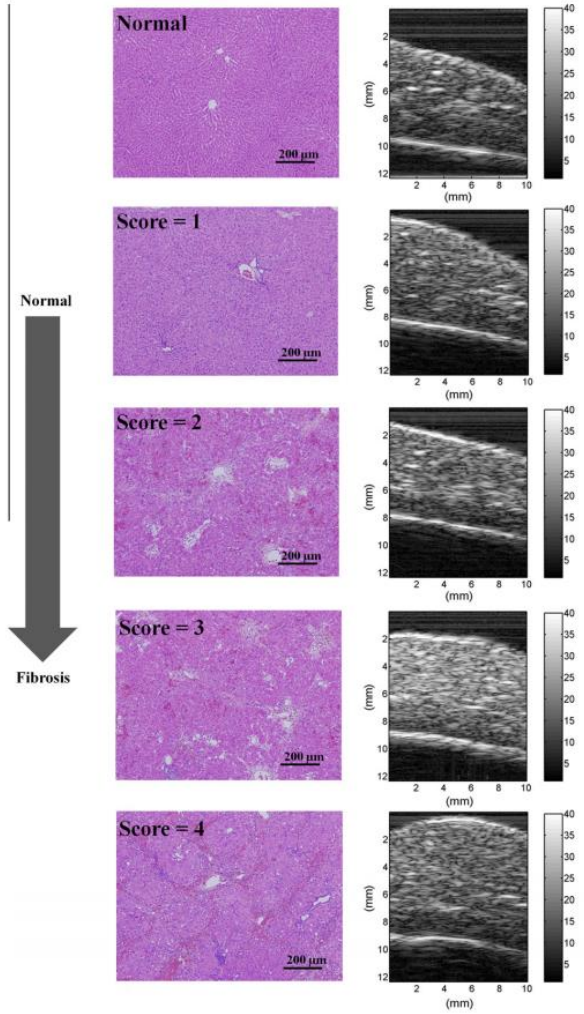


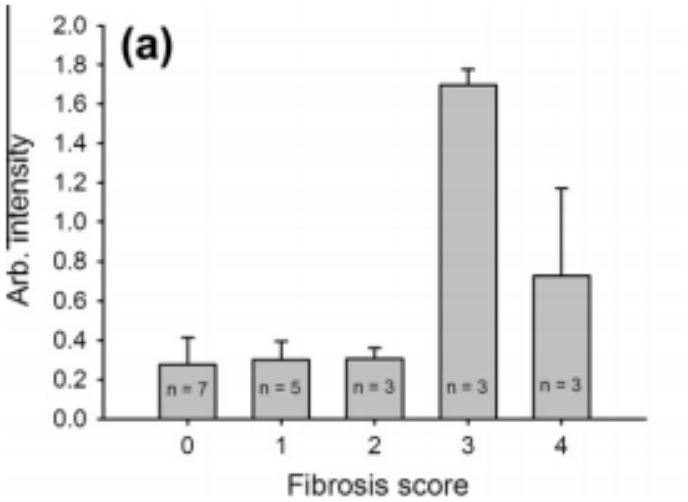


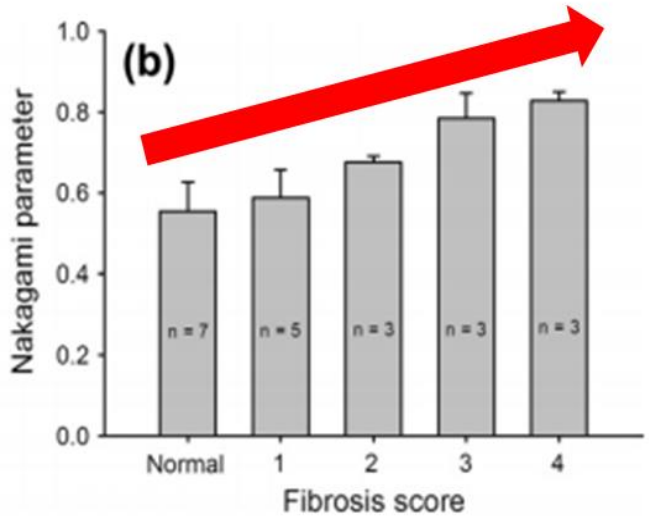
[2]

[1] Liver: Microscopic Anatomy • Copyright © 2011 Pearson Education, Inc.
[2] T. Yamaguchi, H. Hachiya, and N. Kamiyama, "Modeling of the cirrhotic liver considering the liver lobule structure, "Japanese journal of applied physics, vol. 38, no. part 1, pp. 3388-3392, 1999.

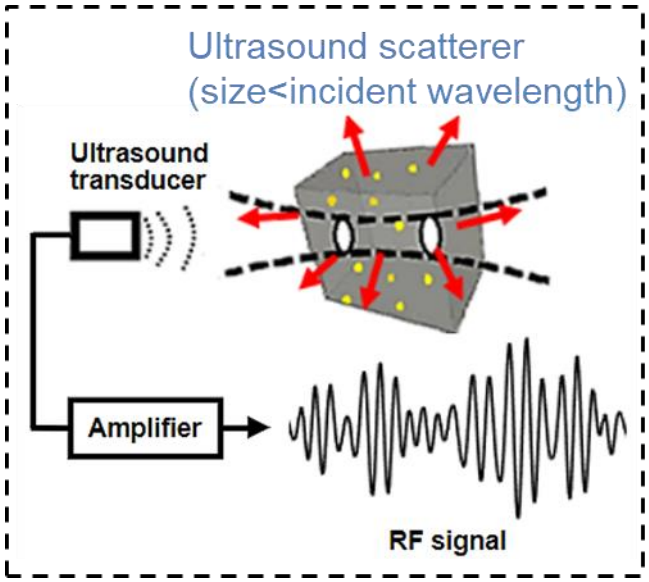
Literature Review – *ex-vivo study*

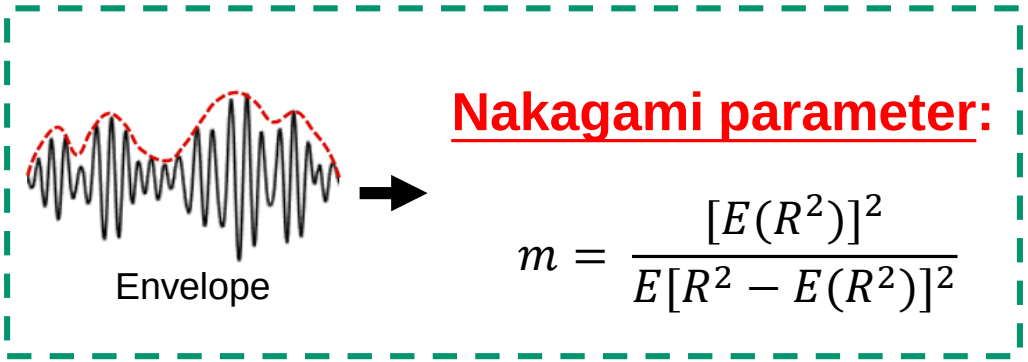


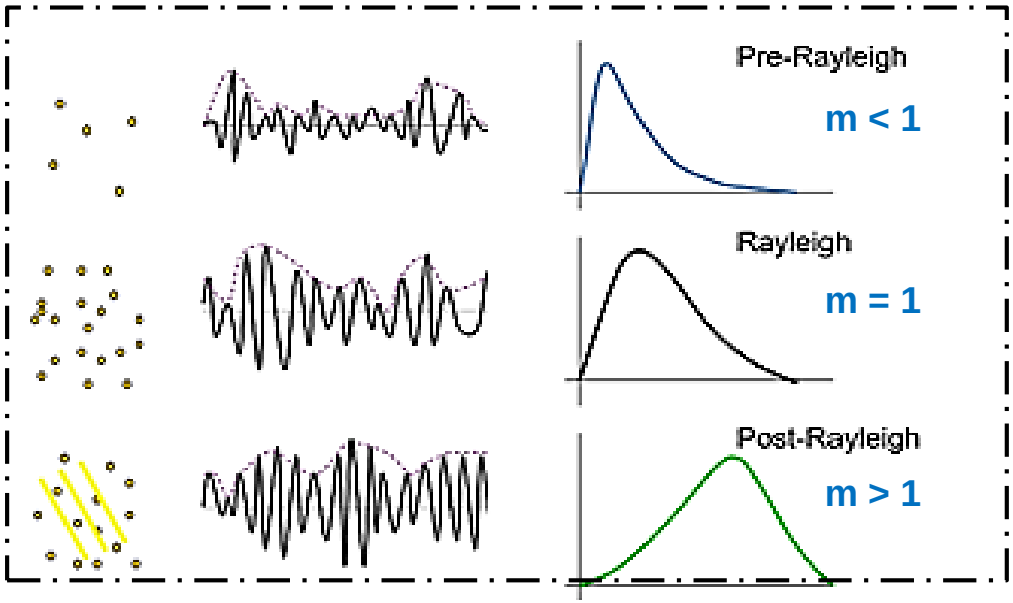




M.-C. Ho et al., "Using ultrasound Nakagami imaging to assess liver fibrosis in rats," Ultrasonics, vol. 52, no. 2, pp. 215-222, 2012.

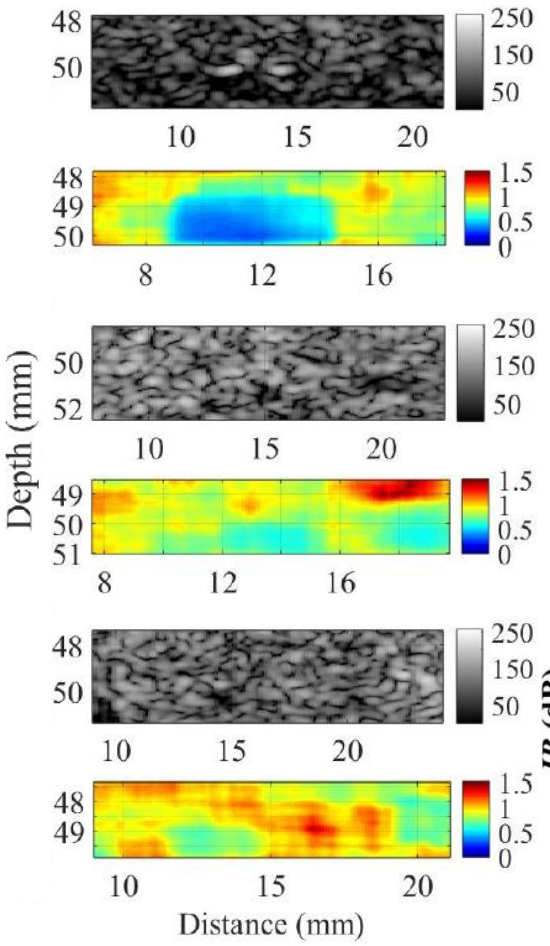




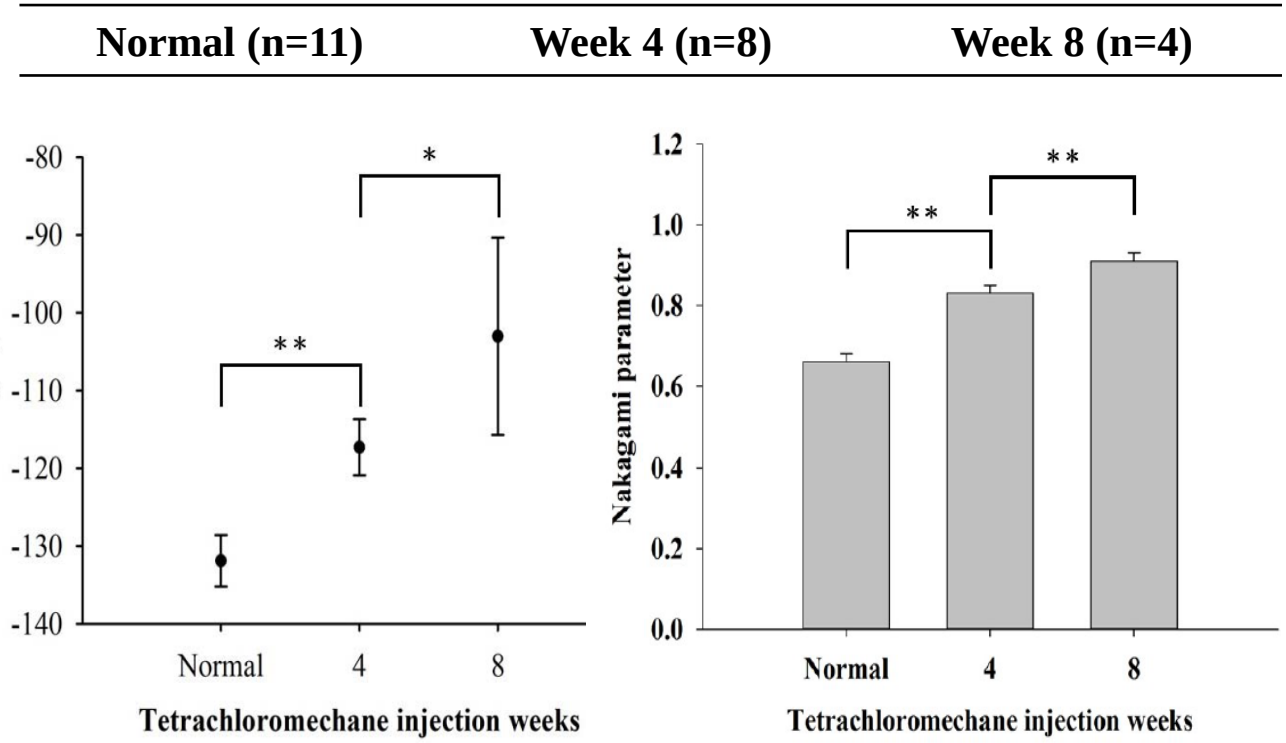


P.M. Shankar, “A general statistical model for ultrasonic backscattering from tissues,” *IEEE Trans. Ultrason. Ferroelec. Freq. Contr.,* 2000.

Literature Review – *in-vivo study*

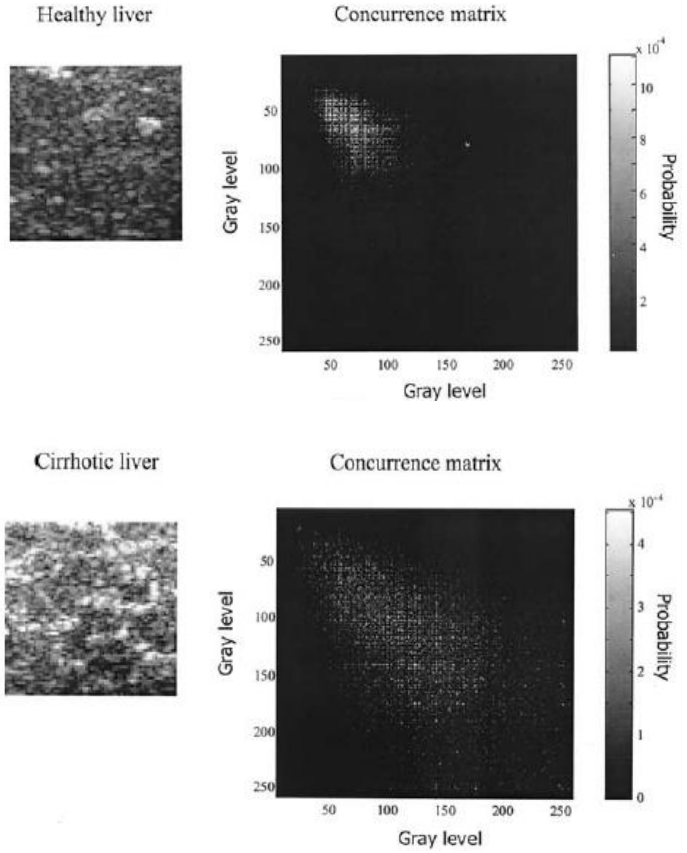


- IB and Nakagami-*m* parameter: increase with liver fibrosis stages
- Nakagami images: shape of backscattering PDF from pre-Rayleigh to post-Rayleigh

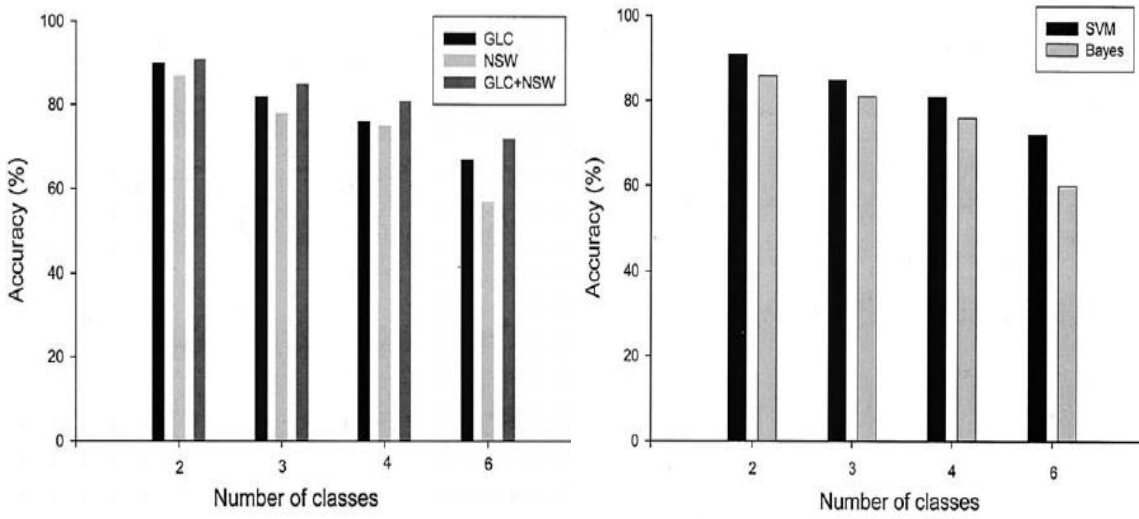


Literature Review – AI with image feature

Liver cirrhosis classified with **Gray-Level Concurrence Matrix** (**GLCM**)



- ✓ Non-separable Wavelet Transform (**NSW**)
- ✓ Support Vector Machine (**SVM**)
- ✓ Bayes Classifier (**Bayes**)



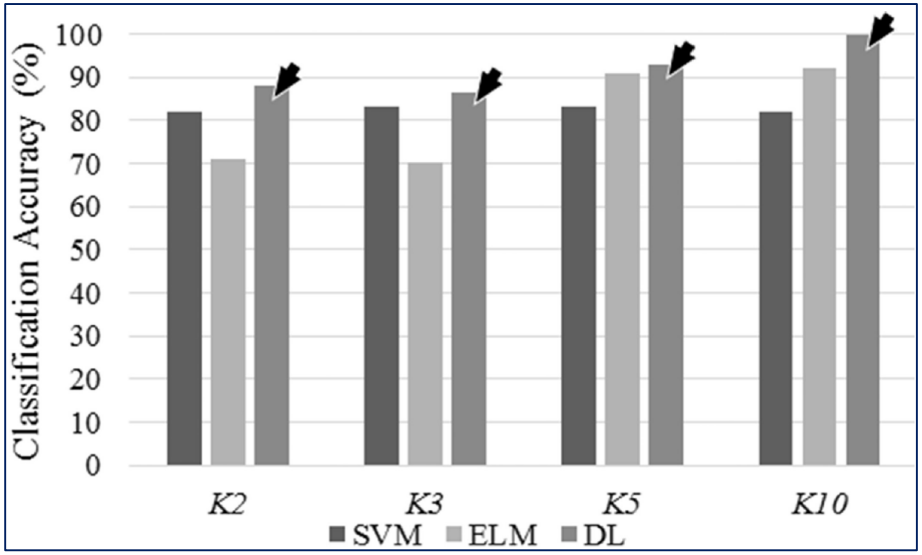
Number of classes	Accuracy in different fibrosis grade (%)						
	5	4	3	2	1	0	Overall
2		90			92		91
3		90		85		60	85
4	80	82.9		85		60	81
6	80	88.6	60	53.3	100	40	72

W.-C. Yeh, S.-W. Huang, and P.-C. Li, "Liver fibrosis grade classification with B-mode ultrasound," Ultrasound in Medicine and Biology, vol. 29, no. 9, pp. 1229-1235, 2003.

Literature Review – AI classification

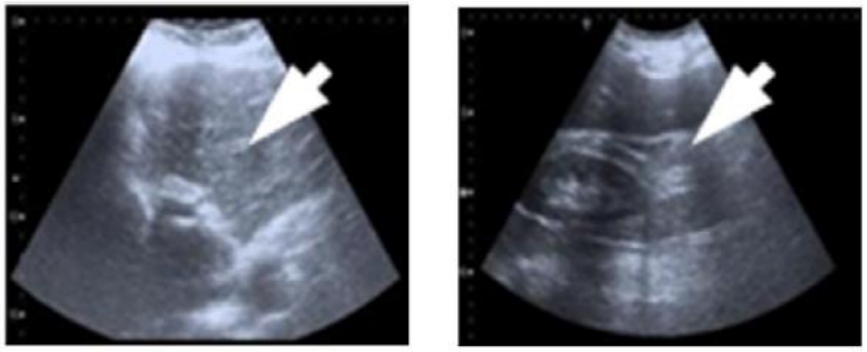
- ✓ Support Vector Machine (SVM)
- ✓ Extreme Learning Machine (ELM)
- ✓ **Deep Learning (DL)** → CNN

CNN has the best performance

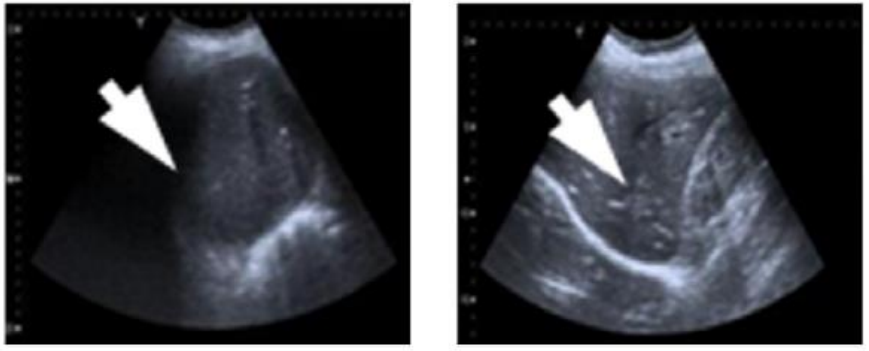


Liver cirrhosis identified with CNN

Normal (N = 27)



Abnormal (N = 36)



M. Biswas et al., "Symtosis: a liver ultrasound tissue characterization and risk stratification in optimized deep learning paradigm," Computer methods and programs in biomedicine, vol. 155, pp. 165-177, 2018.

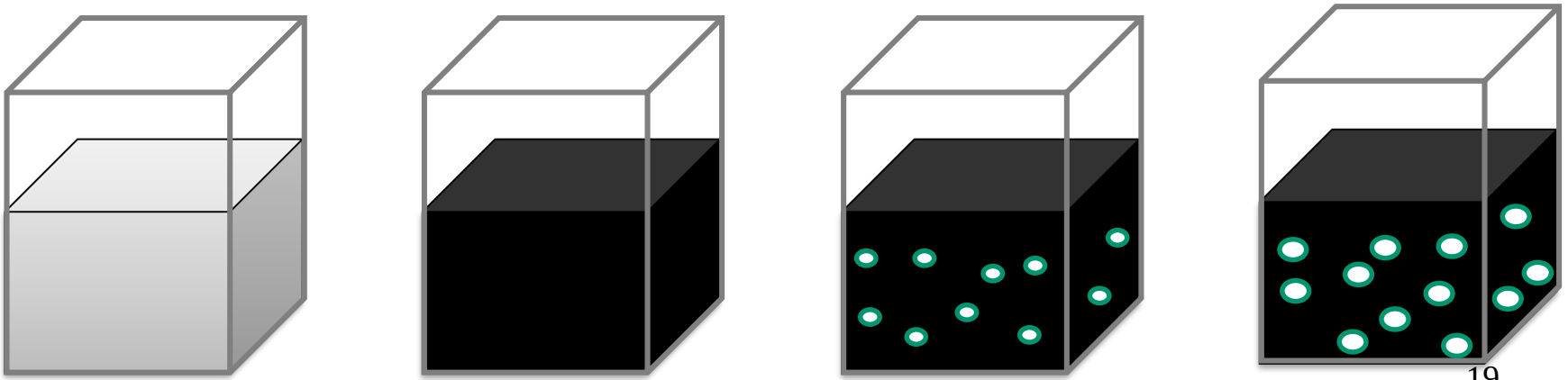
Objectives

- Building CNN models with ultrasonic images for liver fibrosis stages classification
- Consider Nakagami-*m* parameter as ground truth label
- Use machine learning and image processing techniques to improve the accuracy of classification

Materials & Methods – Phantom Simulation

ID	Graphite	Glass bead	DD water	N-propanol	Gelatin	Formaldehyde
A	1.5 %	X	85.43 %	7.72 %	5.04 %	0.05 %
B	3.0 %	X	83.93 %			
C		45 micron				
D		75 micron				

- Acquire 100 images from each phantom (training: 80, testing: 20)



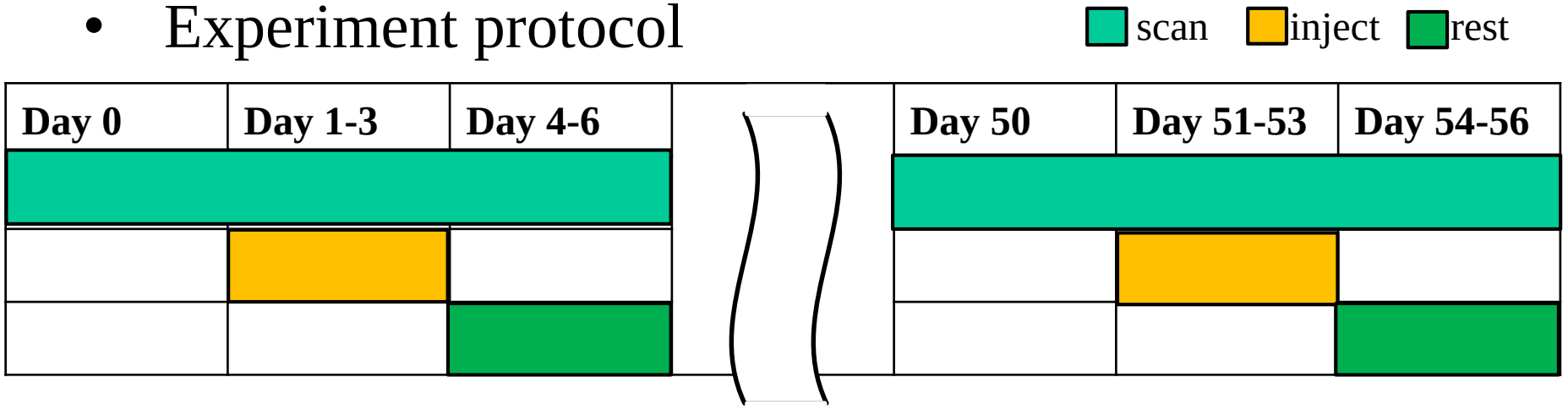
A B C D

Materials & Methods – Animal Model

- SD rats

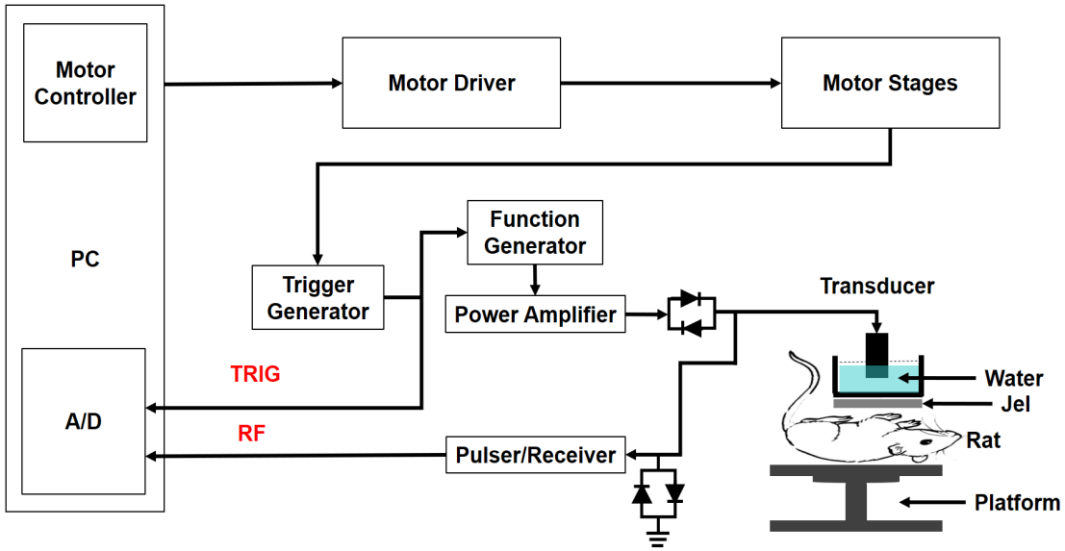
	Numbers of rats	Dosage *	Sacrifice
Control	4	$1\ mL/kg$ olive oil	0, 4^{th}, 8^{th} week
Experiment	15	10% $1\ mL/kg$ CCl_4 in olive oil	4^{th}, 8^{th} week

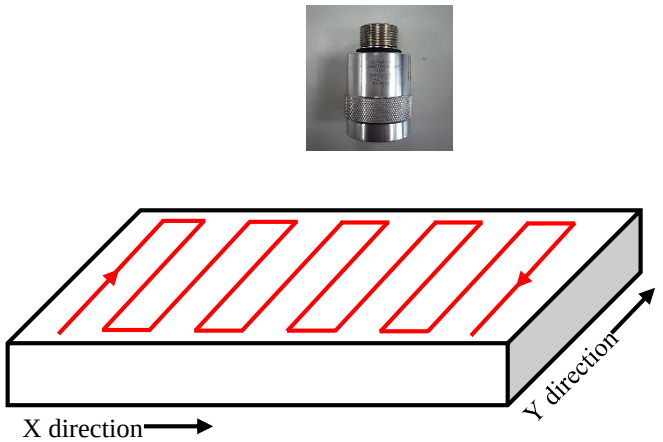
- Experiment protocol



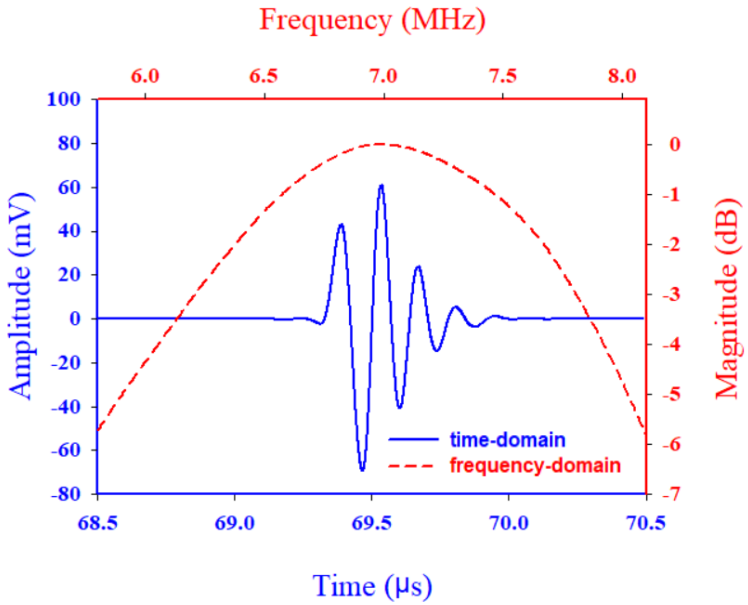
** G. M. Thamiry et al., "Review of experimental models for inducing hepatic cirrhosis by bile duct ligation and carbon tetrachloride injection," Acta Cirúrgica Brasileira, vol. 27, pp. 589-594, 2012.*

Materials & Methods – Experiment Arrangement



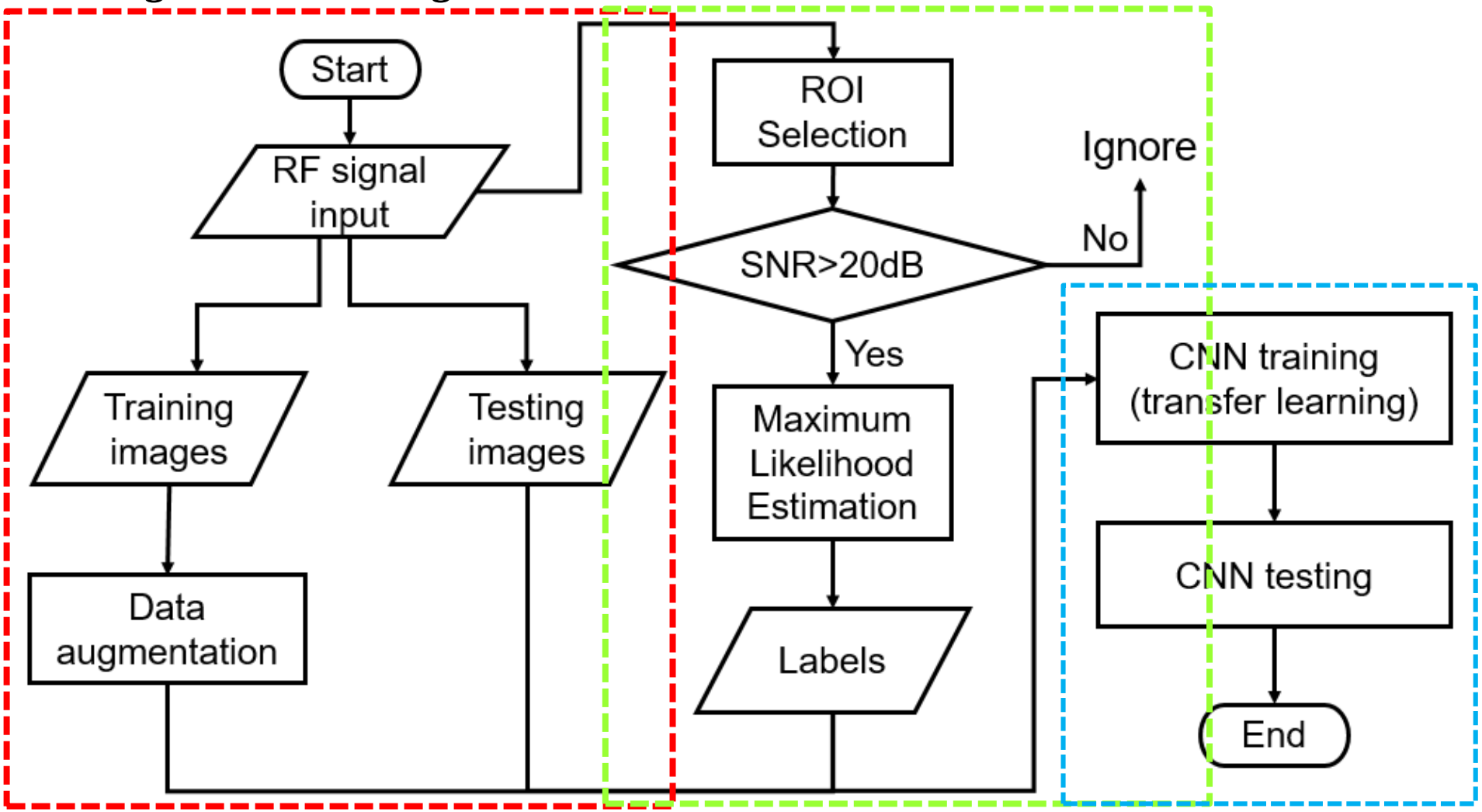


Transducer Characteristics	
Center Frequency	7 MHz
-6 dB Bandwidth	2.3 MHz
f-number	2.67
Depth of Focus	50.80 mm
Aperture Size	19.05 mm



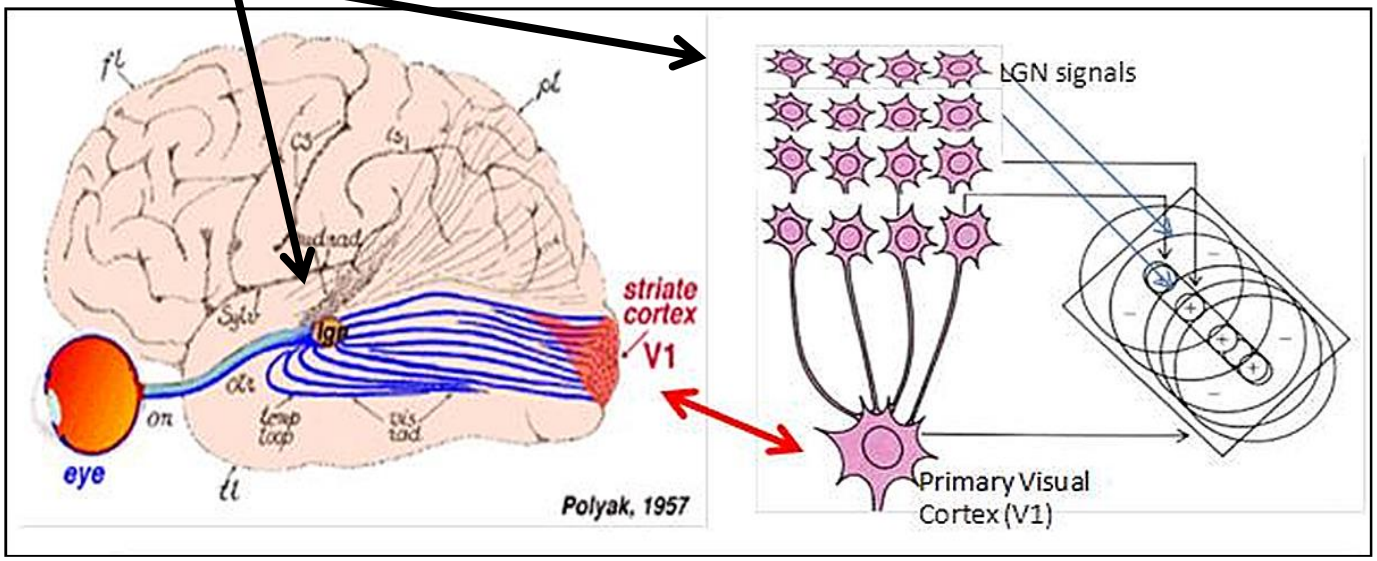
Materials & Methods – Process of Classification

Training N = 17; Testing N = 2



Lateral Geniculate Nucleus (LGN) - axons & synapses - to primary visual cortex (V1)

HD Hubel and TN Wiesel, (1959). "Receptive fields of single noreones in the cat's striate cortex". *J Physiol* **148**(3): 574–591.



Convolution + modulation
to simulate
LGN signals passing to V1 neurons

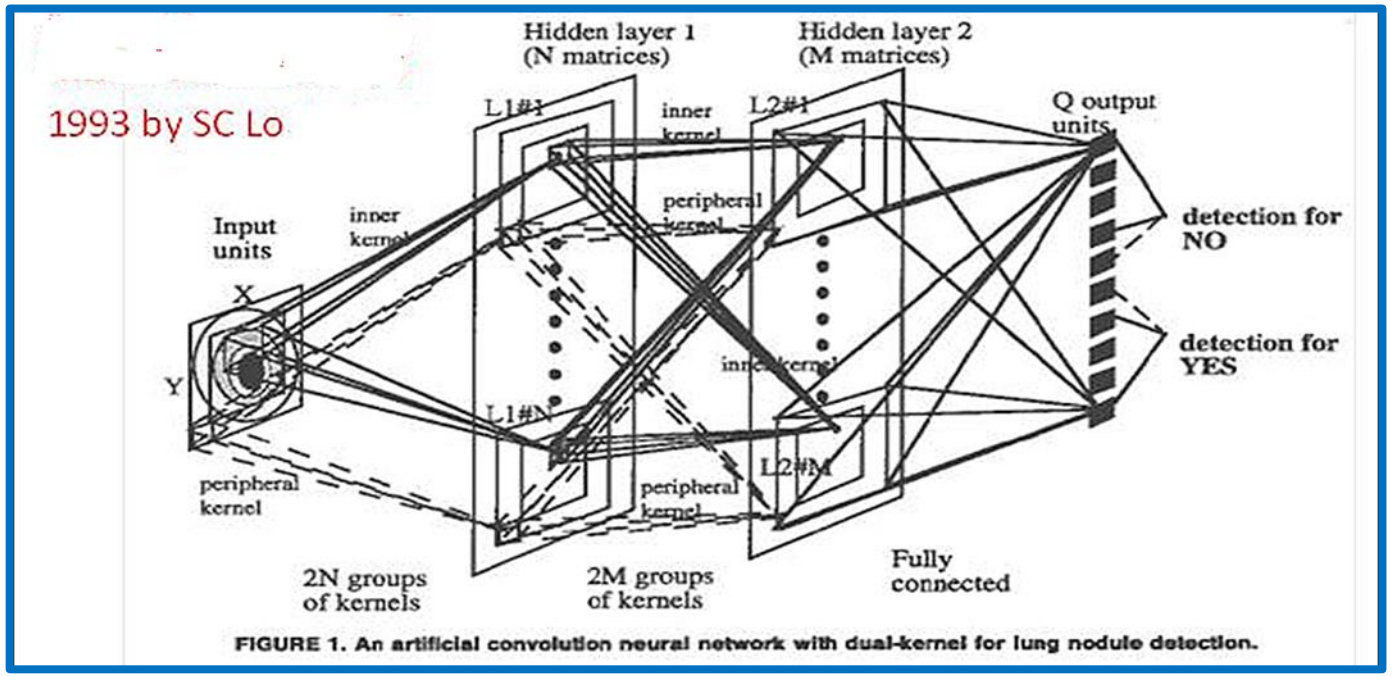
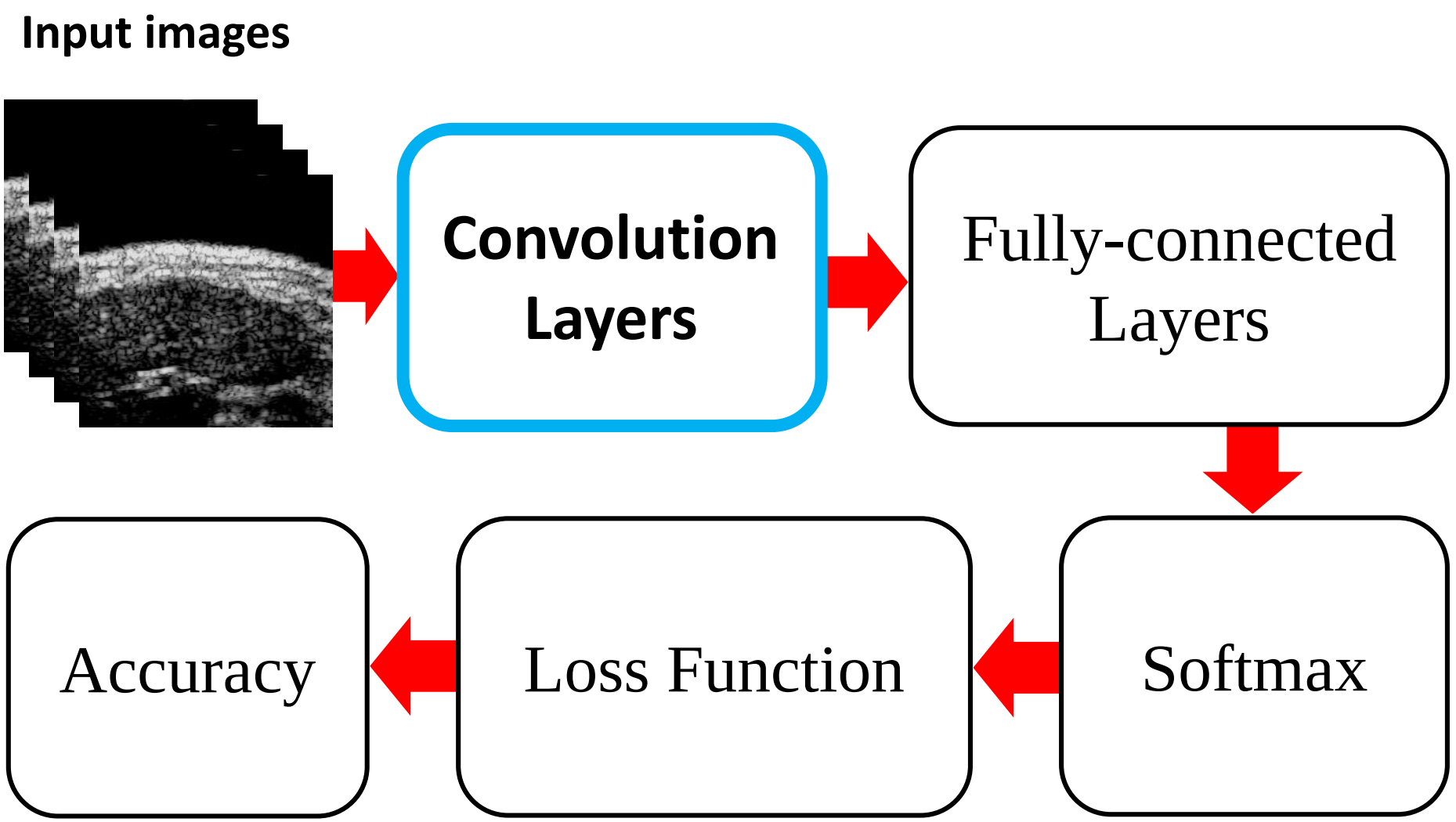
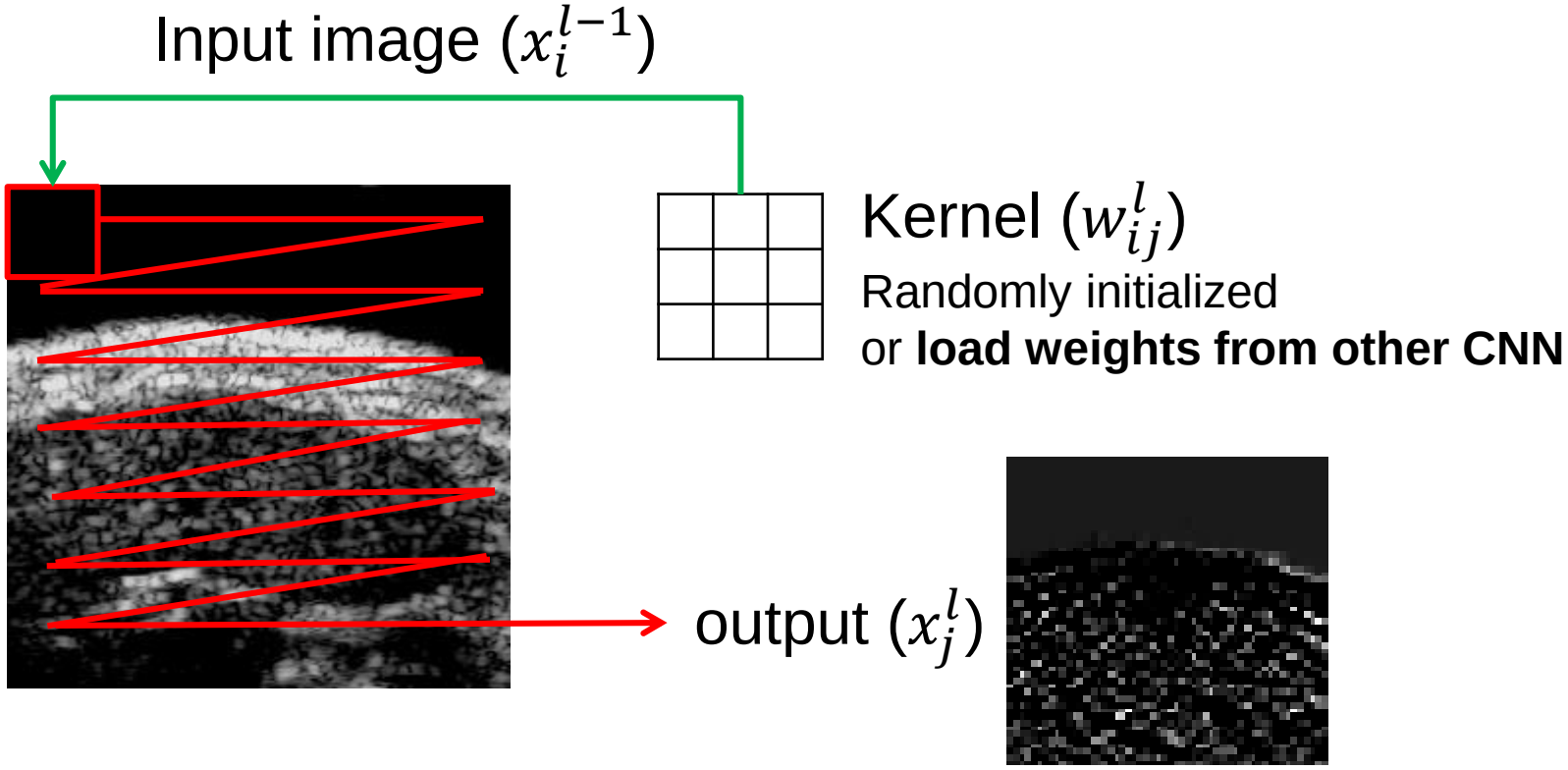


FIGURE 1. An artificial convolution neural network with dual-kernel for lung nodule detection.

Materials & Methods – CNN



Materials & Methods – Convolution Layer



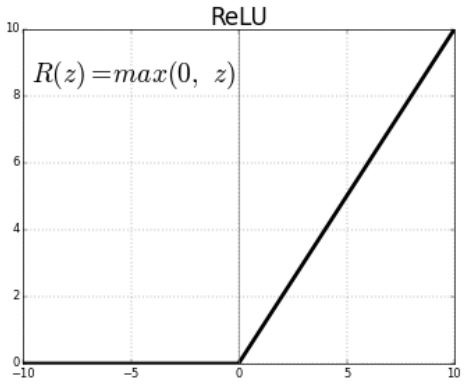
$$x_j^l = F\left(\sum_{i \in M_j} x_i^{l-1} * w_{ij}^l + b_j^l\right)$$

F : activation function

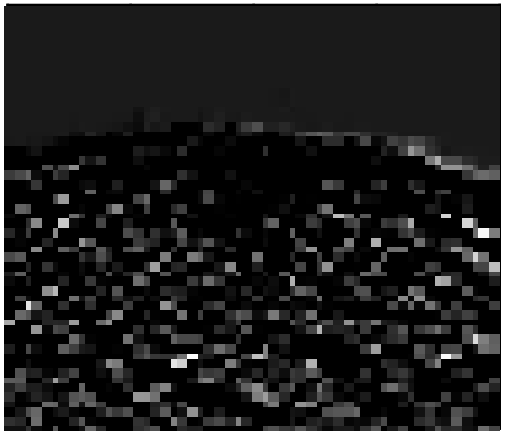
b_j^l : bias

Materials & Methods – Activation Function/Pooling

- Rectified Linear Unit (ReLU)



https://ithelp.ithome.com.tw/articles/10189085

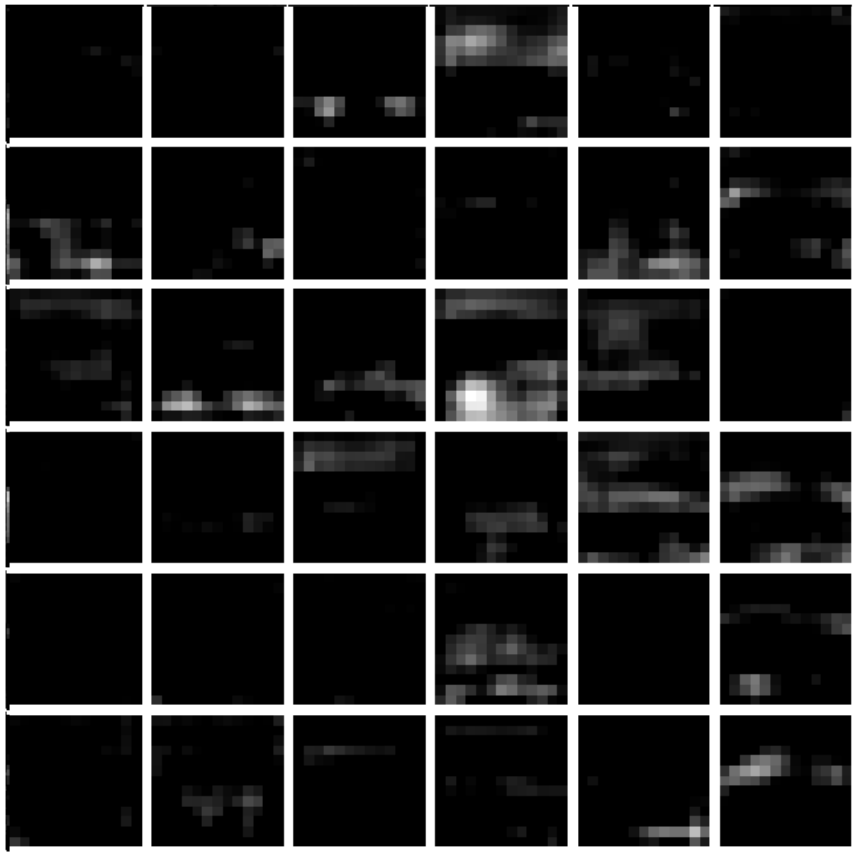


pooling

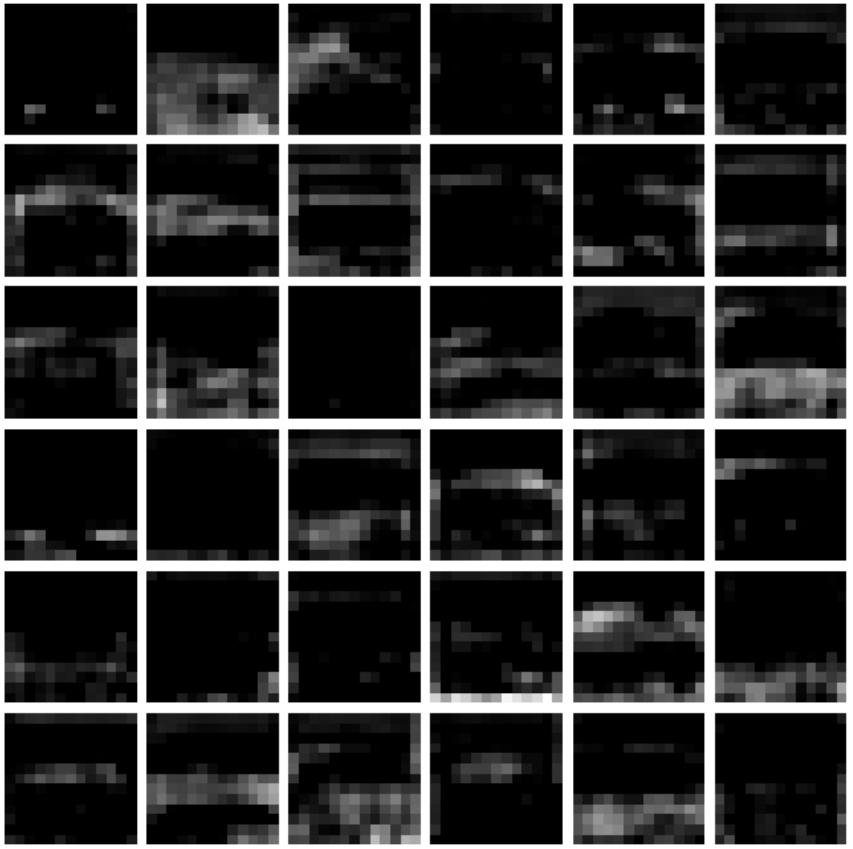
Low-level feature image

High-level feature image

Materials & Methods – Feature Map



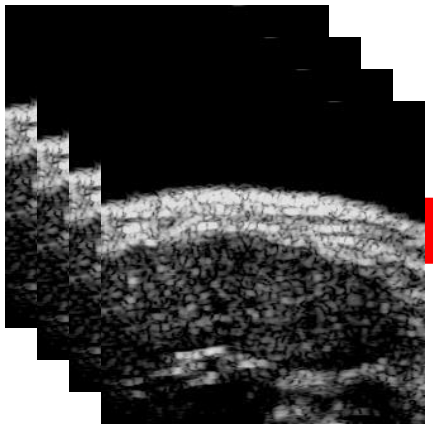
Layer 3



Layer 4

Materials & Methods – CNN

Input images



Convolution Layers

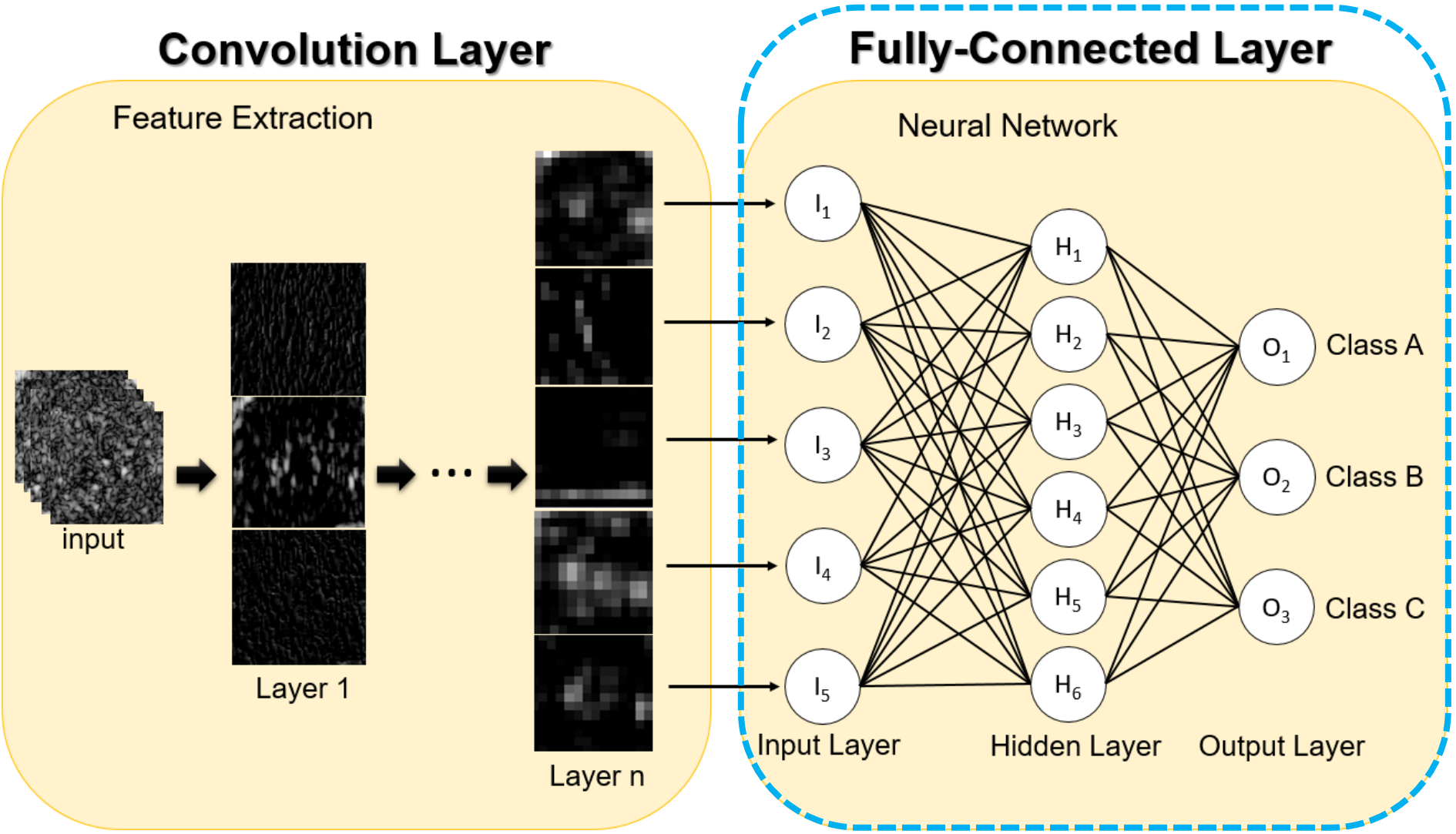
Fully-connected Layers

Softmax

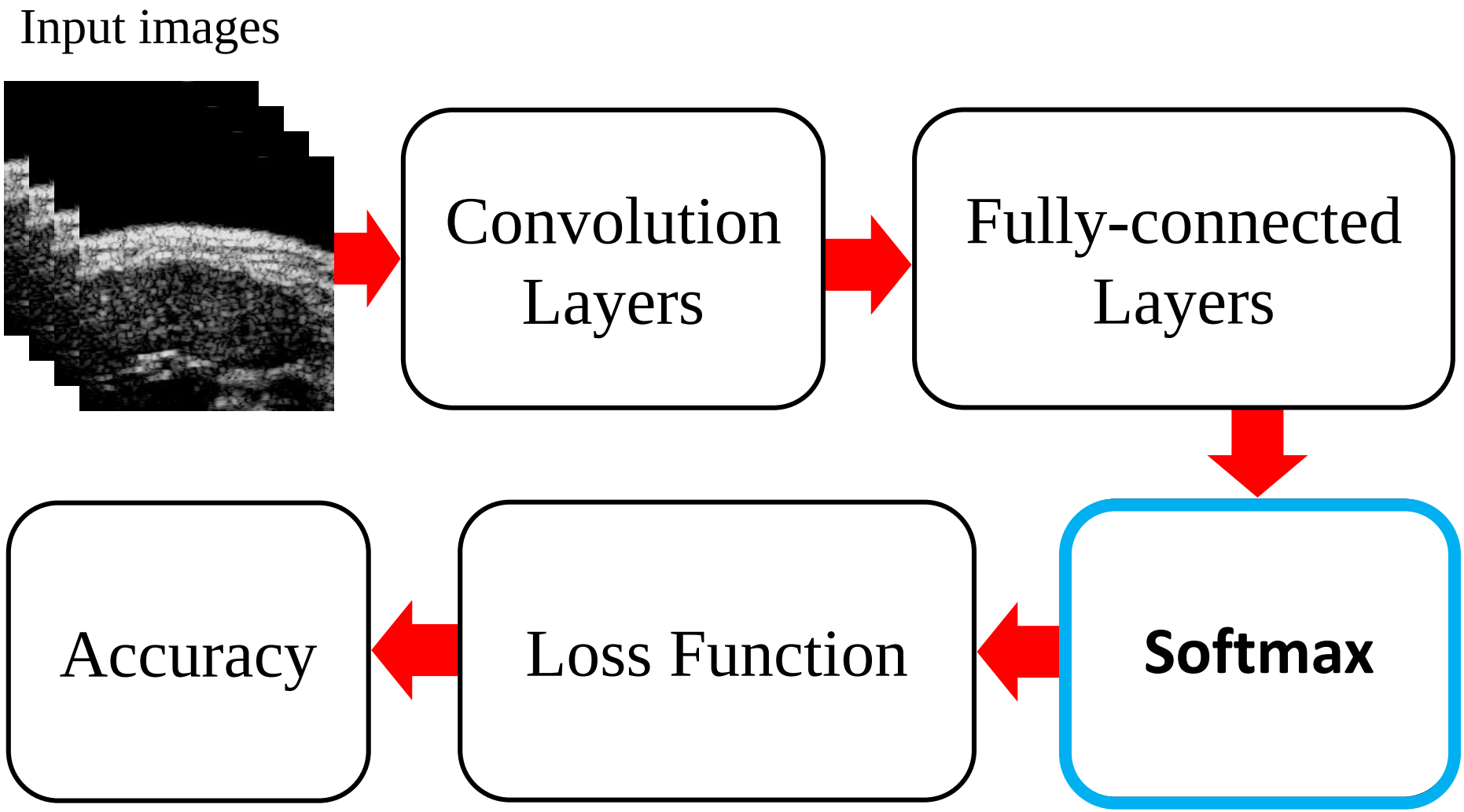
Loss Function

Accuracy

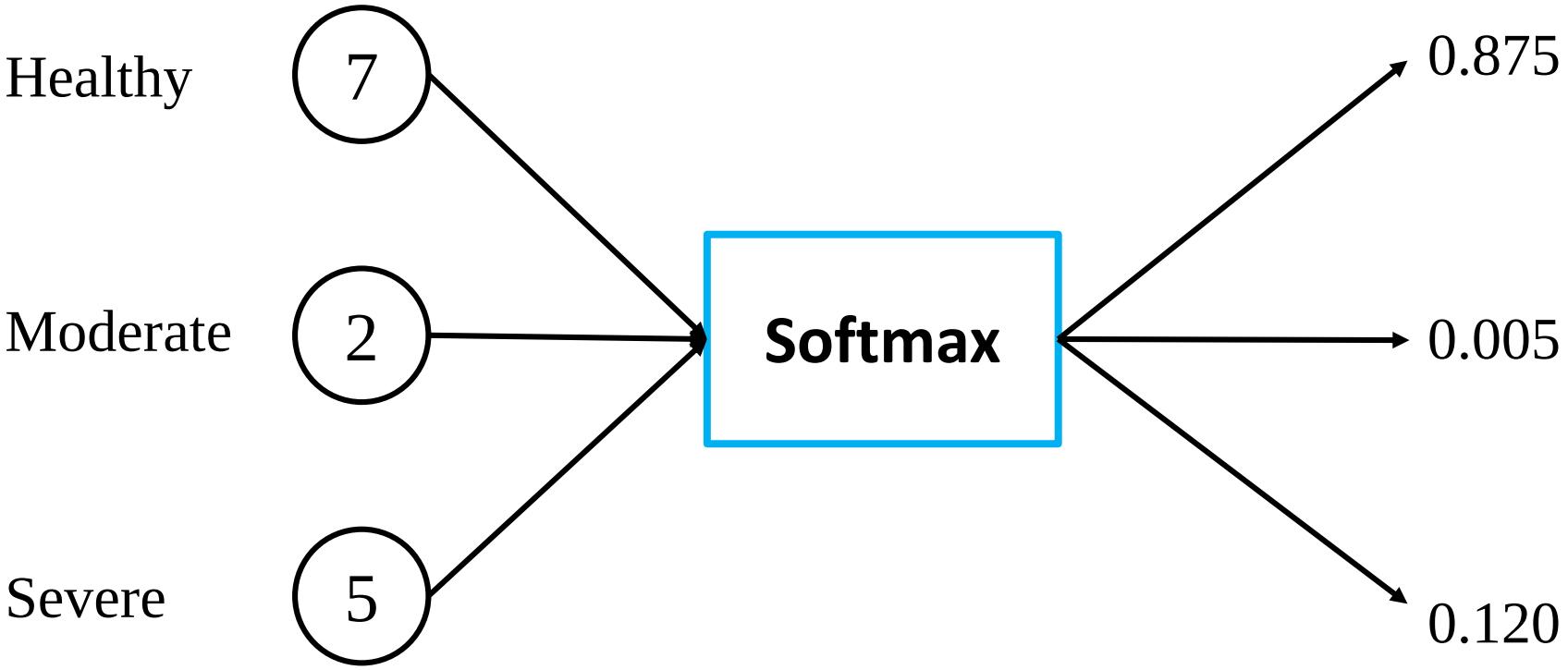
Materials & Methods – Fully-Connected Layer



Materials & Methods – CNN

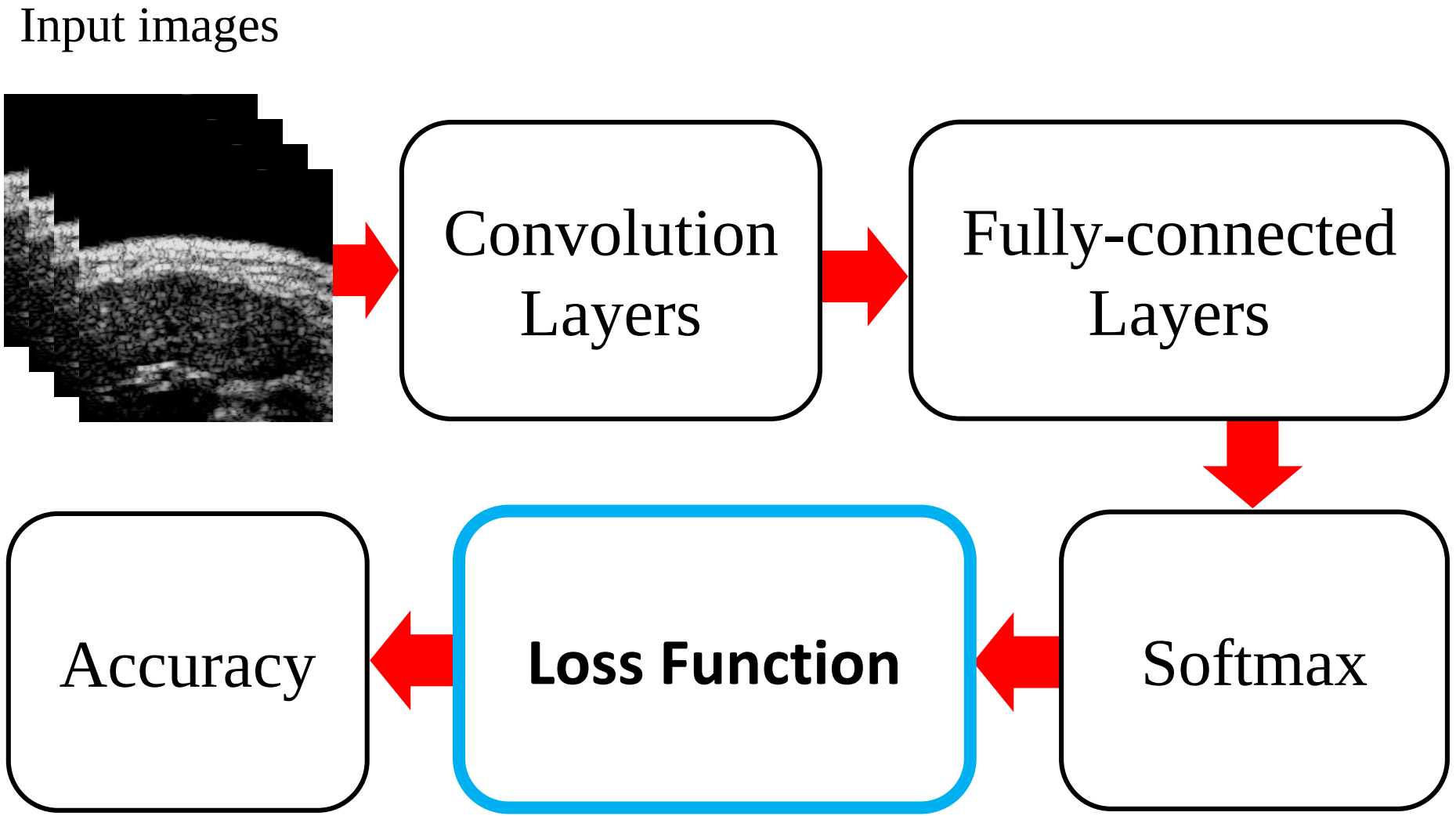


Materials & Methods – Softmax



$$\sigma(z_j) = \frac{e^{z_j}}{\sum_{k=1}^{K} e^{z_k}} \text{ for j} = 1, \ldots, \text{K}$$

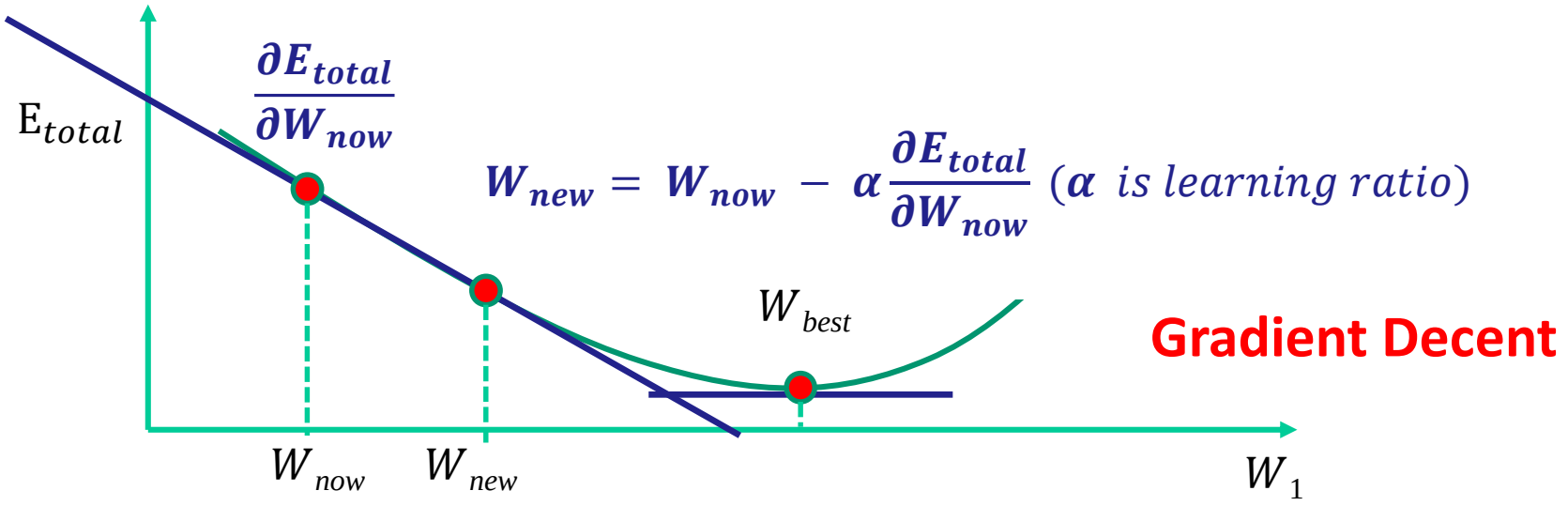
Materials & Methods – CNN



Materials & Methods – Gradient Descent

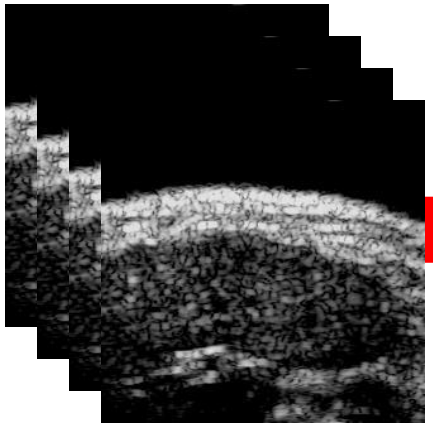
Loss Function

$$\mathrm{E}_{total} = \sum_{i=1}^{n} \frac{1}{2}(label - prediction)^2 = E_{o1} + E_{o2} + E_{o3}$$



Materials & Methods – CNN

Input images



Convolution Layers

Fully-connected Layers

Softmax

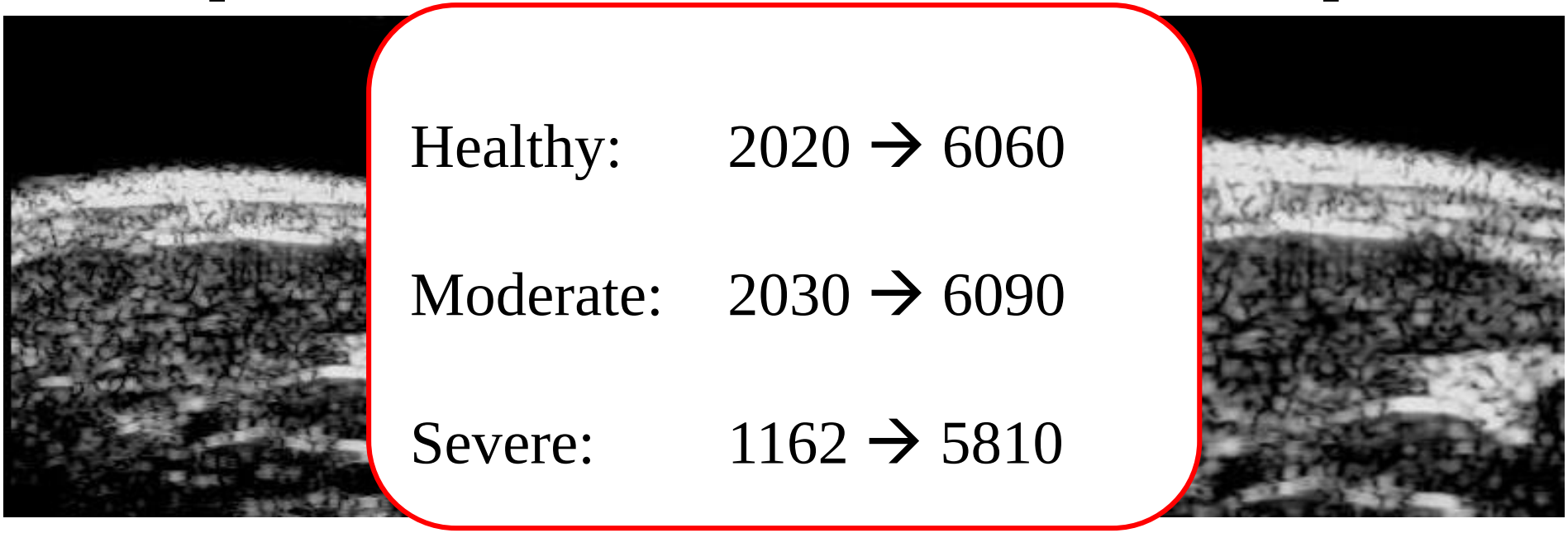
Loss Function

Accuracy

Materials & Methods – Data Augmentation

- **Rat-01**

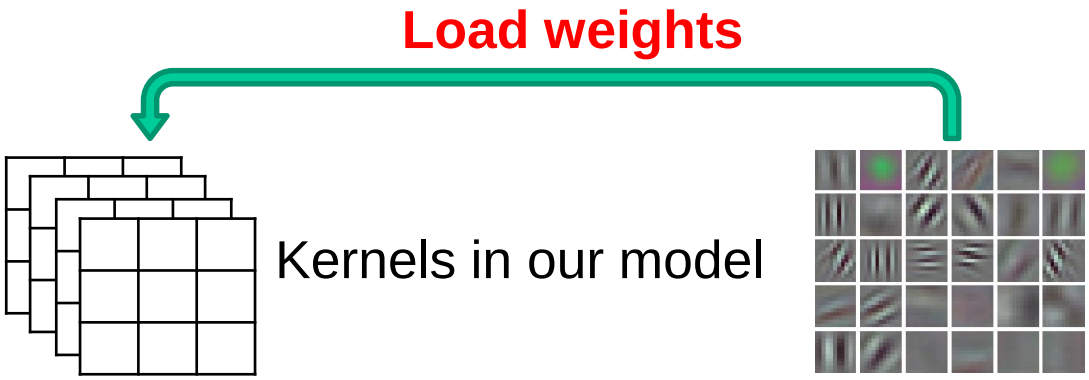
Shifting	**Rotating**	**Zooming**
5 pixels	0~360°	10~50 pixels

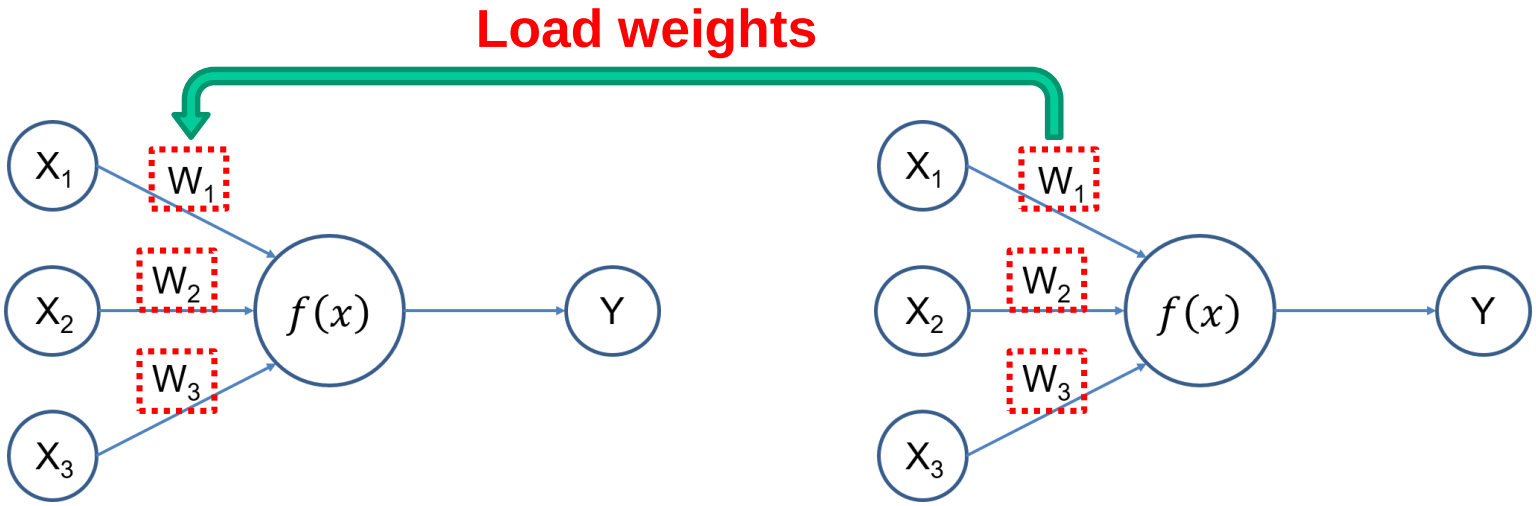


Healthy:	2020 → 6060
Moderate:	2030 → 6090
Severe:	1162 → 5810

** D. Meng, L. Zhang, G. Cao, W. Cao, G. Zhang, and B. Hu, "Liver fibrosis classification based on transfer learning and FCNet for ultrasound images," IEEE Access, 2017.*

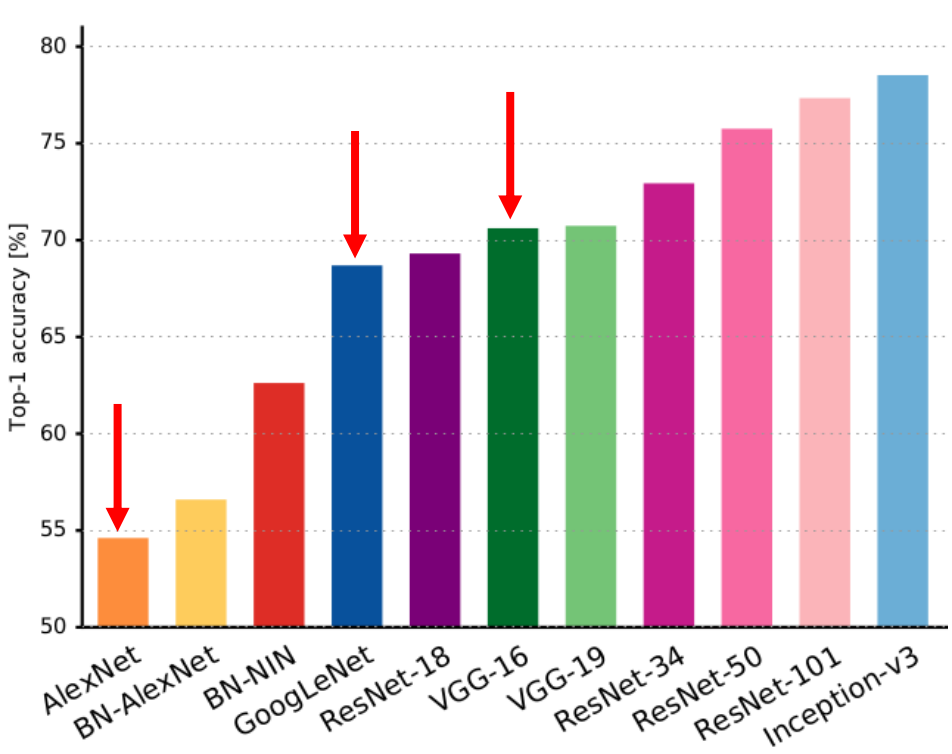
Materials & Methods – Transfer Learning

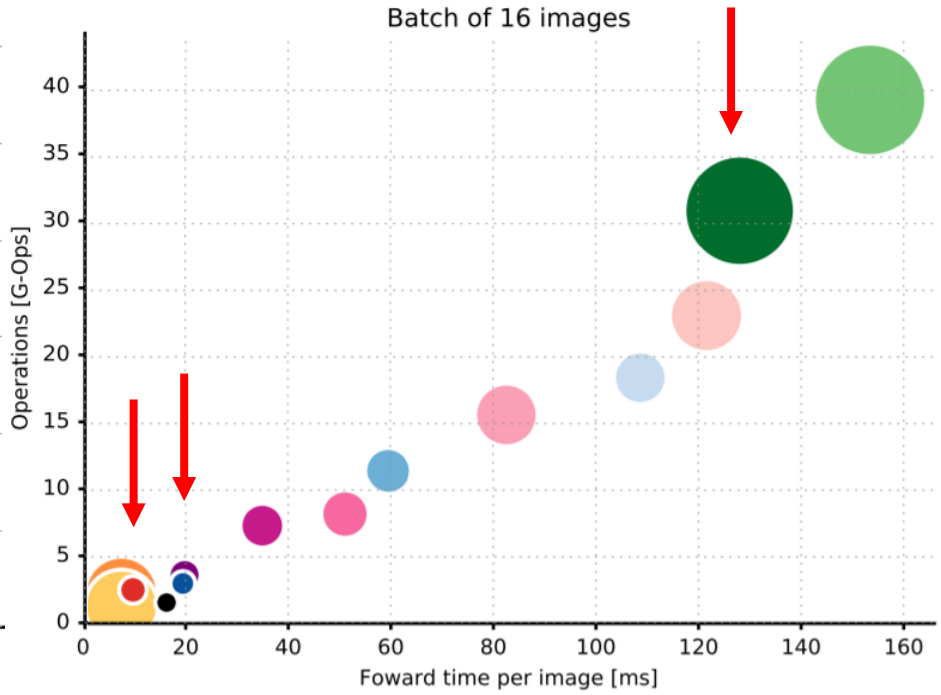




Materials & Methods – CNN Models

- **CNN model selection**

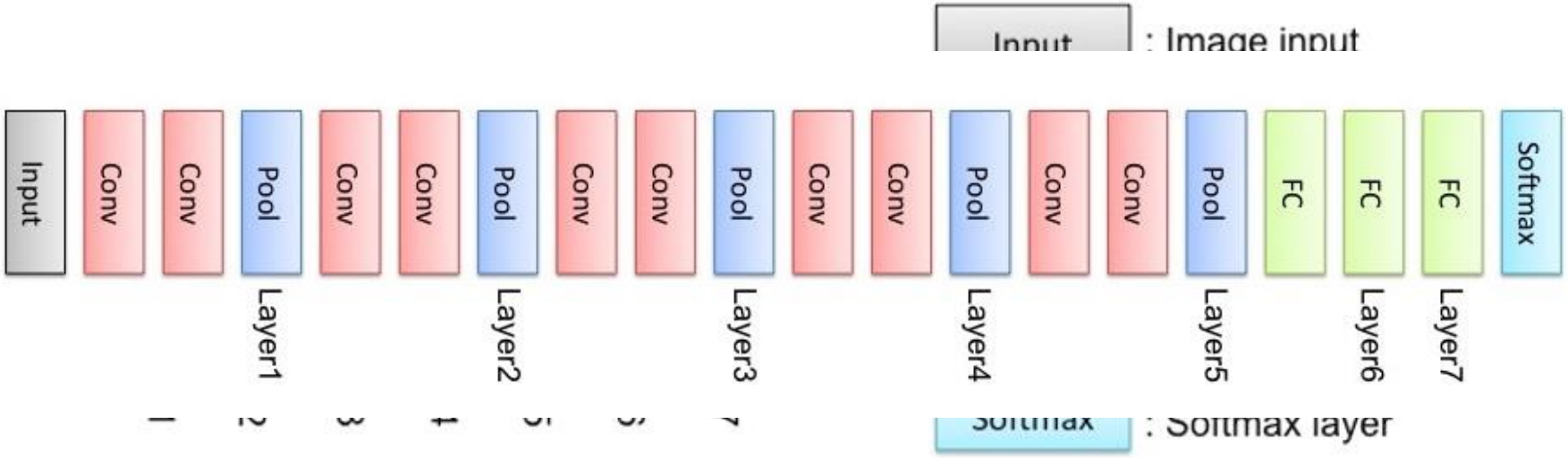




A. Canziani, A. Paszke, and E. Culurciello, "An analysis of deep neural network models for practical applications," arXiv preprint arXiv:1605.07678, 2016.

Materials & Methods – CNN Models

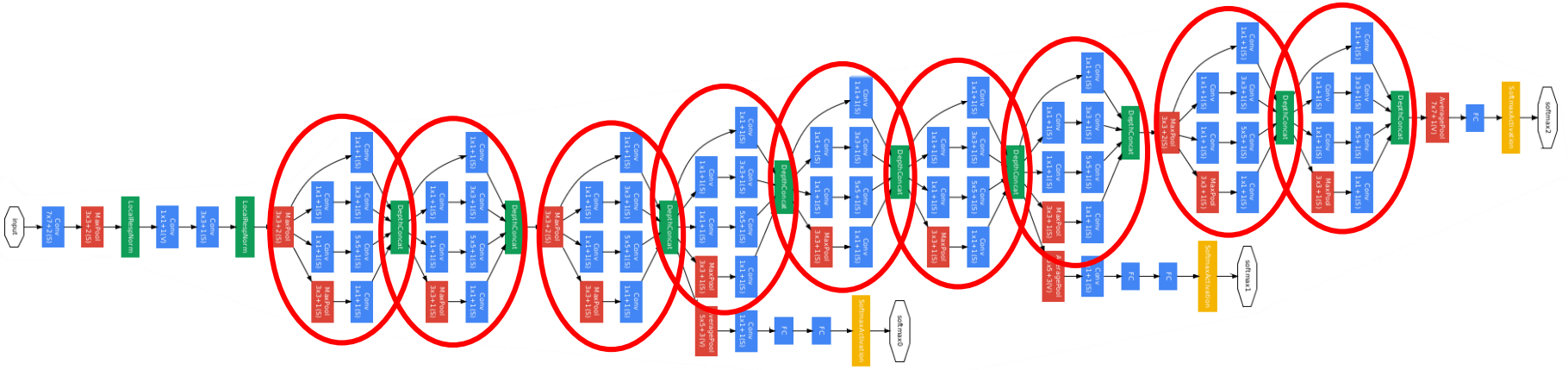
AlexNet (2012)

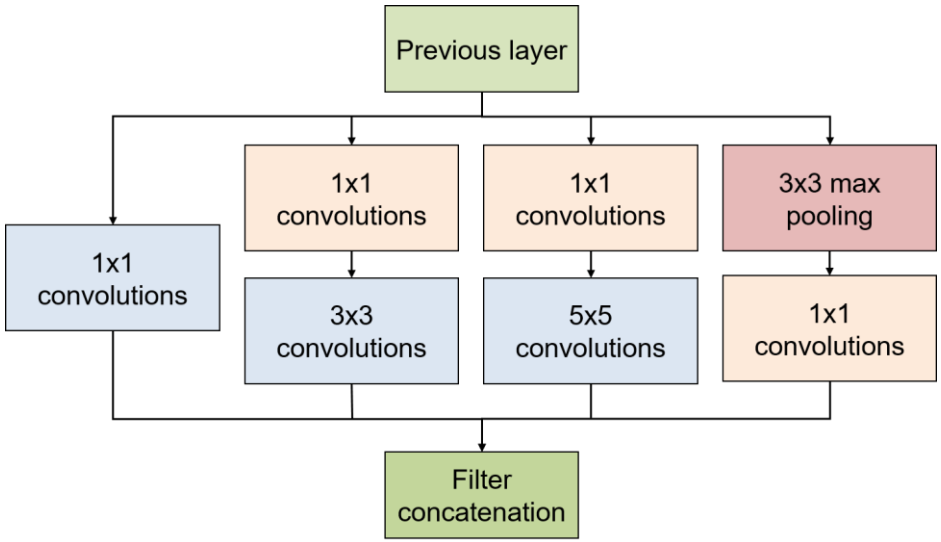


A. Krizhevsky, I. Sutskever, and G. E. Hinton, "Imagenet classification with deep convolutional neural networks," in Advances in information processing systems, 2012, pp. 1097-1105.

Materials & Methods – CNN Models

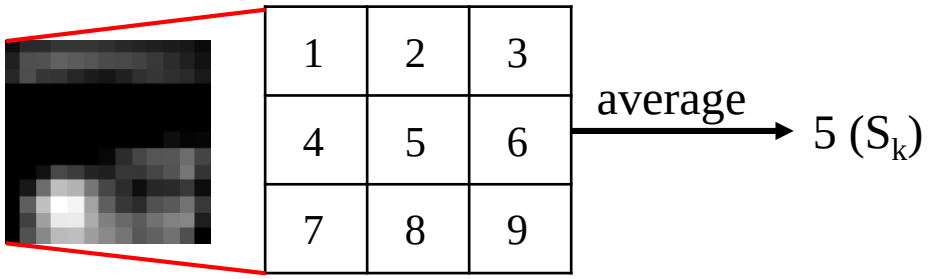
GoogLeNet (2014)

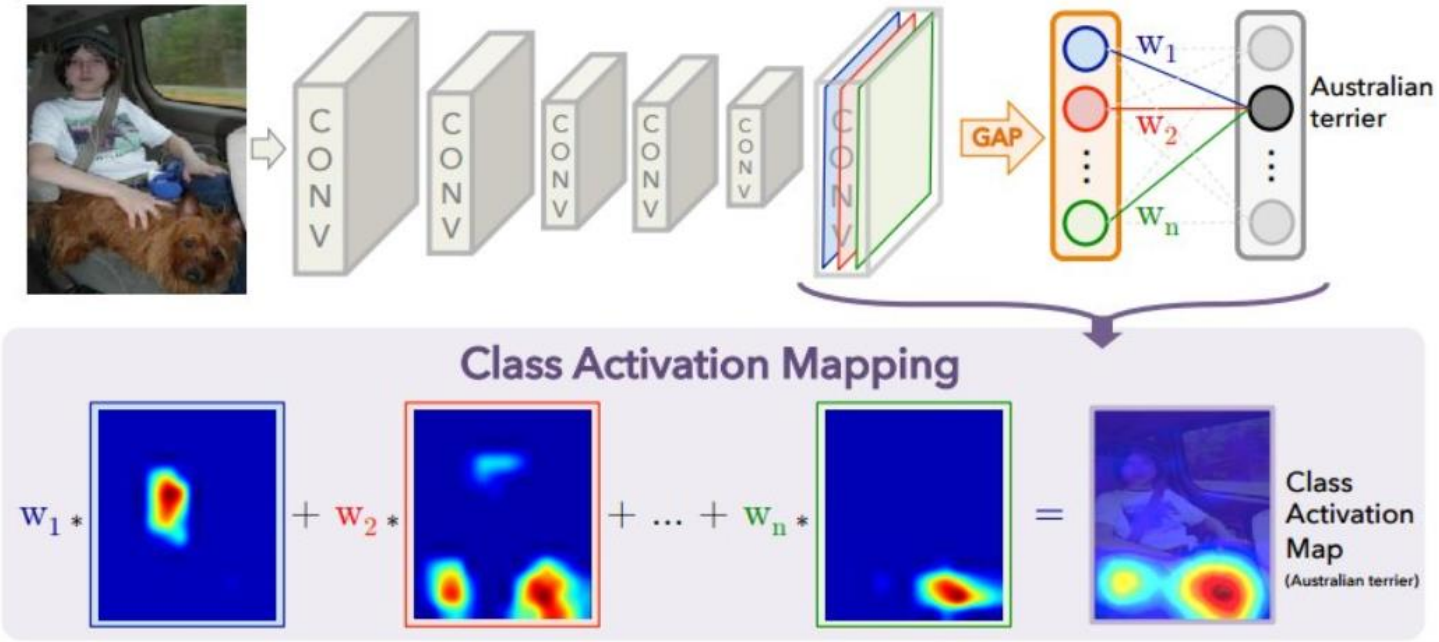




K. Simonyan and A. Zisserman, "Very deep convolutional networks for large-scale image recognition," arXiv preprint arXiv:1409.1556, 2014.

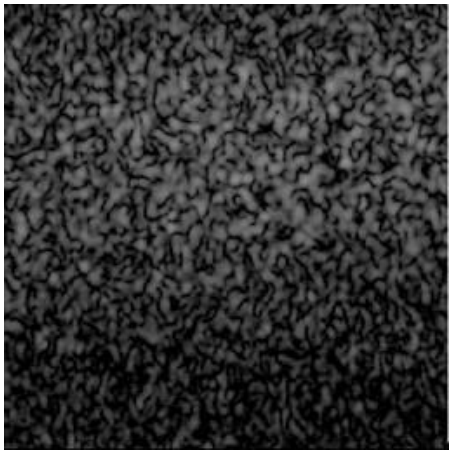
Materials & Methods – Class Activation Map

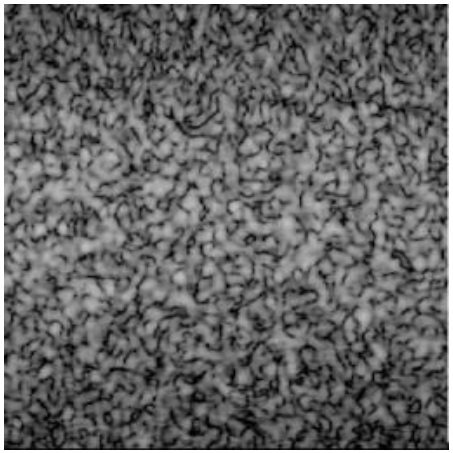


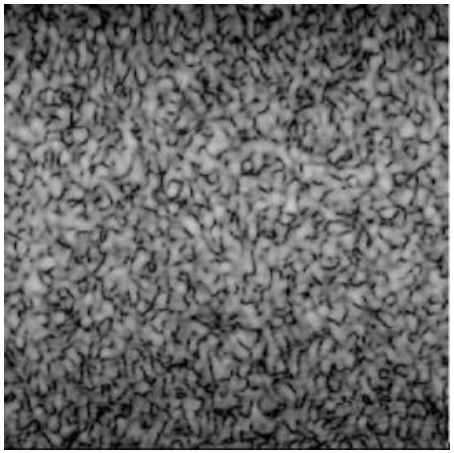


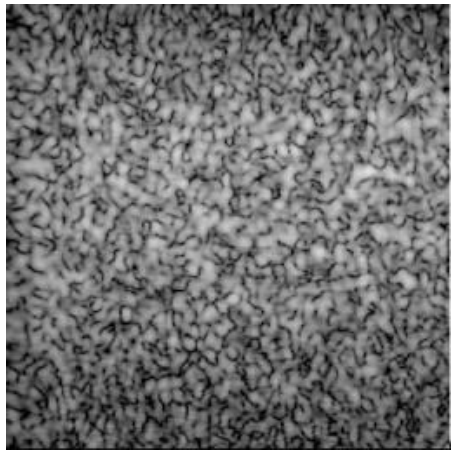
B. Zhou, A. Khosla, A. Lapedriza, A. Oliva, and A. Torralba, "Learning deep features for discriminative localization," in Computer Vision and Pattern Recognition (CVPR), 2016 IEEE Conference on, 2016, pp. 2921-2929: IEEE.

Results & Discussion (1/8) – Phantom


(A) Graphite 1.5%


(B) Graphite 3%

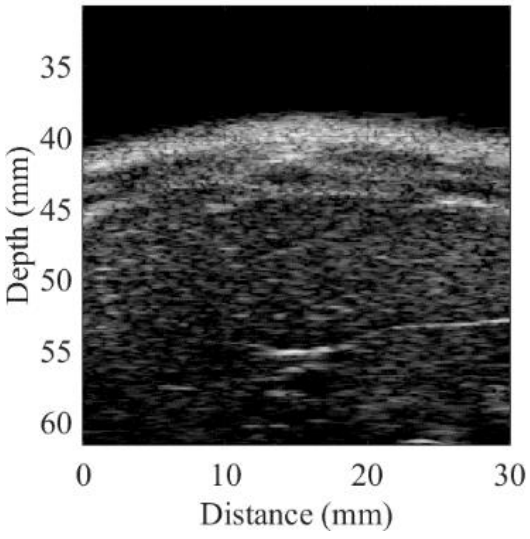

(C) Glass bead 45


(D) Glass bead 75

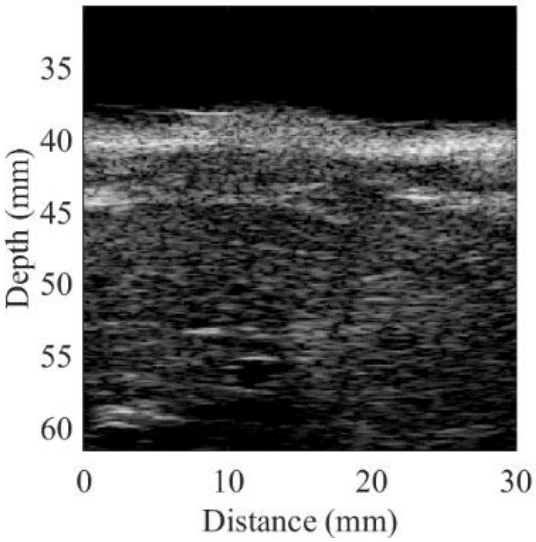
- CNN model could exactly classify whether there were glass beads in the phantom or not.
- The prediction accuracy decreased as (C) and (D) phantoms were divided into different classes.

Results & Discussion (2/8) – Liver Fibrosis

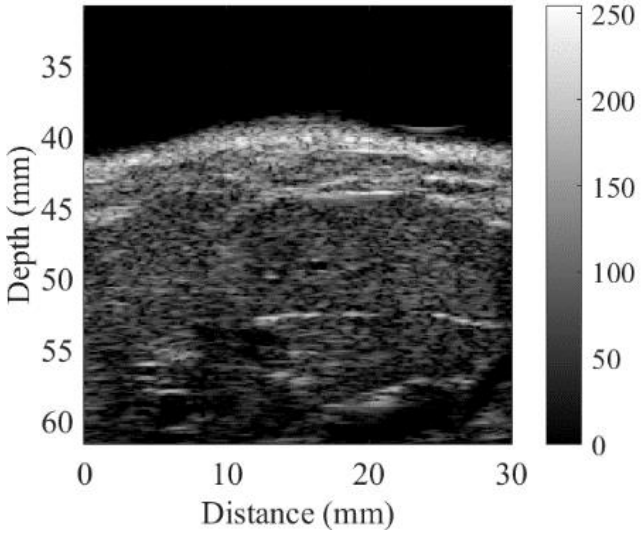
- **Rat-01**



Healthy



Moderate



Severe

Results & Discussion (3/8) – Nakagami-*m*

Patient	Acute Phase: Initial Liver Stiffness (kPa)	Acute Phase: ALT (Units/mL)	After Resolution of the Acute Hepatitic Phase: Liver Stiffness (kPa)	After Resolution of the Acute Hepatitic Phase: ALT (Units/mL)	
3*	21.3	1550	11.6	28	
4	26.3	779	7,9	12	Hepatitis B virus
5	19.4	5382	6.9	5	
10	52.3	151	8.3	23	
13	21.5	151	4.8	11	Toxic
19	13.6	1045	6.8	30	Autoimmune

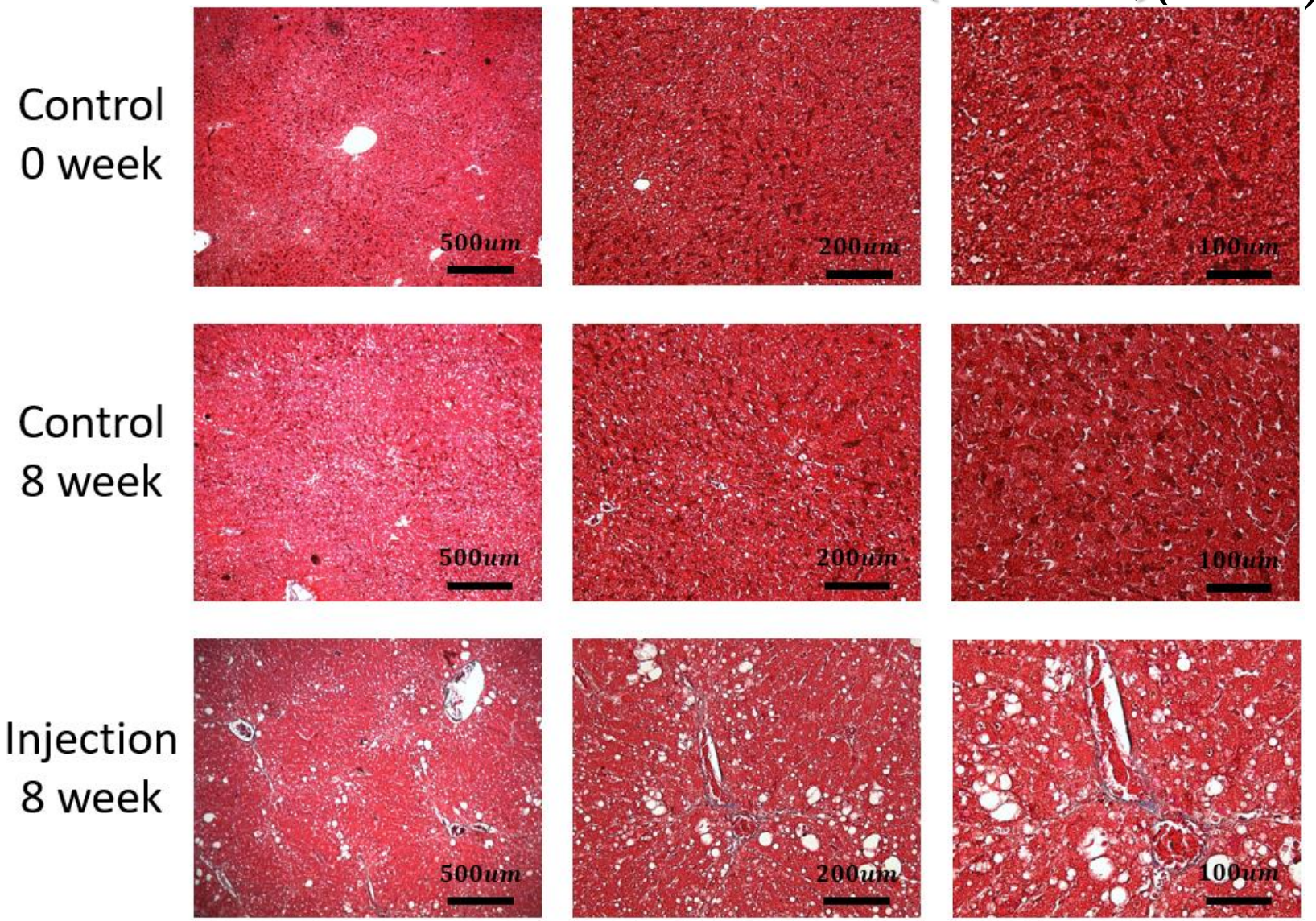
The cutoff value for cirrhosis was 12.5 kPa.

*Patient 3 had a flare of chronic hepatitis B.

A. Sagir, A. Erhardt, M. Schmitt, and D. Häussinger, "Transient elastography is unreliable for detection of cirrhosis in patients with acute liver damage," *Hepatology*, vol. 47, no. 2, pp. 592-595, 2008.

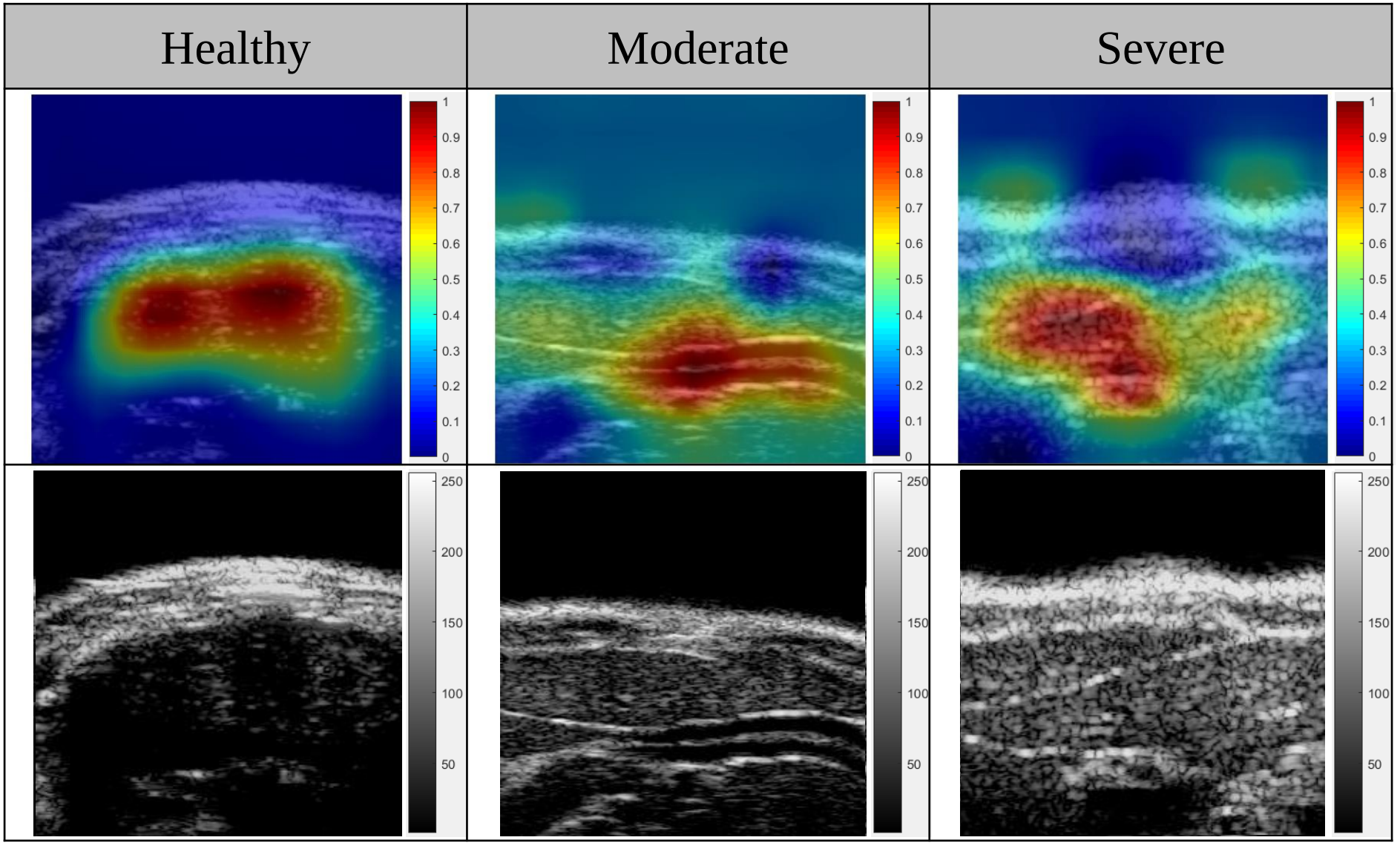
Results & Discussion (4/8)

- **Rat-02, 03, 04 — Tissue Section (Masson)**
- Rat-02, 03, 04 — Tissue Section (H&E)

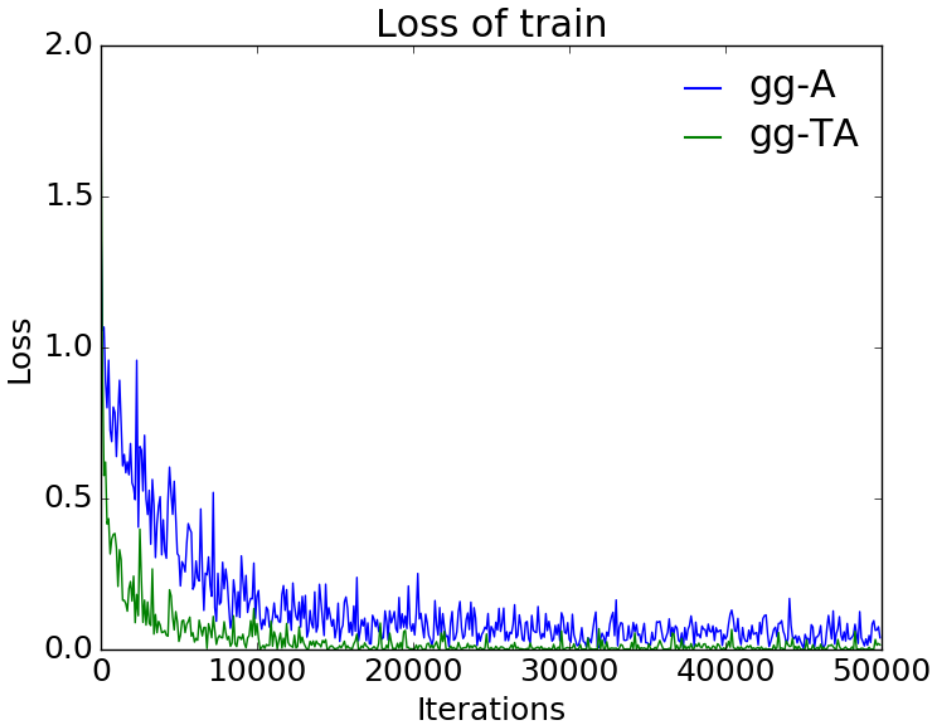


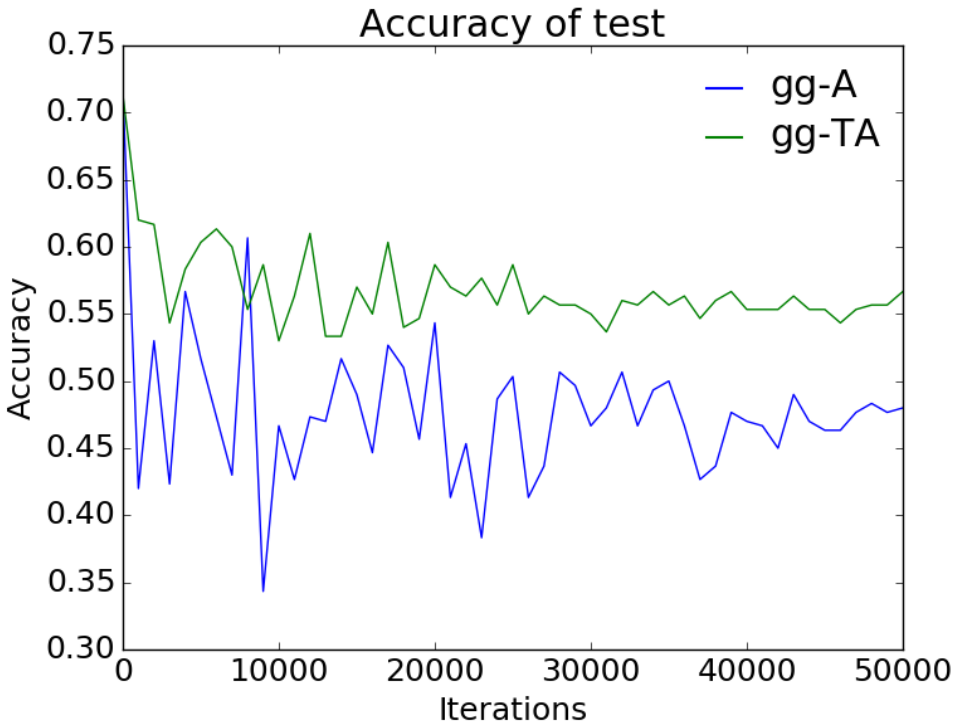
Results & Discussion (5/8)-Class Activation Map

- **Rat-02, 03, 04**



Results & Discussion (6/8) – Loss/Accuracy



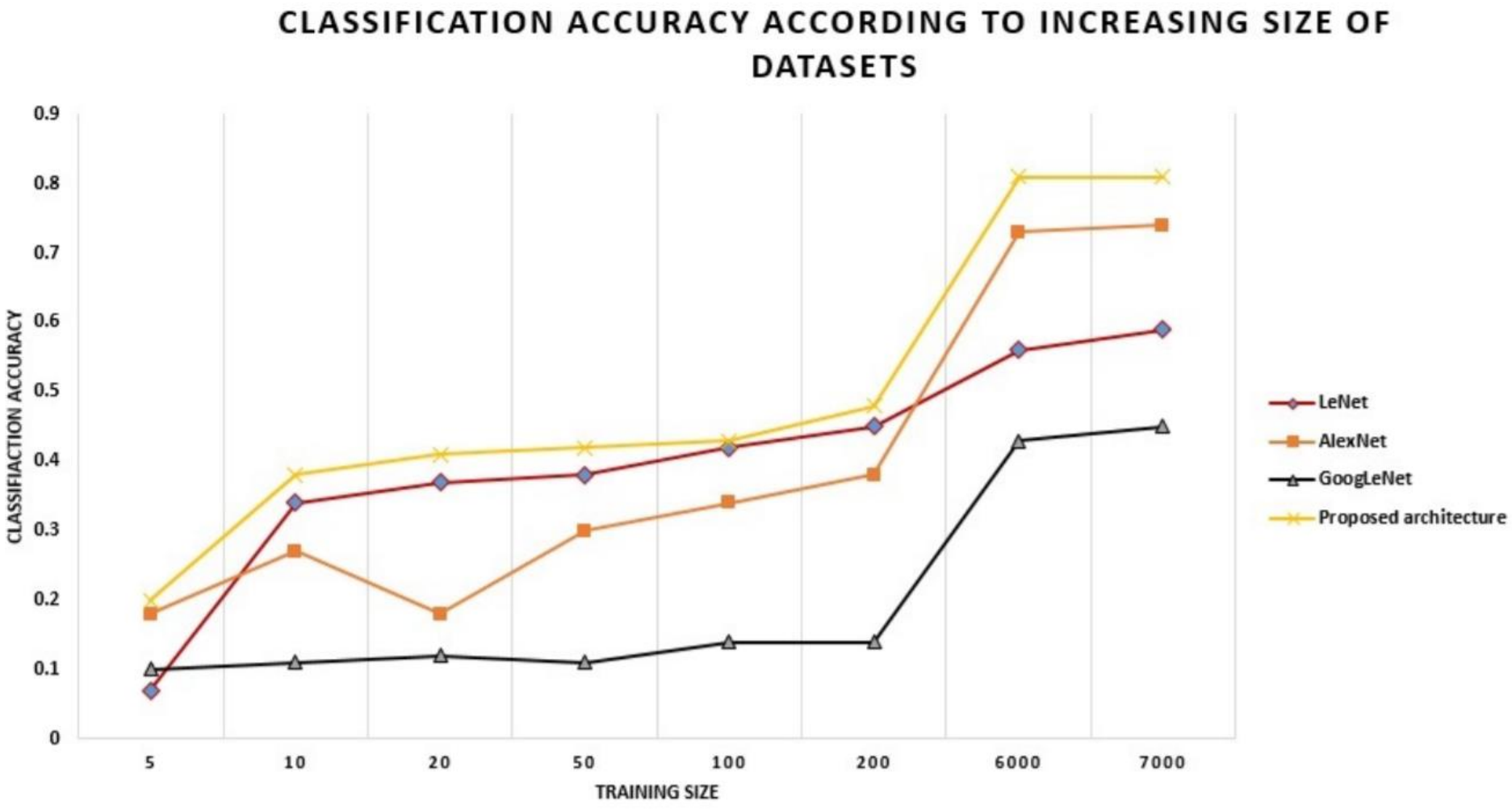


* T = with transfer learning, A = with data augmentation

Results & Discussion (7/8) – Comparison of Different Framework

	Caffe’	Matlab
CPU	Intel® core i7	
GPU	GTX 1080 Ti 11G RAM	
OS	Ubuntu (16.04)	Windows 10
Network	**Computation Time (minutes)**	
AlexNet	139	547
VGGNet	323	2564
GoogleNet	216	822

Results & Discussion (8/8) – Confusion Matrix



S. Khan and S.-P. Yong, "A deep learning architecture for classifying medical images of anatomy object," in *Asia-Pacific Signal and Information Processing Association Annual Summit and Conference (APSIPA ASC), 2017*, 2017, pp. 1661-1668: IEEE.

Conclusion

- We considered Nakagami-*m* parameter as ground truth label and used ultrasonic images to train CNN models for liver fibrosis classification.
- The simpler the model is, the better the classification of medical images are.
- Nakagami-*m* is not suitable for training CNN model; thus, the lack of ground truth label is still a critical problem to be resolved.

Deep convolutional neural networks (DCNN)