Deep Learning Assisted Medical Images Analysis for Automatic Disease Prediction

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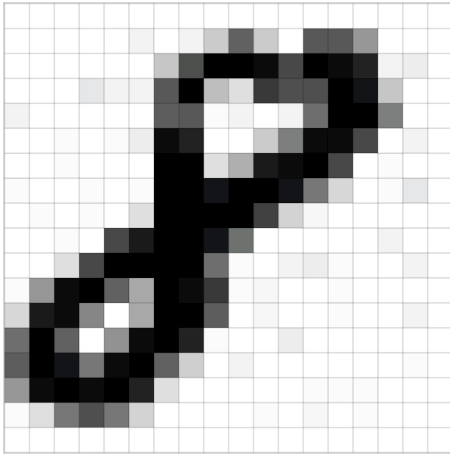
Concept of Artificial Neural Network

How an image is trained in ANN:



Input image

0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	1	12	0	11	39	137	37	0	152	147	84	0	0	0
0	0	1	0	0	0	41	160	250	255	235	162	255	238	206	11	13	0
0	0	0	16	9	9	150	251	45	21	184	159	154	255	233	40	0	0
10	0	0	0	0	0	145	146	3	10	0	11	124	253	255	107	0	0
0	0	3	0	4	15	236	216	0	0	38	109	247	240	169	0	11	0
1	0	2	0	0	0	253	253	23	62	224	241	255	164	0	5	0	0
6	0	0	4	0	3	252	250	228	255	255	234	112	28	0	2	17	0
0	2	1	4	0	21	255	253	251	255	172	31	8	0	1	0	0	0
0	0	4	0	163	225	251	255	229	120	0	0	0	0	0	11	0	0
0	0	21	162	255	255	254	255	126	6	0	10	14	6	0	0	9	0
3	79	242	255	141	66	255	245	189	7	8	0	0	5	0	0	0	0
26	221	237	98	0	67	251	255	144	0	8	0	0	7	0	0	11	0
125	255	141	0	87	244	255	208	3	0	0	13	0	1	0	1	0	0
145	248	228	116	235	255	141	34	0	11	0	1	0	0	0	1	3	0
85	237	253	246	255	210	21	1	0	1	0	0	6	2	4	0	0	0
6	23	112	157	114	32	0	0	0	0	2	0	8	0	7	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

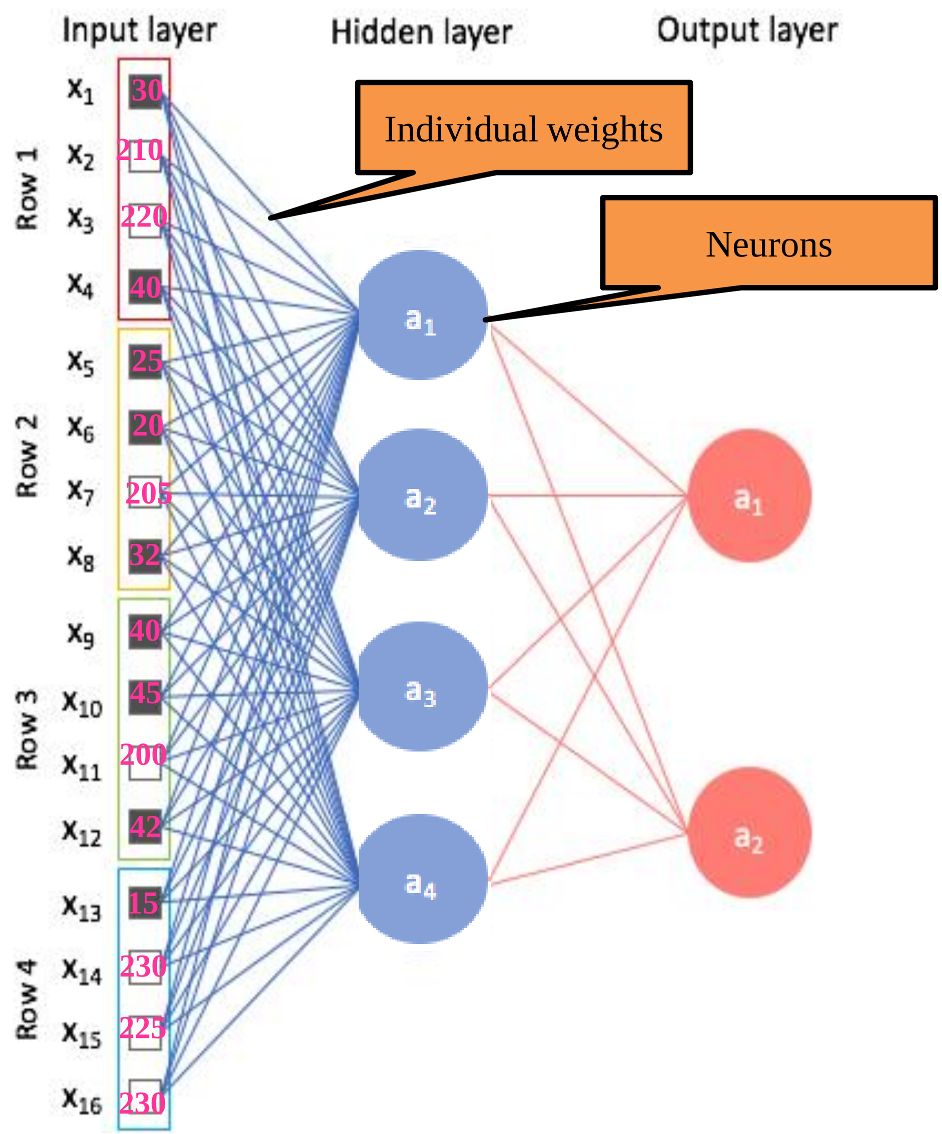
Corresponding pixel

- We can't directly feed this image into the neural network.
- A feed-forward network takes a 1-D vector as input, not a 2-D matrix.
- We need to flatten the 2-D array of pixel values into a 1-D array

How an image is trained in ANN

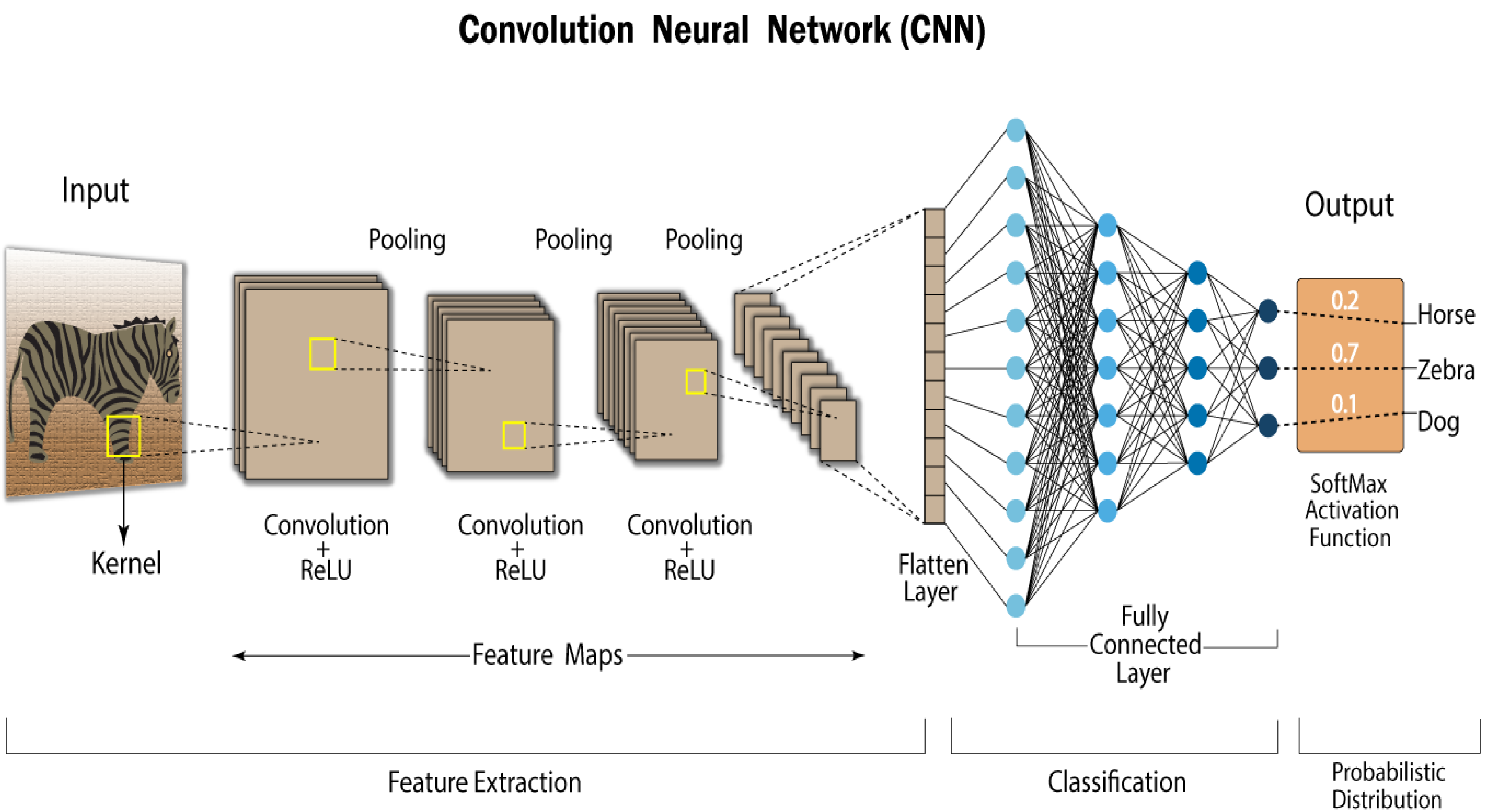
30	210	220	40
25	20	205	32
40	45	200	42
15	230	225	230

Corresponding pixel

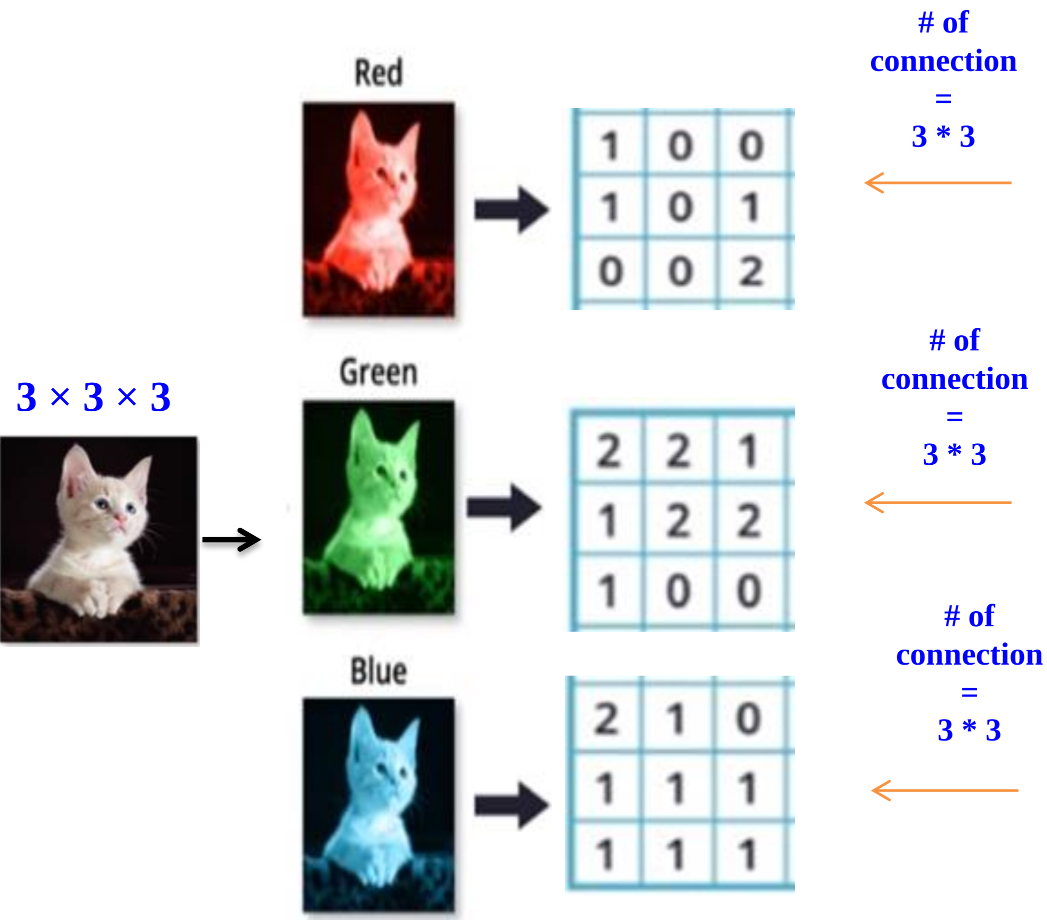


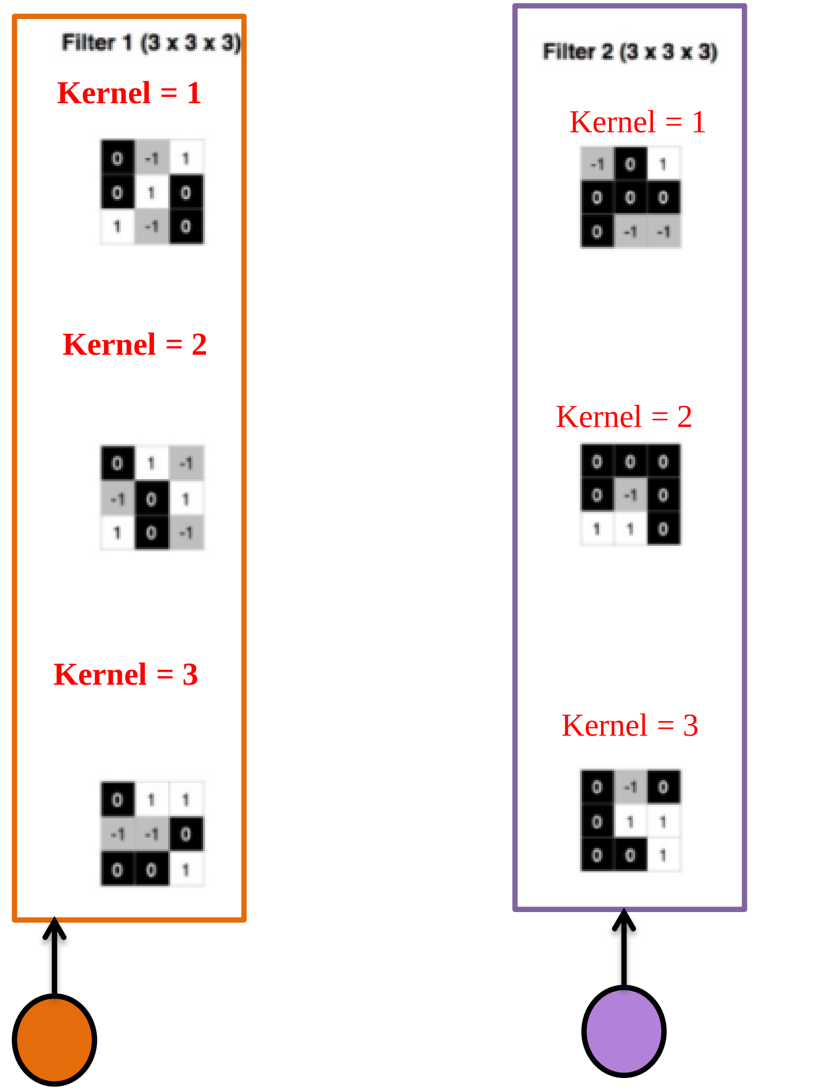
- The input layers of the ANN contain image pixels.
- Treat each individual pixel value as a feature.

Concept of Convolutional Neural Network



Concept of Convolutional Neural Network



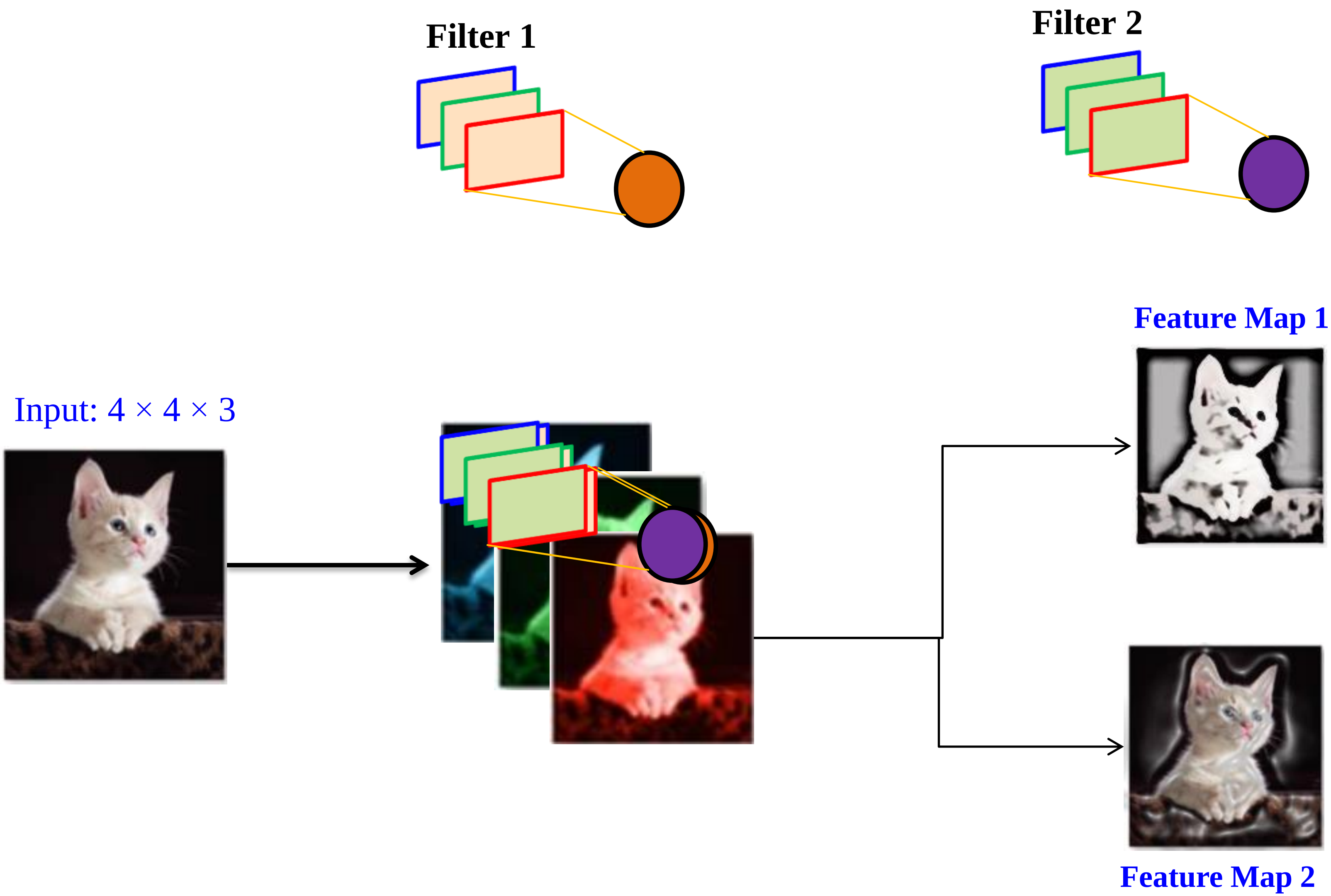


So, total # of connections = 3 * 3 * 3 = 27

Neuron 1
The connectivity to Filter 1 is managed by Neuron 1

Neuron 2
The connectivity to Filter 2 is managed by Neuron 2

Concept of Convolutional Neural Network



How the initial values of the Kernel is decided?

Different Keras Kernel Weight Initializers

Usage of initializers

- Initializers define the way to **set the initial random weights of kernel.**

Call the initial libraries to implement weight initializers:

```
from tensorflow.keras import layers
from tensorflow.keras import initializers
```

Available initializers in Keras:

1. RandomNormal class
2. RandomUniform class
3. TruncatedNormal class
4. Zeros class
5. Ones class
6. Constant class
7. GlorotNormal class
8. GlorotUniform class (Default initializer by Keras)
9. HeNormal class
10. HeUniform class
11. VarianceScaling class
12. Identity class
13. Orthogonal class

List of Hyper-parameters with values

Hyperparameter	Default Value	Usual Value	Range
Hyperparameters related to Training Algorithm			
Learning Rate	0.1*, 0.001#	0.1, 0.01, 0.001, 0.0001	[0,1]
# of Epochs	…	...	[1,2,…,N]
Batch Size	32	32, 64, 128, 256	Power of 2
Momentum (Momentum Decay1)	0.9	0.5-0.9	[0.1-0.9]
Momentum Decay2	0.999	...	[0.1-0.9]
Learning Rate Decay	0.2	0.1, 0.2	[0.1-0.9]
Hyperparameters related to Network structure			
Number of Hidden Units	…	Research Issue	[1,2,…,N]
Dropout	…	20%, 50%, 80%	…
Activation Function	…	ReLU, Sigmoid, Sigmoid	…

***: Stochastic Gradient Descent, #: Adam, RMSprop**

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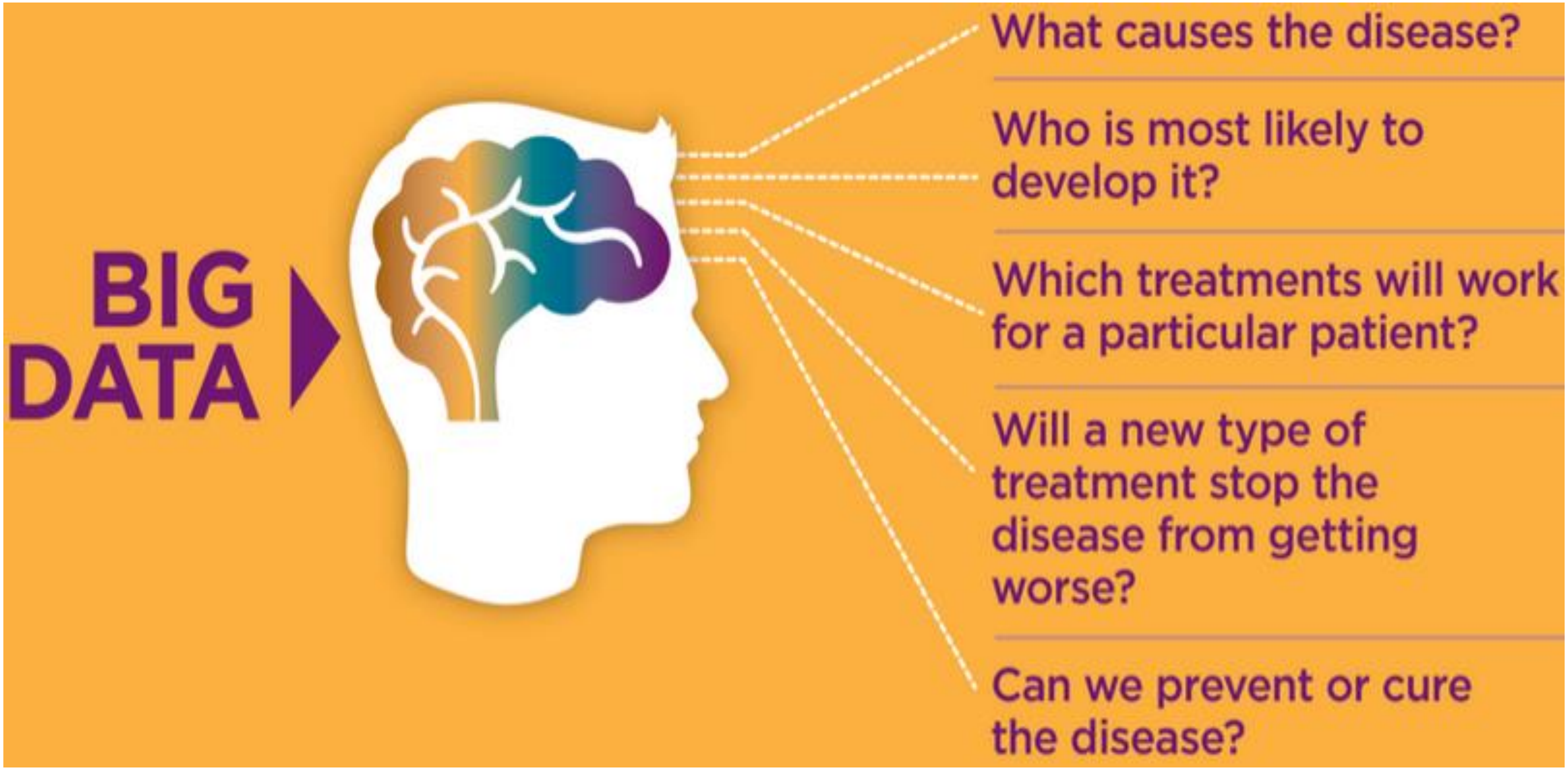
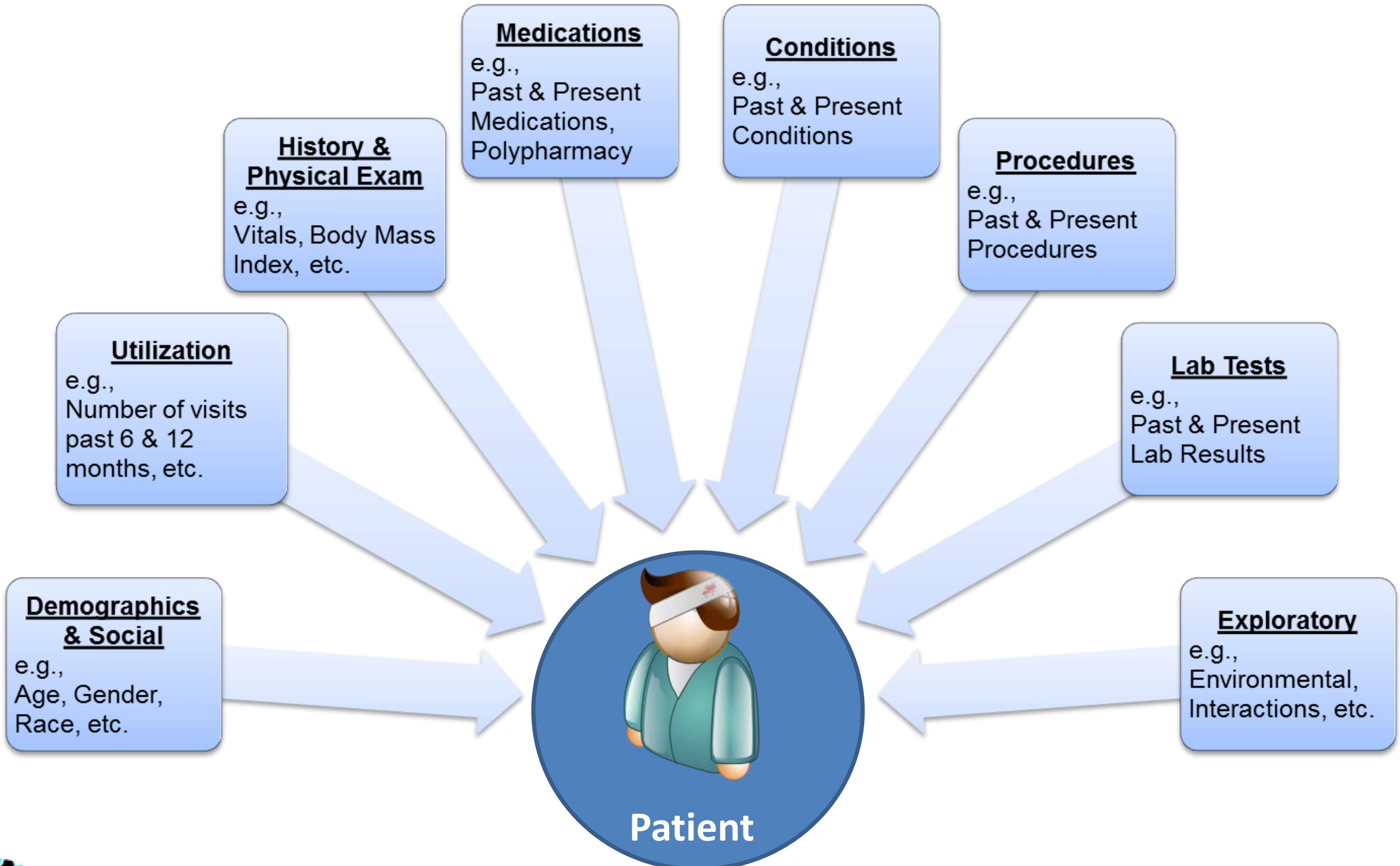
CNN: Network Architecture

- ❑ **Popular networks used in Fully Connected Layers (Dense Layers)**
- ❑ **Sequential CNN Architectures**
  - ❑ **LeNet-5**
  - ❑ **AlexNet**
  - ❑ **VGG16**
  - ❑ **VGG19**
- ❑ **Functional Network Architectures**
  - ❑ **GoogLeNet /Inception V1**
  - ❑ **BN-Inception/Inception V2**
  - ❑ **Inception V3**
  - ❑ **Inception V4**
  - ❑ **ResNet 50**
  - ❑ **ResNet 101**
  - ❑ **ResNet 152**
  - ❑ **InceptionRestV1**
  - ❑ **InceptionRestV2**

Introduction: Big Data in Healthcare

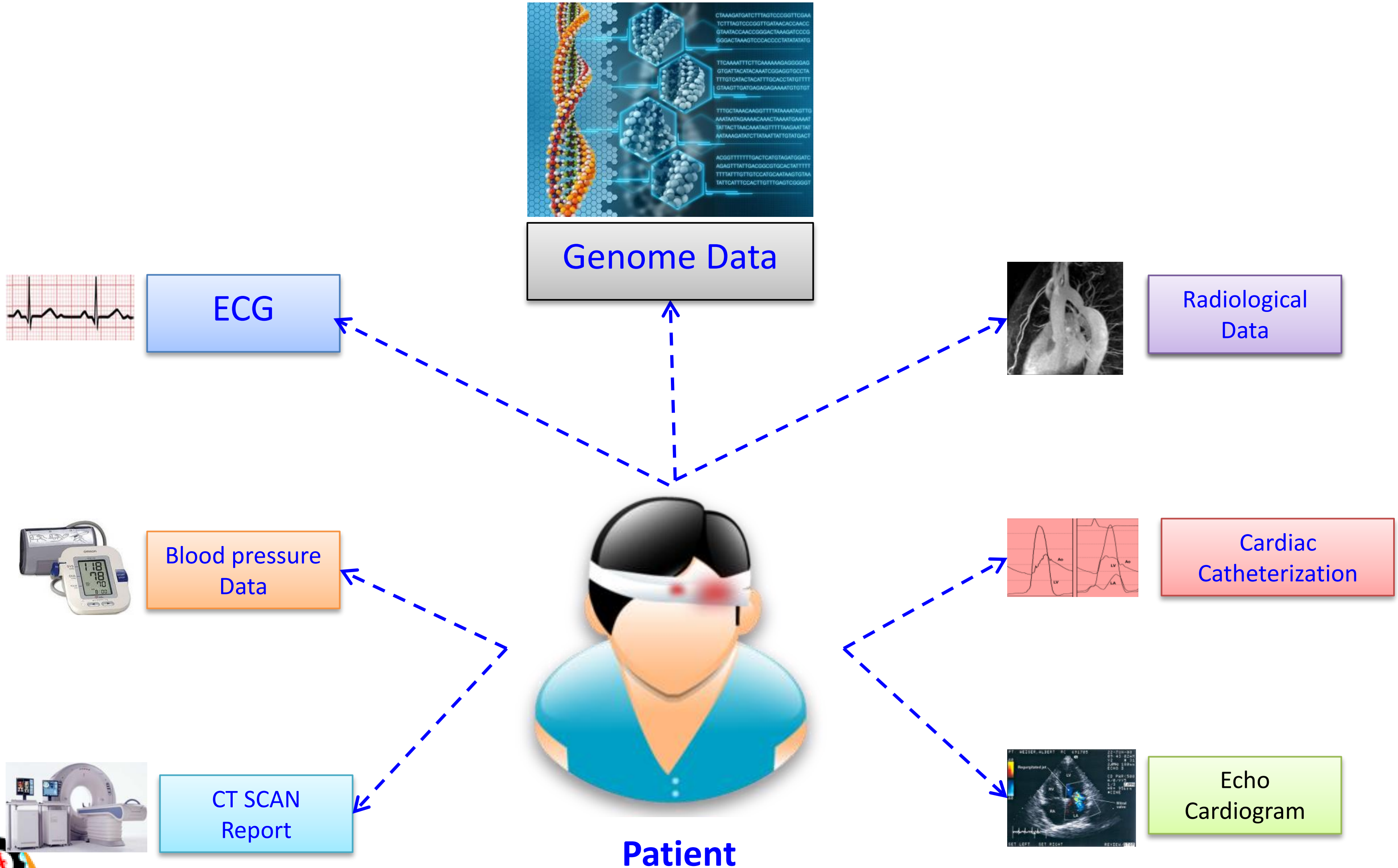


Standard Parameters



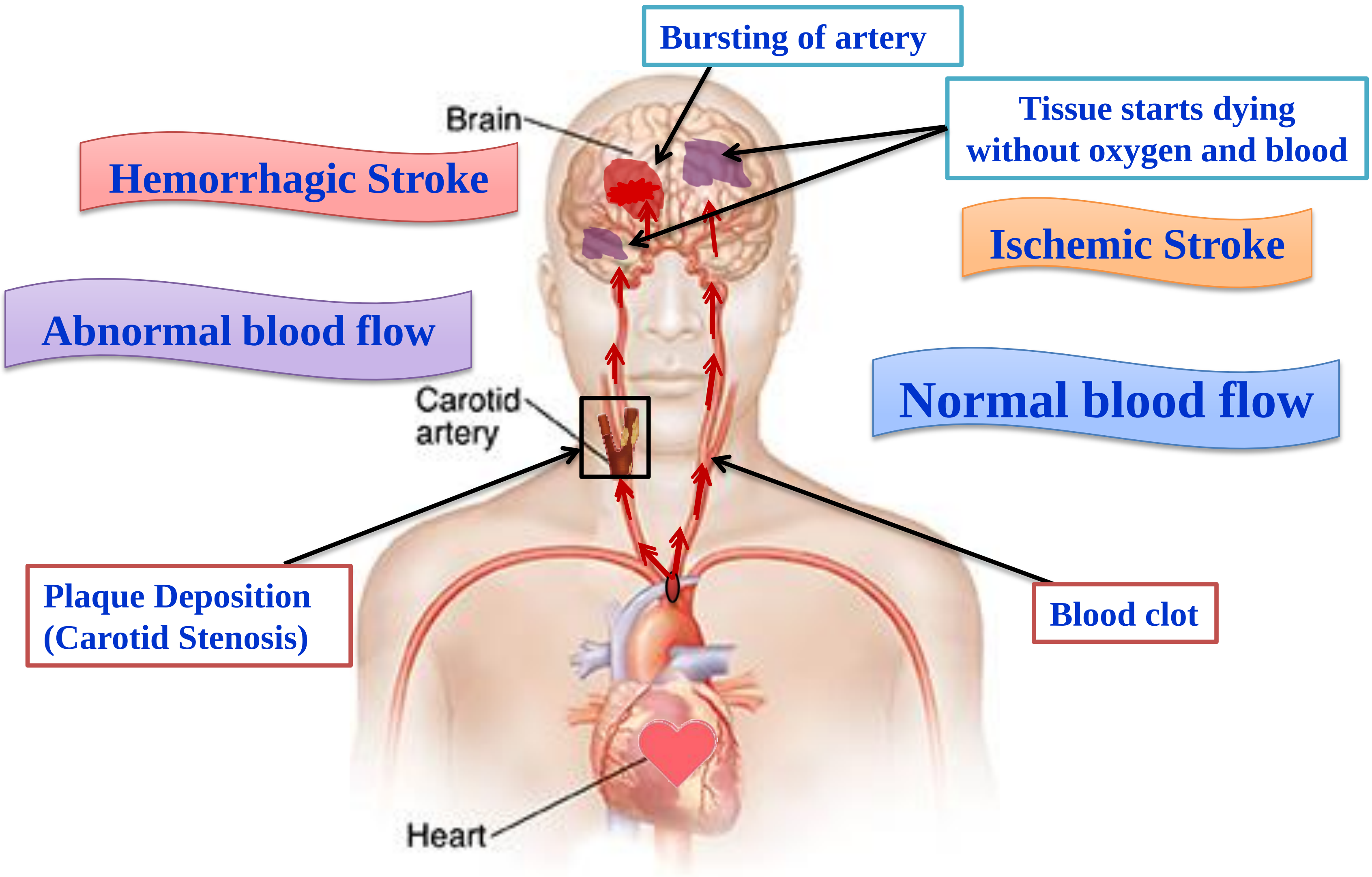
Challenges

- Huge heterogeneous data with diverse dimension.

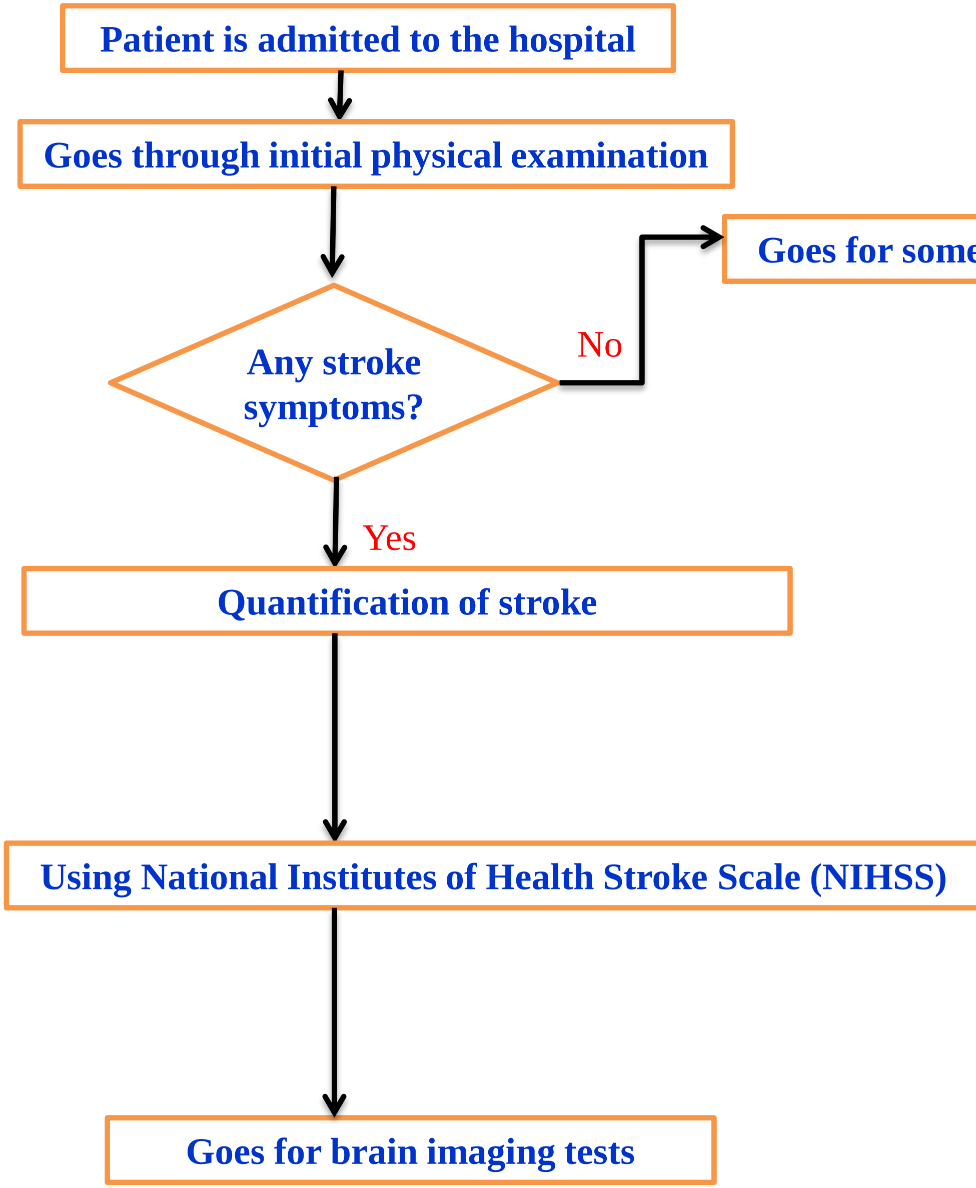


Cerebrovascular Disease (CVD) Image Data Analysis: Applications of Deep Learning

Introduction: Cerebrovascular Disease (CVD)



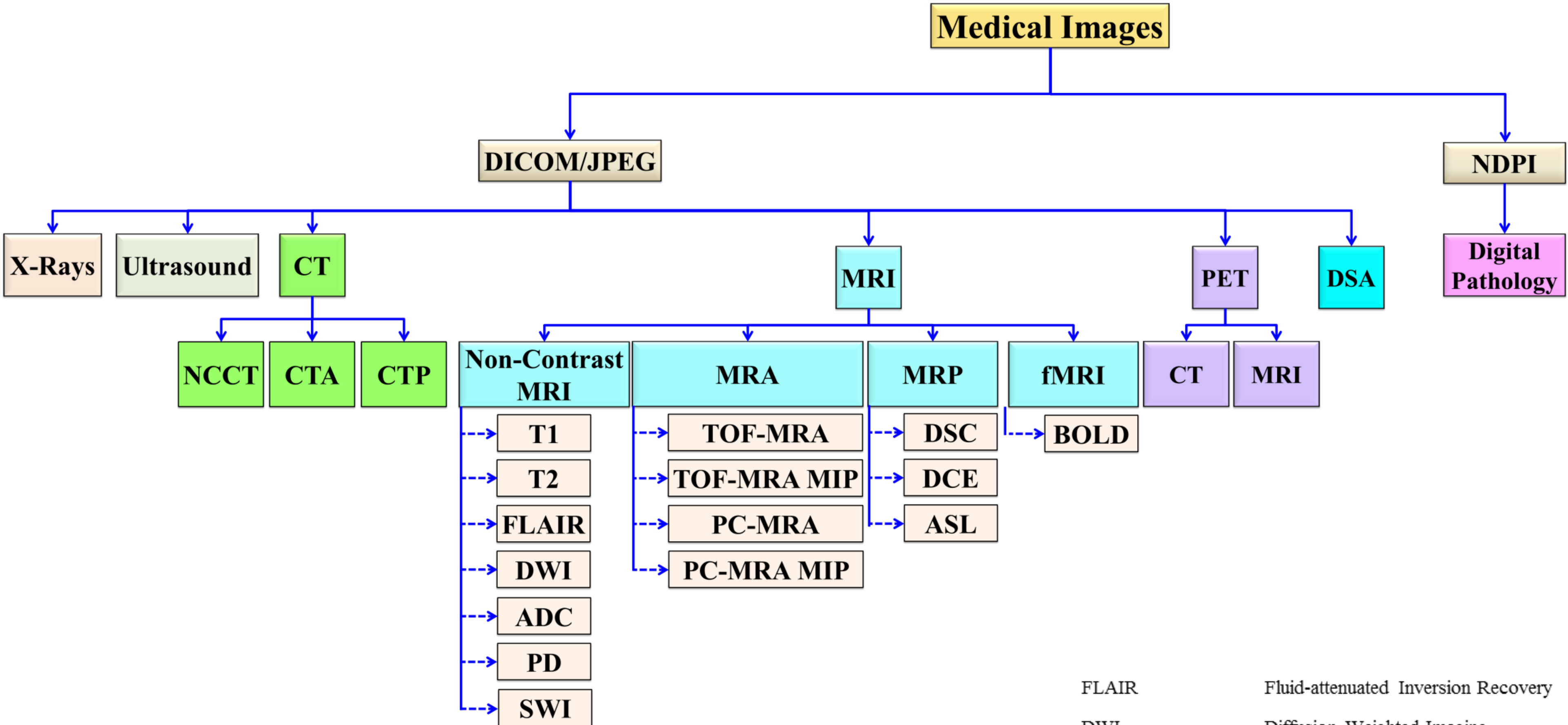
Diagnosis methods



NIHSS SCORE	STROKE SEVERITY	IMPACTED BRAIN DENSITY
0	No Stroke	
0 – 4	Minor Stroke	
5 – 15	Moderate Stroke	
16– 20	Moderate to Severe Stroke	
21 - 42	Severe Stroke	

Courtesy: https://en.wikipedia.org/wiki/National_Institutes_of_Health_Stroke_Scale

Types of Medical Images



CT	Computed Tomography
NCCT	Non-contrast CT
CTA	CT Angiography
CTP	CT Perfusion
MRI	Magnetic Resonance Imaging

MRP	Magnetic Resonance Perfusion
DSC	Dynamic Susceptibility Contrast
DCE	Dynamic Contrast Enhanced
ASL	Arterial Spin Labelling
BOLD	Blood-oxygen-level Dependent
PET	Positron Emission Tomography
DSA	Digital Subtraction Angiography

FLAIR	Fluid-attenuated Inversion Recovery
DWI	Diffusion Weighted Imaging
ADC	Apparent Diffusion Coefficient
PD	Proton Density
SWI	Susceptibility Weighted Imaging
MRA	Magnetic Resonance Angiography
TOF-MRA	Time-of-Flight MRA
TOF-MRA MIP	TOF-MRA Maximum Intensity
PC-MRA	Phase-contrast MRA

Types of brain images

- **Types of brain images**
  - **Computed Tomography (CT)**
    - **Non-Contrast CT (NCCT)**
    - **Contrast CT (CCT)**
      - **CT Angiography (CTA)**
      - **CT Perfusion (CTP)**
  - **Magnetic Resonance Imaging (MRI)**
    - **Non-Contrast MRI**
    - **Contrast MRI**
      - **MR Angiography (MRA)**
      - **MR Perfusion (MRP)**

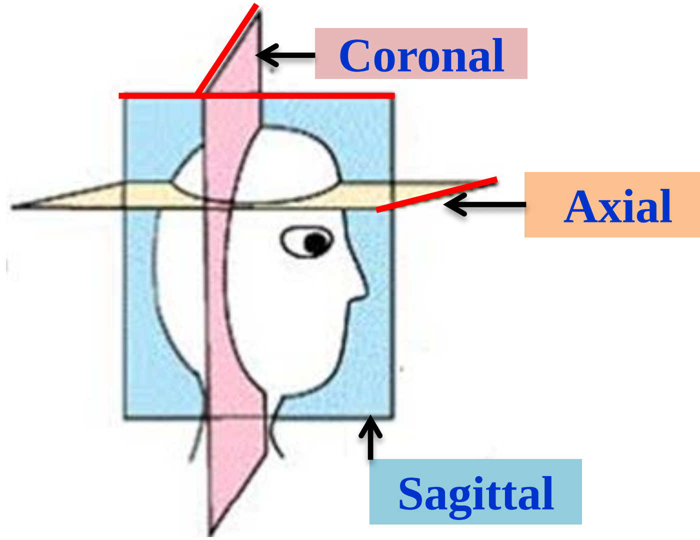
**External iodine-rich material is injected to generate contrast images

Image format

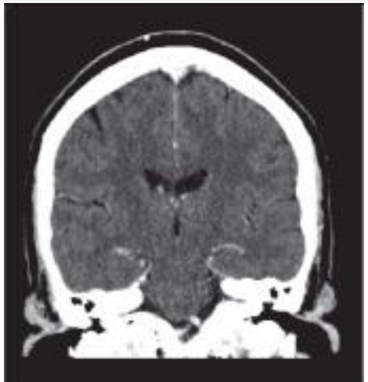
CT/MRI

DICOM (Digital Imaging and Communications in Medicine)

Imaging planes



Coronal
(front and back view)

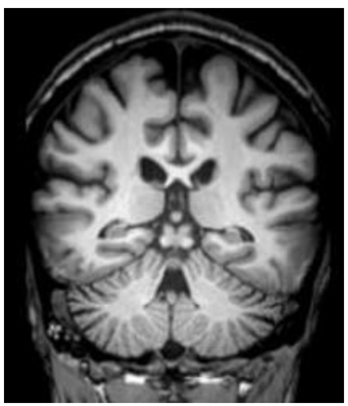


NCCT

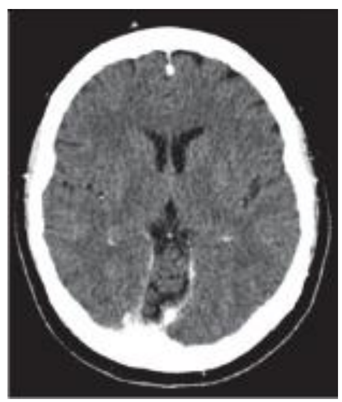
Axial (horizontal view)

Sagittal (lateral view)

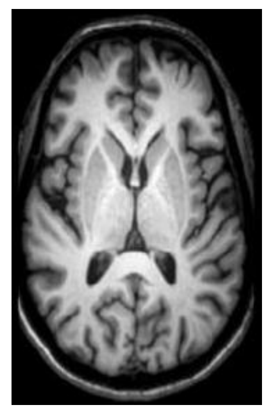
NCCT



MRI



NCCT

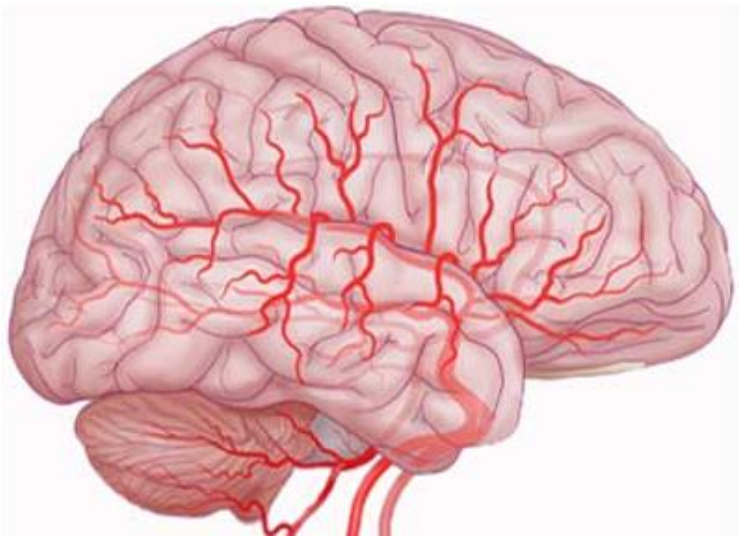


MRI

MRI

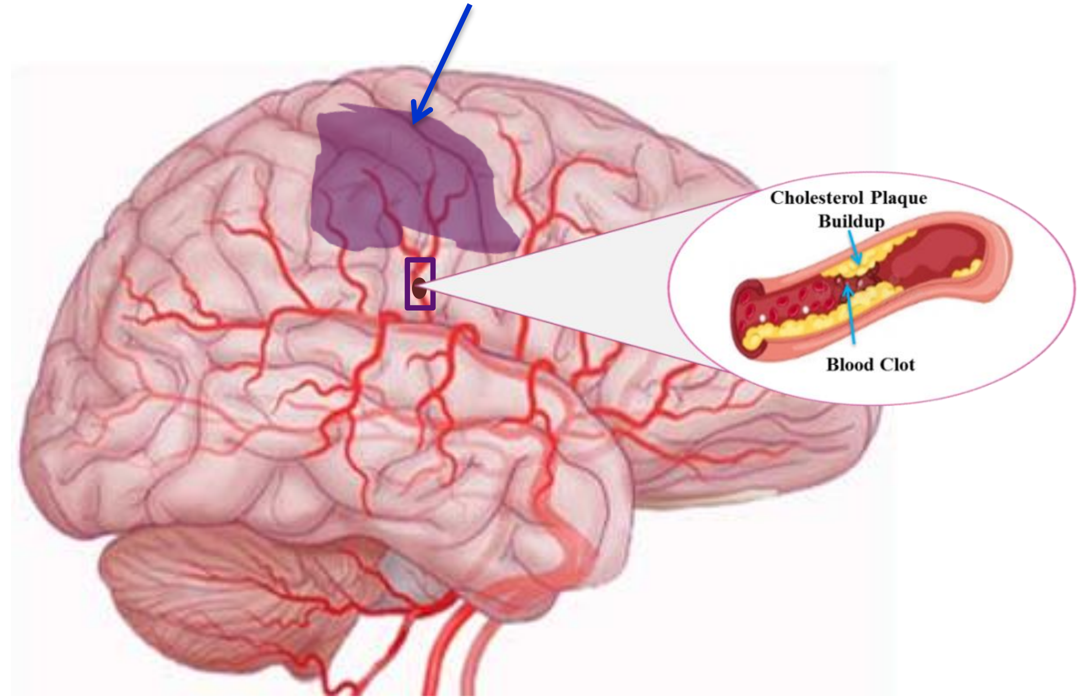
Courtesy: Quantification of Volumetric Changes of Brain in Neurodegenerative Diseases Using Magnetic Resonance Imaging and Stereology

Brain stroke (Ischemia)



Normal Human Brain

Ischemic region



Brain of Ischemic Stroke Patient

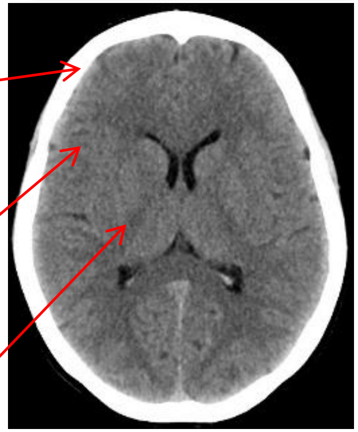
NCCT image of normal brain vs. ischemic brain

Normal brain

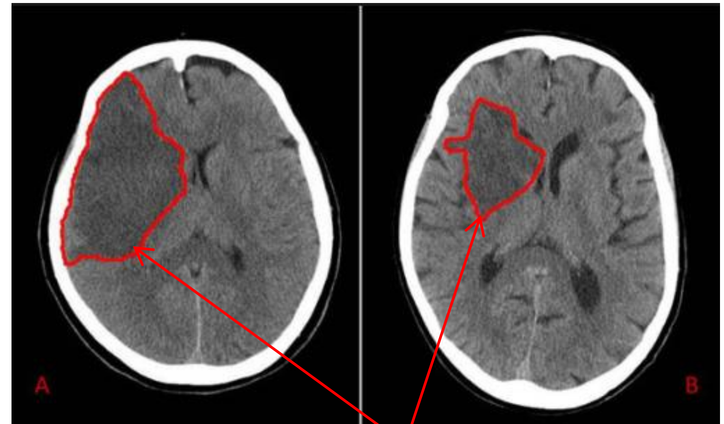
Bone

Blood vessels

Brain tissue



Ischemic brains

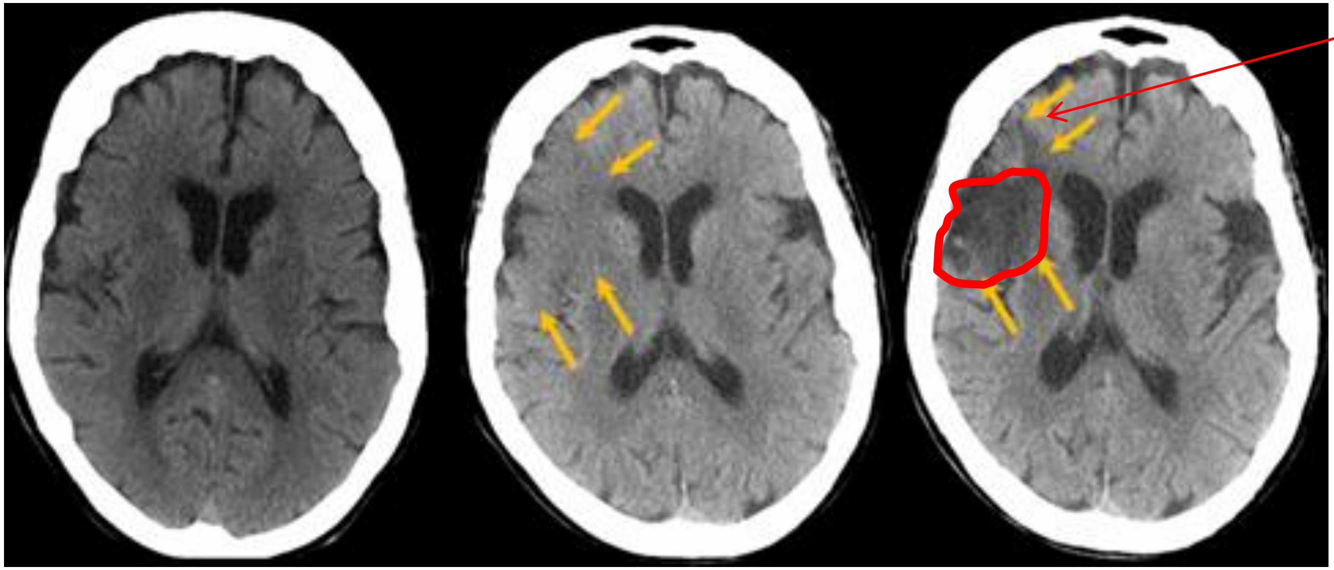


Ischemic region

Color difference between the parts of normal vs. ischemic brain		
Parts	**Colors**	
	Normal brain	**Ischemic brain**
Bone	White	White
Blood vessel	Mostly white	Mostly white
Brain tissue	Mostly gray	Dark gray (Ischemic region)

Courtesy: http://www.uwmedicine.org/health-library/pages/intracerebral-hemorrhage.aspx

Normal progression of infarction



3 hours

1 day

5 days

Ischemic region (the brain tissue color is changed to dark grey)

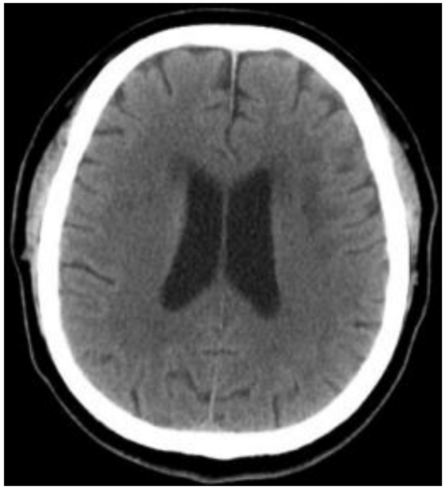
Impression:

In case of unenhanced brain CT image taken within some hours of stroke on-set, it is very difficult to find out the ischemic area by normal human eyes as the changes of color of the brain tissue in the ischemic region is not very prominent.

Motivation (1/8)

** Normally, NCCT image is taken when a patient is admitted to the hospital.

❑ Clinical difficulties:



NCCT image: Normal patient

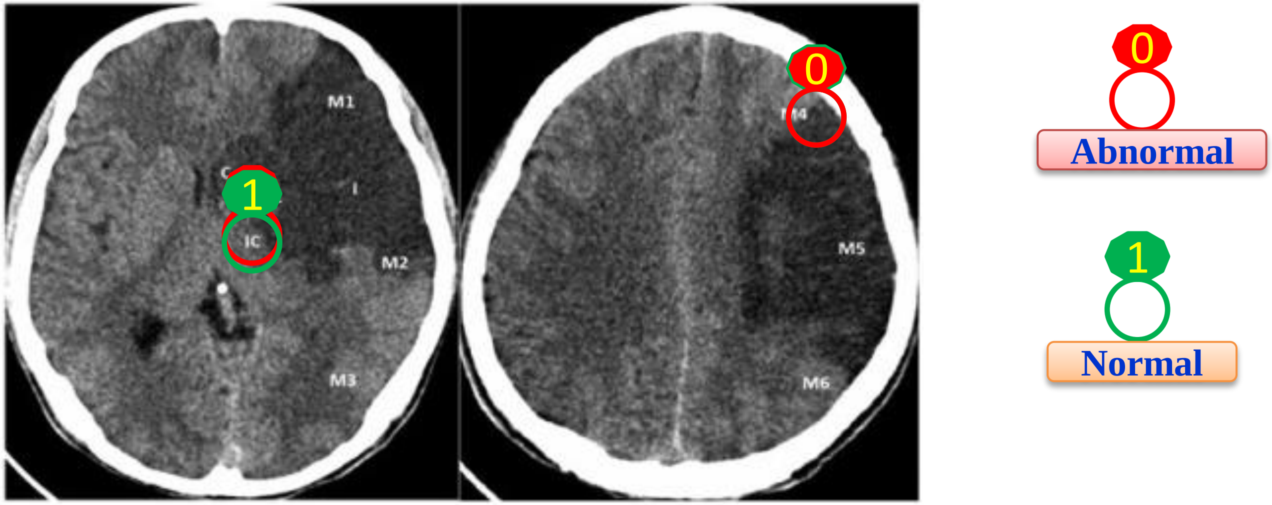
NCCT image: Ischemic stroke patient

- **Difficult to distinguish between the normal and ischemic stroke patients through naked eye**
  - **Due to similar color intensity of the brain tissue.**

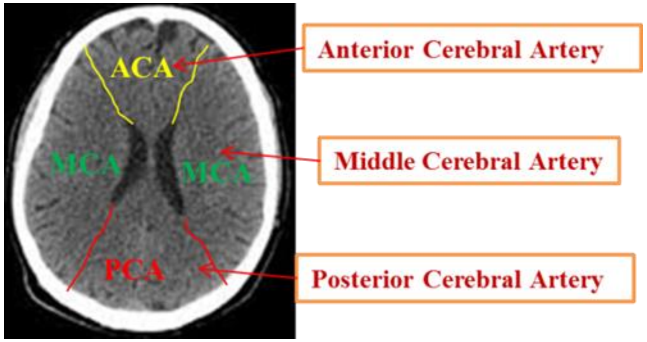
Courtesy: https://analyzedirect.com/documents/guides/IntracerebralHematomaVolumeCT.pdf

❑ Clinical difficulties:

- **Manual quantification of ischemic stroke using Alberta Stroke Programme Early CT Score (ASPECTS) is not accurate.**



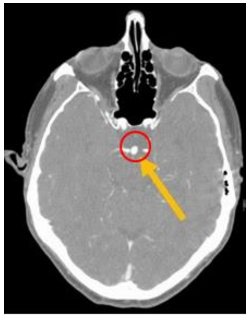
- **Diagnosis results could be different among neurologists.**
- **ASPECT score only focusses the MCA region.**



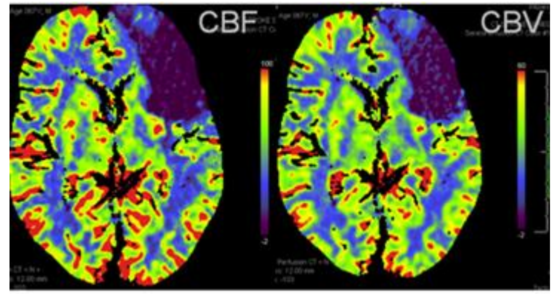
Courtesy: https://teddybrain.wordpress.com/2013/03/16/alberta-stroke-program-early-ct-score-aspects-in-ischemic-stroke/

Motivation (3/8)

❑ Clinical difficulties:



CTA



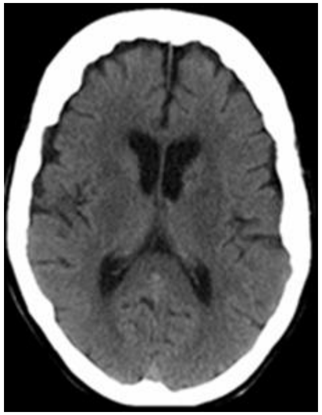
CTP

- **Although the Contrast CT (CCT) image provides more detail about the ischemic region, the imaging methods use high rate iodine-rich contrast material.**

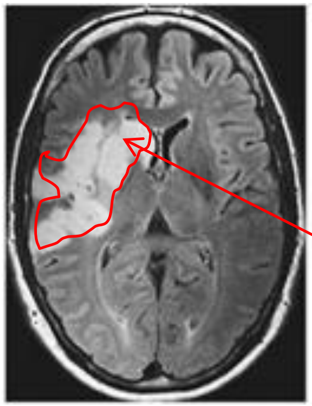
- **These contrast material has many side effects such as**
  - **Chance of cancer.**
  - **Serious allergic reaction to contrast materia**
  - **Health issues based on the radiation dose.**

Courtesy: https://sites.google.com/a/wisc.edu/neuroradiology/image-acquisition/vascular-imaging/cta
http://neuroangio.org/neuroangio-topics/perfusion-primer/

❑ Clinical difficulties:



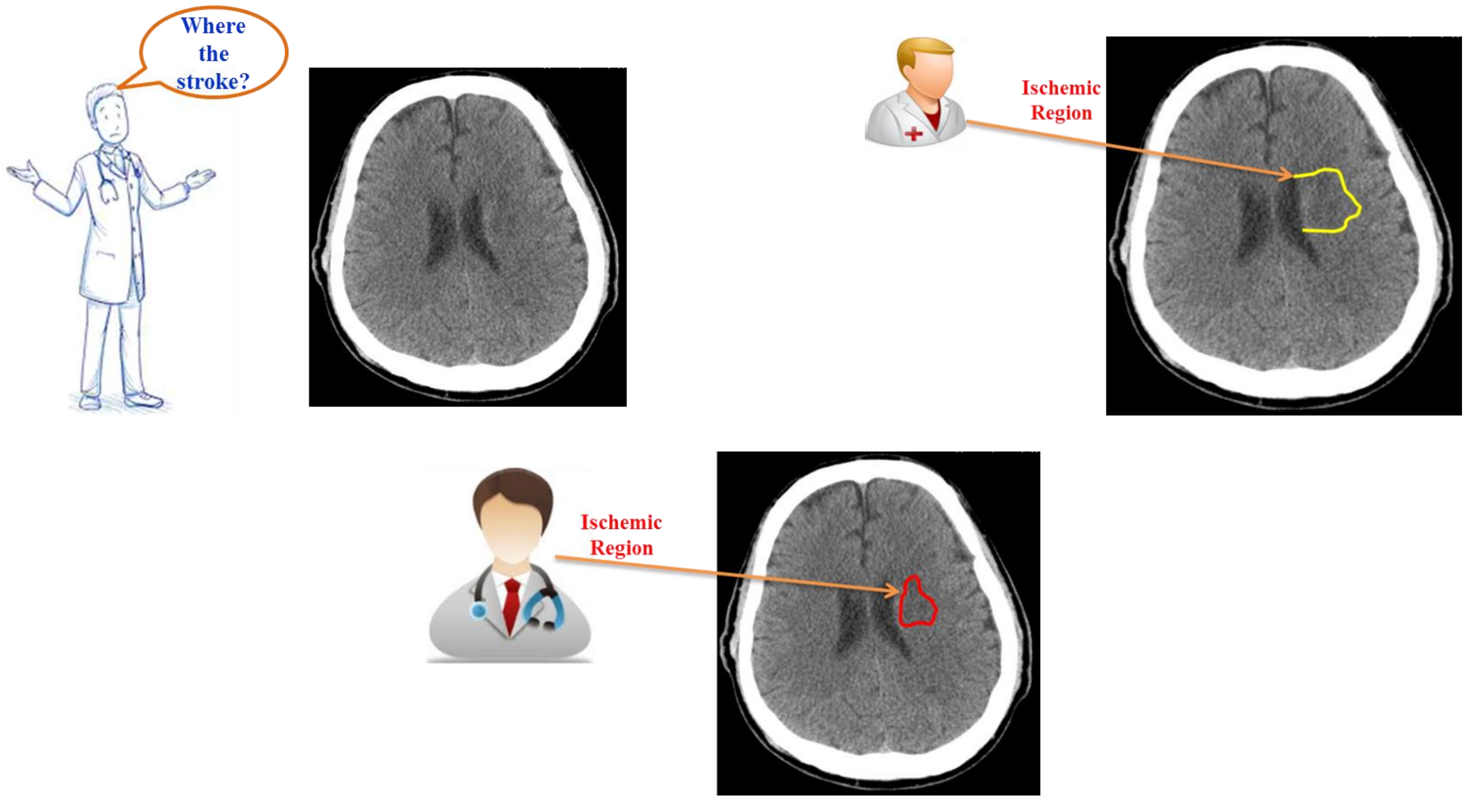
NCCT



MRI

- **Although MRI image provides clear image of ischemic region in comparison to NCCT, MRI has some limitations.**
  - **Time consuming.**
  - **Not always available**
  - **Expensive**

❑ Technical difficulties:

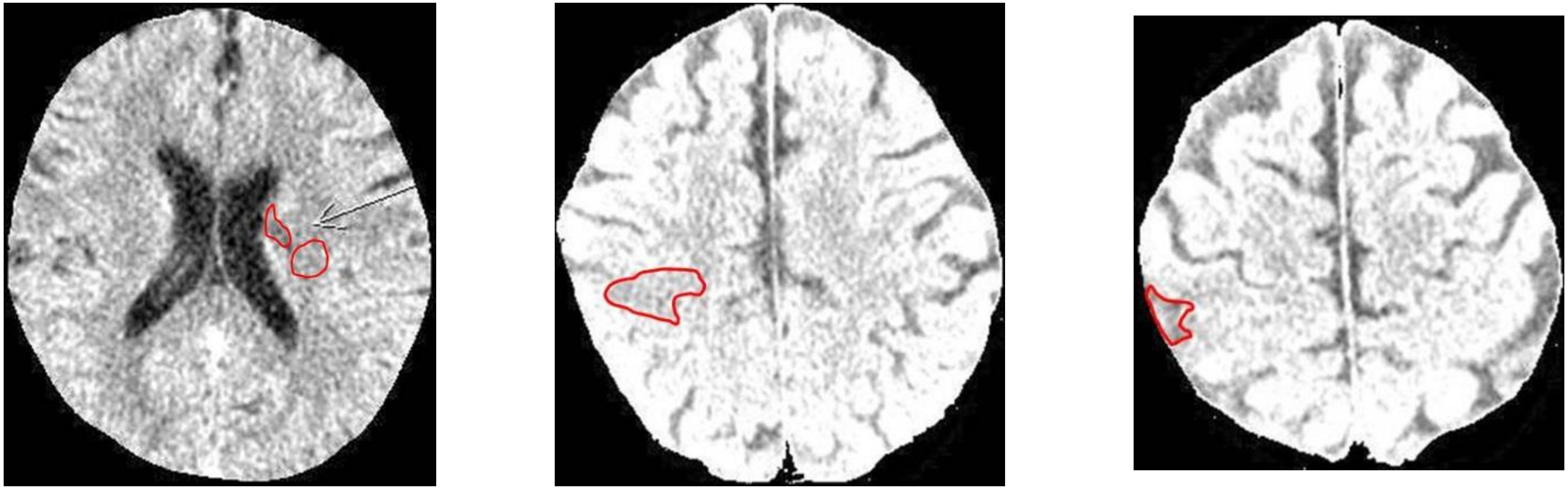


NCCT image: Ischemic stroke patient

- **Localization of ischemic region is bit difficult due to similar color intensity with surrounding tissues.**

Motivation (6/8)

❑ Technical difficulties:

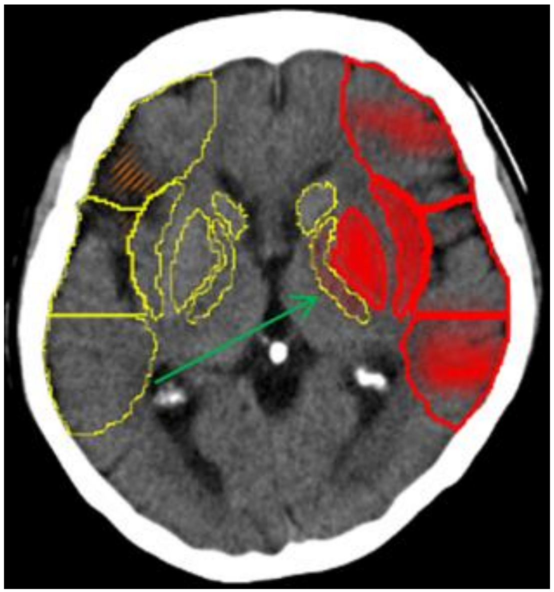


NCCT images: Ischemic stroke patients

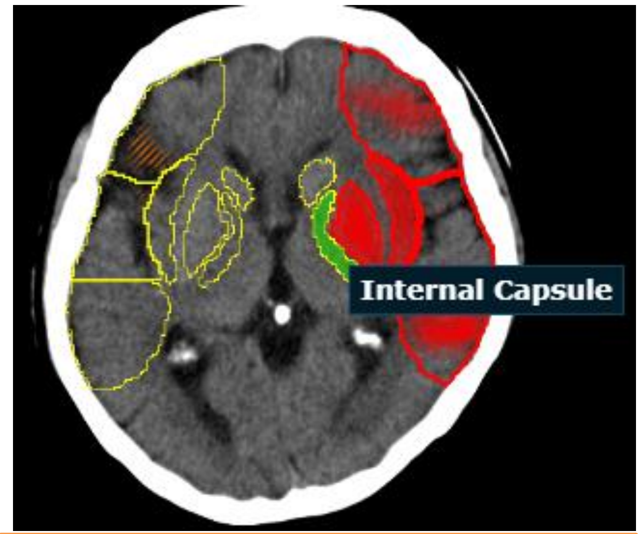
- **No particular location of occurrence of ischemic stroke.**
- **Difficult to determine the area of the ischemic region due to irregular shape.**

❑ Technical difficulties:

- Existing software e-ASPECT (developed by Brainomix) does not provide accurate detection of ischemic stroke region.



Original image
(Internal capsule is affected)



Output
(Display no abnormality in Internal capsule (green color))

- The accuracy depends on the underlying programming
- Needs more cost to purchase and maintain

Courtesy: https://demo.brainomix.com/scan/3?field=study_date_time&order=descending&first=1

❑ Technical difficulties:

- Existing software such as RAPID does not provide accurate detection of ischemic stroke region.

6 affected areas M1, M2, IC, C, I, L Which are marked in red color

The ASPECT score confidence level is 4 instead of 6

❑ The accuracy depends on the underlying programming

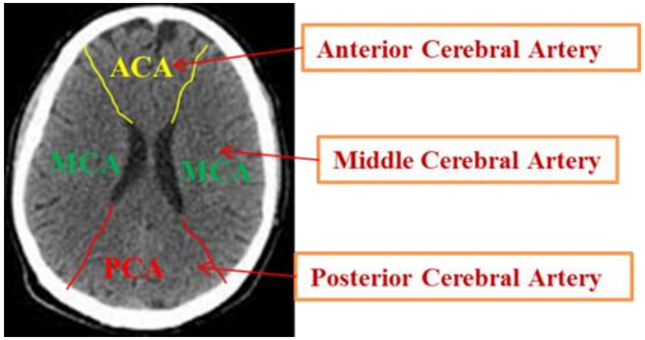
❑ Expensive

Courtesy: Courtesy: Brain ischemia_ CT and MRI techniques in acute ischemic stroke

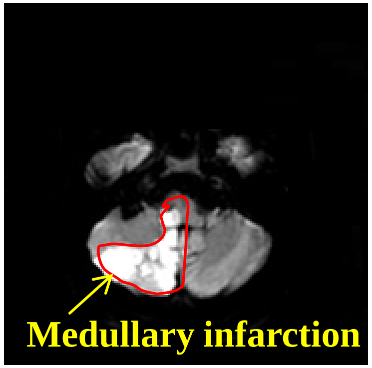
- **Ischemic stroke (NCCT):**
  1. Classification of normal and ischemic stroke patients using deep learning
  2. Localization of ischemic stroke region using deep learning

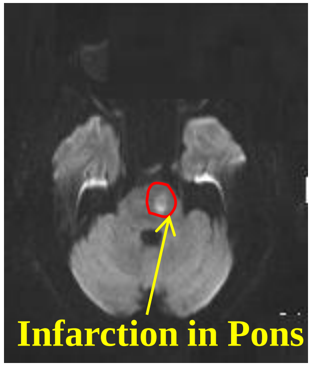
Background of our Analysis (1/5)

- **Considered image type for analysis: NCCT.**
- **Considered regions for analysis:**
  - **Cerebrum (ACA, MCA & PCA regions)**

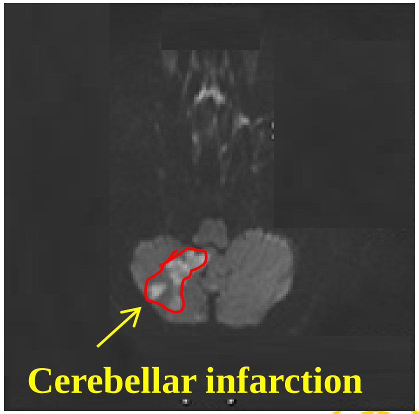


  - **Brain Stem**
    - **Medulla**
    - **Mid-brain**
    - **Pons**





  - **Cerebellum**



Background of our Analysis (2/5)

- **Considered age of the ischemic stroke:**
  - **Age of the Ischemic Stroke** =

Stroke on-set time – Time of the stroke diagnosis (1st NCCT image acquisition time)

Considered age of the ischemic stroke

< 6hr

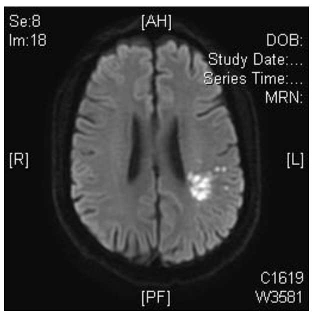
6hr ~ 12 hr

Background of our Analysis (3/5)

- **Considered categories of the ischemic stroke based on stroke visibility:**

Considered categories of ischemic stroke based on stroke visibility

Category 1
(Not visible in NCCT & Visible in DWI)

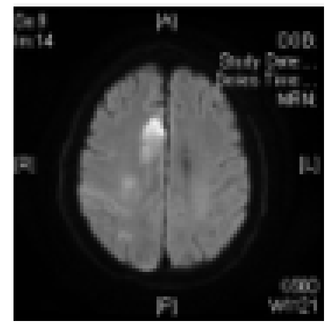


(DWI sequence)

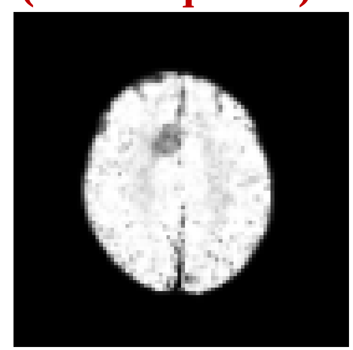
(Corresponding NCCT slice)

Current, considered for analysis

Category 2
(Visible in NCCT & Visible in DWI)



(DWI sequence)

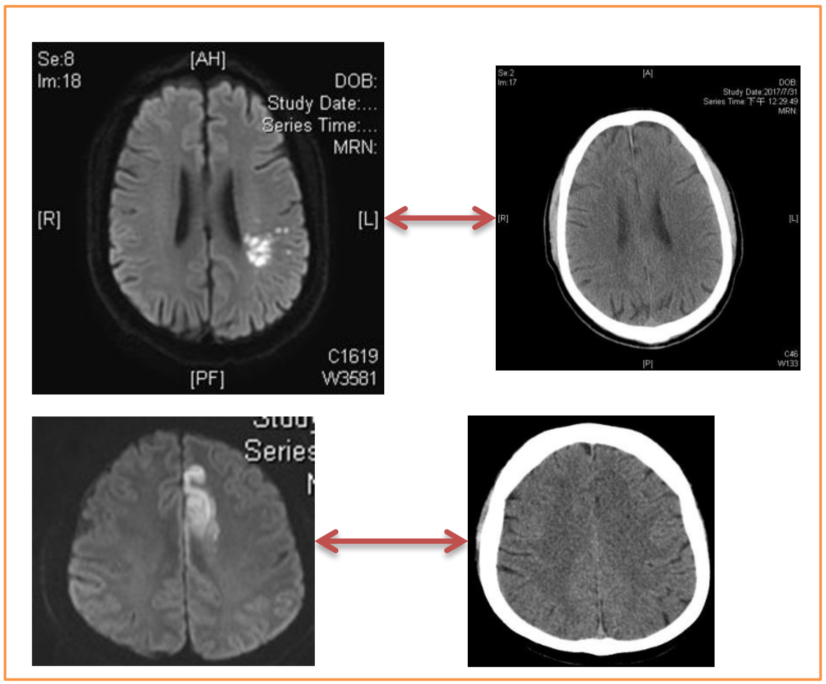


(Corresponding NCCT slice)

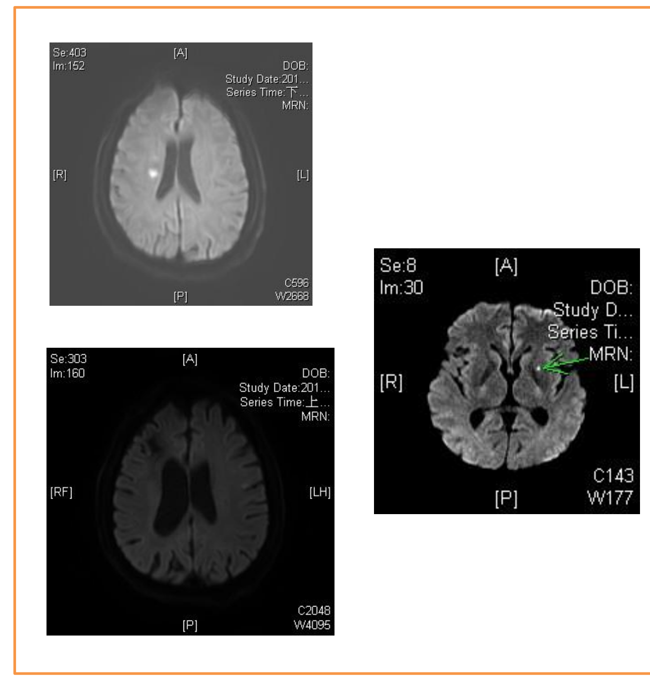
Background of our Analysis (4/5)

Considered categories of ischemic stroke based on size (For Category 1)

Category 1A
Not visible in NCCT, but
Visible: Larger size of
ischemic region in DWI



Category 1B
Not visible in NCCT, but
Visible: Negligible size of ischemic
region in DWI (Lacune)



Summary of tools & framework

Parameters	Description
Image pre-processing tool	**MATLAB R2018a**
Platform	**Ubuntu**
Deep learning frameworks	**TensorFlow**
Deep learning libraries	**Keras, Theano**
CNN architectures	**AlexNet, VGGNet, GoogleNet, Inception, ResNet**

Implementation: Image Analysis Phase (2/2)

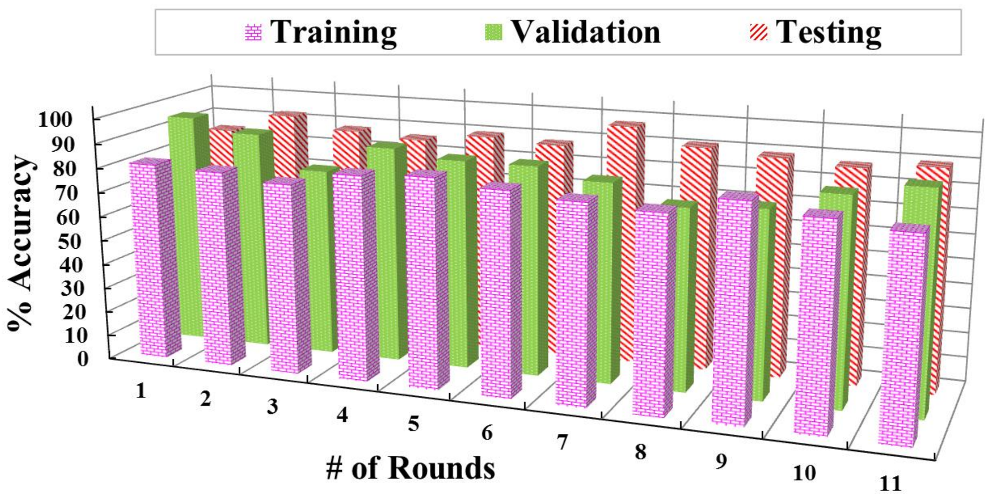
Overview of Implementation Platform:

	Specification
Processor	Intel® Xeon® Scalable Processors, 3 UPI up to 10.4GT/s
Memory	256 GB
GPU	TITAN RTX 24GB * 4
Operating System	Ubuntu 18.04.3 LTS
Kernel	Linux 4.15.0-65-genericx 86_64
NVIDIA-SMI	430.40
CUDA	10.0

Implementation: Patch Classification Phase

Performance Analysis Classification Model (90%_Train:10%_Test):

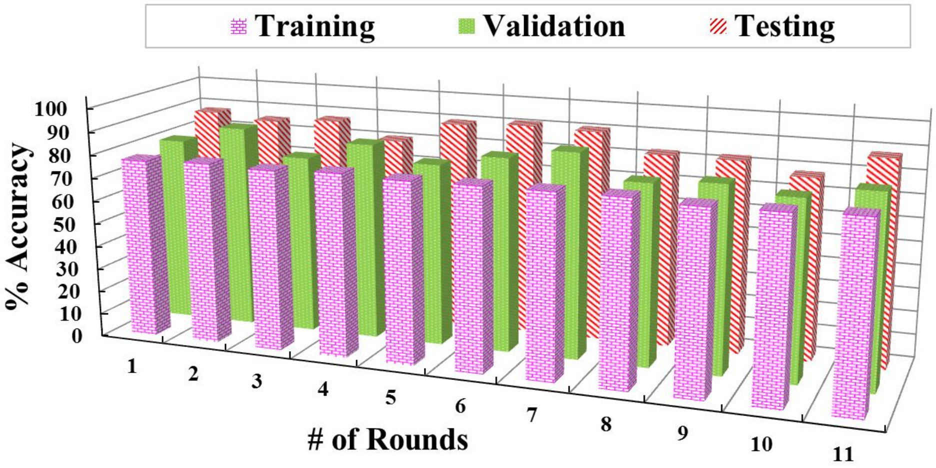
# of Rounds	% of Accuracy		
	Training	Validation	Testing
Round 1	81.18	95.08	84.5
Round 2	80.16	90.00	92.51
Round 3	77.53	76.67	87.95
Round 4	83.28	88.25	86.14
Round 5	84.82	85.26	89.39
Round 6	82.17	85.25	87.86
Round 7	80.02	81.05	97.4
Round 8	78.42	73.63	90.93
Round 9	85.25	75.56	88.88
Round 10	81.24	83.33	87.16
Round 11	78.60	88.16	89.46



Implementation: Patch Classification Phase

Performance Analysis of Case 2 (80%_Train: 20%_Test):

# of Rounds	% of Accuracy		
	Training	Validation	Testing
Round 1	77.18	80.00	87.78
Round 2	78.16	87.50	85.53
Round 3	77.53	76.67	87.47
Round 4	78.62	84.62	80.53
Round 5	77.82	78.18	89.75
Round 6	78.17	83.33	91.18
Round 7	78.32	87.80	90.59
Round 8	78.42	77.50	82.66
Round 9	77.25	79.49	82.66
Round 10	77.64	76.36	77.88
Round 11	78.60	81.25	88.03

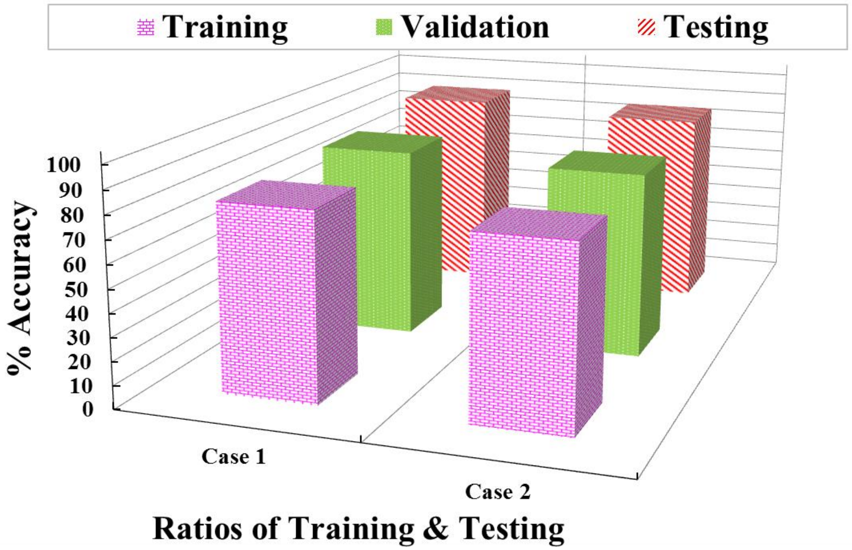


Implementation: Patch Classification Phase

Comparison of Accuracy Case 1 Vs. Case 2:

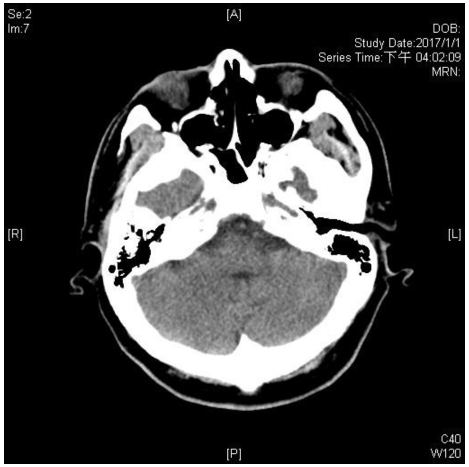
# of Cases	% of Accuracy		
	Training	Validation	Testing
Case 1 (90%_Train: 10%_Test)	81.15	83.34	89.28
Case 2 (80%_Train: 20%_Test)	77.97	81.15	85.82

The % of Accuracy is almost same in both Case 1 & Case 2 signifying the robustness of our Deep Learning Classification model.

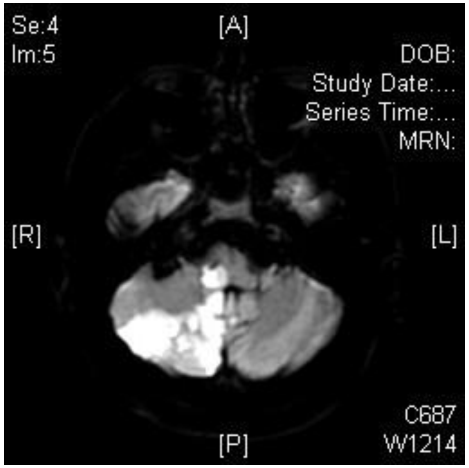


Implementation: Ischemic Stroke Visualization Phase

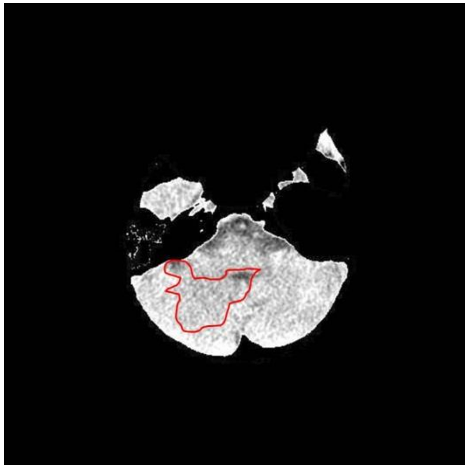
Right Medullary Infarction



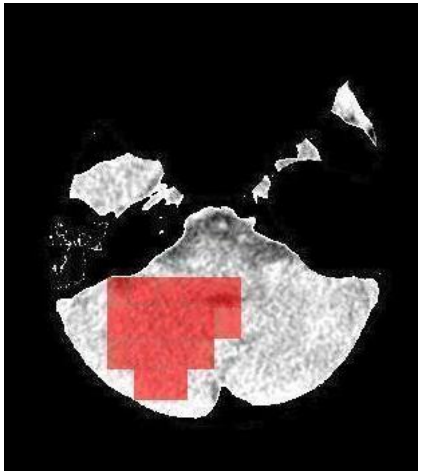
Raw NCCT image



Corresponding DWI image



Ground Truth

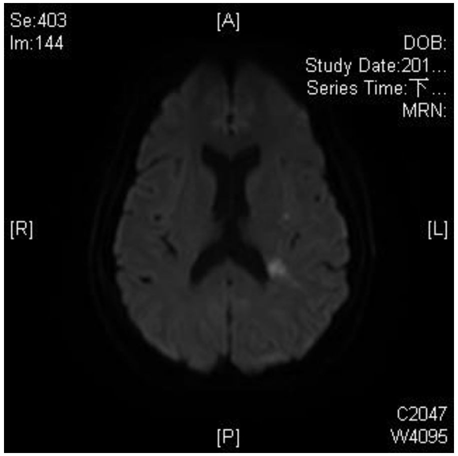


Localized ischemic region

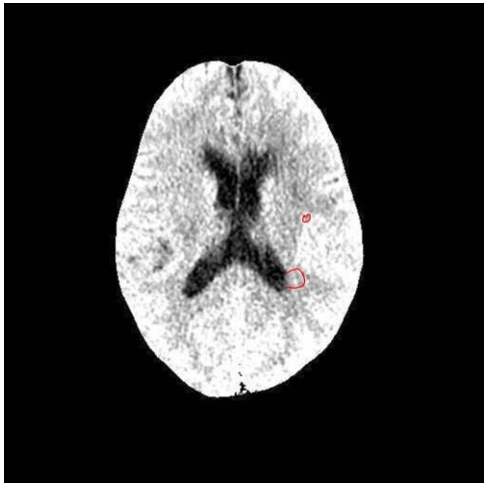
Implementation: Ischemic Stroke Visualization Phase

Left hemisphere Infarction (Lacune : 0.4 cm)

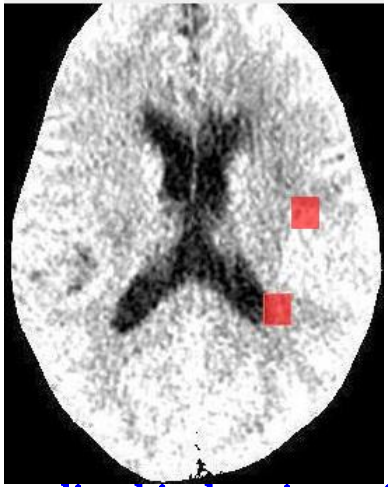
Raw NCCT image



Corresponding DWI image



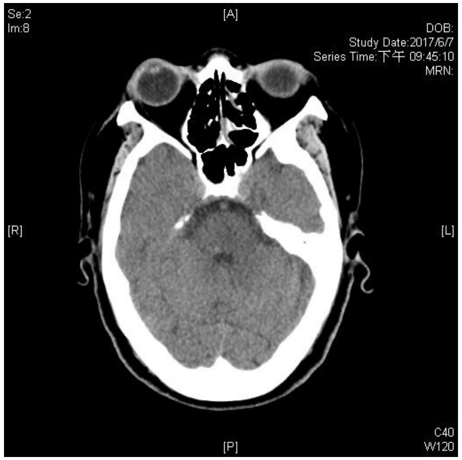
Ground Truth



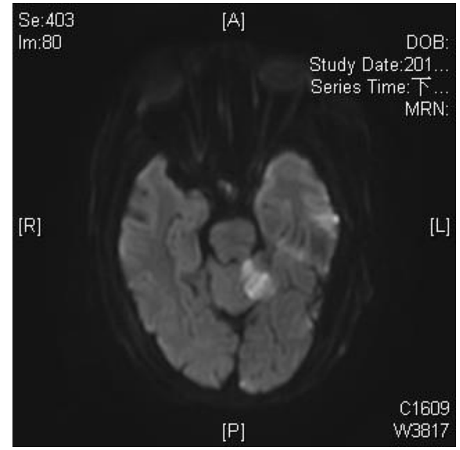
Localized ischemic region

Implementation: Ischemic Stroke Visualization Phase

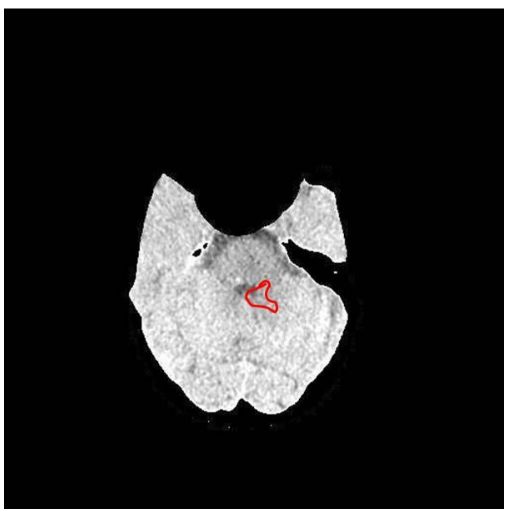
Brain Stem Infarction



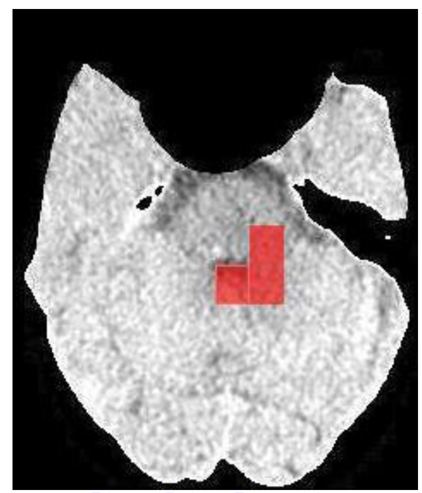
Raw NCCT image



Corresponding DWI image



Ground Truth

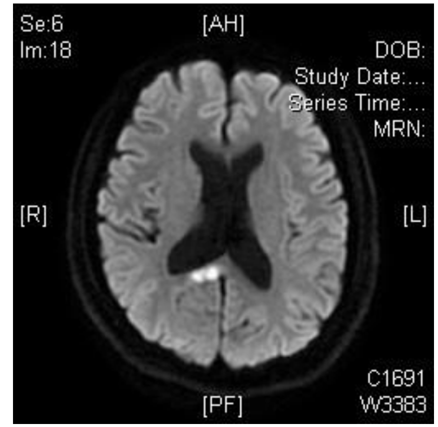


Localized ischemic region

Implementation: Ischemic Stroke Visualization Phase

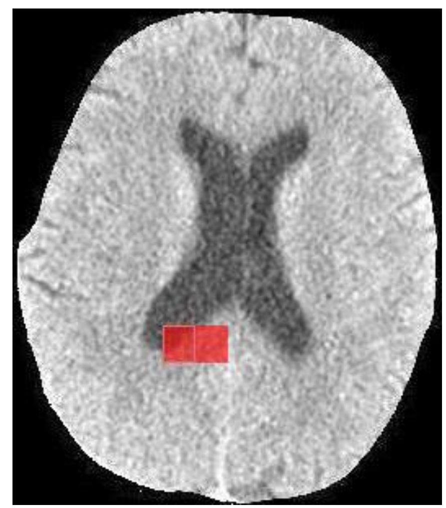
Infarction at Corpus Callosum

Raw NCCT image



Corresponding DWI image

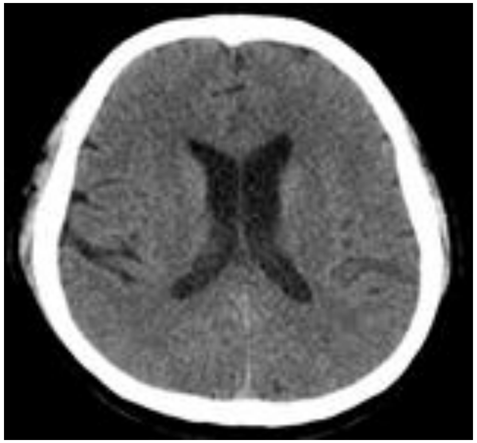
Ground Truth



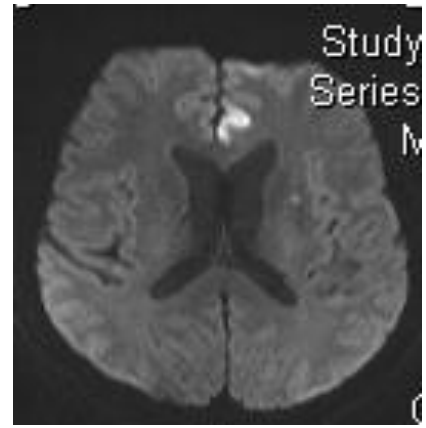
Localized ischemic region

Implementation: Ischemic Stroke Visualization Phase

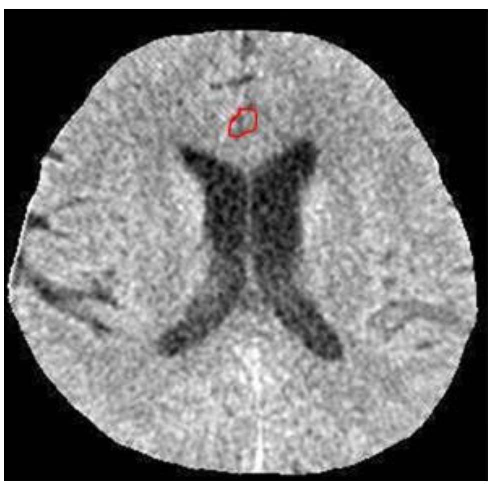
Infarction at ACA Region



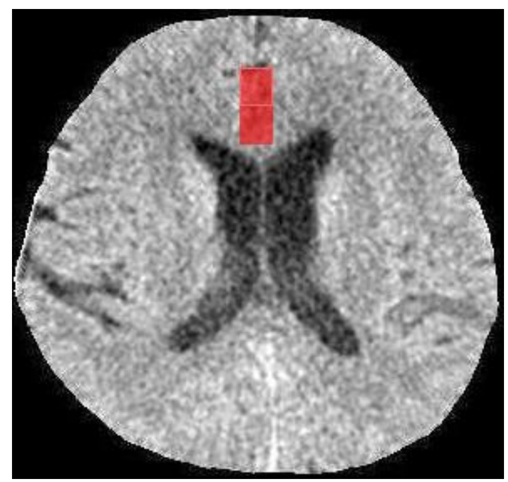
Raw NCCT image



Corresponding DWI image



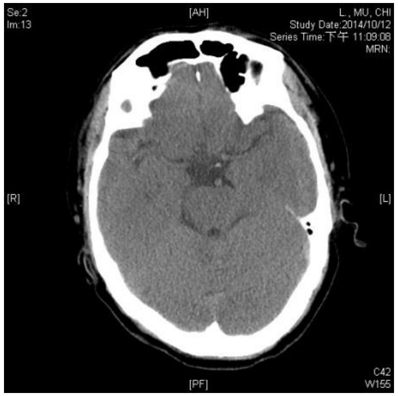
Ground Truth



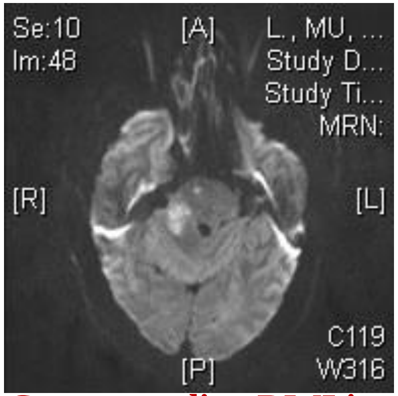
Localized ischemic region

Implementation: Ischemic Stroke Visualization Phase

Infarction at Pons region

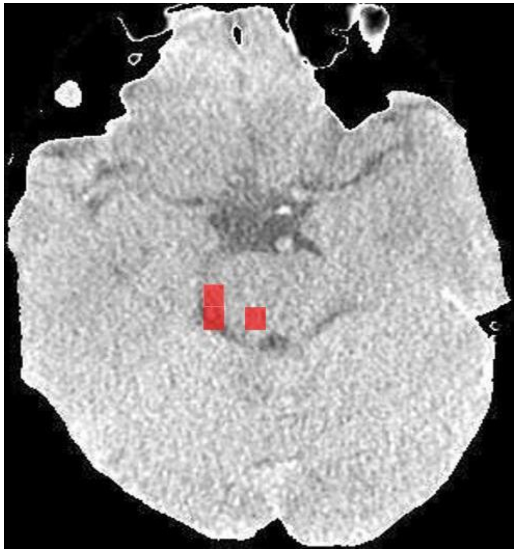


Raw NCCT image



Corresponding DWI image

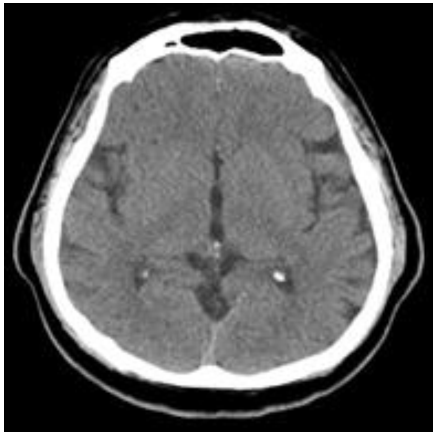
Ground Truth



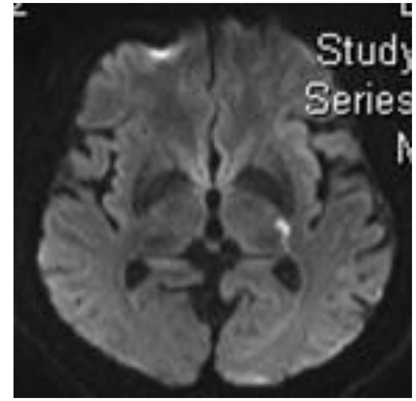
Localized ischemic region

Implementation: Ischemic Stroke Visualization Phase

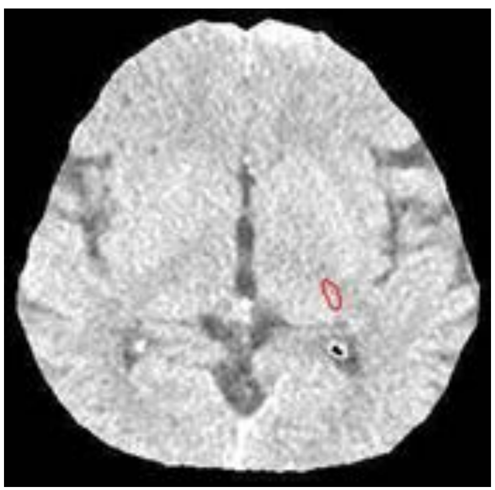
Left-thalamic lacunar infarction



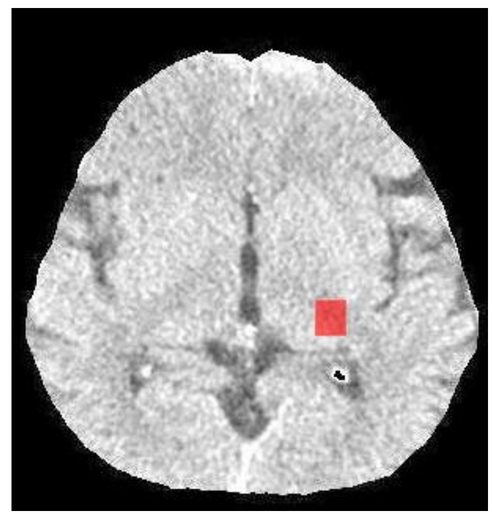
Raw NCCT image



Corresponding DWI image



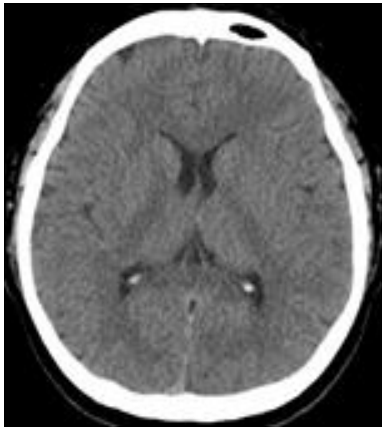
Ground Truth



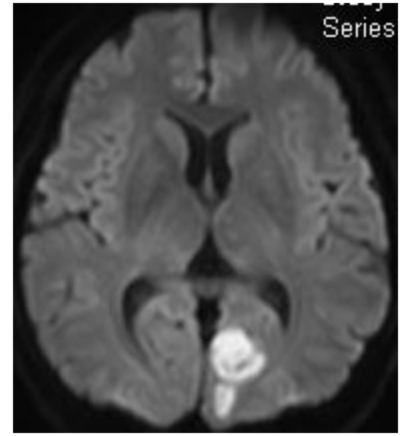
Localized ischemic region

Implementation: Ischemic Stroke Visualization Phase

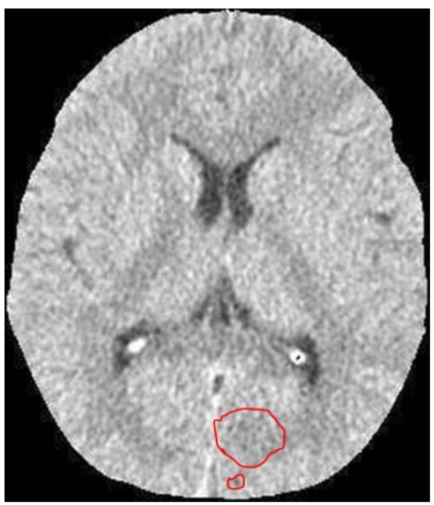
Left PCA territory infarction



Raw NCCT image



Corresponding DWI image



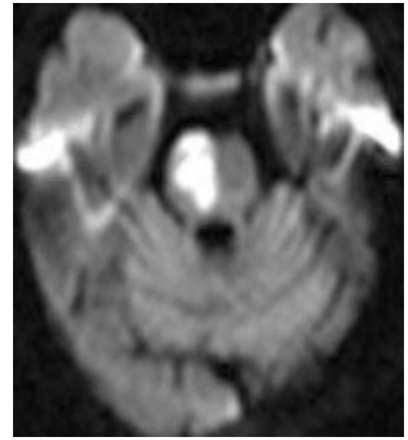
Ground Truth

Localized ischemic region

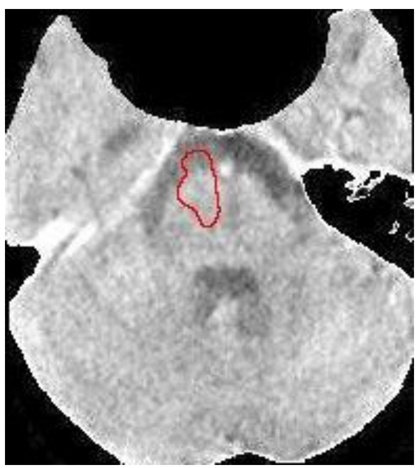
Implementation: Ischemic Stroke Visualization Phase

Infarction at Pons

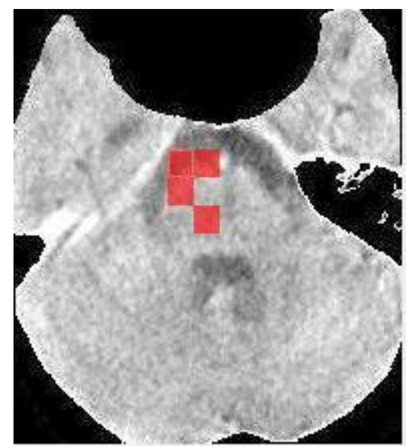
Raw NCCT image



Corresponding DWI image



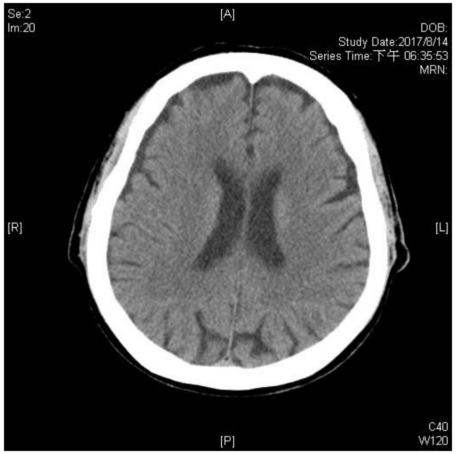
Ground Truth



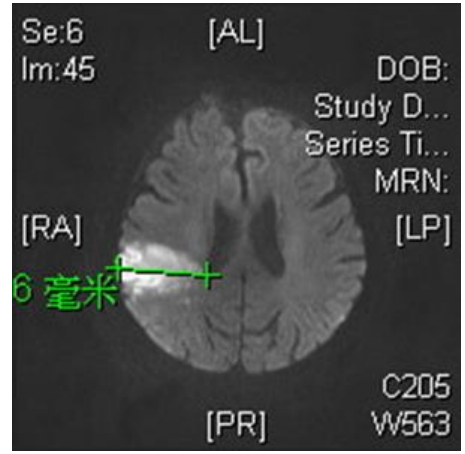
Localized ischemic region

Implementation: Ischemic Stroke Visualization Phase

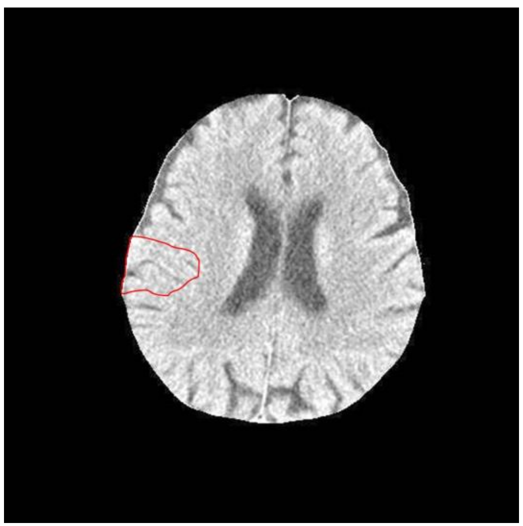
Right hemisphere infarction



Raw NCCT image

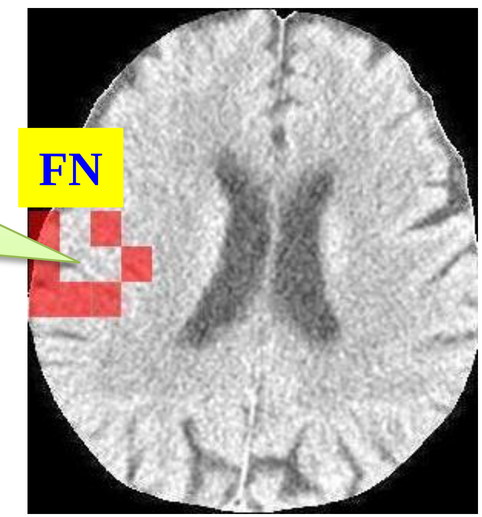


Corresponding DWI image



Ground Truth

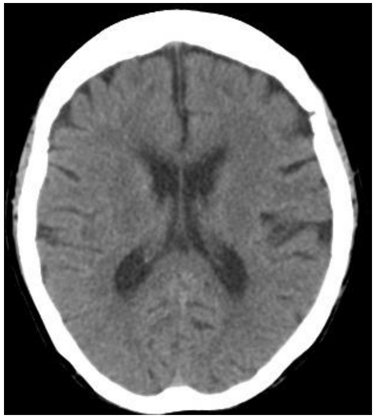
Abnormal patches classified as Normal



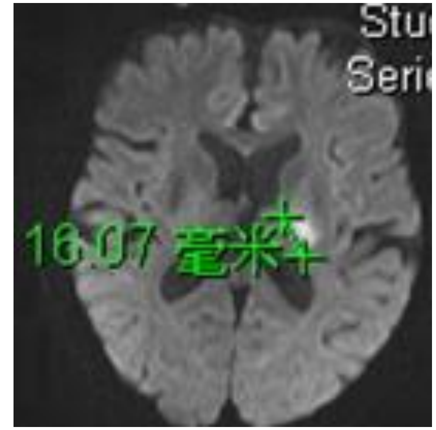
Localized ischemic region

Implementation: Ischemic Stroke Visualization Phase

Left hemisphere infarction



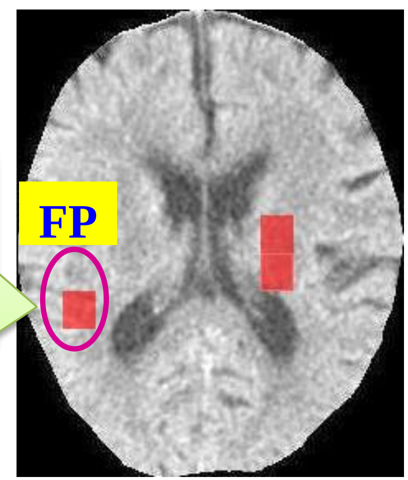
Raw NCCT image



Corresponding DWI image

Ground Truth

Normal patches classified as Abnormal



Localized ischemic region

Performance Analysis of the Designed Classification Model

# of Cases		% of Accuracy		
		Training	Validation	Testing
Case 1: Longer Time Window (0-48 hrs.)	Case 1 (90%_Train: 10%_Test)	81.15	83.34	89.28
	Case 2 (80%_Train: 20%_Test)	77.97	81.15	85.82
Case 2A: Shorter Time Window (0-12 hrs.) & Manual Labeling	Case 1 (90%_Train: 10%_Test)	77.97	78.61	82.96
	Case 2 (80%_Train: 20%_Test)	77.64	79.15	79.01
Case 2B: Shorter Time Window (0-12 hrs.) & Software based Labeling	Case 1 (90%_Train: 10%_Test)	76.91	81.02	80.80
	Case 2 (80%_Train: 20%_Test)	68.02	73.04	78.22

Cardio Embolic Stroke: 3D

DICOM Image
Brain Stroke

3 D Reconstruction
Brain Stroke

• Intracranial Artery Stenosis: 3D

[DICOM Image ICAS]

[3 D Reconstruction ICAS]

Conclusions

- **Applications of Deep Learning in Medical Big Data analysis is huge, challenging and highly essential.**
- Getting real time medical data is bit difficult: **Regulations of a country**
- Ground truth generation is must and **needs help of the experts, which could difficult.**
- **Automatic disease prediction is highly essential**
- It is a challenging research and implementation topics with huge opportunities.
- Minimize the False Negatives
- Minimize False Positives