

ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL

**IMAGE RECONSTRUCTION WITH DEEP LEARNING
AND APPLICATIONS IN MR IMAGES**



Ph.D. THESIS

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Department of Mechatronics Engineering

Mechatronics Engineering Programme

APRIL 2022

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**DERİN ÖĞRENME İLE GÖRÜNTÜ GERİÇATIMI
VE MR GÖRÜNTÜLERİNDE UYGULAMALARI**

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To my parents and spouse,



FOREWORD

This thesis deals with the problem of developing novel deep learning-based techniques for magnetic resonance image reconstruction. The subject of this thesis tackles the long acquisition time limitation of MRI. In this regard, novel deep learning structures have been proposed for fast MRI.

Initially, I would like to express my endless gratitude to Prof. Dr. Ender Mete EKŞİOĞLU who has supported me in all aspects like a real elder brother alongside his invaluable advice for this project. In addition, I should thank the Ph.D. committee members, Prof. Dr. Behçet Uğur TÖREYİN, and Prof. Dr. Aydın KIZILKAYA for their valuable guidance and recommendations.

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ABBREVIATIONS

ADC	: Analog to Digital Converter
ADMM	: Alternating Direction Method of Multipliers
AUTOMAP	: Automated Transform by Manifold Approximation
AMP	: Approximate Message Passing
BM3D	: Block Matching 3D
CNN	: Convolutional Neural Networks
CRNN	: Convolutional Recurrent Neural Networks
CS	: Compressed Sensing
DC	: Data Consistency
DC-CNN	: Deep Cascade-CNN
DCR-GAN	: Densely Connected Residual GAN
DC-WCNN	: Deep Cascade Wavelet-based CNN
DL	: Deep Learning
DWSR	: Deep Wavelet Super-Resolution
DWT	: Discrete Wavelet Transform
FAIR	: Facebook AI Research
FFT	: Fast Fourier Transform
GAN	: Generative Adversarial Networks
GRAPPA	: GeneRalized Autocalibrating Partially Parallel Acquisitions
IFFT	: Inverse Fast Fourier Transform
ISTA	: Iterative Shrinkage-Thresholding Algorithm
IWT	: Inverse Wavelet Transform
MoDL	: Model-based reconstruction using Deep Learning prior
MRI	: Magnetic Resonance Imaging
MSE	: Mean Squar Error
MWCNN	: Multi-Level Wavelet CNN
MWRN	: Multilevel Wavelet Residual Network
NMSE	: Normalized Mean Squared Error
NYU	: New York University
PSNR	: Peak Signal to Noise Ratio
SE block	: Squeeze-and-Excitation block
SISR	: Single Image Super-Resolution
SMASH	: SiMultaneous Acquisition of Spatial Harmonics
SSIM	: Structural Similarity Index Measure
TE	: Time to Echo
UDC	: Updated Data Consistency
VGG	: Visual Geometry Group
WavResNet	: Wavelet Residual Network
ZF	: Zero-Filling



SYMBOLS

b_i	: Bias
$\mathcal{N}$	: Deep network
θ	: Deep model's parameters
n	: Disruption or noise
D	: Discriminator network
G_v	: Encoding gradient
r_{out}	: Estimate of the unobserved part of Fourier information
f_{WCNN}	: Forward mapping of WCNN
G	: Generator network
$\mathcal{L}^{GEN_{adv}}$	: Generative adversarial loss
W_i	: i^{th} layer's weights
k_0	: Input channel size
$\mathcal{F}^{-1}$	: IFFT
$\mathcal{L}$	: Index of the particular convolutional layer
$\overline{M}$	: Inverse of mask function
x_{in}	: Input image (intermediary reconstructed image)
$\hat{x}_i$	: Intermediary outputs of the unfolding blocks
L	: Layers
$\mathcal{L}^{MAE}$	: Mean absolute error
H_θ	: Network quantified function
$\mathcal{F}_{\mathcal{L}}(\cdot)$	: Non-linear convolutional layers
$\mathcal{K}$	: Number of input feature maps
k	: Number of feature maps created by $\mathcal{F}_{\mathcal{L}}$
y	: Observed data in the k-domain
G_ϕ	: Phase encoding gradient
$\circ$	: Point-wise multiplication
f_{vgg}	: Pretrained VGG network
λ	: Rectified linear unit (ReLU)
x_{out}	: Rectified output image
$G_{\phi_{sl}}$	: Slide selection gradient
x_{zf}	: Subsampled image
U	: Subsampling mask function
S	: Sensitivity map
T	: Tesla
$\mathcal{F}_\Omega$	: Undersampled Fourier transform
x_{orig}	: Vectorized form for the ground truth image
$\mathcal{L}^{VGG}$	: VGG loss
α	: Weighting factor



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IMAGE RECONSTRUCTION WITH DEEP LEARNING AND APPLICATIONS IN MR IMAGES

SUMMARY

Magnetic resonance imaging (MRI) is an important modality in clinical imaging because of its non-invasive nature and capability of providing high-quality images, especially for soft tissues. However, it suffers from long data acquisition times. To tackle this drawback, three major approaches for accelerating MR scans have been established. These mainstream approaches include faster imaging based on MRI physics, hardware modification by using multiple coils for parallel imaging, and signal processing techniques by reconstructing MR images from undersampled data acquisition. Much effort has been directed to speed up the scanning operation by utilizing undersampled k-space measurements. Deep learning is offered as one of these powerful solutions for the reconstruction of MR images from subsampled data. Recently, deep learning techniques have shown tremendous results in a variety of image processing applications. With the recent swift improvements of deep networks, their role in MR imaging cannot be overlooked. Due to its superior performance over conventional methods, deep learning algorithms are rapidly being applied in a wide range of domains of MR imaging.

MRI reconstruction techniques based on deep learning have shown their capacity for reducing MRI acquisition time and performance improvement compared to analytical methods. Recent studies in deep learning reveal that the U-Net stands out among the diverse set of deep models as an effective network structure, especially for imaging inverse problems. Initially, the U-Net model was developed to solve segmentation problems for biomedical images while using an annotated dataset. In this thesis, in the first step, the novel application of the U-Net structure was considered for the important inverse problem of MRI reconstruction. Deep networks are particularly efficient for the speed-up of the MR image reconstruction process by decreasing the data acquisition time, and they can significantly reduce the aliasing artifacts caused by the undersampling in the k-space. On the first try, it is aimed to develop a novel and efficient unfolding U-Net framework for reconstructing MR images from undersampled k-space data. The new framework should have improved reconstruction performance when compared to competing methodologies. In this step, a novel unfolding framework utilizing the U-Net as a sub-block is being proposed. The introduced U-Net unfolding structure is applied to the magnetic resonance image reconstruction problem. The connection between the unfolding U-Nets is realized in the form of a recently developed projection-based updated data consistency layer. The novel structure is implemented in the PyTorch environment, which is one of the standards for deep learning implementations. The recently created fastMRI dataset which forms an important benchmark for MRI reconstruction is used for training and testing purposes.

Despite the many challenges in training rather large networks, novel methodologies have enhanced the capability for having clinical-grade MR image reconstruction in real-time. In recent literature, novel developments have facilitated the utilization of deep networks in various image processing inverse problems. In particular, it has been reported multiple times that the performance of deep networks can be improved by using short connections between layers. In the next step of this thesis, a novel MRI reconstruction method is introduced that utilizes such short connections. The dense connections are used inside densely connected residual blocks. Inside these blocks, the feature maps are concatenated to the subsequent layers. In this way, the extracted information is propagated until the last stage of the block. The efficiency of these densely connected residual blocks was evaluated in MRI reconstruction settings, by augmenting different types of effective deep network models with these blocks in novel structures. The quantitative and qualitative results indicate that this original introduction of the densely connected blocks to the MR image reconstruction problem improves the reconstruction performance significantly.

In addition, a novel densely connected residual generative adversarial network (DCR-GAN) is proposed for fast and high-quality reconstruction of MR images. DCR blocks enable the reconstruction network to go deeper by preventing feature loss in the sequential convolutional layers. DCR block concatenates feature maps from multiple steps and gives them as the input to subsequent convolutional layers in a feed-forward manner. In this new model, the DCR block's potential to train relatively deeper structures is utilized to improve quantitative and qualitative reconstruction results in comparison to the other conventional GAN-based models. It can be seen from the reconstruction results that the novel DCR-GAN leads to improved reconstruction results without a significant increase in the parameter complexity or run times.

The GAN-based structures generally suffer from some limitations. They are slow in convergence and they are unstable during the training step. In this work, these limitations of GAN also were addressed by proposing a new wavelet-based structure. To accomplish this, the wavelet transform packet was incorporated into the GAN structure. The wavelet transform is used in the encoding and decoding steps to create this model. In another word, the downsampling and upsampling layers were replaced with Discrete Wavelet Transform (DWT). DWT is used to replace each pooling process during the contraction phase. As DWT is a reversible package, this downsampling approach guarantees that all information can be retained. DWT can also record both the frequency and position information of feature maps, which will aid in the preservation of fine texture. The inverse wavelet transform is employed in the expansion step to upgrade the size of feature maps.

Moreover, recent breakthroughs in this field have inspired us to propose another novel deep unfolding structure for MR image reconstruction. In the last step, the model was trained using not only an iteration of the image itself but also utilizing an updated noise level parameter. The noise level parameter is calculated at each iteration using the error between the network output and the initial zero filling estimate. This new parameter is given as an additional input to the network, and it acts as an evolving regularizer for the image manipulation strength of the network over the unrolling iterations. The introduction of this adaptivity over iterations in the training step also improves the deep

models reconstructed image quality in the inference stage. Empirical results indicate that the recommended technique can convergence to better reconstruction results when compared to state-of-the-art unfolding structures devoid of such an adaptive parameter. The introduction of the additional adaptive parameter results in an incremental increase in the parameter complexity, and the required reconstruction times also stand very similar.

In this thesis, both quantitative and qualitative results were provided and the proposed model's results were evaluated with cutting-edge techniques in the MR image reconstruction field. Three commonly used evaluation metrics of PSNR, SSIM, and NMSE were used to evaluate simulation results. The statistical differences between developed techniques are investigated using the one-way ANOVA method. Additionally, a *t*-test is used to specify the major difference between the means of the two proposed structures. Additionally, the robustness of the proposed densely connected residual models was verified by testing them with another dataset type without retraining them. The other dataset differs in size and body tissue type compared to the training dataset.

The suggested novel structures in this thesis are improved MR image reconstruction performance compared to state-of-the-art techniques regarding all evaluation metrics. They proved their capacity for reconstructing high-quality images. More importantly, the thesis goal was satisfied regarding the acceleration of MR imaging. The proposed models in this thesis are generally considered to be fast enough to be used even in real-time medical imaging.



DERİN ÖĞRENME İLE GÖRÜNTÜ GERİÇATIMI VE MR GÖRÜNTÜLERİNDE UYGULAMALARI

ÖZET

Manyetik rezonans görüntüleme (MRG), girişimsiz doğası ve özellikle yumuşak dokular için yüksek kaliteli görüntüler sağlama yeteneği nedeniyle klinik görüntülemelerde önemli bir yöntemdir. Ancak, uzun süre veri toplama açısından dezavantaj oluşturmaktadır. Bu sıkıntının üstesinden gelmek için, MR taramalarını hızlandırmak için üç ana yaklaşım oluşturulmuştur. Bu ana akım yaklaşımlar, MRI fiziğine dayalı daha hızlı görüntülemeyi, paralel görüntüleme için çoklu bobinler kullanarak donanım modifikasyonunu ve alt örneklenmiş veriden MR görüntülerini geriçatmak sinyal işleme tekniklerini içerir. Yetersiz örneklenmiş k-uzay ölçümlerini kullanarak tarama işlemini hızlandırmak için çok çaba sarf edilmiştir. Alt örneklenmiş verilerden MR görüntülerinin geriçatımı için bu güçlü çözümlerden biri olarak derin öğrenme sunulmaktadır. Son zamanlarda, derin öğrenme teknikleri, çeşitli görüntü işleme uygulamalarında muazzam sonuçlar göstermiştir. Derin ağların son zamanlardaki hızlı gelişmeleri ile MR görüntülemedeki rolleri göz ardı edilemez. Geleneksel yöntemlere göre üstün performansı nedeniyle, derin öğrenme algoritmaları MR görüntülemelerde çok çeşitli alanlarda hızla uygulanmaktadır.

Derin öğrenmeye dayalı MR görüntü geriçatım teknikleri, analitik yöntemlere kıyasla MR görüntü oluşturma süresini azaltma ve performans iyileştirme kapasitelerini göstermiştir. Derin öğrenme konusundaki son araştırmalar, U-Net'in çeşitli derin modeller arasında, özellikle ters problemlerin görüntülenmesi için etkili bir ağ yapısı olarak öne çıktığını ortaya koymaktadır. Başlangıçta, U-Net modeli, etiketli bir veri seti kullanırken biyomedikal görüntüler için segmentasyon problemlerini çözmek için geliştirildi. Bu tezde, ilk adımda, MR görüntü geriçatımının önemli ters problemi için U-Net yapısının yeni bir uygulamasını inceledik. Derin ağlar, veri toplama süresini azaltarak MR görüntüsünün geriçatım sürecinin hızlandırılması için özellikle etkilidirler ve k-uzayda yetersiz örneklemenin neden olduğu örtüşme bozulmalarını önemli ölçüde azaltabilirler. İlk denemede, alt örneklenmiş k-uzay verilerinden MR görüntülerini geriçatım için yeni ve verimli kademeli bir U-Net çerçevesi geliştirmeyi amaçladık. Yeni çerçeve, rakip tekniklerle karşılaştırıldığında iyileştirilmiş geriçatım performansına sahip olmalıdır. Bu bağlamda, U-Net'i bir alt blok olarak kullanan yeni bir kademeli çerçeve önerilmiştir. Tanıtılan U-Net kademeli yapısı, manyetik rezonans görüntü geriçatım problemine uygulanmıştır. Basamaklı U-Net'ler arasındaki bağlantı, yakın zamanda geliştirilmiş, projeksiyon tabanlı güncellenmiş bir veri tutarlılığı katmanı şeklinde gerçekleştirilir. Yeni yapı, derin öğrenme uygulamaları için en çok kullanılan ortam olan PyTorch ortamında gerçekleştirilmiştir. MR görüntü geriçatım için önemli bir kriter oluşturan yakın zamanda önerilen fastMRI veri seti, eğitim ve test amaçlı kullanılmıştır.

Bu oldukça büyük ağların eğitimindeki birçok zorluğa rağmen, yeni yöntemler gerçek zamanlı olarak klinik düzeyde MR görüntü geriçatım sahip olma kabiliyetini artırdı. Yakın zamanlı literatürde verilen yeni gelişmeler, çeşitli görüntü işleme ters problemlerinde derin ağların kullanımını kolaylaştırmıştır. Özellikle, katmanlar arasında kısa bağlantılar kullanılarak derin ağların performansının iyileştirilebileceği birçok kez bildirilmiştir. Bu tezin bir sonraki adımında, bu tür kısa bağlantıları kullanan yeni bir MR görüntü geriçatım yöntemini tanıtıyoruz. Yoğun bağlantılar, yoğun bağlantılı artık blokların içinde kullanılır. Bu blokların içinde, özellik haritaları sonraki katmanlarla birleştirilir. Bu şekilde, çıkarılan bilgi bloğun son aşamasına kadar yayılır. Yeni yapılarda bu bloklarla farklı türde etkili derin ağ modellerini çoğaltarak, bu yoğun bağlantılı artık bloğun MR görüntü geriçatım ayarlarındaki etkinliğini değerlendirdik. Nicel ve nitel sonuçlar, yoğun bağlantılı blokların MR görüntü geriçatım sorununa bu orijinal tanıtımının geriçatım performansını önemli ölçüde iyileştirdiğini göstermektedir.

Ek olarak, MR görüntülerinin hızlı ve yüksek kaliteli geriçatımı için yeni bir yoğun bağlantılı artık üretici rekabetçi ağı (DCR-GAN) önerilmiştir. DCR blokları, sıralı evrişim katmanlarında özellik kaybını önleyerek geriçatım ağının daha derine inmesini sağlar. DCR bloğu, birden fazla adımdan gelen özellik haritalarını birleştirir ve bunları ileri beslemeli bir şekilde sonraki evrişim katmanlarına girdi olarak verir. Bu yeni modelde, DCR bloğunun nispeten daha derin yapıları eğitime potansiyeli, diğer geleneksel GAN tabanlı modellere kıyasla nicel ve nitel geriçatım sonuçlarını iyileştirmek için kullanılır. Geriçatım sonuçlarından, yeni DCR-GAN'ın parametre karmaşıklığında veya çalışma sürelerinde önemli bir artış olmaksızın iyileştirilmiş geriçatım sonuçlarına yol açtığını görebiliriz.

GAN tabanlı yapılar bazı sorunlara sahiptir. Yakınsamada yavaşlırlar ve eğitim aşamasında kararsızdırlar. Bu çalışmada, dalgacık tabanlı yeni bir yapı önerilerek GAN'ın bu sınırlamaları da ele alınmıştır. Bunu başarmak için dalgacık dönüştürme paketini GAN yapısına dahil ettik. Bu modeli oluşturmak için kodlama ve kod çözme adımlarında dalgacık dönüşümü kullanılır. Başka bir deyişle, altörnekleme ve üstörnekleme katmanlarını Ayrık Dalgacık Dönüşümü (DWT) ile değiştirdik. DWT, daralma aşaması sırasında her bir havuzlama işleminin yerini almak için kullanılır. DWT tersine çevrilebilir bir paket olduğundan, bu altörnekleme yaklaşımı, tüm bilgilerin tutulabilmesini garanti eder. DWT ayrıca, ince dokunun korunmasına yardımcı olacak özellik haritalarının hem frekans hem de konum bilgilerini kaydedebilir. Özellik haritalarının boyutunu yükseltmek için genişletme adımında ters dalgacık dönüşümü kullanılır.

Ayrıca, bu alandaki son gelişmeler, MR görüntüsünün geriçatımı için başka bir yeni derin açılım yapısı önermemiz için bize ilham vermiştir. Geliştirilen son yöntemde, modeli sadece görüntü girişini değil, aynı zamanda güncellenmiş bir gürültü seviyesi parametresini kullanarak eğittik. Gürültü seviyesi parametresi, ağ çıkışı ile sıfır doldurma tahmini arasındaki hata kullanılarak her yinelemede hesaplanır. Bu yeni parametre, ağa ek bir girdi olarak verilir ve açılma yinelemeleri üzerinden ağın görüntü işleme gücü için gelişen bir düzenleyici görevi görür. Eğitim adımında yinelemeler üzerinden bu uyarlanabilirliğin tanıtılması, sonuç aşamasında derin modellerin geriçatılmış görüntü kalitesini de geliştirir. Deneysel sonuçlar, önerilen

yöntemin parametrelere önemli miktarda karmaşıklık eklemekten diğer son teknoloji basamaklı yapılara kıyasla daha iyi geriçatım sonuçları ve benzer hız ile yakınsadığını onaylamaktadır.

Tüm çalışmalarımızda önerilen modellerimizi MR görüntü geriçatımında yüksek başarılı tekniklerle değerlendirdik. Hem nicel hem de nitel sonuçlar sağladık. Bu bağlamda, farklı altörnekleme değerleri için PSNR, SSIM ve NMSE gibi üç farklı değerlendirme metriğinin simülasyon sonuçları verilmiştir. Geliştirilen modeller arasındaki performans farkını vurgulamak için istatistiksel değerlendirme testleri yapılmıştır. Simüle edilmiş modellerin tüm değerlendirme metrikleri ve konfigürasyonları açısından istatistiksel önemini vurgulamak için tek yönlü bir varyans analizi (ANOVA) sunduk. ANOVA test bulguları, hem hızlanma faktörleri hem de tüm değerlendirme ölçütleri için 99%'dan fazla güvenilirlik ortaya koymaktadır. Ayrıca, önerilen modellerin etkinliğini doğrulamak için t -test kullanıldı. Bunu yapmak için, tüm modeller t -test ile yüksek başarılı yapılara kıyasla ikili olarak değerlendirildi. Eşleştirilmiş t -testleri, 0,05'lik eşik değerinden daha düşük p -değerleri verdi. Bu sonuç, önerilen yapılarımızda yüzde 95'ten fazla güvenilirlik olduğunu göstermektedir. Önerilen yoğun bağlantılı artık modellerin sağlamlığı, onları yeniden eğitmeden başka bir veri kümesi türüyle test ederek doğrulanmıştır. Diğer veri kümesi, eğitim veri kümesine kıyasla boyut ve vücut dokusu açısından farklıdır.

Tez kapsamında önerilen bu yeni yapılar, tüm değerlendirme ölçütleriyle ilgili olarak en son tekniklerle karşılaştırıldığında MR görüntü geriçatım performansını artırmıştır. Bu yapılar, yüksek kaliteli görüntüleri geriçatım kapasitelerini kanıtladılar. Daha da önemlisi, MR görüntülemenin hızlanmasıyla ilgili olarak tez hedefi karşılandı. Bu tezde önerilen modellerin, genel olarak gerçek zamanlı tıbbi görüntülemeye bile kullanılabilecek kadar hızlı olduğu değerlendirilmiştir.



1. INTRODUCTION

1.1 Magnetic Resonance Imaging

Nowadays, medical imaging is a critical application that provides a great deal of information for the diagnosis and therapy of ailments. Medical image reconstruction as a fundamental part of this field attempts to capture high-quality slices while imposing minimum health risks to the patients. Magnetic resonance imaging (MRI) is one of these medical imaging techniques. Nuclear magnetic resonance imaging, or MRI, is a technology that provides comprehensive slices from body tissue. MRI has gone through a significant evolution in radiology and medicine since its introduction in the early 1970s and afterward a vast field of research has been opened. MRI is a non-invasive important modality for clinical diagnosis because it provides high resolution for soft tissue analysis [1]. This technique can create images by applying a strong magnetic field from different regions of the body that are not visible with other medical imaging modalities like CT scans, ultrasound, or X-rays. It helps physicians look within cartilage, joints, muscles, ligaments, and tendons. A multitude of abnormalities like tumors, spinal cord disorders, and strokes can be detected using this module. Moreover, it has an indisputable share in research activities.

The most significant advantage of MRI over other imaging techniques like x-rays or CT scans is that patients are not in danger of radiation exposure. In this process, you lie down on a mobile cot to scan a certain part of the body tissue. The device creates a strong magnetic field around the area of interest. However, this magnetic field does not impose any pain on the body but you need to tolerate loud noises. In some cases, contrast mediums like gadolinium may even be injected to enhance the quality of images. The Fig. 1.1 explain the MR data acquisition and image reconstruction process.

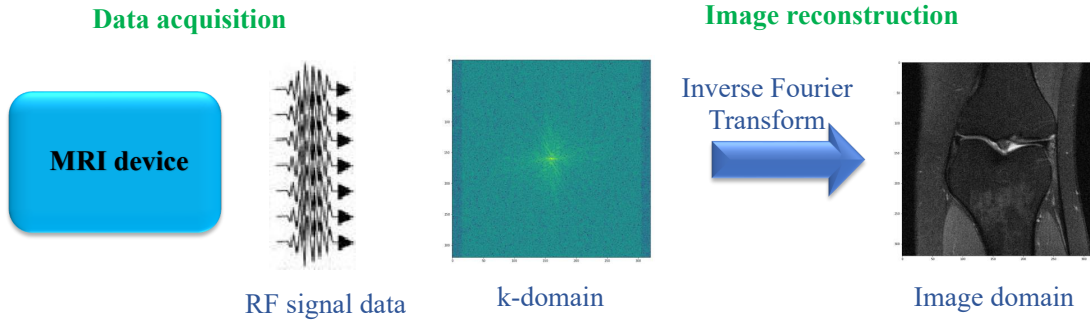


Figure 1.1 : Fully-sampled MR image reconstruction.

Water accounts for the vast majority of the human body. Hydrogen nuclei (protons) in water molecules (H_2O) get aligned in presence of the magnetic field. The Fig. 1.2 summarize the MRI device components. The patients lay down inside the metallic cylinder with the name of the bore. Inside this scanner, there are magnets that create a magnetic field range around two-three T where the magnetic field range of the earth is about $25-65 \mu T$. Sustaining such a massive strength is a tough problem and it necessitates a significant amount of energy and this can be satisfied by using superconductive materials or drastically cutting the resistance. To do so, wires are needed to be maintained at almost $-270^\circ C$. In addition to the main magnetic field, there are three magnets placed in three different directions of X, Y, Z . These additional magnets with lower strength compared to the main one, provide a probability to scan different parts of the body. In this regard, the receiver coils in the X direction will capture the signal from left to right, Y from top to bottom, and Z from head to toe.

As presented in Fig. 1.2, inside the MRI device, the magnets with gradients and radiofrequency hardware serves as an encoding device. The protons capture the magnetic field's energy and rotate their spins. In general, we turn on radio frequency and excite our signal by slide selection gradient $G_{\phi_{sl}}$, next we turn on phase encoding gradient G_{ϕ} , then we sample the signal at Time to Echo TE with our frequency encoding gradient G_v . The protons slowly revert to their initial position as soon as the field is switched off, this process is known as precession. The generated signals during the precession step are sensible by receiver coils. Thereafter, we iterate this process by only changing the phase encoding gradient amplitude to acquire all raw of k-space data. Radiofrequency radiation is transmitted to the patient where it excites the tissue magnetization and radiofrequency signals are emitted from the tissues. To

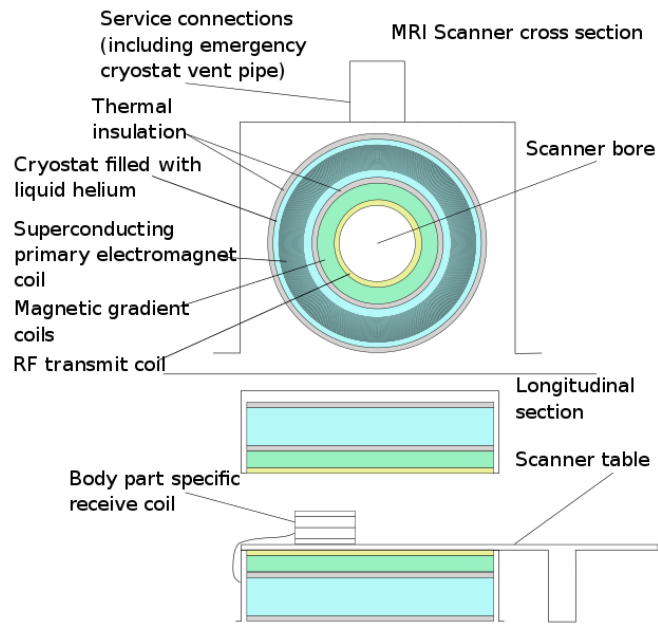


Figure 1.2 : MRI device components [2].

get the proper signals from the right tissues, radiofrequency pulses are properly tuned based on tissue type and tailored to the region of interest. A radiofrequency coil is used to receive a superposition of all the tissue signals. This signal is converted to digital form using an analog to digital converter (ADC) and the digitized form of the signal is usually referred to as raw data or k-space (Fourier space) data.

The protons in different tissues spin back to normal position at different speeds. The MRI scanner uses this feature to differentiate between distinct types of tissue. Additionally, we can adjust the settings of the scanner to generate contrasts between different tissues. Fig. 1.3 presents a particular fully sampled image slice and its associated fully sampled k-space data.

However, the data acquisition process for MR images is relatively long when compared to other imaging methods, because the data acquisition occurs in the k-space (Fourier) domain in a point-wise and successive manner. Moreover, the speed of this sequential data acquisition process is hampered by physiological and hardware constraints [3]. Therefore, the MR image acquisition becomes susceptible to motion artifacts. MR image reconstruction constitutes a trade-off among the acquired amount of k-space data, the quality of the reconstructed images, and reconstruction speed. To tackle these drawbacks, three major approaches for accelerating MR

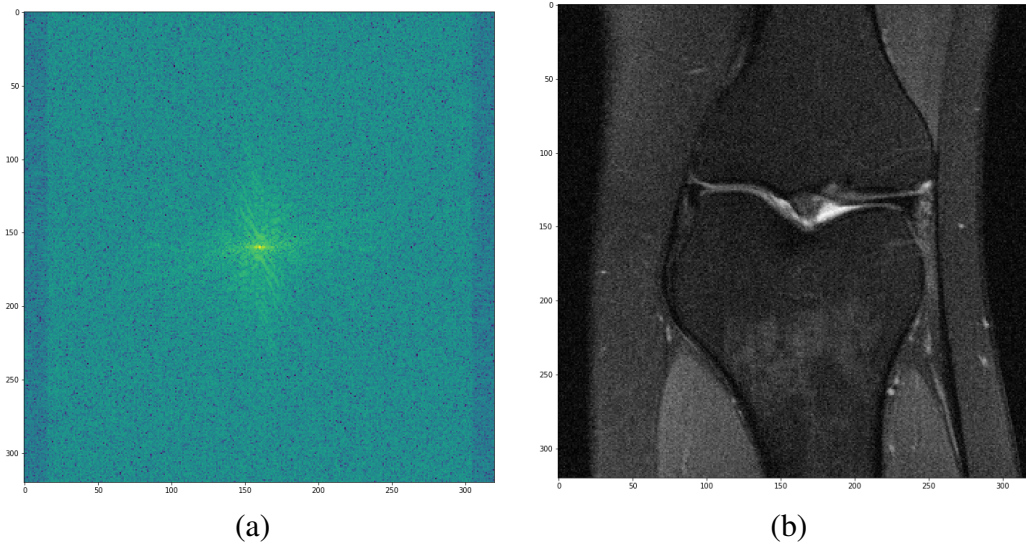


Figure 1.3 : Example for: (a) k-space data, (b) ground truth image.

scans have been established. These mainstreams are included fast imaging based on MRI physics, hardware modification by using multiple coils for parallel imaging, and signal processing techniques by reconstructing MR images from undersampled datasets. These strategies, in conjunction with their variations, have either decreased reconstruction or acquisition time.

In this thesis, we focused on techniques based on signal processing. In late decades, MRI has extended from linear analytic reconstruction techniques like sensitivity encoding (SENSE) [4], GeneRalized Autocalibrating Partially Parallel Acquisitions (GRAPPA) [5], and SiMultaneous Acquisition of Spatial Harmonics (SMASH) [6] to nonlinear iterative reconstructions methods include generalized series (GS) model [7], sparsity [8], statistics distribution regularization [9], low-rank model [10] and so on.

1.2 Deep Neural Networks

Machine learning develops techniques to train computers for solving problems by learning from prior knowledge. Over the last years, machine learning techniques have sparked considerable interest in practically every field of science and technology. The breakthroughs achieved by deep learning are one of the key reasons for its rise in popularity. Deep learning is a subset of machine learning techniques. These models can be trained supervised, semi-supervised, and unsupervised. In unsupervised

learning, models try to detect patterns in the data without humans interfering while in supervised learning the networks are trained based on an already annotated dataset.

Artificial neural networks are introduced to the literature in the 1950s and grasped their popularity from the commencing as a machine learning technique. Image processing applications of artificial neural network structures came to a standstill for a while due to the fact that classical artificial neural network structures are not suitable for processing a large number of training sets and data. Additionally, there was a lack of computational power to train and implement multi-layer structures. At the beginning of the twentieth century, artificial neural networks came to the fore again with developments by the accessibility of large data sets, the development of new and deep, multi-layered artificial neural network structures suitable for this big dataset, and the spread of hardware with the necessary processing power. As structure point view, the neural networks are mainly divided into three layers input, hidden, and output layers. The neural network is originally inspired by the human brain. Inside each layer there are neurons. Neural networks are extremely adaptable and this feature allow them to solve complex problems. However, their training is tough challenge due to their high computational costs. This issue reduce these networks practical application [11]. To tackle these difficulties, deep learning techniques are developed. Deep artificial neural networks structures have emerged as soon as the number of layers of the classical artificial neural network has been increased. In the light of these developments, deep learning structures have been applied with great success in problems such as image classification, object recognition, and image segmentation.

With the introduction of Convolutional Neural Networks (CNNs), the deep learning model is revolutionized. Recent progresses in convolutional neural networks have resulted in promising developments in a variety of medical imaging fields. Conventional machine learning algorithms are trained to execute specific operations using manually created features retrieved from raw data or features extracted from other techniques. However, deep learning models can be trained based on automatically extracted features.

CNNs [12] as one of the deep learning techniques have attracted attention in medical imaging. The CNNs contain various components including convolutional layer, activation function, pooling layer, optimization function, dropout regularization, fully connected layer, and batch normalization. The CNNs are built up of several convolutional layers that produce weights that can be updated by features extracted from former kernels. The convolutional layers result in the feature maps that are characterized by parameters like the number of feature maps, kernel size, padding, stride, dilation, and bias. Activation layers accept feature maps as an input from convolutional layers output.

The nonlinearity of deep networks is a key feature that can be achieved using a nonlinear activation function. Rectified linear units (ReLU), parametric ReLU, sigmoid, logistic, hyperbolic, and Exponential Linear Unit are some common activation functions. In next step, pooling layers are designed to reduce the network computational cost by decreasing the feature map dimension. Moreover, the activation of the network layers can be controlled and adjusted using batch normalization. It can improve model training speed by normalizing the distribution of data.

Training of the deep networks comprise some steps. In first step, weights alongside bias are initialized and input data forward to the network. After creation of the output, the error is computed between target and output data. In this step, different loss function can be optimized like mean square error, cross entropy loss, mean absolute error, and Gaussian negative log likelihood loss. Then features backpropagate to the network and weights are updated. The backpropagation process is commonly used to calculate the parameters of the various layers of a network. The backpropagation process actually calculate the gradients of the previously determined target functions based on the parameters, subsequently, it updates the parameters with respect to the measured gradients [12]. This process continue until achieving the minimum error.

The deep neural networks are strengthened by the introduction of residual connections. Residual networks as a popular deep neural network are proposed for the first time in [13,14] under the title of ResNet. The ResNet architecture is demonstrated in Fig. 1.4. ResNet's skip connection play critical role in maintaining steady training

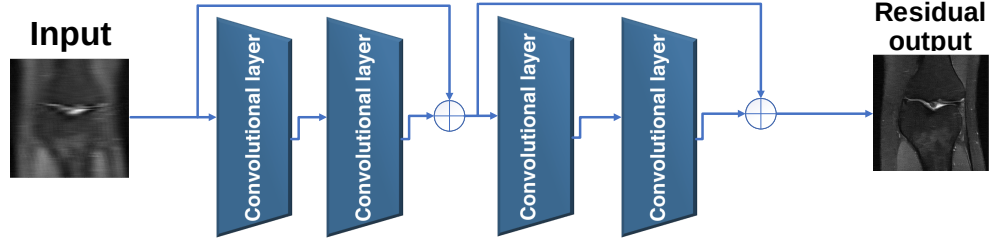


Figure 1.4 : ResNet structure.

of deep networks. Deep neural networks are developed in different applications of biomedical imaging. They are introduced as solutions for text mining and classification of radiology reports [15,16]. They can also reduce the necessity for contrast agents like gadolinium in MR imaging without a considerable decrease in the quality of images [17]. Other applications of deep networks can be summarized as PET-MRI [18,19], theranostics, radiotherapy [20], and radiomics [21]–[23].

1.3 MR Image Reconstruction Based on Deep Learning Techniques

The acquisition of magnetic resonance observation (data) signals is realized by the MR scanner containing a receiving coil. The object to be imaged is exposed to radio frequency radiation at certain angles and frequencies. The main observation equation for obtaining the MR sign can be written with the Fourier integral given below.

$$s(t) = \int_K i(r) e^{-j2\pi k(t)r} dr \quad (1.1)$$

In this integral definition, $s(t)$ denotes the instantly obtained output signal. $i(r)$ represents the spatial back radiation variation of the object to be imaged. r is the spatial position. On the other hand, $k(t)$ denotes the instantly sampled Fourier value in the spatial Fourier domain, also called the k-space. This main equation of MR data acquisition passes through certain stages and turns into a linear observation equation. The frequency coefficients that $k(t)$ scans will form the mask, which selects the coefficients sampled in the Fourier region.

MR image acquisition is a slow process associated with Nyquist–Shannon sampling limitations. This drawback leads to an increase in motion artifacts, patient discomfort, and costs. Deep learning techniques are offered as a solution to address these issues.

Deep learning approaches have recently demonstrated considerable potential in a variety of image processing tasks. With the recent quick improvements of deep networks, their role in MR imaging cannot be neglected. Deep learning approaches are widely used increasingly in a variety of domains in the field of MR imaging due to their outperformance compared to the conventional methods.

Deep learning in MR imaging is mainly concentrated on image reconstruction and segmentation problems. In the current work, we will focus on image reconstruction techniques.

As illustrated in the final part of Section 1.1, deep learning techniques are proposed as a solution for MR imaging to accelerate it. To do so, deep networks reconstruct MR images from subsampled datasets. In this regard, these networks can be trained in the image domain, Fourier domain, or multi-domain. Training datasets are prepared by undersampling fully-sampled datasets in k-space using different mask functions with different acceleration factors. Fig. 1.5 demonstrates four different mask functions.

The main goal in the MR image reconstruction problem is to revert from the observation data to the original image as well as possible. However, to achieve fast MRI, it is desired that the mask have an aggressive acceleration factor, which makes the inverse problem poorly conditioned. In general, the problem can be considered as replacing the missing data in the k-domain, or as a repair operation in the image region. The simplest method for reconstruction is to assume the missing Fourier data to be zero and returns to the image domain directly by inverse discrete Fourier transform. This strategy, also known as a zero filling (ZF) solution, establishes a performance threshold for more complicated reconstruction models.

Here, in Fig. 1.6 the random and equispaced Cartesian undersampling masks are provided with 4-fold, 8-fold, and aggregate acceleration factors. The corresponding zero-filled image is also shown in this figure, and these ZF images are input to the networks.

Image reconstruction problems are one of the important inverse problems in the image processing field. The MRI reconstruction problem remains up-to-date among image reconstruction problems. In the last decade, sparsity and compression sensing

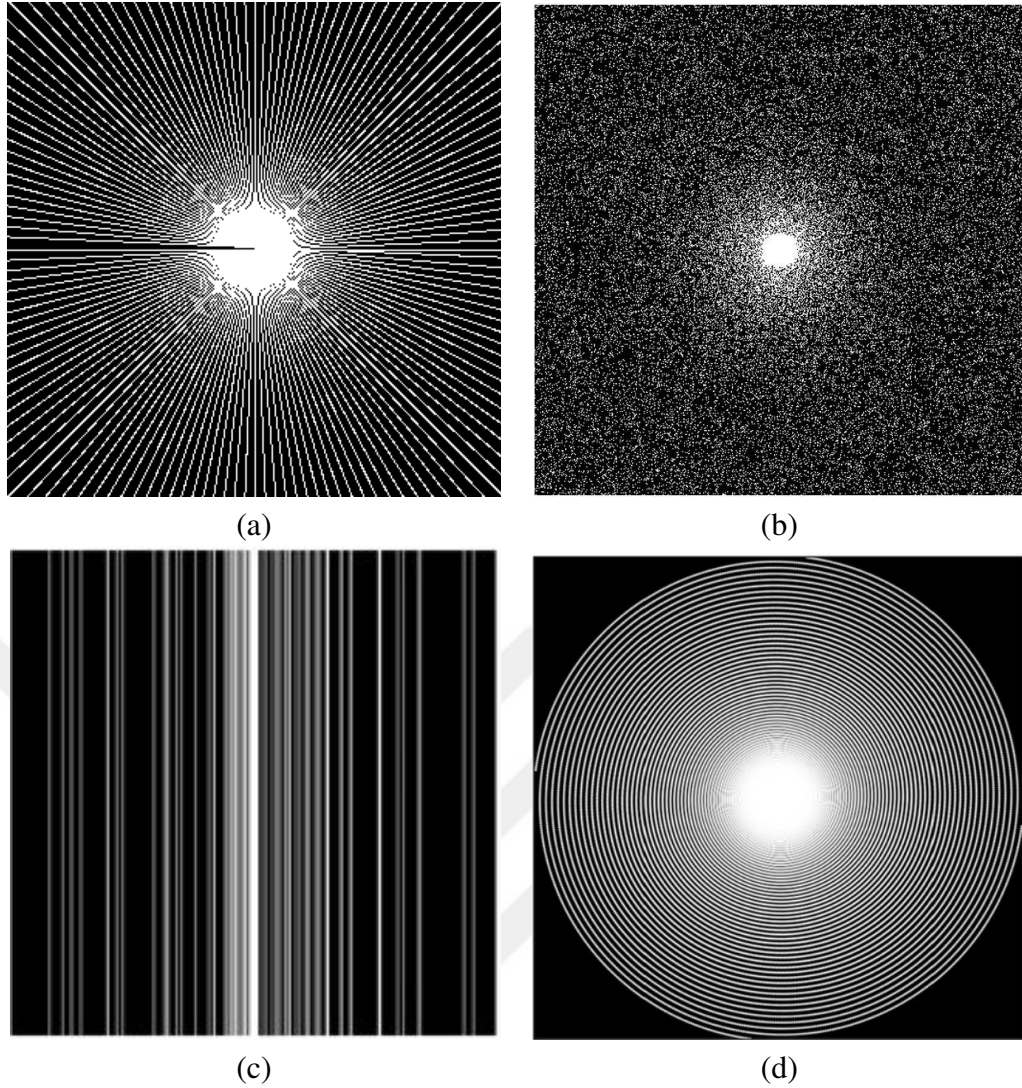


Figure 1.5 : Examples for: (a) radial mask, (b) variable density mask functions (c) cartesian mask and (d) spiral mask.

(CS)-based MRI reconstruction algorithms have attracted attention. The "Sparse MRI" approach which assumes that the searched actual image is sparse in a transform region provided high reconstruction accuracy [24]. While TV norm and wavelet transform norms were used as regularization terms in the Sparse MRI approach, later on, more complex and better performing regularization terms were used. Beyond that, patch-based methods that use non-local processing of patches have also taken the reconstruction performance one step further. However, MR image reconstruction techniques significantly focused on deep learning-based solutions in the last few years. In this work, We will try to summarize here notable examples of suggested solutions using deep learning.

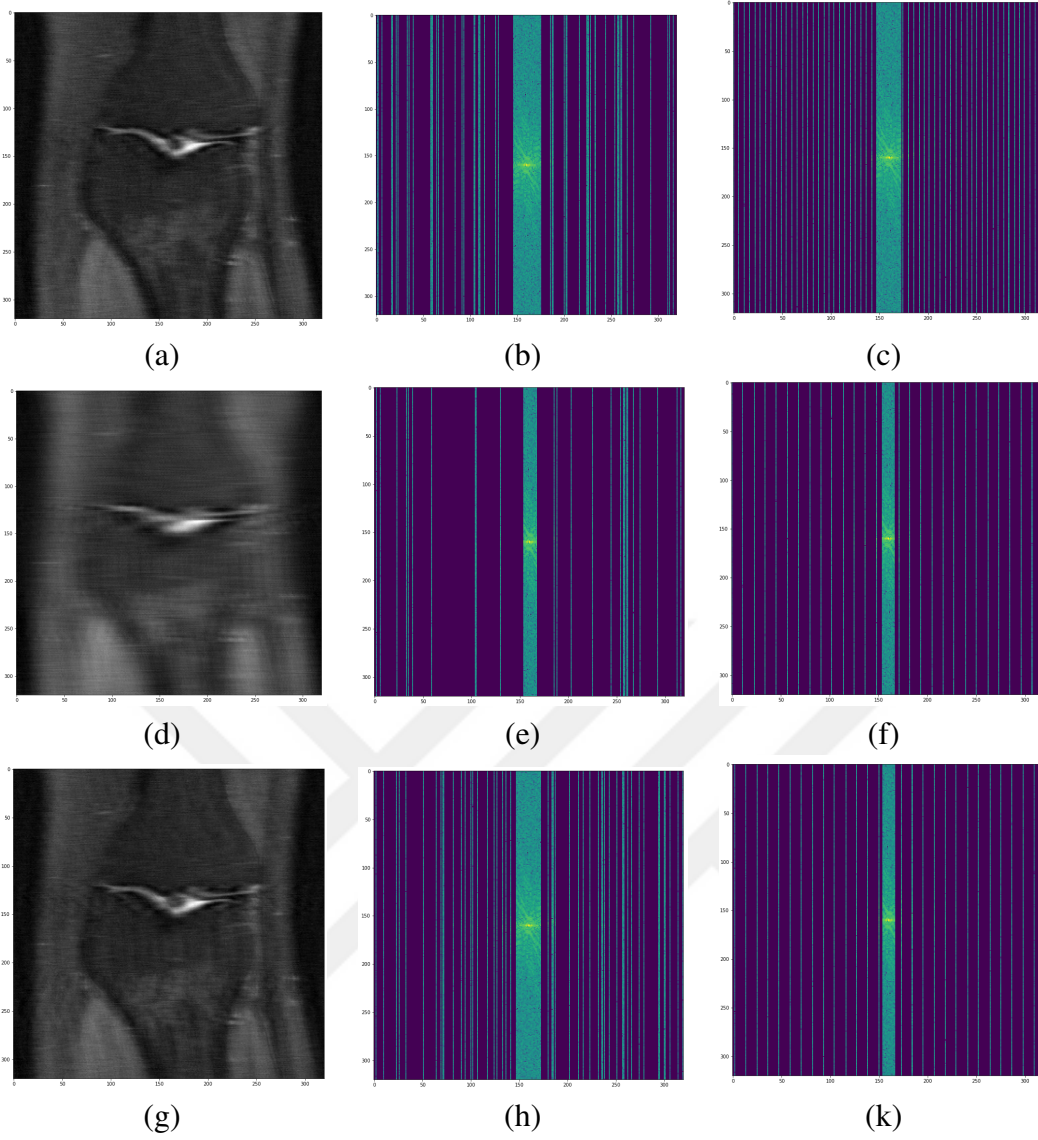


Figure 1.6 : (a) 4-fold zero-filling image, (b) 4-fold undersampled k-space with random mask function, (c) 4-fold undersampled k-space with equispaced mask function, (d) 8-fold zero-filling image, (e) 8-fold undersampled k-space with random mask function, (f) 8-fold undersampled k-space with equispaced mask function, (g) aggregate zero-filling image, (h) aggregate undersampled k-space with random mask function, (k) aggregate undersampled k-space with equispaced mask function.

Deep networks try to reconstruct MR images by learning the perfect way of transforming zero-filled or undersampled k-space data to desired output while minimizing the error between the network output and the grand truth image. MR image reconstruction based on deep learning techniques can be classified into two main groups: data-driven and model-driven unfolding iterative structures. Data-driven ones are end-to-end networks that try to learn from differences between the reconstructed

images and fully-sampled data. On the other hand, model-based approaches use conventional iterative algorithms to tackle the inverse problems.

The MR images are complex-valued in nature and the phase part carries critical information that cannot be easily disregarded in MRI reconstruction [25]. Several studies tried to employ both amplitude and phase information, while some trained by dividing complex images into real and imaginary parts [26]. In study [27], a dynamic reconstruction model is proposed for acquiring high-quality images from aggressively subsampled data with complex values. In [28], a variational network is proposed for reconstructing MR images from undersampled data using the variable density mask function (Fig. 1.5 (c)). Many parameters, like diverse loss functions, can be considered for training different networks with various structures. There is a great deal of deep learning algorithms and publications in MR image reconstruction like [29]–[32]. For using the deep network in clinical MR imaging many factors must be properly addressed. In the next chapters, a comprehensive literature review is provided related to the proposed novel networks.

In this thesis, the application of deep learning to MR image reconstruction has been studied. Novel solutions based on deep learning were proposed for the inverse problem of magnetic resonance image reconstruction and have been tried to develop new deep MR image reconstruction methods. It has been tried to tackle MR imaging difficulties by proposing deep learning-based techniques for swift MR image reconstruction. The significant contributions of this thesis can be reported as follows.

- In the first developed method, an unfolding structure has been proposed for the U-Net pipeline. Also, recently introduced projection-based structures were utilized in the encoding-decoding pathway.
 - The data fidelity block of the MRI reconstruction pipeline was replaced with a recently introduced updated data consistency layer.
 - In literature, unfolding frameworks for MRI reconstruction were trained and tested with rather small datasets, some including up to only 10 fully sampled cardiac MR images. The cascade and projection-based unfolding structures were benchmarked using the recently introduced and rather large fastMRI

dataset. This dataset was firstly developed by a joint group of New York University (NYU) researchers together with a Facebook AI Research (FAIR) team for the fastMRI image reconstruction challenge. This dataset has gained quite attraction in the MRI reconstruction community and has been employed as a benchmark in quite a few recent studies.

- In the second developed method, a novel structure have been introduced by applying densely connected residual blocks inside the generative adversarial network.
 - In another proposed framework, the generative adversarial network limitation was addressed. A novel wavelet-based GAN was offered for a stable training and swift convergence by replacing conventional downsampling and upsampling layers with wavelet packet.
- Motivated by successful applications of dense connections, the densely connected residual blocks were leveraged inside the cutting-edge networks. DCR blocks were used to replace the normal convolutional layers in U-Net and CNN structure.
- Inspired by the conventional iterative thresholding-based reconstruction models, an adaptive noise level parameter was applied to the unfolding structure.

The rest of this thesis can be summarized as follow. In Chapter 2, novel unfolded and projection-based unfolded structures for MR image reconstruction is presented. Chapter 3, provides details about our second study regarding the MR image reconstruction based on densely connected residual generative adversarial network–DCR-GAN. Chapter 4, elaborates the novelties over MR image reconstruction using densely connected residual convolutional networks. In Chapter 5, a novel structure based on deep unfolding pipeline is presented for MRI reconstruction enhanced by adaptive noise maps. In Chapter 6, detailed information about the dataset, experimental setup, and evaluation parameters are discussed. Moreover, the quantitative and qualitative simulation results are comprehensively presented in this chapter. Finally, conclusions are presented in Chapter 7.

2. PROJECTION-BASED UNFOLDED U-NET MODEL FOR MR IMAGE RECONSTRUCTION

2.1 Introduction of Unfolding Structure

Deep networks have facilitated a novel family of reconstruction algorithms from undersampled k-space data. Considering all these issues, a variety of deep learning (DL) and MRI acceleration methods like compressed sensing (CS)-MRI [3,33] have been proposed, with the major research goal being to decrease the acquisition time without significantly reducing image quality. Accordingly, effective CS-MRI models which utilize denoising as a sub-step of iterative reconstruction have been developed [34,35]. In this setting denoisers such as block matching 3D (BM3D) are employed to enforce the sparse prior onto the reconstructed MR images. Using these iterative methods, an opportunity has been provided to improve MRI reconstruction performance by applying a varying regularization parameter. However, the sparsity regularized CS-MRI based reconstruction methods are computationally expensive and rather slow due to the iterative nature of optimization solutions [36]. Newly developed deep learning based frameworks for MR reconstruction enable the researchers to tackle the difficulties related to modeling-based iterative methods. One of these deep frameworks which gained attention in solving the inverse problem of MRI reconstruction was the study performed by Schlemper *et al.* [37,38]. The proposed algorithm incorporates a "Deep unfolded" of Convolutional Neural Networks with interleaved data consistency (DC) stages. The unfolded structure with standard DC layers is given in Fig. 2.1.

The Deep Cascade-CNN (DC-CNN) performs the back-propagation process through the DC block by deriving the Jacobian of this layer. Motivated by the DC-CNN of [37], a cascaded CNN model that utilizes a novel, projection-based updated data consistency layer has been introduced in [39].

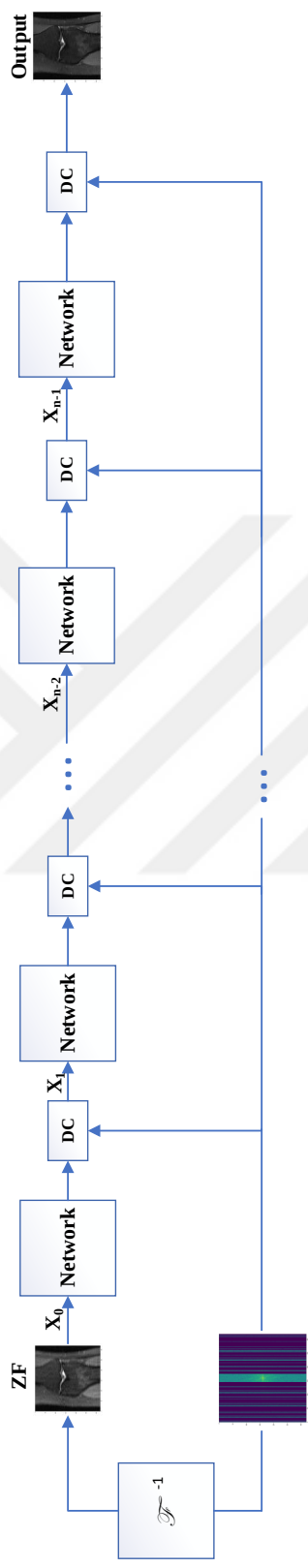


Figure 2.1 : The block diagram of cascade structure with standard DC layer.

Deep learning based methods significantly accelerate the MRI reconstruction process (e.g. for Deep Cascade-MRI each image reconstruction takes around 23ms). Recently, with inspiration from the Deep Cascade model, a compound cascade algorithm has been proposed by Qiao *et al.* [40]. They have applied both data-based and model-based algorithms to achieve better performance compared to other state-of-the-art MRI reconstruction models. The authors have used the iterative Approximate Message Passing (AMP) algorithm alongside the convolutional neural network to de-alias and reconstruct MR images. These two models were connected with data consistency layers to each other. Another study that leveraged DC-layer was conducted by YanWu *et al.* [41]. Their proposed SAT-Net (self-attention convolutional neural network) was developed by using a self-attention CNN and was applied on cartilage images. This deep residual CNN uses long-range dependencies to reconstruct MR images. One more compound network has been put forward by combining the convolutional neural network and parallel imaging. By using this framework, the authors have reconstructed real-time MR images [42]. Using a similar approach, recently a wavelet-based deep cascaded CNN has been put forward by modifying the U-Net model architecture [43]. In this study, they have replaced pooling and unpooling layers in the U-Net model with discrete wavelet transform and inverse wavelet transform, respectively.

MR image reconstruction actually proceeds towards the minimization of a loss function calculated by using the fully-sampled k-space data as the target. The input to the model is the under-sampled k-space data (or the initial rough image estimate calculated using zero-filling) [44]. Based on the same idea, to accelerate the MR imaging S. Wang *et al.* [45] suggested an off-line CNN to identify the connection between MR images that have been acquired from the under-sampled k-space data and the target ground truth data. Their network showed that it can reinstate the details and reconstruct structures that are lost in the masking step.

Besides CNN, U-Net models have been proposed in the literature for automatic segmentation purposes in MR images [46,47]. Attention gated (AG) networks were introduced in [48] for medical image analysis. In this work, the AG model is integrated into CNN and U-net architectures for MR image classification and segmentation problems. Squeeze-and-Excitation block (SE block) was proposed for the first time

in [49]. The SE block updates the features in a channel-wise manner without increasing the computational cost. The USE-Net which employs SE blocks inside a U-Net structure was offered in [50] for zonal MR image segmentation. In this particular study, a combination of three datasets was used for training and testing the model [50]. Despite the fact that the U-Net was originally built for image segmentation problems in bio-imaging, the U-Net has been used as a strong baseline for MR image reconstruction. The U-Net has a strong ability of preserving high-resolution features through concatenation in the up-sampling process. In a recent study [51], a deep learning algorithm based on k-space interpolation using the U-Net has been proposed, where the input and output are in the k-domain and are complex-valued. Hence in this work, the under-sampled k-space measurements have been utilized without performing the Inverse Discrete Fourier transform (IDFT). In another recent work, a framework based on the U-Net for speeding up MR imaging with sub-Nyquist sampling strategies has been developed [52]. Here, the zero-filling image is used as the input to the U-Net model, and the reconstruction is improved by employing the data consistency layer, which provides enforced consistency with the measured k-space data [52]. In [53] on the other hand, CNN models based on the Least Absolute Deviations (LAD-L1) and Least Square Errors (LSE-L2) loss functions have been compared in their capability to achieve fast cardiac MRI reconstruction. The authors showed that their network is almost 150x faster than the compared CS reconstruction method, with even better image quality and for larger acceleration factors [53].

In a comparative study, two deep learning models including residual network and U-Net for MR image reconstruction have been evaluated based on diverse loss functions by using a cardiac MRI dataset. Results reveal that both of the architectures result in similar outputs, and additionally, they found that the utilization of a perceptual loss function outperformed the Dssim, L1, and L2 loss functions [44]. In another study, a variational network that learns the effective priors has been offered, with different acceleration factors, for the purpose of shortening the acquisition and reconstruction time of MR knee images. Additionally, their proposed variational network preserved the original MR image appearance plus pathologies that were not included in the training data set [54].

When adopting deep learning for MR image reconstruction, one should carefully evaluate various features like the effects of loss function choices and network architecture. In [32], the authors put forward a cross-domain CNN called KIKI-net by reconstructing the final output image by forward propagating the under-sampled k-space data through the entire network. They revealed that in terms of restoring tissue structures and removing aliasing artifacts, the combination of K-net and I-net performs much better than the single-domain convolutional neural networks, with an average PSNR improvement of 2.29 dB [32]. Furthermore, another dual-domain architecture has been offered in [55]. In this paper, the authors designed a hybrid framework termed W-net, which operates on both k-space and image domains. Their model in the k-space domain contains a residual U-Net that works with complex values. The structure includes another U-Net in the image domain working with real values. However, in terms of quantitative results, the deep-cascade framework outperforms this model. From a qualitative point of view, the deep-cascade model reconstructs images with better visual quality.

Another state-of-the-art algorithm is the Primal-Dual-Net (PD-net) which was applied to MR images in [56]. This paper implements unrolling of the cross-domain model for MR image reconstruction in the case of aggressively under-sampled k-space data. [57] offers an enhanced recursive residual network that has superior reconstruction abilities with clearly restored structural features and high image quality. Lately, a hybrid CNN has been put forward for MR image reconstruction based on a single-image super-resolution technique. By leveraging the HybridNet, high-quality images have been achieved for three different datasets. The reconstruction PSNR is higher when compared to other deep learning based approaches [58].

Regarding all aforementioned issues, DL-based model realizations from the literature tend to outperform conventional, modeling based reconstruction methods in both reconstruction quality and speed [59]. In this work on the other hand, we introduce an unfolding structure employing U-Net networks. The U-Nets are linked together through the novel updated data consistency (UDC) layer. The introduced new model is trained and tested on the recently introduced fastMRI benchmark dataset [60]. The introduced model's performance is compared with baseline U-Net (Fig. 2.2)

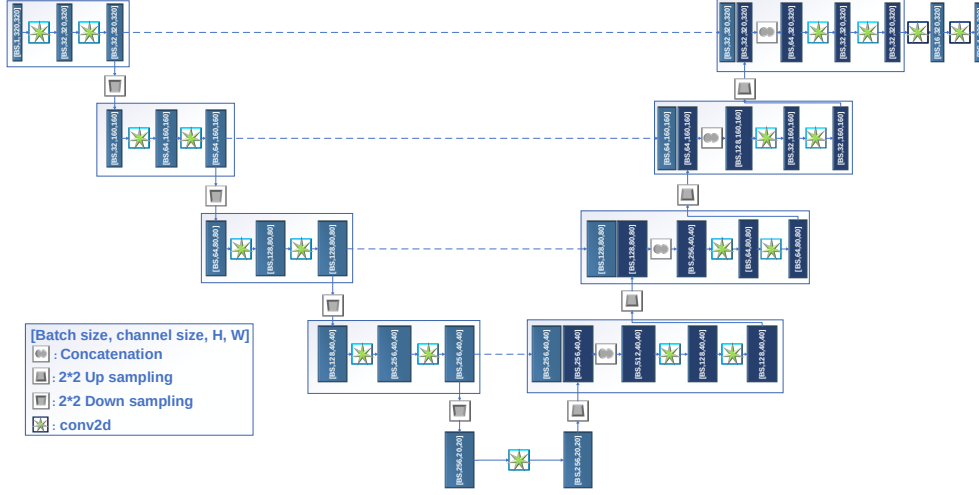


Figure 2.2 : Single-coil baseline U-Net architecture. The feature maps are denoted by the blue rectangular boxes. The slide size and number of channels are presented inside these boxes.

[60]–[62], cascaded CNN [37,38] and projection-based unfolding CNN [39]. The results indicate that the developed unfolding U-Net structure with intermediary UDC layers outperforms all of the mentioned deep learning based MRI reconstruction network variants. The work as detailed in this chapter has been published as a journal paper [63].

2.2 General Framework

In previous works from the literature, MR image reconstruction methodologies based on Convolutional Neural Networks and U-Nets have been offered as successful models. In the MRI reconstruction setting, data is acquired through the following equation:

$$y = \mathcal{F}_{\Omega} x_{orig} + n \quad (2.1)$$

$$x_{zf} = \mathcal{F}^{-1} y \quad (2.2)$$

In this equation, y indicates the observed data in the k -domain, where $\mathcal{F}_{\Omega}$ is the undersampled Fourier transform modeling the data acquisition. n is disruption or noise created in the measurement process. The sequence of selected points used in the MRI acquisition technique is described by Ω and $\Omega \in \{1, 2, 3, \dots, N\}^M$. Here $N \times M$ denotes

the image total pixel size. The IFFT and the subsampled image are shown by $\mathcal{F}^{-1}$ and x_{zf} , respectively. x_{orig} on the other hand, specifies the vectorized form for the ground truth image. In fully sampled data, y fulfill the Nyquist sampling theorem and the MR image can be easily created using an inverse Fourier transform but in undersampled data, different techniques should be applied to address the non-determined properties resulting from undersampling. CS or deep learning methods can be one of these solutions.

$$\mathcal{F}_\Omega = U \mathcal{F} \quad (2.3)$$

$$\mathcal{F}_\Omega = U \mathcal{F} S \quad (2.4)$$

Here, U is the subsampling mask function. $\mathcal{F}$ indicates the FFT and S denotes the sensitivity map for the multicoil volumes.

The MR image reconstruction template attempts to fill in missing points in ZF image. In the training step, it seeks to learn by minimizing the difference between the output or reconstructed slice $\tilde{x}$ and the target image. In this line, the objective is to achieve the most cost-effective H function. As a result, the training step matches up towards the following optimal solution:

$$\tilde{x} = H(x_{zf}) \quad (2.5)$$

$$\operatorname{argmin}_{\theta} \sum_{i=0}^{n_{data}} \|H_{\theta}(\tilde{x}^{(i)} - x_{orig}^{(i)})\| \quad (2.6)$$

Where, H_{θ} denotes the network quantified function, and θ signifies the deep model's parameters.

2.3 Proposed Unfolding Structure

One of the efficient deep models for solving the inverse problem of reconstructing x_{orig} utilizes cascaded CNNs (DC-CNN), and its details are provided in [37,38]. This

DC-CNN model places a data fidelity (or data consistency) layer (DC layer) after each network. Each single CNN reconstructs an intermediary output which goes through the succeeding DC layer as an input. Then, the DC layer enforces the observation data in the k-space domain onto the reconstructed output, with the procedure given in the below equation:

$$x_{out} = \mathcal{F}^{-1} \{ \overline{M} \circ (\mathcal{F} x_{in}) + y \} \quad (2.7)$$

Here, $\mathcal{F}$ and $\mathcal{F}^{-1}$ indicate 2D Discrete Fourier Transform (2D-DFT) and its inverse operator (2D-IDFT), respectively. $\overline{M}$ is the inverse of mask function which has been used for undersampling the ground truth data in the k-space domain. Moreover, “ $\circ$ ” and x_{in} are the point-wise multiplication operator and the input image (intermediary reconstructed image), respectively. A novel, projection-based updated DC layer on the other hand was introduced in [39]. The UDC layer incorporates a secondary output, r_{out} , which corresponds to the estimate of the unobserved part of Fourier information. The UDC layer creates both a rectified output image x_{out} in accordance with the regular DC layer, and also another residual image r_{out} which is defined as follow.

$$r_{out} = \mathcal{F}^{-1} \{ \overline{M} \circ (\mathcal{F} x_{in}) \} \quad (2.8)$$

Fig. 2.3 gives a pictorial description of this updated data consistency layer. These secondary outputs from the UDC layers, alongside the final intermediary reconstructed image, get collected in the concatenation layer near the end of the structure via skip connections.

In this work, we introduce a unfolding deep learning framework that incorporates the U-Net as the building block. We also develop a unfolding model with UDC layers acting as the intermediaries. This novel unfolding U-Net model utilizing UDC layers on the other hand is shown in Fig. 2.4. At the final stage of this novel structure, the last network reconstructs the final image estimate by using the input feature maps coming from the concatenation layer, which brings together the secondary outputs from the UDC layers and the image estimate formed before this final stage.

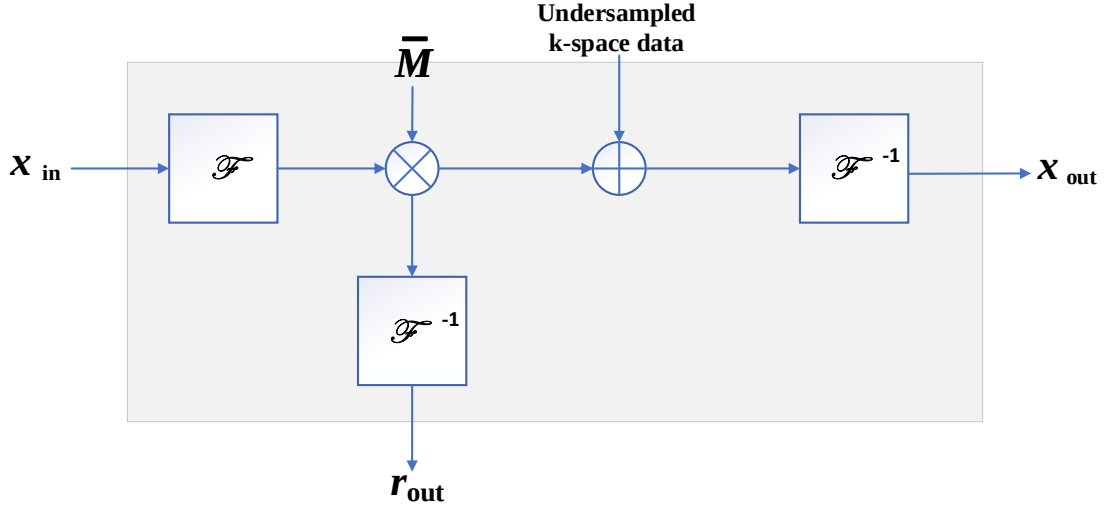


Figure 2.3 : Updated data consistency layer (UDC) block diagram [39].

In this study, to provide a fair overview and comparison, multiple models including standard CNN, cascaded CNN, projection-based unfolded CNN, and U-Nets were trained and validated using the fastMRI dataset. Two different types of masking functions have been utilized with multiple undersampling ratios. The novel models proposed in this work include the unfolded U-Net structure and the projection-based unfolded U-Net structure. These novel structures are depicted in Fig. 2.4.

Their performance results are compared with the previously mentioned models from the literature. In this simulation setting, single-channel ground truth images with real values are undersampled using random and equispaced Cartesian mask functions. Subsequently, zero-filled (ZF) images are given as input to the unfolded blocks of the U-Net with residual network blocks and intermediary DC or UDC layers. However, in the projection-based unfolded U-Net, the fifth block is a reconstruction module with multiple feature maps at its input. The secondary outputs (r_{out}) from the initial UDC layers concatenated with the primary output of the final UDC layer forms the input to this last module. Finally, the loss is calculated between the target image and the final reconstructed image estimate.

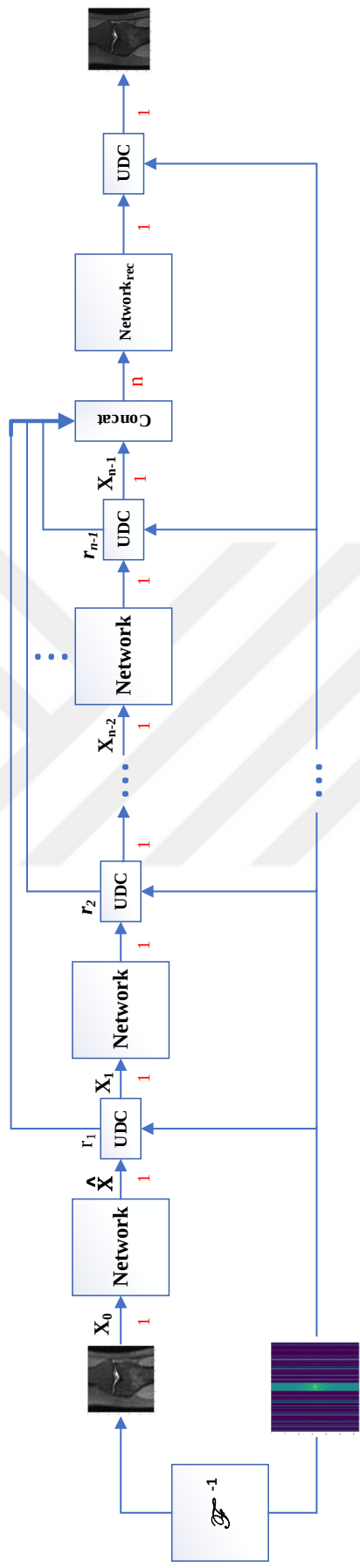


Figure 2.4 : The block diagram for projection-based unfolding structure with updated DC layers. The input and output channel sizes are shown with red values.

Algorithm 1 The steps for the projection-based unfolded network using UDC layers.

```

for  $i = 1 : n - 1$  do
     $\hat{x}_i = \mathcal{N}(x_{i-1})$ 
     $(x_i, r_i) = \text{UDC}(\hat{x}_i, y)$ 
end for
 $\mathbf{R} = [r_1, r_2, \dots, r_{n-1}]$ 
 $\hat{x}_n = \mathcal{N}(x_{n-1}, \mathbf{R})$ 
 $x_n = \text{UDC}(\hat{x}_n, y)$ 

```

In Algorithm 1, we give an algorithmic representation for the unfolded network as introduced in this study. Here $\mathcal{N}$ denotes the deep network as utilized in the recursive, unfolded structure. In our implementation, we take $\mathcal{N}$ to be a U-Net as defined in Fig. 2.4. Here, UDC is the updated data consistency layer. $\hat{x}_i$ are the intermediary outputs of the unfolding blocks. Furthermore, r_i are the secondary residual outputs of the UDC layers. x_i is the rectified image output of the UDC layer. To the best of our knowledge, the proposed scheme gives the first use of U-Nets in a unfolded structure. The UDC is also utilized together with the U-Nets for the first time. This novel unfolded structure which employs the U-Net together with the UDC results in very competitive MRI reconstruction performance.

2.4 Architecture

In this study, all deep networks based on U-Net and CNN have been trained using single-channel MR images with real values. As illustrated in Figs. 2.1 and 2.4, initially inverse Fast Fourier Transform will be applied to the undersampled k-space data. Then, the obtained zero-filling (ZF) images will be normalized as a pre-processing step. These ZF input images will get processed by the deep networks to generate high-quality reconstructed images. Meanwhile, all image slices are center cropped to the size of 320x320 to make all slices from the dataset have the same dimensions.

2.4.1 CNN based networks

The utilized CNN network architecture is the same as the one mentioned in the literature [37,38]. The model is detailed in Fig. 2.5, and it includes five convolution layers. In the first convolutional layer, the input and output channel sizes are set to one

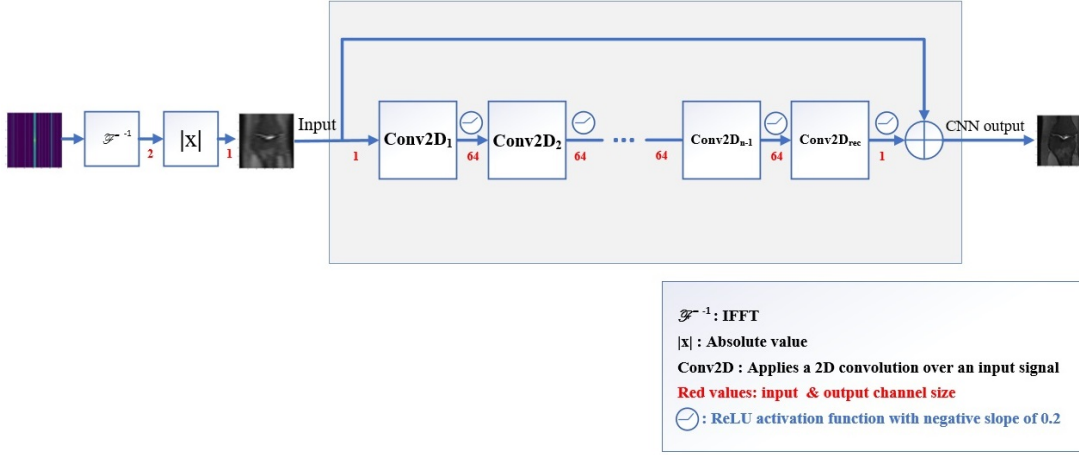


Figure 2.5 : The reconstruction simulation pipeline using the standard CNN architecture.

and 64 respectively, with the filter kernel size equaling three. Subsequent three layers have both input and output channel sizes equal to 64, with the filter kernel size being 3. The final layer, namely C_{rec} will project the 64 input maps into a single image output. Throughout this structure, all convolution layers are followed by ReLU units (rectified linear units) acting as the activation function. Moreover, the input and output of the network are to get a residual network which can improve performance. For the training of all the CNN-based networks, Adam optimizer was utilized with a learning rate of 10^{-4} , weight decay of 10^{-7} , and beta values equal to (0.9, 0.999).

2.4.2 U-Net based networks

In our realizations, we have benefited from the U-Net models for MRI reconstruction as developed and shared by the Facebook AI Research (FAIR) team [60]. The employed U-Net pipeline includes two different deep convolutional networks in the down-sampling and up-sampling paths. The down-sampling path has two blocks of 3x3 convolutions. It employs ReLU as the activation function. These blocks perform down-sampling by using max-pooling layers with stride two to halve the resolution. On the other side, the Up-sampling layer has the same structure as the down-sampling, although it uses bilinear layers to double each spatial dimension. At the output layer, it has a 1x1 convolution layer which makes the output channels to be one. Unlike conventional CNN, our U-Net model has two outputs. In this model, the second output stores residual image which will be carried via skip connection to the input layer of

the final U-Net. This final network will create the ultimate reconstruction based on the residual images and the intermediary rectified image. Furthermore, as a depth of the network, the unfolded and projection-based unfolding U-Net network consists of five U-Net ($n_c=5$) models that each one is connected to a residual layer. As shown in Fig. 2.4 the output of these layers goes inside a UDC layer in order to save the data fidelity.

At the training stage, the deep models are trained by using 973 image volumes. The gradient is calculated as a running average of its recent magnitude (RMSProp) and the error term used is the mean element-wise absolute value difference (L1 loss function) between the reconstructed image and the desired output (ground truth image). Furthermore, during each batch processing step of the training, a random or equispaced (uniform) Cartesian sampling mask is selected to realize the k-domain undersampling. The number of U-Net pooling layers is chosen as four, and the dropout probability is set to zero by default. Additionally, the learning rate is set equal to 0.001. The period for learning rate and the multiplicative factor of learning rate decay are set to 40 and 0.1, respectively. Moreover, the strength of weight decay regularization is chosen as equal to zero.



3. MR IMAGE RECONSTRUCTION BASED ON DENSELY CONNECTED RESIDUAL GENERATIVE ADVERSARIAL NETWORK

3.1 Introduction of GAN Structure

Recently, DL models proved their capability for solving different image processing problems [34]. In this regard, deep learning based methods [39,44,45,51,52,64] came to be an antidote for this issue. Through this path, the deep learning methods are trained using an undersampled dataset. Generative adversarial networks (GANs) as a particular DL framework have presented superb performance in imaging inverse problems in recent literature [65]. GAN models predict the generative framework through an adversarial pipeline. GAN trains two networks at the same time in parallel. In MR image reconstruction, as shown in Fig. 3.1 the generative model G tries to reconstruct high-quality images while the discriminative network D predicts if the result is a ground truth image or it is a reconstructed one. In another point of view, G gives its best to reconstruct such a unique duplicate of a real image that fool D and push it to make mistake and accept the generator result as real one. GAN-based frameworks are proved their potential to predict undersampled k-space data and reconstruct high-resolution images [66].

In [31] a deep de-aliasing GAN has been proposed for reconstructing MR images. In DAGAN, a U-Net structure was used as the generator network [31] and the VGG (Visual Geometry Group) [67] perceptual loss was used alongside generative loss. TM Quan *et al* [68] deployed cyclic loss in residual GAN for MR image reconstruction under name of RefineGAN. In a study, CS-based GAN (GANCS) has been provided by Mardani *et al* [69] for MRI reconstruction. Coupling perceptual loss, pixel-wise, and the cyclic data consistency loss can improve the GAN-based model's performance for image synthesis [70]. Synthesis accuracy can be enriched using information from cross-section neighbors in each volume [70]. Recently, deep networks gained attention due to their promising performance but as they get deeper, their training becomes

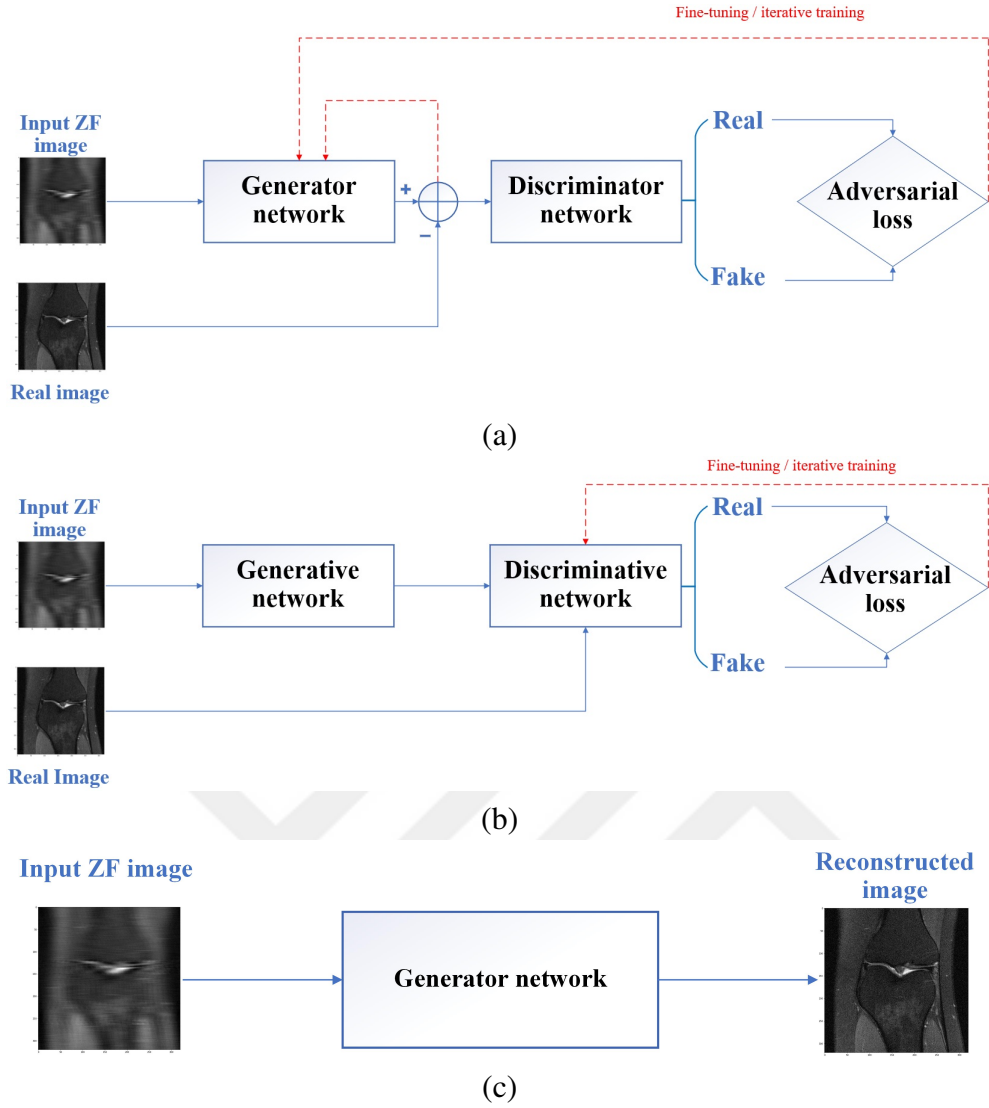


Figure 3.1 : GAN structure: (a) generator network during training step, (b) discriminator network during training step, (c) test step.

more challenging. They need more connections to prevent feature loss and gradient vanishment [71]. To address this drawback, layers during training can be referenced to the input layer by adding them together [13]. Huang *et al* [72] has been demonstrated that employing dense connections among layers can prevent gradient vanishing. Dense connections concatenate receptive fields step by step from all convolutional layers and feed them into the subsequent layer as an input [72]. Then, these residual and dense connections were proved their capacity in various image processing problems. In RDN [73] residual and densely connected networks are coupled together for image restoration. In a study, dense connections are applied to a U-Net based network for image denoising problems [74]. In the MR image segmentation study, the dense

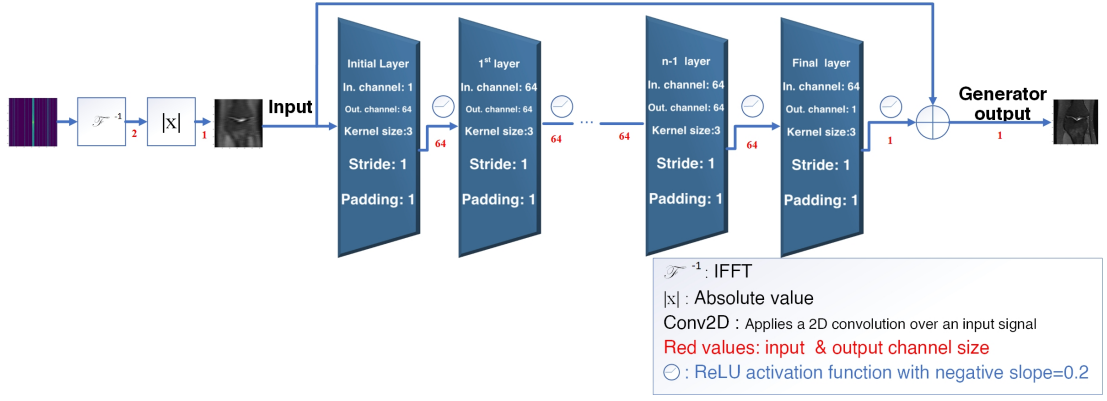


Figure 3.2 : Generative network architecture based on conventional CNN.

connections were added into the U-Net downsampling and upsampling stages [75]. Recently, a wide multimodal dense U-Net has been put forward for reconstructing MR images related to patients who suffer from MS disease [76].

Getting inspired from the vantage points of both GAN-based and densely connected networks, we couple DCR blocks into the generative network. To the best of our knowledge, this is the first time a DCR-GAN structure is being used for MR image reconstruction. The deep networks are applied on initial zero-filling (ZF) image estimates. The ZF images are generated directly from the undersampled k-space data via inverse DFT. For the k-space undersampling we utilize randomized Cartesian mask functions with 4-fold and 8-fold acceleration factors. In this regard, initially we developed a GAN (Fig. 3.1) using standard CNN with five convolutional layers as the generator (Fig. 3.2) and a binary classifier CNN as shown in Fig. 3.3 as the discriminator. We also adopted a VGG loss inside the generator loss. Secondly, we develop a densely connected residual GAN (DCR-GAN) and conduct qualitative and quantitative performance comparisons between these models. In this study, we have used the fastMRI challenge dataset of [60] for both training and testing purposes. The work as discussed in this chapter has been published as a journal paper [77].

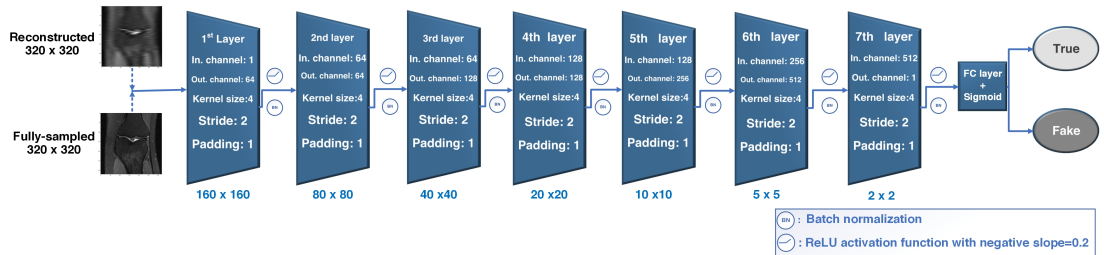


Figure 3.3 : Discriminator network architecture.

3.2 Introduction of Deep Network Structures Based on Wavelet Transforms

The wavelet transform is a useful feature extractor, it contains both spatial and frequency features of an image [78,79]. There are increasing research efforts to explore how wavelet transform operations can be incorporated into image processing problems [80]–[82]. Convolutional operations are good at capturing spatial features, while wavelet transform can capture scale-invariant features based on spectral information. Therefore, it is preferable to consider both spatial and spectral information in a single model [81]. On the other hand, wavelet-based CNN structures presented satisfactory performance in different image processing problems. In a study, a wavelet residual network (WavResNet) and single image super-resolution (SISR) is proposed for image denoising [83]. It has been offered that these wavelet subbands can benefit CNN learning [83]. In [84], the deep wavelet super-resolution (DWSR) method was proposed to recover missing details in the subbands. A multi-level wavelet CNN (MWCNN) model was developed for the first time in [85]. Recently, a deep cascade wavelet-based CNN (DC-WCNN) was developed in [43] to recover fine details in MR image reconstruction. Wavelet transforms [86] provide effective signal separation with time-frequency localization features, while inverse wavelet transform can accurately reconstruct the original signal for wavelet subbands. Motivated by these features, a multilevel wavelet residual network (MWRN) architecture and a progressive training (PTMWRN) scheme to improve image denoising performance was presented in [87]. On the other side, GAN-based structures have some major limitations. These frameworks are unstable during training and they are slow in convergence [88]. GAN also suffers from the vanishing gradient and the problem of balancing training between the Discriminator and the Generative networks [89,90]. Moreover, the GAN is affected by local minimum and convergence. To tackle these limitations of GAN, we proposed a new wavelet-based structure. To do this, we integrated the wavelet transform into the generative part of the GAN structure. This model is developed by applying wavelet transform into the U-Net downsampling-upsampling stages.

3.3 Proposed DCR-GAN Structure

As shown in Fig. 3.1 the ZF images go into the proposed GAN. In general, GAN pipeline includes two competing networks, a generator (G) and a discriminator (D), with training parameters θ_G and θ_D , respectively. G should create fake images which must not be recognizable from ground truth images. To achieve this goal, network D help network G by classifying between fake and real images. Basically, this binary classifier for real samples gives value $D(x_{orig}) = 1$ and for fake data ($\tilde{x}$) = 0. In mathematical terms, D and G play a two-player minimax game which is summarized in the following function:

$$\min_G \max_D V(D, G) = \mathbb{E}_{x_{orig} \sim p_{data}}(x_{orig})[\log(D(x_{orig}))] + \mathbb{E}_{x_{zf} \sim p_{x_{zf}}}(x_{zf})[1 - \log(D(G(x_{zf})))] \quad (3.1)$$

Eq. 3.1 can be optimized by training D to maximize the possibility of correct labeling, while G tries to minimize $\log(1 - D(G(x_{zf})))$ and deceive D to accept the generated image as a real one. In this study, content loss was applied for generator network training. To this end, VGG loss is appended to the mean absolute error.

$$\mathcal{L}_{Total} = \alpha \mathcal{L}_{MAE} + \beta \mathcal{L}_{VGG} + \mathcal{L}_{GEN_{adv}} \quad (3.2)$$

$$\min_{\theta_G} \mathcal{L}_{MAE}(\theta_G) = \|x_{orig} - \tilde{x}\| \quad (3.3)$$

$$\min_{\theta_G} \mathcal{L}_{VGG}(\theta_G) = \frac{1}{2} \|f_{vgg}(x_{orig}) - f_{vgg}(\tilde{x})\|_2^2 \quad (3.4)$$

Here, f_{vgg} denotes the end-to-end function related to the pretrained VGG network. $\mathcal{L}_{MAE}$, $\mathcal{L}_{VGG}$ and $\mathcal{L}_{GEN_{adv}}$ are mean absolute error, VGG loss and generative adversarial loss, respectively. The generator adversarial loss is defined as follows.

$$\min_{\theta_G} \mathcal{L}_{GEN_{adv}}(\theta_G) = -\log(D_{\theta_D}(G_{\theta_G}(x_{zf}))) \quad (3.5)$$

In this study, as in [31] the experimental hyperparameters α and β are set to 15 and 0.025, respectively.

3.4 Proposed Wavelet-Based GAN Structure

In this work, a new wavelet-based GAN is proposed to provide a better trade-off between performance and efficiency. In this regard, We applied this wavelet packet to the generator network of the GAN structure. This model as shown in Fig. 3.4 is based on the U-Net architecture, which consists of a contracting and an expanding subnetwork. Discrete Wavelet Transform (DWT) is deployed in the contraction phase to replace each pooling operation. Since DWT is reversible, it is guaranteed that all information can be stored within downsampling step. Also, DWT can maintain both frequency and location information of feature maps [91,92], which will help preserve detailed texture. In the expanding subnetwork, inverse wavelet transform (IWT) was used to upgrade low-resolution feature maps to high-resolution ones. Despite the U-Net structure that concatenates feature maps from the encoder-decoder stages [93], in the generator network we have adopted elementwise aggregation to enrich the feature maps and reduce the computational burden.

The wavelet-based CNN (WCNN) method can be formulated as an optimization problem:

$$\operatorname{argmin}_{x, \theta} \|x - f_{WCNN}(x_{zf}|\theta)\|_2^2 + \alpha \|F_{\Omega}x_{orig} - y\|_2^2 \quad (3.6)$$

Here f_{WCNN} is forward mapping of WCNN parameterized with θ and α is a weighting factor based on the noise of the obtained data (y). Equation 3.6 forces WCNN to reconstruct x_{orig} in the viewport without any prior knowledge of the data obtained in k-space.

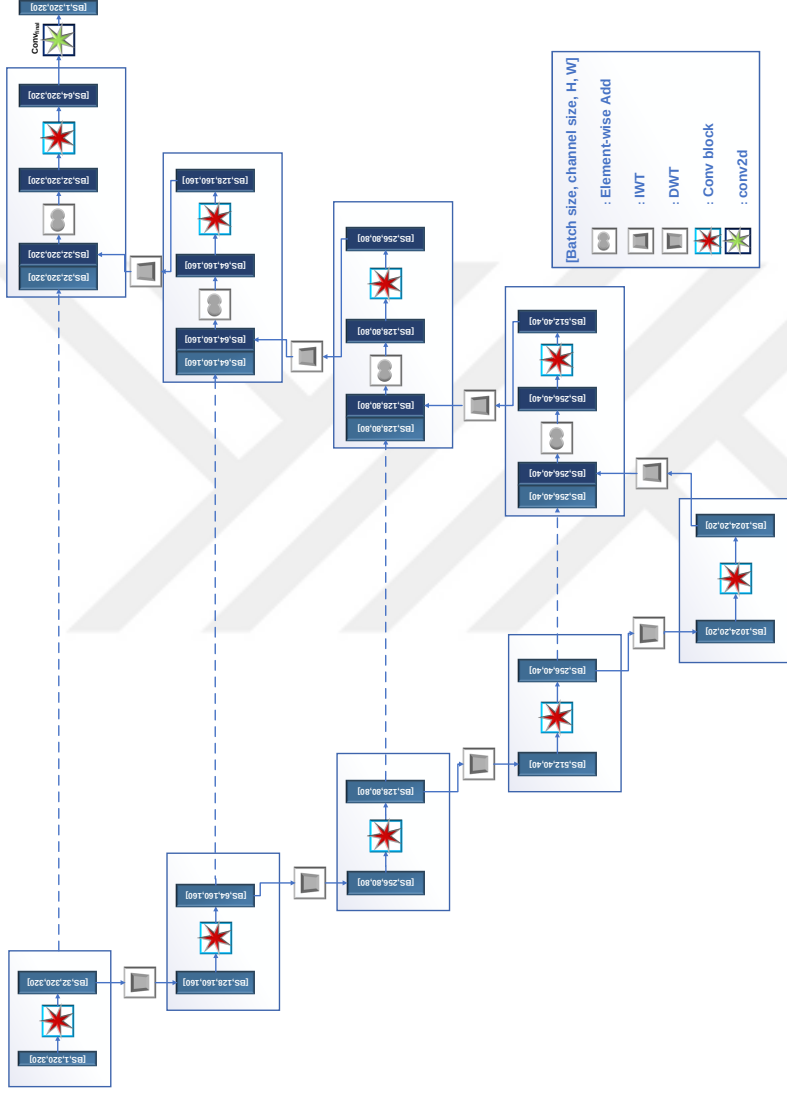


Figure 3.4 : Wavelet-based GAN generative network architecture.

3.5 Architecture

3.5.1 Architecture for proposed DCR-GAN

The GAN model for MR reconstruction is provided in Fig. 3.1. As shown in Fig. 3.2, the generator pipeline includes five convolutional layers with the same training parameters as proposed in [37]. The discriminator network is shown in Fig. 3.3 and is similar to the one which is offered in [66]. This binary classifier includes 7 convolution layers that are followed by leaky-ReLU activation functions and end with a fully-connected layer. In DCR-GAN, initially the generator convolves the single channel ZF image into 64 feature-map, just like the plain CNN. Then these feature-maps are directed through three succeeding DCR blocks. The details of the DCR block can be seen in Fig. 4.3. In the final step, the single channel grayscale image is reconstructed through a reconstruction layer. The overall DCR-GAN generator network is seen in Fig. 3.5. Finally, a DC layer [39] can be applied to the resulting image to improve the reconstruction results.

3.5.2 Architecture for proposed wavelet-based GAN

We proposed a new architecture for GAN generator network to improve training stability and facilitate model convergence. The proposed network's skeleton is the same as U-Net [93], but we have included wavelet package decomposition (WPD) which is a form of the wavelet transform. Both DWT and WPD involve convolution

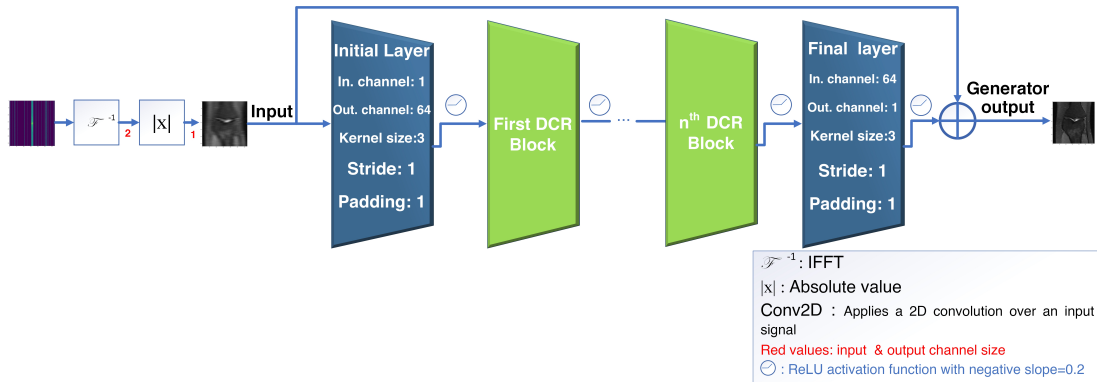


Figure 3.5 : Structure of the novel generator network with n DCR blocks.

of the image with different wavelet filters. The main difference between them is that in WPD the wavelet transform is performed in each subband from the previous level. Conversely, only the low-level low-frequency subband is converted in DWT. The bottom line is that low-level DWT coefficients contain only high-frequency features, whereas each WPD coefficient level contains both high and low-frequency features.





4. MR IMAGE RECONSTRUCTION USING DENSELY CONNECTED RESIDUAL CONVOLUTIONAL NETWORKS

4.1 Introduction of Deep Network Structures Based on Dense Connection

Lately, deep learning-based methods have received attention as a means of accelerating MRI reconstruction. In this regard, some novel deep learning techniques from image processing and computer vision have been applied to this problem. One important example of these successful deep learning methods utilizes domain-transform manifold learning [94]. In this work, automated transform by manifold approximation (AUTOMAP) [94] is adapted to the MRI reconstruction problem using data-driven learning. In another paper, a variational reconstruction network is developed, and it is applied in particular to knee image reconstruction [54]. Among various deep learning models, the U-Net algorithm has gained noticeable success in diverse fields of image processing. Initially, the U-Net [93] had been suggested as an image segmentation framework. However, it has found its way in other image processing inverse problems, including MR image reconstruction. The superiority of the U-Net is attributed to its capability in extracting features with different scales using upsampling (decoder) and downsampling (encoder) stages.

In [95] an encoder-decoder model has been provided for compressed sensing MR image reconstruction. The model has been evaluated using two different datasets. In another study, a wide multimodal U-Net [96] has been proposed for accelerating MRI reconstruction by working on the k-space data in the feed-forward path of encoding. Better perceptual quality has been gained by using this method. In [97], a deep residual U-Net is trained in the k-space domain to reduce the aliasing artifacts. In [52], Hyun et al. provided an improved U-Net based structure by applying a correction step in the k-space.

An increase in the number of convolutional layers and consequent deepening of networks leads to performance improvement. However, due to the concurrent

amplification of the number of parameters, the network becomes more susceptible to gradient loss, and the training procedure becomes prone to failure. Vanishing gradients during the training step hampers the parameter update in the backpropagation procedure [71]. The quest for deeper but still trainable networks motivated researchers to develop designs with an increased number of connections through the use of unrolled solutions, e.g. the cascade network of [37] for MRI reconstruction.

As another approach for the solution of the vanishing gradients problem, in [72] dense connections through densely connected blocks were introduced in the DenseNet setting. This block has found its way to other image processing problems. A hierarchical densely connected network was developed for image denoising in [74]. Converting the model to a hierarchical framework mitigates the memory consumption and alleviates the computational burden. In [73], DenseNet and ResNet were combined leading to the Residual Dense Network and densely connected residual blocks (DCRs). In another recent work, DenseNets have been used for segmentation problems using the encoder-decoder network [75]. In this work, the convolutional neural network in both the downsampling and upsampling stage has been replaced with DenseNets [75]. In yet another study, the dense connection was tested for a super-resolution problem in MRI [98]. In [99] on the other hand, convolutional layers were reused through a super-resolution CNN with dense skip connection.

Encouraged by these successful applications of dense connections, here we are leveraging the use of DCR blocks to the MRI reconstruction problem by using them inside residual convolutional neural networks (CNNs) and encoder-decoder type U-Nets. To the best of our knowledge, this forms the first use of DCR blocks in MR image reconstruction applications.

The application of DCR blocks enables us to make the network deeper and to increase the number of model parameters without the consequent training difficulties and vanishing gradient problems. The extracted feature maps in each step are carried to the following convolutional layers by successive concatenation operations. The qualitative and quantitative results point out that the reconstruction performance of the DCR infused deep networks are considerably enhanced when compared to their

original counterparts. The work as detailed in this chapter has been published as a journal paper [100].

4.2 Proposed Densely Connected Residual Network in MR Image Reconstruction

In our proposed framework (as detailed in Figs. 4.1 and 4.2), a single channel ZF image is fed as input into a convolutional neural network with L layers. The network includes non-linear convolutional layers indicated by the operator $\mathcal{F}_{\mathcal{L}}(\cdot)$. Here, $\mathcal{L}$ is the index of the particular convolutional layer.

$$\mathcal{F}_{\mathcal{L}}(x_i) = \lambda(W_i * x_i + b_i) \quad (4.1)$$

In the above equation, λ is the rectified linear unit (ReLU) activation function [101]. W_i indicates the i^{th} layer's weights, and b_i denotes the bias. Residual connections [13] add input and output and bypass the mapping function $\mathcal{F}_{\mathcal{L}}(\cdot)$ with a skip connection.

$$x_{\mathcal{L}} = \mathcal{F}_{\mathcal{L}}(x_{\mathcal{L}-1}) + x_{\mathcal{L}-1} \quad (4.2)$$

The dense connections [72] as shown in Fig. 4.3 concatenate successive convolutional layers' outputs. Hence, the $\mathcal{L}^{th}$ layer's input will include all the feature maps created by the previous convolutional layers.

$$x_{\mathcal{L}} = \mathcal{F}_{\mathcal{L}}([x_0, x_1, x_2, \dots, x_{\mathcal{L}-1}]) \quad (4.3)$$

The growth rate on the other hand can be defined as follows.

$$\mathcal{K} = k_0 + k \times (\mathcal{L} - 1) \quad (4.4)$$

Here, $\mathcal{K}$ is the number of input feature maps to the $\mathcal{L}^{th}$ layer. k is the number of feature maps created by $\mathcal{F}_{\mathcal{L}}$, and k_0 indicates the input channel size.

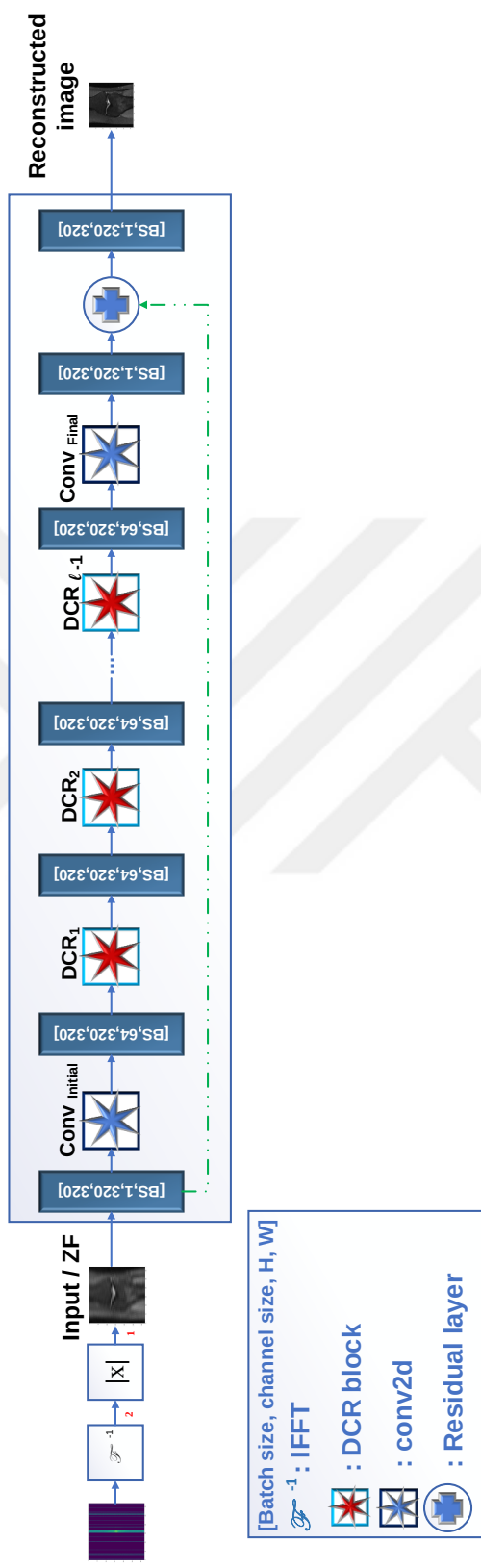


Figure 4.1 : Densely connected residual CNN with L layers.

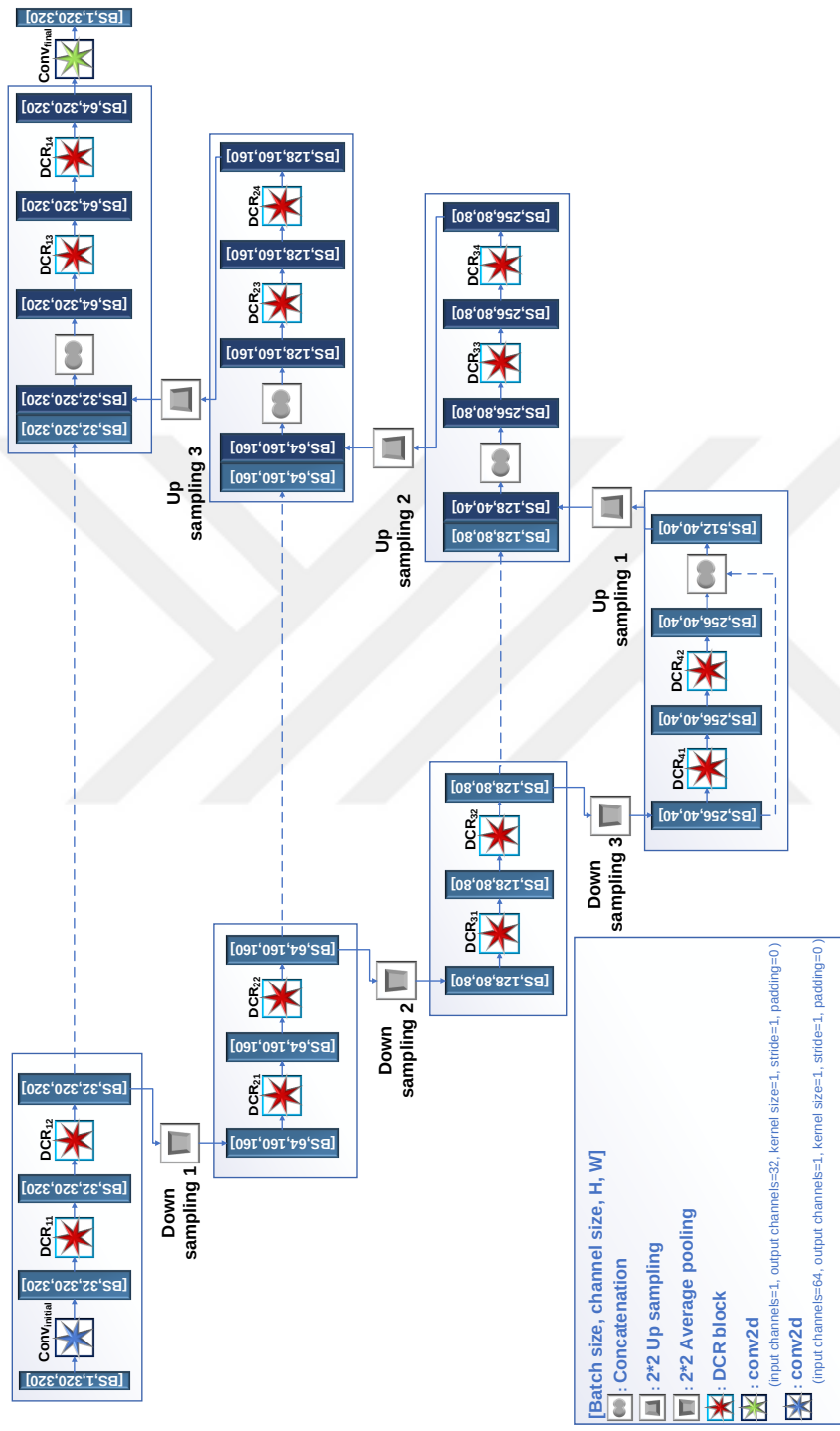


Figure 4.2 : Densely connected residual U-Net.

4.3 Architecture

4.3.1 Densely connected residual CNN based networks

Then, we modified standard CNN into a densely connected residual CNN by adding DCR Blocks as shown in Fig.4.1. In this new structure, the initial and final reconstruction layers are the same as the conventional setup without any change. The three central convolutional layers are replaced by three, eight, and ten DCR blocks. The DCR block as shown in Fig. 4.3 contains three convolutional layers that activate by the ReLU function. Inside DCR block, input and generated feature maps of all layers couple with each other and go through the final convolutional layer which generates 64 feature maps. In the last step, input and output feature maps are added together as a residual output [13].

4.3.2 Modified U-Net structure

Then we modified this structure to the one which has been used in [74] as a DensNet for image denoising problem (with fewer parameters to train). In this regard, we added an initial 1×1 convolutional layer that creates 32 feature-maps from one channel ZF image. The activation functions were changed to Parametric Rectified Linear Unit (PReLU). After final expansion, the final layer reconstructs the final image using only

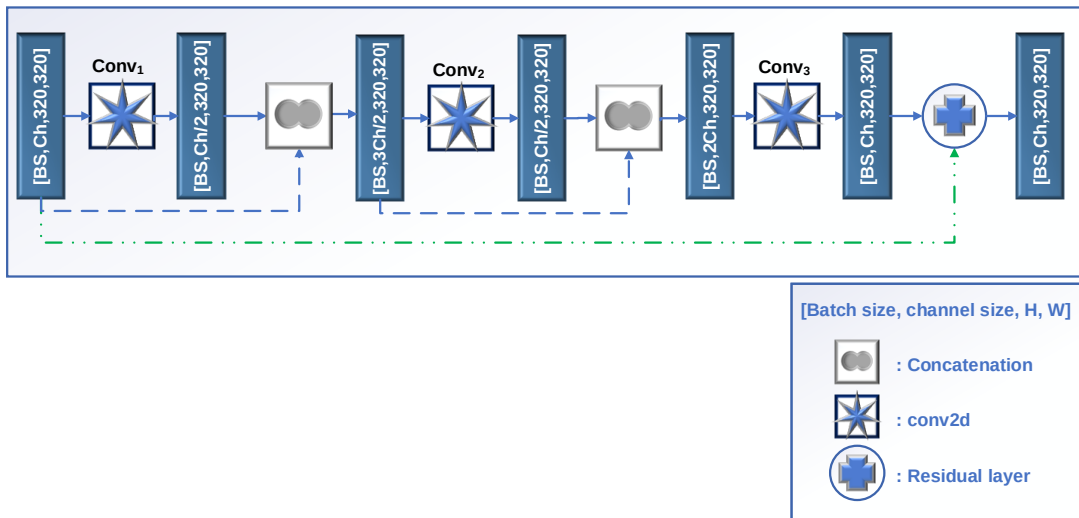


Figure 4.3 : Densely connected residual block.

one 1×1 convolutional layer with input and output channel sizes of 64 and one, respectively. Contrary to the FAIR U-Net, the encoder path reduces the size of the image up to 40×40 (not 20×20). In this U-Net framework, the downsampling is performed by the max-pooling operation. While the max-pooling function half the size of feature maps by stride 2, the convolutional layer doubles the number of feature maps to hinder feature loss. The upsampling path double the size of slices using the pixel-shuffle function with upscaling factor of two. So, as the result of using the sub-pixel interpolation method for the upsampling path, the number of feature maps is alleviated to one quarter. Thereafter, this U-Net pipeline was modified to densely connected residual U-Net as shown in Fig. 4.2. In this proposed structure, the convolutional blocks were replaced by the DCR block. Here, the DCR block again possesses three convolutional layers but these layers are followed by PReLU in contrary to densely connected residual CNN. We set the growth rate of our model to half size of the feature maps.



5. DEEP UNFOLDING ARCHITECTURE FOR MRI RECONSTRUCTION ENHANCED BY ADAPTIVE NOISE MAPS

5.1 Introduction of Adaptive Noise Map

Deep learning-based MR image reconstruction approaches can roughly be classified into unfolding-based [37,46,102]–[104] and non-unfolding-based techniques. Unfolding-based strategies usually begin with an assumed optimization problem the solution of which is a reconstructed image, and thereafter, they unfold an iterative optimization solution to a deep network. As an outcome, the steps arising from iterations are used to build the architecture of an unfolding-based model. CS reconstruction methodology is used in the majority of current unfolding-based deep-learning solutions. The optimization techniques are generally iterative in inherent. The deep-learning techniques based on unfolding provide an opportunity for a better understanding of the relationship between network architecture and efficiency [36]. For the first time, the primitive unrolling iterative network was offered by introducing the Alternating Direction Method of Multipliers (ADMM) [105] in 2016. ADMM-Net was developed based on CS-MRI to optimize the regularization parameters. Inspired by this successful application, researchers introduced novel structures by unrolling networks like Iterative Shrinkage-Thresholding Algorithm (ISTA) with the name of ISTA-Net [106]. At almost the same time, similar structures include Model-based reconstruction using Deep Learning prior (MoDL) [107], cascade CNN, and variational network [54] with the similar principles were introduced by different authors. Schlemper's study [37,38] was one of these deep iterative structures that garnered prominence in tackling the inverse problem of MR image reconstruction. A DC-CNN with DC segments is used in their proposed technique. The variational network [54] combined compressed sensing and deep learning methodologies to accelerate MR image reconstruction using an unrolled scheme. In study [28], the author utilized a variational Networks for variable-density single-shot fast spin-echo

MR imaging. Aggarwal *et al* proposed MoDL [107] by implementing the DC layer inside a variational network to reconstruct MR images in an unrolled platform. In a study, PD-Net was offered by unfolding the primal-dual hybrid gradient (PDHG) pipeline [108] to overcome inverse problems. In [27] another unfolding structure is proposed for cardiac MR image reconstruction. Convolutional recurrent neural networks (CRNN) makes advantage of spatial sequence dependencies as well as the iterative features of standard optimization techniques. later on, LANTERN [109] merged deep learning with the CS-MRI technique for dynamic MR imaging. LANTERN trained adaptively using small dataset with prior knowledge in transient and spars spatial domains. The concatenations of U-Nets have been offered in [110] with the term W-nets for MR image reconstruction. W-nets have been developed in dual-domain. Another unfolded model-based convolutional De-aliasing structure has been proposed for parallel MR imaging by Chen *et al* [111]. This de-aliasing network accelerated aggressively undersampled MRI reconstruction without apparent sensitivity computation. The author designed VS-Net (Variable splitting network) [112] by unfolding the obtained unrolling variable splitting optimization technique to implement a fast MR image reconstruction. In a study, a self-attention convolutional neural network (SAT-Net) was suggested by using a self-attention network and applying the data fidelity layer to the cartilage images [41]. Taking advantage of long-range dependencies, incorporating the DC layer and self-attention pathway into CNNs, effectually speeded up and improved their overall reconstruction result. Qiao *et al* [40] developed a compound unfolding architecture using the Approximate Message Passing (AMP) Algorithm. In comparison to other state-of-the-art MR image reconstruction techniques, they benefited both model-based and data-based methodologies without using the weight-sharing policy in each CNN layer. FFDNet for the first time is proposed by Kai Zhang *et al* [113] as a fast and flexible denoising CNN. The proposed denoiser, namely DRUNet, receives the noise level map as input and further incorporates residual blocks in to the U-Net. Zhang *et al* [103] proposed a Plug-and-Play Image Restoration (IR) model. Generally, plug-and-play IR entails two steps. The first step is an iterative framework that involves solving a data sub-problem and a prior sub-problem alternately. The second step is to use any denoisers to solve the

preceding sub-problem. As an outcome, unlike conventional model-based techniques, plug-and-play IR can use the denoiser to tacitly specify the prior.

Inspiring from unfolding structures, we tried to improve iterative-based models performance by adding an adaptive noise map called σ . To do so, the dissimilarity norm between the reconstructed MR image and the ZF image was used to quantify σ . We defined σ as a trainable parameter that is updated continuously same as the weights. The addition of this dimension to the undersampled input image enhanced the overall performance of the unfolding pipeline. Additionally, the work as given in this chapter has been submitted as a journal paper for possible publication.

5.2 Proposed Structure for Adaptive Noise Level Map

Before, feed forwarding the ZF image into the network we defined a zero-filled initial σ (σ_0) and applied it as a second channel to the input. In this study, we offered a new parameter σ . We defined it as follow:

$$\sigma_i = \frac{\|\tilde{x}_i - x_{zf}\|_F}{\sqrt{N \times M}} \quad (5.1)$$

In Algorithm 2, we provide an algorithmic description for the proposed unfolding structure described in this article. Where, $\mathcal{N}$ is the network that has been adjusted using a specific noise level parameter σ . Here x_i indicates the data consistency layer output.

Algorithm 2 The steps for proposed unfolding structure.

Initialization: $\sigma_0, x_0 = x_{zf}$

for $i = 1 : n - 1$ **do**

$\tilde{x}_i = \mathcal{N}_{\sigma_{i-1}}(x_{i-1})$

$\sigma_i = \frac{\|\tilde{x}_i - x_{zf}\|_F}{\sqrt{N \times M}}$

$x_i = \text{DC}(\tilde{x}_i, y)$

end for

$x_{\text{out}} = x_n$

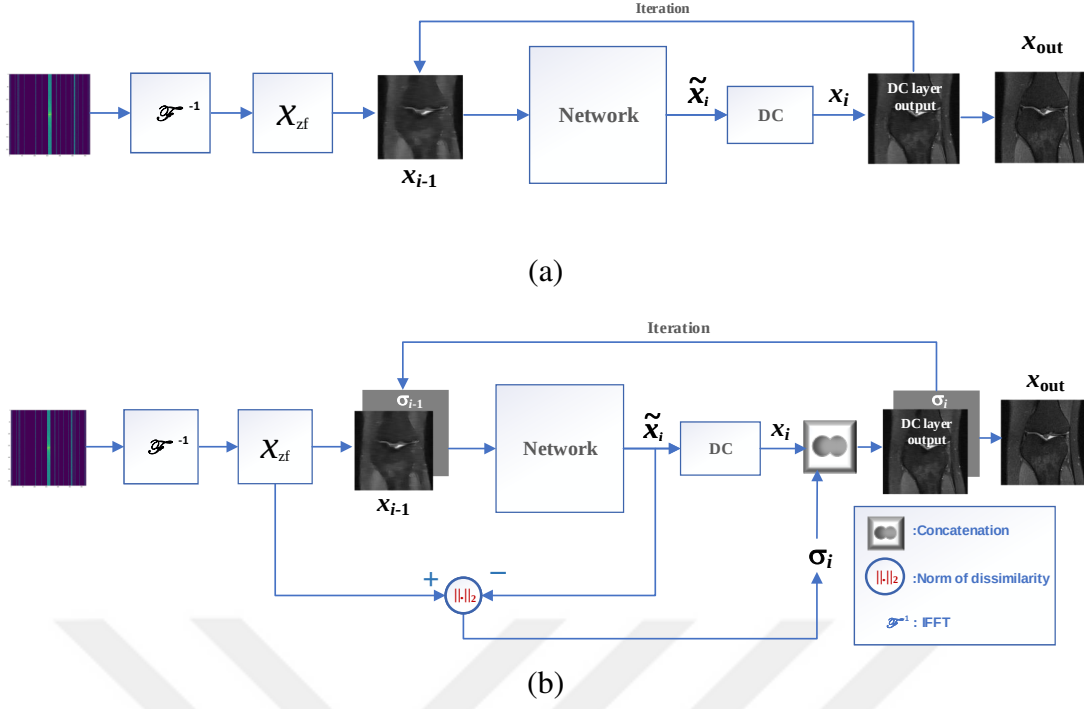


Figure 5.1 : (a) Conventional unfolding structure, (b) proposed unfolding structure.

5.3 Architecture

In this study, we have take advantage of two state-of-the-art models of U-Net and CNN. Conventional and novel proposed unfolding structure is represented in Fig. 5.1. As shown in Fig. 5.1, initially ZF image is created by applying IFFT to the undersampled k-space data. After calculating the absolute value of input tensors, ZF images are normalized. All images are then center cropped to 320×320 pixels to ensure that all slices from the dataset are the same size. Same as Fig. 5.1, these two models were unfolded by performing 5 iterations over each network and implementing the DC layer to each network output.

6. SIMULATION RESULTS

6.1 Dataset

Deep convolutional networks have been proven their performance versus competing state-of-the-art methods in various applications [114]. Hence deep learning based methodologies have found widespread usage, however, their applicability is challenged by the availability of training datasets for the particular application under consideration [93,115]. In the MRI reconstruction setting, some studies tried to solve this problem by eliminating the need for pretraining. As an example, [116] combines the DL-based model with compressed sensing ideas to reconstruct MR images without the need for pretraining, to alleviate the dependency on training datasets. In this reference-driven model, they improved the accuracy and reconstructed MR image quality by leveraging k-space data fidelity. However, the more common effective approach has been the creation and employment of MR image datasets for training deep learning based reconstruction structures aimed at accelerated MR image reconstruction.

The fastMRI dataset presents a very recent and rather complete example for an MR image dataset aimed at MRI reconstruction, complete with the training and testing code for a baseline network [60]. This dataset includes the data for different types of MR images in various formats. Both single and multi-coil images are included. The image data are stored in the form of fully sampled k-space information, reconstructed ground-truth images from the fully sampled data, and DICOM format images.

In this paper, we have employed the single-coil image dataset. There are a total of 1372 single-coil MRI image volumes in the fastMRI dataset. These volumes are divided into four groups of training, validation, test, and challenge subsets. Table 6.1 gives a rundown of the number of volumes and the total number of image slices in these four groups.

Table 6.1 : Data distribution in the fastMRI single-coil dataset [60].

Subset name	Volumes	Slices
Training	973	34742
Validation	199	7135
Test	108	3903
Challenge	92	3305

Each volume includes both the fully sampled k-space data and the corresponding fully sampled single-coil image reconstruction. We start our simulation from the fully sampled and real-valued ground truth images, by subsampling them in the k-space to model the MR data acquisition process. The ZF reconstructions from the subsampled data are used as the input to the networks. Undersampling is performed with three different acceleration strategies and two different masking schemes. Undersampling scenarios include the 4-fold subsampling, 8-fold subsampling, and the aggregate subsampling. In aggregate subsampling, the sampling ratio is randomly set to either four or eight with equal probability for each. Setting the acceleration factor (subsampling ratio) equal to four or eight will result in keeping only 25% or 12.5% of the k-space information, respectively. The ground truth image slices are employed as the target image of the networks, where the network backpropagation error is calculated as the L1 pixel-wise difference between the reconstructed image and target image.

In addition to the fastMRI dataset, we took advantage of the IXI dataset (<https://brain-development.org/ixi-dataset/>) [39,95] to test our trained models' robustness. This dataset includes slices from different types of tissue with different slice sizes compared to the fastMRI dataset.

6.2 Experimental Setup

For the reconstruction simulations of this paper, we utilized Python 3.6 together with Pytorch version 1.4.0. We took advantage of two GPUs in the form of GeForce RTX 2080 Ti with 11GB of memory for each. The batch size was selected as 16 for baseline U-Net and standard CNN realizations. However, the batch size was reduced to four in

the case of the unfolded networks. Meanwhile, the number of training epochs was set to 20, which was observed to be adequate for all of the different network realizations.

6.3 Evaluation Methodology

We tabulate the results evaluating the performance of the different models in the form of three metrics, which include normalized mean squared error (NMSE), peak signal to noise ratio (PSNR), and structural similarity index measure (SSIM). NMSE metric is calculated by measuring the pixel-wise difference between the ground truth and network output images. PSNR is evaluated as the ratio between the maximum possible power of the signal (image intensity across a volume) and the power of the distorting noise that affects the fidelity of its representation. SSIM on the other hand is a perceptual index that measures similarity between images by using mutual dependencies between neighboring pixels. NMSE between the network output image R_i and the desired output G_t is given by the following expression.

$$\text{NMSE}(R_i, G_t) = \frac{\|R_i - G_t\|_2^2}{\|G_t\|_2^2} \quad (6.1)$$

Here, $\|\cdot\|_2^2$ designates the squared Euclidean norm. The PSNR between R_i and G_t is defined as follows.

$$\text{PSNR}(R_i, G_t) = 10 \log_{10} \frac{\max(G_t)^2}{\text{MSE}(R_i, G_t)} \quad (6.2)$$

Here, $\text{MSE}(R_i, G_t)$ is the mean square error between R_i and G_t , which is given by:

$$\text{MSE}(R_i, G_t) = \frac{1}{n} \|R_i - G_t\|_2^2 \quad (6.3)$$

Here, n indicates the number of entries in the ground truth volume G_t . It should be mentioned that lower values for PSNR indicate inferior reconstruction. On the contrary, a lower value for NMSE shows better reconstruction. The SSIM between two image patches P_1 and P_2 is given by:

$$\text{SSIM}(P_1, P_2) = \frac{(2\mu_{P_1}\mu_{P_2} + C_1)(2\sigma_{P_1 P_2} + C_2)}{(\mu_{P_1}^2 + \mu_{P_2}^2 + C_1)(\sigma_{P_1}^2 + \sigma_{P_2}^2 + C_2)} \quad (6.4)$$

Here, μ_{P_1} and μ_{P_2} are the average pixel values of P_1 and P_2 , respectively. $\sigma_{P_1}^2$ and $\sigma_{P_2}^2$ on the other hand, are the corresponding pixel variances. Additionally, $\sigma_{P_1 P_2}$ indicate the covariance value between these two patches. C_1 and C_2 are defined as below to stabilize the division.

$$C_1 = (0.01L)^2 \quad (6.5)$$

$$C_2 = (0.03L)^2 \quad (6.6)$$

L is defined as:

$$L = \max(G_t) \quad (6.7)$$

6.4 Experimental Results

6.4.1 Results for projection-based unfolded U-Net model for MR image reconstruction

6.4.1.1 Quantitative results

In this work, we have implemented the standard CNN and its cascaded variant as used in [37,38]. Another important deep reconstruction paradigm from the literature, which we have realized is the baseline U-Net as implemented in the fastMRI framework [60]. In all of these models, we have employed the regular DC layer for the data fidelity block, as is done in all the original implementations. In addition to these models, we have also implemented the unfolded CNN with UDC layers acting as the linking blocks. The novel models advanced in this study are the unfolded U-Net structures, firstly with the regular DC layer and secondly with the updated DC layer as the linking intermediary blocks. The evaluated quantitative results include PSNR, SSIM, and NMSE. The results are tabulated in Tables 6.2 and 6.3, for different mask types

Table 6.2 : Simulation results for various models with random subsampling mask.

Acceleration	4-fold				8-fold				Aggregate				Runtime (s)
Network	Loss	NMSE	SSIM	PSNR	Loss	NMSE	SSIM	PSNR	Loss	NMSE	SSIM	PSNR	
Zero-filling	-	0.041	0.711	29.876	-	0.077	0.603	26.921	-	0.061	0.651	28.217	0
CNN [37]	0.308	0.034	0.755	30.880	0.451	0.069	0.637	27.462	0.386	0.054	0.688	28.867	0.34
CNN+DC	0.307	0.033	0.759	31.012	0.450	0.067	0.638	27.609	0.385	0.052	0.689	29.041	0.34
Cascade CNN [37,39]	0.280	0.026	0.790	32.412	0.417	0.054	0.654	28.639	0.355	0.042	0.715	30.152	1.75
Projection-based unfolded CNN [39]	0.272	0.0247	0.801	32.872	0.400	0.049	0.678	29.213	0.342	0.038	0.731	30.704	1.83
Baseline U-Net [60]	0.281	0.026	0.785	32.419	0.380	0.043	0.692	29.952	0.335	0.036	0.732	30.934	0.53
Baseline U-Net + DC layer (new)	0.270	0.024	0.801	32.968	0.373	0.040	0.701	30.307	0.326	0.033	0.744	31.358	0.55
Unfolded U-Net (new)	0.261	0.022	0.813	33.585	0.356	0.035	0.715	31.185	0.314	0.030	0.756	32.038	2.76
Projection-based unfolded U-Net (new)	0.260	0.022	0.816	33.685	0.355	0.035	0.719	31.251	0.310	0.029	0.761	32.231	2.77

Table 6.3 : Simulation results for various models with equispaced (uniform) Cartesian subsampling mask.

Acceleration	4-fold				8-fold				Aggregate				Runtime (s)
Network	Loss	NMSE	SSIM	PSNR	Loss	NMSE	SSIM	PSNR	Loss	NMSE	SSIM	PSNR	
Zero-filling	-	0.041	0.709	29.833	-	0.078	0.602	26.898	-	0.061	0.650	28.208	0
CNN	0.306	0.033	0.760	30.934	0.451	0.068	0.640	27.476	0.385	0.053	0.692	28.918	0.32
CNN+DC	0.303	0.032	0.769	31.028	0.450	0.067	0.641	27.624	0.384	0.051	0.694	29.079	0.33
Cascaded CNN	0.280	0.026	0.789	32.379	0.419	0.055	0.654	28.579	0.356	0.042	0.714	30.139	1.72
Projection-based unfolded CNN	0.271	0.024	0.802	32.894	0.399	0.048	0.678	29.217	0.342	0.038	0.731	30.713	1.85
Baseline U-Net	0.274	0.025	0.795	32.763	0.376	0.041	0.698	30.210	0.330	0.034	0.736	31.136	0.49
Baseline U-Net + DC layer	0.269	0.024	0.802	33.037	0.370	0.039	0.703	30.494	0.324	0.032	0.746	31.501	0.53
unfolded U-Net	0.259	0.022	0.816	33.680	0.356	0.035	0.718	31.267	0.312	0.029	0.757	32.168	2.91
Projection-based unfolded U-Net	0.258	0.021	0.818	33.760	0.353	0.034	0.722	31.383	0.309	0.029	0.762	32.326	3.10

and subsampling ratios. From these results, it becomes apparent that projection-based unfolded U-Net with UDC layers performs the best among all the evaluated variants, with the unfolded U-Net using DC layers coming as second. The unfolded U-Net with UDCs has improved performance in all of the calculated metrics. The offered novel methods improved the reconstruction results with respect to all three evaluation indices. This proposed network increases averagely the PSNR performance by almost 1.28 dB and 3.32 dB when compared to the baseline U-Net and the standard CNN, respectively. Furthermore, when we compare Tables 6.2 and 6.3, we notice that almost all of the models get better results with the equispaced, uniform masking function. We can deduce that these two tables verify each other's results when we compare the difference among models.

Note that in these tables, the metrics have been measured using the ground truth (fully sampled) image and the reconstructed image. The run-time has been evaluated for the joint reconstruction of a whole image volume with 32 slices. Additionally, it can be observed that the results obtained in Tables 6.2 and 6.3 verify each other. Furthermore, we have performed statistical assessment tests for the provided quantitative results.

The performed statistical tests include one-way analysis of variance (ANOVA) tests in addition to paired t -tests to confirm the statistical significance of the performance differences throughout all assessment metrics and setups. We set the threshold p -value at $\alpha=0.05$. The ANOVA test results indicated that the p -values for all simulation settings, including different masks, acceleration factors, and assessment metrics are less than a threshold of 0.01, indicating 99% confidence. Moreover, the introduced models' performances were also evaluated pair-wise against the competing CNN, cascade CNN and U-Net results using paired t -tests. The paired t -tests culminated overwhelmingly in p -values less than 0.05, suggesting 95% confidence in the simulation results of our proposed framework.

6.4.1.2 Qualitative results

Figs. 6.1, 6.2 and 6.3 display the reconstructed images by the aforementioned deep networks, for the cases of 8-fold, aggregate and 4-fold acceleration factors, respectively. All these images qualitatively verify the quantitative results as summarized in Table 6.2. We can see that the projection-based unfolding U-Net output images are of a higher perceptual quality than the reconstructed images by the other networks and details are recovered better.

6.4.2 Results for MR image reconstruction based on densely connected residual generative adversarial network

6.4.2.1 Quantitative results

In this study, we developed a novel GAN based structure for MR image reconstruction. We have trained the proposed models using the fastMRI dataset [60]. The fully-sampled k-space is undersampled using random mask function with 4-fold and 8-fold acceleration factors. The simulation results are summarized in Table 6.4 for both undersampling acceleration factors. In Table 6.4, we have evaluated the proposed models performance using three popular performance metrics, namely Normalized Mean Squared Error (NMSE), Peak Signal to Noise Ratio (PSNR) and Structural Similarity Index Measure (SSIM) [51]. As we can infer from Table 6.4, the

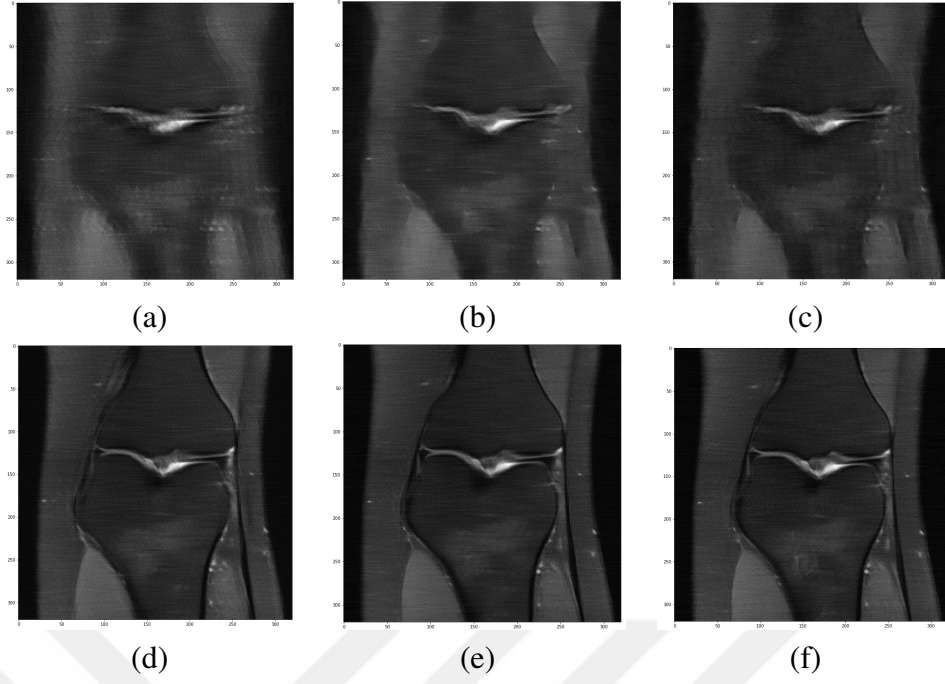


Figure 6.1 : Reconstructed images for 8-fold subsampling with random mask function in the case of (a) standard CNN, (b) cascaded CNN, (c) projection-based unfolded CNN, (d) U-Net baseline, (e) novel unfolded U-Net, (f) novel projection-based unfolded U-Net.

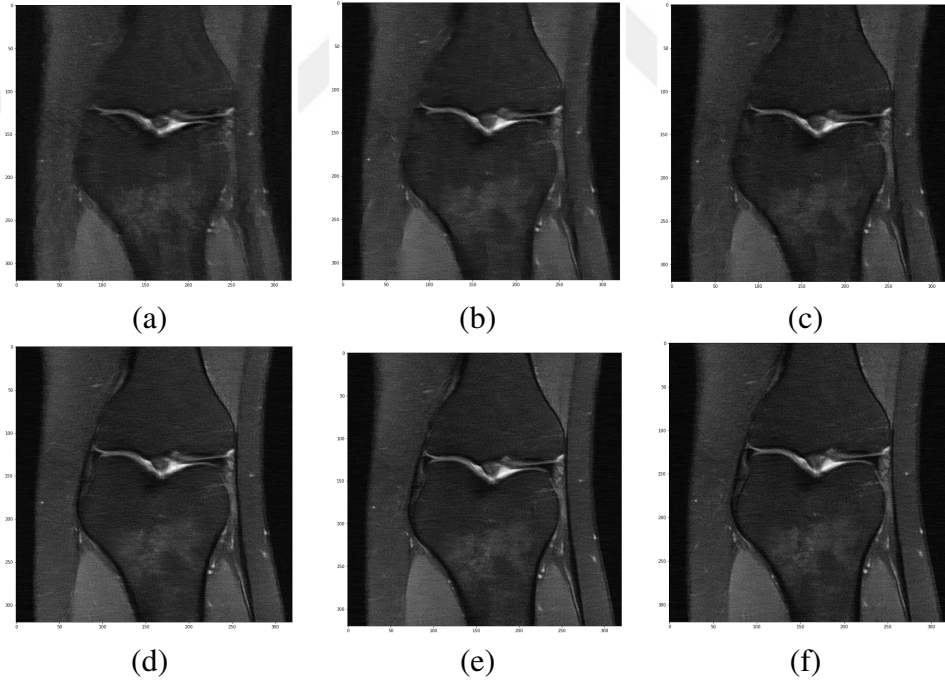


Figure 6.2 : Reconstructed images with random mask function for aggregate subsampling for (a) standard CNN, (b) cascaded CNN, (c) projection-based unfolded CNN, (d) U-Net baseline, (e) novel unfolded U-Net, (f) novel projection-based unfolded U-Net.

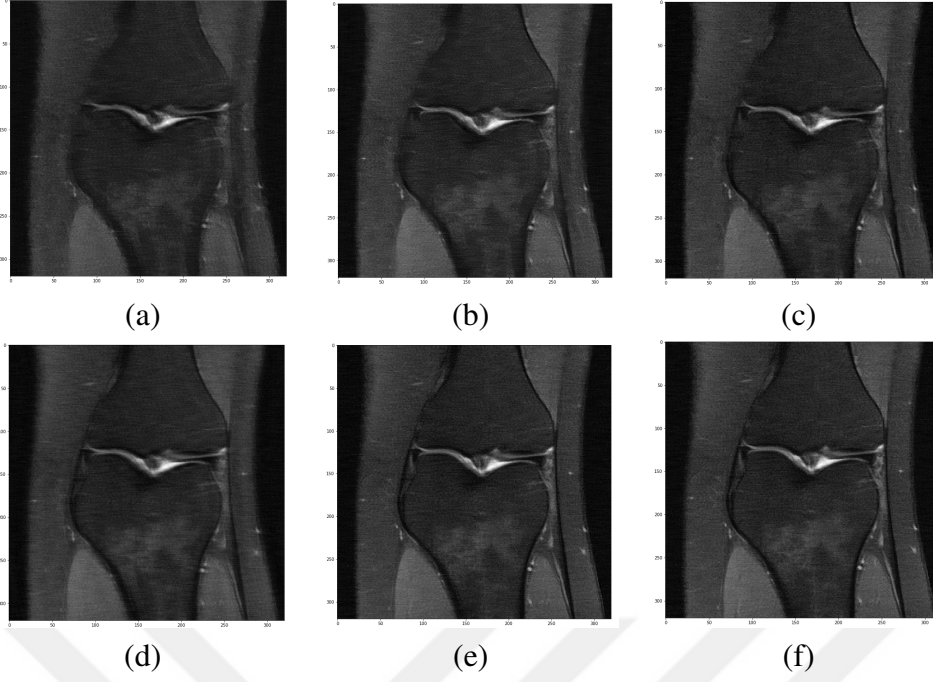


Figure 6.3 : Reconstructed images for 4-fold subsampling with random mask function in the case of (a) standard CNN, (b) cascaded CNN, (c) projection-based unfolded CNN, (d) U-Net baseline, (e) novel unfolded U-Net, (f) novel projection-based unfolded U-Net.

conventional GAN reconstruction results have been improved step by step. Initially, the generative network results have been boosted using the pre-trained VGG loss and application of the data consistency layer to the end of the network. Then the performance healing was continued by unfolding the GAN structure. The better performance was achieved by replacing the regular convolutional layers with DCR blocks. The conventional downsampling and upsampling layers were replaced by the DWT and IWT, respectively. Indeed, the best reconstruction result regarding all three evaluation metrics was attained by unfolding this wavelet-based GAN structure. With an even 8-fold aggressive acceleration factor, the suggested structure increased conventional GAN performance by about 2.62dB in terms of PSNR. We did not utilize the VGG loss while training the DCR-GAN. Although for DCR-GAN we have not applied VGG loss in training, this proposed method achieved promising results in terms of three indices. In addition to this model, we also implemented unfolding wavelet based GAN with DC layers acting as connection blocks. The proposed method achieved promising results for the three evaluation indices. From these results, it appears that the unfolding wavelet-based GAN performed the best among all evaluated

Table 6.4 : Simulation results for various models undersampled by 4-fold and 8-fold acceleration factor.

Acceleration		4-fold				8-fold				Time (s)
Network	Loss	NMSE($\times 10^{-3}$)	SSIM($\times 10^{-3}$)	PSNR	Loss	NMSE($\times 10^{-3}$)	SSIM($\times 10^{-3}$)	PSNR		
ZF	-	41.679	711.59	29.876	-	77.751	603.37	26.921	-	
GAN	0.308	34.317	755.26	30.894	0.451	69.212	637.63	27.466	0.09	
GAN with VGG	0.308	34.152	755.92	30.908	0.451	69.218	639.12	27.474	0.10	
GAN with VGG +DC	0.307	33.176	751.53	31.085	0.449	66.206	634.15	27.671	0.10	
GAN with 3DCR	0.297	31.273	766.34	31.413	0.432	62.106	651.63	27.972	0.29	
GAN with 3DCR +DC	0.299	30.925	759.57	31.501	0.432	59.189	643.37	28.208	0.30	
Unfolded GAN with VGG	0.306	32.443	746.86	31.276	0.436	60.472	632.79	28.123	0.46	
Wavelet based GAN	0.281	26.666	786.12	32.473	0.379	42.984	693.21	29.996	0.42	
Unfolded Wavelet based GAN	0.276	25.381	793.44	32.724	0.379	41.668	692.40	30.086	2.41	

variants. It should be noted that VGG loss was not applied to the wavelet-based GAN structure. Despite this factor, the proposed structure achieved promising results in terms of all three performance indices. In Table 6.4, the reconstruction time is provided for 32 test image slices. The required reconstruction times indicate that these methods are suitable for real-time clinical practice.

6.4.2.2 Qualitative results

In this section, the reconstructed images for all the realized methods for a particular test sample are visualized. The performance of the proposed networks is evaluated by comparing the quality of these output reconstructed images. Fig. 6.4 depicts the original image, the ZF images (undersampled data with 4-fold and 8-fold acceleration factors), resulting images for Conventional GAN and the proposed networks. As shown in Fig. 6.4 the baseline GAN has not fully recovered the details while the proposed networks reconstructed images have better perceptual quality, and they have restored more detail and patterns. Moreover, the proposed structures resulting images have less severe artifacts, and most of the blurring defects have been removed. The quantitative results provided in Table 6.4 confirm the reconstructed images which are provided in Fig. 6.4.

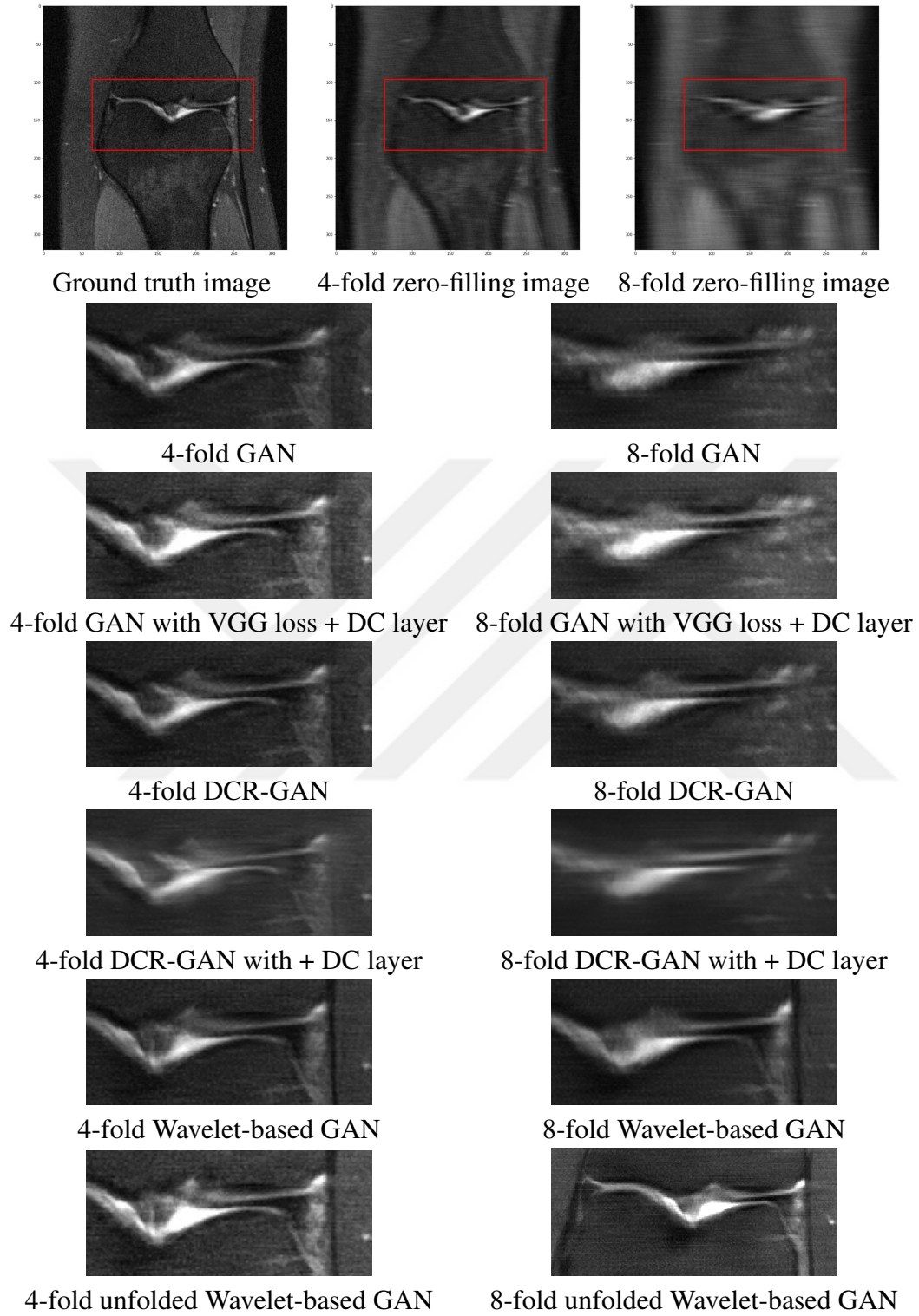


Figure 6.4 : Reconstructed images for 4-fold and 8-fold undersampling with random mask function.

6.4.3 MR image reconstruction using densely connected residual convolutional networks

6.4.3.1 Quantitative results

In current work, we have performed realization for the two novel DCR based networks in addition to various state-of-the-art MR image reconstruction methodologies from the literature. To evaluate the performance of the networks, Normalized Mean Squared Error (NMSE) [117], Structural Similarity Index Measure (SSIM) [118], and Peak Signal to Noise Ratio (PSNR) [119] indices have been used. The results are reported in Tables 6.5 and 6.6, where the methods are ordered with respect to increasing performance. These two tables summarize the simulation results for all the trained networks for both 4-fold and 8-fold acceleration factors. In the preprocessing step, fully-sampled k-space data is undersampled by the random subsampling mask. Afterwards, the data is transformed to the image domain by applying the 2D Inverse Fast Fourier transform (2D-IFFT).

As illustrated in Tables 6.5 and 6.6, the addition of DCR blocks leads to promising results and improved MR image reconstruction performance for both U-Net [60] and standard CNN. Appending 10 DCR blocks to the standard CNN improves reconstruction PSNR about 1.25 dB. It can be noticed that as CNN gets deeper by the addition of more DCR blocks, its results improve in all of the performance metrics. Increasing the number of the DCR blocks in general improves the reconstruction results. However, it was experimentally observed that the addition of more than 10 DCR blocks with the same training hyperparameters resulted in neglectable progress. The densely connected residual U-Net includes a total of 14 DCR blocks. U-Net with DCR is faster than the DCR-CNN in the testing phase, despite its larger number of network parameters. DCR-CNN performs its computations in all convolutional layers on feature maps of a constant pixel size (320×320) without downsampling them. Hence, this leads to slightly reduced reconstruction speed for the DCR-CNN when compared with the DCR based U-Net.

Table 6.5 : Simulation results for fastMRI dataset for 4-fold acceleration factor.

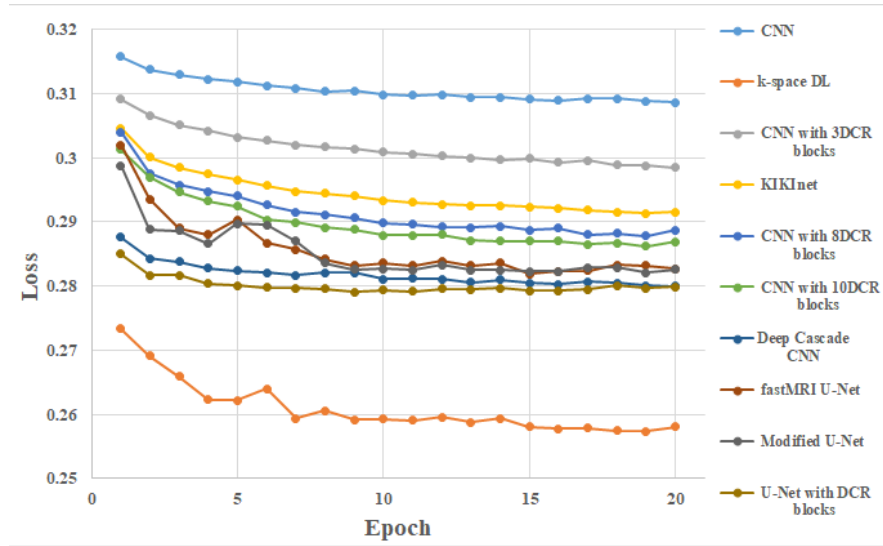
Acceleration factor	4-fold				#Parameter	Time (s)
Network	Loss	NMSE (x10-3)	SSIM(x10-3)	PSNR		
ZF	-	41.679	711.59	29.876	-	-
CS-MRI (TV based) [60,120]	-	36.719±43.52	712.25±224.31	30.846±5.78	-	138.31
CNN [37,38]	0.308	34.259±17.43	755.65±78.76	30.880±2.49	111,744	0.09
k-space DL [51]	0.257	32.060±18.92	763.45±79.35	31.273±2.66	7,756,418	0.17
CNN with 3 DCR blocks	0.298	31.344±17.62	765.97±82.16	31.402±2.69	360,960	0.28
KIKI-net [32,62]	0.291	31.297±17.33	766.52±81.23	31.419±2.78	1,168,128	0.78
CNN with 8 DCR blocks	0.287	28.426±18.09	778.68±84.93	32.038±2.98	960,640	0.73
CNN with 10 DCR blocks	0.286	28.042±18.15	780.73±85.04	32.133±3.03	1,200,512	0.92
Deep Cascade CNN [37,38]	0.280	26.520±18.61	790.00±85.15	32.412±3.14	111,744	0.41
fastMRI U-Net [60,62]	0.281	26.821±18.18	785.93±86.16	32.419±3.17	7,756,097	0.15
Modified U-Net	0.282	26.637±18.25	784.77±85.28	32.466±3.17	6,618,597	0.45
U-Net with DCR	0.279	25.961±18.20	790.14±86.15	32.651±3.27	10,516,083	0.79

Table 6.6 : Simulation results for fastMRI dataset for 8-fold acceleration factor.

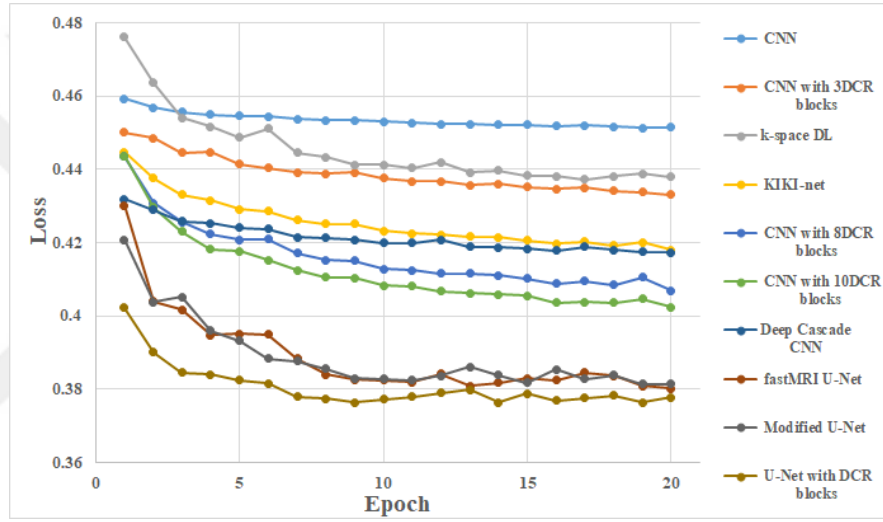
Acceleration	8-fold				#Parameter	Time (s)
Network	Loss	NMSE (x10-3)	SSIM(x10-3)	PSNR		
ZF	-	77.751	603.37	26.921	-	-
CS-MRI (TV based) [60,120]	-	71.921±44.66	608.92±242.23	27.351±4.13	-	134.65
CNN [37,38]	0.451	69.277±19.88	637.76±100.66	27.462±2.01	111,744	0.09
CNN with 3 DCR blocks	0.433	62.360±19.59	650.92±104.83	27.953±2.08	360,960	0.28
KIKI-net [32,62]	0.431	62.103±19.41	644.20±103.54	28.020±2.11	1,168,128	0.78
k-space DL [51]	0.437	58.376±21.89	651.80±103.98	28.292±2.07	7,756,418	0.17
CNN with 8 DCR blocks	0.406	52.318±21.54	670.19±112.73	28.857±2.22	960,640	0.73
CNN with 10 DCR blocks	0.402	50.766±21.94	672.01±115.39	29.026±2.28	1,200,512	0.92
Deep Cascade CNN [37,38]	0.417	54.827±23.25	654.92±113.77	28.639±2.24	111,744	0.41
fastMRI U-Net [60,62]	0.380	43.275±23.47	692.96±118.22	29.952±2.55	7,756,097	0.15
Modified U-Net	0.381	43.234±23.36	691.95±117.12	29.950±2.55	6,618,597	0.50
U-Net with DCR	0.376	41.605±23.67	699.77±117.36	30.198±6.51	10,516,083	0.80

The acquired quantitative results have been compared using statistical assessment tests. To do so, one-way analysis of variance (ANOVA) tests and paired t -tests were applied to verify statistically significant differences among developed networks and their related assessment metrics. These two tests can prove that the acquired reconstruction results are attributed to a specific cause and they are not provided by chance or randomly. In this evaluation, threshold p -values are set to $\alpha=0.05$. For the proposed pipelines, the paired t -tests ended up with the overwhelming suggestion of 95% confidence (p -values ≤ 0.05). The ANOVA test results reported more than 99% confidence by indicating p -values ≤ 0.01 for all the proposed methods, in all different settings including different assessment metrics and acceleration factors.

The testing error loss curves are presented in Figs. 6.5(a) and 6.5(b). In general, this curve gives an idea of how well the model is generalizing through the validation/testing steps. As we can see, the loss value decreases with the increasing number of epochs



(a)



(b)

Figure 6.5 : Testing phase loss curves depending on the epochs; (a) undersampled data with 4-fold acceleration factor (b) undersampled data with an 8-fold acceleration factor.

and converges to a stable point. Moreover, the application of DCR blocks significantly reduced the resulting loss amplitude, when compared to the structures which lack the DCR blocks.

In Fig. 6.6, run time versus PSNR values are given for both the developed networks and also the networks used for comparison. The given time values indicate the time needed for reconstructing 32 slices in the testing phase. It can be concluded that all these frameworks with noticeable reconstruction results can get realized in a real-time

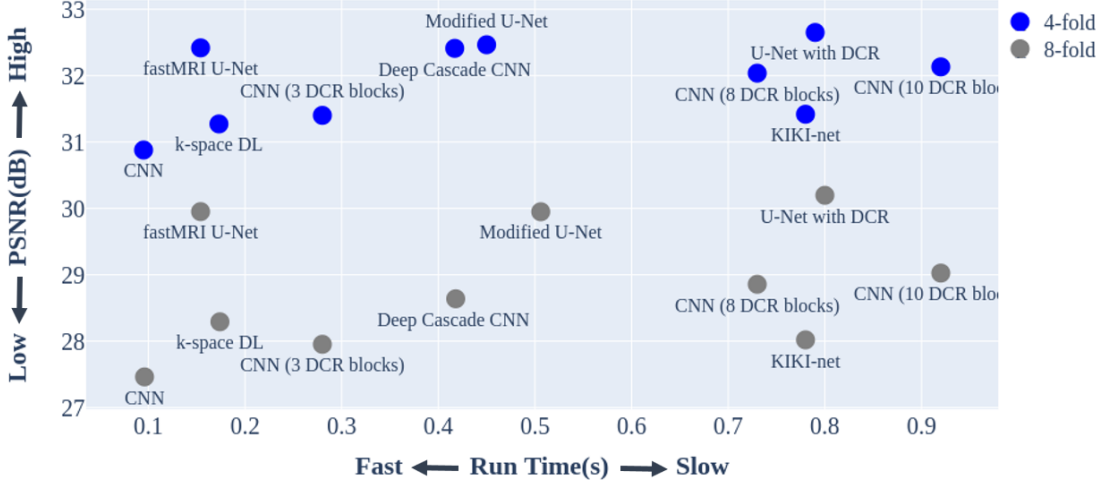


Figure 6.6 : The run time vs. PSNR value of different models.

setting. It can also be seen that the results given for the 4-fold and 8-fold settings complement each other naturally.

The robustness of the proposed structures is emphasized by testing these networks using another dataset. In addition to the benchmark fastMRI dataset, we have tested our trained models using yet another comparatively common dataset, namely the IXI dataset. This dataset contains around 615 lateral brain MR image volumes. Each volume includes 150 real-valued slices of the size 256×256 . The results for the IXI dataset are summarized in Tables 6.7 and 6.8. These results indicate that, the proposed novel models can reconstruct MR images from different parts of the body without the need for retraining. Testing the developed models with the IXI dataset has verified that the proposed novel structures can maintain their improved reconstruction results in comparison to cutting-edge networks. Moreover, the variation of the test dataset size from the training dataset did not affect these structures.

6.4.3.2 Qualitative results

In this study, also a fair qualitative comparison was performed between reconstructed images by two state-of-the-art deep learning models and their densely connected residual form. Figs. 6.7 and 6.8 display the real image, ZF image, Region of Interest (ROI) and error map for images reconstructed by these frameworks. Fig. 6.7 provides the resulting images for undersampled data with 4-fold acceleration factor, whereas Fig. 6.8 is for undersampled data with 8-fold acceleration factor. As we expected

Table 6.7 : Simulation results for IXI dataset for 4-fold acceleration factor.

Acceleration factor	4-fold				#Parameter	Time (s)
Network	Loss	NMSE (x10-3)	SSIM(x10-3)	PSNR		
ZF	-	50.427	727.39	28.078	-	-
CNN [37,38]	0.189	39.281±4.79	751.86±37.03	29.164±1.64	111,744	0.220
k-space DL [51]	0.122	38.011±6.38	758.72±39.62	29.454±1.73	7,756,418	0.485
CNN with 3 DCR blocks	0.181	35.935±4.43	762.43±36.00	29.554±1.66	360,960	0.393
KIKI-net [32,62]	0.174	36.440±5.68	777.40±34.07	29.513±1.70	1,168,128	0.504
CNN with 8 DCR blocks	0.166	31.100±3.58	791.20±29.13	30.176±1.62	960,640	0.416
CNN with 10 DCR blocks	0.165	30.474±3.48	792.65±29.69	30.263±1.62	1,200,512	0.546
Deep Cascade CNN [37,38]	0.164	29.814±4.35	801.91±25.82	30.365±1.73	111,744	0.325
fastMRI U-Net [60,62]	0.162	29.232±3.17	802.21±33.38	30.445±1.61	7,756,097	0.151
Modified U-Net	0.168	30.056±3.17	801.79±39.44	30.320±1.59	6,618,597	0.502
U-Net with DCR	0.164	28.287±3.09	806.03±38.27	30.586±1.59	10,516,083	0.505

Table 6.8 : Simulation results for IXI dataset for 8-fold acceleration factor.

Acceleration factor	8-fold				#Parameter	Time (s)
Network	Loss	NMSE (x10-3)	SSIM(x10-3)	PSNR		
ZF	-	97.763	632.04	25.211	-	-
CNN [37,38]	0.296	90.867±13.20	636.31±50.29	25.523±1.80	111,744	0.221
CNN with 3 DCR blocks	0.283	85.317±11.49	654.08±48.94	25.791±1.76	360,960	0.393
k-space DL [51]	0.295	88.093±14.28	640.11±52.95	25.601±1.81	7,756,418	0.481
KIKI-net [32,62]	0.281	83.825±10.66	663.46±54.12	25.868±1.72	1,168,128	0.504
CNN with 8 DCR blocks	0.271	82.235±10.17	680.08±43.45	25.943±1.67	960,640	0.477
CNN with 10 DCR blocks	0.266	78.691±10.03	680.87±43.31	26.136±1.67	1,200,512	0.550
Deep Cascade CNN [37,38]	0.262	73.726±11.33	689.13±42.32	26.335±1.74	111,744	0.327
fastMRI U-Net [60,62]	0.263	77.472±10.05	684.72±47.74	26.209±1.69	7,756,097	0.151
Modified U-Net	0.273	76.996±10.09	684.79±51.37	26.237±1.70	6,618,597	0.502
U-Net with DCR	0.261	71.911±8.64	696.49±46.59	26.529±1.63	10,516,083	0.505

from Tables 6.5 and 6.6, these figures show that the densely connected residual models restore more detail and pattern whereas the other methods reconstructed more blurred images.

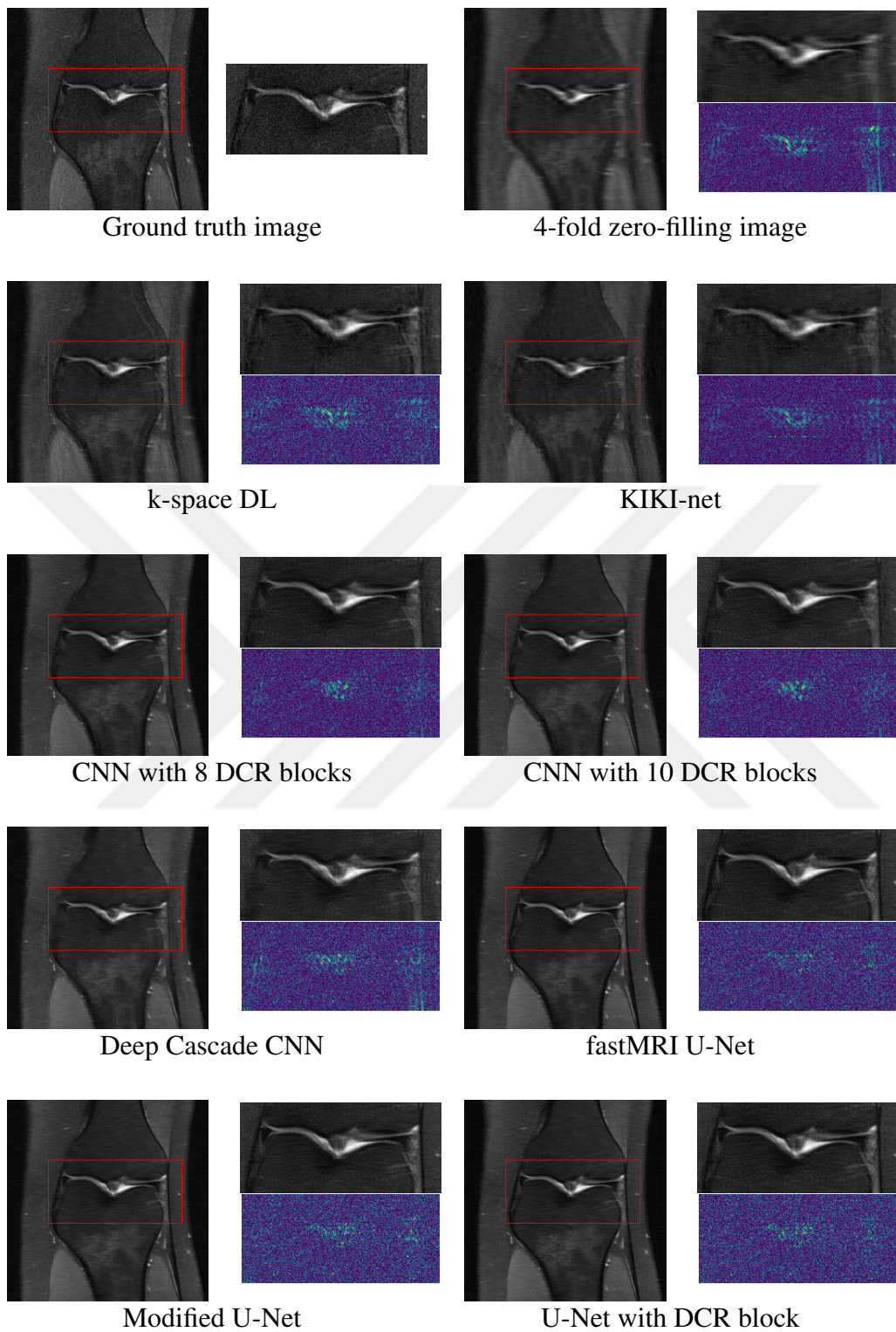


Figure 6.7 : Developed model's reconstruction results, ROI, and error maps for 4-fold undersampled data.

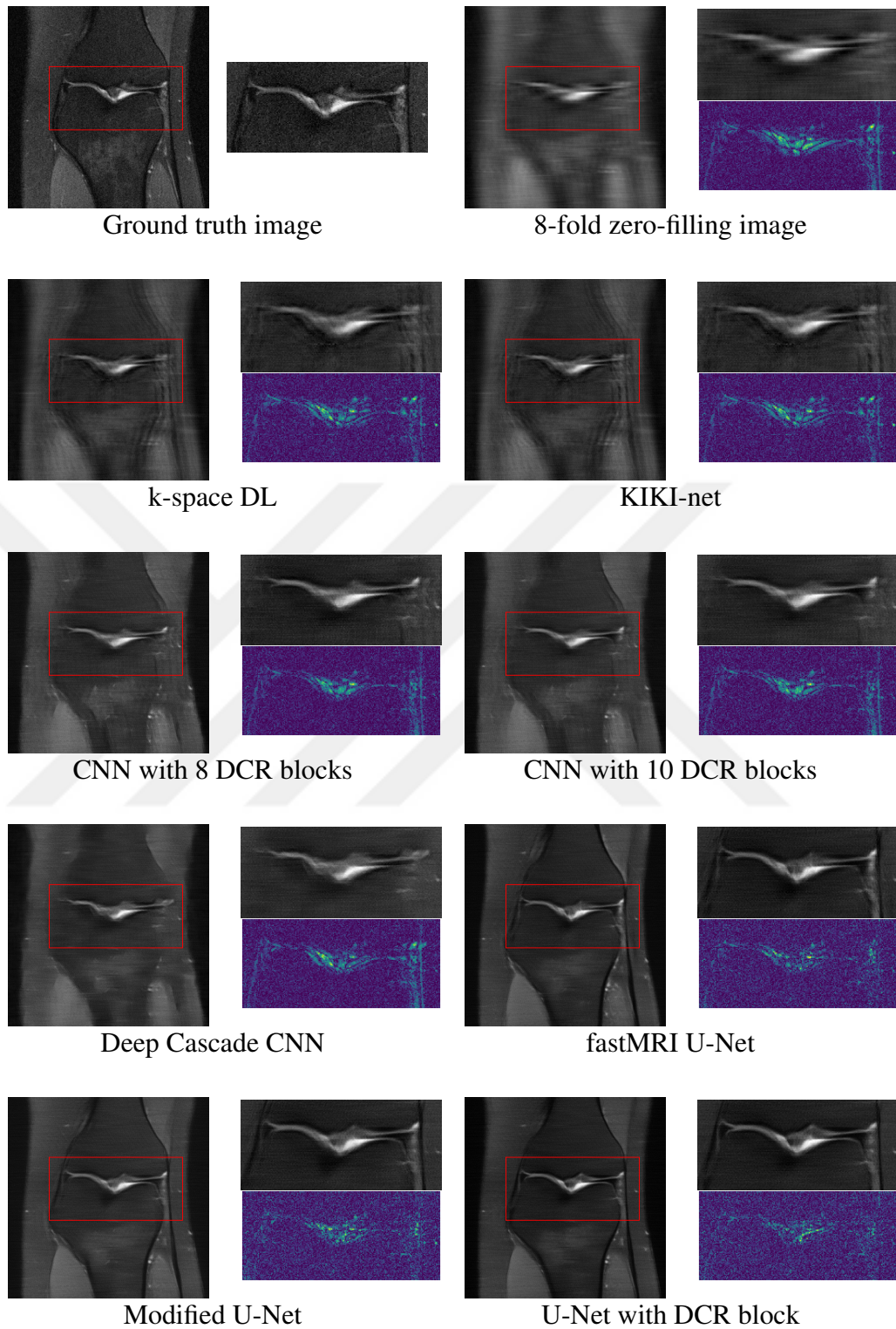


Figure 6.8 : Developed model's reconstruction results, ROI, and error maps for 8-fold undersampled data.

Table 6.9 : Reconstructed image’s PSNR improvement compared to the ZF image.

Network	Acceleration factor	
	4-fold	8-fold
PSNR difference (CNN - ZF)	1.004	0.541
PSNR difference (CNN with 10 DCR blocks - ZF)	2.257	2.105
PSNR difference (U-Net with DCR bloks – ZF)	2.775	3.277

As discussed in the introduction section of this study, the major goal of MR image reconstruction based on deep learning is to speed up MR image reconstruction. To do so, we need to decrease signal acquisition time without significantly reducing image quality. In this regard, more aggressive undersampling with larger acceleration factors are also performed. Deep learning-based advanced methodologies are very effective in fast and high-quality image reconstruction from this reduced acquired data.

In this study, we have trained the deep models by using ZF images as inputs. For the undersampling of k-space data 4-fold and 8-fold acceleration factors have been used. The below table summarizes the PSNR improvements of the reconstructed images when compared to the initial ZF estimate for both 4-fold and 8-fold undersampling cases.

The results in Table 6.9 indicate that the proposed networks are capable to reconstruct high-quality images even with the more aggressive undersampling rates. For both 4-fold and 8-fold undersampling, the proposed frameworks result in significantly better images compared to the ZF estimates.

6.4.4 Results for deep unfolding architecture for MRI reconstruction enhanced by adaptive noise maps

6.4.4.1 Quantitative results

In current work, we have proposed a novel trainable parameter. We enforced this phenomenon into the unfolding structure of state-of-the-art pipelines. A random subsampling function with 4-fold and 8-fold acceleration factor was used to undersample the fully-sampled slices in k-domain. The results of developed simulations and their standard deviations are reported in Tables 6.10 and 6.11 for

Table 6.10 : Simulation results for 4-fold acceleration factor.

Acceleration	4-fold				#Parameter	Time (s)
Network	Loss	NMSE (x10-3)	SSIM(x10-3)	PSNR		
ZF	-	41.679	711.59	29.876	-	-
CNN [37]	0.308	34.259±17.43	755.65±78.76	30.880±2.49	111,744	0.095
Deep Cascade CNN [37]	0.280	26.520±18.61	790.00±85.15	32.412±3.14	111,744	0.417
Unfolding CNN with σ map	0.274	25.225±17.38	797.65±82.30	32.762±3.29	112,896	0.487
U-Net [60,102]	0.281	26.821±18.18	785.93±86.16	32.419±3.17	7,756,097	0.151
Unfolding U-Net [102]	0.261	22.489±17.29	813.83±83.73	33.585±3.72	7,756,097	0.913
Unfolding U-Net with σ map	0.260	22.360±17.28	815.62±83.71	33.631±3.74	7,756,418	1.032

Table 6.11 : Simulation results for 8-fold acceleration factor.

Acceleration	8-fold				#Parameter	Time (s)
Network	Loss	NMSE (x10-3)	SSIM(x10-3)	PSNR		
ZF	-	77.751	603.37	26.921	-	-
CNN [37]	0.451	69.277±19.88	637.76±100.66	27.462±2.01	111,744	0.095
Deep Cascade CNN [37]	0.417	54.785±22.32	655.84±112.67	28.639±2.20	111,744	0.417
Unfolding CNN with σ map	0.405	50.772±22.59	670.04±113.30	29.037±2.30	112,896	0.487
U-Net [60,102]	0.380	43.275±23.47	692.96±118.22	29.952±2.55	7,756,097	0.151
Unfolding U-Net [102]	0.356	35.791±24.64	715.45±125.47	31.185±3.19	7,756,097	0.913
Unfolding U-Net with σ map	0.355	35.589±24.43	717.78±124.31	31.267±3.12	7,756,418	1.032

two undersampling acceleration factor. The proposed novelty improved reconstruction results based on PSNR, NMSE, and SSIM indices. The concatenation of adaptive noise parameter to the input image simply enhanced the reconstruction results of prominent and robust unfolded structures of CNN [37] and U-Net [102]. By comparing suggested structures with deep cascade CNN and unfolded U-Net, we can see that the network performance has improved without a significant increase in parameter quantity and computational costs, and this fact ended in a minor increase in time. In both of the result tables, the best performance belongs to the unfolded U-net structure with an adaptive noise level parameter. We can observe an almost 3.8 dB improvement in unfolded U-net structure with σ in comparison to the conventional CNN with an even 8-fold aggressive acceleration factor. The reconstruction results in these two tables verify each other as soon as we calculate the amount of improvement between the proposed architecture and other developed pipelines. The time for reconstruction of 32 slices using developed models are provided. These reconstruction timeframes are appropriate for real-time clinical applications.

In this work, we used statistical evaluation tools to assess the acquired quantitative results. To do so, One-way analysis of variance tryouts and paired t -tests were used to confirm the statistical significance of the simulated models in terms of all evaluation

Table 6.12 : ANOVA (one-way analysis of variance) results.

Acceleration factor	<i>p</i> -value			Result
	NMSE	SSIM	PSNR	
4x	3.01E-10	2.71E-14	1.34E-20	H ₀ rejected
8x	2.43E-45	1.06E-12	2.33E-48	H ₀ rejected

indices and configurations. In this setup, the threshold p -value is set as $\alpha = 0.05$. In Table 6.12, the ANOVA test findings reveal more than 99% reliability for both of acceleration factors and all evaluation metrics. As indicated in result section of Table 6.12, the null hypothesis, which states that the population means of the different networks are identical, is rejected. In addition, the effectiveness of the proposed models was assessed pair-wised in comparison to that of state-of-the-art structures by t -test. The paired t -tests yielded p -values less than the threshold value of 0.05, indicating more than 95 percent reliability in our suggested structures.

In Fig. 6.9, the σ evolution were given for each iteration of unfolding structure. In this figure, each point indicates the average σ value for all slices of full dataset in a specified epoch of training. As we can see σ value evolve through each iteration and training epoch with almost similar growth rate and slop. Moreover, The σ value in the test step over each iteration overlaps through similar boundaries with the last epoch of the training step.

6.4.4.2 Qualitative results

This section provides a visualized analogy between the proposed novel structures and state-of-the-art networks. Fig. 6.10 depicts a specific slice in the K-domain and subsampled representations of the same slice with 4-fold and 8-fold acceleration factors. One particular reconstructed image from the test sample is displayed in this section. The suggested models' performance was assessed by making a comparison of their generated images. The reconstruction results are demonstrated in Fig. 6.11 and 6.12. These figures also include the ground-truth, ZF images, Region of Interest (ROI) and error map. Apparently, the proposed unfolding structures are recovered more patterns and presented richer perceptual quality. Furthermore, the suggested designs' output images have fewer significant artifacts and the majority of the blurring

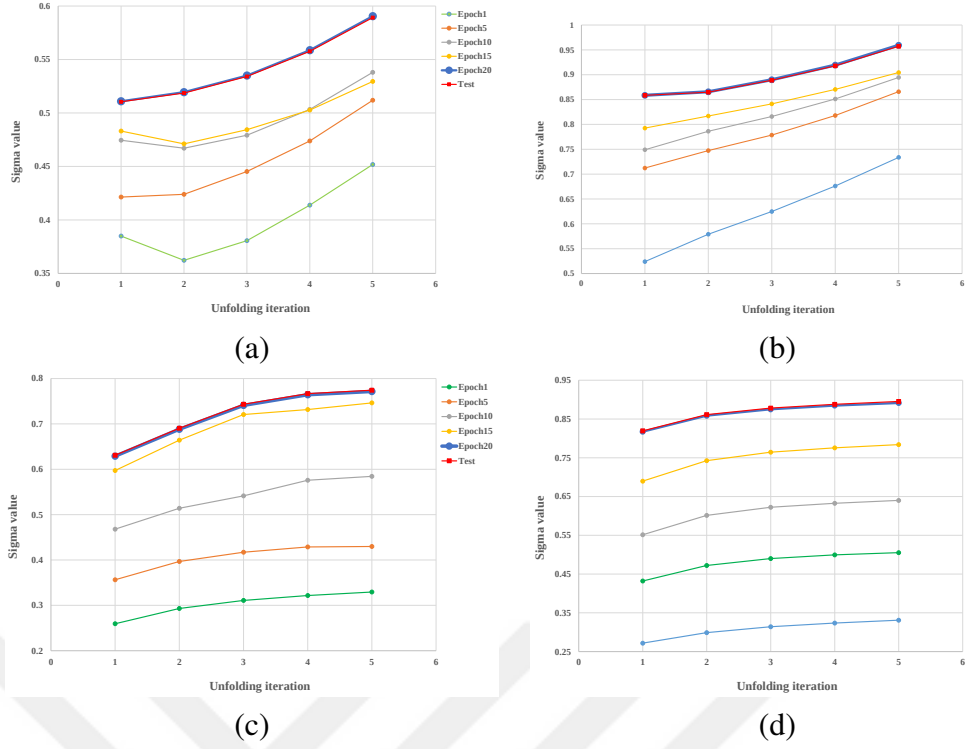


Figure 6.9 : Sigma evolution during the iterations: (a) unfolding CNN for 4-fold acceleration factor, (b) unfolding CNN for 8-fold acceleration factor.

issues have been addressed. As can be observed, the quantitative findings in Tables 6.10 and 6.11 match the reconstruction results in Figs. 6.11 and 6.12.

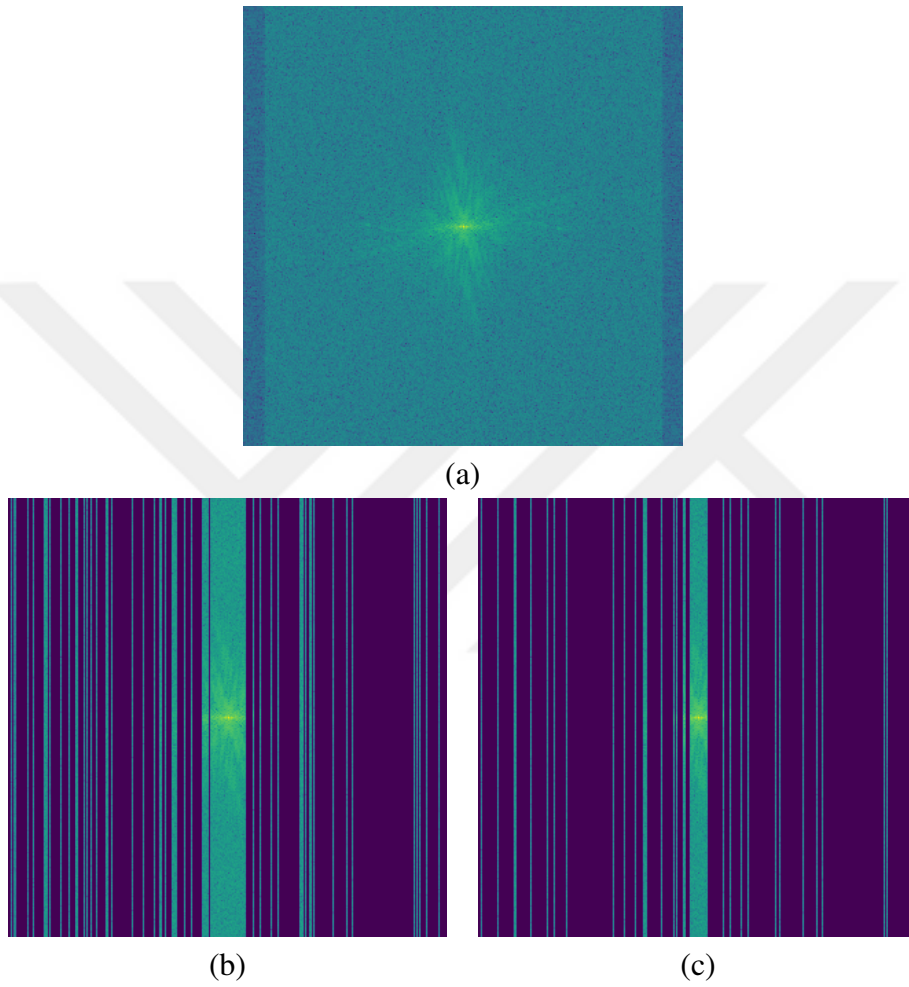


Figure 6.10 : Specific k-domain examples: (a) k-space, (b) subsampled k-space data with 4-fold acceleration factor, (c) subsampled k-space data with 8-fold acceleration factor.

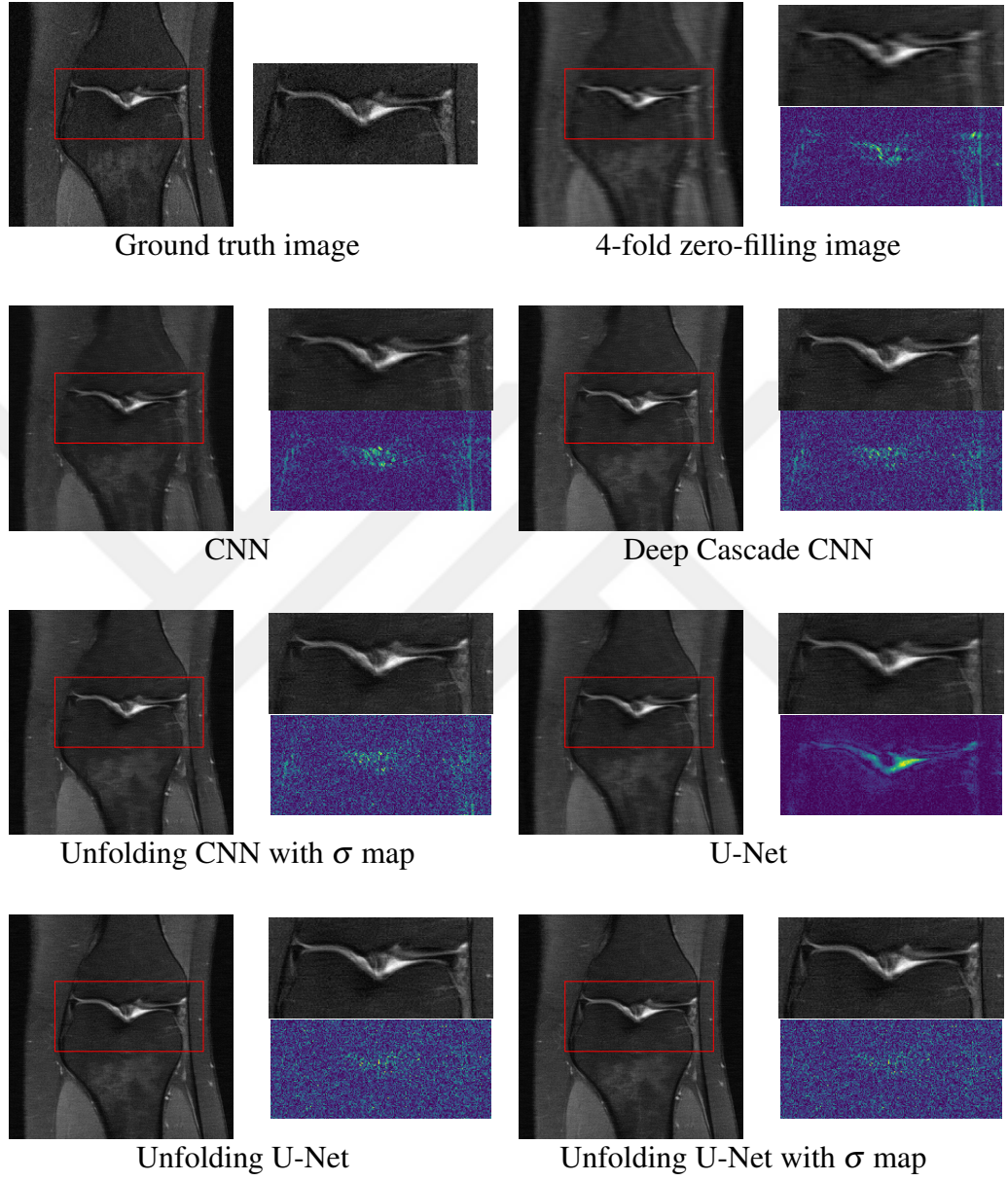


Figure 6.11 : Proposed techniques' reconstructed images, ROI, and error maps for 4-fold undersampled slices.

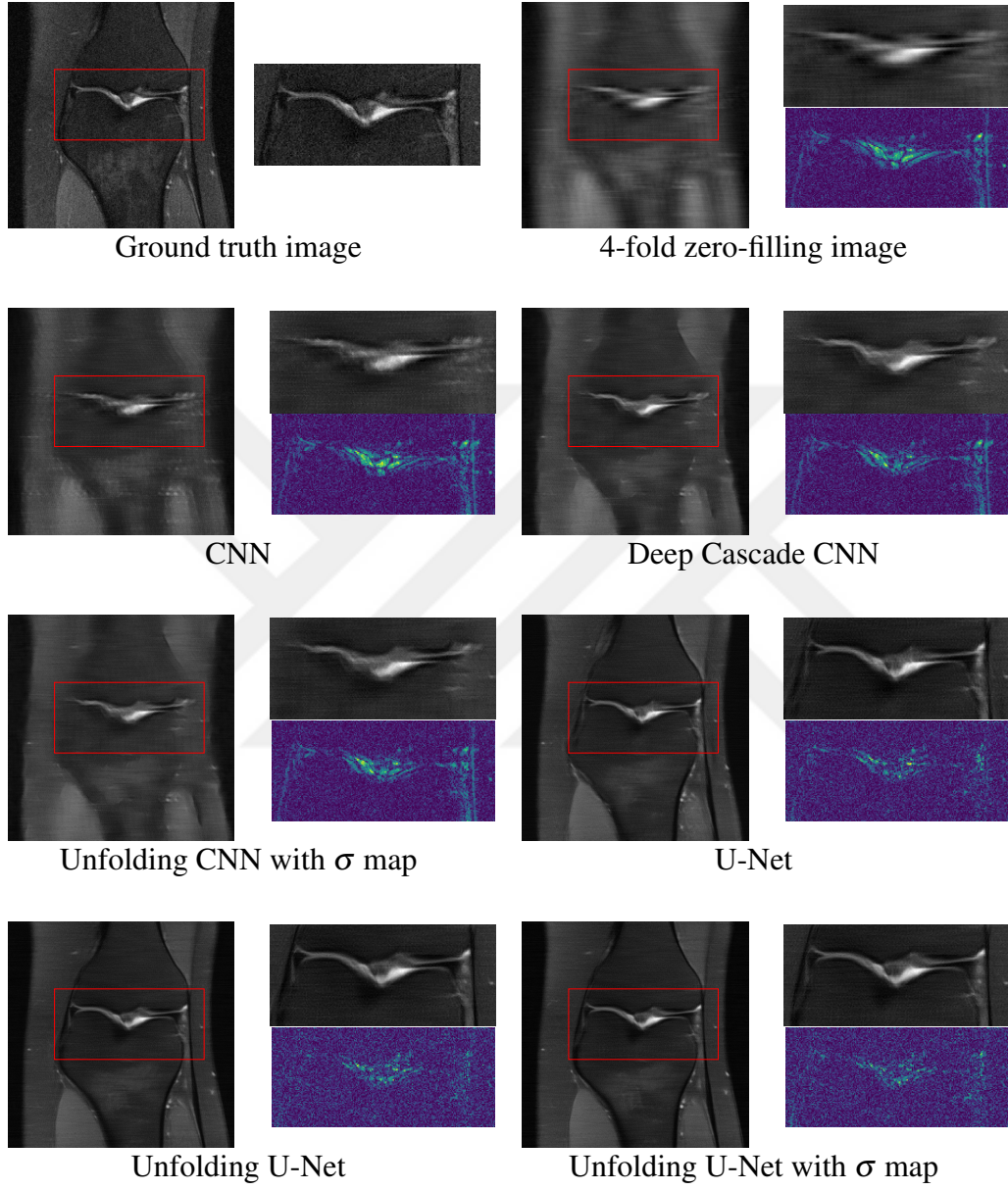


Figure 6.12 : Proposed techniques' reconstructed images, ROI, and error maps for 8-fold undersampled slices.

7. CONCLUSIONS

MR imaging is one of the key non-invasive modalities among clinical imaging techniques due to its ability to acquire high-contrast images from soft tissues. MRI is a technique that produces detailed images from different part of body tissue. However, despite its popularity and advantages, the required data acquisition and image formation process is a rather lengthy operation. During this reconstruction procedure, patients need to be motionless in order to acquire high-quality images without artifacts. MRI data are acquired in the k-space, and the data acquisition process necessitates a tradeoff between reconstruction quality and reconstruction time. As a possible solution to this drawback, various MRI acceleration methods include DL techniques have been introduced. These pipelines have led to both faster and better reconstruction of MR images from subsampled k-space data acquired in the Fourier domain. We have walked in a similar pathway and developed some novel structures based on deep learning for MR image reconstruction.

In initial study, we proposed a novel projection-based unfolded U-Net structure for the important problem of MRI reconstruction from highly undersampled k-space observation data and compared it with state-of-the-art techniques. We evaluated the introduced model's applicability and performance by using the rather recent fastMRI dataset as a benchmark. Random and uniform Cartesian undersampling masks of differing ratios have been employed to model the MRI data acquisition in the k-space. The zero-filling image estimate forms the input to the realized networks. The U-Net is employed as the building block of the novel unfolded U-Net structure. The intermediary updated data consistency layers firstly rectify the reconstructed images at their input and forward these rectified images to the successive network stage. The UDC also creates a secondary output, which gets collected at a later stage of the structure for further processing. Applying this novel method in a residual setting, we observed that the projection-based unfolding U-Net structure with UDCs outperforms

a variety of previously introduced deep networks that are aimed at MRI reconstruction. The introduced novel model can produce images with improved SNR results. The results for the new model can maintain texture details better when compared to the prior networks.

Furthermore, in recent years densely connected deep residual networks have shown their capacity for improving performance results in various image processing problems. Inspired by this fact, in second step of this thesis, dense connections are applied inside a generative adversarial network for MR image reconstruction. Appending DCR blocks to the generative network improves the qualitative and quantitative reconstruction results of the plain CNN based generator structure. We conducted simulations comparing the quantitative and qualitative performance results for the proposed structure and other methods from literature. Results reveal that in MR image reconstruction, the proposed DCR-GAN can compete with potent models from the literature. DCR-GAN with just three DCR blocks inside the generative network can get promising results for both 4-fold acceleration factor and the more aggressive 8-fold acceleration factor.

Motivated by this successful application of dense connections in GAN structure, in third step of this project, we proposed an MR image reconstruction pipeline that includes a residual densely connected structure. The quantitative and qualitative results are summarized for images reconstructed from undersampled data with 4-fold and 8-fold acceleration factors. By coupling the DCR blocks into two state-of-the-art deep learning frameworks, promising simulation results have been obtained. The MR image reconstruction results indicate improved performance when compared to the original structures lacking dense connections. The results again imply that DCR blocks provide a possible solution for further deepening of MR reconstruction network structures, without the information loss problem which is usually associated with increased depth. The results showcase that increasing the number of DCR blocks, translates into improved reconstruction performance. These results are observed in both cases when CNN-based and U-Net based networks are augmented with DCR blocks. The PSNR results for densely connected CNN structure with ten DCR blocks are improved significantly in comparison to the plain CNN, where the improvement

lies around 1.25 - 1.56 dB. Moreover, statistical evaluation tests were realized, and the statistical significance of the improved results was verified. In conclusion, the introduced novel use of dense connections in the form of DCR blocks has shown great potential for possible use in MRI reconstruction deep models.

In last step of this thesis, inspired by promising results of unfold structures in MRI reconstruction as indicated in recent literature, we applied adoptive noise map called σ into unfolding structure. The proposed model improves the performance of these unfolding structures without leading to any complexity increase. The adoption of an adaptively calculated noise level parameter at the input of the network results in better reconstruction performance. We conducted a comparison among models using quantitative and qualitative results. According to presented findings, the offered trainable parameter boosted the robust unfolding manifold outcomes. In future work, the effectiveness of this proposed parameter can be tested by applying it to model-based structures or even by evaluating its performance in other image processing problems like denoising.

The contributions of this thesis can be summarized as follows.

- An unfolding architecture for the U-Net framework has been offered.
 - The U-Net model was integrated into recently introduced projection-based structures. In this regard, the data fidelity block in the unfolding network was replaced with an updated data consistency layer.
 - In the recent studies, researchers have trained and tested unfolding frameworks for MRI reconstruction using relatively small data, some including up to only 10 fully sampled cardiac MR images. The cascade and projection-based unfolding structures have been benchmarked using the recently introduced and rather large fastMRI dataset. This dataset was firstly developed by a joint group of New York University (NYU) researchers together with a Facebook AI Research (FAIR) team for the fastMRI image reconstruction challenge. This dataset has gained quite attraction in the MRI reconstruction community and has been employed as a benchmark in quite a few recent studies.

- A novel variation of generative adversarial networks was introduced by applying densely connected residual blocks inside the generative network.
 - Additionally in this thesis, some limitations related to the generative adversarial networks were addressed. To do so, a novel wavelet-based GAN with a stable training and fast convergence was suggested. In this regard, the conventional downsampling and upsampling blocks were replaced with wavelet packet.
- Inspired by successful applications of dense connections, the densely connected residual blocks were utilized inside the state-of-the-art networks. In this regard, the standard convolutional layers inside U-Net and CNN were replaced by DCR blocks.
- Motivated by the conventional iterative unfolding reconstruction models, an adaptive noise level parameter was implemented inside the unfolding U-Net and CNN.

In this thesis, MR imaging drawbacks related to long data acquisition time have been addressed. The novel structures based on deep learning methods were proposed for swift MR image reconstruction with high-quality representation. The proposed structures were compared with state-of-the-art techniques by employing commonly used evaluation metrics, namely SSIM, NMSE, and PSNR. Moreover, the statistical significance for the results of the offered networks was emphasized by performing statistical assessment tests. These statistical tests approved the performance difference between proposed models and state-of-the-art techniques. Additionally, the proposed networks in this thesis are robust enough to be tested by another dataset with even different types of tissue and different slice sizes. We approved this robustness by testing our proposed models with the IXI dataset without retraining in [100]. As represented in our result tables, our newly offered networks are fast enough to be used even in real-time practical medical imaging. This thesis resulted in two journal papers [63,100] and one conference paper [77]. Moreover, the work as given in Chapter 5 has been submitted as a journal paper for possible publication.

Image super-resolution is another widespread field of study that has been integrated into various imaging modalities. Recently, numerous promising approaches have been introduced in this field based on deep learning techniques. In future works, the effectiveness of the image super-resolution techniques based on deep learning can be investigated for the MR image reconstruction problem. The proposed models in this thesis also can be applied to the super-resolution problem for MR image reconstruction.





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- Külekci, M. O., Habib, I., and **Aghabiglou, A.** (2019). Privacy–Preserving Text Similarity via Non-Prefix-Free Codes. In *International Conference on Similarity Search and Applications*, (pp. 94-102). Springer, Cham.

