Contrast Synthesis with Uncertainty Estimation

Using Deep Learning Approach

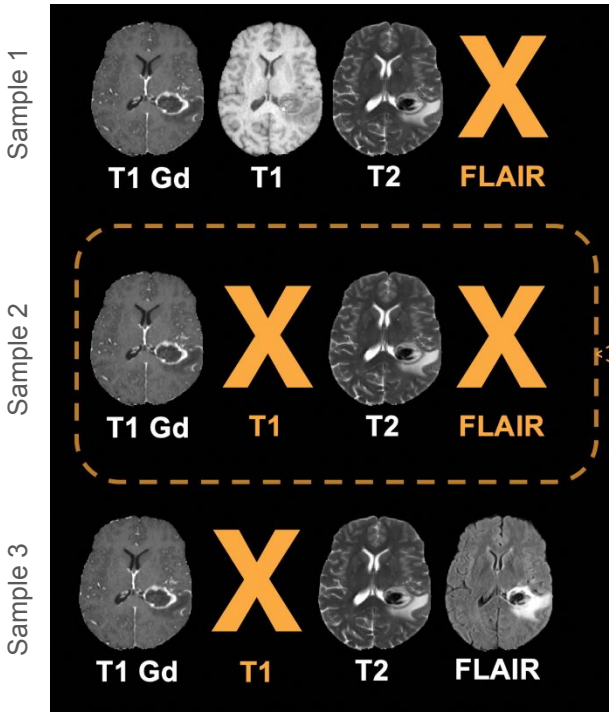
Presenter: Sachin Salim
Advisor: Dr. Anand Joshi

Introduction

- In medical imaging tasks such as segmentation and biomarker identification, datasets often include multiple MRI contrasts like T1w, T1Gd, T2w, T2-FLAIR, T2-DWI, etc.

- **Challenge:** Some sequences are often missing from individual patient datasets:
  - Example: Dataset A may lack FLAIR, while Dataset B may be missing T1w and FLAIR.

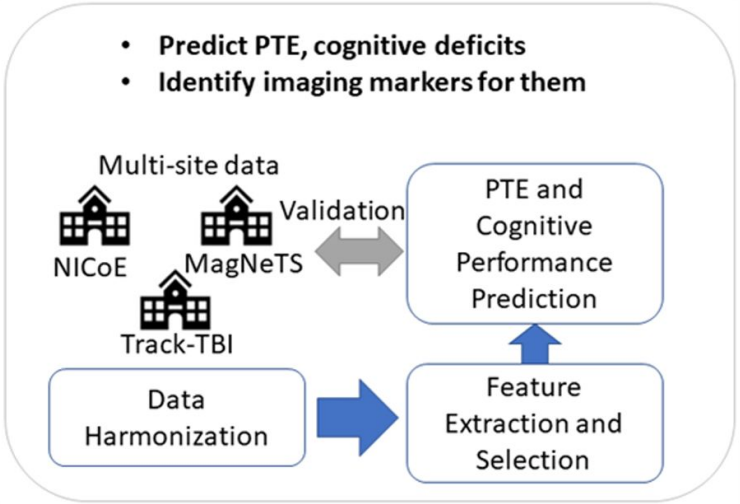
- **Impact:** These missing sequences present challenges when directly using the dataset for modeling



pubs.rsna.org/doi/full/10.1148/radiol.2021203786

Why This Problem Matters to Us

- In the grant-funded ongoing project on identifying biomarkers for post-traumatic epilepsy (PTE) in traumatic brain injury (TBI) patients, we utilize MRI datasets like NICoE and TRACK-TBI
- These datasets have missing contrasts which makes it challenging for machine learning analysis
- Hence it's crucial to develop data imputation techniques to avoid altering our existing model pipelines to effectively manage missing data



PTE Project Narrative Grant

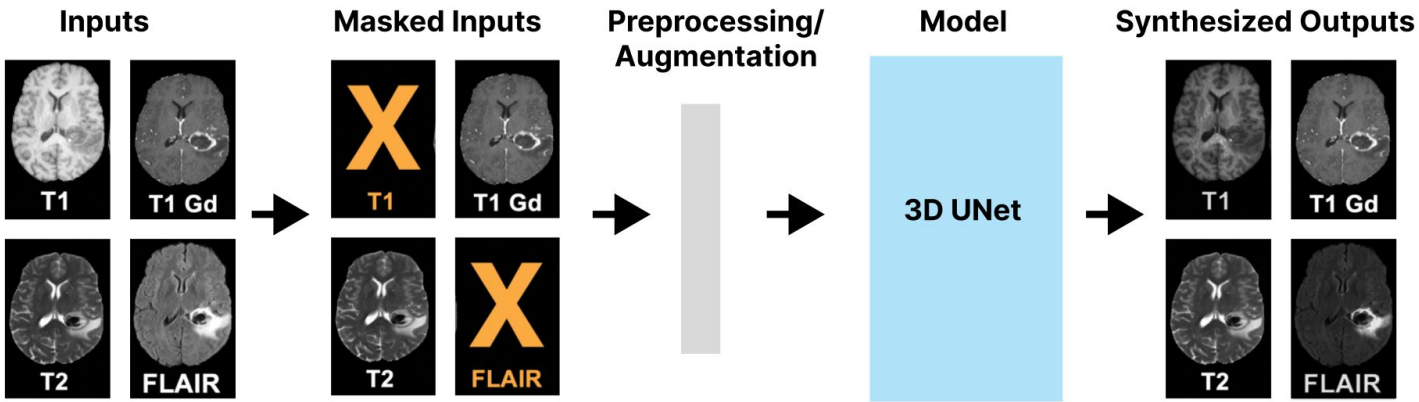
More info

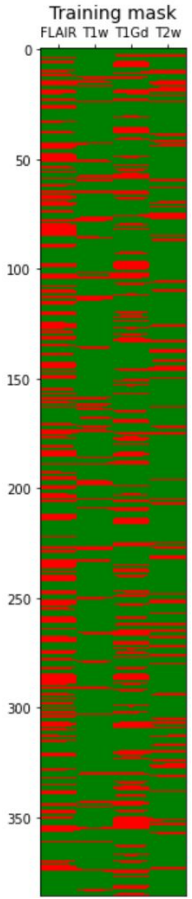
Problem Statement

- Consider x_i : multi-contrast 3D Brain MRI volume of sample i
- x_i has dimension: CxWxHxD
  - In our task: C=4, W=H=240, D=155
- $x_i = [x_i^{(1)}, x_i^{(2)}, x_i^{(3)}, x_i^{(4)}]$
- x_i may be missing one or more contrast $x_i^{(k)}$

- Say C be the set of all contrasts and C_{-k} be the set of contrasts without k
- Our objective is to learn $p_k(x^{(k)}|x^{(C_{-k})})$ so that $x^{(k)}$ can be synthesised when other contrasts are known

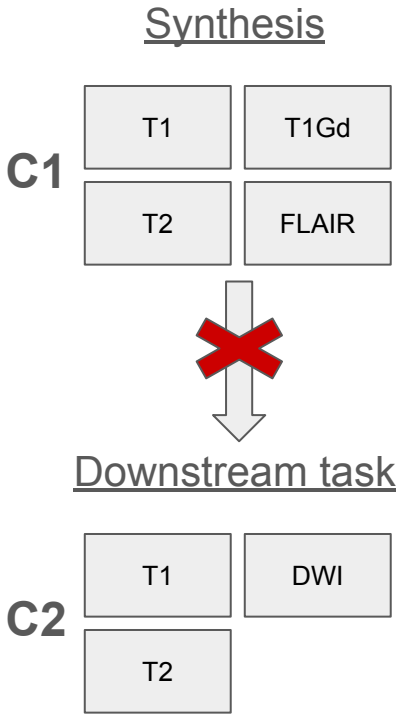
Method 1 (Mixed Contrast Synthesis - **MCS**)



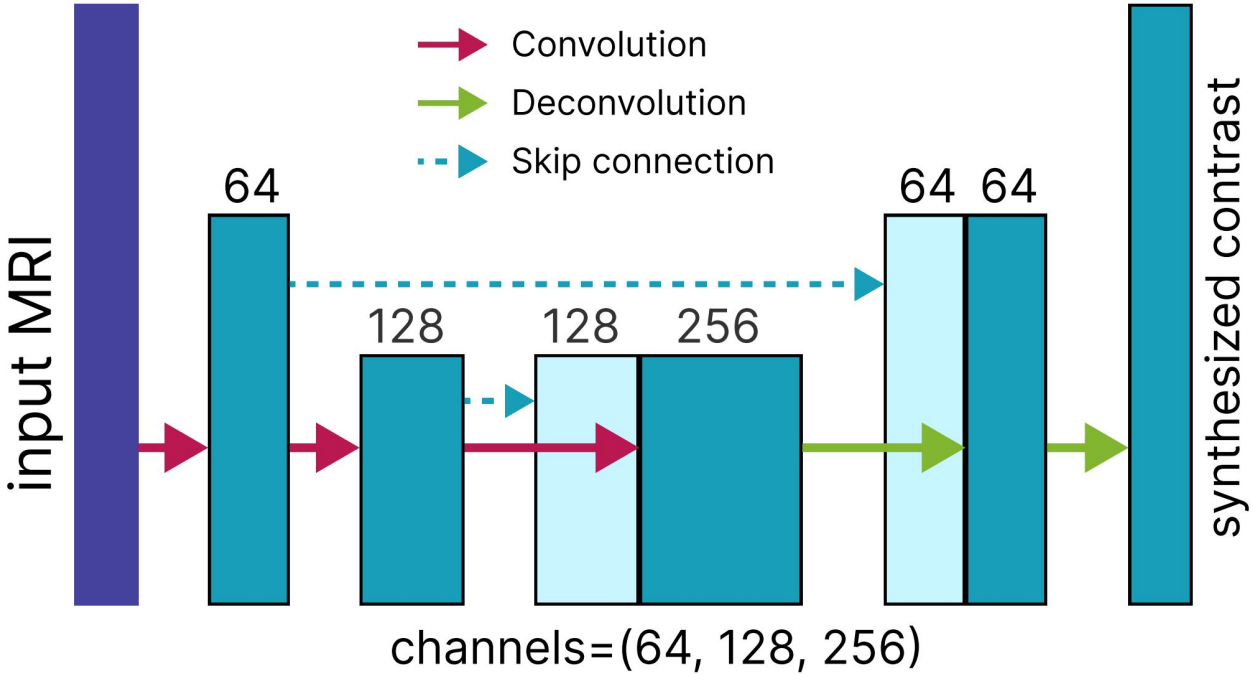


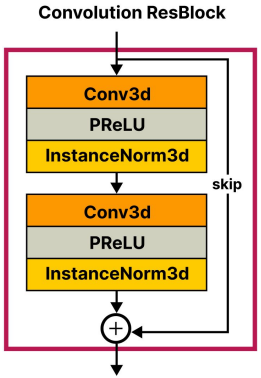
Drawback of MCS

- Say, a model is trained using MCS method for T1, T1Gd, T2, FLAIR (Contrast set C1).
- Say our primary objective is Lesion detection on a dataset (with some missing contrasts) that has T1, DWI, T2 (Contrast set C2).
- The MCS model we trained on C1 wouldn't be able to synthesise missing contrasts on C2 since they're different.
- So MCS would only work if C1 and C2 are exactly same.



Model


Convolution
Deconvolution
Skip connection
input MRI
64
128
128
256
64
64
synthesized contrast
channels=(64, 128, 256)


Convolution ResBlock
Conv3d
PReLU
InstanceNorm3d
Conv3d
PReLU
InstanceNorm3d
skip

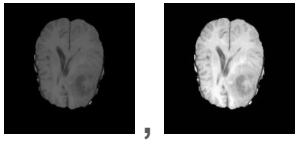
Loss functions

- Various loss functions were considered to synthesize contrasts (along with uncertainty)
- The tumor segmentation results using these were suspiciously low (~10 DICE) so I kept uncertainty-prediction aside for now, to focus on a simpler problem first.

Gaussian Log Likelihood Loss

$$\text{loss} = \frac{1}{2}\left(\log\left(\max\left(\text{var},\ \text{eps}\right)\right) + \frac{\left(\text{input} - \text{target}\right)^2}{\max\left(\text{var},\ \text{eps}\right)}\right) + \text{const.}$$

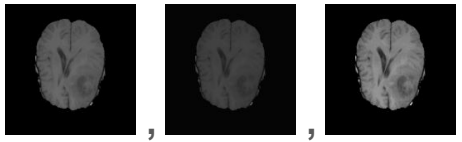
mean var



Quantile Loss

$$\rho_\alpha(y, \hat{y}) := \begin{cases} \alpha(y - \hat{y}) & \text{if } (y - \hat{y}) > 0 \\ (1 - \alpha)(y - \hat{y}) & \text{otherwise.} \end{cases}$$

median (α=0.5) qL (α=0.023) qH (α=0.977)

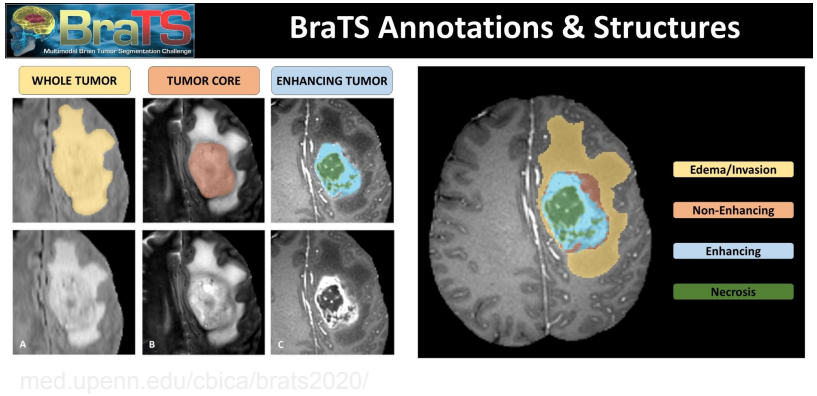


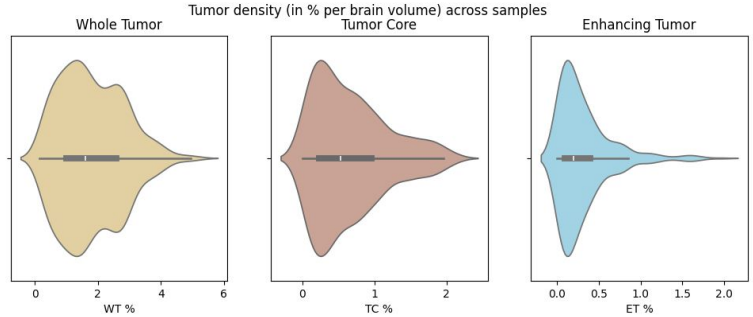
* Contrasts shown here are for representational purpose

Our implementation

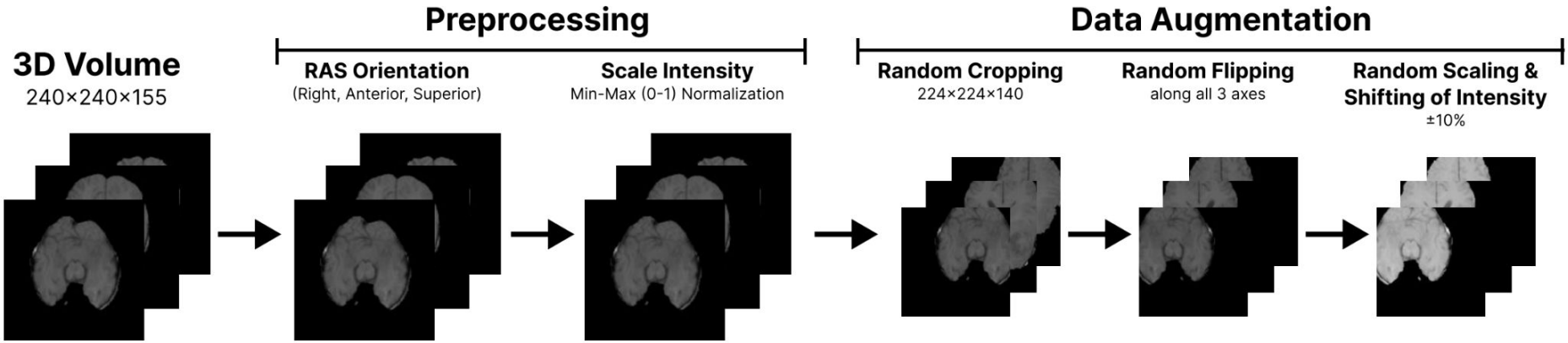
Dataset

- We use BraTS 2017 dataset
- This dataset is ideally used for Tumor Segmentation and contains no healthy subjects; every sample includes a tumor





Dataset Preprocessing

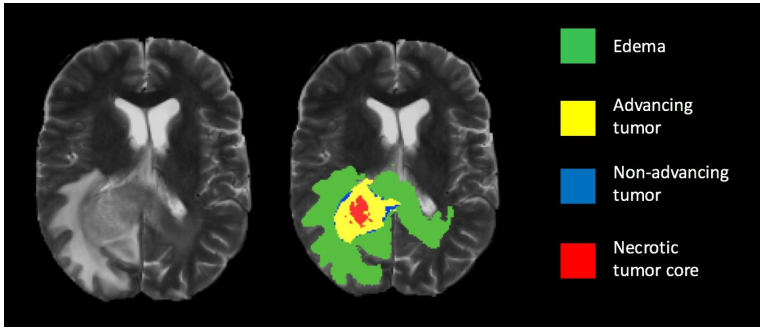


Evaluation: Synthesis quality

- Evaluate the quality of generated MRI sequence images using:
  - Mean Squared Error (MSE)
  - Mean Absolute Error (MAE)
  - Peak Signal-to-Noise Ratio (PSNR) $PSNR = 10 \cdot \log_{10}\left(\frac{MAX_I^2}{MSE}\right)$
  - Structural Similarity Index (SSIM)
    - measures similarity based on luminance, contrast, and structure $\mathrm{SSIM}(\mathbf{x},\mathbf{y}) = \frac{(2\mu_x\mu_y + C_1)(2\sigma_{xy} + C_2)}{(\mu_x^2 + \mu_y^2 + C_1)\,(\sigma_x^2 + \sigma_y^2 + C_2)}.$

Evaluation: Synthesis effectiveness

- To demonstrate the effectiveness of synthesis, select a downstream task like tumor segmentation on the BraTS dataset and compare the results using the Dice similarity coefficient
- Evaluate performance against segmentation without imputation (lower bound) and with complete data (upper bound)

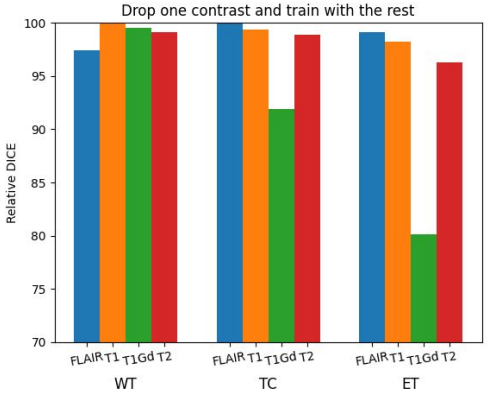


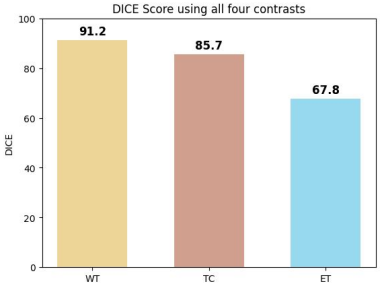
medium.com/@lfoster49203/

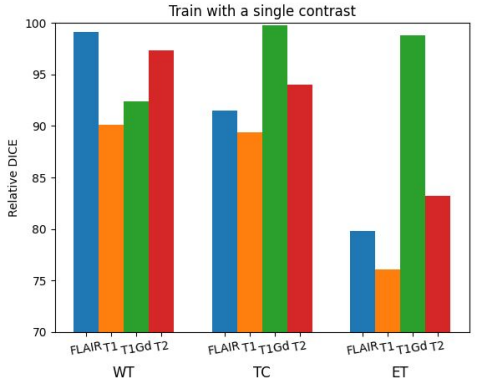
Results

Brain Tumor Segmentation: Insights

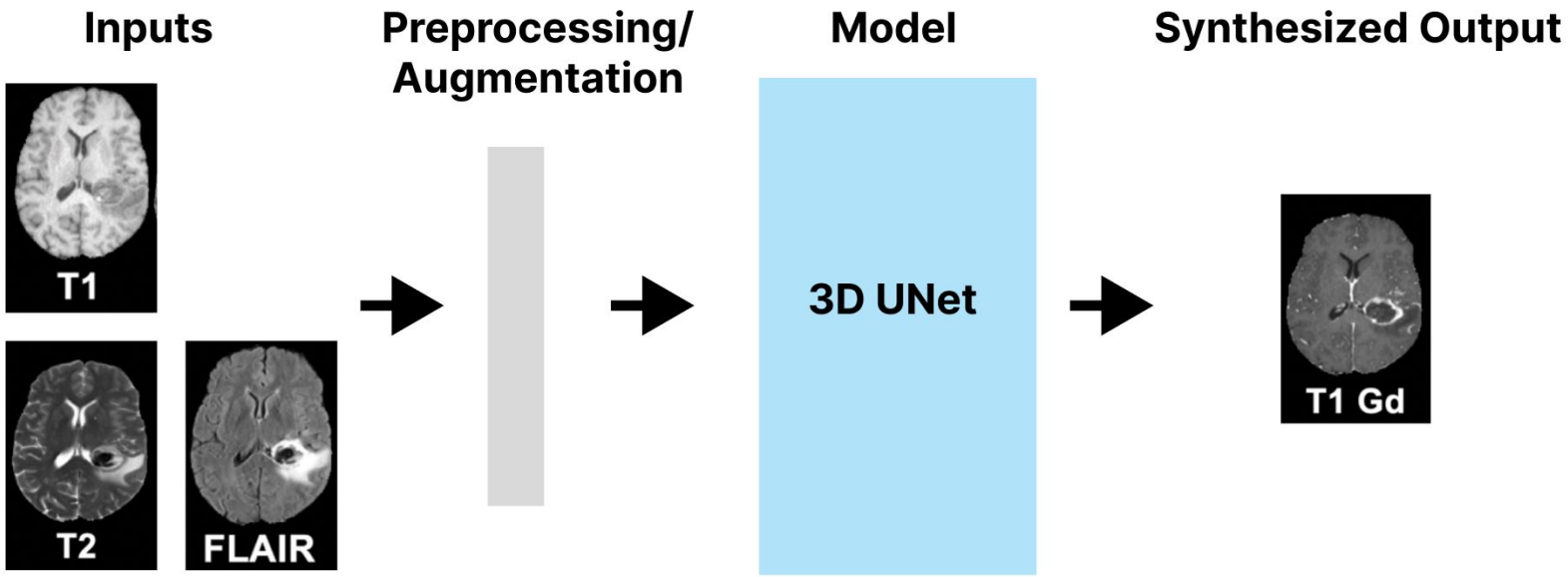
- As seen from these plots, T1Gd plays a vital role in segmenting Tumor Core and Enhancing Tumor regions
- So I considered dropping T1Gd contrast and replacing it with synthesized contrast to compare tumor segmentation results





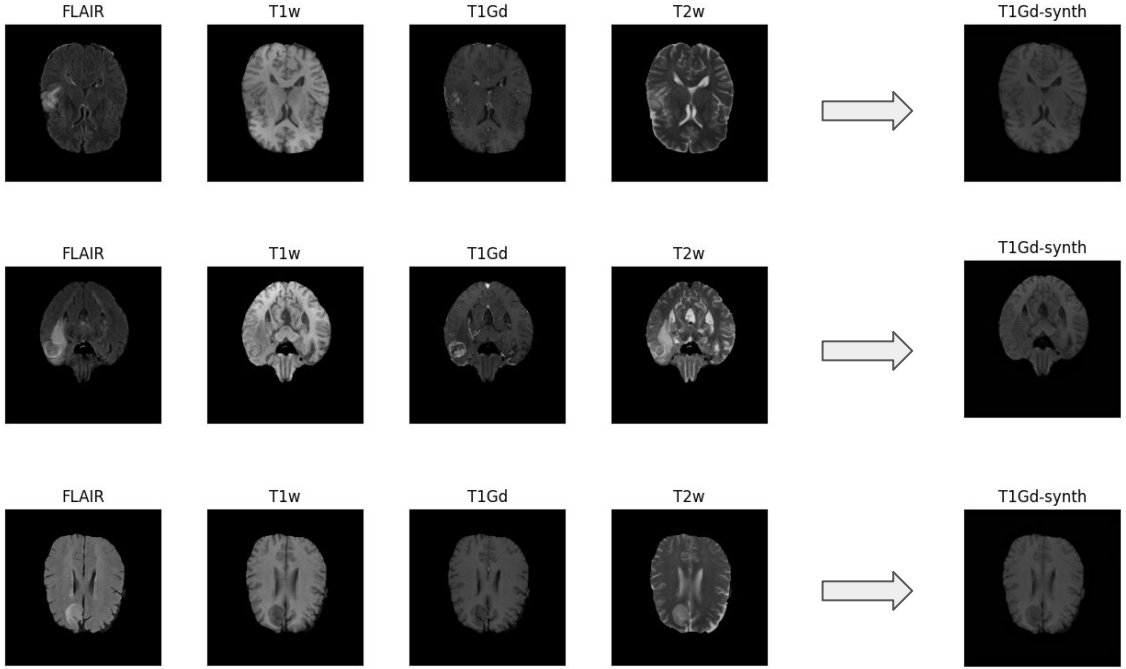


T1Gd Synthesis



* Contrasts shown here are for representational purpose

Results: T1Gd Synthesis



Results: T1Gd Synthesis

Evaluation scores of gT1Gd (ground-truth) with sT1Gd (synthetic), Zero (empty), T1w and mT1Gd (mean)

	sT1Gd	**Zero**	**T1w**	**mT1Gd**
MSE	**0.0008**	0.0125	0.0048	0.0021
MAE	**0.0116**	0.0425	0.0211	0.0159
PSNR	**31.7**	19.3	26.3	27.2
SSIM	0.8719	0.8198	**0.9412**	0.8843

Results: T1Gd Synthesis

Comparison with other Medical Image Synthesis Methods

	Ours	HRC	MedGAN
MAE	**0.012**	0.029	N/A
PSNR	**31.3**	30.0	27.0
SSIM	0.872	**0.923**	0.901

HRC: Synthesizing MR Image Contrast Enhancement Using 3D High-Resolution ConvNets", Chen 2023
MedGAN: "MedGAN:Medical image translation using GANs", Armaniousetal 2020

Results: T1Gd Synthesis

Ablation study

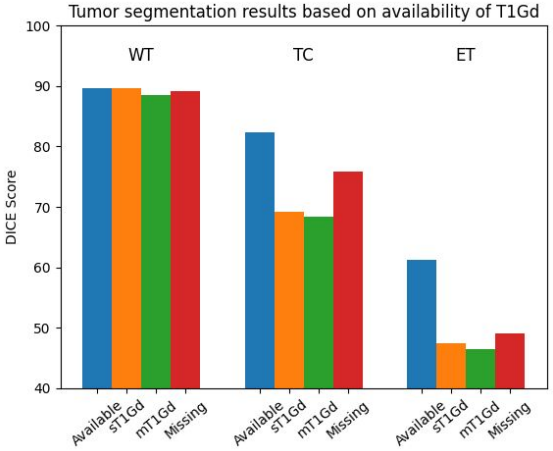
Size of model

	(4, 8, 16)	(64, 128, 256)
MSE	0.0009	**0.0008**
MAE	0.0121	**0.0116**
PSNR	31.3	**31.7**
SSIM	0.8396	**0.8719**

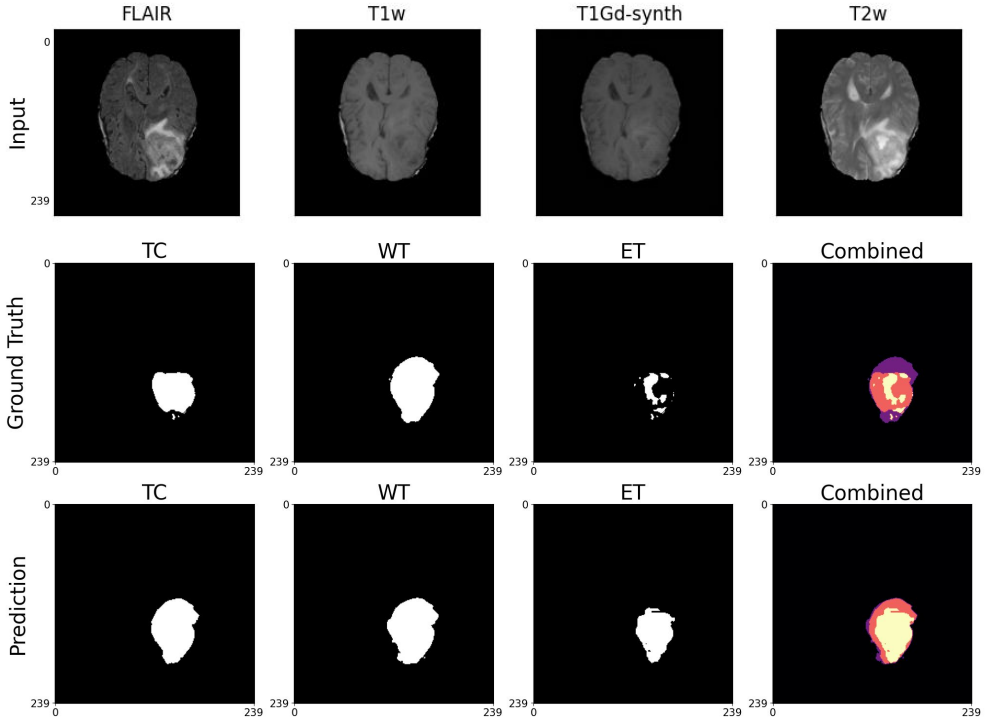
Loss function

	MSE	MAE
MSE	**0.0009**	0.0012
MAE	**0.0121**	0.0138
PSNR	**31.3**	30.0
SSIM	**0.8396**	0.7976

Brain Tumor Segmentation

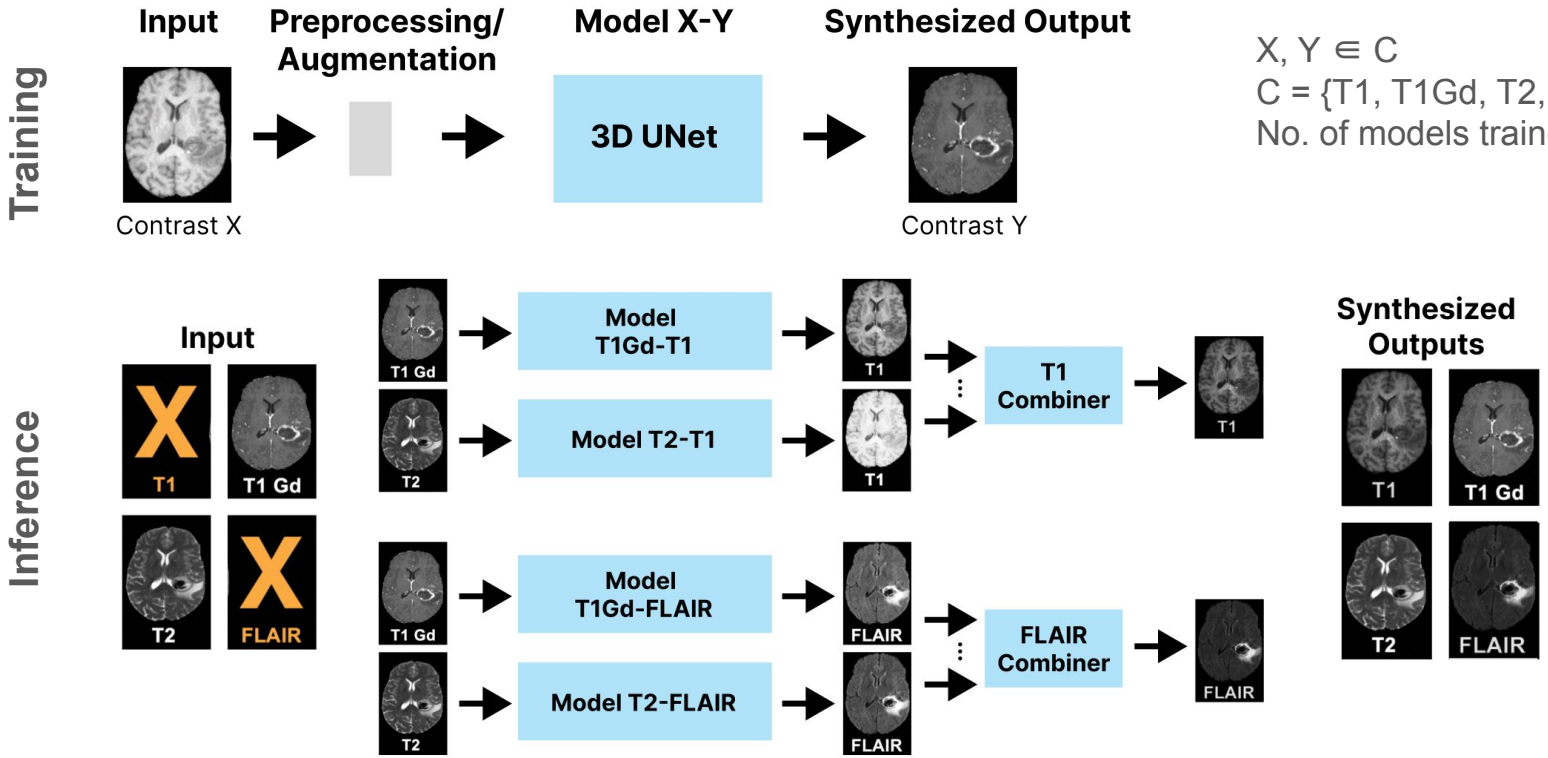


	WT	TC	ET
Available	89.7	82.4	61.2
Synthesized	89.7	69.2	47.4
Mean	88.6	68.4	46.5
Missing	89.2	75.8	49



Next Work

Method 2 (Ensemble of Single Contrast Synthesis - **ESCS**)



Expected kernel for missing features in support vector machines (Anderson et al., 2011)

- The expected kernel is defined as the average similarity between two feature vectors, taking into account the uncertainty due to missing values. Mathematically, it is expressed as:

$$K_{\exp}(p_{X_i}, p_{X_j}) \triangleq \mathrm{E}_{X_i, X_j}\left[K\left(X_i, X_j\right)\right]$$
$$= \iint p_{X_i}(x_i) p_{X_j}(x_j) K(x_i, x_j) dx_i dx_j.$$

- Some examples of expected kernels:
  - Expected Inner Product Kernel: $K(x_i, x_j) = x_i^T x_j$

$$\Rightarrow K_{\exp}^{\mathrm{lin}}(p_{X_i}, p_{X_j}) = m_i^T m_j + \delta_{i=j} \mathrm{tr}\ \Sigma_i,$$

  - Expected RBF kernel $K(x_i, x_j) = \exp\left(-\frac{\gamma}{2}\|x_i - x_j\|^2\right)$

$$\Rightarrow K_{\exp}^{\mathrm{rbf}}(p_{X_i}, p_{X_j}) = \frac{\exp\left(-\frac{1}{2}(m_i - m_j)^T \left(\Sigma_i + \Sigma_k + \gamma^{-1} I\right)^{-1} (m_i - m_j)\right)}{\left|\gamma\Sigma_i + \gamma\Sigma_j + I\right|^{\frac{1}{2}}}$$

SVM with missing features

Solved by QP (Quadratic Programming)
Anderson et al (2011)

$$\underset{c,b,\xi}{\text{minimize}}\ \frac{1}{2}c^T K_{\text{exp}} c + C\sum_{i=1}^{n}\xi_i$$

$$\text{s.t. } y_i\left(c^T k_{\text{exp},i} + b\right) \geq 1 - \xi_i$$

$$\xi_i \geq 0,$$

where $k_{\text{exp},i} \triangleq [K_{\text{exp}}(p_{X_1}, p_{X_i}), \ldots, K_{\text{exp}}(p_{X_n}, p_{X_i})]^T$

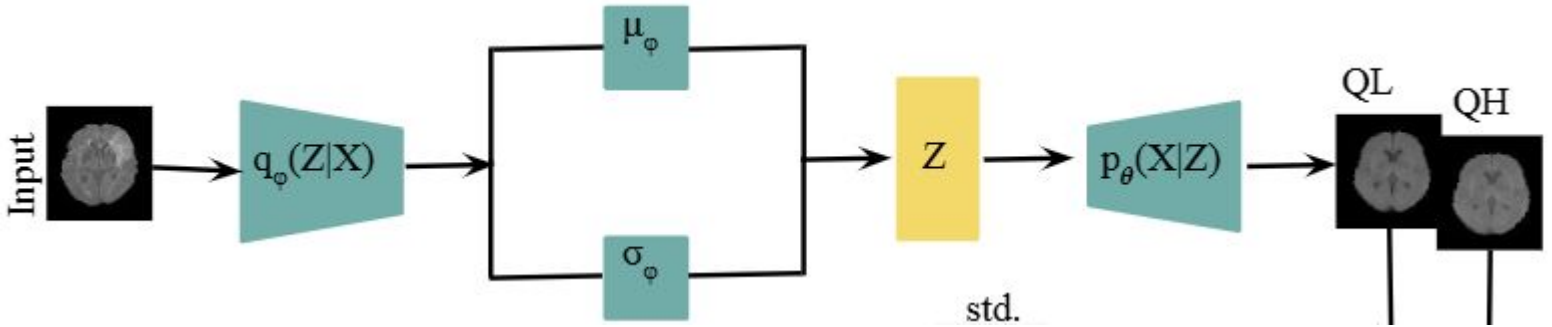
Solved by SOCP (Second Order Cone Programming)
Shivaswamy et al. (2006)

$$\underset{c,b,\xi}{\text{minimize}}\ \frac{1}{2}c^T \hat{K} c + C\sum_{i=1}^{n}\xi_i$$

$$\text{s.t. } y_i\left(c^T \hat{k}_i + b\right) \geq 1 - \xi_i + \tau_i \|c\|_{\Sigma_i^k}$$

$$\xi_i \geq 0$$

- Conditional Expected Kernel Embeddings for Robust Lesion Segmentation in Multimodal Brain MRI with Missing Modalities



Estimate conditional probability of image modalities P(Xi)


Thank
you!

Appendix

Contrast availability in TRACK-TBI

- For instance, in TRACK-TBI data (n=252), there are 9 different contrasts present
- But not all of them are available for every sample