Chapter 2

Theoretical Background

Highlights of the Chapter

- *Understanding of segmentation using deep learning based methods.*
- *Analysing Denoising methods based on conventional deep learning approaches.*
- *Overview of deep learning based methods for classification of medical images.*
- *Understanding of transfer learning based approaches for medical image processing.*

This chapter encompasses the traditional approaches developed and utilized for segmentation, denoising and classification of medical images. The chapter gives a brief overview of the deep learning-based methodologies for various tasks in medical image processing. The considerable advancement in the field of deep learning has paved the way for automatic feature extraction networks. These networks are capable of producing exceedingly good results as compared to conventional methods without being fed with the handcrafted features. This versatile capability of deep learning-based networks is making them more popular in the medical imaging field.

2.1 Segmentation using deep learning based methods

Image segmentation is the process of partitioning the image into multiple components so that each component is meaningful. The segmentation problem can be viewed as a labelling problem in which a label is assigned to each pixel, indicating a particular region in the image [26] [27]. Moreover, segmentation can be considered as a process of extracting the boundaries of different objects in the image so that the image is divided into meaningfully connected regions. The medical images are acquired using various modalities such as ultrasound, Computed Tomography (CT), Positron Emission Tomography (PET), Magnetic Resonance

Imaging (MRI) etc. These modalities provide invaluable access to view the interior organs of the human body. This allows clinical experts to plan the medical diagnosis of the patients suffering from various diseases [28]. The extraction of useful information is reasonably necessary from the images acquired using various modalities. The disease affected regions should be delineated for the medical analysis and planning of the treatment. For this purpose, an efficient segmentation method is required which can clearly distinguish the unhealthy tissues from the healthy tissues with the least possible error. Accurate segmentation plays a vital role in medical analysis as the correct delineation of anatomical structures is of utmost importance. The manual segmentation by the medical experts can provide reliable results, but it could be time-consuming and subject to observer variability. Thus the automatic methods of segmentation are required to deal with such issues without compromising the accuracy and reliability of the results. For example, detecting tumour inside the human body and precisely outlining the region of the tumour are the basic requirements of the effective automatic segmentation process [29]. The periodic acquisition of growth of the tumour and prediction of its evolution are also the requirements of this process.

The recent advancement in the field of deep learning has provided the way for accurate and effective segmentation models, which can produce outstanding results for a better understanding of the disease. These networks automatically learn the complex features independently, and depending upon that, learning various medical imaging tasks can be accomplished. This property of the deep learning-based networks has motivated the researchers to focus more on the network architecture rather than handcrafted features. Deep learning networks take the patches extracted from the input images and deploy convolution filters and local subsampling to concentrate on more complex features. The output produced by each convolution layer is termed a feature map. These feature maps are topologically arranged responses to the particular features of the images. The consecutive convolutional layers produce various levels of feature maps which are utilised while performing specific assignments of medical imaging. The feature extraction is basically subjected to the three steps:

1. Convolution of Kernels
2. Application of non-linear activation function on intermediate inputs
3. Pooling

The feature maps (Q_S) are associated to every kernel which are computed using the following equation:

$$Q_s = b_s + \sum_n G_{sn} * I_n \quad (2.1)$$

Where the r^{th} input channel is denoted by I_n, G_{sn} denotes the sub-kernel of the channel, and b_s represents the bias term. The element-wise non-linearity is applied to the output of the convolution kernels for obtaining the features, which are the non-linear transformation of the input. The pooling operation is performed to pool out the features according to the assignment being performed. Various types of pooling operators are available such as max-pooling, average pooling etc. Finally, the segmentation operation is performed by assigning a label to each pixel in the image, forming the connected regions with similar characteristics.

The literature reports various deep learning-based segmentation networks which perform effective segmentation for various medical applications. In this regard, Olaf Ronneberger proposed an efficient deep learning-based network capable of being trained on very few images [30]. This network was termed as U-net because of its U-shaped arrangement of layers. U-net produced reliable and accurate segmentation results for various medical imaging applications. The activity profile model was used by Li et al. for the segmentation of liver tumour in abdominal CT images [31]. For segmentation of cardiac MR images and prostate MR images, Tsai et al. proposed a shape-based method incorporated using horizontal sets [32]. Lalonde et al. proposed an approach based on the Hausdorff template for disc inspection [33]. Urban et al. used 3D CNN model for MRI glioma segmentation. Multichannel intensity information from small patches around each labelled points was used by Zikic D. et al. for the segmentation of brain tumours [34]. Kamnitsas et al. developed a dual path CNN incorporated with two parallel paths with similar receptive fields, and the other path received patches from subsample representation [35]. Christ et al. showed a cascaded FCN based approach which was implemented using a series of FCN [36]. V-Net proposed by Milletari et al. [37] provided better feature representation by avoiding vanishing gradient problem. Table 2.1 shows some recently proposed image segmentation techniques.

Table 2-1: Selected previous significant work for segmentation of medical images

Author and Year	**Title of Paper**	**Method**
H. Fu, J. Cheng, Y. Xu, D. W. K. Wong, J. Liu, and X. Cao, 2018. [38]	Joint optic disc and cup segmentation based on multi-label deep network and polar transformation.	Deep Learning-based architecture termed as M-Net to solve OD and OC problems.
Y. Onishi, A. Teramoto, M. Tsujimoto, T. Tsukamoto, K. Saito, H.Toyama,K. Imaizumi, and H. Fujita, 2020. [39]	Multiplanar analysis for Pulmonary nodule classification in CT images using deep convolutional neural network and generative adversarial networks.	GAN based method for pulmonary nodule classification.
Y. Gao, J. M. Phillips, Y. Zheng, R. Min, P. T. Fletcher, and G. Gerig, 2018. [40]	Fully convolutional structured LSTM networks for joint 4D medical image segmentation.	Deep Learning-based framework termed as FCSLSTM for 4D image segmentation with FCN.
H. Seo, C. Huang, M. Bassenne, R. Xiao, and L. Xing 2019. [41]	Modified U-net (MU-net) with incorporation of object-dependent high level features for improved liver and liver-tumor segmentation in CT images.	U-Net modified using a residual path, deconvolution for efficient Segmentation.
X. Chen, R. Zhang, and P. Yan, 2019. [42]	Feature fusion encoder decoder network for automatic liver lesion segmentation.	A feature fusion method is based on the attention mechanism.

W. Tang, D. Zou, S. Yang, and J. Shi, 2018. [43]	Dsl: Automatic liver segmentation with faster R-CNN and deeplab.	DSL (detection and segmentation laboratory) method based on Faster R-CNN and DeepLab.
M. A. Al-Antari, M. A. Al-Masni, M.-T. Choi, S.-M. Han, and T.-S. Kim, 2018. [44]	A fully integrated computer-aided diagnosis system for digital X-ray mammograms via deep learning detection, segmentation, and classification.	Full resolution convolutional network (FrCN) for segmentation of breast mass.
Y. Yan, P.-H. Conze, E. Decenci`ere, M. Lamard, G. Quellec, B. Cochener, and G. Coatrieux, 2019. [45]	Cascaded multi-scale convolutional encoder decoders for breast mass segmentation in high-resolution mammograms.	A multi-scale cascade of deep convolutional encoder-decoders without any pre-detection scheme for mass breast segmentation.

2.2 Denoising using deep learning based methods

The noise gets introduced in the MR images at the time of the acquisition of the image because of many factors. The raw data of MR images is Fourier transform, which is known as raw data. This data is complex and corrupted with Gaussian noise. Inverse Fourier transform of this data is taken to form the images, and after this process, the distribution of noise changes to Rician distribution. This noise causes uncertainty as to whether a spatial location represents actual tissue information of the subject or a true signal may be affected by encoding scheme or effect of neighbourhood and so on [46] [47]. These undesirable effects, caused by the noise, should be removed by some mathematical modelling or software [48]. Henkelman R. M. was probably the first to estimate the actual signal intensity from noisy MRI data. The relation between noise and signal can be established with the help of second-order moment of Rician distribution and expressed as follows:

$$\mu_2 = E\{M^2\} = A^2 + 2\sigma_n^2 \quad (2.2)$$

Hence, $A^2 = \mu_2 - 2\sigma_n^2$ (2.3)

Where is signal level without noise, is the noise variance and is the second-order moment. The quality of the original signal gets reduced in the presence of noise. So, it is reasonably necessary to have some denoising methods suited to remove the Rician distributed noise while preserving the details of the original signals present in the images [49]. The images with reduced noise contents helps the medical practitioners to diagnose the disease more accurately [50]. In this regard, many conventional methods have been modified accordingly to adjust the nature of MRI data. The details of the boundary and tissue-related information should be preserved precisely after the denoising process. Many algorithms designed for edge detection have failed to distinguish between the edges of the different types of tissues. The boundaries of the standard and pathological tissues are most affected by the presence of noise in the MR images; thereby, it becomes challenging to identify the tissues affected by some disease. The deep learning-based methods evolved in the recent past have provided efficient solutions to cope with noise in magnetic resonance images. These methods do not require prior estimation of noise, thus reducing the chances of errors. Deep learning models are self-capable of learning and producing more relevant results from the clinical point of view.

Table 2-2: Selected previous significant work for image denoising

Author and Year	**Title of Paper**	**Method**
Andrew D. Missert, Lifeng Yu, Shuai Leng, Joel G. Fletcher, and Cynthia H. McCollough, 2020. [51]	Synthesizing images from multiple kernels using a deep convolutional neural Network.	CNN architecture consisting of repeated blocks of residual units used to denoise the CT images.
Masafumi Kidoh, Kensuke Shinoda, Mika Kitajima, Kenzo Isogawa, Masahito Nambu, Hiroyuki Uetani, Kosuke Morita, Takeshi Nakaura, Machiko Tateishi, Yuichi Yamashita, and Yasuyuki Yamashita, 2019. [52]	Deep Learning Based Noise Reduction for Brain MR Imaging: Tests on Phantoms and Healthy Volunteers.	Denoising convolutional neural network (DnCNN) was used to denoise brain MR images.
Jiang D, Dou W, Vosters L, Xu X, Sun Y, Tan T, 2018. [53]	Denoising of 3D magnetic resonance images with multi-channel residual learning of convolutional neural network	Deep learning based model directly applied for the denoising of Rician noise.
José V. Manjón and Pierrick Coupe, 2019. [54]	MRI denoising using Deep Learning and Non-local averaging.	A two stage approach in which a patch based CNN blindly denoises the images while in the second stage denoised image is used as guided image.

Da-in Eun, Ryoungwoo Jang, Woo Seok Ha, Hyunna Lee, Seung Chai Jung and Namkug Kim, 2020. [55]	Deep-learning-based image quality enhancement of compressed sensing magnetic resonance imaging of vessel wall: comparison of self-supervised and unsupervised approaches.	Two different denoising algorithm, one self-supervised and other unsupervised used to denoise the clinical images.
Magauiya Zhussip, Shakarim Soltanayev, Se Young Chun, 2019. [56]	Training deep learning based image denoisers from undersampled measurements without ground truth and without image prior.	Two denoising methods based on denoiser-approximate message passing (D-AMP) and Stein's unbiased risk estimator (SURE) theories are proposeb.
A. Benou, R. Veksler, A. Friedman, T. Riklin Raviv, 2017. [57]	Ensemble of expert deep neural networks for spatio-temporal denoising of contrast-enhanced MRI sequences.	A novel spatio-temporal framework based on Deep Neural Networks (DNNs) to address the DCE-MRI denoising.
Kai Zhang, Wangmeng Zuo, Yunjin Chen, Deyu Meng, and Lei Zhang, 2016. [58]	Beyond a Gaussian Denoiser: Residual Learning of Deep CNN for Image Denoising.	Residual learning and batch normalization based discriminative deep learning approach for denoising.
Ruihua Wang, Xiongwu Xiao, ID , Bingxuan Guo, Qianqing Qin, and Ruizhi Chen, 2018. [59]	An Effective Image Denoising Method for UAV Images via Improved Generative Adversarial Networks.	GAN based approach for tracing the relationship between noisy and clean images.
Guang Yang , Simiao Yu, Hao Dong, Greg Slabaugh, Pier Luigi Dragotti, Xujiong Ye , Fangde Liu, Simon Arridge, Jennifer Keegan, Yike Guo, and David Firmin, 2017. [60]	DAGAN: Deep De-Aliasing Generative Adversarial Networks for Fast Compressed Sensing MRI Reconstruction.	Generative Adversarial Networks-based model (DAGAN) for reconstruct CS-MRI.
Forest Agostinelli, Michael R. Anderson and Honglak Lee, 2013. [61]	Adaptive Multi-Column Deep Neural Networks with Application to Robust Image Denoising.	Adaptive multi-column stacked sparse denoising autoencoder for denoising.

2.3 Classification using deep learning based methods

The image data of various related disease is analysed slice by slice through visual inspection, which requires time, prone to human error and sometimes unable to exploit invaluable information. The accurate and precise medical image classification is the rising demand of the current time to ease the burden on the medical systems as the reliable classification mechanism can detect the disease in the early stage for prevention of human lives [62]. For example, the Covid-19 related infection, if detected in the early stage, can save precious lives. The medical images have a varying internal structure with different texture and pixel intensities which are to be analysed to determine the disease. In the recent past, deep learning-based computer-aided analysis has provided a reliable and accurate solution for the classification of medical image data. The primary aim of medical image classification is to classify the images into various classes for helping the clinical practitioners.

The deep learning-based model extracts the features of various classes and uses those features for building the classification networks, which can classify the image dataset according to the requirement [63] [64]. These methods do not require handcrafted features for training as they are self-capable of feature extraction. The deep learning model gets trained using the input data, which is known as learning. The model predicts the class and receives feedback for accuracy. Accordingly, the model adjusts the error automatically. The model's training is a back and forth process that requires several iterations to produce noble predictions. Overall, deep learning-based methods have provided a reliable and perfect solution to medical image classification. Table 2-3 shows some previously proposed selected literature on image classification using a deep learning-based approach.

Table 2-3: Selected previous significant work for classification of images

Author and Year	Title of Paper	Method
A. Krizhevsky, I. Sutskever, and G. E. Hinton, 2012. [65]	Imagenet classification with deep convolutional neural networks	Very Large deep neural network for classification of 1.2 million high resolution images
Karen Simonyan and Andrew Zisserman, 2012. [66]	Very deep convolutional networks for large-scale image recognition.	Very deep CNN used for large scale image classification.
Hoo-Chang Shin, Holger R. Roth, Mingchen Gao, Le Lu, Ziyue Xu, Isabella Nogues, Jianhua Yao, Daniel Mollura, Ronald M. 2016. [67]	Deep Convolutional Neural Networks for Computer-Aided Detection: CNN Architectures, Dataset Characteristics and Transfer Learning.	Deep CNN used for computer aided detection problem
Adrian Barbu, Michael Suehling, Xun Xu, David Liu, S. Kevin Zhou, Dorin Comaniciu, 2012. [68]	Automatic Detection and Segmentation of Lymph Nodes from CT Data.	Learning based method for automatic detection of lymph nodes.
Qi Dou, Hao Chen, Lequan Yu, Lei Zhao, Jing Qin, Defeng Wang, Vincent CT Mok, Lin Shi and Pheng-Ann Heng, 2016. [69]	Automatic Detection of Cerebral Microbleeds from MR Images via 3D Convolutional Neural Networks	3D CNN used for detection of cerebral microbleeds from MR images
Tsung-Han Chan, Kui Jia, Shenghua Gao, Jiwen Lu, Zinan Zeng, and Yi Ma, 2015. [70]	PCANet: A Simple Deep Learning Baseline for Image Classification?	Deep learning network for image classification using cascaded PCA
Rui Zeng , Jiasong Wu , Zhuhong Shao, Yang Chen, Beijing Chen, Lotfi Senhadji, Huazhong Shu, 2016. [71]	Color image classification via quaternion principal component analysis network.	Quaternion principal component analysis network (QPCANet) for colour image classification
C. Szegedy, W. Liu, Y. Jia, P. Sermanet, S. Reed, D. Anguelov, 2015. [72]	Going deeper with convolutions.	Deep CNN Inception net for large scale classification.
Mark Sandler Andrew Howard Menglong Zhu Andrey Zhmoginov Liang-Chieh Chen, 2019. [73]	MobileNetV2: Inverted Residuals and Linear Bottlenecks.	MobileNet V2 architecture for improving the performance of mobile models.
Francois Chollet, 2017. [74]	Xception: Deep learning with depthwise separable convolutions.	Deep learning model based on depth wise separable convolution for image classification.

2.4 Transfer learning for image processing

Transfer learning is the approach that utilizes the knowledge obtained from one domain to perform specific tasks in other domains. It is a machine learning method that utilizes the pre-trained model on a new problem [75]. In this approach, the early and the middle layers of the network is reused while only the final layers are trained, which are used to perform the specific tasks. It helps leverage the labelled data of the task it was initially trained on. Transfer learning helps in reducing the time to train the network and reduces the use of complex computation facilities such as GPUs. This approach eliminates the need of training the model from scratch by using the features obtained from pre-trained models [76]. To improve the target's task-specific efficiency, the transfer learning-based approaches to transfer the knowledge from source to target. The transfer learning-based methods are categorized into three categories, namely 1) Inductive Transfer learning, 2) Transductive Transfer Learning, 3) Unsupervised Transfer Learning. The task of source and target are the same in Inductive Transfer learning, while in Transductive learning, the task of source and target are different. Unsupervised transfer learning is the same as inductive learning, but the target tasks are unsupervised. The transfer learning-based approaches are flexible as they allow the task, testing and domain to be different. The motivation behind transfer learning is that the previous knowledge can be used for performing new tasks. Table 2-4 shows some selected works of literature on transfer learning.

Table 2-4: Selected previous significant work on Transfer Learning.

Author and Year	**Title of Paper**	**Method**
Maxime Oquab, Leon Bottou, Ivan Laptev1, Josef Sivic, 2014. [77]	Learning and Transferring Mid-level Image Representations Using Convolutional Neural Networks.	This work proposes the transfer of image representations learned by CNN for visual recognition tasks.
Yuhai Yu, Hongfei Lin, Jiana Meng, Xiaocong Wei, Hai Guo and Zhehuan Zhao, 2017. [78]	Deep Transfer Learning for Modality Classification of Medical Images.	Deep CNN (VGGNet and ResNet) used for the transfer of knowledge or performing image classification.
Hiba Chougrad,a, Hamid Zouaki, Omar Alheyane, 2018. [79]	Deep Convolutional Neural Networks for breast cancer screening.	Transfer learning-based approach for classification of mammography mass lesions.
Aayush Jaiswal, Neha Gianchandani, Dilbag Singh, Vijay Kumar and Manjit Kaur, 2020. [80]	Classification of the COVID-19 infected patients using DenseNet201 based deep transfer learning.	Transfer learning based on DenseNet 201 for classification of Covid-19 infected images.
Ravi K. Samala, Heang-Ping Chan, Lubomir Hadjiiski, Mark A. Helvie, Jun Wei and Kenny Cha, 2016. [81]	Mass detection in digital breast tomosynthesis: Deep convolutional neural network with transfer learning from mammography.	Computer-based approach for detection of digital breast tomosynthesis (DBT) volume using transfer learning.
Nima Tajbakhsh, Jae Y. Shin, Suryakanth R. Gurudu, R. Todd Hurst, Christopher B. Kendall, Michael B. Gotway, and Jianming Liang, 2017. [82]	Convolutional Neural Networks for Medical Image Analysis: Full Training or Fine Tuning?	Study of deep CNN with fine-tuning for eliminating the need for training from scratch.

The concept of deep learning and transfer learning is utilized in the presented thesis for medical image segmentation, denoising and classification. Critical review of existing algorithms helped to understand how previously proposed algorithms encounter the major challenges of this field. Further, the concepts have been utilized to meet the goals of the thesis.

The general block diagrams for depicting the the process of segmentation, denoising and classification using deep learning are shown in figure 2.1 (a), (b), (c).

Figure 2.1 (a): Block diagram for the flow of Segmentation Process

Figure 2.1 (b): Block diagram for the flow of Denoising Process

Figure 2.1 (c): Block diagram for the flow of Classification Process