RS-Net: Regression-Segmentation 3D CNN for Synthesis of Full Resolution Missing Brain MRI in the Presence of Tumours

Raghav Mehta, Tal Arbel

Centre for Intelligent Machines
McGill University

McGill
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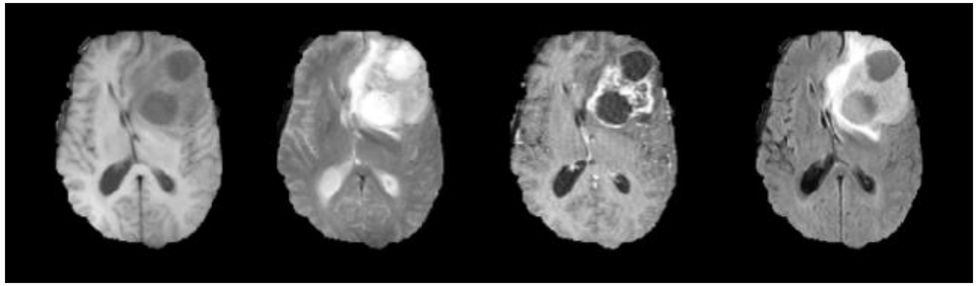
Intelligent Machines

SASHIMI MICCAI 2018

Motivation

- Availability of different modalities of MRI assists in better analysis of disease
  - Improved segmentation of pathology [1]



T1 T2 T1c FLAIR

[1] Havaei et al., MICCAI 2016

Motivation

- Availability of different modalities of MRI assists in better analysis of disease
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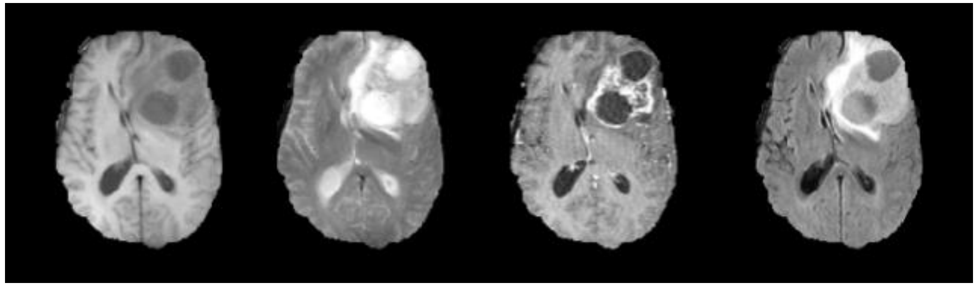
- In real clinical practice, not all modalities are always available due to various reasons
  - Cost and time constraints
  - Image corruption due to noise, patient movement
  - Inappropriate acquisition parameters



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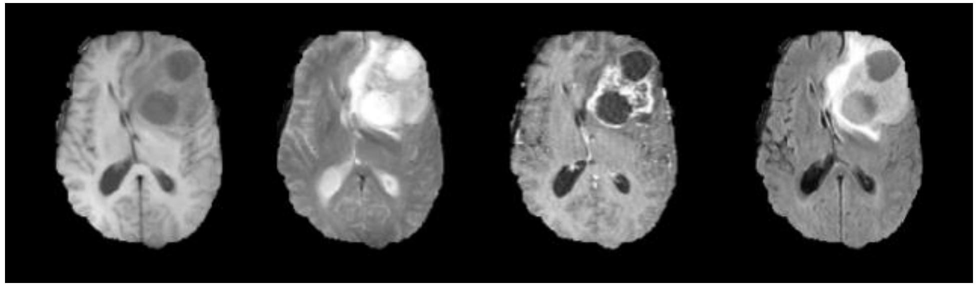
  - Improved segmentation of pathology [1]
- In real clinical practice, not all modalities are always available due to various reasons
  - Cost and time constraints
  - Image corruption due to noise, patient movement
  - Inappropriate acquisition parameters
- Synthesized missing modality can be used by clinicians for better diagnosis
- This can also assist in improving automatic pathology segmentation [2]



T1 T2 T1c FLAIR

[1] Havaei et al., MICCAI 2016
[2] Tulder et al., MICCAI 2015

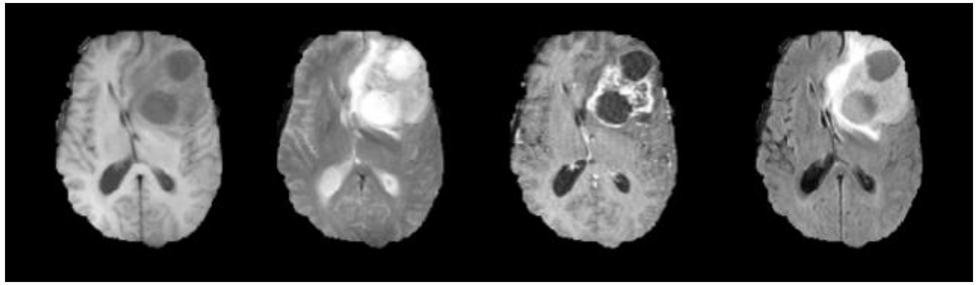
Related Work (Modality Synthesis)

	Dataset	Synthesis Type	Evaluation Metrics
Modality Propagation [3]	Diseased / Pathology	Uni-modal	Correlation Co-efficient (CC)
REPLICA [4]	Healthy / Pathology	Uni-modal / Multi-modal	PSNR, SSIM, UQI
MIMECS [5]	Healthy / Pathology	Uni-modal / Multi-modal	Tissue Segmentation / Visual Comparison
LSDN [6]	Healthy	Uni-modal	PSNR
2D-CNN [7]	Pathology	Uni-modal / Multi-modal	MSE, PSNR, SSIM
2D-GAN [8]	Pathology	Uni-modal	MAE, PSNR

[3] Ye et al., MICCAI 2013
[4] Jog et al., MIA 2016
[5] Roy et al., TMI 2013
[6] Van Nguyen et al., MICCAI 2015
[7] Chartsias et al., TMI 2017
[8] Wolterink et al., SASHIMI MICCAI 2017

In this Paper…

- Method specifically designed for synthesizing MR sequence with pathology



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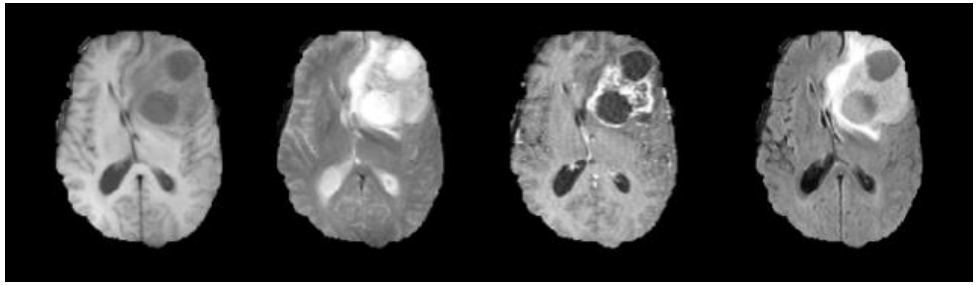

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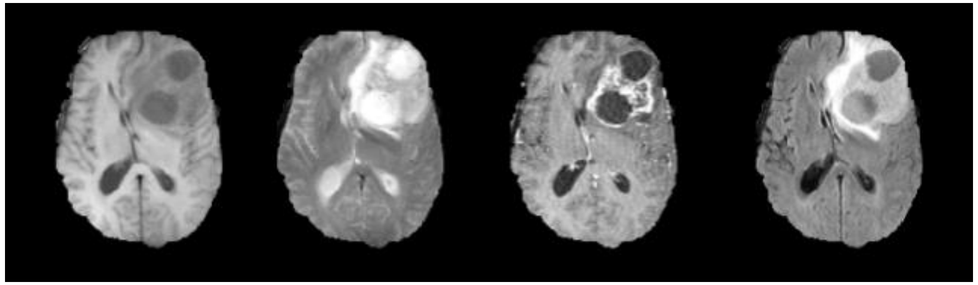
- Multimodal synthesis of missing MR sequence
- Synthesis quantification using on MC-dropout [9] based uncertainty estimation



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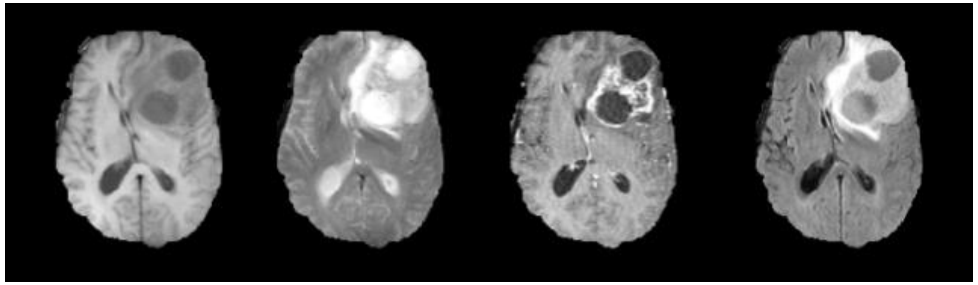
- Experiments on publicly available large-scale brain tumour dataset (BraTS 2017)



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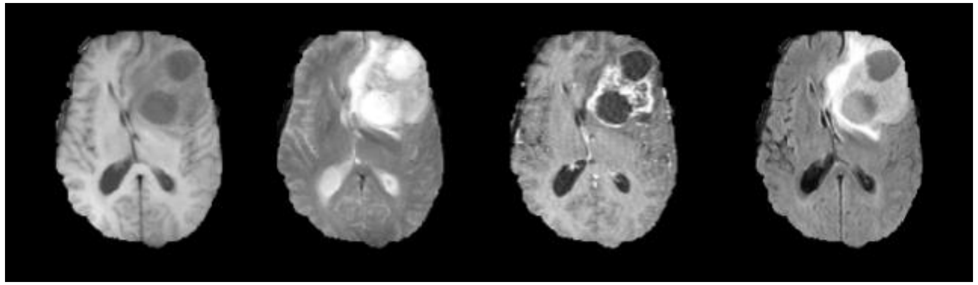
- Experiments on publicly available large-scale brain tumour dataset (BraTS 2017)
- Evaluation based on downstream segmentation task



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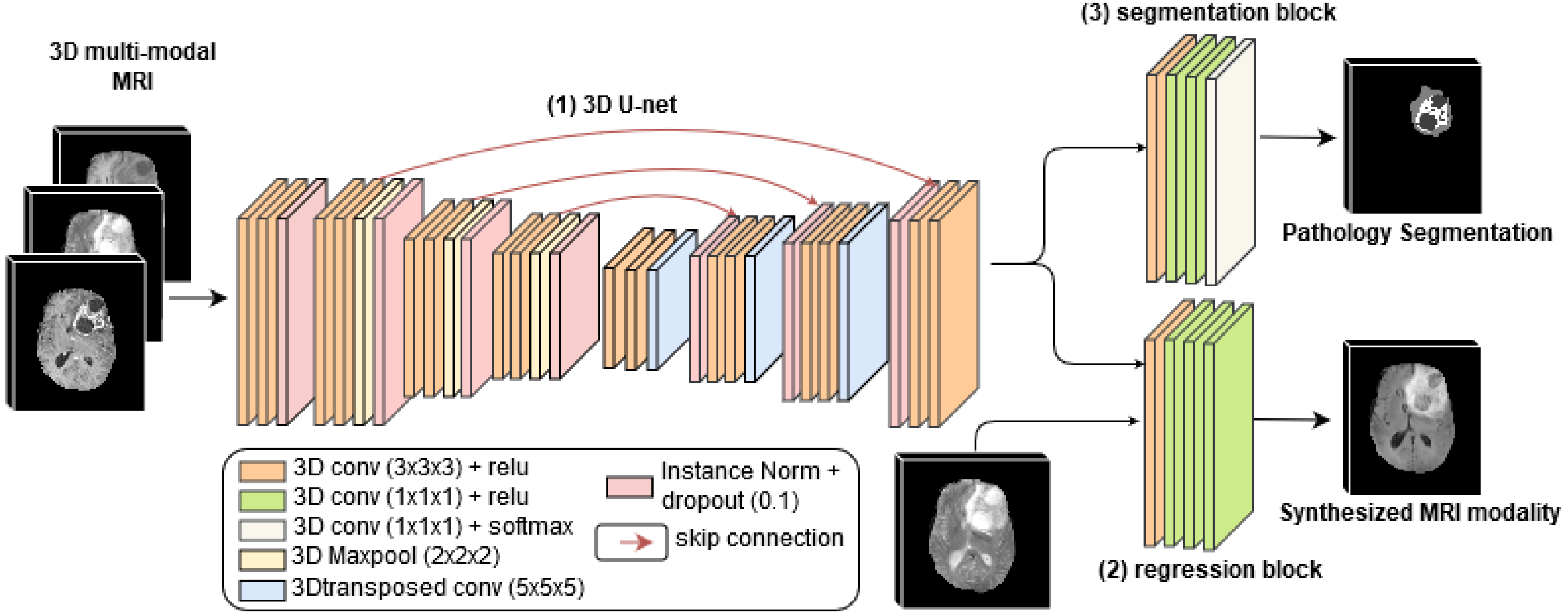
Proposed Method (RS-Net)



[10] Cicek et al., MICCAI 2016
[11] Ulyanov et al., arXiv:1607.08022.

Loss Function

- Weighted combination of Mean Squared Error (MSE), for synthesis, and Categorical Cross Entropy (CCE), for segmentation.

$$L^i = \lambda_1 (w_n^i * MSE)^i + \lambda_2 (w_n^i * CCE)^i$$

Loss Function

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- Weights for each samples according to its true label.

Which is real and which is synthesized?

T2

Which is real and which is synthesized?

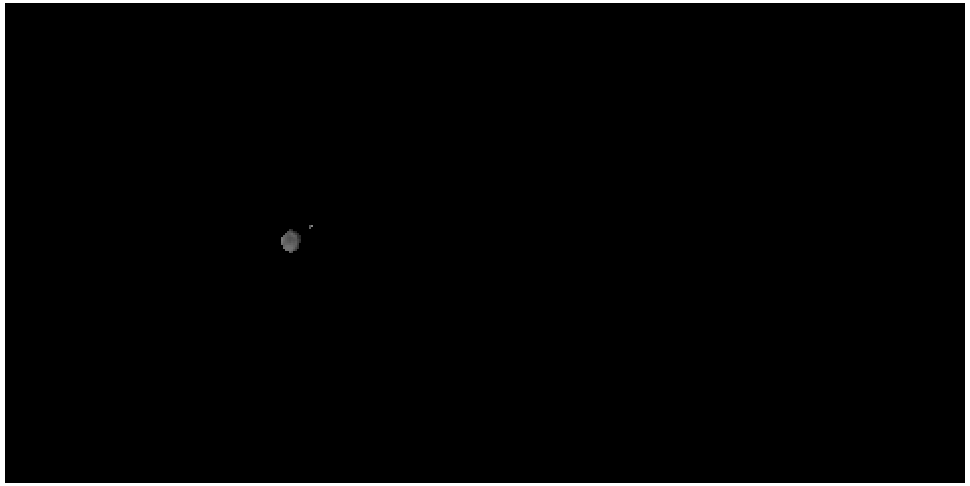
Real

Synthesized

T2

3D visualization

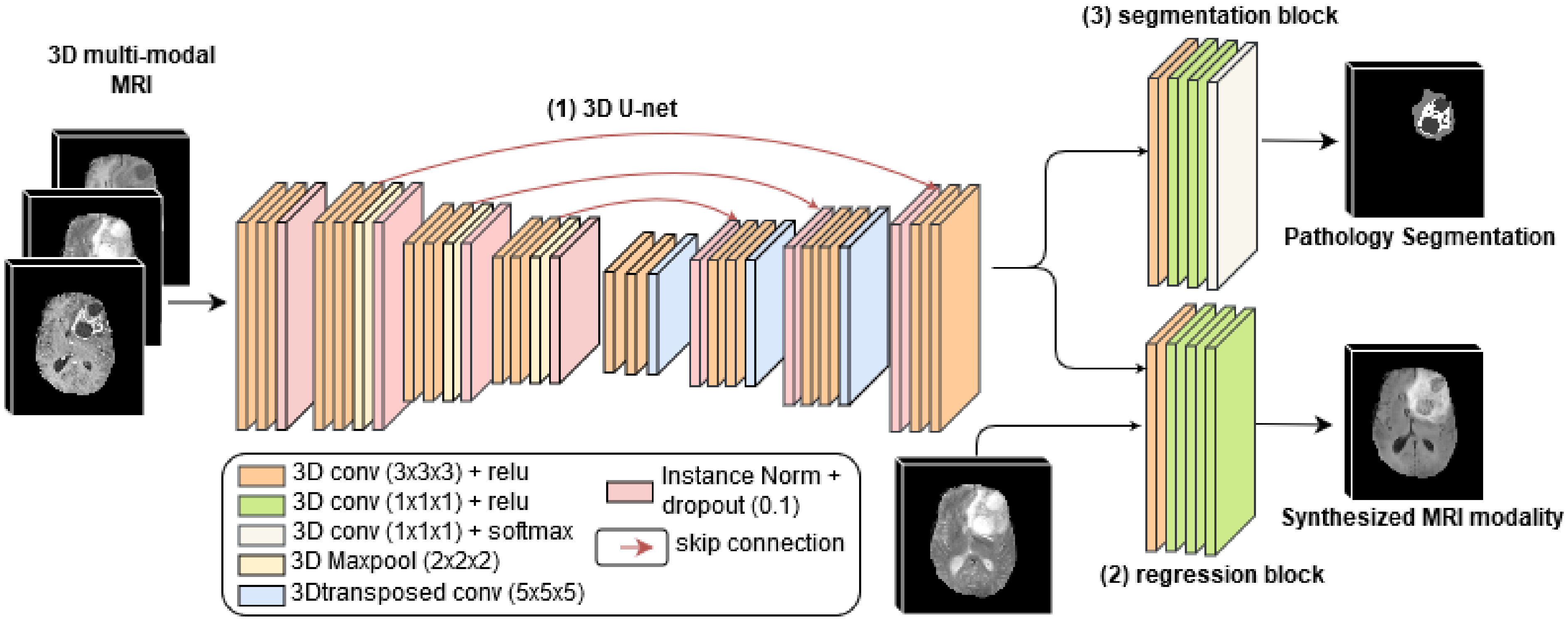
Real



Synthesized

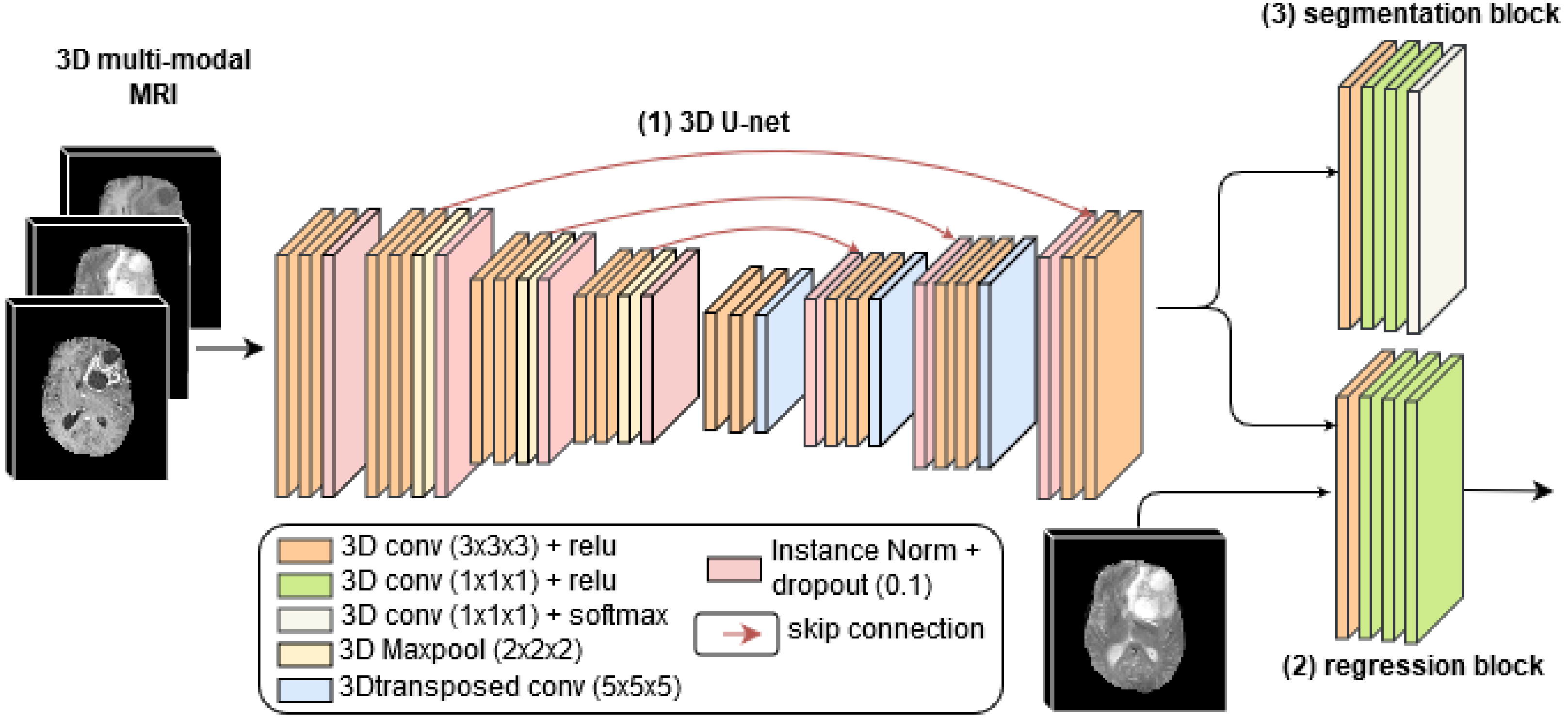
T1c

Synthesis Uncertainty



RS-Net

Synthesis Uncertainty



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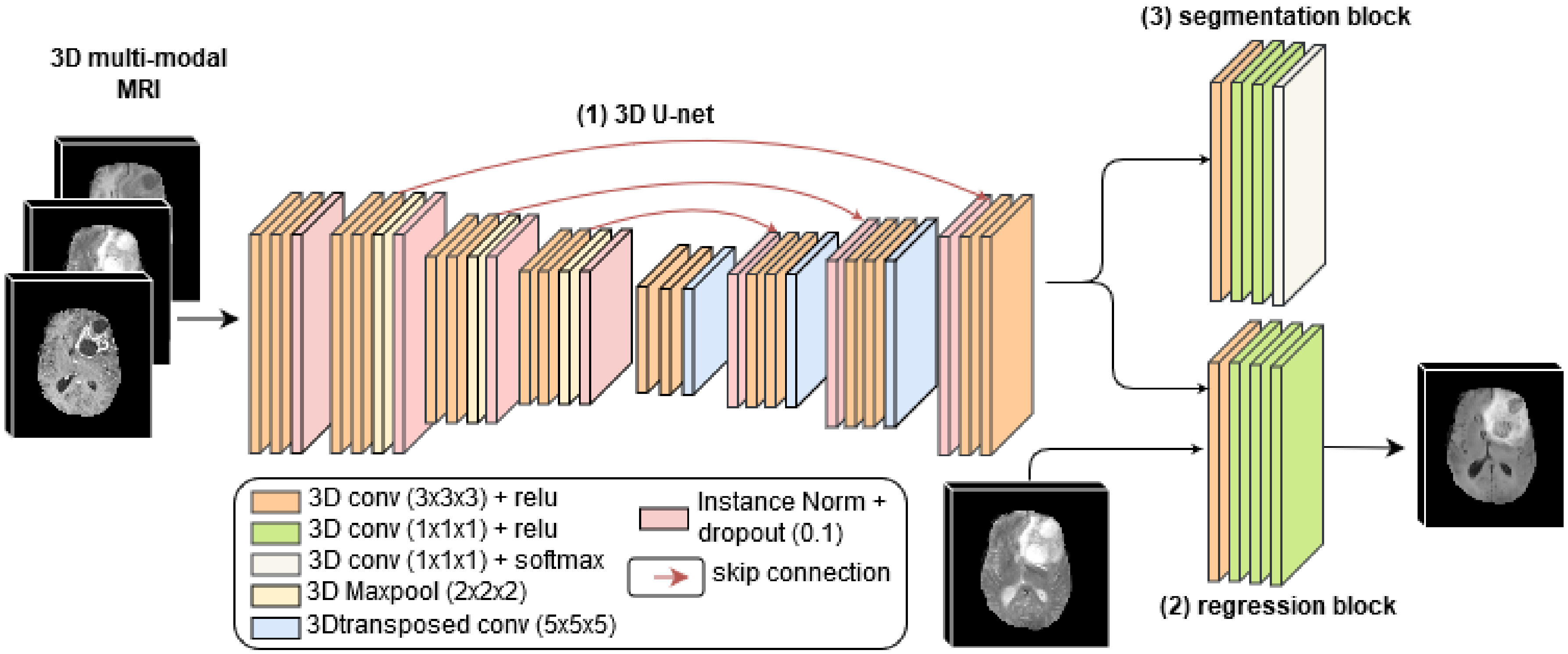

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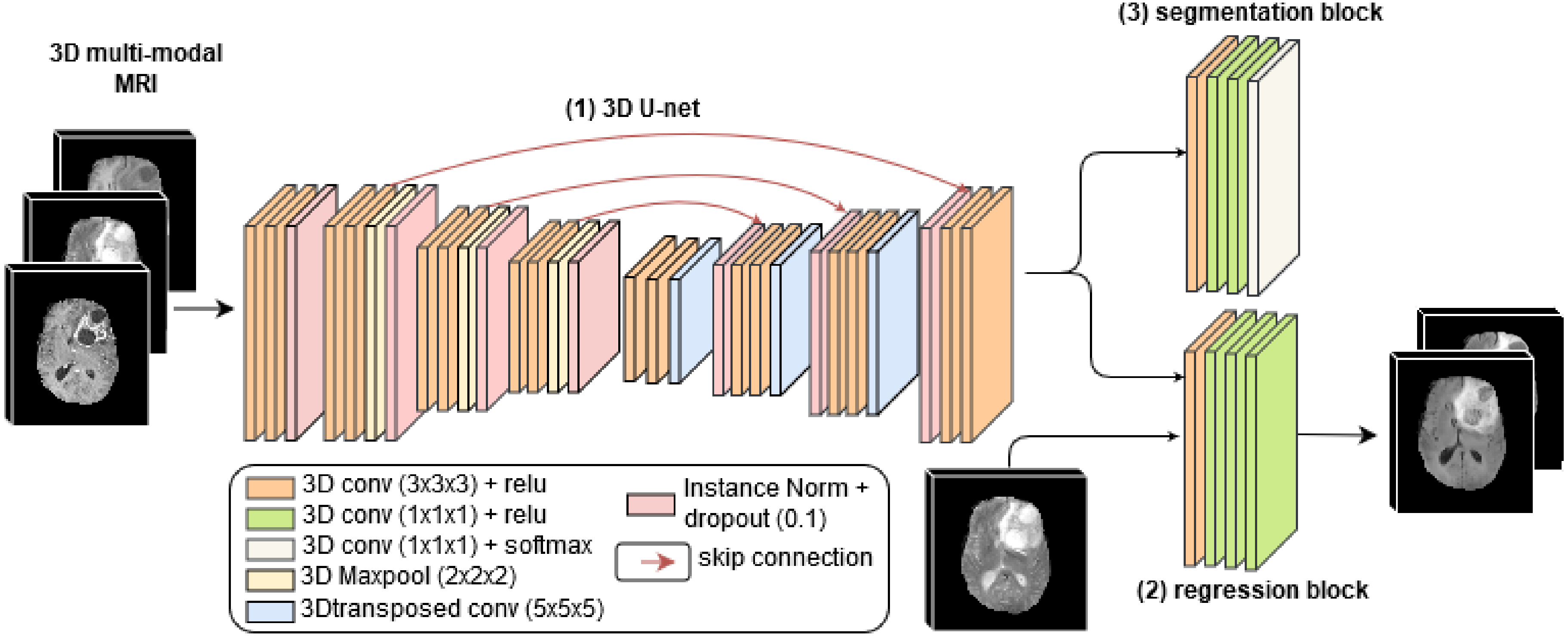

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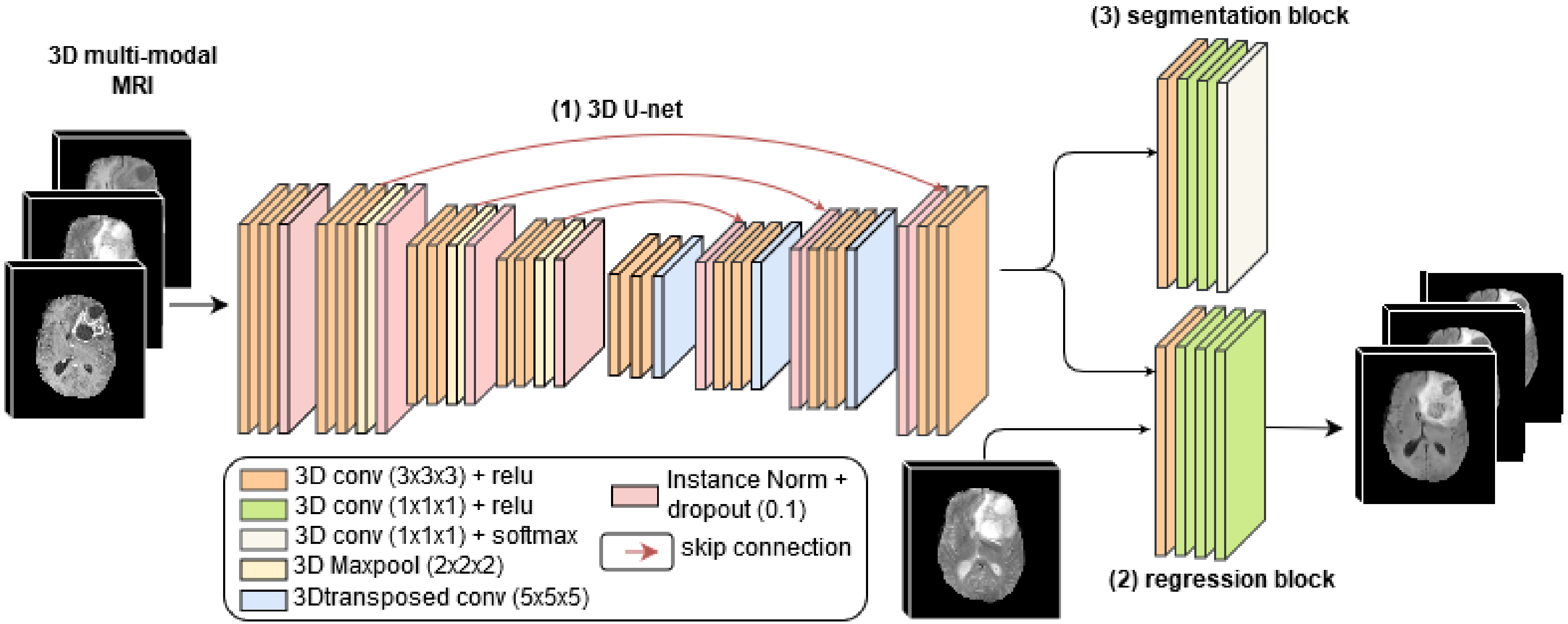

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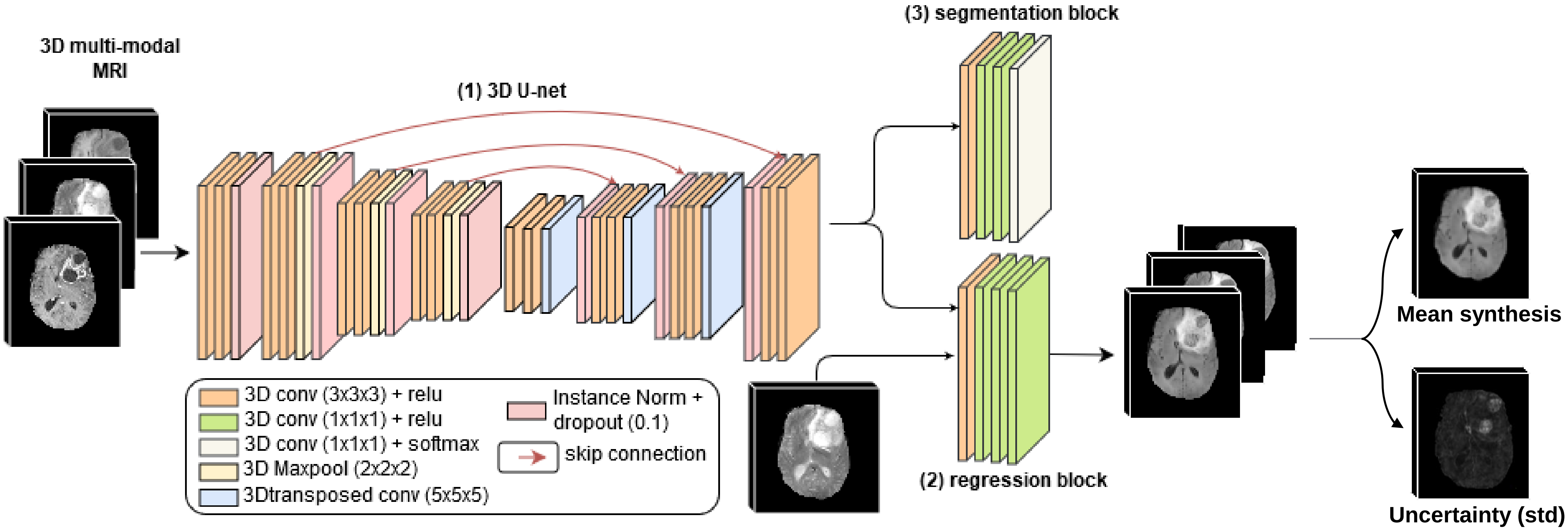

RS-Net

Experiments on BraTS 2017 dataset

Dataset and Pre-processing

- 2017 Brain Tumour Segmentation (BraTS) [12] challenge dataset
  - 4 modalities (T1, T2, FLAIR, T1c)
  - Resolution: 1x1x1 mm^3
  - Dimensions: 184 x 200 x 152
  - Manual marking for 3 types of tumour (edema, necrotic core, and enhancing core)
- Pre-processing
  - Skull stripping
  - Co-registration
  - Intensity Normalization (mean subtraction, divide by standard deviation, re-mapping to 0-1)

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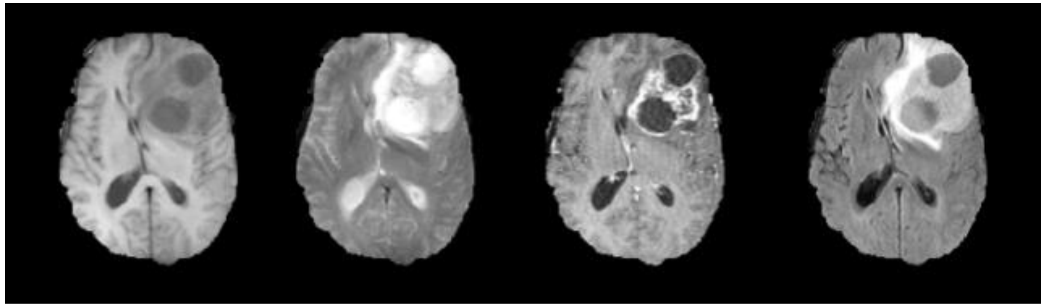
  - Co-registration
  - Intensity Normalization (mean subtraction, divide by standard deviation, re-mapping to 0-1)
- BraTS 2017 Training data (285 patients) for training (228) and validation (57)
- BraTS 2017 Validation data (46 patients) for testing

[12] Menze et al., TMI 2015

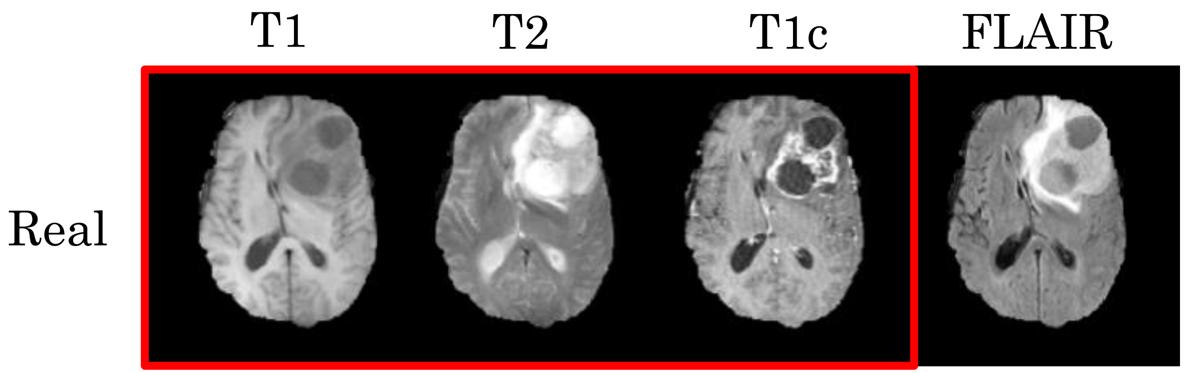
3 -to- 1 synthesis

T1 T2 T1c FLAIR

Real



3 -to- 1 synthesis



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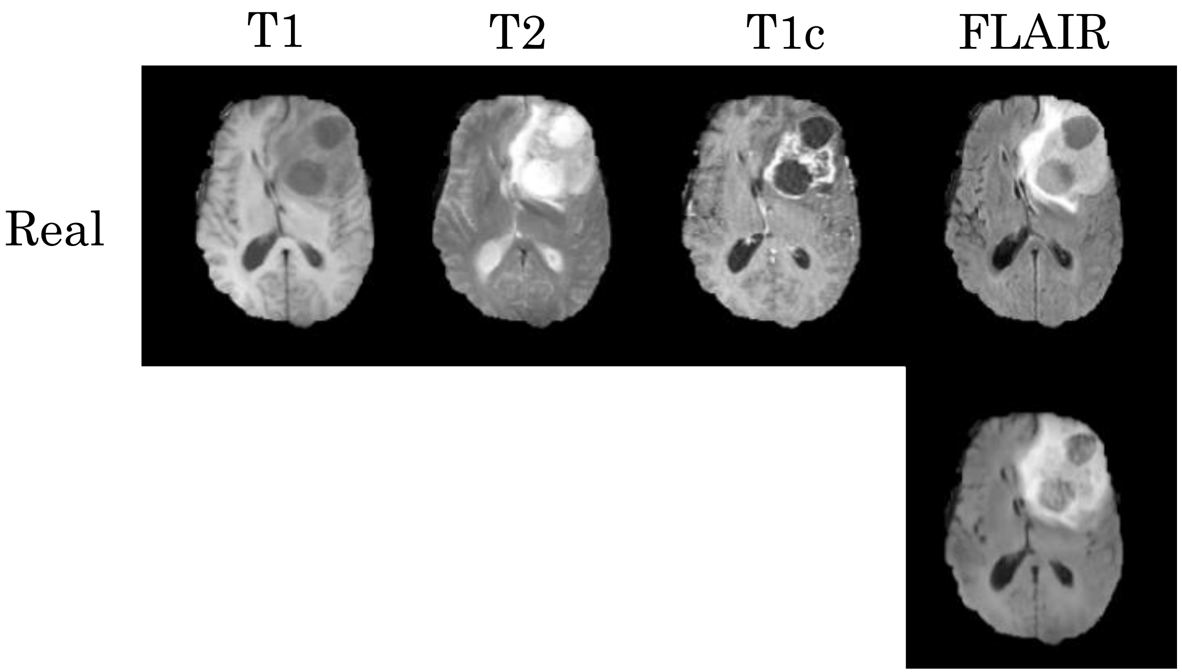
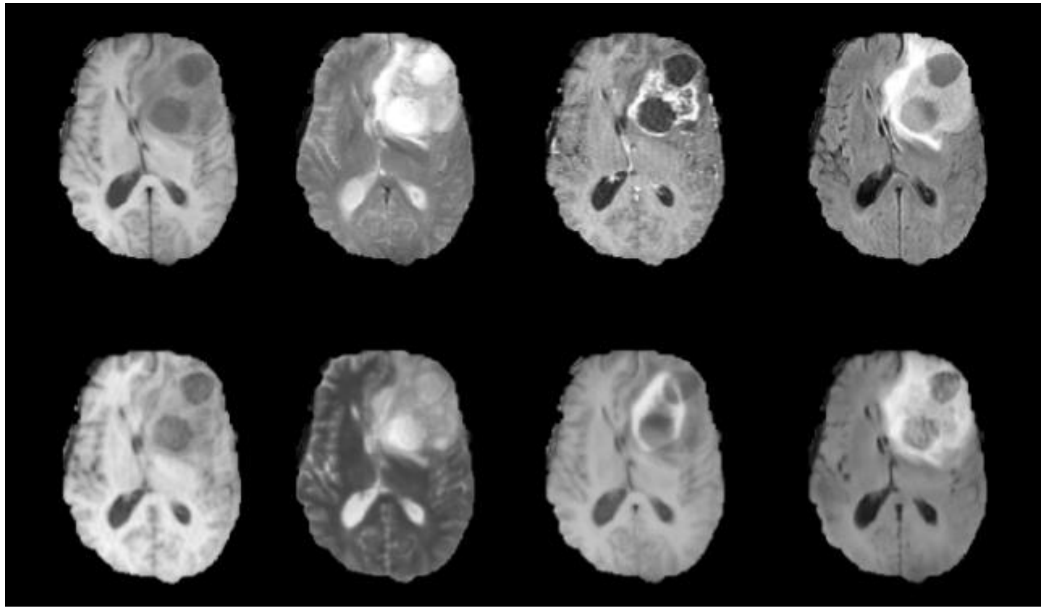


3 -to- 1 synthesis

T1 T2 T1c FLAIR

Real

Synthesis



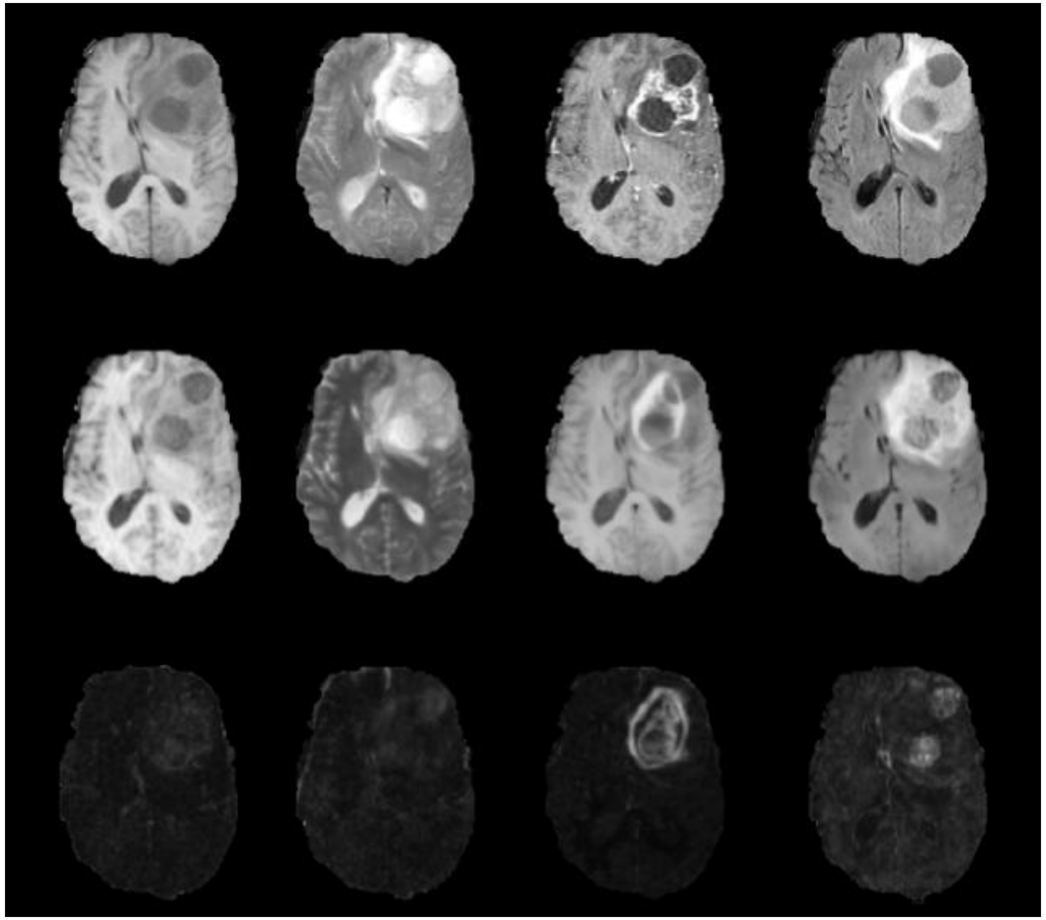
3 -to- 1 synthesis

T1 T2 T1c FLAIR

Real

Synthesis

Uncertainty



Quantitative Evaluation

- Standard Evaluation metrics [4,6,7,8]
  - Peak Signal to Noise Ration (PSNR)
  - Mean Squared Error (MSE)
  - Structure Similarity Index (SSIM)

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- Global metrics, Useful for quantitative evaluation of the whole MRI
- Here, interested in evaluating synthesis performance in the area of tumour
- Tumour Segmentation (whole, core, and enhancing) evaluation
  - Dice Coefficient
  - $DICE(A,B) = \frac{2\,|\,A \cap B\,|}{|\,A \cup B\,|} * 100$

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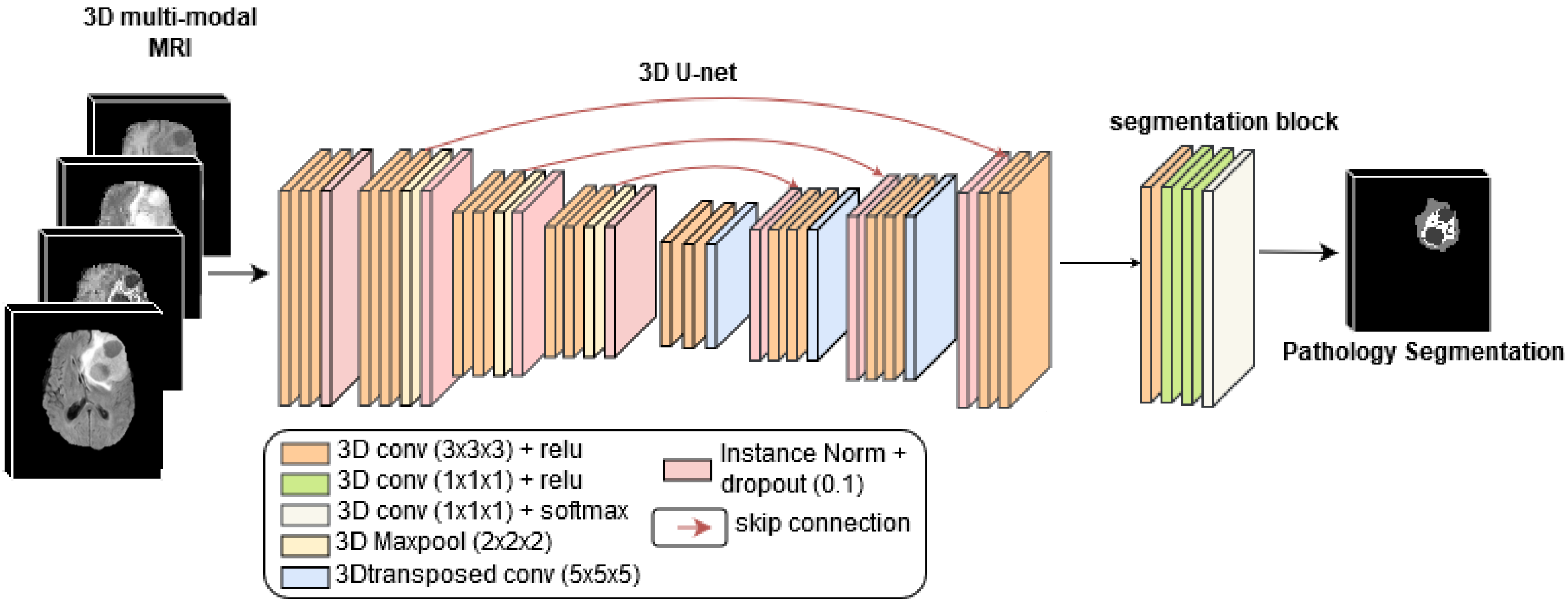
Segmentation Network (S-Net)



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Replacing real with synthetic MRI Volumes

	T1	T2	FLAIR	T1ce	DE	DT	DC
Real	✓	✓	✓	✓	68.2	87.9	75.7

✓ Real MRI

DE: Dice Enhance
DT: Dice Tumour
DC: Dice Core

Replacing real with synthetic MRI Volumes

	T1	T2	FLAIR	T1ce	DE	DT	DC
Real	✓	✓	✓	✓	**68.2**	**87.9**	**75.7**
T1 Synthesis	$\odot$	✓	✓	✓	67.6	87.9	75.5

✓ Real MRI

$\odot$ Synthesised MRI (RS-Net)

DE: Dice Enhance
DT: Dice Tumour
DC: Dice Core

Replacing real with synthetic MRI Volumes

	T1	T2	FLAIR	T1ce	DE	DT	DC
Real	✓	✓	✓	✓	**68.2**	**87.9**	**75.7**
T2 Synthesis	✓	⊙	✓	✓	66.3	87.3	75.6

✓ Real MRI

⊙ Synthesised MRI (RS-Net)

DE: Dice Enhance
DT: Dice Tumour
DC: Dice Core

Replacing real with synthetic MRI Volumes

	T1	T2	FLAIR	T1ce	DE	DT	DC
Real	✓	✓	✓	✓	**68.2**	**87.9**	**75.7**
FLAIR Synthesis	✓	✓	⊙	✓	66.8	83.6	73.1

✓ Real MRI

⊙ Synthesised MRI (RS-Net)

DE: Dice Enhance
DT: Dice Tumour
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Replacing real with synthetic MRI Volumes

	T1	T2	FLAIR	T1ce	DE	DT	DC
Real	✓	✓	✓	✓	**68.2**	**87.9**	**75.7**
T1ce Synthesis	✓	✓	✓	⊙	24.8	87.3	54.0

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Replacing real with synthetic MRI Volumes

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T1 Synthesis	⊙	✓	✓	✓	67.6	87.9	75.5
T2 Synthesis	✓	⊙	✓	✓	66.3	87.3	75.6
FLAIR Synthesis	✓	✓	⊙	✓	66.8	83.6	73.1
T1ce Synthesis	✓	✓	✓	⊙	24.8	87.3	54.0

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⊙ Synthesised MRI (RS-Net)

DE: Dice Enhance
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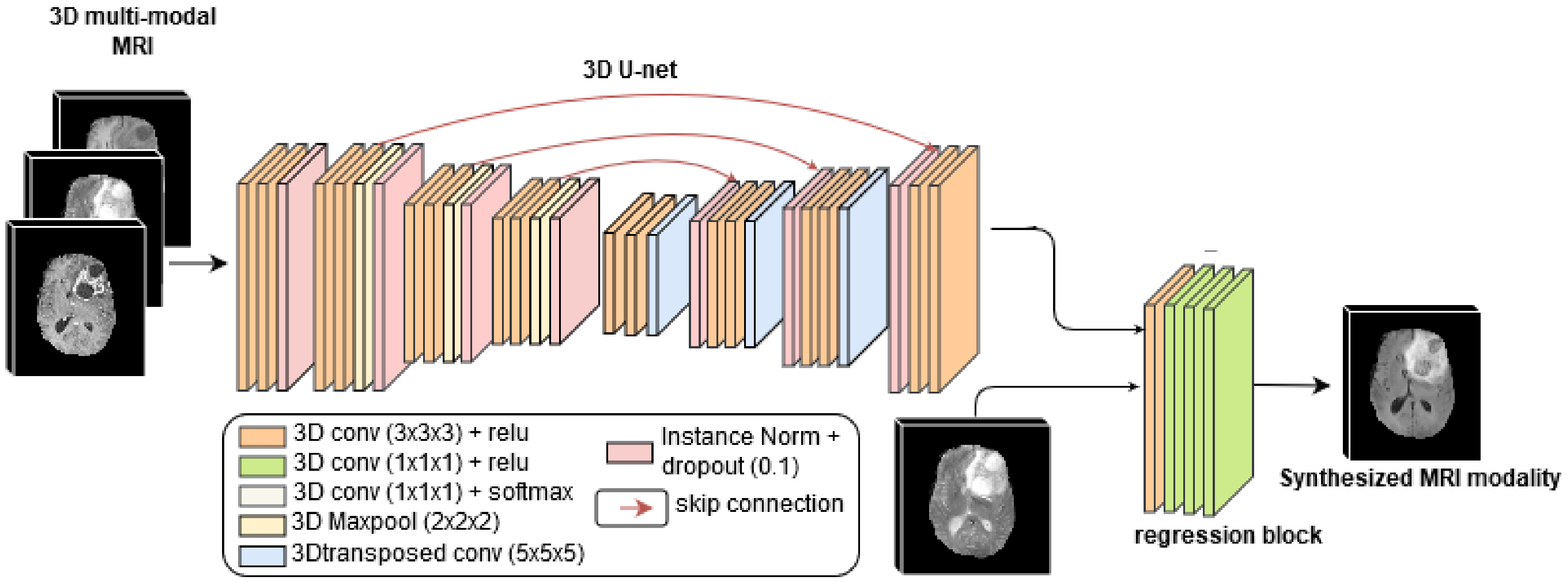
Regression-only Network (R-Net)



R-Net

Comparison of RS-Net and R-Net

	T1	T2	FLAIR	T1ce	DE	DT	DC
Real	✓	✓	✓	✓	**68.2**	**87.9**	**75.7**
T1 Synthesis	⊙	✓	✓	✓	67.6	87.9	75.5
	•	✓	✓	✓	67.5	87.8	75.3

✓ Real MRI
⊙ Synthesised MRI (RS-Net)
• Synthesised MRI (R-Net)

DE: Dice Enhance
DT: Dice Tumour
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Comparison of RS-Net and R-Net

	T1	T2	FLAIR	T1ce	DE	DT	DC
Real	✓	✓	✓	✓	**68.2**	**87.9**	**75.7**
T2 Synthesis	✓	⊙	✓	✓	66.3	87.3	75.6
	✓	●	✓	✓	66.1	87.2	75.4

✓ Real MRI

⊙ Synthesised MRI (RS-Net)

● Synthesised MRI (R-Net)

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FLAIR Synthesis	✓	✓	⊙	✓	66.8	83.6	73.1
	✓	✓	•	✓	62.9	81.3	71.5

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T1ce Synthesis	✓	✓	✓	⊙	24.8	87.3	54.0
	✓	✓	✓	•	24.1	85.9	53.9

✓ Real MRI
⊙ Synthesised MRI (RS-Net)
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	•	✓	✓	✓	67.5	87.8	75.3
T2 Synthesis	✓	⊙	✓	✓	66.3	87.3	75.6
	✓	•	✓	✓	66.1	87.2	75.4
FLAIR Synthesis	✓	✓	⊙	✓	66.8	83.6	73.1
	✓	✓	•	✓	62.9	81.3	71.5
T1ce Synthesis	✓	✓	✓	⊙	24.8	87.3	54.0
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Comparison of RS-Net against other methods

Comparison of RS-Net against other methods

- Comparison against following state-of-the-art methods:
  - 2D Convolutional Neural Network (2D CNN) [7]
  - Regression Ensembles with Patch Learning for Image Contrast Agreement (REPLICA) [4]
  - Patch-based Location Sensitive Deep Network (LSDN) [6]

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- Two Experiments:
  - T1 -to- T2 synthesis
  - T1 -to- FLAIR synthesis

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Dataset and Pre-processing

- 2015 Brain Tumour Segmentation (BraTS) [12] challenge dataset
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- Pre-processing
  - Skull stripping
  - Co-registration
  - Intensity Normalization (Divide by mean)

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- Pre-processing
  - Skull stripping
  - Co-registration
  - Intensity Normalization (Divide by mean)
- BraTS 2015 Training Low-Grade Glioma cases (54 patients)
- 5 fold cross validation with 42, 6, and 6 cases respectively for training, validation, and testing.

[12] Menze et al., TMI 2015

Evaluation Metrics

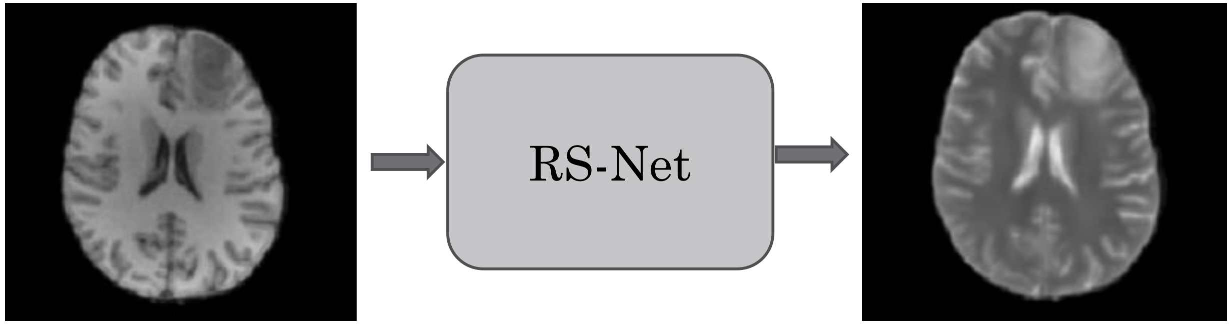
- Structure Similarity Index (SSIM)

$$\mathrm{SSIM} = \frac{(2\mu_x\mu_{x\prime}+c_1)(2\sigma_{xx\prime}+c_2)}{(\mu_x^2+\mu_{x\prime}^2+c_1)(\sigma_x^2+\sigma_{x\prime}^2+c_2)}$$

- Peak Signal -to- Noise Ratio (PSNR)

$$\mathrm{PSNR} = log_{10}(\frac{MAX_I^2}{MSE})$$

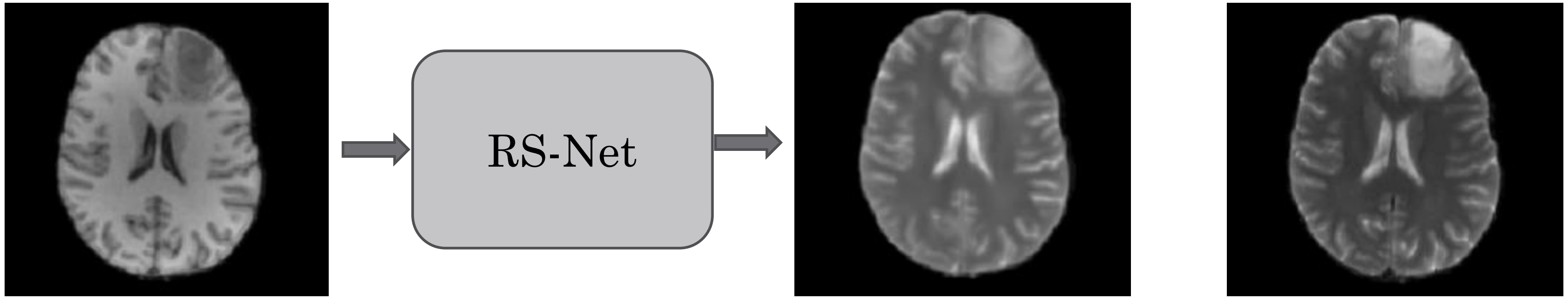
T1 -to- T2 synthesis



Input T1 MRI

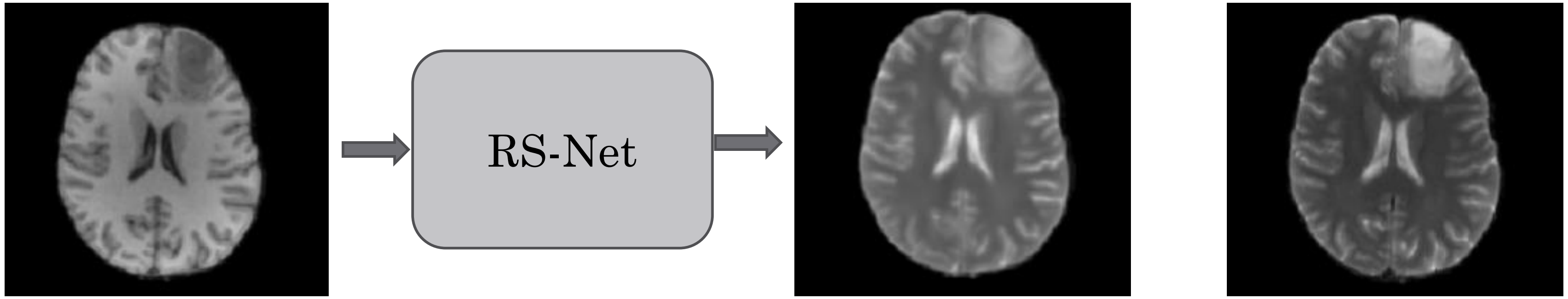
Synthesised T2 MRI

T1 -to- T2 synthesis



Input T1 MRI | Synthesised T2 MRI | Real T2 MRI

T1 -to- T2 synthesis



Input T1 MRI

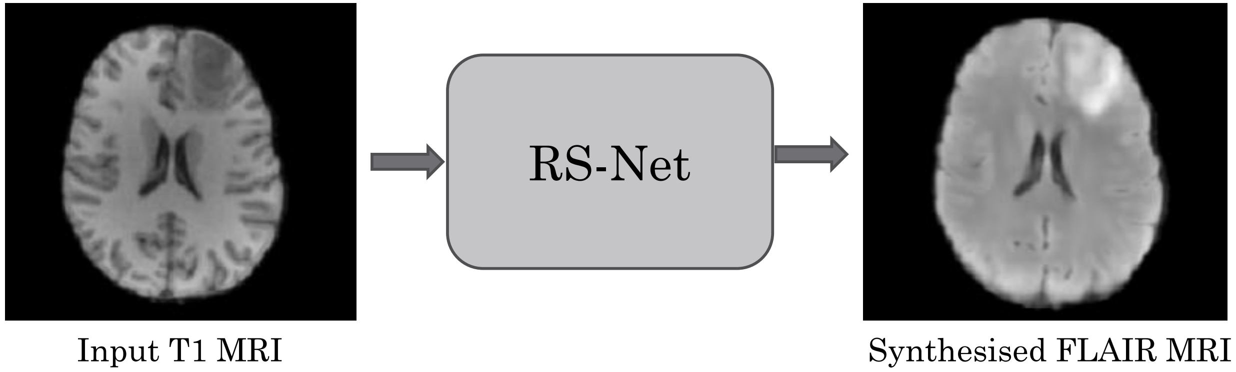
Synthesised T2 MRI

Real T2 MRI

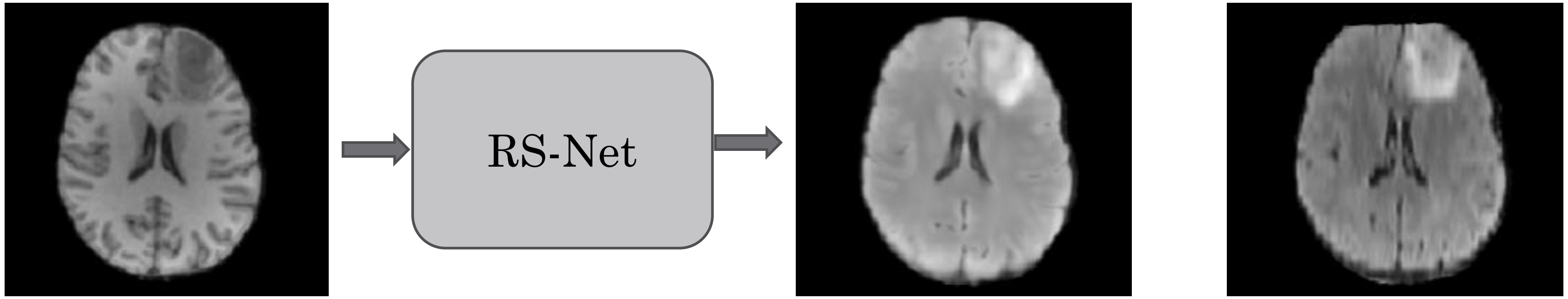
	REPLICA [4]	LSDN [6]	2D-CNN [7]	RS-Net (proposed)
SSIM	0.901 (0.01)	0.909 (0.02)	0.929 (0.17)	**0.934 (0.02)**
PSNR	28.62 (1.69)	30.12 (1.62)	30.96 (1.85)	**31.13 (1.78)**

[4] Jog et al., MIA 2015
[6] Van Nguyen et al., MICCAI 2015
[7] Chartsias et al., TMI 2017

T1 -to- FLAIR synthesis

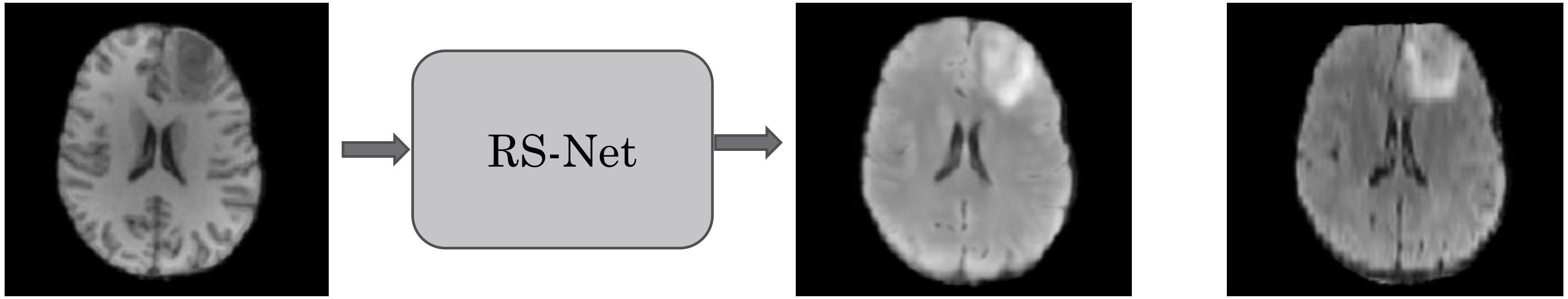


T1 -to- FLAIR synthesis



Input T1 MRI | Synthesised FLAIR MRI | Real FLAIR MRI

T1 -to- FLAIR synthesis



Input T1 MRI | Synthesised FLAIR MRI | Real FLAIR MRI

	REPLICA [4]	LSDN [6]	2D-CNN [7]	RS-Net (proposed)
SSIM	0.870 (0.01)	0.887 (0.01)	0.897 (0.01)	**0.900 (0.01)**
PSNR	28.32 (1.38)	29.68 (1.56)	30.32 (1.61)	**30.88 (1.84)**

[4] Jog et al., MIA 2015
[6] Van Nguyen et al., MICCAI 2015
[7] Chartsias et al., TMI 2017

Conclusion

- Proposed a 3D CNN for the combined task of Synthesis and Segmentation
  - High quality synthesis even for tumour regions

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  - Real MRI can be replaced with Synthesised MRI with minimum degradation in tumour segmentation accuracy
  - Combined Synthesis-Segmentation improves quality over only Synthesis, especially for FLAIR, T1c
- T1c synthesis is still an open and challenging task

Questions?

Real

Synthesized

T2

3D visualization

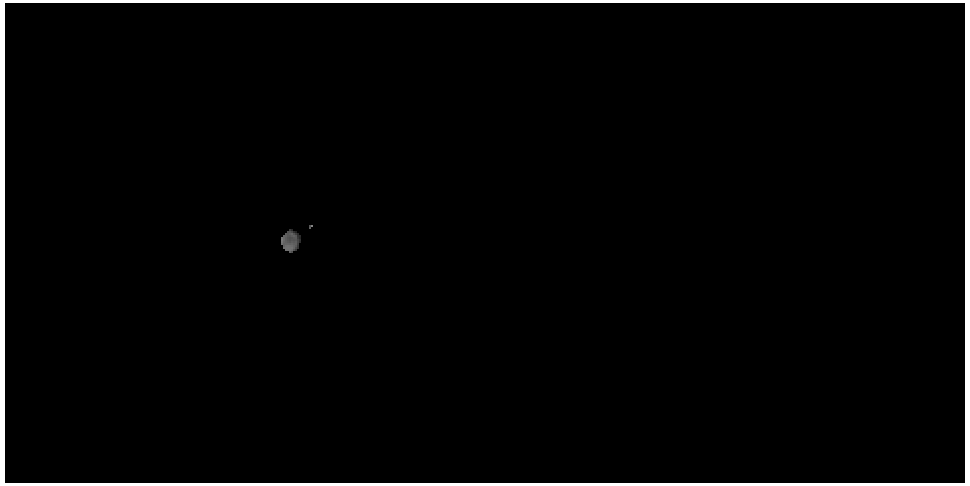
Real

Synthesized

T1

3D visualization

Real

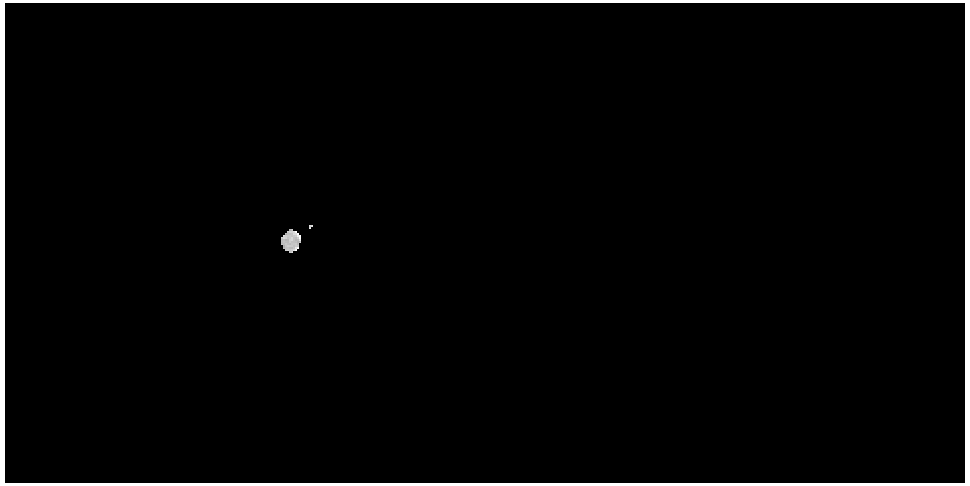


Synthesized

T1c

3D visualization

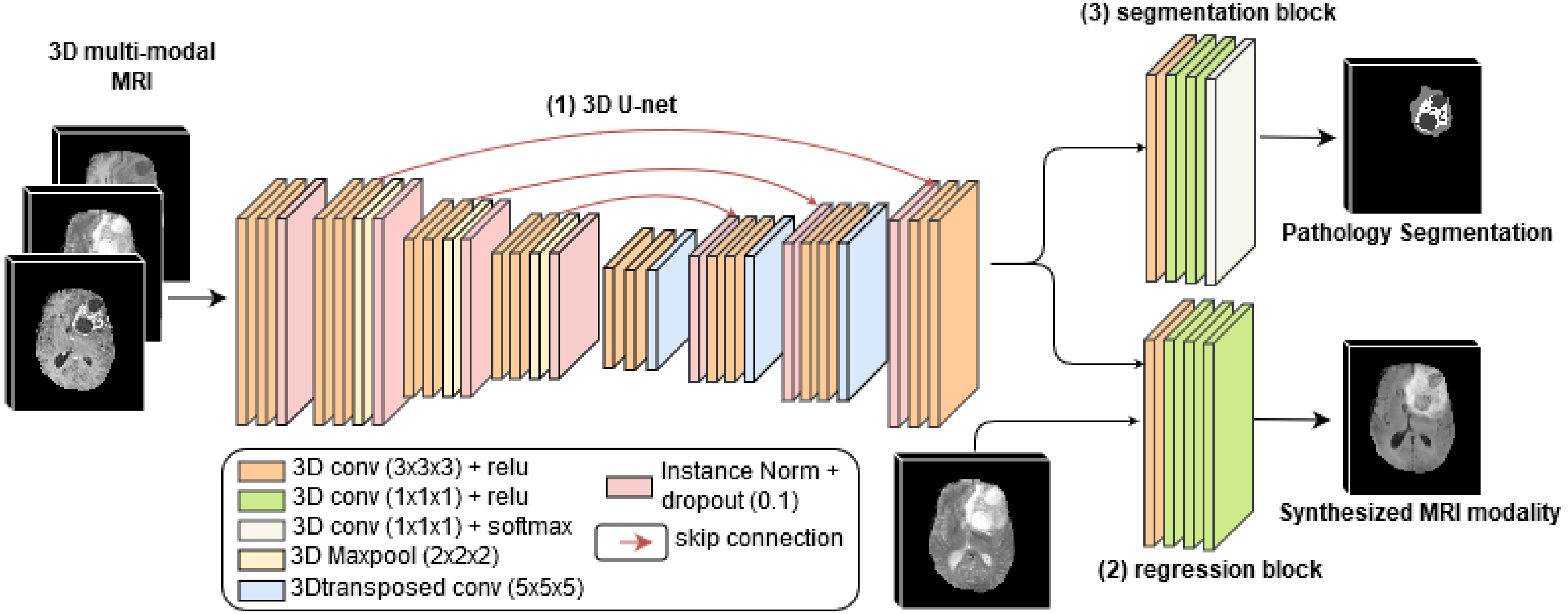
Real



Synthesized

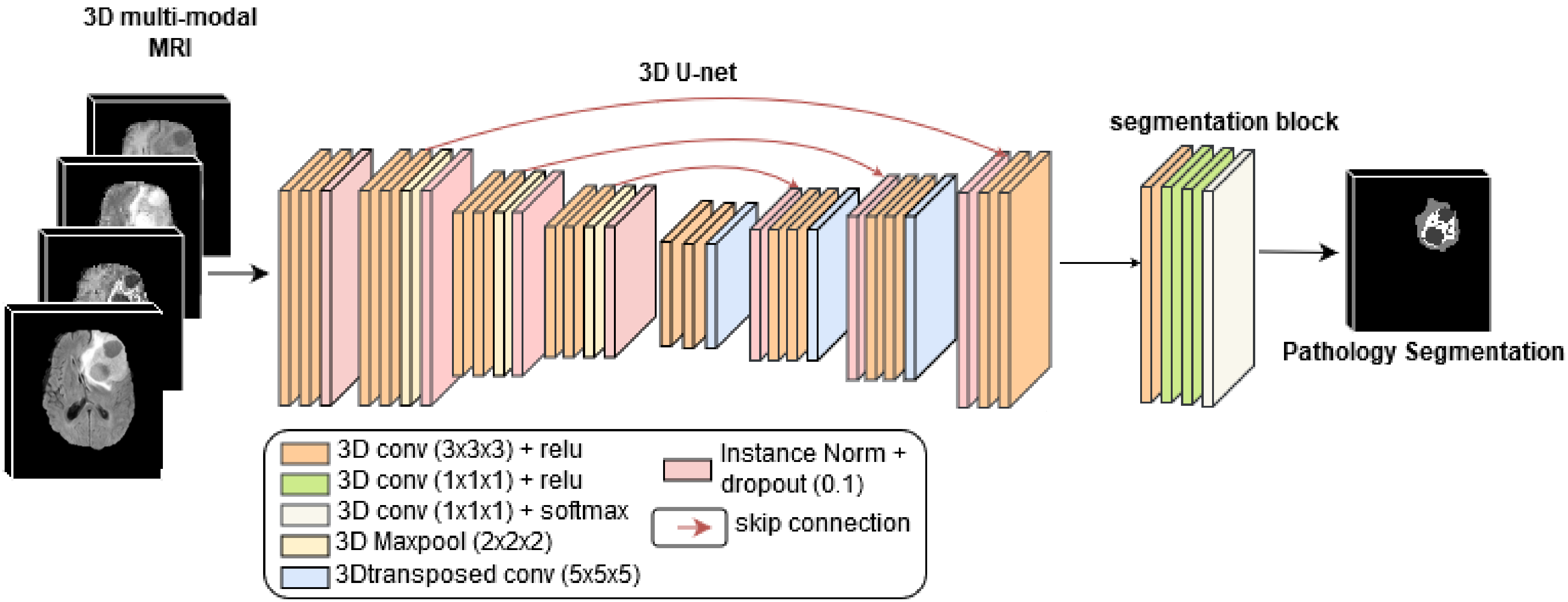
FLAIR

Performance of Segmentation part of RS-Net



RS-Net

Performance of Segmentation part of RS-Net



S-Net

Performance of Segmentation part of RS-Net

	T1	T2	FLAIR	T1ce	DE	DT	DC
Real	✓	✓	✓	✓	**68.2**	**87.9**	**75.7**
T1 Synthesis	⊙	✓	✓	✓	67.6	87.9	75.5
	×	✓	✓	✓	66.4	85.2	71.0
T2 Synthesis	✓	⊙	✓	✓	66.3	87.3	75.6
	✓	×	✓	✓	66.5	87.0	71.1
FLAIR Synthesis	✓	✓	⊙	✓	66.8	83.6	73.1
	✓	✓	×	✓	70.5	82.6	74.0
T1ce Synthesis	✓	✓	✓	⊙	24.8	87.3	54.0
	✓	✓	✓	×	23.1	86.5	52.0

✓ Real MRI

⊙ Synthesised MRI (RS-Net)

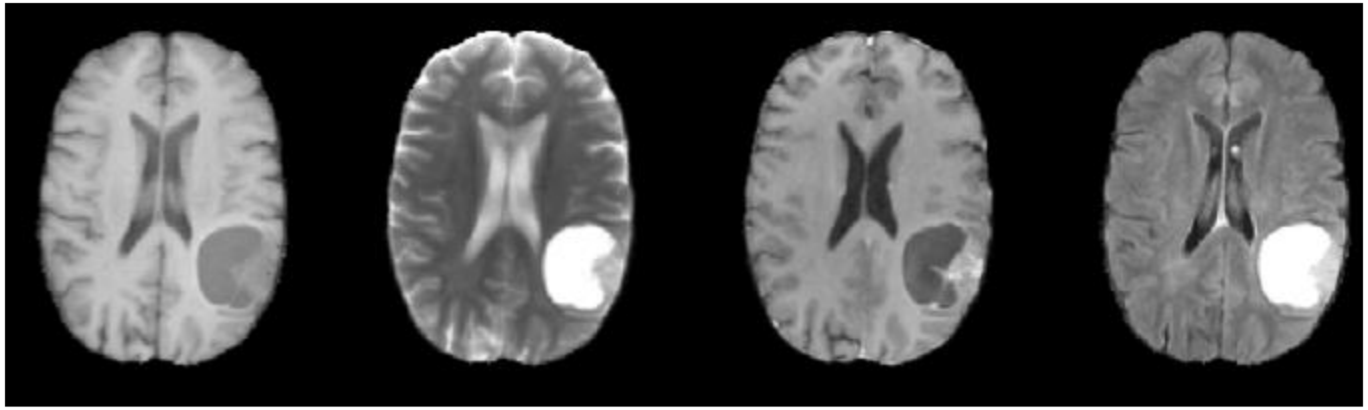
× Segmentation output of RS-Net without MR volume

DE: Dice Enhance
DT: Dice Tumour
DC: Dice Core

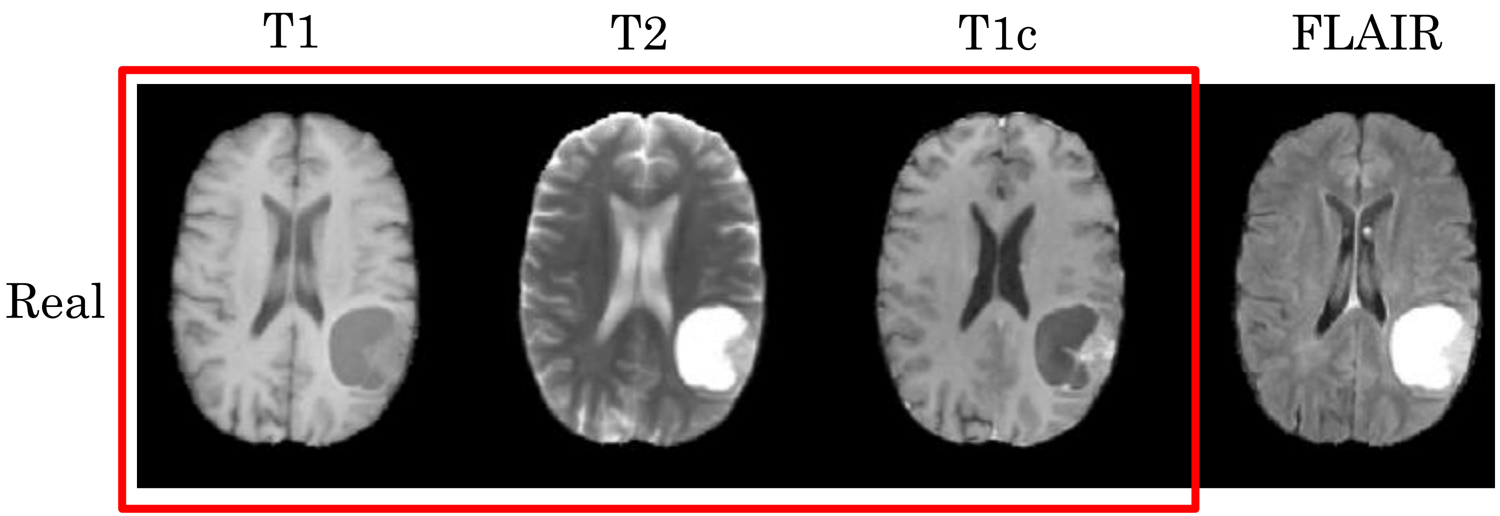
3 -to- 1 synthesis

	T1	T2	T1c	FLAIR

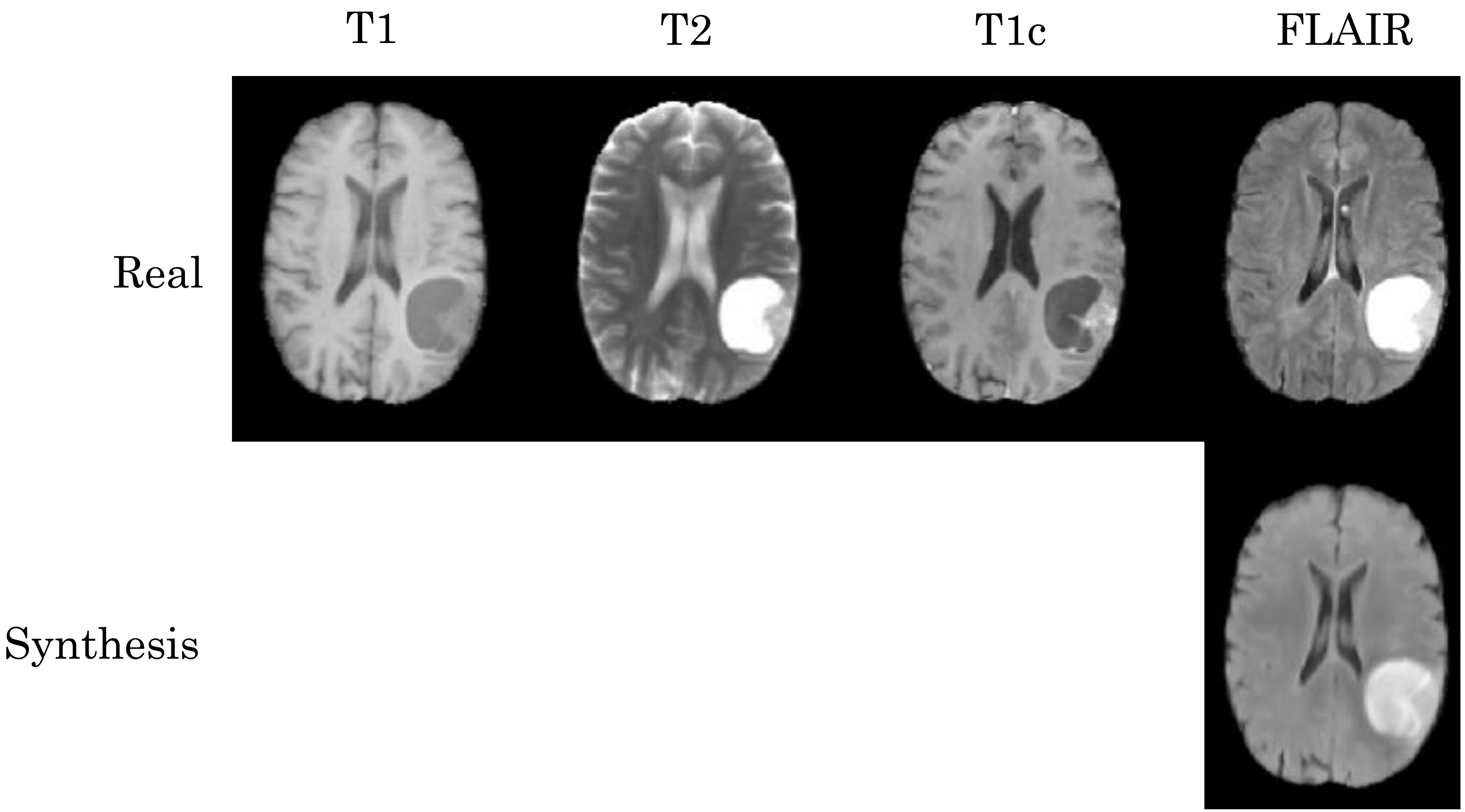
Real



3 -to- 1 synthesis



3 -to- 1 synthesis



3 -to- 1 synthesis

	T1	T2	T1c	FLAIR
Real				
Synthesis