Medical/Bio Research Topics II: Week 06 (10.10.2025)

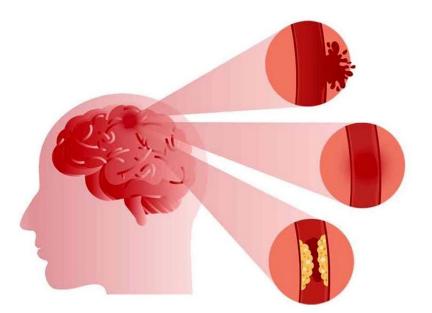
Hands-on Al Segmentation Model Development (1):
Data and Prediction Problem

인공지능 분할 모델 개발 실습 (1): 데이터 및 예측 문제

Stroke

Medical condition in which poor blood flow to the brain

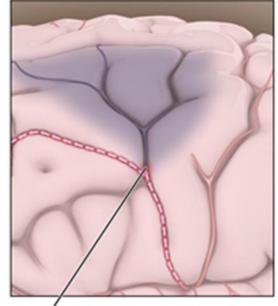
causes cell death



[https://mewarhospitals.com/stroke-causes-symptoms-and-treatment/]

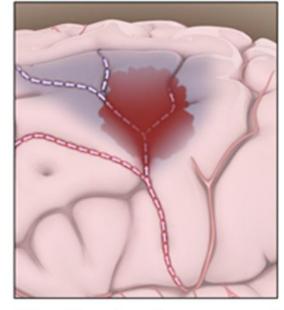
- Two types of stroke
 - Ischemic ('ischein' (to restrain) + 'haima' (blood)) stroke
 - Most common type of stroke
 - State where blood supply to a specific area is reduced or blocked
 - The brain cannot get oxygen and nutrients from the blood, so that brain cells begin to die within minutes
 - Hemorrhagic ('haima' (blood) + 'rhegnynai' (to burst forth)) stroke
 - State where a blood vessel has ruptured, causing bleeding
 - The leaked blood results in pressure on brain cells, damaging them

Ischemic stroke



A clot blocking blood flow to an area of the brain

Hemorrhagic stroke



Bleeding inside or around brain tissue

[https://myhealth.alberta.ca/Health/Pages/conditions.aspx?hwid=tp12720]

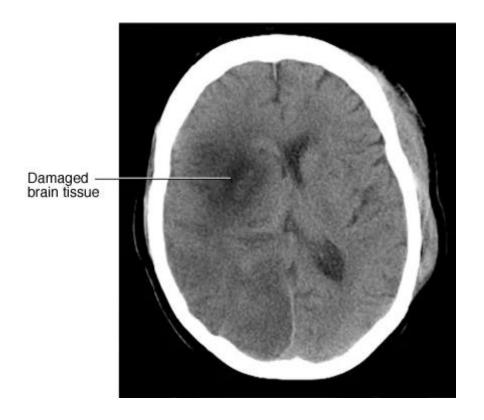
Ischemic vs. Hemorrhagic Stroke

Medical emergency

- Signs and symptoms
 - Trouble speaking and understanding what others are saying
 - Paralysis or numbness of the face, arm, or leg
 - Problems seeing in one or both eyes
 - Headache
 - Trouble walking
- Early treatment can reduce brain damage and other complications

Diagnosis

- Determines the type of stroke
- Rules out other possible causes of symptoms
- Tests
 - Physical exam
 - Blood tests
 - CT
 - MRI

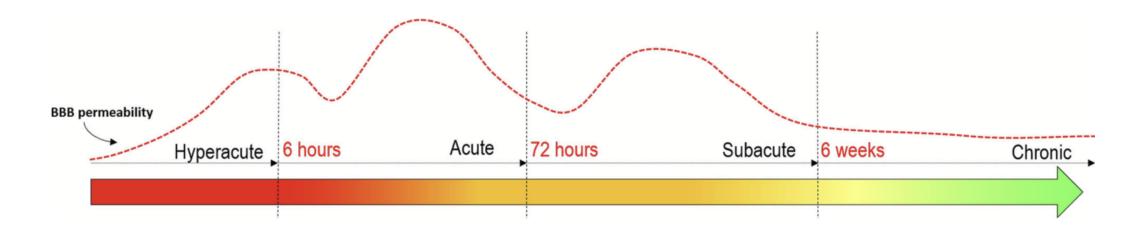


[https://www.mayoclinic.org/diseases-conditions/stroke/diagnosis-treatment/drc-20350119]

CT Scan of Brain Tissue Damaged by Stroke

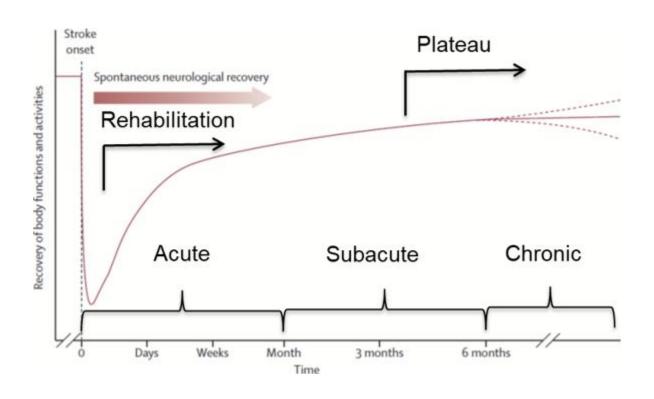
- Emergency treatment
 - Depends on the type of stroke
 - Ischemic stroke
 - Intravenous injection of recombinant tissue plasminogen activator (TPA) to dissolve the blood clot
 - Usually given through a vein in the arm within 4.5 hours of symptom onset
 - Endovascular therapy to directly remove the blood clot
 - Mechanical thrombectomy recommended within 6 hours of symptom onset
 - Hemorrhagic stroke
 - Surgery to remove the blood and relieve pressure on the brain
 - Endovascular therapy to cause blood to clot

- Stages of stroke
 - Acute phase: hours to days after onset
 - Subacute phase: days to weeks
 - Chronic phase: weeks onwards



Rehabilitation therapy

- For most stroke survivors depending on the area of the brain involved and the amount of tissue damaged
- Focuses on helping to recover as much function as possible and return to independent living
- May begin before discharge and continue after discharge in a rehabilitation unit, as an outpatient, or at home
- After getting proper treatment during stroke attacks, most of the neurological recovery happens within 3-6 months
 - Most commonly, a stroke recovery plateau occurs around 3-6 months after stroke, in which little or no gains in function happen

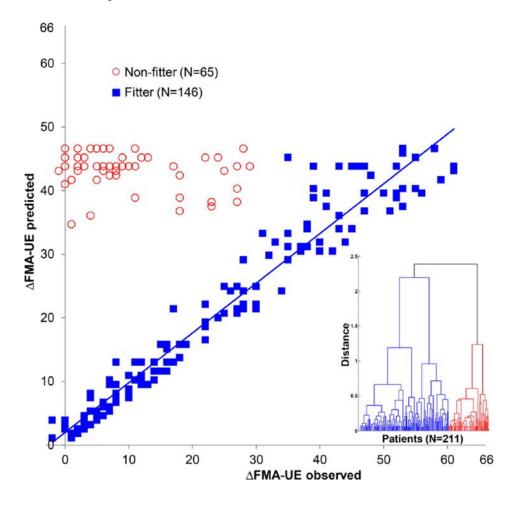


- Proportional recovery rule
 - The degree of natural recovery up to a stroke recovery plateau is proportional to initial functional impairment [Winters et al., 2015]

 Applied to different functional domains including upper and lower limb motor, aphasia, and neglect

$$\Delta FMA-UE_{observed} = FMA-UE_{6months} - FMA-UE_{initial}$$

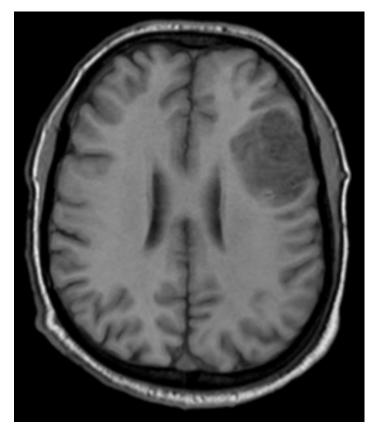
 $\Delta FMA-UE_{predicted} = 0.7 \times (66 - FMA-UE_{initial}) + 0.4$



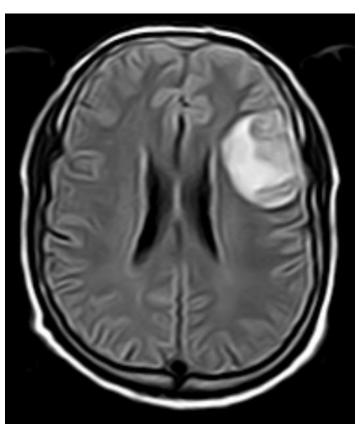
[Winters et al., 2015]

Stroke Lesion

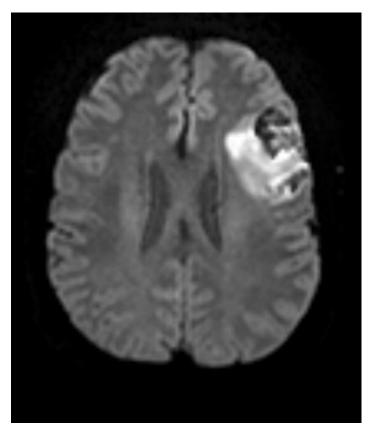
- Ischemic lesion
 - Acute ischemic lesion
 - Subacute/chronic infarct (permanent tissue damage)
- Hemorrhagic lesion
 - Intracerebral hemorrhage (ICH)
 - Subarachnoid hemorrhage (SAH)







FLAIR

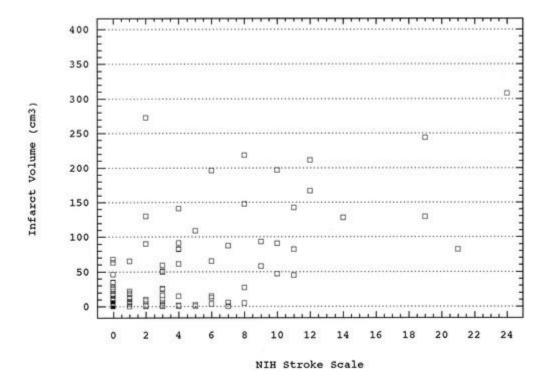


Diffusion-weighted

[https://www.mayoclinic.org/diseases-conditions/stroke/diagnosis-treatment/drc-20350119]

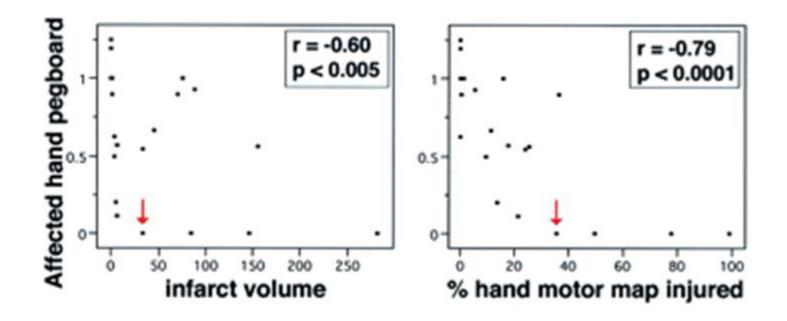
Stroke Lesion Displayed as Altered Signals in MRI

- Brain-behaviour relationship in stroke rehabilitation
 - Lesion size
 - Lesion volume correlates with clinical outcome

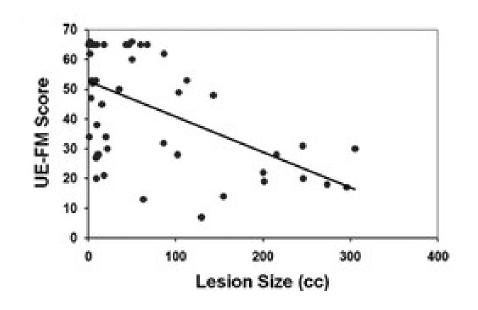


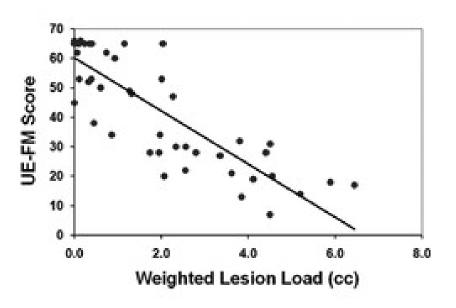
Lesion location

 Motor performance correlates with the fraction of hand motor map injured more strongly than with lesion volume



- Lesion load: Lesion overlap with extant brain structures
 - Motor impairment correlates with the proportion of the corticospinal tract injured more strongly than with lesion volume



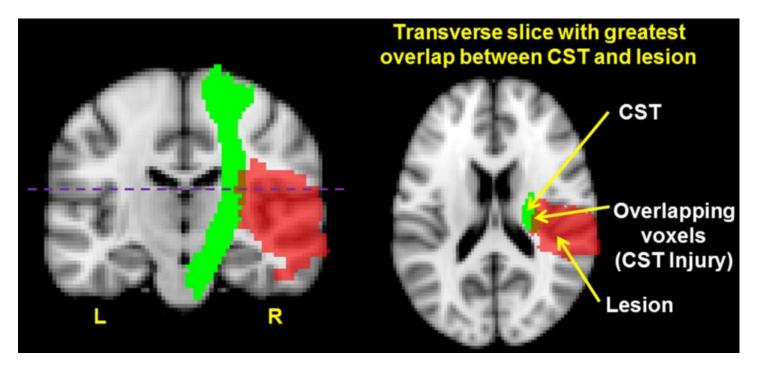


CST Injury =

Number of overlapping voxels between the CST and lesion for the transverse slice

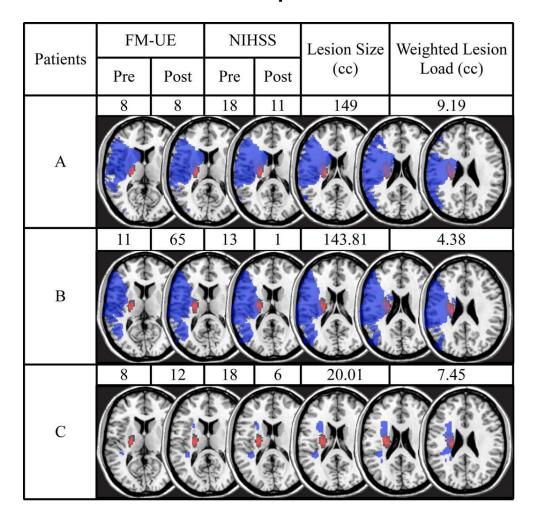
Total number of CST voxels for the transverse slice

 $\times 100\%$



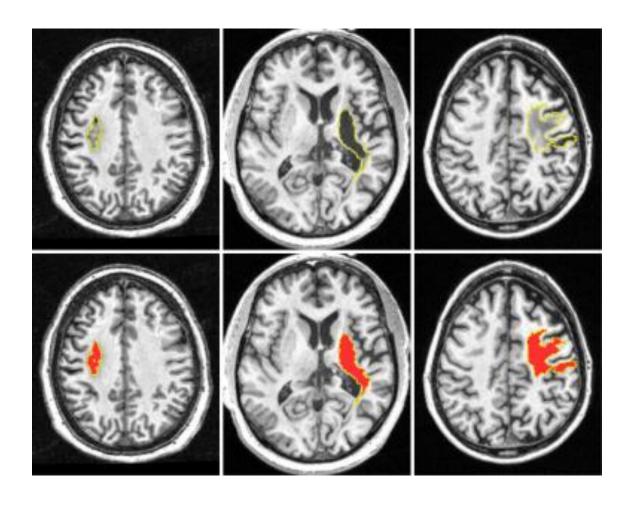
[Lam et al., 2020]

• Corticospinal tract lesion load can predict motor outcome



Lesion Segmentation

- Critical in stroke rehabilitation research
 - For the quantification of lesion burden
 - For accurate image processing
- Still faces challenges and difficulties primarily due to variations of lesions in terms of shape, size, and location
- Manual segmentation remains the gold standard, but it is time-consuming, subjective, and requires neuroanatomical expertise



[Wu et al., 2023]

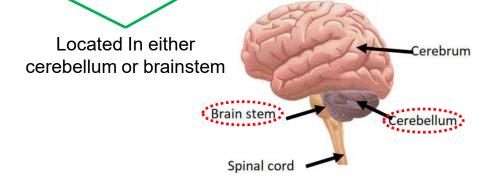
Variations in Stroke Lesions

- Anatomical Tracings of Lesions After Stroke (ATLAS) R2.0 dataset [https://fcon_1000.projects.nitrc.org/indi/retro/atlas.html]
 - Primarily led by the Mark and Mary Stevens Neuroimaging and Informatics Institute at the University of Southern California (USC)
 - Released in 2021 by expanding upon and replacing ATLAS R1.2 released in 2018
 - Largest dataset of its kind
 - Intended to be a resource for the scientific community to develop more accurate lesion segmentation algorithms
 - Derived from diverse, multi-site data from 44 research cohorts worldwide

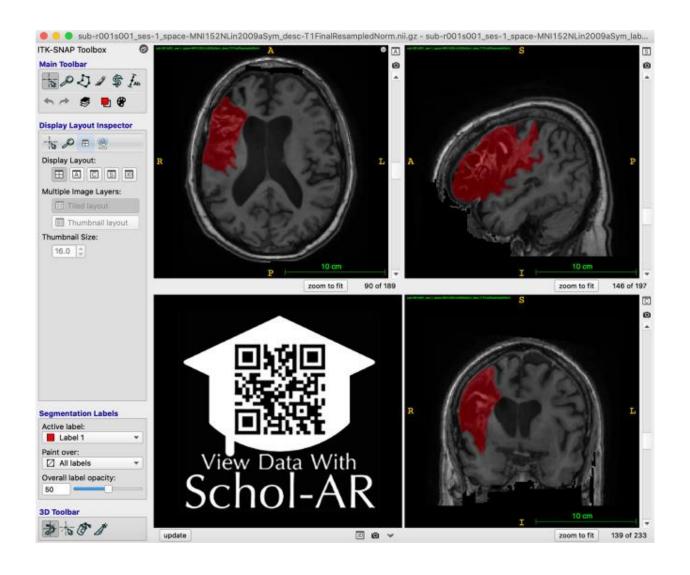
- Includes T1-weighted MRI scans and manually segmented lesion masks (n = 1,271)
 - Training and test sets derived from 33 research cohorts
 - Samples from each research cohort are randomly assigned to either training or test sets so that they have similar compositions
 - Training set (n = 655): publicly released T1-weighted MRI scans and lesion masks
 - Test set (n = 300): publicly released T1-weighted MRI scans and hidden lesion masks
 - Generalizability set derived from 11 new cohorts
 - To test the performance of trained algorithms on completely unseen data
 - Generalizability set (n = 316): completely hidden T1-weighted MRI scans and lesion masks from separate cohorts

- T1-weighted MRI data
 - Collected on 1.5 Tesla and 3 Tesla MR scanners
 - Each cohort was collected on a single scanner using the same parameters except for 2 cohorts
 - High-resolution with the voxel size of 1 mm³ or higher
- Lesion masks [Liew et al., 2022]
 - Number of lesions and lesion location were manually recorded

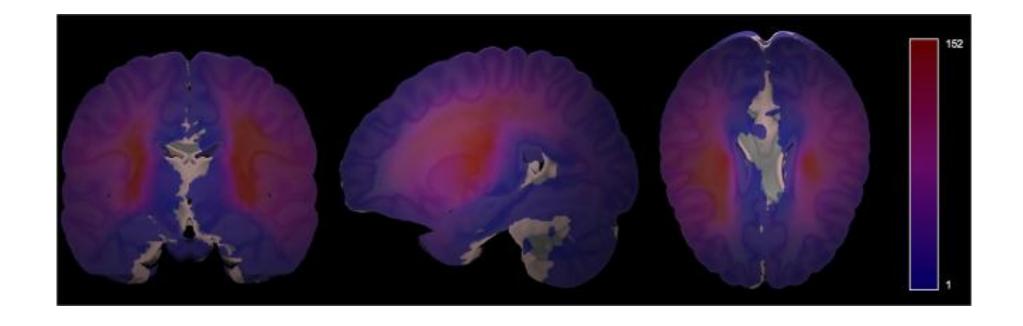
	Subjects with One Lesion			Subjects with Multiple Lesions		
	Left	Right	Other	Unilateral	Bilateral	Other
Training data (n = 655)	173 (26.4%)	187 (28.5%)	46 (7.0%)	47 (7.2%)	121 (18.5%)	81 (12.4%)
Testing data (n = 300)	88 (29.3%)	95 (31.7%)	23 (7.7%)	16 (5.3%)	43 (14.3%)	35 (11.7%)



- Lesion identification and manual tracing
 - By using ITK-SNAP [http://www.itksnap.org/]
 - White matter hyperintensities of presumed vascular origin and perivascular spaces were excluded from lesion masks as much as possible
 - All identified lesions for each subject were reviewed for quality control by two additional trained raters



[Liew et al., 2022]



[Liew et al., 2022]

Image Segmentation

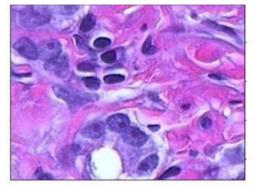
- Technique in digital image processing and analysis to partition an image into multiple parts or areas, often based on the characteristics of the pixels/voxels in the image
 - Involves converting an image into a collection of regions of pixels/voxels that are represented by a mask or a labeled image
- A common application in medical imaging is to detect and label pixels/voxels that represent an abnormality in the brain or other organs

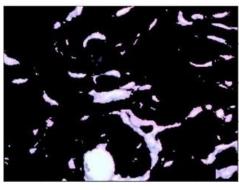
- Algorithms and techniques [https://www.mathworks.com/discovery/image-segmentation.html]
 - Developed over the years using domain-specific knowledge to effectively solve segmentation problems in specific application areas such as medical imaging, automated driving, video surveillance, and machine vision
 - Thresholding
 - Performs thresholding on a greyscale or color image to create a binary image

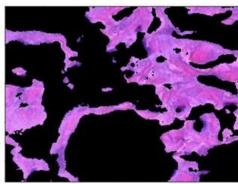


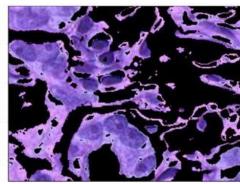
Clustering

- Creates a segmented labeled image using a specific clustering algorithm such as K-means clustering
- For example, to distinguish between tissue types in an image of body tissue stained with hematoxylin and eosin









- Graph-based segmentation
 - Enables to segment an image into foreground and background areas



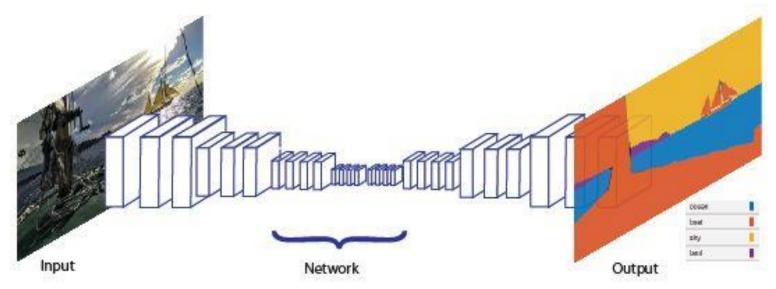


Region growing

 Examines neighboring pixels/voxels of initial seed points and determines iteratively whether the pixel neighbors should be added to the area

Deep Learning-based Image Segmentation

 Associates every pixel/voxel of an image with a class label by using neural networks



[https://www.mathworks.com/discovery/image-segmentation.html]

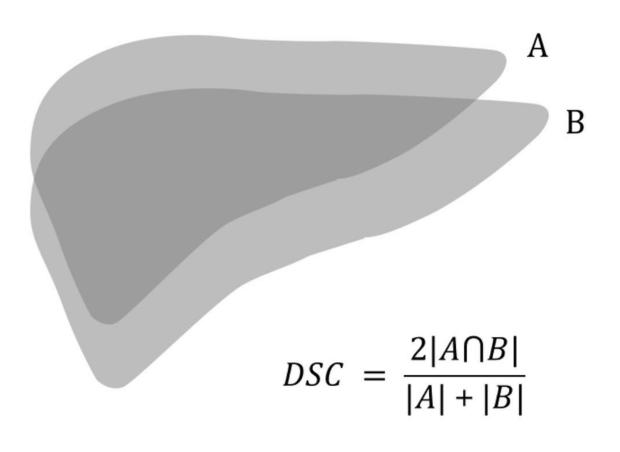
- Leverages the power of deep learning algorithms to analyze image features at various scales, offering improved accuracy and efficiency compared to traditional methods
- Processes the entire image in smaller sections vs. holistically
 - Patch-based inference
 - Extracts fixed-size patches from the volume (e.g., 96×96×96) and processes them sequentially or with overlap
 - Memory-efficient, but involves redundant computation from overlap
 - Full-image inference
 - Processes the entire volume (or large region) in a single forward pass
 - Preserves global context without redundant computation, but requires high memory

Segmentation performance

- Dice similarity coefficient (DSC, Dice-Sørensen coefficient or Dice coefficient) [Dice, 1945]
 - 2 * |X ∩ Y| / (|X| + |Y|), where X and Y are the predicted and ground truth segmentations
 - Measures the overlap between predicted and ground truth segmentations
 - F₁ score that is a harmonic mean of precision and recall
 - Precision (True Positive Value (TPV)) = TP / (TP + FP)
 - Recall (sensitivity) = TP / (TP + FN)
 - $-F_1$ score = 2 / ((1 / precision) + (1 / recall)) = 2TP / (2TP + FP + FN)
 - Range: 0 (no overlap) to 1 (perfect overlap)
 - Sensitive to both false positives and false negatives

		Predicted cond	lition		
	Total population = P + N	Positive (PP)	Negative (PN)	Informedness, bookmaker informedness (BM) = TPR + TNR - 1	Prevalence threshold (PT) $= \frac{\sqrt{TPR \times FPR} - FPR}{TPR - FPR}$
Actual condition	Positive (P)	True positive (TP), hit	False negative (FN), type II error, miss, underestimation	True positive rate (TPR), recall, sensitivity (SEN), probability of detection, hit rate, power $= \frac{TP}{P} = 1 - FNR$	False negative rate (FNR), miss rate $= \frac{FN}{P} = 1 - TPR$
Actual	Negative (N)	False positive (FP), type I error, false alarm, overestimation	True negative (TN), correct rejection	False positive rate (FPR), probability of false alarm, fall-out $= \frac{FP}{N} = 1 - TNR$	True negative rate (TNR), specificity (SPC), selectivity $= \frac{TN}{N} = 1 - FPR$
	Prevalence $= \frac{P}{P+N}$	Positive predictive value (PPV), $precision$ $= \frac{TP}{PP} = 1 - FDR$	False omission rate (FOR) $= \frac{FN}{PN} = 1 - NPV$	Positive likelihood ratio (LR+) = TPR FPR	Negative likelihood ratio (LR-) = FNR TNR
	Accuracy (ACC) $= \frac{TP + TN}{P + N}$	False discovery rate (FDR) $= \frac{FP}{PP} = 1 - PPV$	Negative predictive value (NPV) = $\frac{TN}{PN}$ = 1 - FOR	Markedness (MK), deltaP (Δp) = PPV + NPV - 1	Diagnostic odds ratio (DOR) = LR+ LR-
	Balanced accuracy (BA) $= \frac{TPR + TNR}{2}$	$F_{1} \text{ score}$ $= \frac{2PPV \times TPR}{PPV + TPR} = \frac{2TP}{2TP + FP + FN}$	Fowlkes–Mallows index (FM) = √PPV×TPR	Matthews correlation coefficient (MCC) =√TPR×TNR×PPV×NPV -√FNR×FPR×FOR×FDR	Threat score (TS), critical success index (CSI), Jaccard index = TP TP + FN + FP

[https://en.wikipedia.org/wiki/Confusion_matrix]



DSC: Dice similarity coefficient



[Lee et al., 2018; https://www.mathworks.com/help/images/ref/dice.html]

Computation of DSC

- Intersection over Union (IoU, Jaccard Index)
 - |X ∩ Y| / |X ∪ Y|
 - Measures the overlap ratio of the intersection to the union of predicted and ground truth segmentations
 - Range: 0 (no overlap) to 1 (perfect overlap)
 - Stricter than DSC by penalizing errors more heavily
- Mean Intersection over Union (mIoU)
 - Average of IoU scores for all classes
 - Provides an overall measure of segmentation quality across multiple classes
 - Range: 0 (no overlap) to 1 (perfect overlap)
 - Useful for multi-class segmentation tasks

Hausdorff distance

- max(h(X,Y), h(Y,X)), where h(X,Y) = max(min(d(x,y))) for x in X, y in Y and h(Y,X) = max(min(d(y,x))) for y in Y, x in X
- Measures the maximum distance between the boundaries of predicted and ground truth segmentations
- Range: 0 to ∞ (lower is better)
- Sensitive to outliers, useful for evaluating boundary accuracy
- Average Surface Distance (ASD)
 - Average of distances between surfaces of predicted and ground truth segmentations
 - Measures the average error in boundary delineation
 - 0 to ∞ (lower is better)
 - Less sensitive to outliers than Hausdorff Distance

Accuracy

- (Correctly Classified Elements) / (Total Elements) = (TP + TN) / (Total Elements)
- Measures the proportion of elements correctly classified across all classes
- Range: 0 (completely incorrect classification) to 1 (perfect classification)
- Sensitivity and specificity
 - Sensitivity = TP / (TP + FN), specificity = TN / (TN + FP)
 - Measure the model's ability to correctly identify positive and negative cases
 - Range: 0 (complete failure to detect positive/negative cases) to 1 (perfect detection of positive/negative cases)
- Area Under the Receiver Operating Characteristic Curve (AUC-ROC)
 - Measures the model's ability to distinguish between classes
 - Range: 0.5 (random guessing) to 1 (perfect classification)

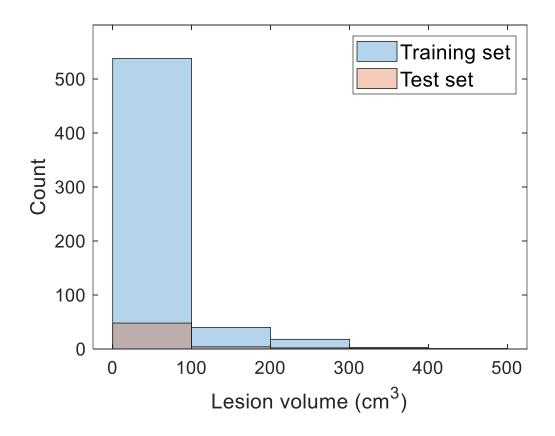
- Deep learning-based lesion segmentation
 - Specific application of image segmentation to medical images by targeting abnormal tissues or pathological regions
 - Challenges
 - Class imbalance (lesions often small compared to healthy tissue)
 - Varying in lesion shape, size, and location
 - Artifacts and noise common in medical images
 - Data considerations
 - Often works with 3D volumetric images (CT, MRI scans)
 - Requires expert annotations, which can be costly and time-consuming
 - Employs data augmentation to efficiently use limited training data
 - May benefit from multi-modal data integration

Performance metrics

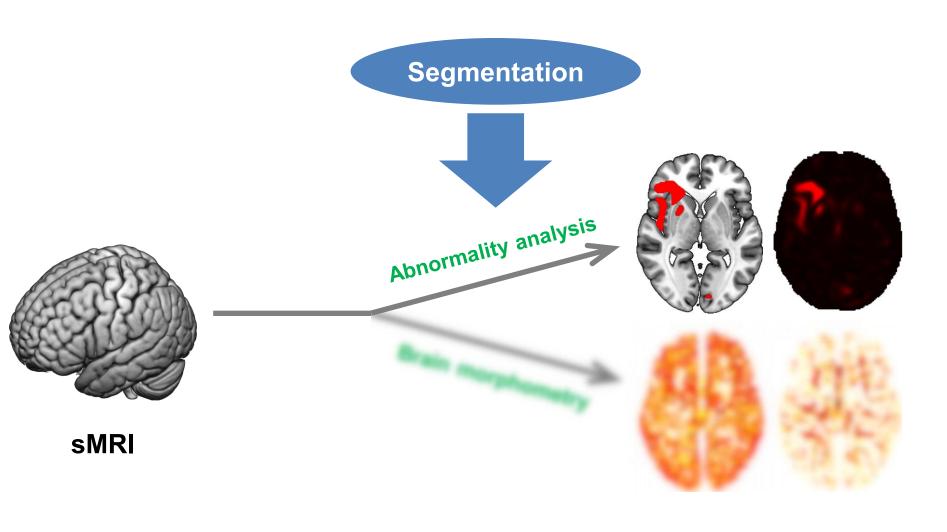
- Usually uses domain-specific metrics like DSC and Hausdorff distance
- Emphasizes both quantitative accuracy and clinical relevance
- Specialized architectures
 - Uses common segmentation models such as U-Net and its variants
 - Ability to capture both local and global context
 - Skip connections that preserve fine details, crucial for precise lesion boundaries
 - Designed to handle medical imaging specificities

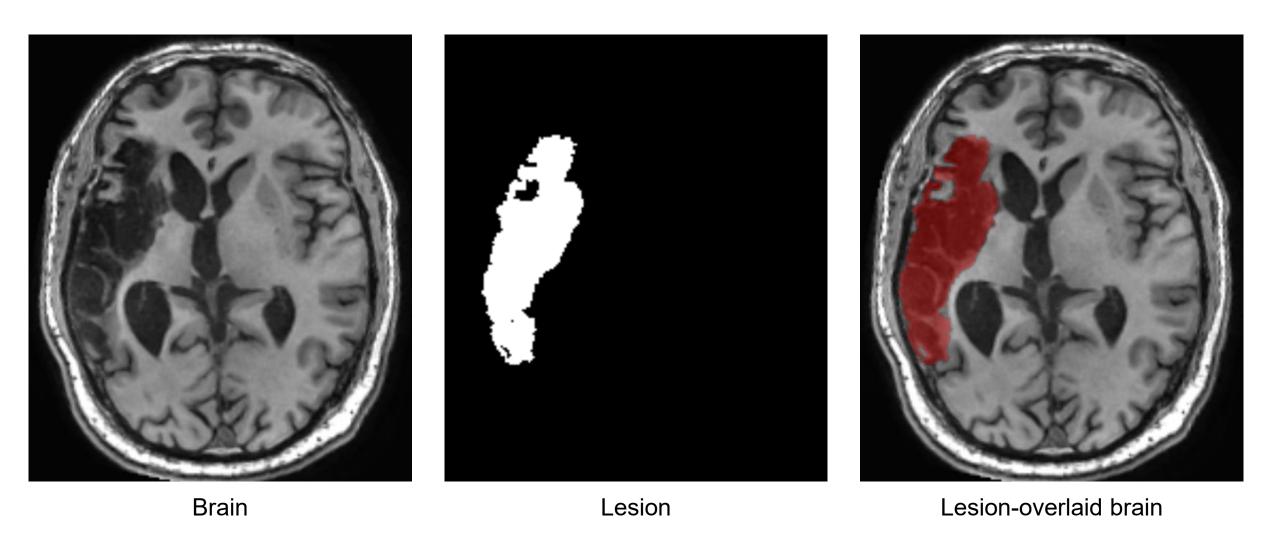
Dataset

- ATLAS R2.0 dataset for training (n = 655)
 - Training set: n = 600
 - T1-weighted MRI scans: train/Brain/001-600.nii.gz
 - Lesion masks: train/Lesion/001-600.nii.gz
 - Test set: n = 55
 - T1-weighted MRI scans: test/Brain/001-055.nii.gz
 - Lesion masks: hidden

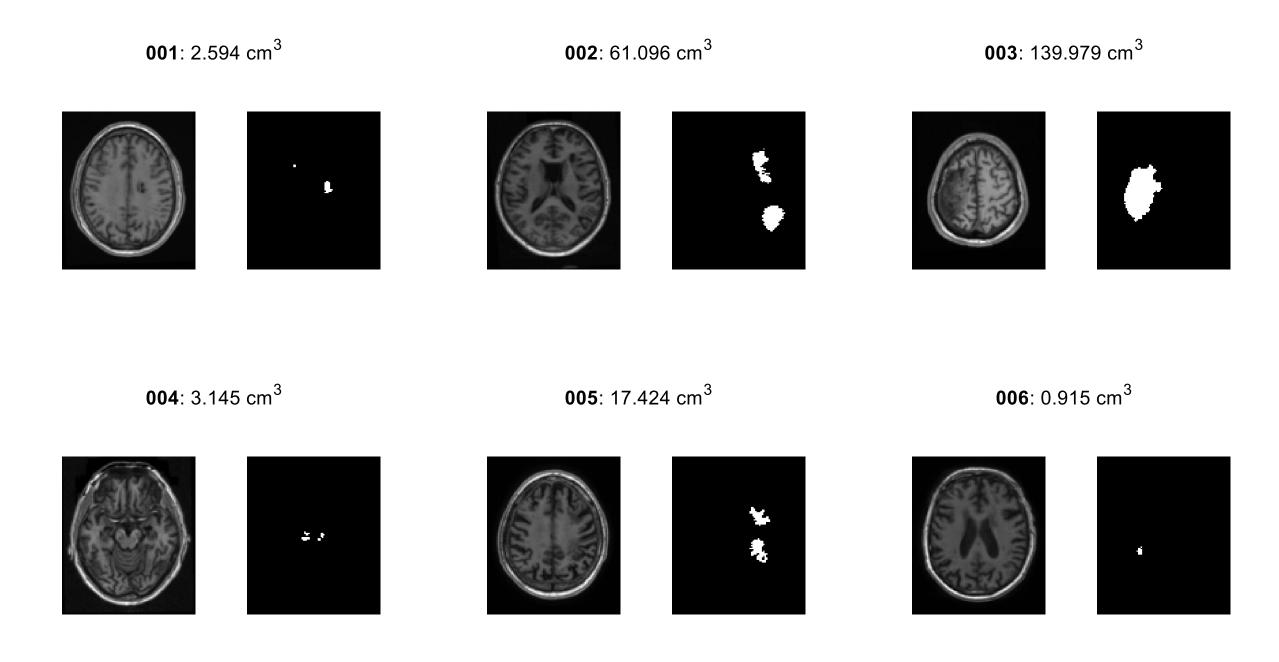


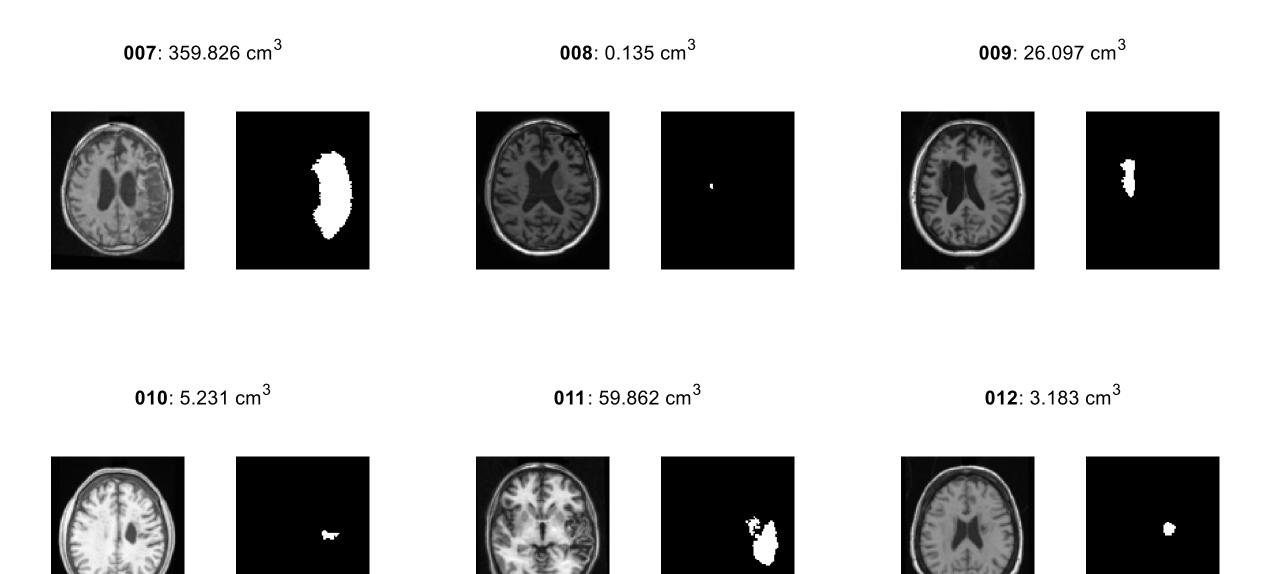
Distribution of Lesion Volume

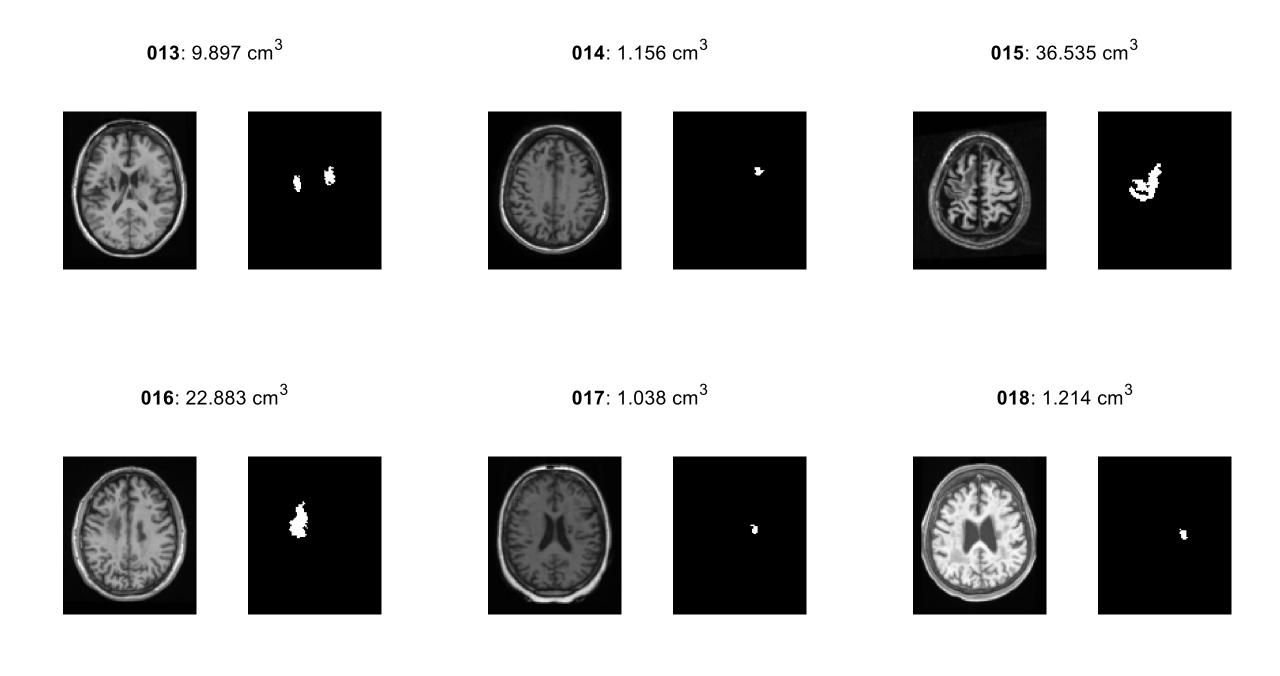


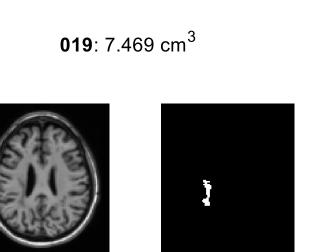


Example Pair of a T1-weighted MRI Scan and a Lesion Mask

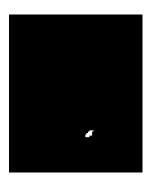








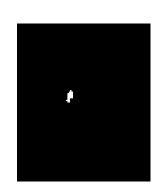






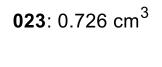
021: 1.180 cm³

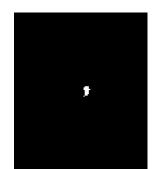
024: 67.076 cm³



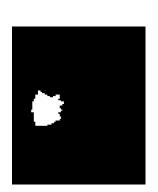
022: 34.330 cm³





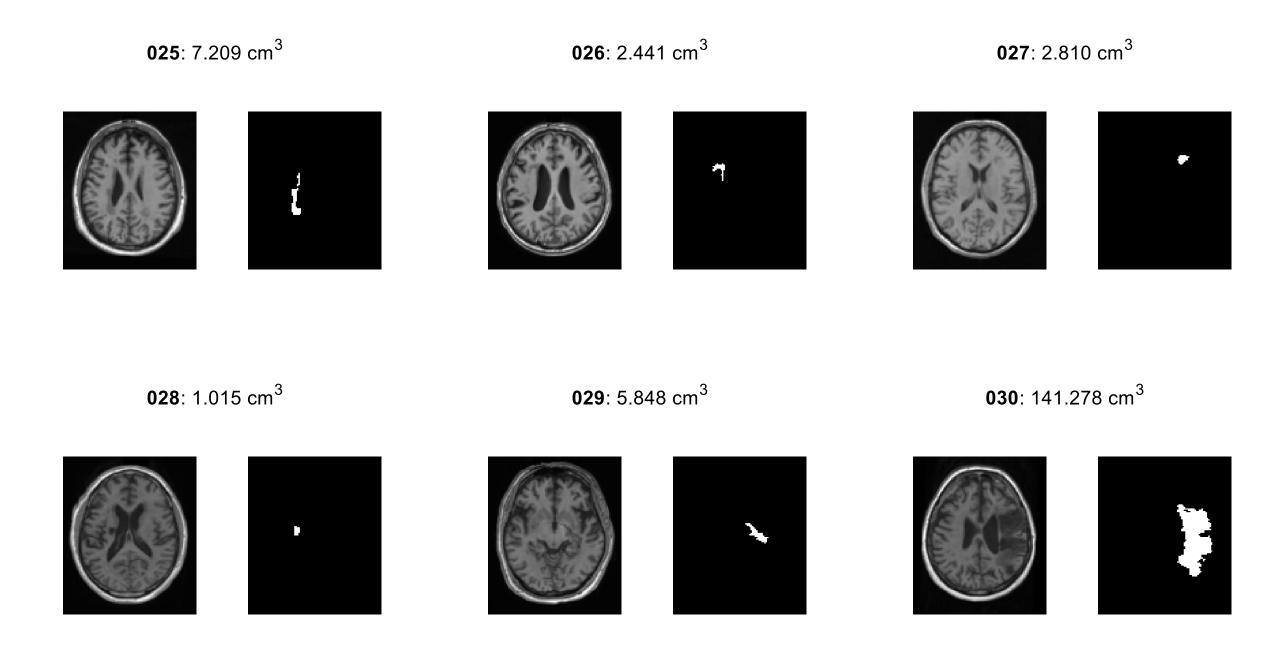


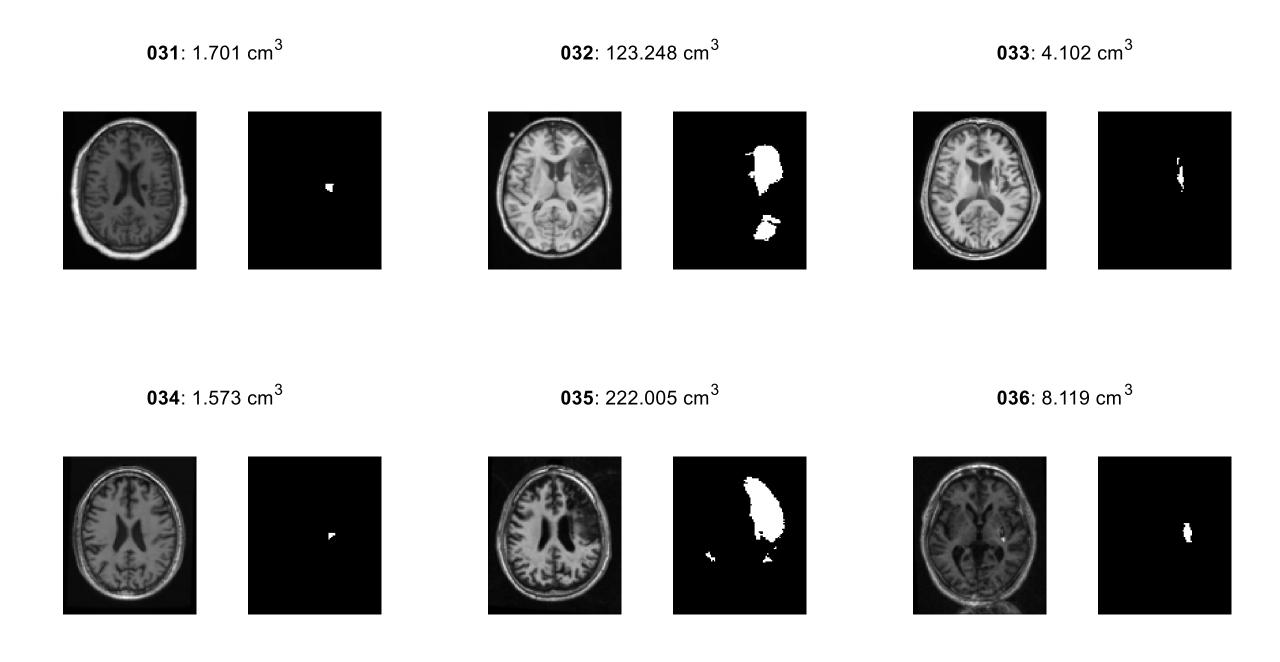




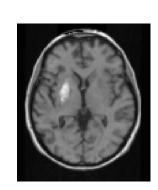


020: 0.375 cm³

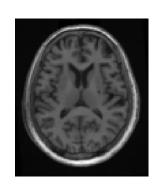


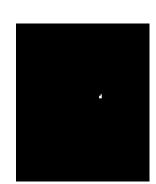


037: 66.057 cm³



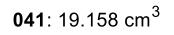




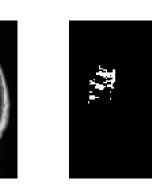


040: 1.806 cm³



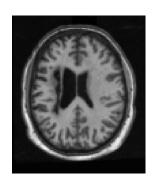


038: 130.660 cm³



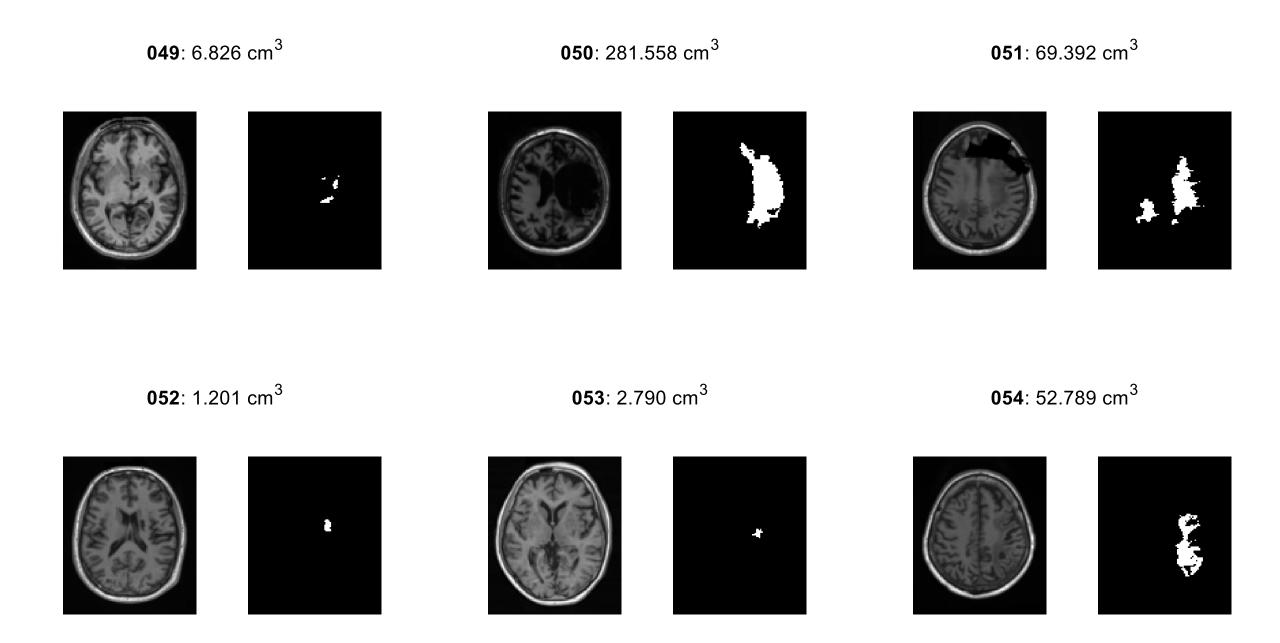
042: 40.818 cm³

039: 0.089 cm³





043: 6.161 cm³ **045**: 13.653 cm³ **044**: 14.618 cm³ **046**: 16.615 cm³ **047**: 5.247 cm³ **048**: 19.138 cm³



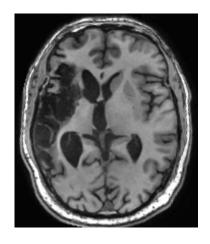
055: 47.632 cm³





- Raw T1-weighted image and lesion mask
 - Raw T1-weighted image in native space
 - Lesion mask in native space

Raw T1-weighted image



Lesion mask



Image specifications:

Dimensions: $98 \times 116 \times 94$

Voxel size: $2.0 \text{ mm} \times 2.0 \text{ mm} \times 2.0 \text{ mm}$

Raw T1-weighted Image and Lesion Mask

- Segmentation label map
 - Lesion mask
- Lesion segmentation performance
 - Mean DSC for the test set (n = 55)
 - Average of the overlap between predicted and manually annotated lesion masks across the test set
 - Ranges from 0 to 1

Article	Method	Reported Dice	Code Publicly Available	n	Validation Method	Input size 2D/3D (H, W, D)
					Cross-validation	
Basak et al., 2021	DFENet	0.546	no	229	5-fold cross-validation	2D 192, 192 or 3D 192, 192, 4
Hui et al., 2020	PSPF and U-Net	0.593	no	239	6-fold cross-validation	2D 176, 176
Lu et al., 2020	EDCL w/ 3D Unet	0.148 (0.584)**	no	239	5-fold cross-validation	3D 64, 64, 64
Qi et al., 2019	X-Net	0.487	yes	229	5-fold cross-validation	2D 192, 224
Zhang et al., 2020	MI-UNet	0.567	no	229	5-fold cross-validation	2D 233, 197 or 3D 49, 49, 49
					One hold-out Train, Validation, Test	
Chen et al., 2018	U-Net/GMM*	0.500/0.170	no	220	unclear/0, 0, 100 (%)	2D 128, 128 or 256, 256
Chen et al., 2020	VAE*/GMVAE*	0.110/0.120	no	220	0, 0, 100/0, 0, 100 (%)	2D 200, 200
Kervadec et al., 2020	Enet	0.474	yes	229	203, 26, 0	unclear
Liu et al., 2019	MSDF-Net	0.558	no	229	160, 69, 0	2D 224, 177
Paing et al., 2021	3D U-Net	0.668	no	239	60, 20, 20 (%)	3D 197, 233, 189
Qi et al., 2020	U-Net	0.518	no	229	120, 40, 69	2D 224, 192
Sahayam et al., 2020	MUDCap3	0.670	no	229	160, 69, 0	3D 256, 256, 256
Tomita et al., 2020	3D-ResU-Net	0.640	yes	239	76, 11, 13 (%)	3D 144, 172, 168
Wang et al., 2020	CPGAN	0.617	no	239	129, 40, 60	2D 256, 256
Xue et al., 2020	U-Net (9 paths)	0.540	yes	54	0, 0, 54	3D 192, 224, 192
Yang et al., 2019	CLCI-Net	0.581	yes	220	55, 18, 27 (%)	2D 224-233, 176-197
Zhou et al., 2019	D-Unet	0.535	no	229	80, 20, 0 (%)	2D 192, 192 or 3D 192, 192, 4

[Liew et al., 2022]

Demo Dataset

- Simulated images and labels
 - Training dataset: n = 40
 - Images: Image/0-39.nii.gz
 - Masks: Label/0-39.nii.gz

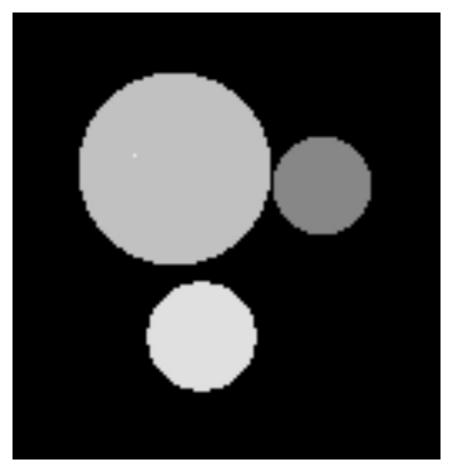




Image Label

Example Pair of an Image and a Label Mask