

DRINet for Medical Image Segmentation

Liang Chen, Paul Bentley, Kensaku Mori, Kazunari Misawa, Michitaka Fujiwara, Daniel Rueckert *Fellow IEEE*

Abstract—Convolutional neural networks (CNNs) have revolutionized medical image analysis over the past few years. The U-Net architecture is one of the most well-known CNN architectures for semantic segmentation and has achieved remarkable successes in many different medical image segmentation applications. The U-Net architecture consists of standard convolution layers, pooling layers, and upsampling layers. These convolution layers learn representative features of input images and construct segmentations based on the features. However, the features learned by standard convolution layers are not distinctive when the differences among different categories are subtle in terms of intensity, location, shape, and size. In this paper, we propose a novel CNN architecture, called Dense-Res-Inception Net (DRINet), which addresses this challenging problem. The proposed DRINet consists of three blocks, namely a convolutional block with dense connections, a deconvolutional block with residual Inception modules, and an unpooling block. Our proposed architecture outperforms the U-Net in three different challenging applications, namely multi-class segmentation of cerebrospinal fluid (CSF) on brain CT images, multi-organ segmentation on abdominal CT images, multi-class brain tumour segmentation on MR images.

Index Terms—Convolutional neural network, medical image segmentation, brain atrophy, abdominal organ segmentation.

I. INTRODUCTION

Significant progress has been achieved in the field of medical image analysis in recent years due to the advent of CNNs [1]. Within medical imaging, the problem of image segmentation has been one of the major challenges. Segmentation is a pre-requisite for many different types of clinical applications, including brain segmentation [2], cardiac ventricle segmentation [3], abdominal organ segmentation [4], and cell segmentation in biological images [5]. In these applications, the results of the segmentation are usually used to derive quantitative measurements or biomarkers for subsequent diagnosis and treatment planning.

Among the different approaches that use CNNs for medical image segmentation, the U-Net architecture [5] and its 3D extension [6] are widely used because of their flexible architectures. In the first part of the U-Net architecture (analysis path), deep features are learned while the second part of the U-Net architecture (synthesis path) performs segmentation based on these learned features. Training the two parts of the network in an end-to-end fashion yields good segmentation results. As

the number of features in the first part of network is reduced because of convolutions and poolings, skip connections are used to allow dense feature maps from the analysis path to propagate to the corresponding layers in the synthesis part of the network, which improves the performance significantly.

However, the limitation of the U-Net architecture is its scalability. Specifically, deeper networks learn more representative features and result in better performance. Adding more layers to the network enlarges the parameter space, which allows the network to learn more representative features. However, this also increases the difficulties in training the network because gradients are likely to vanish during training. Therefore, the challenge is to make the network wider and deeper without gradient vanishing.

In computer vision, the state-of-the-art CNN architectures include the densely connected convolutional network (DenseNet) [7], [8] and the Inception-ResNet [9]. The DenseNet approach consists of a number of dense blocks with pooling layers between them to reduce the size of the feature maps. Within each dense block, layers are directly connected with all of their preceding layers, which is implemented via concatenation of feature maps in subsequent layers. This dense architecture has a number of advantages: Firstly, the concatenation of feature maps enables deep supervision so that gradients are propagated more easily to preceding layers, which makes the network training easier. Secondly, bottleneck layers (convolution layers with 1-by-1 kernels) are used to control the growth rate of parameters in the network. Finally, in the DenseNet architecture the final classifier uses features from all layers (instead of only features from the last layer as in standard CNN approaches), leading to improved classification performance.

The Inception network [10] is a CNN architecture which uses the Inception modules and allows for very deep networks. The main purpose of the Inception modules are: 1) to increase the depth and width of networks without adding more parameters; and 2) to achieve multi-scale features for processing. These are achieved by carefully designing structures of the Inception modules. The latest version of the Inception architecture [9] also uses residual connections, i.e. Inception-ResNet. Fig. 1 shows an overview of the Inception-ResNet: a stem convolution block, stacks of inception and reduction blocks, and the classifier. The stem block consists of a number of standard convolution and pooling layers, reducing the size of feature maps in lower layers (the ones close to the input). This aims to be memory efficient in training but is not strictly necessary. Each inception block consists of number of inception modules. The reduction blocks are inception modules with dimension reduction. An inception module consists of a number of branches of convolution

L. Chen is with the Department of Computing and the Division of Brain Sciences, Department of Medicine, Imperial College London, UK, SW7 2AZ, e-mail: liang.chen12@imperial.ac.uk.

P. Bentley is with the Division of Brain Sciences, Department of Medicine, Imperial College London.

K. Mori is with Graduate School of Informatics, Nagoya University.

K. Misawa is with Aichi Cancer Center.

M. Fujiwara is with Nagoya University Hospital.

D. Rueckert is with the Department of Computing, Imperial College London.

94 layers. In each branch, a bottleneck layer reduces the number
 95 of feature maps. The feature maps are then processed by
 96 convolution layers with different sizes of kernels in different
 97 branches. The output of all branches are finally aggregated as
 98 the output of the inception module.

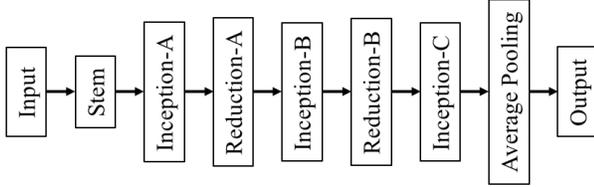


Fig. 1. The overall schema of the Inception-ResNet [9]. The whole architecture consists of some Inception and Reduction blocks. Each block contains a number of modules. The detailed structures in different blocks vary slightly.

99 Inspired by the DenseNet and the Inception-ResNet, we
 100 propose an architecture consisting of dense connection blocks,
 101 residual Inception blocks, and unpooling blocks. We term this
 102 architecture Dense-Res-Inception Net (DRINet). We apply the
 103 proposed DRINet architecture for three challenging clinical
 104 segmentation problems, namely multi-class segmentation of
 105 brain CSF in CT images, abdominal multi-organ segmenta-
 106 tion in CT images, and brain tumour segmentation (BraTS)
 107 in multi-modal MR images. The former two problems are
 108 based on clinical datasets while the last one is based on
 109 a publically benchmark dataset. Our main contributions are:
 110 1) a novel combination of the dense connections with the
 111 inception structure to address segmentation problems. The
 112 use of dense connection blocks, residual inception blocks,
 113 and the unpooling blocks achieve high performance while
 114 maintaining computational efficiency; 2) easy and flexible
 115 implementation of the proposed network architecture; 3) state-
 116 of-the-art segmentation performance for challenging image
 117 segmentation tasks.

118 II. RELATED WORK

119 The basic CNN architecture for many semantic segmenta-
 120 tion problems is the fully convolutional network (FCN), shown
 121 in Fig. 2(a), which consists of cascaded convolution, pooling,
 122 and deconvolution layers. Convolution and pooling layers form
 123 the analysis path while the convolution and deconvolution
 124 layers form the synthesis path. The analysis path and the
 125 synthesis path are usually symmetric.

126 The U-Net (Fig. 2(b)) is the FCN with skip layers between
 127 layers in analysis path and synthesis path. The skip layers
 128 are implemented via concatenations and they allow deep
 129 supervision for the network. As such, the errors can propagate
 130 easily through the network. Therefore, the skip layers improve
 131 the network performance. In addition, residual connections can
 132 be used in the U-Net, which results in the Res-U-Net (Fig.
 133 2(c)). In the Res-U-Net, the residual learning is implemented
 134 using the bottleneck building blocks with residual connections,
 135 which were used in the ResNet-50/101/152 architectures [11].

136 The DeepLab approach [12] involved atrous convolutions
 137 and poolings within the CNN architecture to solve segmenta-
 138 tion problems, as well as conditional random field (CRF) mod-
 139 els for post processing. Based on the DeepLab architecture,

Chen et al. [13] proposed the latest DeepLabV3 architecture. 140
 In DeepLabV3, a simple synthesis path is used. This synthesis 141
 path only consists of very few convolution layers, which is 142
 different from the synthesis path used in the FCN and the U- 143
 Net architectures. Skip connections are used to connect the 144
 analysis path and the synthesis path. 145

The DenseNet was extended in a fully convolutional fashion 146
 so that it can be used for segmentation tasks [14]. Specifically, 147
 an upsampling transition module was proposed in correspon- 148
 dence to the downsampling transition module in the original 149
 DenseNet. In addition, the macro-architecture of the fully 150
 convolutional DenseNet is similar to the U-Net where skip 151
 connections are used. 152

Finally, the Pyramid Scene Parsing Network (PSPNet) [15] 153
 was proposed to solve the challenging scene parsing problem. 154
 In the scene parsing problem, prior knowledge could be 155
 incorporated in CNNs to improve performance. For example, 156
 cars are likely to be on the road while they should not be in the 157
 sky. Global context is required to incorporate these priors. The 158
 pyramid pooling module in the PSPNet investigate features in 159
 multiple levels, achieving the state-of-the-art performance. 160

161 III. DRINET

162 A. Overview

Fig. 2(d) demonstrates our proposed DRINet architecture. 163
 Similar to the FCN, the DRINet has an analysis path and a 164
 synthesis path. Stacks of dense connection blocks, instead of 165
 standard convolution layers make up the analysis path, which 166
 is inspired by the DenseNet. The synthesis path consists of 167
 residual inception blocks and unpooling blocks, which are 168
 inspired by the Res-Inception Net. To be more efficient in 169
 terms of memory, the DRINet has no skip connections. 170

171 B. Dense connection block

We employ convolutional dense connection blocks [7] in 172
 the analysis path, which are shown in Fig. 3. Formally, 173
 let us assume x_l is the output of the l^{th} layer and $f(\cdot)$ 174
 is a convolution function followed by batch normalization 175
 (BN) [16] and rectified linear unit (ReLU). In the standard 176
 convolution layer, we have: 177

$$x_{l+1} = f(x_l) \quad (1)$$

while in the dense connection block [7] we have 178

$$x_{l+1} = f(x_l) \circ x_l. \quad (2)$$

Here \circ indicates concatenation. 179

The number of output channels from standard convolution 180
 layers are usually fixed and typically 64 or 128. As a result, 181
 it is expensive in terms of memory to concatenate the outputs 182
 of preceding convolution layers. In addition, the concatenation 183
 also leads to many redundant features. Therefore, Huang et al. 184
 [7] propose to use 1×1 convolutions to reduce the output size. 185
 As shown in Fig. 3, within a dense connection block, the size 186
 of the output channel for each convolution layer k_i is typically 187
 small, e.g. 12 or 24 and this is commonly referred to as the 188
 growth rate of the network. 189

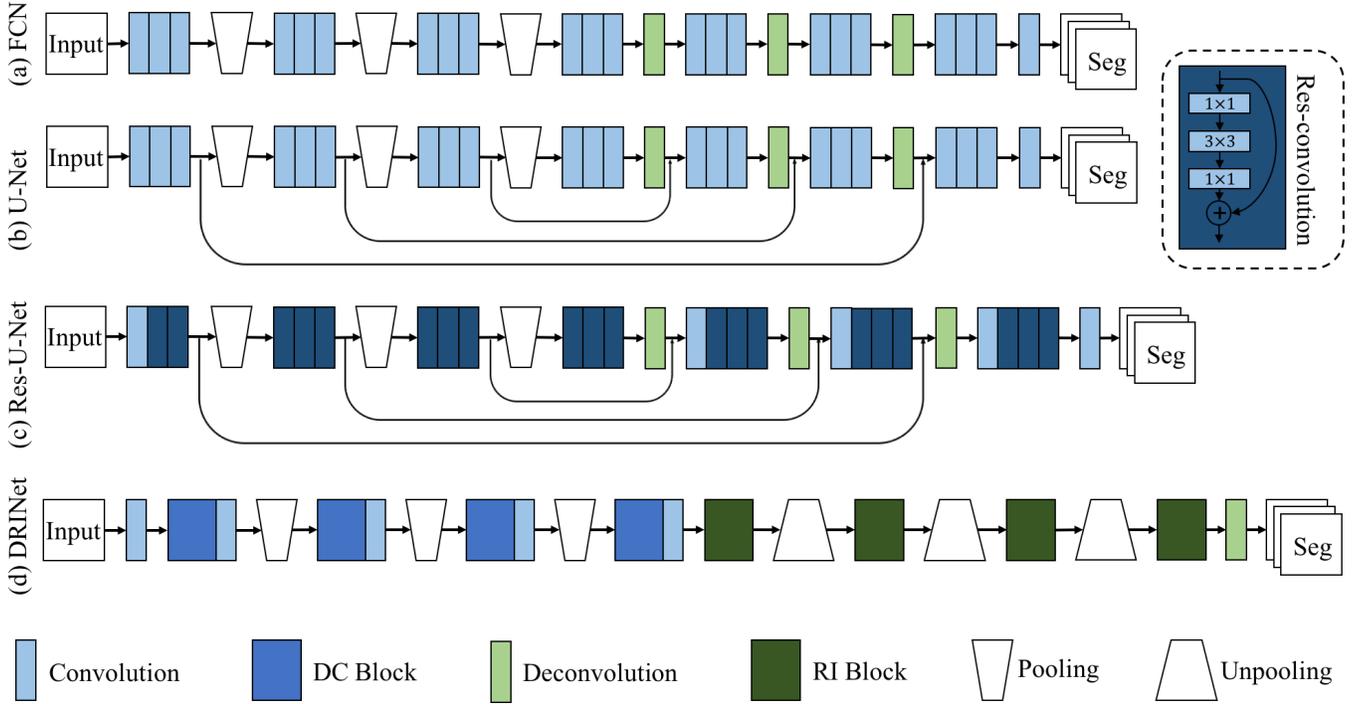


Fig. 2. Overview of the FCN, the U-Net, the Res-U-Net and the DRINet. DC block and RI block represent the dense connection block and the residual Inception block. In the DRINet, the DC, RI, and unpooling blocks are depicted in Fig. 3, 4, and 5, respectively. In the Res-U-Net, the residual convolution means the bottleneck building block used in the ResNet-50/101/152 [11].

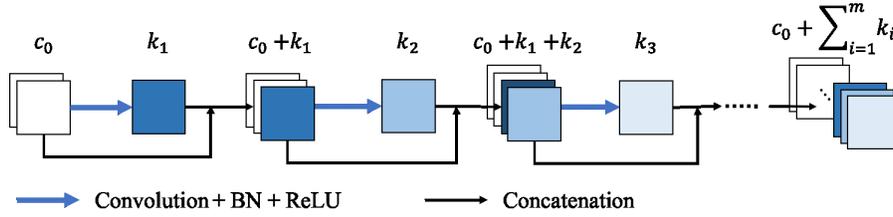


Fig. 3. A dense connection block contains m convolution layers. The output channel number of each convolution layer k_i is the growth rate. BN and ReLU apply on every convolution layer. The input and output of a convolution layer is concatenated so deep supervision is allowed.

190 Using dense connection blocks in the analysis path leads
 191 to three major advantages: 1) Gradient propagation through
 192 the network is more efficient. Conventionally, it is difficult
 193 to ensure that gradients backpropagate to lower layers in the
 194 network. Therefore, it is important to use dense connection
 195 blocks to alleviate the effect of vanishing gradients. 2) The
 196 input to the synthesis path consists of feature maps output from
 197 all preceding layers, instead of only the last layer, which reuses
 198 the feature maps. 3) It is easy to use the growth rate to control
 199 the parameter space, resulting in good network performance.
 200 The latter two advantages will be verified in the following
 201 experiments.

202 C. Residual Inception block

203 In the synthesis path of the DRINet, we propose to use
 204 the residual Inception blocks, which is depicted in Fig. 4.
 205 Similar to the original inception modules [10], the idea is
 206 to aggregate feature maps from different branches, where the
 207 input feature maps are convolved using kernels in different

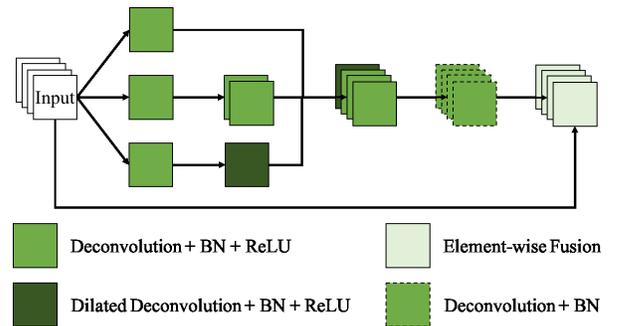


Fig. 4. A residual Inception block is an Inception module with residual connections. An Inception module is a weighted combination of features maps from a few branches. Each branch process the input feature maps using deconvolutions with different kernel sizes.

sizes. The residual connections make the learning easier since
 a residual inception block learns a function with reference to
 the input feature maps, instead of learning an unreferenced
 function.

In terms of the kernel sizes in convolutions, it is difficult to determine the optimal size for each convolution. In the FCN and the U-Net, the kernel size of convolutions is fixed as 3×3 . In the inception module, convolutions of different kernel sizes are used in parallel. In implementation, the feature maps are combined using concatenation and a deconvolution layer with 1×1 kernel learns the combination weights. The deconvolutions are transposed convolutions. In the proposed Inception modules, deconvolutions work the same as the convolutions. The purpose of this is to differentiate with convolutions in the analysis path in symbols.

Unlike the Inception Res-Net [9] having various inception modules, we propose to use identical inception blocks in the DRINet, which is easy to implement. We propose to aggregate feature maps convolved by three kernels, namely 1×1 , 3×3 , and 5×5 . Inspired by the DeepLab [17], the deconvolution with a 5×5 kernel is replaced by a dilated deconvolution with a 3×3 kernel, which is more efficient in memory. To further limit the size of the parameter space, a bottleneck deconvolution is used in each branch.

Formally, let $g(\cdot)$ denotes a deconvolution function followed by BN and ReLU and $g_b(\cdot)$ and $g_d(\cdot)$ represent bottleneck and dilated deconvolution respectively. As a result we obtain

$$x_{l+1} = g_b(g_b(x_l) \circ g(g_b(x_l)) \circ g_d(g_b(x_l))) + x_l. \quad (3)$$

D. Unpooling block

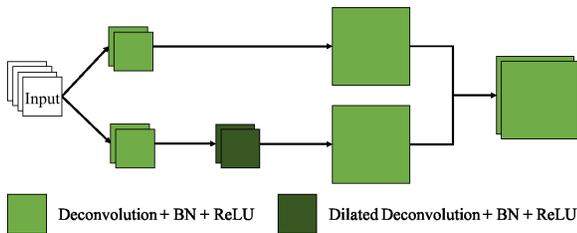


Fig. 5. An unpooling block is a mini Inception module and it upsamples the input feature maps.

We propose an unpooling block shown in Fig. 5 to upsample the feature maps in the synthesis path. The unpooling block can be viewed as a mini inception module, which combines upsampled feature maps from two branches. In each branch, the input feature maps are convolved using kernels in different sizes, namely 1×1 and 5×5 . The resulting feature maps are then upsampled using a deconvolution layer with stride 2. Again, the deconvolution with a 5×5 kernel is replaced by a dilated deconvolution with a 3×3 kernel in order to ensure memory efficiency. Also, to limit the parameter space, the input feature maps are firstly convolved by a bottleneck layer in each branch, which is similar to the residual inception block. The combination of upsampled feature maps is achieved via concatenation. Formally, let $g^2(\cdot)$ denotes the deconvolution function with stride 2. The upsampled feature maps are therefore:

$$x_{l+1} = g^2(g_b(x_l)) \circ g^2(g_d(g_b(x_l))). \quad (4)$$

The major advantage of the proposed unpooling block is the aggregation of different upsampled feature maps. Specifically,

simply upsampling the input feature maps using a deconvolution layer is likely to produce errors. For instance, a small error in the input feature maps is likely to be enlarged, which finally results in errors in the segmentation results. In contrast, convolving the input feature maps with different kernels leads to different intermediate feature maps. Upsampling these feature maps separately and combining them together reduce the effect of errors.

E. Evaluation metrics

In multi-class segmentation on brain CSF and abdominal organs, we use the well-known Dice coefficient as well as sensitivity (SE) and precision (PR) for evaluation. In evaluation in the BraTS challenge, we use the same metrics used in the challenge, namely the Dice coefficient, the SE, the specificity (SP), and the Hausdorff95 distance. The Hausdorff95 distance is a robust version of the standard Hausdorff distance, which measures 95 quantile of the distance between two surfaces, instead of the maximum.

F. Implementation details

In this work, we use cross-entropy as the loss function for all networks. We use the Adam method [18] for optimization with the following parameters: $\beta_1 = 0.9, \beta_2 = 0.999, \epsilon = 1e - 8$. An initial learning rate of $1e - 3$ is utilized. The weights are all initialised from a truncated normal distribution of standard deviation of 0.01. Batch normalization [16] layers are employed in all convolution and deconvolution layers except the last convolution/deconvolution layer. There are three convolution layers in each dense connection block and the kernel size is 3×3 with stride 1. There are three residual inception modules in each residual Inception block. For the standard deconvolution layers in the residual Inception module, the kernel size is 3×3 and the stride is 1. All networks used in this paper are implemented on the Tensorflow¹ platform.

IV. EXPERIMENTS AND RESULTS

A. CSF segmentation in CT images

Overview: Assessment of CSF volume, within ventricles and cortical sulci, is important for numerous neurological and neurosurgical applications. In many applications where rapid assessment is required (e.g. stroke), CT is preferred over MRI [19]. A common condition requiring the quantification of CSF is hydrocephalus (ventricular enlargement), a potentially life-threatening, but reversible condition; caused by a wide range of pathologies including hemorrhage, edema or tumours [20]. In these cases, CSF space quantification, especially comparison of ventricular to sulcal compartments, is important for distinguishing hydrocephalus from atrophy (due to age-related ischemia or degeneration) [21]. Standard quantification methods rely upon simple measurement of ventricular spans [22]. However, given the complex ventricular shape, these are imprecise, vary between observers and do not allow for accurate estimation of sulcal CSF [23].

¹<https://www.tensorflow.org/>

The challenges for multi-class CSF segmentation in CT are three-fold: 1) clinical CT images are often acquired as stacks of 2D image slices with large slice thickness. Thus, each slice is usually separately analyzed, however the position of the patient’s head is usually highly variable. Therefore, the CSF on each 2D image slice can vary significantly in terms of its configuration and shape; 2) patients often have background disease (e.g. old infarcts) which can have similar intensities to CSF. 3) at the borders of different categories of CSF, segmentation errors often occur. Many existing methods [24]–[32] are not robust to these problems. To the best of our knowledge, this is the first attempt to solve the multi-class CSF segmentation problem in CT images.

Dataset: CT scans from 133 stroke patients were collected from two local hospitals. All clinical CT scans were collected retrospectively from local PACS databases and anonymized before performing research. Ethical approval was obtained from the Imperial College Joint Research Office. The scans were acquired on three types of CT scanners (GE, Siemens, and Toshiba). The thicknesses of image slices range from 1mm to 7mm and the voxel spacing in plane is approximately 0.4×0.4 mm. The image size is 512×512 . Table I displays the demographic information of the patients.

The training and validation datasets consist of 781 2D image slices randomly chosen from 101 subjects. 500 of these images were used for training and 281 for validation. A separate test set containing 32 subjects was used. The training, validation, and testing datasets were manually annotated by a human expert. The CSF was segmented into three categories: 1) CSF in the ventricles, 2) CSF in the cerebral cortical sulci, fissures, arachnoid cysts, and 3) other CSF spaces, namely: basal and brainstem cisterns, cerebellar sulci, infratentorial arachnoid cysts. For these image slices, a threshold was chosen to obtain a coarse segmentation on the whole CSF and then the expert edited them using the MRICron software². The suprasellar cistern was bisected, such that CSF anterior to a line joining the bilateral anterior most parts of the cerebral peduncles/midbrain was classified within the cerebral compartment (reflecting atrophy of medial temporal and orbitofrontal cortices, and including Sylvian cisterns); while CSF posterior to this line (including interpeduncular, crural and ambient cisterns) was classified within the third cisternal compartment.

TABLE I

DEMOGRAPHICS OF PATIENTS IN THE CSF SEGMENTATION EXPERIMENT. THE NIHSS IS THE NATIONAL INSTITUTES OF HEALTH STROKE SCORE WHICH MEASURES PATIENTS’ FUNCTIONAL SEVERITY ON ADMISSION.

Age (years)	mean \pm std	71 \pm 14
	range	28-94
Gender	male %	52.63
NIHSS	mean \pm std	10 \pm 6.03
	range	1-27

Pre-processing and augmentation: In this work, we do not perform resampling on the CT images. This is because the thickness of the clinical CT images is large (up to 7mm) and

resampling the images can introduce inaccuracies and interpolation artefacts. In terms of the image intensity normalization, we employed the similar strategy as described in [17]. We normalized CT images on a per slice basis. This means for each slice, background (i.e. air, bone) was excluded and the remaining intensities were normalized to zero mean and unit deviation. We randomly cropped 128×128 patches from the slice to construct the training set. In this way, the training set contains sufficient number of patches. As our CNNs are fully convolutional, in the testing stage, the input can be the entire image slice.

Results: We use the FCN, the U-Net, and the Res-U-Net as baselines. The baseline networks are compared to the DRINet with various growth rates. The results are displayed in Table II.

The FCN and the U-Net perform similarly well in terms of Dice. The results suggest that segmenting the CSF in ventricles is relatively easy while segmenting CSF around brainstem is challenging. As depicted in Fig. 6, the CSF around brainstem is likely to be misclassified. In addition, the skip connections in the U-Net do not improve the segmentation results in this case.

Changing the U-Net architecture into the Res-U-Net architecture makes the network deeper and reduces the number of training parameters. According to [11], this change should only marginally influence on the results. However, the Dice score of the CSF around brainstem decreases under the Res-U-Net architecture. This result indicates that reducing parameters is problematic although the network uses the residual connections.

The growth rate is the key hyper-parameter in the DRINet because it controls the network parameter space and performance. Changing the growth rate allows to compare the performance between baseline networks and the DRINets with a similar number of parameters. Table II shows the results evaluating the effects of growth rate. The DRINet with a growth rate of 12 has a similar number of parameters as the Res-U-Net. This DRINet segments the CSF around brainstem significantly better than the Res-U-Net. The DRINet with a growth rate 24 is comparable to the FCN and the U-Net in terms of the size of parameter space. It performs better than the FCN and the U-Net in terms of the CSF in ventricles and around brainstem. If the growth rate increases to 48, the DRINet performs best in all three parts of the CSF segmentation, as well as the whole CSF segmentation. When the growth rate becomes very large (e.g. 64), the DRINet is likely to overfit and the performance decreases. In the following experiments, a growth rate of 48 is used.

Huang et al. [8] noted that a larger growth rate in the higher layers is beneficial for the performance of network. In our experiments, we evaluate this strategy using growth rates like 12, 24, 36, 48 in each dense connection block. Comparing DRINets using identical growth rate and increasing growth rates, which have similar number of parameters, the DRINets using increasing growth rates do not perform significantly better in any part of CSF segmentations.

Run time: Pre-processing was performed on a desktop PC with an Core i7-3770 processor and 32GB RAM. CNNs

²<https://people.cas.sc.edu/rorden/mricron/index.html>

TABLE II

PERFORMANCE COMPARISON AMONG THE BASELINE CNNs AND THE DRINET WITH DIFFERENT GROWTH RATES. THE NUMBERS UNDER THE DRINET INDICATE THE GROWTH RATES IN EACH DENSE CONNECTION BLOCK.

		Dice (%)				SE (%)			PR (%)			# params
		Ventricles	Cortex	Brainstem	Total	Ventricles	Cortex	Brainstem	Ventricles	Cortex	Brainstem	
FCN	val	83.29	76.71	80.74	84.16	90.17	80.06	79.48	93.47	85.13	83.19	2.71M
	test	92.89	89.01	85.25	90.91	92.86	88.50	86.73	94.76	91.18	84.52	
U-Net [5]	val	82.67	76.10	80.45	84.65	90.07	83.72	78.50	93.24	82.60	83.28	2.91M
	test	92.45	89.18	85.20	91.03	92.18	91.70	85.31	94.44	88.22	85.73	
Res-U-Net	val	81.66	73.99	76.34	84.15	89.72	79.48	75.84	92.84	85.50	81.67	0.96M
	test	91.64	88.73	82.94	90.76	91.54	87.67	82.43	93.81	91.39	84.34	
DRINet 12,12,12,12	val	84.98	76.87	86.72	82.96	87.24	75.47	76.99	95.87	89.49	88.71	0.85M
	test	92.13	87.77	86.08	89.37	88.76	82.78	82.99	97.52	95.75	90.29	
DRINet 24,24,24,24	val	85.08	80.70	90.87	84.44	91.32	79.67	82.57	93.21	87.12	85.58	2.80M
	test	93.84	89.97	88.40	91.27	94.78	88.34	89.55	94.27	93.23	87.91	
DRINet 36,36,36,36	val	85.00	80.19	90.08	84.67	89.97	81.73	81.18	94.30	85.57	86.71	5.85M
	test	93.70	90.33	88.48	91.52	92.80	90.23	88.22	96.20	91.93	89.45	
DRINet 48,48,48,48	val	87.39	80.00	91.08	84.89	91.06	82.36	82.18	93.59	85.29	86.74	10.03M
	test	94.28	90.64	88.96	91.85	94.19	91.00	89.39	95.55	91.74	89.24	
DRINet 64,64,64,64	val	86.97	79.95	90.58	84.62	90.63	80.51	81.15	93.96	86.64	88.33	17.33M
	test	94.15	90.20	88.96	91.53	94.27	88.78	87.43	95.37	93.37	91.28	
DRINet 12,24,36,48	val	85.74	79.38	87.92	84.55	90.88	81.81	82.21	93.50	85.40	85.21	4.11M
	test	93.87	90.26	88.15	91.50	93.95	90.32	88.91	95.38	91.77	88.15	
DRINet 24,36,48,64	val	86.98	79.63	90.84	84.69	93.90	85.75	87.32	90.74	81.58	81.30	8.03M
	test	94.27	90.16	88.82	91.51	94.19	89.53	87.83	95.68	92.45	90.53	
DRINet 36,48,64,80	val	86.45	80.08	89.68	84.72	89.86	80.96	82.10	94.58	86.43	87.22	13.70M
	test	93.76	90.27	88.82	91.46	92.44	89.38	88.59	96.64	92.79	89.76	

408 were trained and tested on an NVIDIA TITAN XP GPU
 409 processor except for the DRINets with large growth rates
 410 (e.g. 48, 64), which were trained on two GPUs to keep the
 411 batch size sufficiently large. On average it took 44.46s for the
 412 DRINet to segment the CSF in one image. The training time
 413 of the DRINet with the best performance was 21.37 hours. In
 414 contrast, the U-Net is faster with 11.44 hours for training and
 415 23.56s per image for testing. Although the DRINet is slower,
 416 its run time is acceptable.

417 B. Multi-organ segmentation

418 **Overview:** Segmenting abdominal organs is important for
 419 clinical diagnosis and surgery planning [33]. There are two
 420 major challenges in the multi-organ segmentation problem:
 421 1) Abdominal organs are highly deformable and mobile and
 422 therefore can have various shapes and sizes; 2) the contrast
 423 between organs is often poor making it difficult to identify
 424 boundaries between organs.

425 Abdominal organ segmentation is a popular topic for which
 426 many solutions have been proposed. Many methods were
 427 based on statistical shape models [34] or multi-atlas segmen-
 428 tation [34]–[38]. Using recent deep learning approaches, the
 429 segmentation accuracy has significantly improved, particularly
 430 for smaller organs (e.g. pancreas). Furthermore, deep learning
 431 approaches are much faster than conventional methods [4],
 432 [39], [40].

433 **Dataset:** 3D abdominal CT scans were used in this exper-
 434 iment to evaluate the performance of the DRINet. Image ac-
 435 quisition parameters and patient demographics for the dataset
 436 used here can be found in [37].

437 Pre-processing and augmentation were carried out in similar
 438 manner to those for CSF segmentation. The only difference is

439 that in the CSF segmentation, the image intensity normaliza-
 440 tion is performed per slice while in this multi-organ segmen-
 441 tation task, the image intensity is normalized per volume. The
 442 128×128 image patches were randomly cropped to develop
 443 the training set.

444 We used the same the experimental settings and CNN con-
 445 figurations as in the previous experiments, so no parameters
 446 tuning is performed in this experiment. The purpose is to
 447 validate the flexibility of the DRINet. Therefore, we only
 448 split the whole dataset into a training set (75 subjects) and
 449 a separate testing set (75 subjects).

450 **Baseline:** Again, the U-Net and the Res-U-Net are used
 451 as baselines. Table III displays the segmentation results. The
 452 performance of the U-Net and the Res-U-Net is comparable.
 453 The Res-U-Net provides better PR but worse SE than the U-
 454 Net in segmenting the pancreas and kidneys. As mentioned
 455 above, the pancreas is the most challenging organ to segment
 456 because of its thin and various structure. The strength of the
 457 proposed DRINet is demonstrated by the fact that it is able
 458 to segment the challenging organs significantly better than the
 459 baseline CNNs approaches.

460 **Comparison with existing methods:** We compare the
 461 DRINet with existing methods evaluated on the same dataset.
 462 [36] and [37] proposed methods based on conventional ma-
 463 chine learning approaches. According to the results (displayed
 464 in Table IV) they have achieved fairly good segmentations in
 465 terms of kidneys, liver, and spleen. The method proposed by
 466 Tong et al. [37] is much faster than the one proposed by Wolz
 467 et al. [36]. The 3D FCN proposed by Roth et al. [4] is the
 468 state-of-the-art method based on deep CNNs. It is clear that the
 469 3D FCN achieves significantly better results in the pancreas
 470 segmentation. Furthermore the inference time is significantly

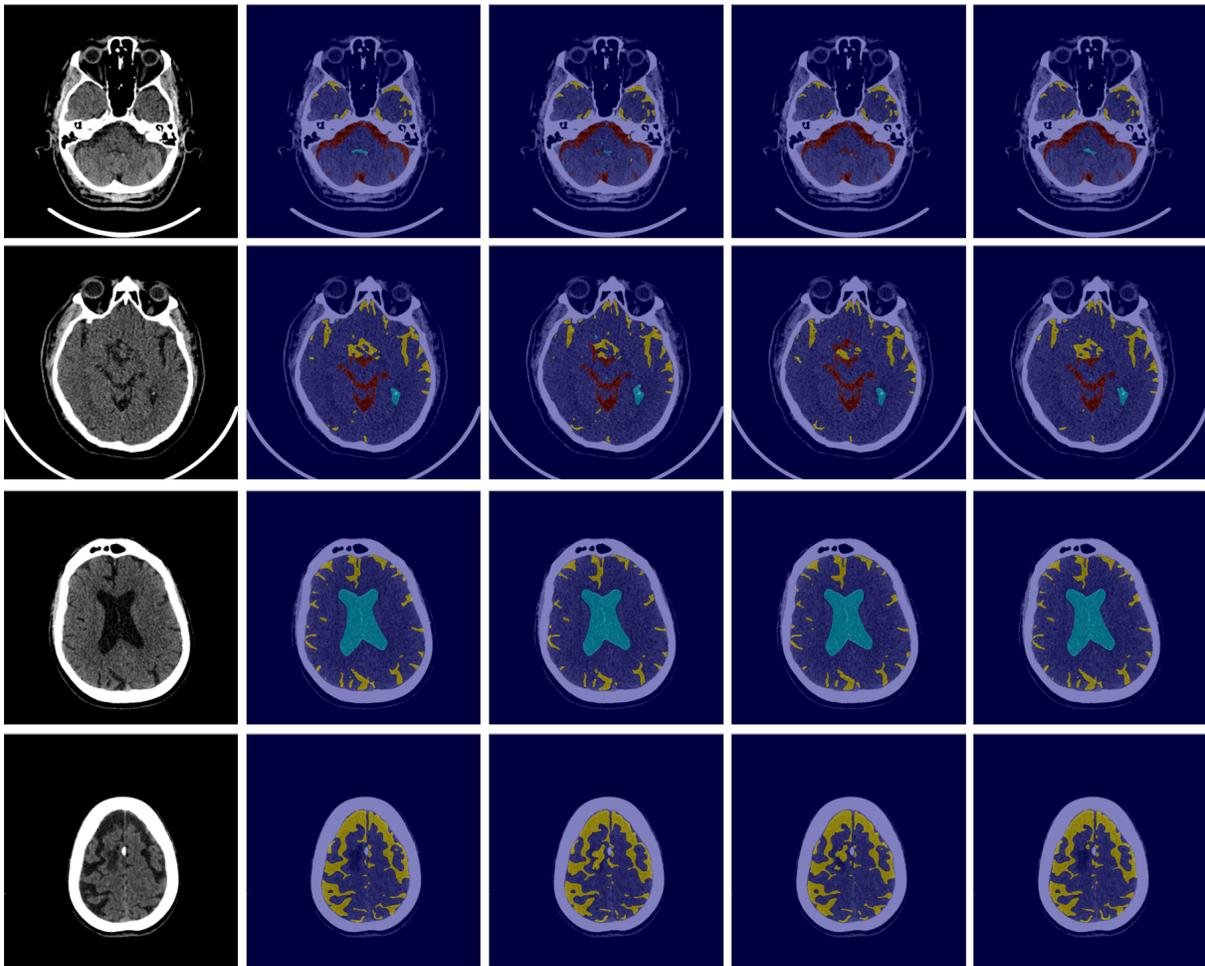


Fig. 6. The visual examples of multi-class CSF segmentations. The first column displays the original images. The second column shows the manual references. The following columns demonstrate the segmentations of the U-Net, the Res-U-Net, and the DRINet.

TABLE III
PERFORMANCE COMPARISON AMONG THE U-NET, THE RES-U-NET AND THE DRINET. THE DRINET OUTPERFORMED THE BASELINE CNNs, PARTICULARLY IN TERMS OF THE PANCREAS.

	Dice (%)				SE (%)				PR (%)			
	Pancreas	Kidneys	Liver	Spleen	Pancreas	Kidneys	Liver	Spleen	Pancreas	Kidneys	Liver	Spleen
U-Net [5]	80.09	95.80	94.70	94.72	74.89	95.86	92.79	93.13	87.98	95.85	96.65	95.98
Res-U-Net	79.09	95.41	96.20	94.71	72.41	93.72	96.15	92.92	89.49	97.28	96.26	95.94
DRINet	83.42	95.96	96.57	95.64	80.29	95.84	96.69	95.63	87.95	96.20	96.47	96.13

471 reduced. However, in terms of the other organs, namely the
 472 kidneys, liver, and spleen, the 3D FCN did not offer significant
 473 improvements.

474 The DRINet outperforms the 3D FCN achieving the state-
 475 of-the-art based on this dataset. Specifically, it improves the
 476 pancreas segmentation further from the 3D FCN. In addition,
 477 the DRINet promotes the segmentation on other organs as
 478 well. Note that the DRINet is only based on 2D image
 479 slices without using 3D contextual information. Therefore, this
 480 experiment verifies the DRINet is powerful and robust in the
 481 multi-organ segmentation problem.

TABLE IV
PERFORMANCE COMPARISON AMONG DIFFERENT ALGORITHMS. IT IS CLEAR THAT THE DRINET IS SUPERIOR TO THE EXISTING METHODS.

	Dice (%)				Time (h)
	Pancreas	Kidneys	Liver	Spleen	
Wolz et al. [36]	69.60	92.50	94.00	92.00	51
Tong et al. [37]	69.80	93.40	94.90	91.90	0.5
Roth et al. [4]	82.20	-	95.40	92.80	0.07
DRINet	83.42	95.96	96.57	95.64	0.02

C. Brain Tumour Segmentation

Overview: Brain tumours are routinely diagnosed using
 multi-modal MRI, including native T1-weighted (T1), post-

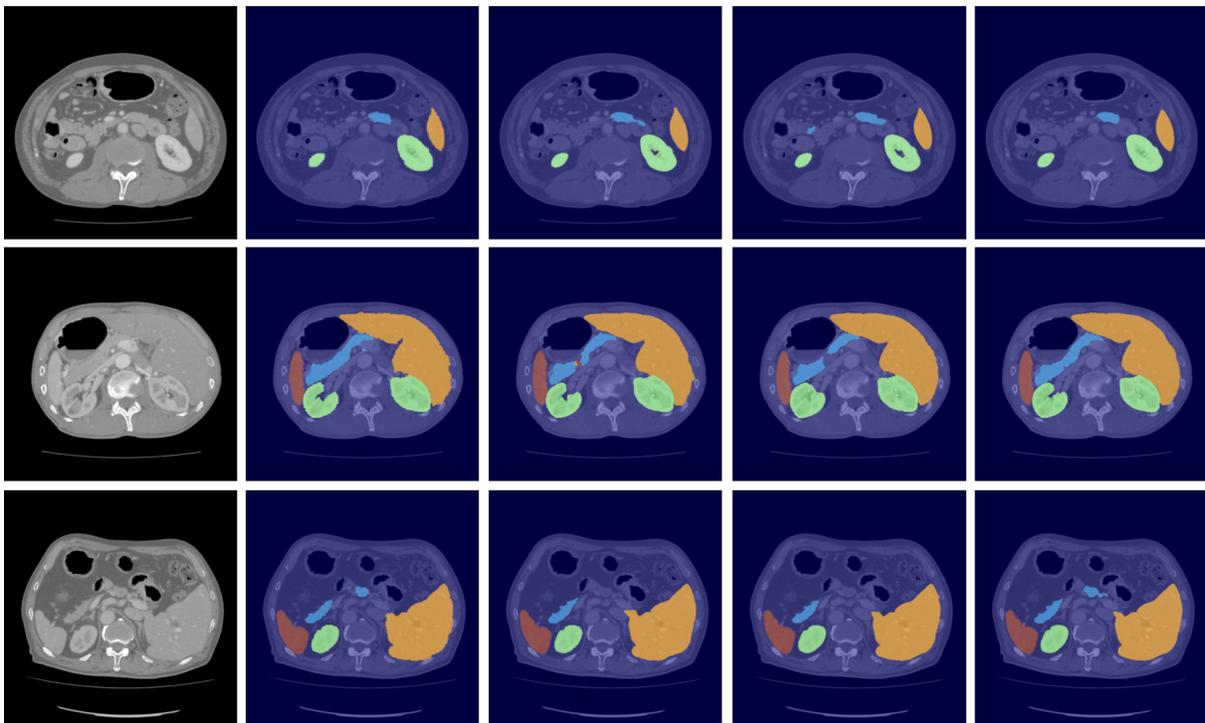


Fig. 7. The visual examples of abdominal multi-organ segmentations. The first column displays the original images. The second column shows the manual references. The following columns demonstrate the segmentations of the U-Net, the Res-U-Net, and the DRINet.

485 contrast T1-weighted (T1-Gd), T2-weighted (T2), and T2 fluid
 486 attenuated inversion recovery (FLAIR) image sequences [41].
 487 Quantification of the tumours based on the multi-modal MRI
 488 benefits the diagnosis and treatment [42]. Segmenting tumours
 489 into necrotic and non-enhancing tumours, the peritumoral
 490 edema, and gadolinium enhancing tumours has been a popular
 491 research topic [43].

492 **Dataset:** We propose to use the training dataset of the
 493 BraTS 2017 challenge. There are 285 subjects in total and we
 494 randomly select 50 for training and the remaining 235 ones
 495 for testing. The segmentation is based on 2D patches of size
 496 of 64×64 . Since the training patch size is smaller compared to
 497 that in the previous experiments, all CNNs in this experiments
 498 have two downsampling and upsampling process and all the
 499 other network configurations are fixed. According to [43], the
 500 images have been preprocessed: images were co-registered
 501 into the same anatomical template; skulls were stripped; voxels
 502 were resampled to isotropic resolution ($1mm^3$). We normalise
 503 the image intensities into zero mean and unit deviation. No
 504 post-processing trick is used in any case. The evaluation is
 505 based on the whole tumour region, the tumour core region,
 506 and the enhancing tumour core region, instead of individual
 507 tumour structures.

508 **Results:** On this benchmark dataset, we evaluate the three
 509 key components of the DRINet: the dense connection block,
 510 the residual Inception block, and the unpooling block. We set
 511 the FCN as the baseline CNN and separately add one of the
 512 proposed blocks to verify its contribution. We also compare
 513 their performance with the U-Net and the DRINet.

514 Table V shows the results: In terms of the whole tumour
 515 structure, the added blocks do not affect the Dice scores signif-

icantly. The dense connection block and the residual Inception
 block increase the sensitivity and the Hausdorff distances and
 decrease the specificity, which means they increase the number
 of false positives (FPs). In contrast, the unpooling block
 decreases the sensitivity and Hausdorff distance and increases
 the specificity, which means it reduces FPs but introduces FNs.
 Combining them together results in a trade-off between FNs
 and FPs. Therefore, the overall performance increases.

In terms of the tumour core and enhanced core, the three
 blocks increase the Dice scores and specificity while decreasing
 their sensitivity and Hausdorff distances. This means the
 overall performance for the segmentation of the tumour core
 and the enhanced core is improved. However, since their sizes
 are fairly small, some FNs occur.

The DRINet with three powerful blocks achieves better
 segmentation results than the U-Net in terms of the dice scores,
 the sensitivity, and the Hausdorff distances. Regarding the Res-
 U-Net, since the parameter space is small, it cannot perform
 as well as the U-Net in this case. Fig. 8 shows that the training
 error of the Res-U-Net is larger than that of the U-Net and
 the DRINet. Therefore, the Dice coefficients given by the
 Res-U-Net on tumours are the worst among all the CNNs.
 According to the low sensitivity, the high specificity, and the
 low Hausdorff distance, it is clear that the segmentation results
 by the Res-U-Net have many FNs but few FPs.

V. DISCUSSION AND CONCLUSION

In this paper, a novel CNN architecture, DRINet, is proposed.
 The DRINet has three key features, namely the use of dense
 connection blocks, residual inception blocks, and the unpooling
 blocks. These blocks deepen and widen the network

TABLE V
THE SEGMENTATION RESULTS OF DIFFERENT NETWORKS. THE ENTRIES IN BOLD HIGHLIGHT THE BEST COMPARABLE RESULTS.

Network	Dice (%)			SE (%)			SP (%)			Hausdorff95 (mm)		
	Whole	Core	Enh.	Whole	Core	Enh.	Whole	Core	Enh.	Whole	Core	Enh.
U-Net [5]	81.51	71.30	63.05	81.69	72.51	79.70	99.86	99.92	99.94	42.07	34.44	36.46
Res-U-Net	71.50	67.75	60.06	60.25	66.06	68.27	99.97	99.93	99.97	21.98	25.00	27.56
FCN	81.42	70.4	61.49	80.84	77.12	80.76	99.85	99.80	99.92	42.19	47.24	44.08
FCN+dense	81.09	71.98	63.29	84.90	74.81	78.56	99.80	99.91	99.95	48.34	39.36	36.56
FCN+RI	81.89	72.30	63.25	85.26	74.29	78.02	99.82	99.91	99.95	47.38	36.49	33.97
FCN+unpool	81.81	71.43	63.93	78.56	70.53	75.80	99.91	99.94	99.96	33.37	28.39	27.12
DRINet	83.47	73.21	64.98	84.53	74.93	80.35	99.86	99.92	99.94	36.4	25.59	30.31

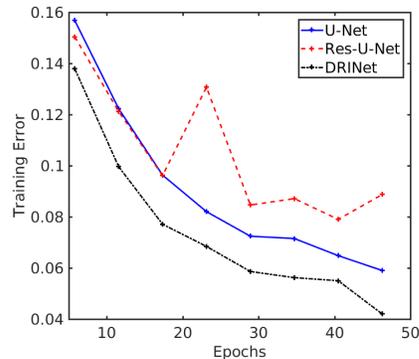


Fig. 8. The training error comparisons among different CNNs.

546 significantly and the parameter space can be controlled via
547 the growth rate. The gradient propagation is improved due
548 to the dense connections and residual connections. As a
549 result, the performance of the DRINet is significantly im-
550 proved when compared to the standard U-Net. In addition,
551 the DRINet architecture is highly flexible: Within a block,
552 the convolution/deconvolution layers can be changed adaptively.
553 It is therefore easy to integrate the blocks into other CNN
554 architectures.

555 In this paper, we focus on evaluating the performance
556 of the proposed DRINet and each of its components. The
557 segmentation results of each problem can be improved using
558 some domain knowledge and post-processing. For instance, in
559 the brain CSF segmentation problem, a brain mask could be
560 added. In the abdominal organ segmentation task, 3D contex-
561 tual information could be included. In the BraTS problem, the
562 CRF model could be used to remove FPs.

563 Among the three experiments, the multi-class CSF segmen-
564 tation on CT images is novel. To the best of our knowledge,
565 we are the first to attempt on this problem and the proposed
566 DRINet results in good segmentation. In the future, we plan
567 to extend the proposed approach to segment lesions as well as
568 CSF using a single DRINet. This is useful in clinical settings
569 for prognostication after stroke [44] or estimating cerebral
570 haemorrhage risk [45], [46].

571 In the context of abdominal multi-organ segmentation, the
572 DRINet achieves very good results although the segmentation
573 is based on 2D CT image slices. Our results show that the
574 DRINet improves the segmentation on small and various
575 organs like pancreas as well as big organs like liver. It is

of interest to extend its ability to segment more challenging
organs such as arteries and veins, which could make the
DRINet more useful in clinics.

A limitation of the DRINet approach is that the increase
of the growth rate results in many more parameters, which
may lead the training more difficult and testing slower. In the
future, the research could focus on simplifying the network
structure while maintaining its ability.

ACKNOWLEDGMENT

This work is supported by the NIHR Grant i4i: Decision-
assist software for management of acute ischemic stroke using
brain-imaging machine-learning (Ref: II-LA-0814-20007) and
JSPS Kakenhi (26108006, 17K20099). We acknowledge the
kind donation of the GPUs from the NVidia.

REFERENCES

- [1] H. Greenspan, B. van Ginneken, and R. M. Summers, "Guest editorial deep learning in medical imaging: Overview and future promise of an exciting new technique," *IEEE Transactions on Medical Imaging*, vol. 35, no. 5, pp. 1153–1159, 2016.
- [2] A. de Brebisson and G. Montana, "Deep neural networks for anatomical brain segmentation," in *CVPR Workshops*, 2015, pp. 20–28.
- [3] M. Avendi, A. Kheradvar, and H. Jafarkhani, "A combined deep-learning and deformable-model approach to fully automatic segmentation of the left ventricle in cardiac MRI," *Medical Image Analysis*, vol. 30, pp. 108–119, 2016.
- [4] H. R. Roth, H. Oda, Y. Hayashi, M. Oda, N. Shimizu, M. Fujiwara, K. Misawa, and K. Mori, "Hierarchical 3D fully convolutional networks for multi-organ segmentation," *arXiv preprint:1704.06382*, 2017.
- [5] O. Ronneberger, P. Fischer, and T. Brox, "U-net: Convolutional networks for biomedical image segmentation," in *MICCAI*, 2015, pp. 234–241.
- [6] Ö. Çiçek, A. Abdulkadir, S. S. Lienkamp, T. Brox, and O. Ronneberger, "3D U-net: learning dense volumetric segmentation from sparse annotation," in *MICCAI*, 2016, pp. 424–432.
- [7] G. Huang, Z. Liu, K. Q. Weinberger, and L. van der Maaten, "Densely connected convolutional networks," in *CVPR*, 2016, pp. 4700–4708.
- [8] G. Huang, D. Chen, T. Li, F. Wu, L. van der Maaten, and K. Q. Weinberger, "Multi-scale dense convolutional networks for efficient prediction," in *ICLR*, 2018.
- [9] C. Szegedy, S. Ioffe, V. Vanhoucke, and A. A. Alemi, "Inception-v4, Inception-ResNet and the impact of residual connections on learning," in *AAAI*, 2017, pp. 4278–4284.
- [10] C. Szegedy, W. Liu, Y. Jia, P. Sermanet, S. Reed, D. Anguelov, D. Erhan, V. Vanhoucke, and A. Rabinovich, "Going deeper with convolutions," in *CVPR*, 2015, pp. 1–9.
- [11] K. He, X. Zhang, S. Ren, and J. Sun, "Deep residual learning for image recognition," in *CVPR*, 2016, pp. 770–778.
- [12] L.-C. Chen, G. Papandreou, I. Kokkinos, K. Murphy, and A. L. Yuille, "DeepLab: semantic image segmentation with deep convolutional nets, atrous convolution, and fully connected CRFs," *IEEE Transactions on Pattern Analysis and Machine Intelligence*, vol. PP, no. 99, pp. 1–1, 2017.

- [13] L.-C. Chen, G. Papandreou, F. Schroff, and H. Adam, "Rethinking atrous convolution for semantic image segmentation," *arXiv preprint arXiv:1706.05587*, 2017.
- [14] S. Jégou, M. Drozdal, D. Vazquez, A. Romero, and Y. Bengio, "The one hundred layers tiramisu: Fully convolutional densenets for semantic segmentation," in *CVPR Workshops*, 2017, pp. 1175–1183.
- [15] H. Zhao, J. Shi, X. Qi, X. Wang, and J. Jia, "Pyramid scene parsing network," in *CVPR*, 2017, pp. 2881–2890.
- [16] S. Ioffe and C. Szegedy, "Batch normalization: Accelerating deep network training by reducing internal covariate shift," in *ICML*, 2015, pp. 448–456.
- [17] L. Chen, P. Bentley, and D. Rueckert, "Fully automatic acute ischemic lesion segmentation in DWI using convolutional neural networks," *NeuroImage: Clinical*, 2017.
- [18] D. Kingma and J. Ba, "Adam: A method for stochastic optimization," in *ICLR*, 2015.
- [19] N. Sanossian, K. A. Fu, D. S. Liebeskind, S. Starkman, S. Hamilton, J. P. Villablanca, A. M. Burgos, R. Conwit, and J. L. Saver, "Utilization of emergent neuroimaging for thrombolysis-eligible stroke patients," *Journal of Neuroimaging*, vol. 27, no. 1, pp. 59–64, 2017.
- [20] I. K. Pople, "Hydrocephalus and shunts: what the neurologist should know," *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 73, no. suppl 1, pp. i17–i22, 2002.
- [21] M. A. Williams and N. R. Relkin, "Diagnosis and management of idiopathic normal-pressure hydrocephalus," *Neurology: Clinical Practice*, vol. 3, no. 5, pp. 375–385, 2013.
- [22] A. V. Kulkarni, J. M. Drake, D. C. Armstrong, and P. B. Dirks, "Measurement of ventricular size: reliability of the frontal and occipital horn ratio compared to subjective assessment," *Pediatric Neurosurgery*, vol. 31, no. 2, pp. 65–70, 1999.
- [23] F. Pasquier, D. Leys, J. G. Weerts, F. Mounier-Vehier, F. Barkhof, and P. Scheltens, "Inter- and intraobserver reproducibility of cerebral atrophy assessment on MRI scans with hemispheric infarcts," *European Neurology*, vol. 36, no. 5, pp. 268–272, 1996.
- [24] T. Sandor, D. Metcalf, and Y.-J. Kim, "Segmentation of brain CT images using the concept of region growing," *International Journal of Bio-Medical Computing*, vol. 29, no. 2, pp. 133–147, 1991.
- [25] U. E. Ruttimann, E. M. Joyce, D. E. Rio, and M. J. Eckardt, "Fully automated segmentation of cerebrospinal fluid in computed tomography," *Psychiatry Research: Neuroimaging*, vol. 50, no. 2, pp. 101–119, 1993.
- [26] T. H. Lee, M. F. A. Fauzi, and R. Komiya, "Segmentation of CT brain images using K-means and EM clustering," in *Fifth International Conference on Computer Graphics, Imaging and Visualisation*, 2008, pp. 339–344.
- [27] —, "Segmentation of CT brain images using unsupervised clusterings," *Journal of Visualization*, vol. 12, no. 2, pp. 131–138, 2009.
- [28] W. Chen and K. Najarian, "Segmentation of ventricles in brain CT images using gaussian mixture model method," in *International Conference on Complex Medical Engineering*, 2009, pp. 1–6.
- [29] V. Gupta, W. Ambrosius, G. Qian, A. Blazejewska, R. Kazmierski, A. Urbanik, and W. L. Nowinski, "Automatic segmentation of cerebrospinal fluid, white and gray matter in unenhanced computed tomography images," *Academic Radiology*, vol. 17, no. 11, pp. 1350–1358, 2010.
- [30] L. Poh, V. Gupta, A. Johnson, R. Kazmierski, and W. L. Nowinski, "Automatic segmentation of ventricular cerebrospinal fluid from ischemic stroke CT images," *Neuroinformatics*, vol. 10, no. 2, pp. 159–172, 2012.
- [31] X. Qian, J. Wang, S. Guo, and Q. Li, "An active contour model for medical image segmentation with application to brain CT image," *Medical Physics*, vol. 40, no. 2, 2013.
- [32] X. Qian, Y. Lin, Y. Zhao, X. Yue, B. Lu, and J. Wang, "Objective ventricle segmentation in brain CT with ischemic stroke based on anatomical knowledge," *BioMed Research International*, vol. 2017, 2017.
- [33] M. G. Linguraru, J. A. Pura, V. Pamulapati, and R. M. Summers, "Statistical 4D graphs for multi-organ abdominal segmentation from multiphase CT," *Medical Image Analysis*, vol. 16, no. 4, pp. 904–914, 2012.
- [34] T. Okada, R. Shimada, M. Hori, M. Nakamoto, Y.-W. Chen, H. Nakamura, and Y. Sato, "Automated segmentation of the liver from 3D CT images using probabilistic atlas and multilevel statistical shape model," *Academic Radiology*, vol. 15, no. 11, pp. 1390–1403, 2008.
- [35] Z. Wang, K. K. Bhatia, B. Glocker, A. Marvao, T. Dawes, K. Misawa, K. Mori, and D. Rueckert, "Geodesic patch-based segmentation," in *MICCAI*, 2014, pp. 666–673.
- [36] R. Wolz, C. Chu, K. Misawa, M. Fujiwara, K. Mori, and D. Rueckert, "Automated abdominal multi-organ segmentation with subject-specific atlas generation," *IEEE Transactions on Medical Imaging*, vol. 32, no. 9, pp. 1723–1730, 2013.
- [37] T. Tong, R. Wolz, Z. Wang, Q. Gao, K. Misawa, M. Fujiwara, K. Mori, J. V. Hajnal, and D. Rueckert, "Discriminative dictionary learning for abdominal multi-organ segmentation," *Medical Image Analysis*, vol. 23, no. 1, pp. 92–104, 2015.
- [38] C. Chu, M. Oda, T. Kitasaka, K. Misawa, M. Fujiwara, Y. Hayashi, Y. Nimura, D. Rueckert, and K. Mori, "Multi-organ segmentation based on spatially-divided probabilistic atlas from 3D abdominal CT images," in *MICCAI*, 2013, pp. 165–172.
- [39] H. R. Roth, L. Lu, N. Lay, A. P. Harrison, A. Farag, A. Sohn, and R. M. Summers, "Spatial aggregation of holistically-nested convolutional neural networks for automated pancreas localization and segmentation," *arXiv preprint:1702.00045*, 2017.
- [40] J. Cai, L. Lu, Y. Xie, F. Xing, and L. Yang, "Improving deep pancreas segmentation in CT and MRI images via recurrent neural contextual learning and direct loss function," *arXiv preprint:1707.04912*, 2017.
- [41] S. Bakas, H. Akbari, A. Sotiras, M. Bilello, M. Rozycki, J. S. Kirby, J. B. Freymann, K. Farahani, and C. Davatzikos, "Advancing the cancer genome atlas glioma mri collections with expert segmentation labels and radiomic features," *Scientific data*, vol. 4, p. 170117, 2017.
- [42] S. Bakas, H. Akbari, A. Sotiras, M. Bilello, M. Rozycki, J. Kirby, J. Freymann, K. Farahani, and C. Davatzikos, "Segmentation labels and radiomic features for the pre-operative scans of the tcga-1gg collection," *The Cancer Imaging Archive*, 2017.
- [43] B. H. Menze, A. Jakab, S. Bauer, J. Kalpathy-Cramer, K. Farahani, J. Kirby, Y. Burren, N. Porz, J. Slotboom, R. Wiest *et al.*, "The multimodal brain tumor image segmentation benchmark (brats)," *IEEE Transactions on Medical Imaging*, vol. 34, no. 10, pp. 1993–2024, 2015.
- [44] I.-. C. Group *et al.*, "Association between brain imaging signs, early and late outcomes, and response to intravenous alteplase after acute ischaemic stroke in the third International Stroke Trial (IST-3): secondary analysis of a randomised controlled trial," *The Lancet Neurology*, vol. 14, no. 5, pp. 485–496, 2015.
- [45] P. Fotiadis, S. van Rooden, J. van der Grond, A. Schultz, S. Martinez-Ramirez, E. Auriel, Y. Reijmer, A. M. van Opstal, A. Ayres, K. M. Schwab *et al.*, "Cortical atrophy in patients with cerebral amyloid angiopathy: a case-control study," *The Lancet Neurology*, vol. 15, no. 8, pp. 811–819, 2016.
- [46] C. M. Dunham, D. A. Hoffman, G. S. Huang, L. A. Omert, D. J. Gemmel, and R. Merrell, "Traumatic intracranial hemorrhage correlates with preinjury brain atrophy, but not with antithrombotic agent use: a retrospective study," *PloS One*, vol. 9, no. 10, p. e109473, 2014.