Image Inpainting to Improve the Registration Performance of Multiple Sclerosis (MS) Patient Brain with Brain Atlas

by

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DECLARATION OF CANDIDATE

It is hereby declared that this thesis or any part of it has not been submitted elsewhere for the award of any degree or diploma.

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DEDICATION

I would like to dedicate this thesis to my family who supported me through both good and tough times. They always give me the motivation to move forward in my life.

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ABSTRACT

Multiple sclerosis (MS) is an inflammatory autoimmune disease of the central nervous system which damage the myelin layer of White Matter (WM) and Grey Matter (GM). The loss of myelin layer (demyelination) exposes the WM and GM, which is viewed as lesions in the MRI brain scans. Loss of this layer will distort or interrupt the flow of signals from the brain to the parts of the body. To treat and monitor the progression of MS in standardized way, patient MRI brain scans are registered with brain atlas. Brain atlas is composed of serial sections along different anatomical planes of the healthy or diseased developing brain. However, in this registration step, the MS lesions create a strong distortion in the output transformation which creates a bias in registered image. In this thesis, we propose a novel image inpainting technique to reduce such bias. Image inpainting is used to reconstruct the lost or deteriorated parts of image data. We inpaint the MS lesions to make it appear like healthy tissue and register this inpainted MS brain with the brain atlas, and add the masked lesions afterwards. To evaluate the performance of our proposed inpainting algorithm, we employ a two-step evaluation process. Firstly, we inpaint distorted 2D images and artificial MS lesions in 3D MRI image data with our proposed and state-of-the-art methods. Secondly, we register the inpainted brain with an atlas and compare its performance with the ground truth. This two-step evaluation indicates that the proposed inpainted algorithm performs comparatively better than other state-of-the-art methods and it also increases the registration performance and significantly reduces the bias previously created by the MS lesions. The quantitative analysis has given the idea that comparative parameters known as dice and jaccard score are manifesting better performance with respect to the present ones.

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LIST OF ACRONYMS

Abbreviated Form	Descrption
MS	Multiple Sclerosis
CNS	Central Nervous System
WM	White Matter
GM	Grey Matter
MSF	Multiple Sclerosis Foundation
BET	Brain Extraction Tool
SUSAN	Smallest Univalue Segment Assimilating Nucleus
FSL	FMRIB sofware library
FLIRT	FMRIB's Linear Image Registration Tool
FNIRT	FMRIB's Nonlinear Image Registration Tool
TE	Echo Time
TR	Repetative Time
DOF	Degrees of Freedom
US	Ultra Sound
MRI	Magnetic Resonance Imaging
CT	Computational Tomography
T1WI	T1 weighted image
T2WI	T2 weighted image
PDWI	Proton Density weighted image

Chapter 1: Introduction

1.1 Problem Definition

Multiple Sclerosis (MS) is an unpredictable, often disabling disease of the Central Nervous System (CNS) that disrupts the flow of information within the brain, and between the brain and body [1]. It is the most common auto immune disorder affecting CNS [2] and it affects the brain and spinal cord alike.

MS involves an immune-mediated process in which an abnormal response of the body's immune system is directed against the CNS, which is made up of the brain, spinal cord and optic nerves. The exact antigen, in other words target that the immune cells are sensitized to attack still remains unknown, which is why MS is considered by many experts to be "immune-mediated" rather than "autoimmune."

Within the CNS, the immune system attacks myelin, the fatty substance that surrounds and insulates the nerve fibers, as well as the nerve fibers themselves.

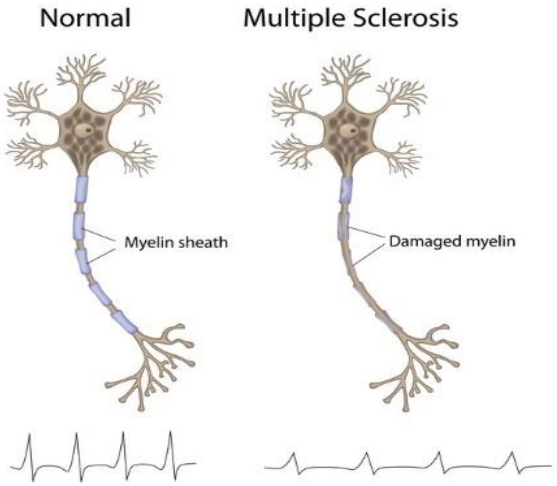


Figure 1.1: Differences between normal and damaged myelin of a neuron.

The damaged myelin forms scar tissue (sclerosis), which gives the disease its name.

When any part of the myelin sheath or nerve fiber is damaged or destroyed, nerve impulses traveling to and from the brain and spinal cord are distorted or interrupted, producing a wide variety of symptoms [3].

The MSF (Multiple Sclerosis Foundation) estimates that more than 400,000 people in the USA, around 100,000 people in the UK have MS and about 2.5 million people around the world have MS [4]. In 2013, about 2.3 million people were affected globally with rates varying widely in different regions and among different populations [5, 6]. The disease usually begins between the ages of 20 and 50 and is twice as common in women as in men [7].

Timely and effective treatment can relieve MS symptoms and delay disease progression [3].

To diagnose and treat patients with MS and other neurological diseases, it is a common practice to use brain atlas [8]. A brain atlas is composed of serial sections along different anatomical planes of the healthy or diseased developing brain where each relevant brain structure is assigned a number of coordinates to define its outline or volume [9].

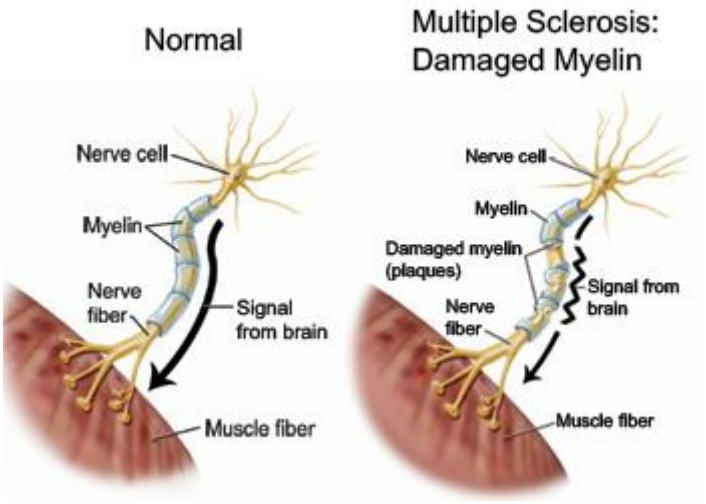


Figure 1.2: Myelin layer of healthy brain and severe MS.

Registering a patient brain with brain atlas is the most common way to build it. One of the objectives of image registration is to allow the characterization of the morphology of different subjects' brains helps to make anatomical comparison among different populations [10].

While the cause is not clear, the underlying mechanism is thought to be either destruction by the immune system or failure of the myelin-producing cells [6]. Proposed causes for this include genetics and environmental factors such as being triggered by a

viral infection [2]. MS is usually diagnosed based on the presenting signs and symptoms and the results of supporting medical tests [6].

The three main characteristics of MS are the formation of lesions in the central nervous system (also called plaques), inflammation, and the destruction of myelin sheaths of neurons. These features interact in a complex and not yet fully understood manner to produce the breakdown of nerve tissue and in turn the signs and symptoms of the disease [2]. Additionally, MS is believed to be an immune-mediated disorder that develops from an interaction of the individual's genetics and as yet unidentified environmental causes [3]. Damage is believed to be caused, at least in part, by attack on the nervous system by a person's own immune system [2].

1.2 Research Challenges:

For MS patients, lesions can be found at White Matter (WM) and Grey Matter (GM). WM lesions are more common, prominent and can easily be detected by traditional imaging technique. Such MS lesions create distortion in the registration step in the brain atlas.

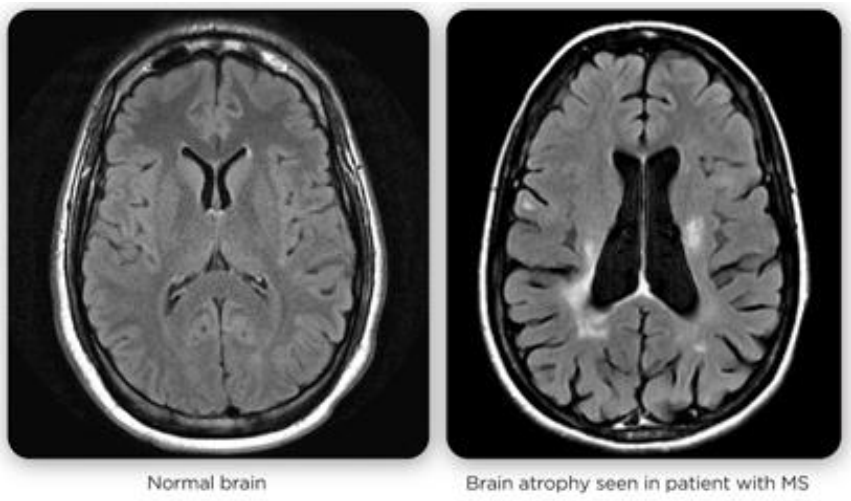


Figure 1.3: Brain atrophy of a Normal brain & MS affected Brain.

This is because, WM lesions look like GM and as registration techniques use mutual information like brightness, color, shape, relative position; these lesions can be

mistaken as GM in WM creating distortion in the registration step. To reduce such unwanted distortion, many researchers have used different techniques.

One is spatial normalization [11] where the subject brain is deformed to correspond to the same location in the target brain (i.e. the atlas). It is often performed in research-based functional neuroimaging where one wants to find common brain activation across multiple human subjects. But, the problem is comparisons of group activation data for patients with brain lesions with data from controls must still be treated with severe caution [12].

Second way to deal with MS lesion bias is to use seed points. Seed points can be processed with intuitive heuristics which provide improved segmentation accuracy while facilitating quick and natural point placement. But, the method does not account for normal variations in intensity [13].

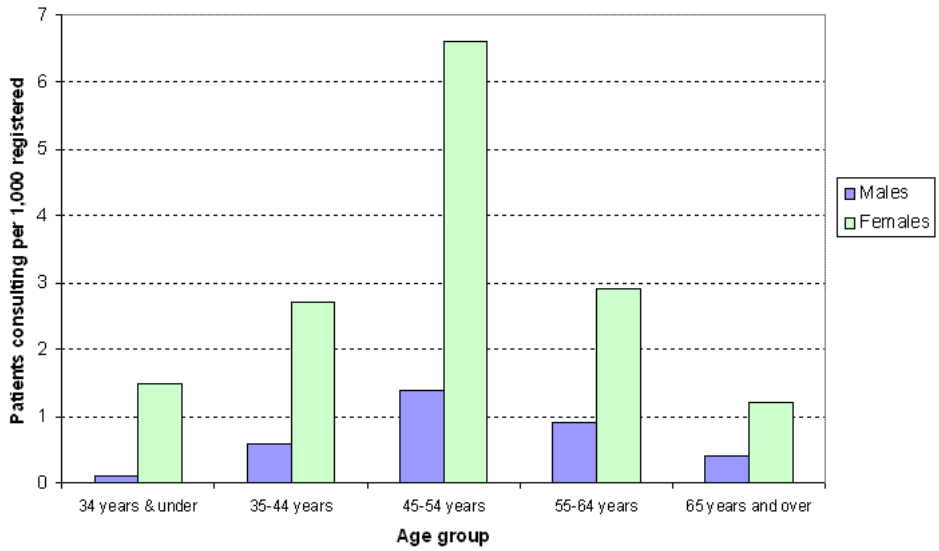


Figure 1.4: Bar Chart showing different age group of people affected by MS.

Finally another method is Image Inpainting technique. Image inpainting is the process of reconstructing lost or deteriorated parts of images [14]. It is mathematically highly ill posed process. There are many inpainting algorithms available for traditional structural 2D images such as harmonic inpainting technique [15], Mumford shah algorithm [16], and Transport inpainting algorithm [17] and so on.

In this Thesis, we are proposing a novel inpainting technique to reduce the bias in the registration step caused by MS lesions because this method is computationally efficient as well as fully automated and robust once the lesions have been detected.

The aim of this Thesis is to firstly identify problems associated with the registration of MS patient brain with Brain atlas. To propose a solution to the registration problem possibly by inpainting technique.

To evaluate if the proposed inpainting algorithm can contribute to traditional 2D images as well as 3D MRI images and further investigate its applications in medical imaging modalities.

The proposed inpainting method is believed to have potential scintillating applications in MRI as well as traditional 2D images. Of course, to check whether it suits perfectly or not, we need to register the image with some reference and register that. Then we can have an idea about the superiority of our proposed method over current ones.

First, this method will be used to inpaint random 2d images and then MRI images distorted with MS lesions. The comparative performance will then be evaluated to access if the inpainted image can reduce the bias in the registration step.

1.3 Thesis Objectives

First, the target is to get accustomed with the traditional methods existing successfully in this field. And, then our goal is to improve the registration performance by giving a try to utilize a novel inpainting algorithm beforehand.

The main objective is to propose a novel inpainting algorithm for inpainting the MS lesions in the brain MRI for better performance in the registration step after thoroughgoing perusal of the state-of-the-art inpainting methods already utilized in 2D images.

However, more particularly, the objectives can be concluded as the followings.

i. The aim of this Thesis is to firstly identify problems associated with the registration of MS patient brain with Brain atlas.
ii. To propose a solution to the registration problem possibly by inpainting technique.
iii. To evaluate if the proposed inpainting algorithm can contribute to traditional 2D images as well as 3D MRI images and further investigate its applications in medical imaging modalities.

1.4 Thesis Outline

MS is believed to be an immune-mediated disorder that develops from an interaction of the individual's genetics and as yet unidentified environmental causes. Damage is believed to be caused, at least in part, by attack on the nervous system by a person's own immune system.

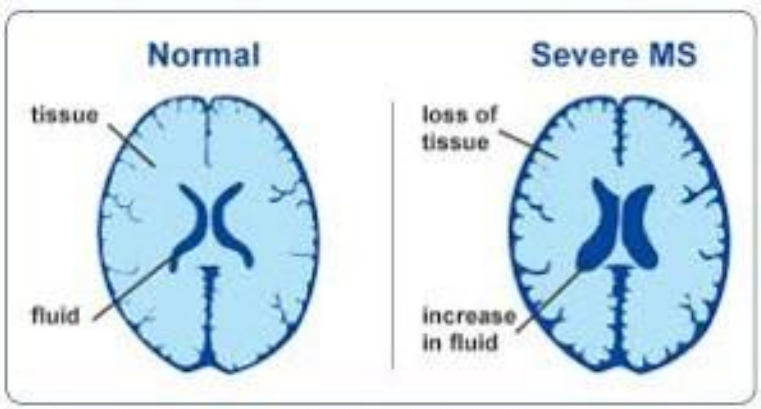


Figure 1.5: Difference showing Normal brain and MS affected one.

Chapter 2 provides background for Multiple Sclerosis patient's state. It includes the causes, affects, diagnosis, and importance and pernicious affects as well. It also illustrates why we need to detect early and have to have a good registration later to have all the information about the corpus colosum of the brain. It also defines the necessity to inpaint the patient brain firstly for the registration part by delineating the other state-of-the-art techniques to reduce the distortion.

The basics of the state-of-the-art inpainting techniques are given and also associated drawbacks are analysed. This chapter finally includes the novel inpainting algorithm of our proposed method to inpaint the images.

In chapter 3, Image registration procedures have been dealt with. Different kinds of registrations, their advantages as well as disadvantages with associated conditions are then scrutinized. The procedure to register the healthy brain with brain atlas has been discussed thoroughly.

In Chapter 4, results by getting registration with the inpainted patient brain has been manifested comparing using the traditional ones with our novel inpainted technique.

Finally, our thesis book provides the Discussion with regards to the interpretations obtained from the results and also its relevance for future investigations in MS affected brains. Each chapter is filled with results we achieve both qualitatively and quantitatively.

Chapter 2: Related Background

2.1 Introduction to Multiple Sclerosis (MS)

Multiple sclerosis (MS) is a demyelinating disease in which the insulating covers of nerve cells in the brain and spinal cord are damaged [18]. This damage disrupts the ability of parts of the nervous system to communicate, resulting in a range of signs and symptoms, including physical, mental, and sometimes psychiatric problems.

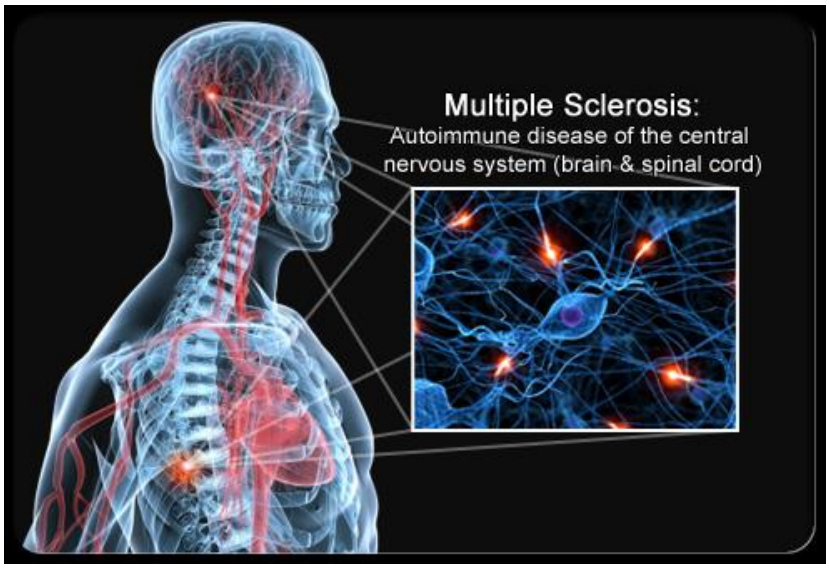


Figure 2.1: Scalp view of an MS affected Brain.

MS takes several forms, with new symptoms either occurring in isolated attacks (relapsing forms) or building up over time (progressive forms) [19]. In severe cases, the patient becomes paralyzed or blind while in milder cases there may be numbness in the limbs and other several parts or organs of the body. This damage disrupts the ability of parts of the nervous system to communicate resulting in a range of signs and symptoms including physical, mental and sometimes psychological problems as well.

2.2 Signs and Symptoms of MS

Signs and symptoms are not mandatory for an MS patient. It is possible that it may not show any signs until a certain stage. And the exact cause is still unknown to the researchers. But still some early symptoms can be identified by researches oriented through it. Once again, it is stated that signs are not necessary for MS.

Early symptoms may include total weakness, fatigue, vertigo, tingling, numbness, blurred vision and even problem with balance and coordination.

Early symptoms:

- Weakness
- Fatigue
- Vertigo
- Tingling
- Numbness
- blurred vision
- problems with balance and coordination

Besides these early most common symptoms, some other lesser impacting signs can be concise below. Other less important signs and symptoms can be included as muscle stiffness, speech and swallowing problems, cognitive dysfunction, thinking problems, mood swing, sexual dysfunction and last but not least urinary problems.

Other less important signs:

- muscle stiffness
- speech and swallowing problems
- Cognitive dysfunction
- thinking problems i.e. mood swing
- sexual dysfunction
- urinary problems

2.3 Some Basics of MS

2.3.1 Causes

MS is believed to have a genetic component as people with a first degree relative with the disease have a higher incidence than the general population. But it is not considered as hereditary.

The exact cause of multiple sclerosis is still unknown, but it is believed to be any combination of the following factors by researchers. They can be –

- Immunologic
- Environmental
- Infectious
- Smoking
- Stress
- Vaccination
- genetic factors or,
- Combination of the above.

2.3.2 Mechanism to affect

It is a demyelinating disease in which the insulating covers of nerve cells in the brain and spinal cord are damaged gradually. This damage disrupts the ability of parts of the nervous system.

2.3.3 Necessity of Early Diagnosis

While the cause is not clear, the underlying mechanism is thought to be either destruction by the immune system or failure of the myelin-producing cells [20]. Proposed causes for this include genetics and environmental factors such as being triggered by a viral infection.[21, 22] MS is usually diagnosed based on the presenting signs and symptoms and the results of supporting medical tests.[23]

2.3.4 Cure of MS

There is no known cure for multiple sclerosis. Physical therapy can help with people's ability to function [18]. Medications used to treat MS, while modestly effective, can have side effects and be poorly tolerated. Many people pursue alternative treatments, despite a lack of evidence [24]. Treatments attempt to improve function after an attack and prevent new attacks [25].

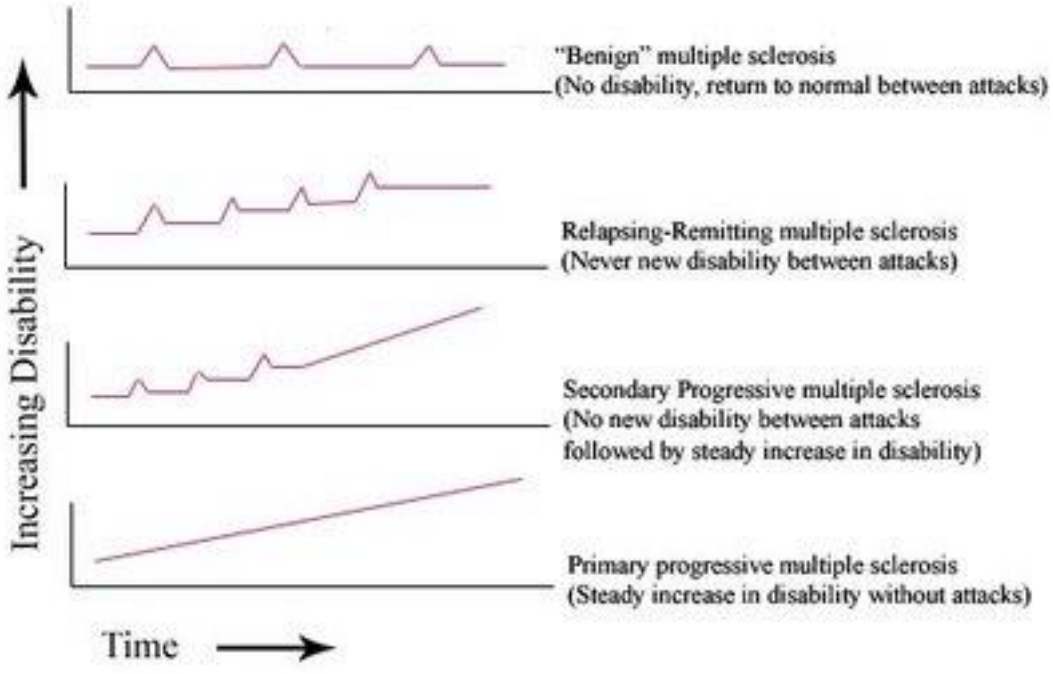


Figure 2.2: Increasing disability with time progression for MS patient brain.

The long-term outcome is difficult to predict, with good outcomes more often seen in women, those who develop the disease early in life, those with a relapsing course, and those who initially experienced few attacks [26]. Life expectancy is on average 5 to 10 years lower than that of an unaffected population [27].

As we know that the exact causes are still not known, so we need to have an early detection to have a less affect to our brain as well as central nervous system (CNS).

2.3.5 Role of MRI to diagnose MS

MRI is the investigative tool of choice for neurological cancers, as it has better resolution than CT and offers better visualization of the posterior fossa. The contrast provided between grey and white matter makes it the best choice for many conditions of the central nervous system, including demyelinating diseases, dementia, cerebrovascular disease, infectious diseases and epilepsy [7].

Since many images are taken milliseconds apart, it shows how the brain responds to different stimuli; researchers can then study both the functional and structural brain abnormalities in psychological disorders [8]. MRI is also used in MRI-guided stereotactic surgery and radiosurgery for treatment of intracranial tumors, arteriovenous malformations and other surgically treatable conditions using a device known as the N-localizer [9].

MRI allows doctors to see lesions in the central nervous system. It's important to note, however, that not all lesions are due to MS and not all people with MS have lesions.

According to the National MS Society, MRI shows no lesions in five percent of patients with "clinically definite MS" at time of diagnosis.

It's important to note that the number of lesions doesn't always indicate severity of symptoms.

2.3.6 Definition of MRI

Magnetic resonance imaging (MRI) is a medical imaging technique used in radiology to form pictures of the anatomy and the physiological processes of the body in both health and disease. MRI scanners use strong magnetic fields, radio waves, and field gradients to generate images of the inside of the body.

Functional MRI (fMRI), introduced later, is used to understand how different parts of the brain respond to external stimuli or passive activity in a resting state. In some extensive level, Blood oxygenation level dependent (BOLD) fMRI measures the hemodynamic response to transient neural activity resulting from a change.

Researchers use statistical methods to construct a 3D parametric map of the brain which indicates the regions of the cortex that demonstrate a significant change in activity in response to the task. fMRI has applications in behavioural and cognitive research, and in planning neurosurgery of eloquent brain areas [29][30].

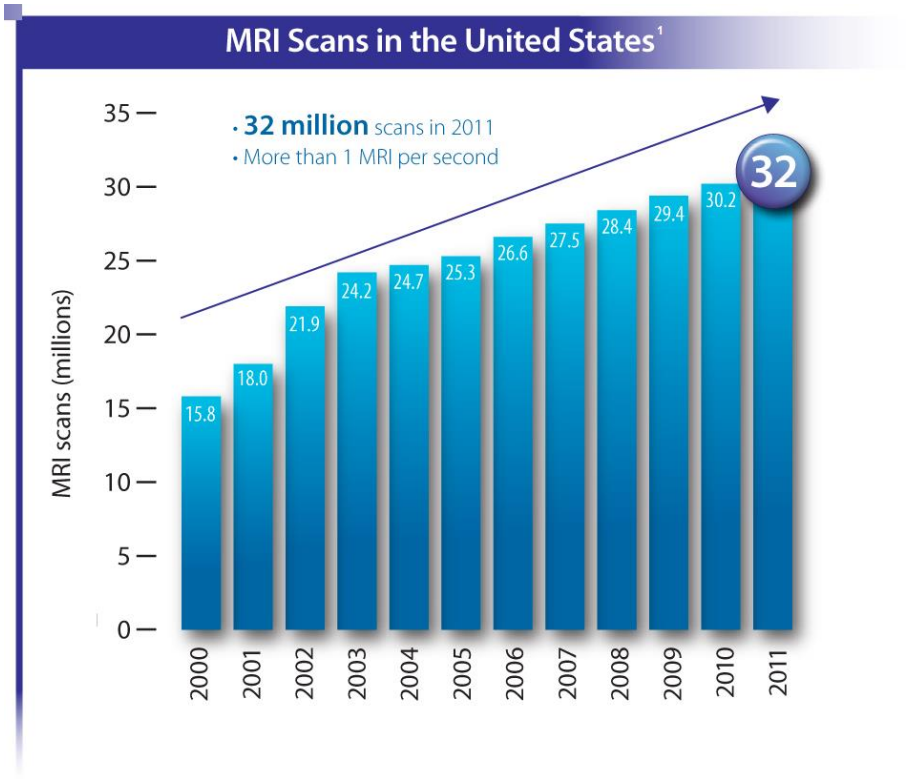


Figure 2.3: Bar Chart showing MRI scan used in United States [24].

In research settings, structural MRI or functional MRI (fMRI) can be combined with EEG (electroencephalography) under the condition that the EEG equipment is MR compatible. Although EEG equipment (electrodes, amplifiers and peripherals) are either approved for research or clinical use, the same MR Safe, MR Conditional and MR Unsafe terminology applies. With the growth of the use of MR technology, the U.S. Food & Drug Administration [FDA] recognized the need for a consensus on standards of practice, and the FDA sought out ASTM International [ASTM] to achieve them. Committee F04[31] of ASTM developed F2503, Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment.[32]

2.3.7 Applications of MRI

Every MRI scanner has a powerful radio transmitter that generates the electromagnetic field that excites the spins. If the body absorbs the energy, heating occurs. For this reason, the transmitter rate at which energy is absorbed by the body must be limited It has been claimed that tattoos made with iron containing dyes can lead to burns on the subject's body [33]. Cosmetics are very unlikely to undergo heating, as well as body lotions, since the outcome of the reactions between those with the radio waves is unknown. The best option for clothes is 100% cotton.

- MRI has a wide range of applications in medical diagnosis and over 25,000 scanners are estimated to be in use worldwide [34]. MRI affects diagnosis and treatment in many specialties although the effect on improved health outcomes is uncertain [35].
- Since MRI does not use any ionizing radiation, its use is generally favoured in preference to CT when either modality could yield the same information [36].
- Although, in certain cases, MRI is not preferred as it can be more expensive, time-consuming, and claustrophobia-exacerbating.

The MRI System must attend to periodic maintenance from the manufacturer, Gradients and RF transmit must attend factory specifications. In some systems there are parts responsible for the measurement of the power absorption limiter that must be periodically replaced for a new one (Recalibrate in factory). There are several positions strictly forbidden during measurement such as crossing arms and legs, and the patient's body cannot create loops of any kind for the RF during the measurement. Unusual patient heating cases must be reported to the appropriate regulatory agency for further investigation.

2.3.8 Medical Uses of MRI

MRI has a wide range of applications in medical diagnosis and over 25,000 scanners are estimated to be in use worldwide.[34] MRI affects diagnosis and treatment in many specialties although the effect on improved health outcomes is uncertain. Since MRI does not use any ionizing radiation, its use is generally favored in preference to CT when either modality could yield the same information.[35] In certain cases, MRI is not preferred as it can be more expensive, time-consuming, and claustrophobia-exacerbating.

MRI is in general a safe technique but the number of incidents causing patient harm has risen. Contraindications to MRI include most cochlear implants and cardiac pacemakers, shrapnel and metallic foreign bodies in the eyes. The safety of MRI during the first trimester of pregnancy is uncertain, but it may be preferable to other options. The sustained increase in demand for MRI within the healthcare industry has led to concerns about cost effectiveness and over diagnosis.[35]

- **Neuroimaging:** MRI is the investigative tool of choice for neurological cancers, as it has better resolution than CT and offers better visualization of the posterior fossa. The contrast provided between grey and white matter makes it the best choice for many conditions of the CNS, dementia, cerebrovascular disease, infectious diseases and epilepsy.[7]
- **Cardiovascular:** Cardiac MRI is complementary to other imaging techniques, such as echocardiography, cardiac CT and nuclear medicine. Its primary applications include any kind of the assessment of the myocardial ischemia and viability, cardiomyopathies, myocarditis, iron overload, vascular diseases and congenital heart disease [23].
- **Liver and gastrointenstial imaging:** Hepatobiliary MR is used to detect and characterize lesions of the liver, pancreas and bile ducts. Focal or diffuse disorders of the liver may be evaluated using diffusion-weighted, opposed-phase imaging and dynamic contrast enhancement sequences. Extracellular contrast agents are widely used in liver MRI and newer hepatobiliary contrast agents also provide the opportunity to perform functional biliary imaging.

Anatomical imaging of the bile ducts is achieved by using a heavily T2-weighted sequence in magnetic resonance cholangiopancreatography (MRCP).

2.3.9 Lesion

As it has already been said that our nerves have a protective covering called myelin. In MS, the body's immune system mistakenly attacks myelin, causing inflammation and damage. The resulting scar tissue is called a lesion.

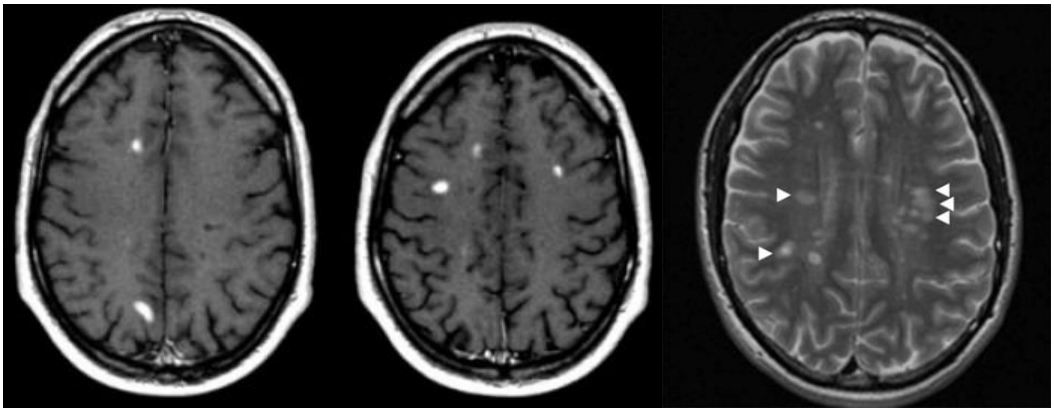
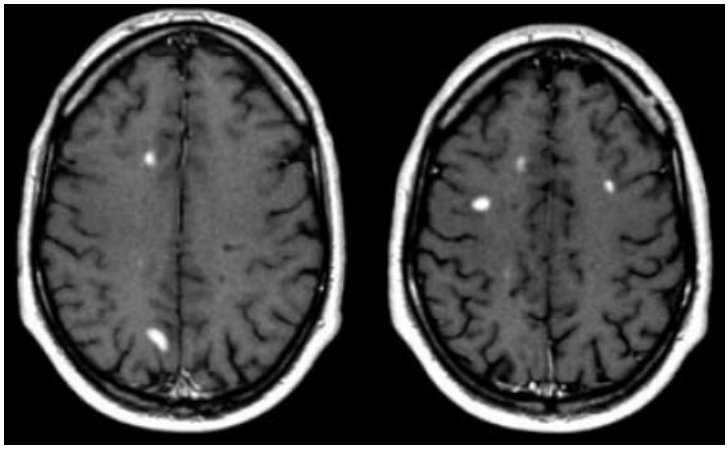


Figure 2.4: Detection of lesion in MRI images (axial view)

Some lesions are inactive and don't cause any symptoms. Active lesions, those that are just forming or expanding, can cause a wide variety of symptoms, depending on where they are located and how big they are. The name "multiple sclerosis" means "multiple scars."

Lesions are important for diagnosis as well as prevention. Now this lesions are not stable in time to time. So, MRI should be taken into account with time also to find the

discrepancies of the lesions located in the image. Those differences will also delineate the status of the patients. For example, if we look in the following image



(a) (b)

Figure 2.5: Two different time stages of an MRI brain images (axial view).

On the left, a patient brain MRI has been taken into account and after 3 months the same patient brain MRI is re-examined which is depicted in the right one. Now we can have a good, not so deep though, idea about the situation of this patient with the help pf the location of lesions [44].

Typical findings for MS as seen in this case are: Multiple enhancing lesions, many of these lesions 'touch the cortex', and also these enhancing lesions all are new lesions. So this finding is proof of dissemination in time.

The name multiple sclerosis refers to the scars (sclerae – better known as plaques or lesions) that form in the nervous system. These lesions most commonly affect the white matter in the optic nerve, brain stem, basal ganglia, and spinal cord, or white matter tracts close to the lateral ventricles.[2] The function of white matter cells is to carry signals between grey matter areas, where the processing is done, and the rest of the body. The peripheral nervous system is rarely involved.[3]

A repair process, called remyelination, takes place in early phases of the disease, but the oligodendrocytes are unable to completely rebuild the cell's myelin sheath

[62]. Repeated attacks lead to successively less effective remyelinations, until a scar-like plaque is built up around the damaged axons [70].

2.3.10 Brain Images in MRI

There are actually three anatomical planes through which one can take the image. MRI images are also not different from those. We can have a good idea from those three type of anatomical planes for MRI images as well.

An anatomical plane is a hypothetical plane used to transect the human body, in order to describe the location of structures or the direction of movements. In human and animal anatomy, three principal planes are used:

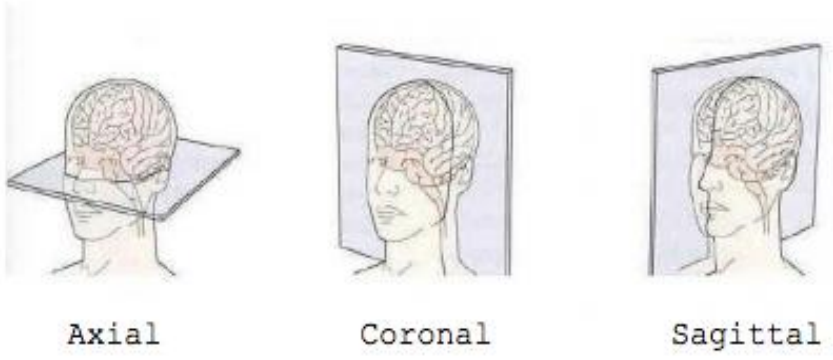


Figure 2.6: Three type of views for anatomical images.

- The sagittal plane (anteroposterior) is a plane parallel to the sagittal suture. It divides the body into left and right.
- The coronal plane (frontal) or frontal plane divides the body into dorsal and ventral (back and front, or posterior and anterior) portions.

- The transverse plane (horizontal) or axial plane divides the body into cranial and caudal (head and tail) portions.

Now, if we use MRI scan of this views then we will get something like as followed.

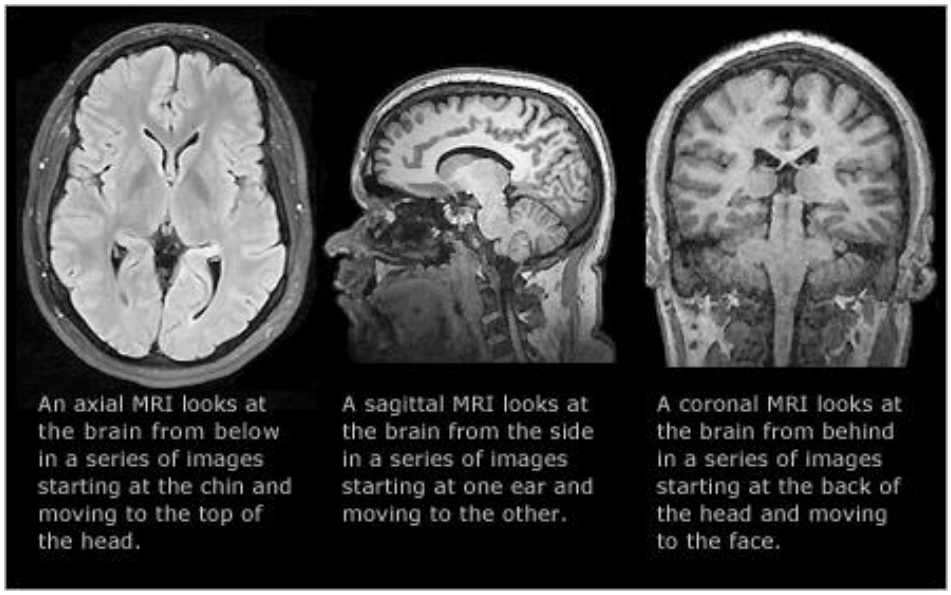


Figure 2.7: Three type of views for MRI Brain images

- An axial MRI looks at the brain from below in a series of images starting at the chin and moving to the top pf the head.
- A sagittal MRI looks at the brain from the side in a series of images starting at one ear and moving to the other.
- And a coronal MRI looks at the brain form behind in a series of images beginning at the back of the head and moving to the face.

2.3.11 MRI over CT scan or US

Comparative Analysis:

MRI is much more suitable over CT scan or ultrasound (US) in many different ways. They can be-

- MRI is usually painless medical test.
- MR imaging uses a powerful magnetic field, radio waves and a computer to produce detailed pictures of organs, soft tissues, bone and virtually all other internal body structures.
- In ultrasound (US), image quality is way much worse than MRI or CT scan and next to impossible with the barrier of scalp.

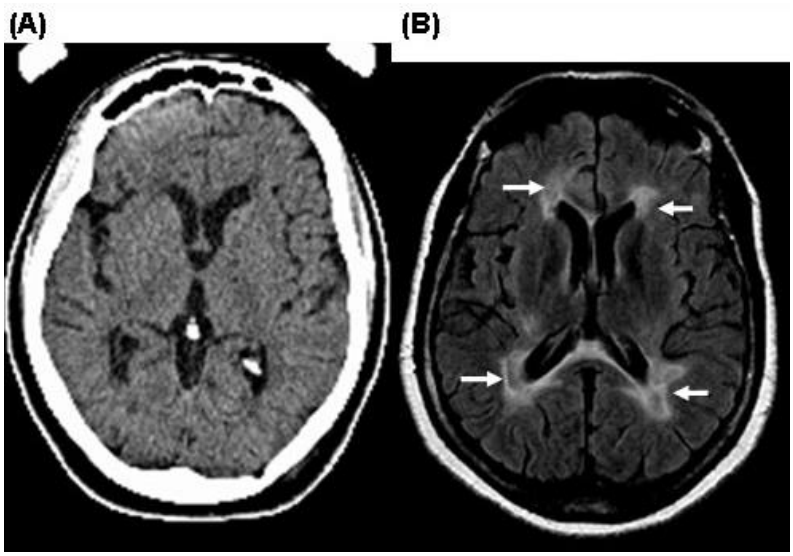


Figure 2.8: (A) CT scan and (B) MRI showing the increased sensitivity that MRI adds in visualizing brain lesions, such as those in MS (arrows).

Table 2.1: Comparisons between CT scan and MRI in terms of significance and efficiency.

Subjects	MRI and CT
Usability and wideness	MRI is new compared to CT. CT is more widely used than MRI in OECD countries with a mean of 132 vs. 46 exams per 1000 population performed respectively [45].
Statistics of CT and MRI	A concern is the potential for CT to contribute to radiation-induced cancer and in 2007 it was estimated that 0.4% of current cancers in the United States were due to CTs performed in the past, and that in the future this figure may rise to 1.5–2% based on historical rates of CT usage.[47] An Australian study found that one in every 1800 CT scans was associated with an excess cancer [46].
Ionizing affect	An advantage of MRI is that no ionizing radiation is used and so it is recommended over CT when either approach could yield the same diagnostic information [47].
Cost	However, although the cost of MRI has fallen, making it more competitive with CT, there are not many common imaging scenarios in which MRI can simply replace CT, although this substitution has been suggested for the imaging of liver disease [48].
CNR and accuracy	MRI has high CNR. It has high accuracy as well. But, limited spatial resolution of MRI in axial direction (slice thickness) which is improved by CT scan but with high radiation and contrast dose.

CT scan:

CT scan makes use of computer-processed combinations of many X-ray images taken from different angles to produce cross-sectional (tomographic) images (virtual "slices") of specific areas of a scanned object, allowing the user to see inside the object without cutting.

As X-ray CT is the most common form of CT in medicine and various other contexts, the term computed tomography alone (or CT) is often used to refer to X-ray CT, although other types exist, such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT).

Older and less preferred terms that also refer to X-ray CT are computed axial tomography (CAT scan) and computer-aided/assisted tomography. X-ray CT is a form of radiography, although the word "radiography" used alone usually refers, by wide convention, to non-tomographic radiography.

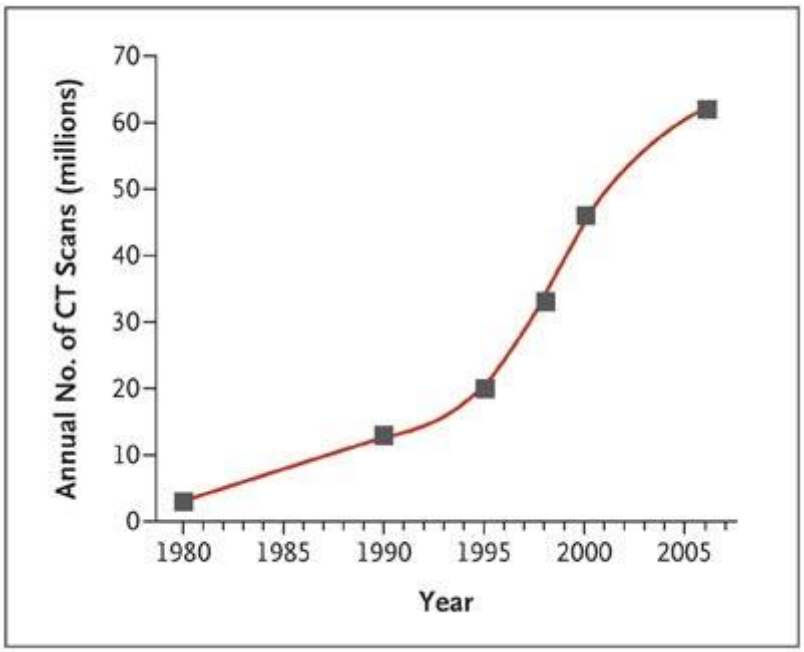


Figure 2.9: Graph Chart showing annual numbers of CT scan [6].

Use of CT has increased dramatically over the last two decades in many countries.[6] An estimated 72 million scans were performed in the United States in 2007.[7] One study estimated that as many as 0.4% of current cancers in the United

States are due to CTs performed in the past and that this may increase to as high as 1.5 to 2% with 2007 rates of CT use [8] however, this estimate is disputed [9] as there is not a consensus about the existence of damage from low levels of radiation. Kidney problems may occasionally occur following intravenous contrast agents used in some types of studies.[10]

Advantages:

There are several advantages that CT has over traditional 2D medical radiography.

First, CT completely eliminates the superimposition of images of structures outside the area of interest.

Second, because of the inherent high-contrast resolution of CT, differences between tissues that differ in physical density by less than 1% can be distinguished.

Finally, data from a single CT imaging procedure consisting of either multiple contiguous or one helical scan can be viewed as images in the axial, coronal, or sagittal planes, depending on the diagnostic task. This is referred to as multiplanar reformatted imaging,

There are some basics of CT scan. Using those properties we can have a good idea about the basics. They can be illustrated as the following-

- Better for bony lesions.
- Sensitive to acute hemorrhage.
- Chronic hemorrhage may be subtle.
- 60% acute strokes visualized.
- Posterior fossa degraded by artefact.
- Poor resolution of demyelinating lesions.
- Metal artifacts (skull plates, clips)
- Axial and coronal images
- Ionized contrast agent. Risk is ionizing radiation

X-ray:

X-radiation (composed of X-rays) is a form of electromagnetic radiation.

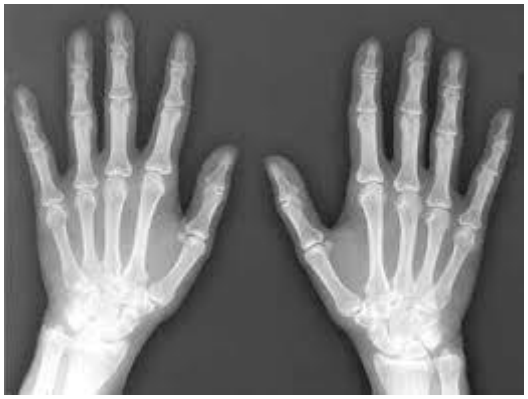


Figure 2.10: X-Ray of two hands of one patient.

Most X-rays ave a wavelength ranging from 0.01 to 10 nanometers, corresponding to frequenciesin the range 30 petahertz to 30 exahertz (3×1016 Hz to 3×1019 Hz) and energies in the range 100 eV to 100 keV. X-ray wavelengths are shorter than those of UV rays and typically longer than those of gamma rays.

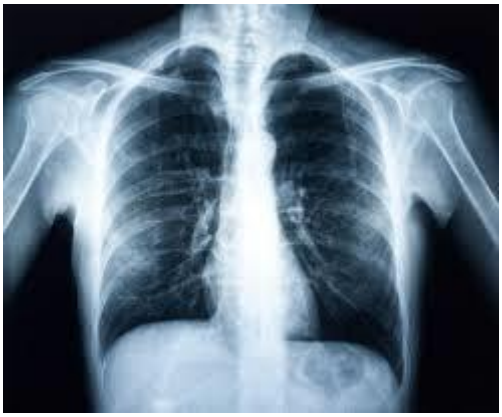


Figure 2.11: Chest X-Ray.

In many langages, X-radiation is referred to with terms meaning Röntgen radiation, after Wilhelm Röntgen who is usually credited as its discoverer, and who had named it X-radiation to signify an unknown type of radiation [63]. Spelling of X-ray(s) in the English language includes the variants x-ray(s), xray(s), and X ray(s) [64].

Medical Use:

- Radiograph
- Computed Tomography
- Fluoroscopy
- Radiotherapy

Adverse effects:

Diagnostic X-rays (primarily from CT scans due to the large dose used) increase the risk of developmental problems and cancer in those exposed. X-rays are classified as a carcinogen by both the World Health Organization's International Agency for Research on Cancer and the U.S. government.[65] It is estimated that 0.4% of current cancers in the United States are due to computed tomography (CT scans) performed in the past and that this may increase to as high as 1.5-2% with 2007 rates of CT usage.[66]

MRI:

- Better for soft tissue delineation
- Insensitive to acute hemorrhage
- Chronic hemorrhage is well seen
- 80% acute strokes visualized
- Demyelinating lesions well seen in all stages
- Ferromagnetic artifacts
- Axial, sagittal, angled as well as coronal images
- Paramagnetic contrast agent. Risk is magnetic field

2.4 State of the Art techniques to solve the distortion

There are some traditional methods which are currently utilized to solve the distortion in the registration step. As, the prime target was to firstly get to know the pros and cons of the state-of-the-art methods.

So some basic methods are in the following. Fundamental and brief description of those and the limitations as well as drawbacks are now going to be stated altogether to have a pellucid idea.

There are some good ways to solve the distortion part in the registration step. Of which spatial normalization, using the seed points are worthy of mention as with some others as well. So we need to know the reasons behind choosing the inpainting case instead of these with associated drawbacks.

Although it is unlikely to posit that ours one is the supreme one, rather we are using inpainting for these drawbacks.

2.4.1 Spatial normalization

In neuroimaging, spatial normalization is an image processing step, more specifically an image registration method. Human brains differ in size and shape, and one goal of spatial normalization is to deform human brain scans so one location in one subject's brain scan corresponds to the same location in another subject's brain scan.

It is often performed in research-based functional neuroimaging where one wants to find common brain activation across multiple human subjects. The brain scan can be obtained from magnetic resonance imaging (MRI) or positron emission tomography (PET) scanners.

Overview:

- One is spatial normalization [11] where the subject brain is deformed to correspond to the same location in the target brain (i.e. the atlas).
- It is often performed in research-based functional neuroimaging where one wants to find common brain activation across multiple human subjects.

Alternatively, many advanced methods for spatial normalization are building on structure preserving transformations homeomorphisms and diffeomorphisms since they carry smooth sub manifolds smoothly during transformation. Diffeomorphisms are generated in the modern field of Computational Anatomy based on diffeomoirphic flows, also called diffeomorphicmapping.

However, such transformations via diffeomorphisms are not additive, although they form a group with function composition and acting non-linearly on the images via group action. For this reason, flows which generalize the ideas of additive groups allow for generating large deformations that preserve topology, providing 1-1 and onto transformations.

Computational methods for generating such transformation are often called which provide flows of diffeomorphisms as the main computational tool for connecting coordinate systems corresponding to the geodesic flows of Computational Anatomy.

Associated drawback:

The problem is comparisons of group activation data for patients with brain lesions with data from controls must still be treated with severe caution [12].

2.4.2 Using Seed points

Seed-based region growing (SBRG) has been widely used as a segmentation method for medical images. The selection of initial seed point in SBRG is the crucial part before the segmentation process is carried out. Most of the region growing methods identify the seed point manually which involve human interaction and require prior information about the image. In this paper, an automated initial seed point selection for SBRG algorithm is proposed.

The proposed method is tested on 50 mammogram images confirmed by a radiologist to consist microcalcifications. The performance is evaluated using Receiving Operator Curve (ROC) based on level of detection. Experimental results show that the method has successfully segmented the microcalcifications with 0.98 accuracy.

Overview:

- Second way to deal with MS lesion bias is to use seed points.
- Seed points can be processed with intuitive heuristics which provide improved segmentation accuracy while facilitating quick and natural point placement.

Associated Drawback:

But, the method does not account for normal variations in intensity [13]

2.5 Inpainting

To inpaint a damaged image or an ancient painting with missing regions is to guess and fill in the lost image information in such a consistent way that the restored image or painting seems as natural as its original version.

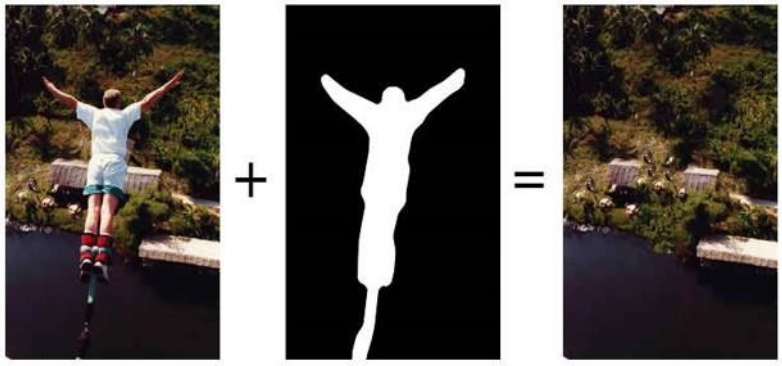


Figure 2.12: Image Inpainting to get the desired ones.

The word “inpainting” was initially invented by museum or art restoration workers [51, 52]. The concept of digital inpainting was only recently introduced into digital image processing [53], who were the first group to develop inpainting models based on high order PDEs.

Earlier related works based on second order PDEs and variational techniques can be found in [54] and [55].

Image inpainting is the process of reconstructing lost or deteriorated parts of images [14].It is mathematically highly ill posed process. There are many inpainting algorithms available for traditional structural 2D images.

2.6 Important Applications of Inpainting

The inpainting problem has also been carried out in the context of image interpolation [56], image replacement [57], and error concealment [58, 59], although these works are more based on statistical and algorithmic approaches.

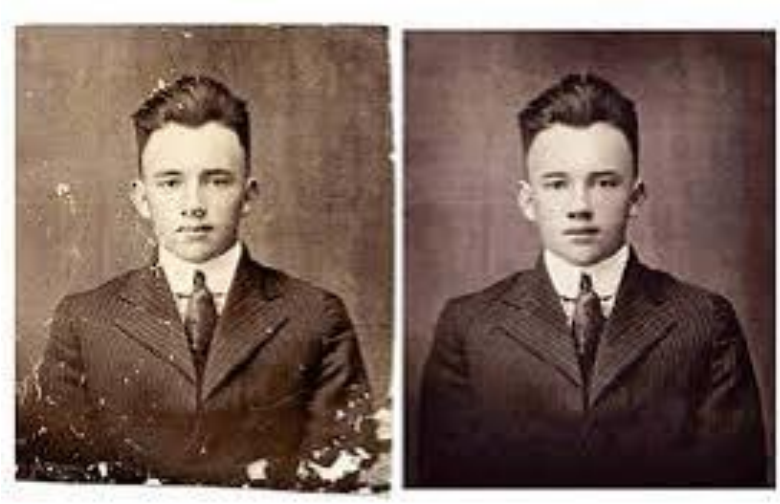


Figure 2.13: Image Restoration.

Important applications of digital inpainting include

a) digital restoration of ancient paintings for conservation purposes [51, 52],
b) restoring aged or damaged photographs and films [56, 60],
c) text removal and object removal in images for special effects [53],
d) disocclusion in vision research [55, 61],
e) digital zooming and edge-based image coding and so on

2.7 Image Inpainting techniques

There are many image inpainting algorithm available such as Harmonic inpainting, Transport inpainting, Mumford Shah inpainting [10] etc. All of these algorithms are part of structural image inpainting. Structural inpainting fills out the empty parts in the image by using local structural information only.

Figure 2.14: Image Inpainting by interpolation technique.

Now, they are described a little bit as followed.

2.7.1 Harmonic

Harmonic inpainting uses second order diffusion technique for inpainting. Its evaluation describes a multi scale analysis of an image that is a family of transformation, which when applied to a given image produces, a sequence of new images just like solving the heat equation [11].

It constitutes a smooth and linear interpolation process that roughly fills in missing gray values by averaging the given gray values on the boundary of inpainting domain.

But it does not show good results on the edges of lost data.

The contrast and noise parameters λ and σ give the user the liberty to adapt nonlinear diffusion scale-spaces to the desired purpose in order to reward interesting features with a longer lifetime. Suitable values for them should result in a natural way from the specific problem. In this sense, the time t is rather a parameter of importance, with respect to the specified task, than a descriptor of spatial scale. The traditional opinion that the evolution parameter t of scale-spaces should be related to the spatial scale reflects the assumption that a scale-space analysis should be uncommitted.

It is clear, however, that nonlinear diffusion filtering is a young field which has certainly not reached its final state yet. Thus, we can expect a lot of new results in the near future.

2.7.2 Transport

Transport inpainting works on third or higher order inpainting process. It's mainly a curvature driven diffusion [12].

But it lacks of simplicity. Mumford and Shah imposes a segmentation model which is based on the idea of decomposing an image into piecewise smooth parts that are separated by an edge set [13].

It is the higher order extension of the approach by an Euler elastic regularization.

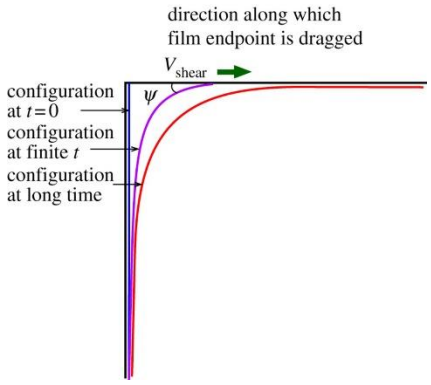


Figure 2.15: Curvature Driven Diffusion.

Two approaches can diminish this noise effect. First, one can get denoising the available part of the original image before applying the Curvature Driven Diffusion (CDD) inpainting scheme. However, due to the topological complexity of a general inpainting

domain, the implementation of most edge enhancing denoising schemes is often nontrivial. The second approach is to intrinsically build the denoising action in to the CDD inpainting scheme, which appears more natural for the human inpainting and disocclusion process. Human observers seem to be the master in detecting features from the available portion of a noisy image, and at the same time, extending them into the inpainting domain.

Such methodology also appears in other mathematical models in image and vision analysis. One famous example is the Mumford–Shah segmentation model [13], in which segmentation and denoising are carried out simultaneously.

2.7.3 Mumford Shah

Though Mumford and Shah Model reduces complexity but it needs fine tuning to get superior performance.

In this thesis, we extend these methods to propose a new inpainting algorithm that can be used to fill out the MS lesions in the brain as well as distortions in 2D images.

In spite of all this, the piece-wise smooth model is serviceable on certain scales and to a certain approximation. Restating these ideas, the segmentation problem in computer vision consists in computing a decomposition of the domain of the image.

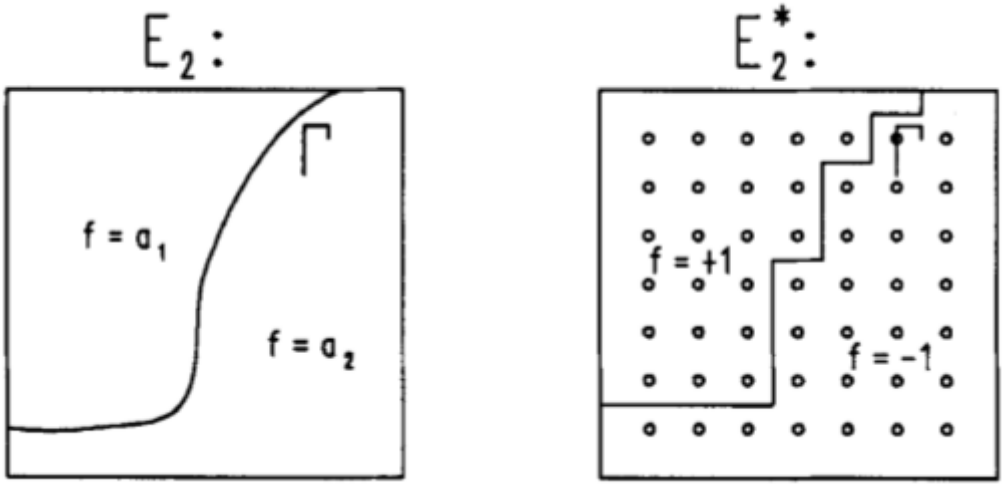


Figure 2.16: Continuous versus discrete segmentation.

The purpose of this improved method is to introduce and study the most basic properties of three new variational problems which are suggested by applications to computer vision. In computer vision, a fundamental problem is to appropriately decompose the domain R of a function g(x, y) of two variables.

2.8 Novel Inpainting Technique

Image inpainting is one of the most used image processing technique used by the professional restorers.

In this thesis, we propose an inpainting algorithm to fill out the MS lesions for delineating the effects of lesions on registration bias.

The inpainted MS brain is morphometrically more feasible in terms of registration accuracy and reduction of bias when calculating the output transformation matrix. Once the transformation matrix is calculated it can be used to add the masked MS lesions into the registered brain atlas. In this thesis, we also investigate if such preprocessing step (i.e. inpainting) contributes to the registration accuracy.

In our thesis a method is proposed that applies to the registration of MS brains. MS creates lesions in WM and GM but the lesions in the cortical or deep GM are difficult to understand in traditional T1 images. So, only WM lesions will be appreciated and this method can easily be extended to GM lesions.

For that reason we need to cover some necessary steps before applying inpainting technique.

2.8.1 Data

To get raw brain data, we are using Human Connectome Project (HCP) [28] open source data of healthy brains. The dataset was provided by HCP database which was composed of 5 set of patients data.

After qualitatively analyzing, we chose the suitable one to work with.

Every set was composed of a 3D acquired T1w, a T2w and a PDw image and a lesion mask created from the image. The data is acquired by MRI scanning. The image dimensions for 3D acquired T1w was 256 x 320 x 320 voxels with voxel size 1.171 x 1.171 x 1 mm.

Now the data we have got from the HCP open source database are in .nii format. We need to make it correct by using .mat format to work further with this. So, we need to use MATLAB and take those data's into the usable format. Then, we can proceed to the next task which is pre-processing.

2.8.2 Pre-processing

To extract the brain matter from the whole brain scan, we used Brain Extraction Tool (BET) [29]. BET deletes non-brain tissues like skull, tongue from an MRI image and extracts the brain matters from it.

After BET, reduction of noise from our data has been done with Structure preserving noise reduction method named SUSAN [30]. For carrying out these operations, we used FMRIB Software Library (FSL) is utilized which is an open source software.

As at the scope of this work, we did not have MS patient data so created artificial lesions in the healthy brain and performed our analysis to test the feasibility of our proposed algorithm.

Presumptuously considering about the inherent noise in our image we decided to apply a nonlinear digital filtering technique, in our case we considered the median filter. We did not thoroughly look about the conditions in which it preserves edges as edge preservation is not our primary focus.

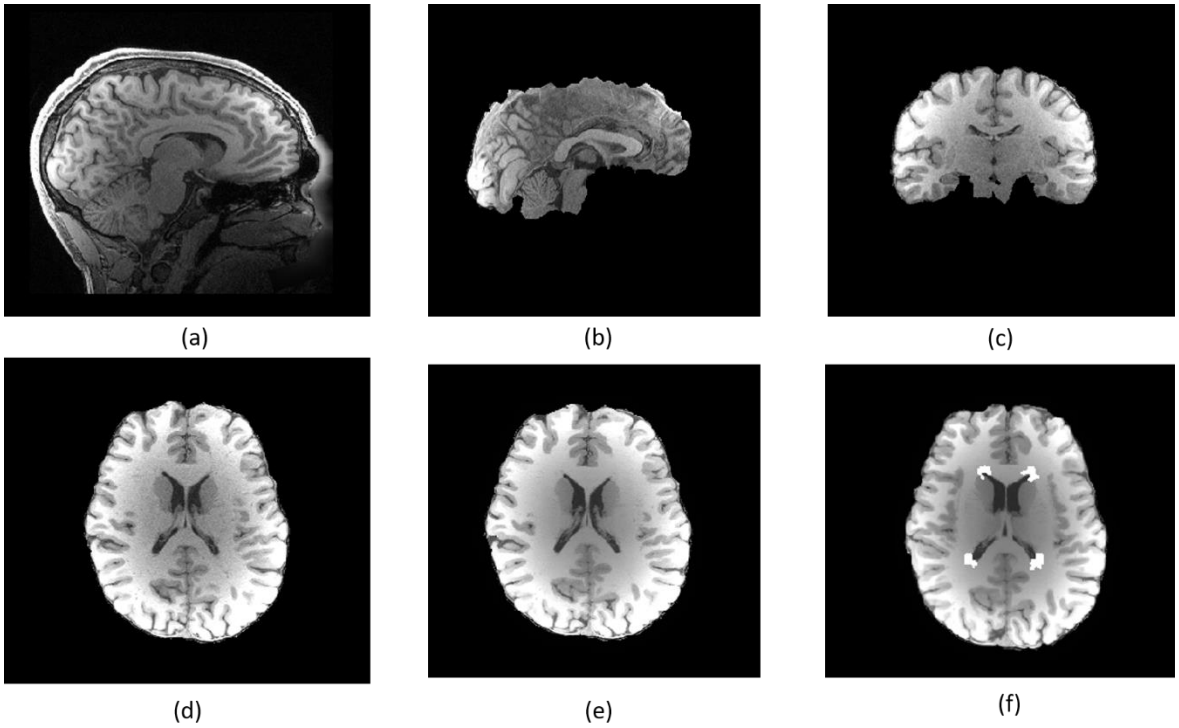


Figure 2.17: Different stages of pre-processing (a) Raw image of the whole, (b) brain extracted, (c) Orientation changed (coronal view), (d) Orientation corrected (axial view), (e) SUSAN filtered & (f) applied lesioned mask

So, after considering about the inherent noise in our image we decided to apply a nonlinear digital filtering technique, in our case we considered the median filter. We did not thoroughly look about the conditions in which it preserves edges as edge preservation is not our primary focus. The tradeoff was in presence of noise median filter do blur image but as we already applied some prior noise degradation mechanism in our image as a result noise level in our image becomes significantly low as a result blurring because of this noise can be almost ignored.

2.8.3 Inpainting Algorithm

We implemented the state-of-the-art inpainting algorithms like harmonic, Mumford-Shah, transport. The proposed algorithm has low complexity and it does not solely depend on neighbourhood points for inpainting process. During the analysis of previous

proposed methods we speculated the possibility of improvement by the exploitation of Total Variation (TV) model proposed in [22].

According to the variational methodology it is more convenient to solve the unconstrained TV inpainting problem

$$J[u] = \int_{EUD} |\nabla u| dxdy + \frac{\lambda}{2} \int_{E} |u - u^0|^2 dxdy \quad \text{…. …. …. …. …. (2.1)}$$

where, λ is the lagrange multiplier for the constrained variational problem. If we give larger value of this lagrange multiplier, we can get some clearer view of the image. On the other hand, if we give smaller value, image will be blurred a little bit.

Euler-lagrange equation for the minimization of energy functional J is

$$-\nabla \cdot \left(\frac{\nabla u}{|\nabla u|} \right) + \lambda_e \left(u - u^0 \right) = 0 \quad \text{… … …. ….. … (2.2)}$$

For all $z = (x, y) \in E \cup D$. The extended lagrange multiplier λ_e contains two different value for two different regions

$$\lambda_e = \lambda \text{ for } z \in E \quad \text{… …. …. …. ….. …. …. (2.3)}$$

$$0 \text{ for } z \in D$$

The infinitesimal steepest descent equation for $J[u]$ is following

$$\frac{\partial u}{\partial t} = \nabla \cdot \left(\frac{\nabla u}{|\nabla u|} \right) + \lambda_e \left(u - u^0 \right) \quad \text{… … ….. …. …. (2.4)}$$

Since λe takes two different values, (2.3) or (2.4) is a two-phase problem, and the interface is the boundary Γ of the inpainting domain. From the numerical point of view, in all of the above differential equations we replace the curvature term

$$\nabla \cdot \left(\frac{\nabla u}{|\nabla u|} \right) \quad \text{by} \quad \nabla \cdot \left(\frac{\nabla u}{|\nabla u|_a} \right), \qquad \text{…. …. ….. …. …. (2.5)}$$

where, the "lifted" absolute value is defined by

$$|s|_a := \sqrt{s^2 + a^2} \qquad \text{… … … …. …. ….. …… ….. (2.6)}$$

for some (usually small) positive lifting parameter a.

We are thus actually minimizing

$$J_\lambda^a[u] = \int_{E \cup D} \sqrt{a^2 + |\nabla u|^2}\, dxdy + \frac{\lambda}{2} \int_E |u - u^0|^2 dxdy. \qquad \text{…. … (2.7)}$$

As in most processing tasks involving thresholding's (like denoising and edge detection), the lifting parameter an also plays a thresholding role. In smooth regions where |∇u|<<a, the model tries to imitate the harmonic inpainting, while along edges where |∇u|>>a, the model resumes the TV inpainting.

On the other hand, from the theoretical point of view, the lifting parameter a also better conditions the TV inpainting model (2.1). In a noise-free situation, (2.1) is reduced to a boundary value problem:

$$\nabla \cdot \left(\frac{\nabla u}{|\nabla u|} \right) = 0, \quad x \in D; \qquad u|_{\partial D} = u^0|_{\partial D}.$$

… …. . …. (2.8)

Since λ_e takes two different values for two different regions it is a two phase problem and the interface is the boundary of the inpainting domain.

This approach initiates with a lesioned image where we artificially inserted some region to imitate MS lesion in practical cases. Details of insertion of region is included in the inpainting the lesion part. In the original image a gradient analysis of the whole image is operated. From which the gradient similarity with the lesioned part is observed by optical evaluation.

Necessary filtering, rotation and conversion of image for the ease of usage and denoising gives a clear view of the respective image.

In the original TV inpainting approach the inpainted value of the target pixel has been found out with the help of adjacent neighborhood. On the contrary in our approach due to almost same value neighborhood we concentrated on a neighborhood which has almost same gradient as our targeted region by optical evaluation of the gradient of whole image.

Suppose, the target pixel is O. Then according to the figure O' is the corresponding point of another neighborhood which is almost 18×18 pixel away from our target pixel. We found out this neighborhood by gradient matching by optical evaluation.

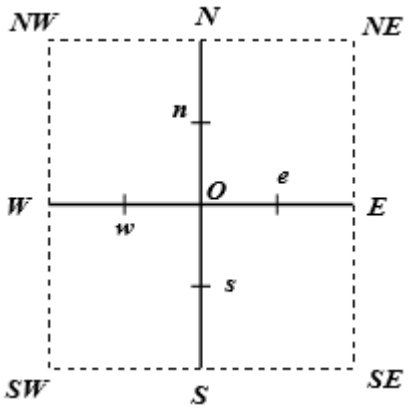


Figure 2.18: A target pixel O and its neighbors.

Let E, N, W, S denotes its four adjacent pixels. For example, e, n, w, s the corresponding four midway points. Now this midway points are not available from the image .By doing some algebraic manipulation we found the divergence of this mid points by this equation

$$\left|\nabla u_e\right| = \frac{1}{h}\sqrt{\left(u_E - u_0\right)^2 + \left[\left(u_{NE} + u_N - u_S - u_{SE}\right)/4\right]^2} \quad \text{... …. … (2.9)}$$

Some variations on this formula may render better and improved performances. Due to concentrated focus on a working algorithm it was not viable for us to explore them.

The weights of this midway points are necessary to implement our proposed algorithm which was found by following equation

$$w_p = \frac{1}{\left|u_p\right|} \quad \text{.. …. …. ….. ….. …… …. (2.10)}$$

Actually we want to approximate the value of our inpainted point with the help of an equation which in nature signifies a low pass filter. According to our guideline paper a Jacobi iteration scheme is used. In this specialized scenario this iteration is somewhat observed ancillary.

$$u_o = \sum h_{OP} u_p + h_{OO} u_o^0 \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.11)$$

Illustrated equation more or less represents a low pass filter. Smoothing of the image by decreasing the disparity among the value of pixels was our intended purpose. Low pass filter was assumed to give an upper hand on this requisite.

Second part of this equation deals with the original value of our intended pixel to be inpainted. Original value multiplied with an appropriate filter coefficient abided by a specified equation should assist us.

First part deals with all the values of neighborhood points of that pixel to be inpainted. Cumulative value of them multiplied with a necessary filter coefficient is our prior need.

$$h_{OP} = \frac{w_p}{\sum_{Q \in \lambda_o} w_Q + \lambda_e} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.12)$$

λ_o signifies all the neighborhood pixel values.

$$h_{OO} = \frac{\lambda_e}{\sum_{Q \in \lambda_o} w_Q + \lambda_e} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.13)$$

This specified filter coefficients must coincide with a given constraint to align with the attributes of a low pass filter for smoothing purpose.

$$\sum_{P\in\lambda_0} h_{OP} + h_{OO} = 1 \quad \text{…. …. ….. …… …. (2.14)}$$

Since the applied filter was a low pass filter. Moreover, any iteration is not going to be included in this propsed approach it must abides by the maximum principle.

Freezing the filter coefficients (to linearize the equations), and adopting the Gauss–Jacobi iteration scheme for linear systems, at each step n, we update u(n−1) to u(n) by

$$u_O^{(n)} = \sum_{P\in\Lambda_O} h_{OP}^{(n-1)} u_P^{(n-1)} + h_{OO}^{(n-1)} u_O^{(n-1)} \quad \text{…. .. …. … ….. (2.15)}$$

where h(n−1) = h(u(n−1)). Since h is a low pass filter, the iterative algorithm is stable and satisfies the maximum principle [9]. In particular, the gray value interval [0, 1] is always preserved during the iterating process. Useful variations of the algorithm can be obtained by altering the definition wP or |∇up| in (2.10). For instance, instead of (2.9), we can also try

$$|\nabla u_e| \simeq \frac{1}{h}\sqrt{(u_E - u_O)^2 + [(u_{NE} - u_{SE})/2]^2}. \quad \text{… …. … ….. (2.16)}$$

For some small number a, to avoid a zero divisor in smooth regions. Notice that choosing a large a brings the TV model closer to the harmonic inpainting (especially computationally, since the spatial step size h is set to 1, and u takes values from the finite gray-scale interval [0, 1]).

In addition, as a gets bigger, the convergence of the iteration scheme speeds up. The size of the extension domain E is also easily determined. If the image is clean, E can simply be the boundary of the inpainting domain D.

In implementation, the weights w_P are “lifted” to

$$w_P = \frac{1}{|\nabla u_p|_a} = \frac{1}{\sqrt{a^2 + |\nabla u_p|^2}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (2.17)$$

Otherwise, to clean up statistical noise and extract reliable image information near the boundary, one can choose E with a reasonable size, e.g., several pixels wide, as practiced in image processing [21]. If, as for the inpainting of an old photo, the entire image is contaminated by noise, then one should take E to be the complement of D, to simultaneously clean and inpaint the photo.

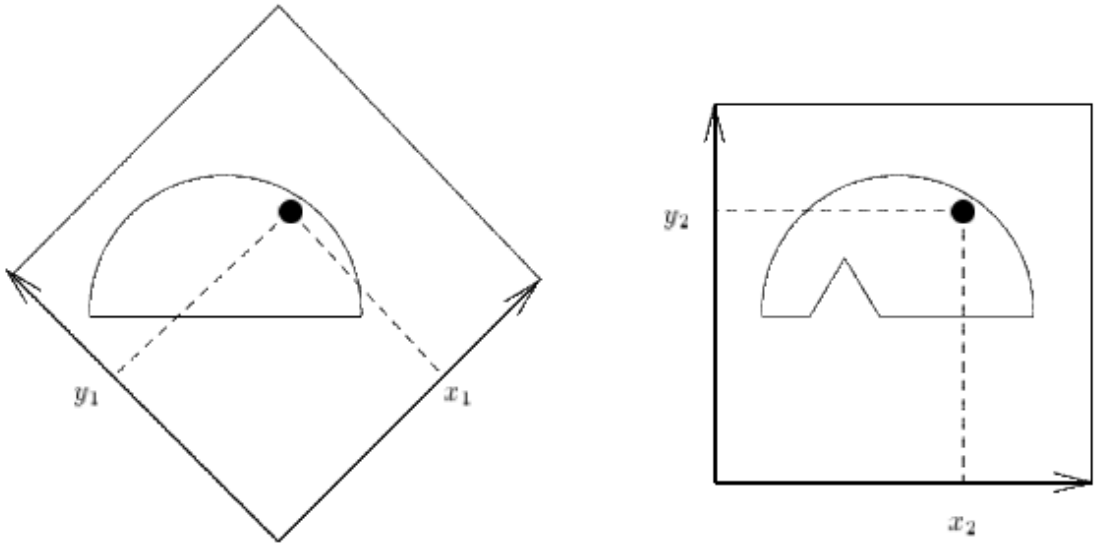
Chapter 3: Image Registration

Registration of one brain image to a brain atlas or a healthy brain is done so that the common features overlap and deviations from the healthy brain are apparent.

Given two images, the aim of registration is to find the transformation that maps the voxels from one image (the reference) to the voxels of the other (the floating image). Image registration is the process of transforming different sets of data into one coordinate system.

Data may be multiple photographs, data from different sensors, times, depths, or viewpoints [1]. It is used in computer vision, medical imaging [2]. military automatic target recognition, and compiling and analyzing images and data from satellites. Registration is necessary in order to be able to compare or integrate the data obtained from these different measurements.

3.1 Registration



(a) (b)

Figure 3.1: Registration of source image (a) with target image (b). Image (a) has been rotated so that the object will have same orientation as in image (b) [49].

The determination of a one-to-one mapping between the coordinates in one space and those in another, such that points in the two spaces that correspond to the same anatomical point are mapped to each other [49].

Image registration algorithms can also be classified according to the transformation models they use to relate the target image space to the reference image space. The first broad category of transformation models includes linear transformations, which include rotation, scaling, translation, and other affine transforms. [4] Linear transformations are global in nature, thus, they cannot model local geometric differences between images.[3]

For registration of a brain with an abnormal structure e.g. tumor or lesions, the invertibility of the transformation is not possible as these structures are not present in atlas.

In other words, establishing correspondence between features in sets of images to infer correspondence away from those features is known to be the mechanism of Image registration.

3.2 Classifications

Image registration or image alignment algorithms can be classified into intensity-based and feature-based. [3] One of the images is referred to as the reference or source and the others are respectively referred to as the target, sensed or subject images.

Image registration involves spatially registering the target image(s) to align with the reference image.[3] Intensity-based methods compare intensity patterns in images via correlation metrics, while feature-based methods find correspondence between image features such as points, lines, and contours [3]. Intensity-based methods register entire images or sub-images. If sub-images are registered, centers of corresponding sub images are treated as corresponding feature points.

Feature-based methods establish a correspondence between a numbers of especially distinct points in images. Knowing the correspondence between a numbers of points in images, a geometrical transformation is then determined to map the target image to the reference images, thereby establishing point-by-point correspondence between the reference and target images [3].

3.3 Applications

- To look for differences in the same type of images taken at different times, e.g.:

– Mapping Pre and post contrast agent

  - Digital Subtraction Angiography (DSA)
  - MRI with Gadolinium tracer

– Mapping Structural Changes

  - Different stages in tumor growth (Before and After treatment)
  - Neuro degenerative disease-> Quantifying tissue loss patterns

– Detecting Changes due to function

  - Functional MRI (fMRI) Before and After brain stimulus
  - Associated Problems:
    - ✓ Subject scanned multiple times -> removed from scanner
    - ✓ We cannot easily fix/know patient location and orientation with respect to imaging system
    - ✓ Need to remove differences in patient positioning to detect true differences in patient images [50].

3.4 Registration is Preponderant

Registration of the MS brain to a brain atlas is an essential step for analyzing brain structures. This is because the human brain has significant variation in its morphometry where any standardized diagnosis on the basic of morphometry can be erroneous.

Use of brain atlases enable us to segment images using a prelabeled atlas [31], to follow the evolution of brain structures in longitudinal studies [32] or for morphometry [33]. For treatment, diagnosis and evaluating the progression of MS, such registration to brain atlas is very common.

However, losing the myelin layer, the MS lesions appears different than rest of the surrounding anatomy in MRI image. This creates a registration bias and automated segmentation performance.

In- deed, intensity driven non-rigid registration algorithms assume that the two images being registered have the same structures but these lesions are present in the patient and not in the reference image [34]. This distortion of the transformation will be an important problem to solve.

Some studies have investigated possible methodological reasons to explain changes in GM volume with increasing WM damage [35], [36], and [37]. These studies have suggested that WM lesions may affect mean WM intensity values and shift segmentation boundaries, thus leading to inaccuracies in the GM segmentation considered for atrophy quantification.

Higher white matter lesions artificially reduced the total GM volumes [38] which further add to the registration bias.

3.5 Some Features of Registration

There are some basic features of registration techniques which we should know to work further with this phenomena. So some fundamental features are described brifly in the following.

3.5.1 Cost Function Weighting

Weighting volumes can be specified using -refweight, -inweight (or both). This allows the cost function to have a different weighting at each voxel, which is useful for excluding areas (weight=0) of no interest, or increasing the weighting around important structures such as the ventricles. Note that this is different from masking the original images, as masking introduces artificial boundaries whereas weighting does not.

3.5.2 Degrees of freedom

Choose from 6, 7, 9 or 12 Degrees of Freedom (DOF) for full 3D registrations. Also includes a 3DOF 2D-to-2D registration mode which is selected using the -2D option. Note that it does not perform any search in 2D mode, and cannot deal with 2D to 3D registrations. More flexible DOF options are provided by the specific schedule files provided in $FSLDIR/etc/flirtsch.

3.5.3 Interpolation Methods

This includes Nearest Neighbour, a family of Sinc-based methods (three window types - rectangular, Hanning and Blackman) with configurable window width, and spline (a highly efficient method, with similar output characteristics to sinc). The interpolation is only used for the final transformation (and in applyxfm), not in the registration calculations.

3.5.4 Cost Function

This includes the within-modality functions Least Squares and Normalised Correlation, as well as the between-modality functions Correlation Ratio (the default), Mutual Information and Normalised Mutual Information. In addition, there is the BBR cost function which utilises a segmentation of the reference image to define a boundary, and it is the intensity differences in the input image, across the transformed boundary, that contribute to the cost.

3.6 Different Registration approaches

To solve the problem of registering a brain with tumors to a healthy brain, biomechanical model of the tumor growth was planted in the reference image before and after the registration [39], [40] to mimic the effect that a tumor would have if it was on the healthy brain.

The biomechanical model of the tumor or the "tumor seed" would push the surrounding tissues of the brain and would account for the distortion in the transformation that was to be caused by the "real" tumor.

But a "tumor seed" cannot model the WM lesions as the lesions replace healthy tissues rather than pushing them like tumors. Another approach is to ameliorate the effect of the abnormal growths e.g. tumors [41], focal lesions [42] in registration by masking the regions of interest. The voxels that contain the lesions are removed from the similarity metric of the registration which means the cost function will only be applied on the voxels which are "healthy".

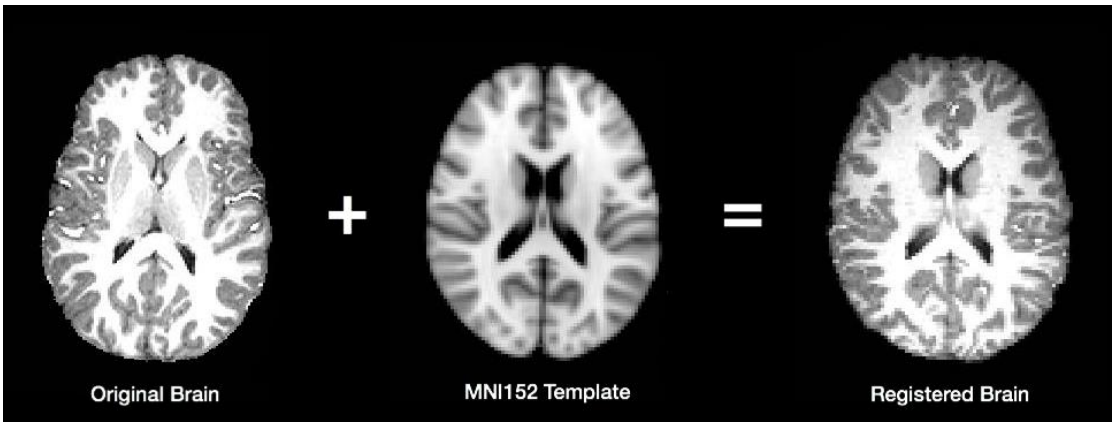


Figure 3.2: Registration of source image (left one) with target image (middle one). Finally the last one is the registered one.

Furthermore, in [43], different brain structures are segmented and parameterized to find the optimum transformation to match these structures. This takes care of the MS lesions bias as the lesions do not appear in these structures.

Three approaches are distinguished. They are-

- Removing the lesions from the patient image.
- Adding the lesions to the atlas and aligning.
- Removing the influence of the lesions during the registration.

In this work, the MS lesions are inpainted created before performing registration to make the lesions look like healthy brain tissue. This is a fully automated process as the mask used to create the lesions are known a priori. Thus, it is an easy preprocessing step before registration.

3.7 Brain Atlas

A geometric transformation maps locations in one image to new locations in another image. The step of determining the correct geometric transformation parameters is key to the image registration process.

Image registration is often used as a preliminary step in other image processing applications. For example, you can use image registration to align satellite images or to align medical images captured with different diagnostic modalities (MRI and SPECT). Image registration allows you to compare common features in different images. For example, you might discover how a river has migrated, how an area became flooded, or whether a tumor is visible in an MRI or SPECT image.

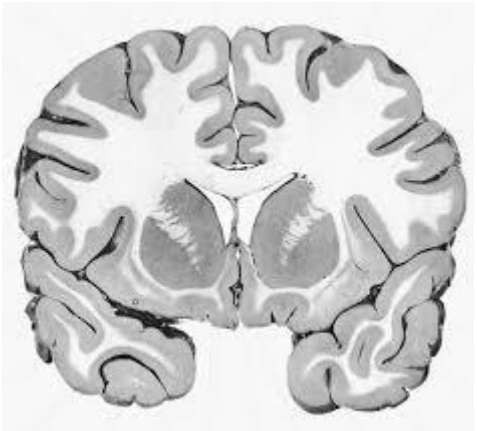


Figure 3.3: Brain Atlas in MRI scan.

A brain atlas is composed of serial sections along different anatomical planes of the healthy or diseased developing brain. Here each relevant brain structure is assigned a number of coordinates to define its outline or volume. Registering a patient brain with brain atlas is the most common way to build it.

Now we have already applied our proposed inpainting technique to the patient brain with lesions after BET and SUSAN. Now we need to register the patient brain with brain Atlas.

3.8 Registration with brain Atlas

Registration are of two kinds named functional and structural. Here in our thesis, we work with the structural registration or voxel based registration. The prime aim of registration is to find the transformation that maps the voxels from one image (the reference) to the voxels of the other (the floating image).

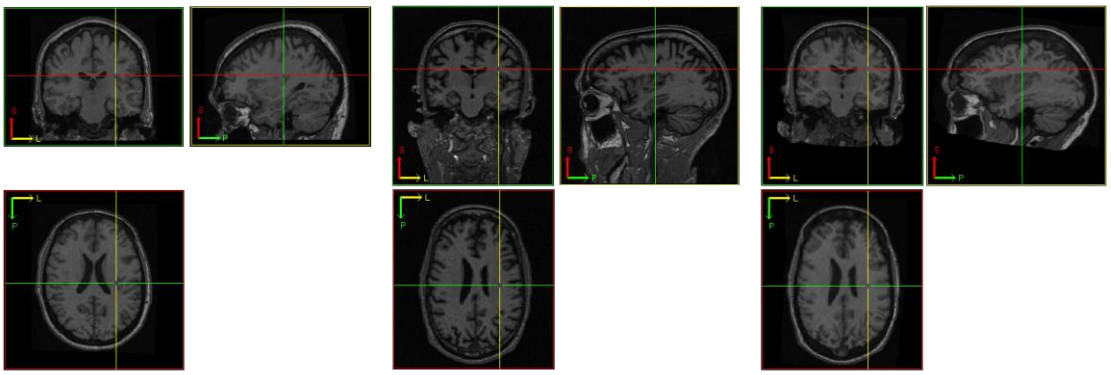


Figure 3.4: Registration of source images (a) with target images (b) to get the registered images (c) with sagittal, coronal and axial views in MRI.

After the inpainting step, we perform FLIRT to brain using the inpainted image. FLIRT (FMRIBs Linear Image Registration Tool) is a fully automated robust and accurate tool for linear (affine) intra- and inter-modal brain image registration with 2D or 3D images.

It is based around a multi-start, multi-resolution global optimization method. In addition, it can be run with a number of different transformation models (degrees of freedom) and it implements a general cost function weighting scheme for all cost functions.

3.8.1 FLIRT

- Main Options

The simplest use of FLIRT is to register two single volumes together. This is done by choosing the Input image -> Reference image mode in the top box, then filling in the Reference image and Input image boxes with the appropriate images. The result is a registered image which will be saved to the location specified in the Output image box. All other options/boxes can be left at their default values.

The second mode of operation is a two stage registration which takes an input Low res image and two target images. It initially registers the low res image to a High res image and then registers this high res image to the final Reference image. The two resulting transformations are concatenated and then applied to the original low res image to create an Output image that is a version of the low res image transformed (resliced) to the reference image space.

- Secondary Images

Apply the estimated transform to other (secondary) images, which were originally aligned with the input/low-res image, in order to align them with the reference image.

- Model/DOF

For 3D to 3D mode, the DOF can be set to 12 (affine), 9 (traditional), 7 (global rescale) or 6 (rigid body). In 2D to 2D mode only 3 DOF (rigid body) transformations are allowed. For each registration, we used trilinear interpolation technique and affine registration (12 DOF).

For FLIRT, an input and a reference volume is to be taken; the calculated affine transformation that registers the input to the reference which is to be saved as an affine matrix; and output volume where the transform is applied to the input volume to align it with the reference volume.

3.8.2 Some related functions

- Search - select the angular range over which the initial optimisation search stage is performed.
- Cost Functions - select the desired cost function from a range of inter- and intra-modal functions.
- Interpolation - select the interpolation method to be used in the final (reslice) transformation (it is not used for the estimation stage - trilinear interpolation is always used for the estimation of the transformation). The options for this final interpolation method are: Tri-Linear; Nearest Neighbour and * Sinc. If Sinc is chosen, further window parameters (type of windowing function and window width) can also be specified.
- Weighting Volumes - impose voxel-wise weighting to reference and/or input images, to affects the cost function. The weighting images must be the same size as the image they are weighting (e.g. refweight and reference images) and the voxel values of the weighting image represent how much weighting that particular voxel is given in the cost function.

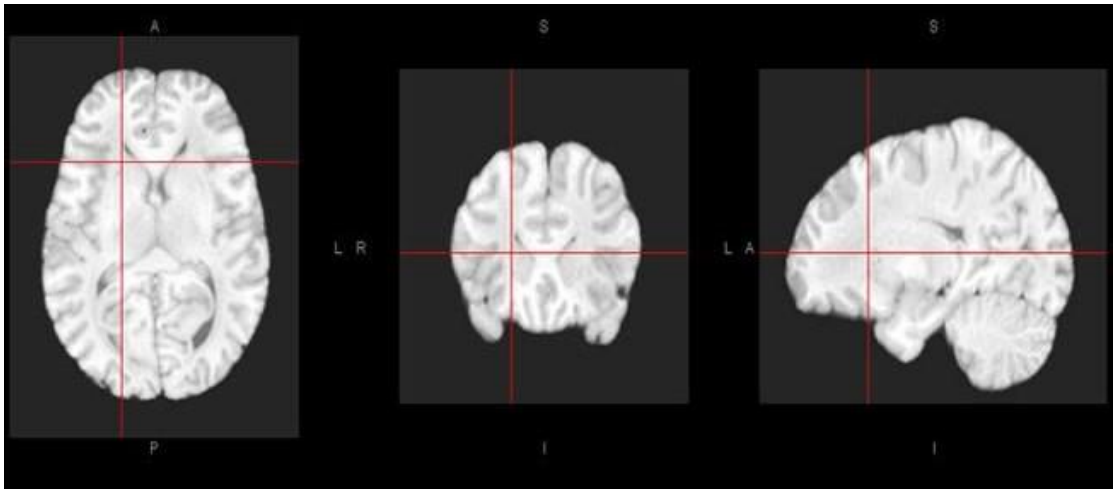


Figure 3.5: Three types of views of brain MRI with mapping.

In this way very accurate registrations can be made between pathological and "normal" images. This cannot be achieved by masking the images prior to registration, as that induces artificial boundaries which bias the registration.

Therefore, by setting weights to zero, some areas of the image can be effectively ignored, which is useful in masking out pathologies so that they do not affect the registration.

Furthermore, some areas can be given extra weighting (such as the ventricles) so that the registration is most accurate near these structures, but still uses information from the rest of the image (e.g. the cortical surface) to improve the robustness of the registration.

Affine transformation has 6 parameters. So, it needs 3 pairs of corresponding points. Usually it uses more than 3 pairs to obtain best fitting affine parameters. Affine transformation is a simple linear transformation. This transformation can change shape: it includes scaling, rotation, translation, and shearing. In addition, FLIRT can also be used to apply a saved transformation to a volume.

For these usages the reference volume must still be specified as this sets the voxel and image dimensions of the resulting volume. Firstly we do the registration with the healthy brain and reference MNI152 template [23]. The result is to be used as ground truth. Then we register the lesioned image as well as inpainted image with the reference one.

3.9 Overview of the proposed framework

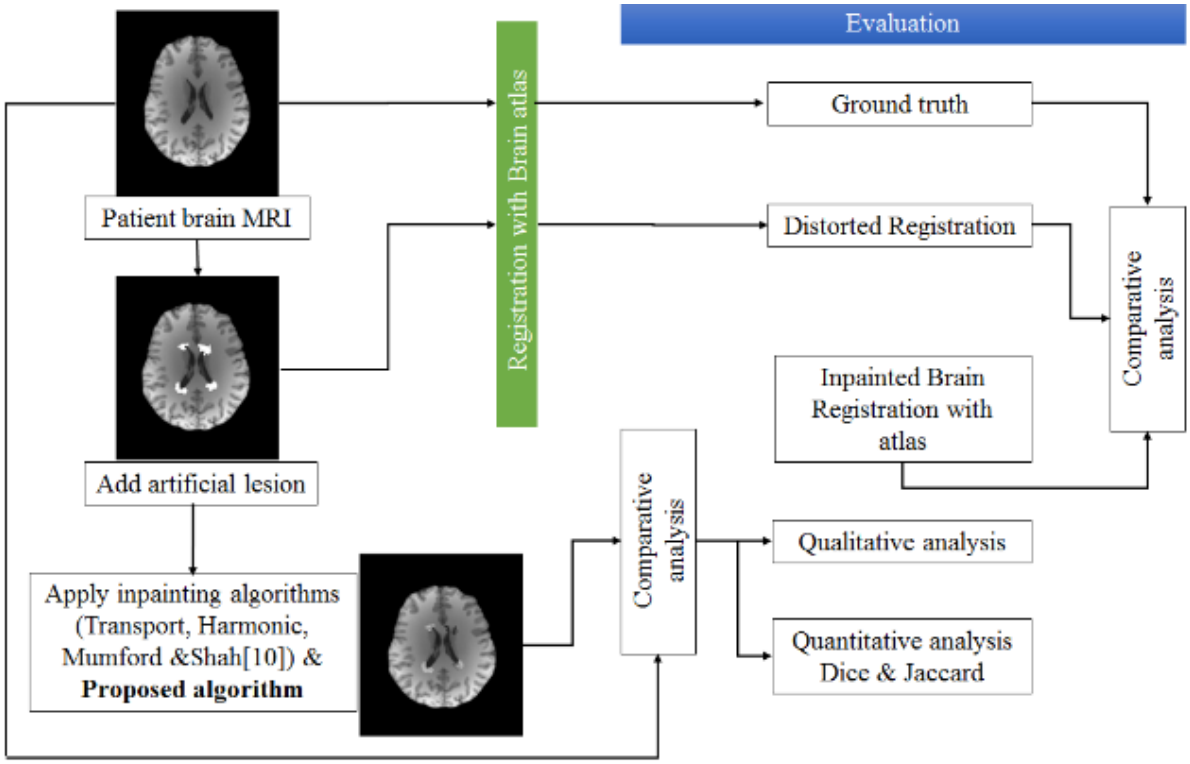


Figure 3.6: Eclectic view of the proposed framework.

So, we finally got registered healthy, lesioned and inpainted image. For quantitative analysis with the lesioned and inpainted ones, dice and jaccard scores has been calculated. Finally we can come to a conclusion that our proposed inpainting method has an improved effect to remove the bias in case of registration with brain atlas.

Chapter 4: Performance analysis

To evaluate our results we at first apply some image pre-processing using BET (Brain Extraction Tool) in our data. Then after this pre-processing we use (logical) mask to create artificial lesions and then apply our algorithm to test its feasibility.

For comparing our results, we use standard comparison method Jaccard and Dice with the other inpainting algorithm (Transport, Mumford Shah, Harmonic etc.) For our justification we also applied the same procedure in a normal image to see how it works on the real image.

Firstly, we will be seeing utilizing only white lesions added artificially. Then, we will look over the lesions being slightly greyish (both light grey and dark grey) as well as mixed type artificial lesion. For 2D image, we will do the performance analysis. And afterwards we will be discussing about the MRI image.

We will be conducting two different types of results. They are-

- Qualitative Analysis
- Quantitative analysis

4.1 Image Contrast Modalities

There are lots of types of images can be formed through the MRI images. For simplicity we will be discussing about mainly three types of images. They are T1 weighted image, T2 weighted image and proton density weighted image.

To know it better we should have some idea about Repetition Time (TR) & Echo Time (TE).

- **Repetition Time (TR):** the time difference between one RF wave pulse to another.
- **Echo Time (TE):** The TE is the time between the initial 90 degree RF pulse and the echo signal that we got from the gradient coils.

4.1.1 T1 weighted image

T1 weighted image (also referred to as T1WI or "spin-lattice" relaxation time) is one of the basic pulse sequences in MRI and demonstrates differences in the T1 relaxation times of tissues.

A T1WI relies upon the longitudinal relaxation of a tissue's net magnetisation vector (NMV). Basically, spins aligned in an external field (B_0) are put into the transverse plane by an RF pulse. They then slide back toward the original equilibrium of B_0. Not all tissues get back to equilibrium equally quickly, and a tissue's T1 reflects the amount of time its protons' spins realign with the main magnetic field (B_0).

T1 weighting tends to have short TE (<40 ms) and TR (<750 ms) times.

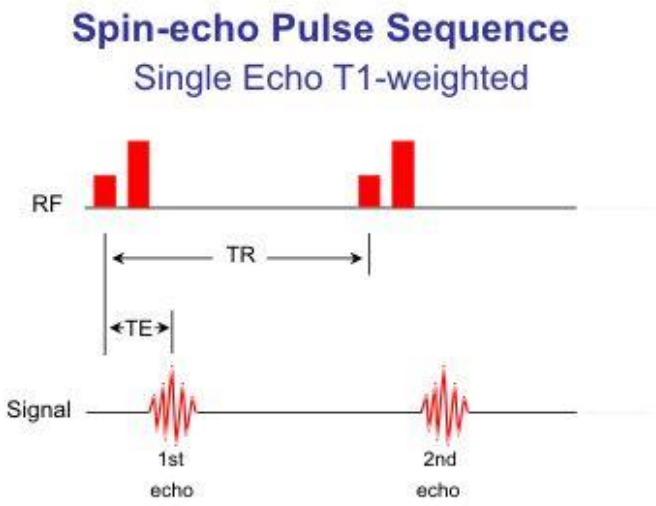


Figure 4.1: TE and TR for T1 weighted image.

Properties:

Fat quickly realigns its longitudinal magnetization with B0, and it therefore appears bright on a T1 weighted image.

Conversely, water has much slower longitudinal magnetization realignment after an RF pulse, and therefore has less transverse magnetization after a RF pulse. Thus, water has low signal and appears dark.

4.1.2 T2 weighted image

T2 weighted image (also referred to as T2WI "T2 weighted image") is one of the basic pulse sequences in MRI. The sequence weighting highlights differences in the T2 relaxation time of tissues.

A T2WI relies upon the transverse relaxation (also known as "spin-spin" relaxation) of the net magnetization vector (NMV). T2 weighting tends to require long TE(>2000 ms) and TR(80 ms) times.

After an RF excitation pulse, spins are decaying from their aligned precession in the transverse plane. Differences in this decay are captured in T2 weighting.

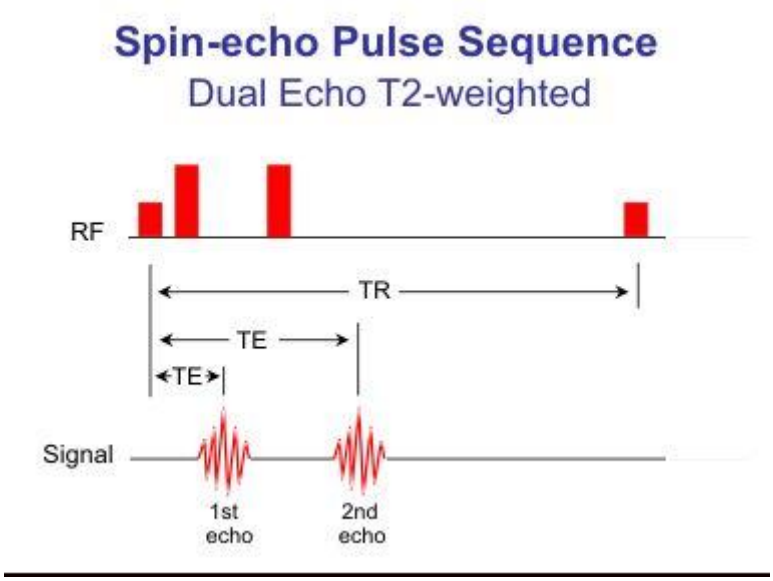


Figure 4.2: TE and TR for T2 weighted image.

Properties:

- Basically it's a brighter version of MRI images.
- Fat: intermediate-bright; fluid: bright.

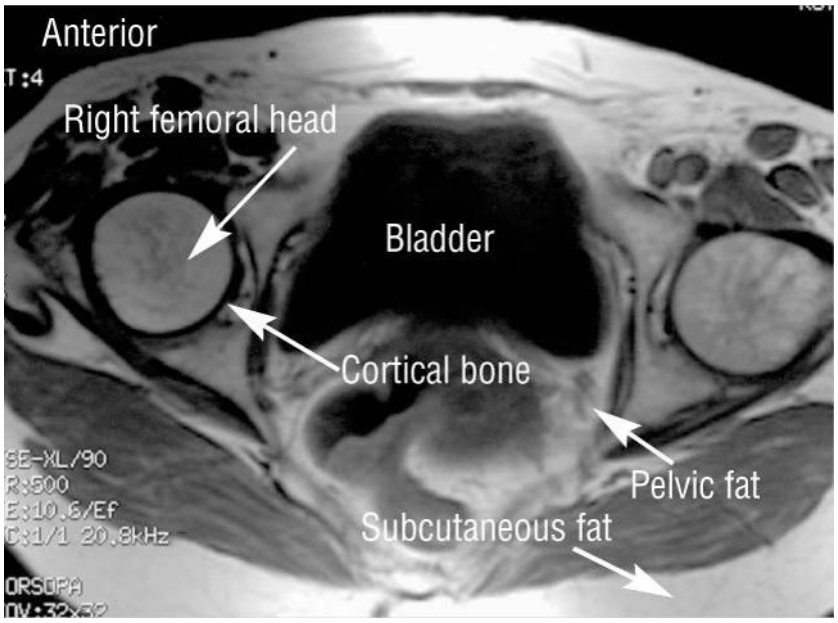


Figure 4.3: T1 weighted image of axial pelvis.

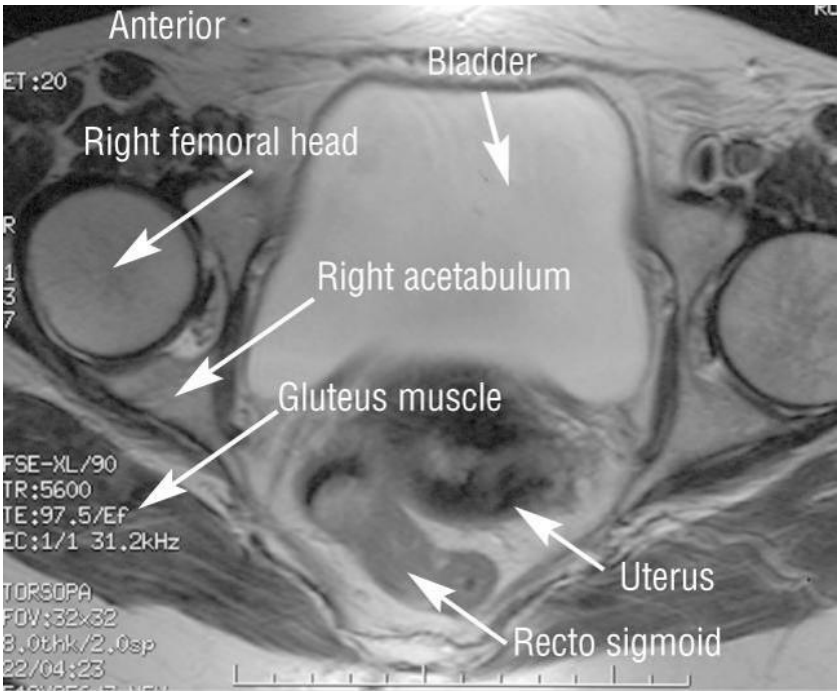


Figure 4.4: T2 weighted image of axial pelvis.

4.1.3 Proton Density (PD) weighted image

When an MRI sequence is set to produce a PD-weighted image, it is the tissues with the higher concentration or density of protons (hydrogen atoms) which produce the strongest signals and appear the brightest on the image.

Proton density weighted sequence produces contrast mainly by minimizing the impact of T1 and T2 differences with long TR (2000-5000ms) and short TE (10-20).

The easiest way to identify PD weighted images is to compare the fluid against the fat signal. Fluids normally appear as grayish white, almost similar appearance as the fat in the body.

Properties:

Bone marrow: - equal to or higher than that of muscle (fatty marrow is usually bright)
Fat – bright (slightly darker than the fat signal in T1 images)
Fluids – bright (darker than the fluid signal in T2 images)
White matter - darker than bright gray
Gray matter - bright gray
Moving blood- dark
Muscles-gray
Bone - dark
Air - dark

4.2 Qualitative Analysis

4.2.1 For 2-D image

Figure 4.5: Original image (Upper left), Masked Image (Upper right), Inpainted image (Lower Middle) for transpose inpainting Method

Figure 4.6: Original image (Upper left), Masked Image (Upper right), Inpainted image (Lower Middle) for Mumford Shah inpainting method

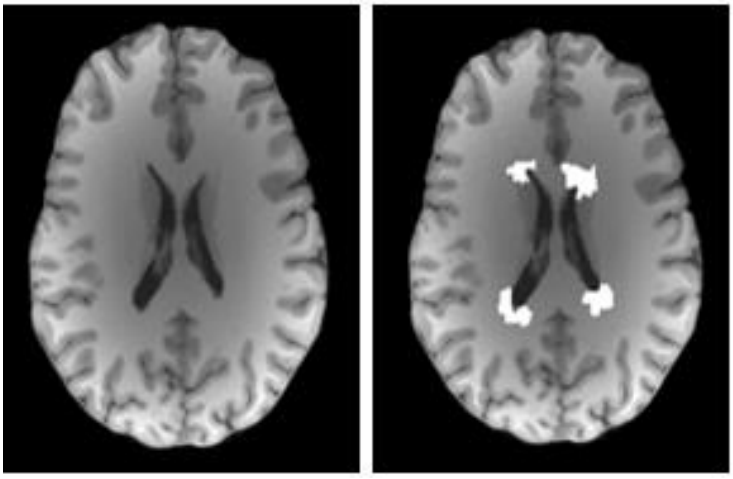
Figure 4.7: Original image (Upper left), Masked Image (Upper right), Inpainted image (Lower Middle) for Harmonic inpainting method.

Figure 4.8: Original image (Upper left), Masked Image (Upper right), Inpainted image (Lower Middle) for our proposed inpainting method

4.2.2 For 3-D MRI image

Now after completing the 2D random images, our next target is to utilize that inpainting algorithm for a patient with his brain MRI images.

But, due to some circumstances as stated earlier, we firstly take the healthy patient data. Then, artificially give it some lesions to mimic like a patient brain image just like the following.

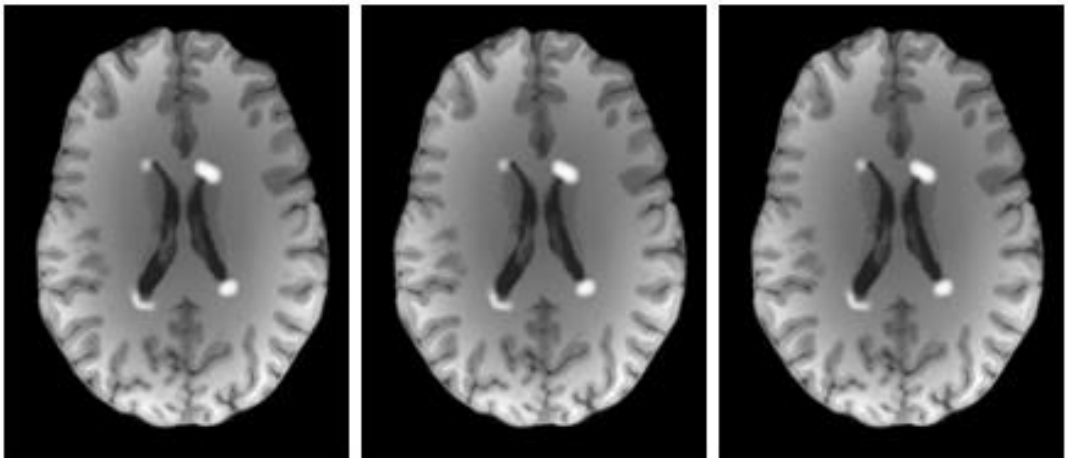


(a) (b)

Figure 4.9: (a) MRI T1 brain image of a healthy patient, (b) lesions are added artificially to mimic the MS lesions.

After getting the mimicking done, now we are going to use the traditional inpainting techniques (i.e. harmonic, Mumford shah, transport) to inpaint the lesioned image. Now, these techniques are used as they are the state-of-the-art methods for inpainting generally 2D images.

But we will check the workability of those in MRI images by visual as well as dice and jaccard scores (dice and jaccard scores are used to compare the images quantitatively).



(a) (b) (c)

Figure 4.10: The lesions in the artificially created MS brain are inpainted using (a) harmonic, (b) transport, and (c) Mumford and shah inpainting technique

Now that we have utilized the traditional methods, we can visually compare the effectiveness of these state-of-the-art methods.

Our next task is to use our proposed inpainting algorithm of this thesis to inpaint the lesions which we artificially structured in the healthy patient brain beforehand. After using the inpainting technique proposed in our method, we will have something like the following.

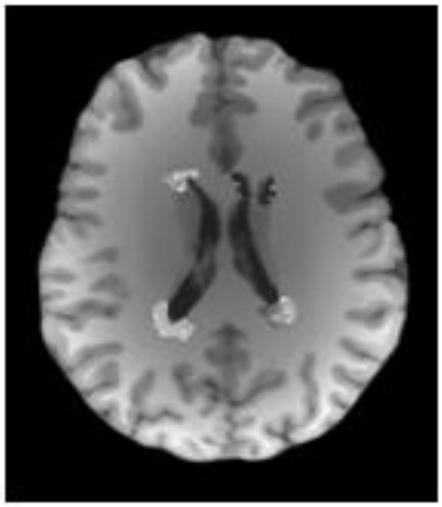
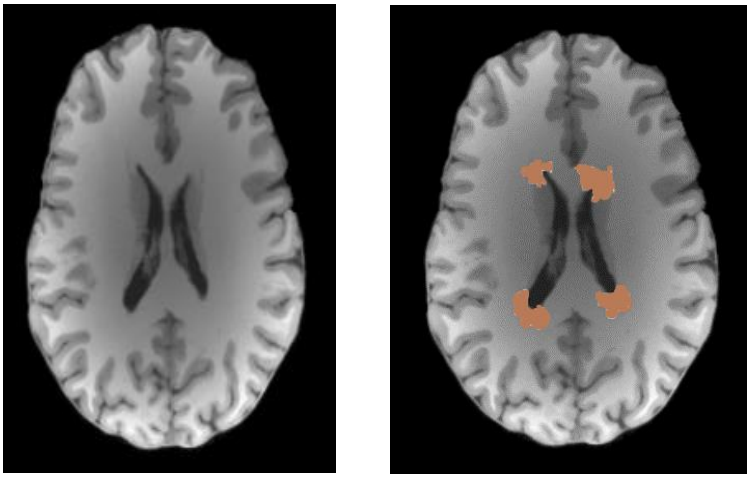


Figure 4.11: The lesions in the artificially created MS brain are inpainted using proposed inpainting algorithm

So, now if we compare qualitatively those traditional methods with this proposed one, it is conspicuously better inpainted. But even here, the lesions are not fully gone, some slight parts are still present.

Now as we have introduced only the white lesions artificially, we need to check by giving some other type of lesions as well. So we firstly give all the greyish artificial masks, then give the mixed type masks i.e. having both white and greyish lesions with different orientation as well.

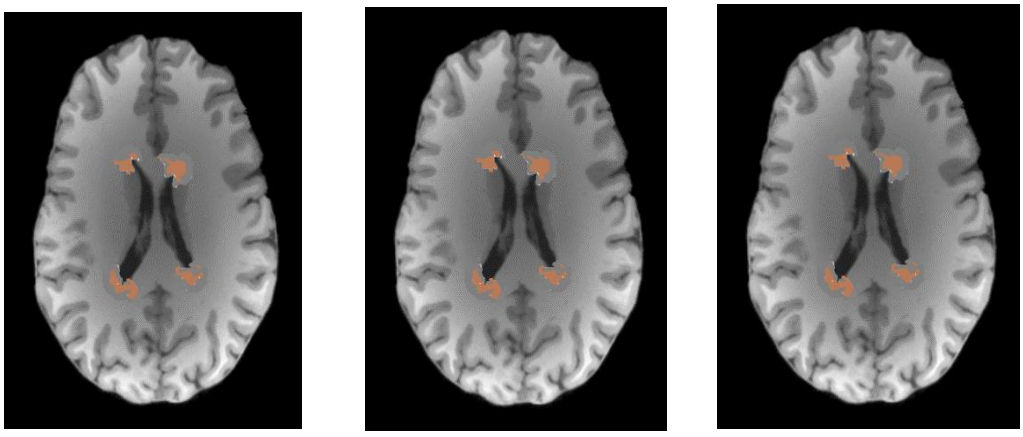
So, we firstly take the healthy patient data. Then, artificially give it some grey type lesions to mimic like a patient brain image just like the following.



(a) (b)

Figure 4.12: (a) MRI T1 brain image of a healthy patient, (b) lesions are added artificially to mimic the MS lesions.

After getting the mimicking done, now we are going to use the traditional inpainting techniques (i.e. harmonic, Mumford shah, transport) to inpaint the lesioned image. Now, these techniques are used as they are the state-of-the-art methods for inpainting generally 2D images.



(a) (b) (c)

Figure 4.13: The lesions in the artificially created MS brain are inpainted using (a) harmonic, (b) transport, and (c) Mumford and shah inpainting technique

Now that we have utilized the traditional methods, we can visually compare the effectiveness of these state-of-the-art methods. Our next task is to use our proposed inpainting algorithm of this thesis to inpaint the lesions which we artificially structured in the healthy patient brain beforehand. After using the inpainting technique proposed in our method, we will have something like the following.

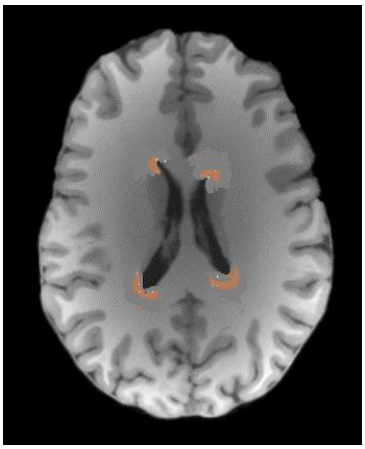
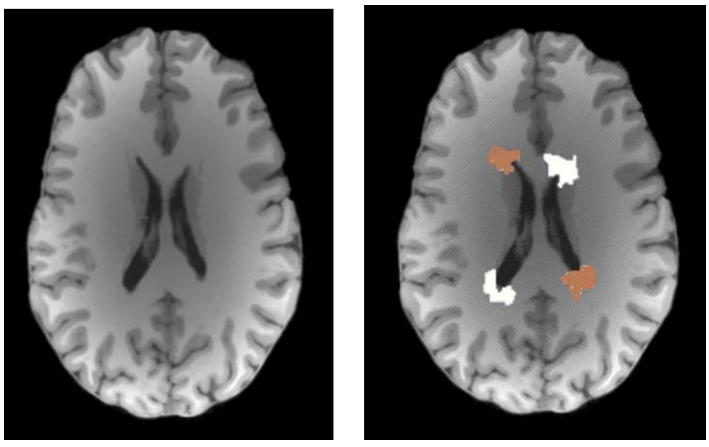


Figure 4.14: The lesions in the artificially created MS brain are inpainted using proposed inpainting algorithm

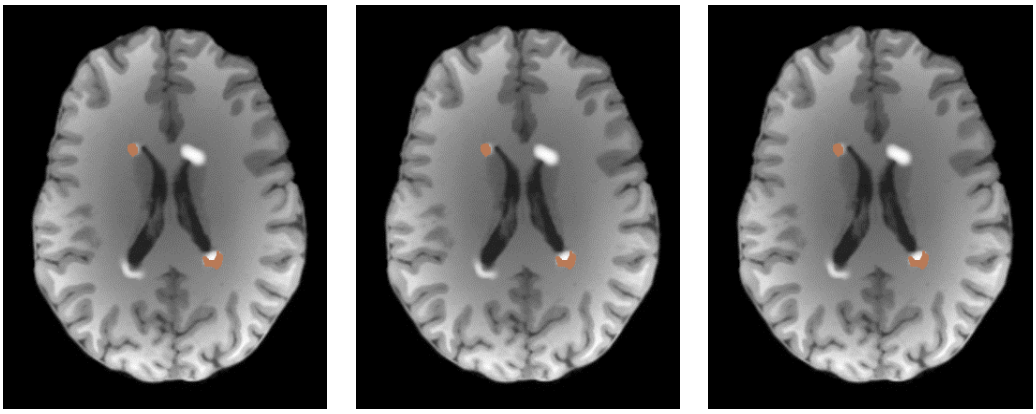
Now if we apply mixed lesions.



(a) (b)

Figure 4.15: (a) MRI T1 brain image of a healthy patient, (b) lesions are added artificially to mimic the MS lesions.

After getting the mimicking done, now we are going to use the traditional inpainting techniques (i.e. harmonic, Mumford shah, transport) to inpaint the lesioned image.



(a) (b) (c)

Figure 4.16: The lesions in the artificially created MS brain are inpainted using (a) harmonic, (b) transport, and (c) Mumford and shah inpainting technique

Now that we have utilized the traditional methods, we can visually compare the effectiveness of these state-of-the-art methods.

Our next task is to use our proposed inpainting algorithm of this thesis to inpaint the lesions which we artificially structured in the healthy patient brain beforehand. After using the inpainting technique proposed in our method, we will have something like the following.

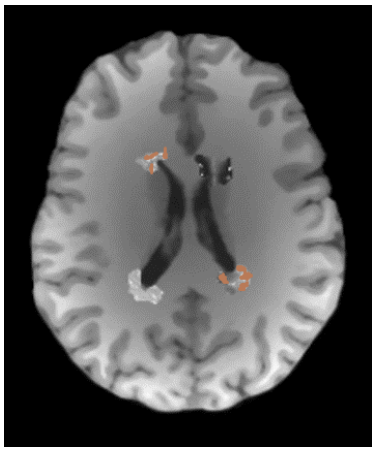
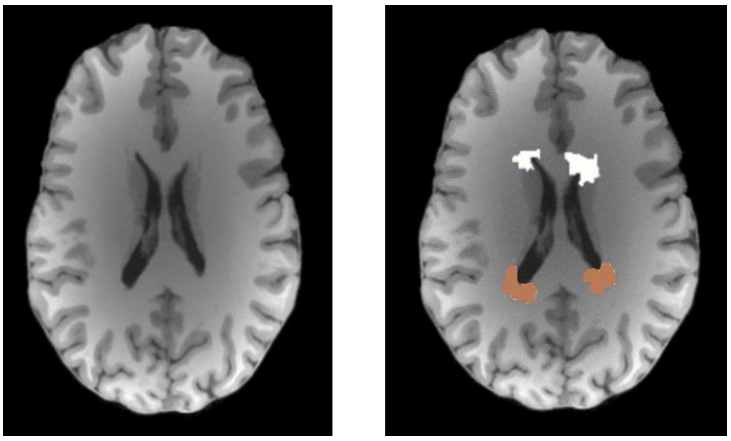


Figure 4.17: The lesions in the artificially created MS brain are inpainted using proposed inpainting algorithm.

Now, again, if we apply different orientation of mixed lesions.

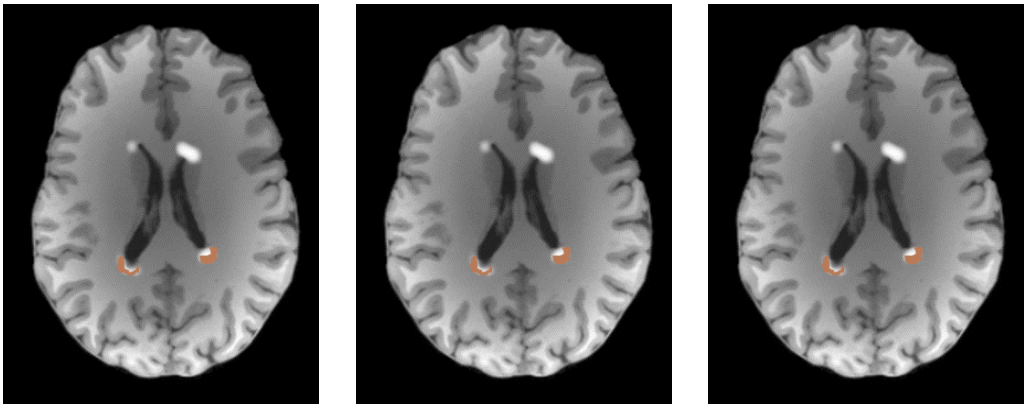


(a) (b)

Figure 4.18: (a) MRI T1 brain image of a healthy patient, (b) lesions are added artificially to mimic the MS lesions.

After getting the mimicking done, now we are going to use the traditional inpainting techniques (i.e. harmonic, Mumford shah, transport) to inpaint the lesioned image. Now, these techniques are used as they are the state-of-the-art methods for inpainting generally 2D images.

But we will check the workability of those in MRI images by visual as well as dice and jaccard scores (dice and jaccard scores are used to compare the images quantitatively).



(a) (b) (c)

Figure 4.19: The lesions in the artificially created MS brain are inpainted using (a) harmonic, (b) transport, and (c) Mumford and shah inpainting technique

Now that we have utilized the traditional methods, we can visually compare the effectiveness of these state-of-the-art methods.

Our next task is to use our proposed inpainting algorithm of this thesis to inpaint the lesions which we artificially structured in the healthy patient brain beforehand. After using the inpainting technique proposed in our method, we will have something like the following.

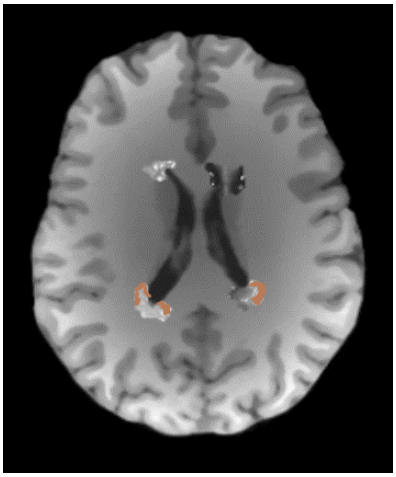


Figure 4.20: The lesions in the artificially created MS brain are inpainted using proposed inpainting algorithm.

4.3 Quantitative Analysis

4.3.1 For 2-D image

First we have used this inpainting methods to inpaint 2-D images. We have used the traditional methods and finally we started to utilize our proposed method to work with.

Table 4.1: Dice and jaccard scores for comparison among different inpainting techniques in case of 2D images.

2 Dimensional Images		
Methodology	Jaccard Score	Dice Score
Harmonic [11]	.8911	.9424
Mumford n Shah [13]	.9970	.9985
Transport [12]	.8468	.9171
Proposed method	.9989	.9987

4.3.2 For 3-D MRI image

After using 2D images, we intended to use the 3D MRI images of the patient's brain collected form human connectome project (HCP) [28] database. Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images are given below.

For patient 1 (P1), T1 weighted image we have the following.

Table 4.2: Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images (for Patient 1 T1WI).

MRI data		
Methodology	Jaccard Score	Dice Score
Harmonic [15]	.9811	.9905
Mumford n Shah [17]	.9547	.9978
Transport [16]	.9687	.9841
Proposed method	.9891	.9854

This is one patients brain MRI T1 weighted image (T1WI) shown in above. In the similar way, we have used 5 patients both T1 weighted images as well as T2 weighted image (T2WI).

The statistics are given in the following.

For patient 1, T2 weighted image we have the following.

Table 4.3: Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images (for patient 1 T2WI).

MRI data		
Methodology	Jaccard Score	Dice Score
Harmonic	.9793	.9705
Mumford n Shah	.9547	.9778
Transport	.9587	.9741
Proposed method	.9791	.9804

Now in the similar way, we have used this methods (the traditional ones as well as the proposed one) to the different patients, four patients' data, to be exact. And we got better results in case of our proposed method for inpainting cases which are illustrated in the following tables.

Table 4.4: Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images (for patient 2).

MRI data			
Methodology		Jaccard Score	Dice Score
Harmonic	T1WI	.9654	.9725
	T2WI	.9583	.9689
Mumford n Shah	T1WI	.9689	.9699
	T2WI	.9547	.9609
Transport	T1WI	.9705	.9856
	T2WI	.9687	.9841
Proposed method	T1WI	.9742	.9849
	T2WI	.9691	.9854

Table 4.5: Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images (for patient 3).

MRI data			
Methodology		Jaccard Score	Dice Score
Harmonic	T1WI	.9761	.9804
	T2WI	.9699	.9795
Mumford n Shah	T1WI	.9821	.9874
	T2WI	.9801	.9797
Transport	T1WI	.9701	.9789
	T2WI	.9687	.9697
Proposed method	T1WI	.9819	.9880
	T2WI	.9803	.9797

Table 4.6: Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images (for patient 4).

MRI data			
Methodology		Jaccard Score	Dice Score
Harmonic	T1WI	.9418	.9385
	T2WI	.9385	.9336
Mumford n Shah	T1WI	.9401	.9393
	T2WI	.9356	.9299
Transport	T1WI	.9399	.9302
	T2WI	.9287	.9241
Proposed method	T1WI	.9421	.9395
	T2WI	.9379	.9340

Table 4.7: Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images (for patient 5).

MRI data			
Methodology		Jaccard Score	Dice Score
Harmonic	T1WI	.9602	.9687
	T2WI	.9571	.9597
Mumford n Shah	T1WI	.9612	.9626
	T2WI	.9577	.9595
Transport	T1WI	.9502	.9584
	T2WI	.9487	.9501
Proposed method	T1WI	.9610	.9691
	T2WI	.9578	.9598

If we apply greyish lesions, we will get the following results for patient 1 MRI data.

Table 4.8: Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images (for patient 1).

MRI data			
Methodology		Jaccard Score	Dice Score
Harmonic	T1WI	.9654	.9725
	T2WI	.9583	.9689
Mumford n Shah	T1WI	.9689	.9699
	T2WI	.9547	.9609
Transport	T1WI	.9705	.9856
	T2WI	.9687	.9841
Proposed method	T1WI	.9742	.9849
	T2WI	.9691	.9854

If we apply mixed lesions, we will get the following results for patient 1 MRI data.

Table 4.9: Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images (for patient 1).

MRI data			
Methodology		Jaccard Score	Dice Score
Harmonic	T1WI	.9761	.9804
	T2WI	.9699	.9795
Mumford n Shah	T1WI	.9821	.9874
	T2WI	.9801	.9797
Transport	T1WI	.9701	.9789
	T2WI	.9687	.9697
Proposed method	T1WI	.9819	.9880
	T2WI	.9803	.9797

If we apply mixed lesions, we will get the following results for patient 1 MRI data.

Table 4.10: Dice and jaccard scores for comparison among different inpainting techniques in case of 3D MRI images (for patient 1).

MRI data			
Methodology		Jaccard Score	Dice Score
Harmonic	T1WI	.9418	.9385
	T2WI	.9385	.9336
Mumford n Shah	T1WI	.9401	.9393
	T2WI	.9356	.9299
Transport	T1WI	.9399	.9302
	T2WI	.9287	.9241
Proposed method	T1WI	.9421	.9395
	T2WI	.9379	.9340

Further, we investigated the effect of inpainting the MS lesion in the registration step. To do that, we created the ground truth by registering the healthy brain to the brain atlas. We compared the distorted registration output generated by registering an MS brain with the brain atlas with the ground truth.

We have found that the Dice and Jaccard value are 0.8486 and 0.8086 respectively.

This proves that, lesions create distortion in registration by deviating from the ground truth, and by inpainting this effect can be ameliorated.

4.3.3 Bar Chart:

Now, we can have a look over the following bar chart. Here, we can easily have a idea about the difference or improvement of the proposed method corresponding to the state-of-the-art methods inpainting methods.

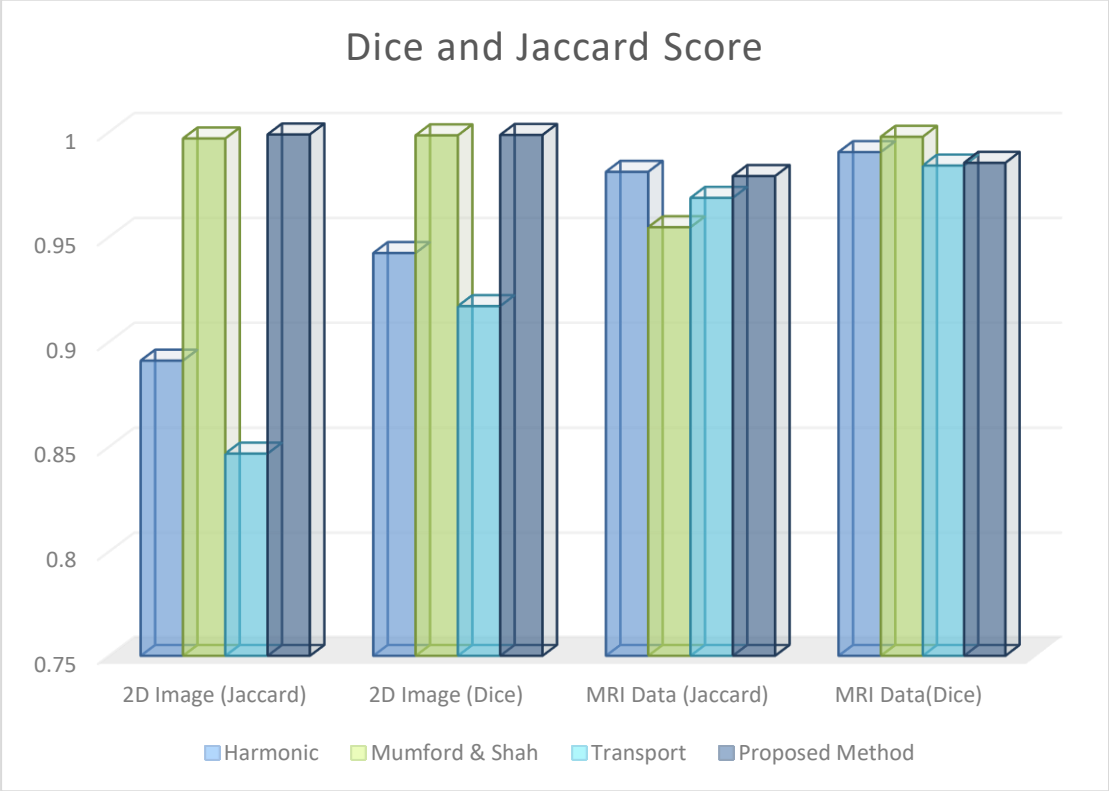


Figure 4.21: Bar chart showing the comparison among different state-of-the-at methods and our proposed method.

4.3.4 Comparison using Graphs:

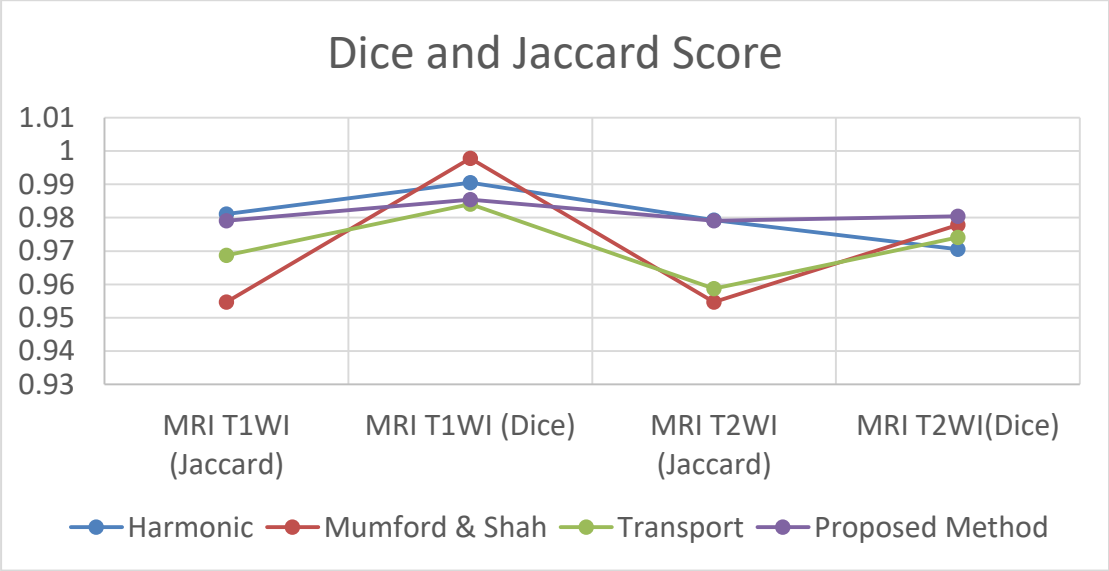


Figure 4.22: Dice and Jaccard score for patient 1.

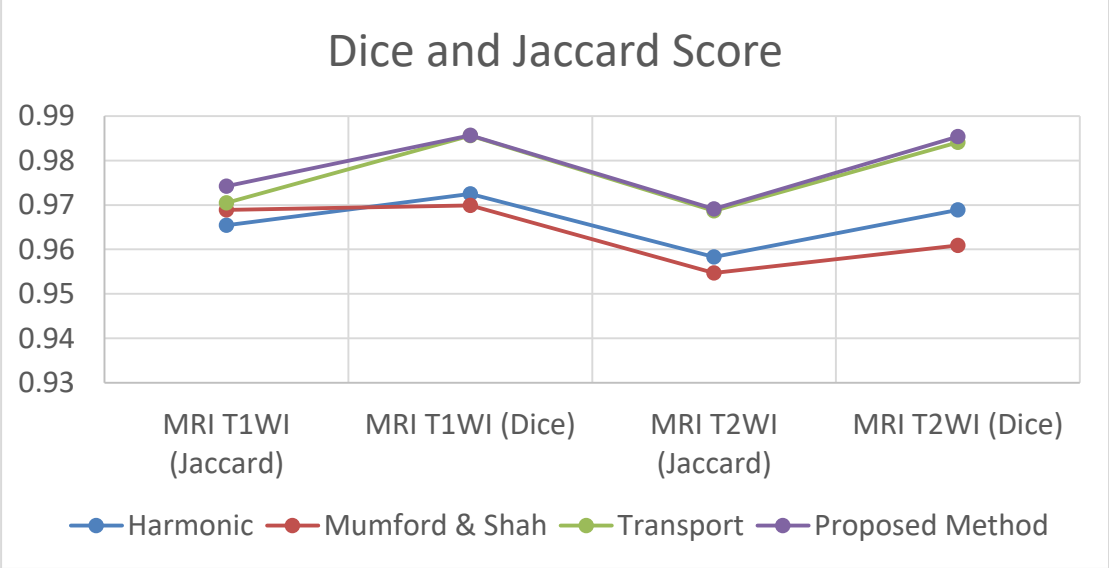


Figure 4.23: Dice and Jaccard score for patient 2.

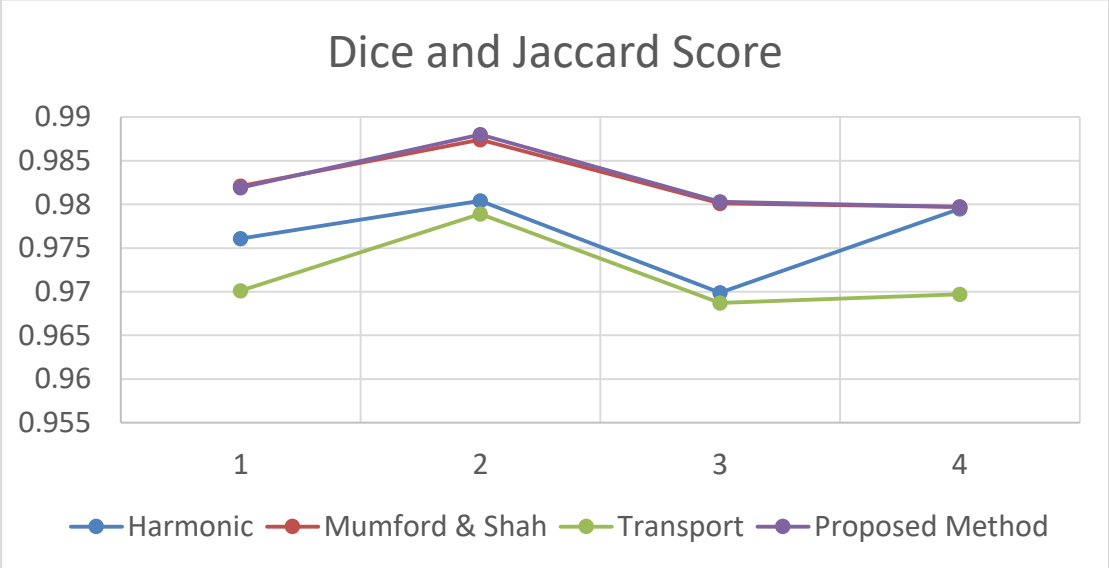


Figure 4.24: Dice and Jaccard score for patient 3.

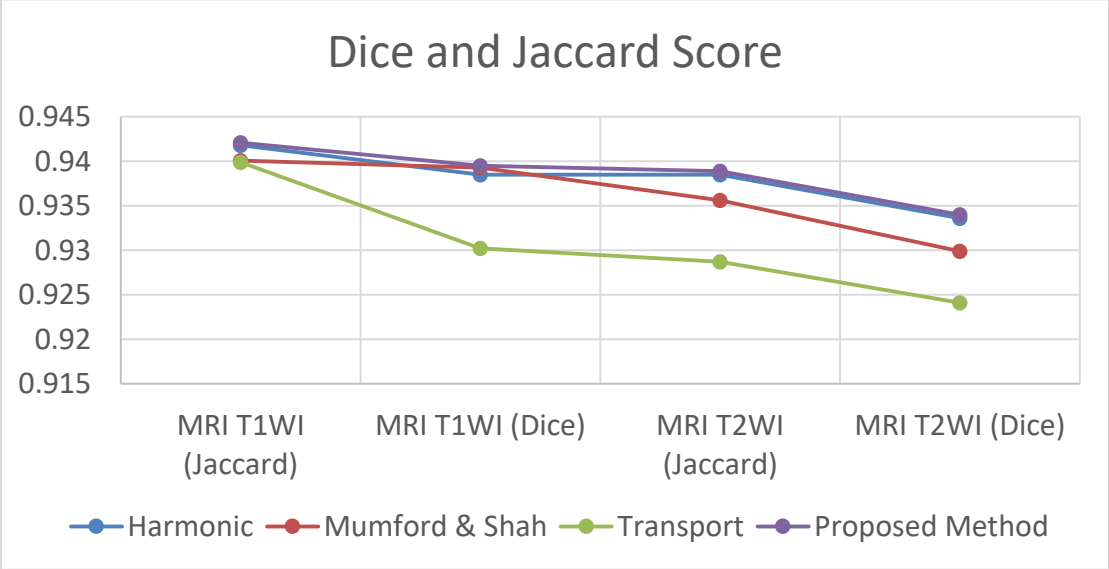


Figure 4.25: Dice and Jaccard score for patient 4.

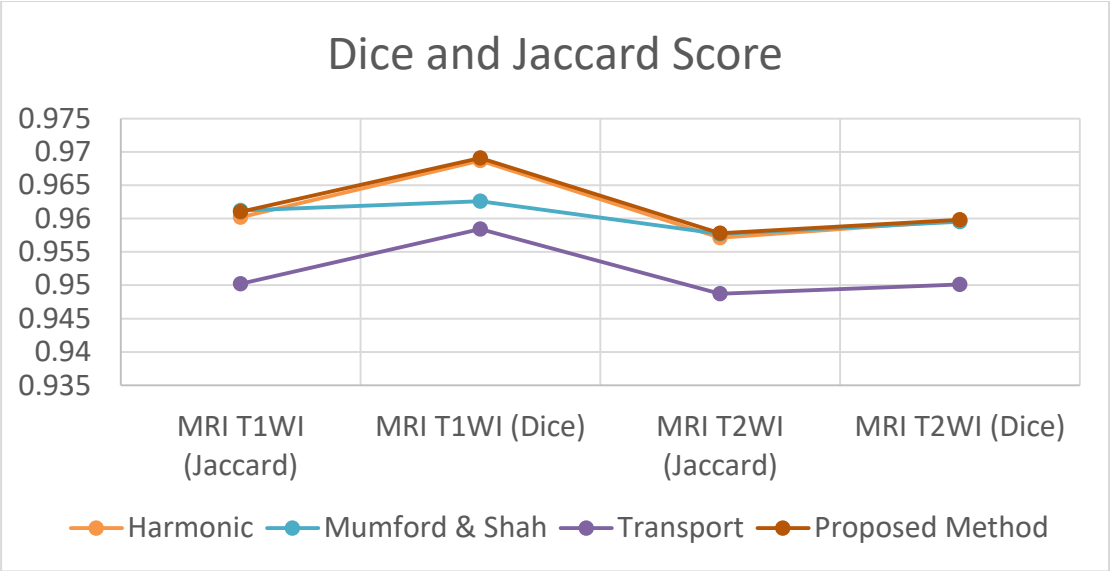


Figure 4.26: Dice and Jaccard score for patient 5.

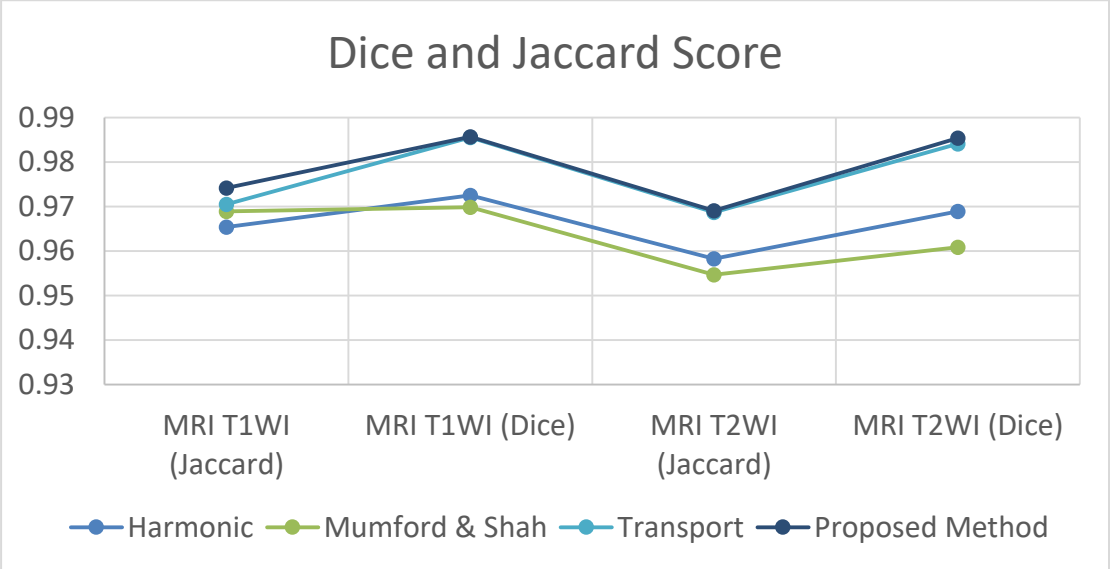


Figure 4.27: Dice and Jaccard score for patient 1 (greyish lesion).

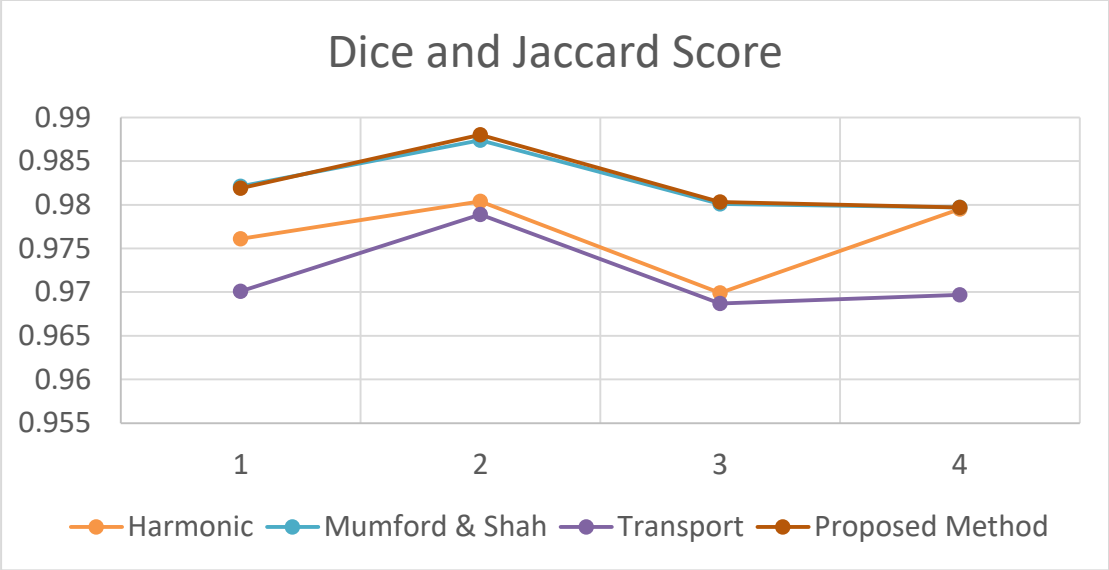


Figure 4.28: Dice and Jaccard score for patient 1 (mixed lesion).

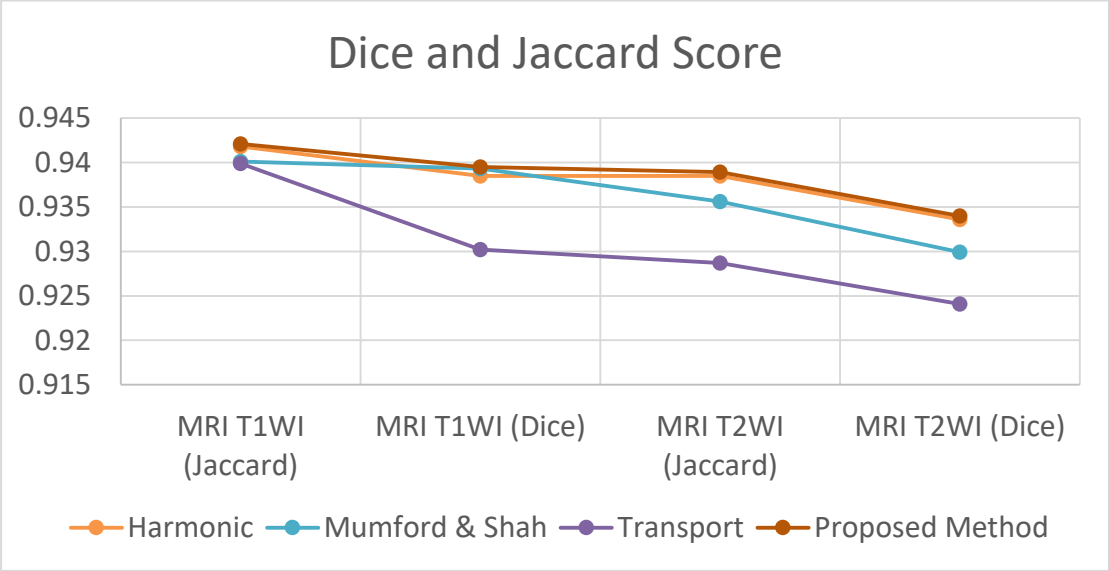


Figure 4.29: Dice and Jaccard score for patient 1 (mixed lesion).

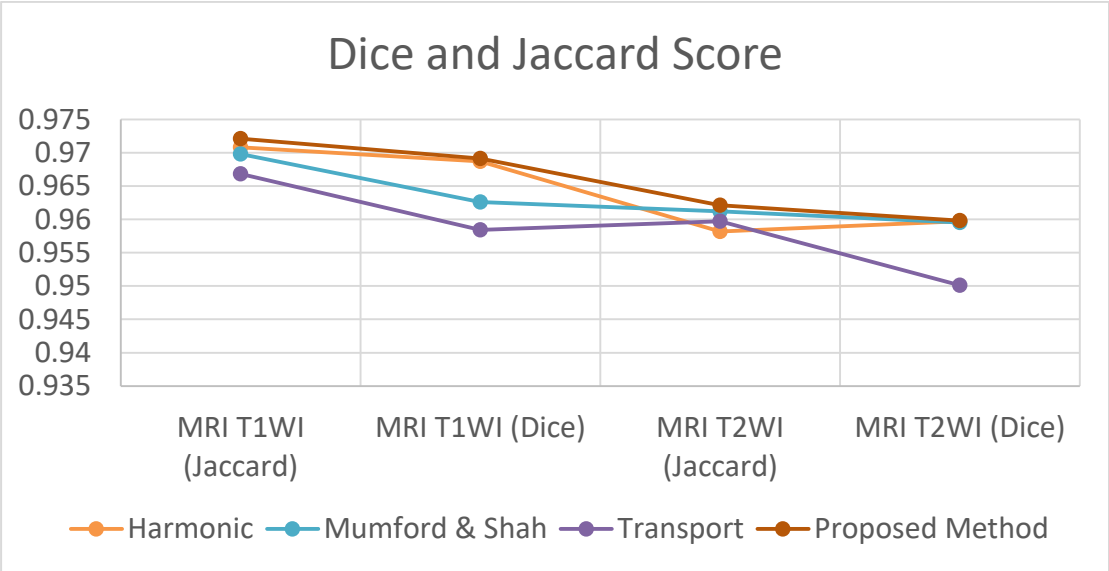


Figure 4.30: Dice and Jaccard score for patient 2 (greyish lesion).

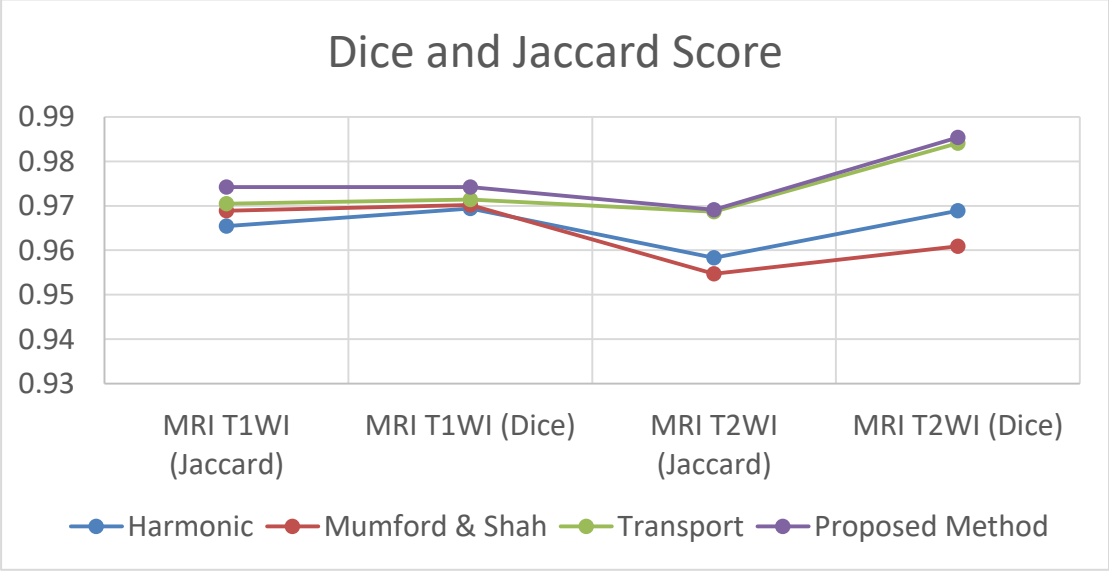


Figure 4.31: Dice and Jaccard score for patient 2 (mixed lesion).

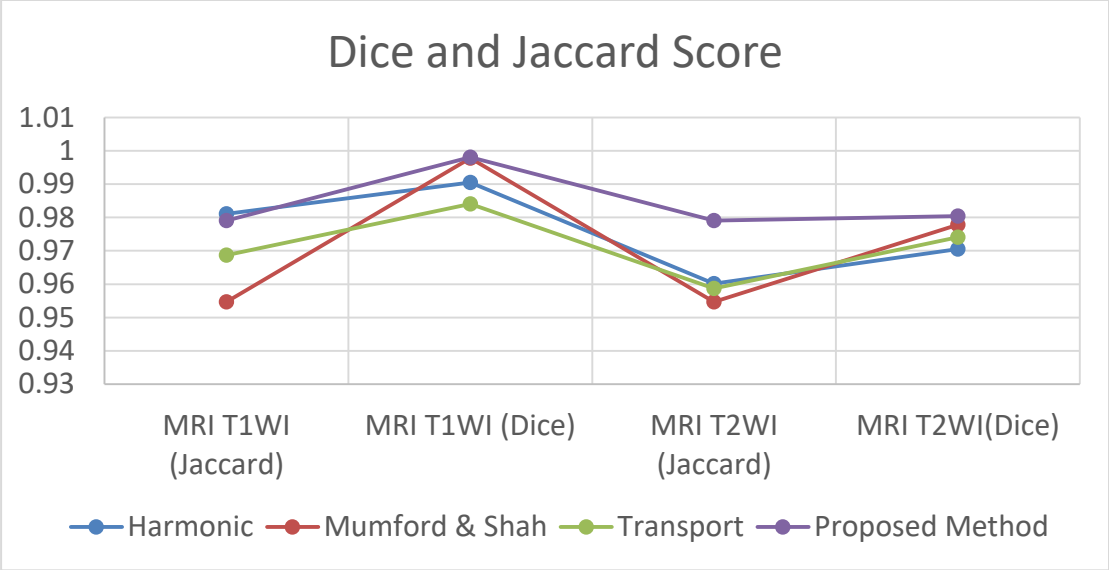


Figure 4.32: Dice and Jaccard score for patient 2 (mixed lesion).

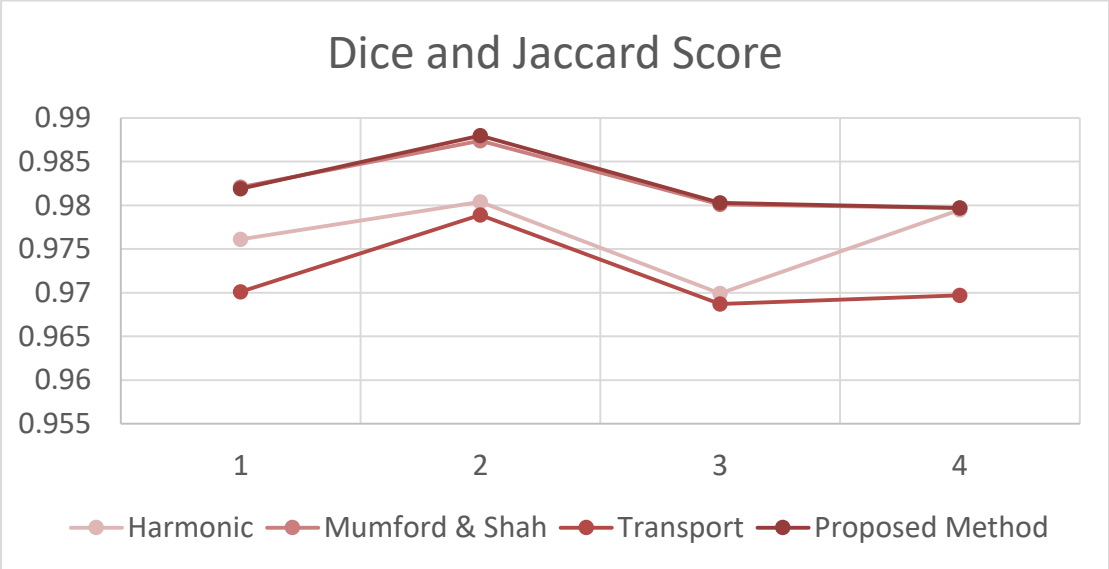


Figure 4.33: Dice and Jaccard score for patient 3 (greyish lesion).

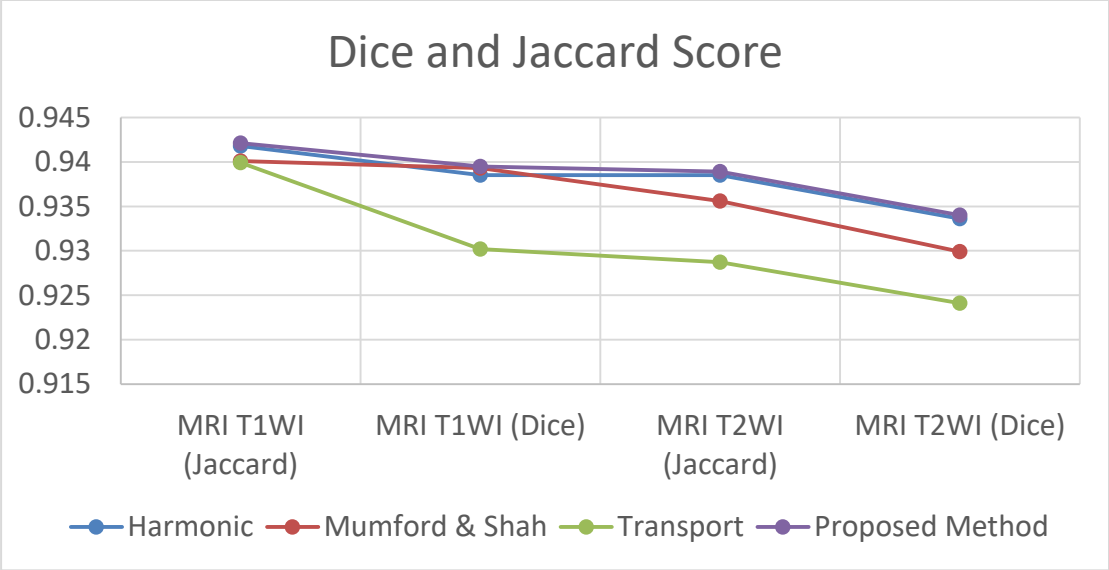


Figure 4.34: Dice and Jaccard score for patient 3 (mixed lesion).

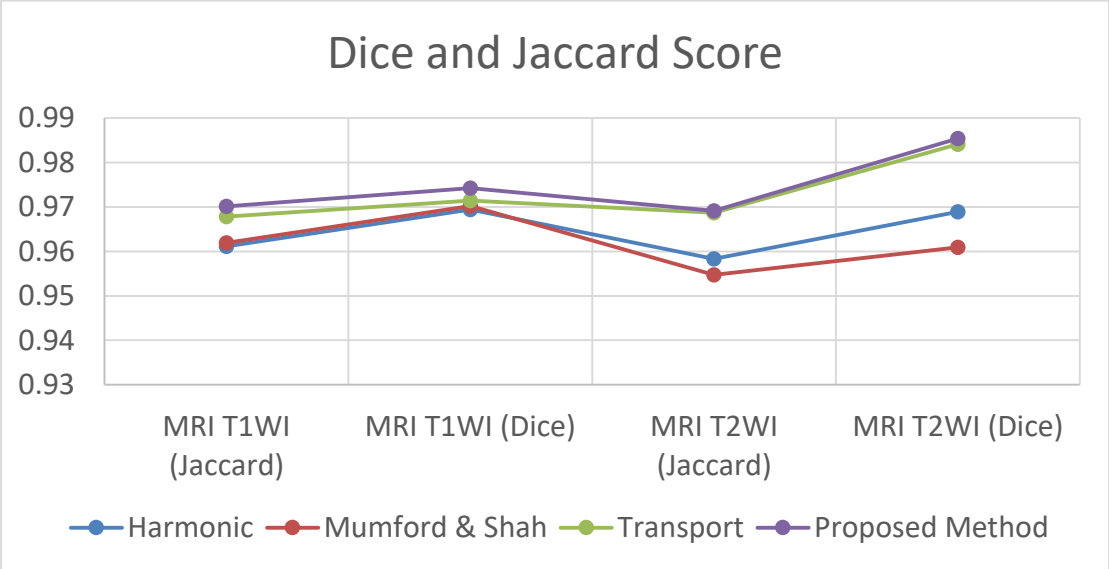


Figure 4.35: Dice and Jaccard score for patient 3 (mixed lesion).

It is showing the difference between different Methodologies. Dice and jaccard scores are taken to implement the visibility among the traditional methods and our proposed method.

Chapter 5: Conclusion

5.1 Synopsis

In chapter 1, we have discussed the introduction to the topic, in other words, the definition if the problem which is intended to solve through this thesis. We have also demonstrated the challenges of the research as well as thesis objectives and possible outcomes.

Chapter 2 provided the related background for Multiple Sclerosis patient's state. It is indeed a pernicious disease. It included the causes, affects, diagnosis, and importance and pernicious affects as well. It also illustrated why we needed to detect early and have to have a good registration later to have all the information about the corpus colosum of the brain.

It also demonstrated the necessity to inpaint the patient brain firstly for the registration part by delineating the other state-of-the-art techniques to reduce the distortion. The basics of the state-of-the-art inpainting techniques were then given and also associated drawbacks were analyzed. This chapter finally included the novel inpainting algorithm of our proposed method to inpaint the images.

In chapter 3, Image registration procedures had been dealt with. Different kinds of registrations, their advantages as well as disadvantages with associated conditions were then scrutinized. The procedure to register the healthy brain with brain atlas had been discussed thoroughly.

In Chapter 4, results by getting registration with the inpainted patient brain has been manifested comparing using the traditional ones with our novel inpainted technique.

5.2 Future works

Inpainting the white matter lesion is an easy preprocessing step and it can be used before any registration especially when one is working with MS patients. Furthermore, if one is creating an atlas of any patient population, WM lesions can create further bias as there is no standard template to register with.

The different intensities in the same part of the brain will cause the floating image to deform in some unwanted way.

- But with inpainting, any brain with MS lesions can be used as the reference image or the floating image of the registration algorithm. This is not the case with the Cost Function Masking method.
- In fact, if a mask is used to remove the influence of the lesions from the floating image, the voxels of the reference image is mapped to that masked region having a null cost.

Further, the improvement in Dice and Jaccard may seem very little, but this is proportional to the resolution of the floating image, template and largely on the size of the lesions. As the WM lesions are smaller compared to the total WM mask the change in Dice and Jaccard are ought to be small. But this plays a vital role when one tries to create an atlas of MS patient brains.

As the lesion location change longitudinally they will have a cumulative error effect on the created atlas which may deform the whole atlas in an unwanted way and it will be very hard to trace back the root of the problem. So small change in the performance can have significant impact.

Furthermore, in this work a lower resolution template was selected i.e. MNI152 2mm template to make the calculations faster (by an order of 2) in an ordinary machine. Some previous discrete results using higher resolution template i.e. MNI152 1mm template resulted in superior improvement of Jaccard and Dice coefficient. But for the scope of this project the lower resolution template was selected to evaluate the relative performance of different inpainting methods using different transformation matrix. If better performance is of essence then the same process can be repeated for the entire test subjects ensuing higher precision.

With the current progress of the work, it can be propitious that several future goals can be achieved.Future work may be extending the inpainting approach to different contrast modalities e.g. PDw and use our proposed algorithm in real MS patient data.

References

[1] Compston A, Coles A, "*Multiple sclerosis*". Lancet. 359 (9313): 1221–31.

[2] Berer K, Krishnamoorthy G, "*Microbial view of central nervous system autoimmunity*". National MS Society, FEBS Letters. S0014-5793 (14): 00293–2.

[3] Nakahara J, Maeda M, Aiso S, Suzuki N "*Current concepts in multiple sclerosis: autoimmunity versus oligodendrogliopathy*."Clinical reviews in allergy & immunology. 42 (1): 26–34

[4] http://www.healthline.com/health/multiple-sclerosis/facts-statistics-infographic

[5] David Rodriguez G., Susan D *"Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013*:" a systematic analysis for the Global Burden of Disease Study 2013.

[6] World Health Organization (2008). "*Atlas: Multiple Sclerosis Resources in the World 2008 Geneva: World Health Organization."* pp. 15–16. ISBN 92-4-156375-3.

[7] Milo R, Kahana E (March 2010). "*Multiple sclerosis: geoepidemiology, genetics and the environment*". Autoimmune Rev 9 (5): A387–94

[8] David Alexander Dickie, Dominic E. Job, David Rodriguez Gonzalez, Susan D. Shenkin, and Joanna M. Wardlaw "*Use of Brain MRI Atlases to Determine Boundaries of Age-Related Pathology: The Importance of Statistical Method"* (April 2014).

[9] https://en.wikipedia.org/wiki/Brain_atlas

[10] John Ashburner, Jesper L. Andersson, and Karl J. Friston, *"High-Dimensional Image Registration Using Symmetric Priors."*

[11] Matthew Bretta, 1, Alexander P. Leffb, Chris Rordenc, John Ashburnerd, *"Spatial Normalization of Brain Images with Focal Lesions Using Cost Function Masking"*.

[12] Michael Sdika, Daniel Pelletier, *" Non-rigid registration of Multiple Sclerosis Brain Images using Lesion inpainting for morphometry or Lesion mapping."*

[13] Jon McAusland, Roger C. Tam ; Erick Wong ; Andrew Riddehough ; David K. B. Li, *"Optimizing the Use of Radiologist Seed Points for Improved Multiple Sclerosis Lesion Segmentation."*

[14] https://en.wikipedia.org/wiki/Spatial_normalization

[15] J. Weickert, *"Anisotropic diffusion in image processing, vol. 1, teubner, stuttgart, germany, 1998,"* View at MathSciNet.

[16] T. F. Chan and J. Shen, *"Nontexture inpainting by curvature-driven diffusions,"*Journal of Visual Communication and Image Representation, vol. 12, no. 4, pp. 436–449, 2001.

[17] D. Mumford and J. Shah, *"Optimal approximations by piecewise smooth functions and associated variational problems,"* Communications on pure and applied mathematics, vol. 42, no. 5, pp. 577–685, 1989.

[18] Jian-Feng Cai, Raymond H. Chan, Zuowei Shen, *"A framelet-based image inpainting algorithm"*

[19] Selim Esedoglu and Jianhong Shen, *"Digital inpainting based on the Mumford–Shah–Euler image model"*

[20] Aurélie Bugeau, Marcelo Bertalmio; Vicent Caselles ; Guillermo Sapiro, *"A Comprehensive Framework for Image Inpainting"* (February 2012).

[21] NINDS Multiple Sclerosis Information Page". *National Institute of Neurological Disorders and Stroke*." November 19, 2015. Retrieved 6 March 2016.
[22] Lublin FD, Reingold SC "Defining the clinical course of multiple sclerosis: results of an international survey". Neurology 46 (4): 907–11(April 1996).
[23] Aiso S, Suzuki N *"Current concepts in multiple sclerosis: autoimmunity versus oligodendrogliopathy."* Clinical reviews in allergy & immunology. (February 2012).
[24] Compston A, Coles A (April 2002). "*Multiple sclerosis"*. *Lancet*359 (9313)
[25] Ascherio A, Munger KL (April 2007). *"Environmental risk factors for multiple sclerosis. Part I: the role of infection"*. Annals of Neurology 61 (4): 288–99
[26] Tsang BK, Macdonell R (December 2011). *"Multiple sclerosis- diagnosis, management and prognosis"*. Australian family physician 40 (12): 948–55.
[27] Huntley A (January 2006). "A review of the evidence for efficacy of complementary and alternative medicines in MS". *Int MS J* 13 (1): 5–12, 4.
[28] C. A., C. A (April 2002). "Multiple sclerosis". *Lancet*359 (9313): 1221–31
[29] Weinshenker BG (1994). "Natural history of multiple sclerosis". *Annals of Neurology* 36 (Suppl): S6–11
[30] Compston A, Coles A (October 2008). *"Multiple sclerosis"*. Lancet 372 (9648): 1502–17
[31] R. Stefanescu, O. Commowick, G. Malandain, P.-Y. Bondiau, N. Ayache, and X. Pennec, *"Non-rigid atlas to subject registration with pathologies for conformal brain radiotherapy,"* in Medical Image Computing and Computer-Assisted Intervention–MICCAI 2004. Springer, 2004, pp. 704–711.
[32] M. Brett, A. P. Leff, C. Rorden, and J. Ashburner, *"Spatial normalization of brain images with focal lesions using cost function masking,"* Neuroimage, vol. 14, no. 2, pp. 486–500, 2001.
[33] S. Walden, "*The Ravished Image*", St. Martin's Press, New York
[34] Olletti, P.M.; Shinbane, J; S, Shellock; F. G. (2011). *"MR-conditional" pacemakers: the radiologist's role in multidisciplinary management"*. AJR Am J Roentgenol.
[35] Andal C. Archibold, *"Hospital Details Failures Leading to M.R.I. Fatality,"* The New York Times
[36] Hartwig, Valentina; Giovannetti, Giulio; Vanello, Nicola; Lombardi, Massimo; Landini, Luigi; Simi, Silvana (2009). *"Biological Effects and Safety in Magnetic Resonance Imaging: A Review"*. International Journal of Environmental Research and Public Health.
[37] https://humanconnectome.org/
[38] S.M. Smith, "*Fast robust automated brain extraction. Human Brain Mapping"*, 17(3):143-155, November 2002.
[39] S.M. Smith and J.M. Brady. SUSAN – "*a new approach to low level image processing. International Journal of Computer Vision"*, 23(1):45–78, May 1997.
[40] S. Warfield, A. Robatino, J. Dengler, F. Jolesz, and R. Kikinis, *"Nonlinear registration and template driven segmentation,"* Brain Warping, vol. 4, pp. 67–84, 1999.
[41] D. Rey, G. Subsol, H. Delingette, and N. Ayache, *"Automatic detection and segmentation of evolving processes in 3d medical images: Application to multiple sclerosis,"* Medical Image Analysis, vol. 6, no. 2, pp. 163–179, 2002.
[42] J. Ashburner, C. Hutton, R. Frackowiak, I. Johnsrude, C. Price, K. Friston et al., *"Identifying global anatomical differences: deformation-based morphometry,"* Human brain mapping, vol. 6, no. 5-6, pp. 348–357, 1998.

[43] M. Brett, A. P. Leff, C. Rorden, and J. Ashburner, *"Spatial normalization of brain images with focal lesions using cost function masking,"* Neuroimage, vol. 14, no. 2, pp. 486–500, 2001.

[44] A. Ceccarelli, M. A. Rocca, P. Valsasina, M. Rodegher, E. Pagani, A. Falini, G. Comi, and M. Filippi, *"A multiparametric evaluation of regional brain damage in patients with primary progressive multiple sclerosis,"* Human brain mapping, vol. 30, no. 9, pp. 3009–3019, 2009.

[45] J. Chen,S. Narayanan, D. Collins, S. Smith, P. Matthews, and D. Arnold, *"Relating neocortical pathology to disability progression in multiple sclerosis using mri,"* Neuroimage, vol. 23, no. 3, pp. 1168–1175, 2004.

[46] K. Nakamura and E. Fisher, *"Segmentation of brain magnetic resonance images for measurement of gray matter atrophy in multiple sclerosis patients,"* Neuroimage, vol. 44, no. 3, pp. 769–776, 2009.

[47] R. Gelineau-Morel, V. Tomassini, M. Jenkinson, H. Johansen-Berg, P. M. Matthews, and J. Palace, *"The effect of hypointense white matter lesions on automated gray matter segmentation in multiple sclerosis,"* Human brain mapping, vol. 33, no. 12, pp. 2802–2814, 2012.

[48] S. K. Kyriacou, C. Davatzikos, S. J. Zinreich, and R. N. Bryan, *"Nonlinear elastic registration of brain images with tumor pathology using a biomechanical model [mri],"* Medical Imaging, IEEE Transactions on, vol. 18, no. 7, pp. 580–592, 1999.

[49] B. Dawant, S. Hartmann, S. Pan, and S. Gadamsetty, *"Brain atlas deformation in the presence of small and large space-occupying tumors,"* Computer Aided Surgery, vol. 7, no. 1, pp. 1–10, 2002.

[50] D. S. Meier and E. Fisher, *"Atlas-based anatomic labeling in neurodegenerative disease via structure-driven atlas warping,"* Journal of Neuroimaging, vol. 15, no. 1, pp. 16–26, 2005.

[51] M. Inglese, " Multiple sclerosis: New insights and trends" American Journal of Neuroradiology 27:954-957, May 2006

[52] *"Health at a Glance 2011"*. Health at a Glance. OECD. 2011.

[53] Mathews JD, Forsythe AV, Brady Z, Butler MW, Goergen SK, Byrnes GB, Giles GG, *"Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians"*. BMJ.

[54] Wallace AB; Anderson PR,*"iRefer"*. Royal College of Radiologists.

[55] Semelka RC, Armao DM, Elias J, Huda W *"Imaging strategies to reduce the risk of radiation in CT studies, including selective substitution with MRI"*. J Magn Reson Imaging. 25 (5): 900–9(2007).

[56] Calvin R. Maurer, J. Michael Fitzpatrick, *"A review of medical image registration"*, Interactive Image-Guided Neurosurgery, American Association of neurological surgeons, 1993, pp. 17-44

[57] Gerardo Hermosillo K.-H. Herrmann, Guillaume Bousquet, Luca Bogoni, Kallol Chaudhuri," *Image Registration in Medical Imaging: Applications, Methods, and Clinical Evaluation"* Multi-Modality State-of-the-Art Medical Image Segmentation and Registration Methodologies,pp 263-313,Date: 11 February 2011

[58] G. Emile-Male, "*The Restorer's Handbook of Easel Painting*", Van Nostrand Reinhold, New York.

[59] M. Bertalmio, G. Sapiro, V. Caselles, and C. Ballester, "*Image inpainting"*, in Proceedings of SIGGRAPH 2000, New Orleans, LA, 2000.

[60] V. Caselles, J.-M. Morel, and C. Sbert, *"An axiomatic approach to image interpolation,"* IEEE Trans. Image Process., 7 (1998), pp. 376–386.

[61] S. Masnou and J.-M. Morel, *"Level-lines based disocclusion"*, Proceedings of the 5th IEEE International Conference on Image Processing, Chicago, IL, 1998, pp. 259–263.
[62] A. C. Kokaram, R. D. Morris, W. J. Fitzgerald, and P. J. W. Rayner, "*Interpolation of missing data in image sequences*", IEEE Trans. Image Process., 11 (1995), pp. 1509–1519.
[63] H. Igehy and L. Pereira, "*Image replacement through texture synthesis",* in Proceedings of the 1997 IEEE International Conference on Image Processing.
[64] K.-H. Jung, J.-H. Chang, and C. W. Lee, "*Error concealment technique using data for blockbased image coding"*, SPIE, 2308 (1994), pp. 1466–1477.
[65] W. Kwok and H. Sun, *"Multidirectional interpolation for spatial error concealment"*, IEEE Trans. Consumer Electronics, 39 (1993).
[66] A. C. Kokaram, R. D. Morris, W. J. Fitzgerald, and P. J. W. Rayner, "*Detection of missing data in image sequences*", IEEE Trans. Image Process., 11 (1995), pp. 1496–1508.
[67] M. Nitzberg, D. Mumford, and T. Shiota, "*Filtering, Segmentation, and Depth"*, Lecture Notes in Comput. Sci. 662, Springer-Verlag, Berlin, 1993.
[68] Chari DM (2007). "*Remyelination in multiple sclerosis*". Int. Rev. Neurobiol. 79: 589–620
[69] Novelline, Robert, "*Squire's Fundamentals of Radiology"*. Harvard University Press. 5th edition. ISBN 0-674-83339-2.
[70] David Attwood, "*Soft X-rays and extreme ultraviolet radiation."* Cambridge University. p. 2. ISBN 978-0-521-65214-8.
[71] Roobottom CA, Mitchell G, Morgan-Hughes G (2010). *"Radiation-reduction strategies in cardiac computed tomographic angiography"*. Clin Radiol. 65 (11): 859–67. doi:10.1016/j.crad.2010.04.021
[72] Brenner DJ, Hall EJ (2007). *"Computed tomography—an increasing source of radiation exposure"*. N. Engl. J. Med. 357 (22): 2277–84.