Cost comparative analysis of two-tiered and multi-tiered approaches to MRI for multiple sclerosis and prostate cancer

Farshad Safaei Ardakani

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By: **Farshad Safaei Ardakani**

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Signed by the Final Examining Committee:

______________________ Chair
Dr. Susan Liscouet-Hanke

______________________ External Examiner
Dr. Ketra Schmitt

______________________ Examiner
Dr. Akif A. Bulgak

______________________ Supervisor
Dr. Masoumeh Kazemi Zanjani

______________________ Co-supervisor
Dr. Khashayar Rafat Zand, MD FRCPC Director of body MRI
Assistant Prof. of Radiology UMass Memorial Medical Center
Adjunct Prof. of Radiology McGill University Health Center

Approved by ______________________
Martin D. Pugh, Chair
Department of Mechanical and Industrial Engineering
2019

____
Amir Asif, Dean
Faculty of Engineering and Computer Science

Abstract

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Farshad Safaei Ardakani

Every year, a vast amount of money is spent across Canada for healthcare. In fact, Canada healthcare system has been spending more than numerous other countries, yet the outcome is not proportional to the efforts and budget that have been used. A big chunk of the pie of expense surplus comes from over-utilization of resources. Most notably, around 20 % to 50 % of this cost stems from the high-tech imaging modality, especially MRI scanners. This over-utilization in MRI procedures leads to higher costs for the system and patients, longer waiting time, and patients' dissatisfaction. Researchers have developed methods to improve patient experience and the population's health while reducing the per capita cost of healthcare. Motivated by the mentioned facts, the primary purpose of this thesis is to compare two-tiered and multi-tiered approaches to MRI for the diagnostics of multiple sclerosis (MS) and prostate cancer (PC) diagnosis in a community-based practice in a large metropolitan area in Canada. The goal is to identify the best procedure protocol in terms of cost, efficiency and throughput. In particular, our contributions are two-fold. First, we compare different MRI procedures to MS diagnostics based on referring physician specialization (i.e. neurologists and non-neurologists referrals). We further investigate the dependency between the test results and referral pattern via conducting a statistical hypothesis test. Our second contribution revolves around the comparison between two-tiered and multi-tiered MRI procedures for PC diagnostics in terms of cost and efficiency. Through a decision tree analysis, we demonstrate that two-tiered MS MRI approach and two-tiered MpMRI for PC turns out to be the most cost efficient methods with the lowest number of adverse events while improving patients experience through reducing the number of callbacks and venipuncture/contrast complications.

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Chapter 1

Introduction

In This chapter, we first present motivation of this study. Afterwards, we clarify the objectives and finally, state the outlines of this thesis.

1.1 Motivation

Studies around healthcare services have grown recently due to the lack of efficiency in this sector. Canada healthcare services have been spending more than most of the other countries; Total health expenditure is expected to reach $253.5 billion or $6,839 per capita in 2018 (OECD, 2019); yet the outcome is not meeting the expectations compared to other countries, (Erickson, Rockwern, Koltov, & McLean, 2017), (Hovanesyan, Rubio, Novak, Budoff, & Rich, 2017).

Since the establishment of Medicare in the 1960s, Canada's health care system has experienced an ongoing continuous period of growth. The only exception was this growth in the early to mid-1990s, when federal and provincial governments faced a reduction in budget deficits. The ratio of health to GDP is estimated to be 11.3% in 2018 (CIHI, 2018). With an increase in real costs of more than 10% per annum for nearly a decade, health care costs rise to their highest historical level - in absolute dollars or percentage of GDP.

According to (CIHI, 2018), while growth in health care costs has been observed in all sections, yet the highest percentage increase is not in traditional medical services and hospitals. Together, these two sectors dropped according to the percentage of public health care spending in Canada from 74.7% in 1975 to 51.4% in 2018. Decreasing cost proportions in these two main areas has been described with growth in areas such as medicine, home care, public health and diagnostic services.

There are many explanations for the higher costs such as health insurance, administrative costs, prescription drugs and diagnostic testing; yet the most important contributor to the cost of healthcare is over-utilization. This over-utilization has two sides: 1) The high volume of services such as hospitalization, office visits, tests and procedures; and 2) Expensive tests, and procedures (Emanuel & Fuchs, 2008).

Advanced medical technologies bring higher cost of services. Accordingly, the primary driver of healthcare costs in developed countries are medical technologies such as medical imaging. During the past decade, the cost of medical imaging has grown twice the rate of other technologies in healthcare sector. The demands and benefits of medical imaging are unquestionable, but some publications have suggested that around 20%-50% of these high-tech imaging procedures cannot provide the information that can improve patient welfare or reduce the treatments procedure and therefore might be unnecessary and lead to the over-utilization of the MRI scanners, doctors, and specialists (Hendee et al., 2010), (Iglehart, 2006).

Among different medical imaging technologies, magnetic resonance imaging (MRI) is the primary diagnostic procedure for multiple sclerosis (MS) and prostate cancer (PC). MRI is a medical imaging system utilized in radiology to form detailed images of the anatomy and the physiological processes of the body (Smith-Bindman et al., 2012).

Studies from different provinces indicate that the prevalence of multiple sclerosis (MS) among Canadians is one of the highest in the world. The estimation of Canadians reported a diagnosis of MS is 93,500 based on the most recent data in 2011. Women are more likely to have MS compared to men, around two to three times. This imbalance in the sex ratio is increasing in several countries. In Canada, there are 2.6 women diagnosed with MS for every man with the same condition,leading to the prevalence estimates of 419 cases per 100,000 women and 159 cases per 100,000 men.

The most observed cancer in men is prostate cancer (161,360 out of 836,150 cases per year). The death rate of cancer is 1650 per day for men. Detection of cancer in early stages increases the potential of effective medical treatment. Although it is an vital part of medical care, early detection is still challenging (de Rooij, Hamoen, Fütterer, Barentsz, & Rovers, 2014). For public health, prostate cancer (PC) costs $ 12billion per year, considering 200,000 new cases each year in the United States. Roughly $ 4.8 billion of cost is related to overestimation of cancer treatment and cancer detection (Merrill & Stephenson, 2000). There is no precise study of overestimation and over-treatment of the prostate cancer; however, it is estimated to be around 17 % to 50 % of screening results.

There are different protocols of diagnosing the disease for both MS and PC MRI procedures. In Canada, brain MRI imaging can be conducted without pre-authorization or referral from a neurologist. After a departmental utilization review, it is observed that only a small portion of positive scans in MRIs, performed for assessment of MS, referred by non-neurologists. For PC MRI procedure, a full MRI test or abbreviated MRI test can be performed. The advantages of the abbreviated test are the lower price and shorter period for performing the test. However, there is a disadvantage for this test, which is of lower accuracy in categorizing the results.

One well-known way to study the cost of medical imaging is Comparative Effectiveness. Comparative Effectiveness research means to objectively compare the results of one approach to managing a surgical procedure, disease, or technical procedure or test with another one. By comparing two (or more) approaches the cost of the system can be reduced, the efficiency can be improved, while managing the utilization (Hendee et al., 2010).

1.2 Objectives

The primary purpose of this study is to compare different diagnostic protocols for MS MRI diagnosis and PC MRI diagnosis to find out the best procedure protocol in terms of cost (to the healthcare system and patient), efficiency and throughput. In particular, we aim to investigate:

1. The comparison between different MRI procedures based on different referring physician specialization (i.e. neurologists and non-neurologists) in a community-based practice in a large metropolitan area in Canada. Our goal is to compare the cost, efficiency, and throughput of different MRI procedures for diagnosing MS. We also aim to conduct a statistical test on the data to assess the dependency of the results.

2. The comparison between different MRI procedures for PC diagnostics in a community based in a large metropolitan area in Canada. Our goal is to compare the cost, efficiency, and throughput of different MRI procedures for diagnosing PC.

1.3 Thesis outline

To provide the relevant context, the rest of the thesis is organized as follows:

Chapter 1 provides an overview and a summary of the significant contributions made in the thesis.

Chapter 2 presents a comprehensive background and literature review on Comparative effectiveness analytic and two-tiered approaching for MRI applications, as well as their modules and the corresponding processing methods.

Chapter 3 introduces the definition of the diseases (MS and PC) as well as the diagnostic procedure of both diseases.

Chapter 4 provides the statistical test of dependency related to referral pattern.

Chapter 5 describes the data collection, methodology and results for our first objective, which is a comparison of different MRI procedures for diagnosing MS.

Chapter 6 describes the data collection, methodology and results for the second objective, which is comparison of different MRI procedures for diagnosing PC.

Chapter 7 concludes the thesis and provides some directions for future work.

Chapter 2

Literature Review

In this chapter, we review studies and researches related to the comparison of different MRI procedures. Afterwards, the gaps in the existing studies are presented.

With the goal of reducing MRI utilization for patients with low back pain, (Fried, Andrew, Ring, & Pastel, 2018) proposed the inclusion of a simple epidemiologic statement in MRI reports. They compared treatment utilization rates between patients whose radiology reports for MRI low back included the statement with those whose reports did not include the statement. The studied population was patients with lumber MR imaging. They compared baseline patient characteristics by performing Pearson X^2 tests for categorized variables and a t-test for age at index MR imaging. For other characteristics such as sex, low back pain weakness and numbness, the severity of findings at MR images, a log-binomial test was used.

There is a vast emerging literature favouring the adoption of two-tiered MRI protocols based on patient population data. (Sharma et al., 2013) compared the diagnostic efficiency and potential cost implications of conventional and two-tiered MRI approaches in the management of patients with headache. They apply a two-tiered to increase the efficiency of utilization of the scanner, reduce the cost and to have less burden on patients. They study the feasibilities and implications from the patient, payer and imaging facility perspective. They calculated sensitivity and specificity for two-tiered and conventional MRI and using Fisher exact two-tailed test as independence test.

In (Sharma et al., 2014), the comparison of comprehensive MRI and T2-weighted imaging have been investigated with the same approaches as (Sharma et al., 2013). In the paper, a decision tree was developed to compare the cost-effectiveness of a proposed two-tiered model with conventional MRI. In the two-tiered strategy, the comprehensive MRI involved only as a second step. They hypothesized that utilization of proposed two-tiered MRI has significant cost saving with highly similar results as comprehensive MRI.

Recent studies have shown that abbreviated protocol (AP) of MRI is helpful for detection of breast cancer. The results also proved that the performance of AP outperforms mammography (MG).CT scan and MRI has been used to detect acute appendicitis in children. Given the recent concerns regarding ionizing radiation in CT and being time-consuming and requiring the use of sedation or anesthesia for traditional MRI, (Zens et al., 2018) developed a quick MRI abdomen and pelvis protocol without the using of contrast or demand for sedation. The purpose of the study was to describe the quick MRI as a fast, cost-effective and accurate alternative to CT and traditional MRI for evaluation of postoperative abscess (POA). The subjects of this study were children under age of 18 diagnosed with acute appendicitis that required cross-sectional imaging to evaluate for the presence of am intra-abdominal fluid collection. The chi-squared and independent t-tests with p values less than 0.05 were used as the test of independence.

(Chen, Huang, Shen, Liu, & Xu, 2017) investigated the usefulness and economical aspects of using AP compared to a full diagnostic protocol (FDM). The study included data of 356 women who had dense breast examined. They used one-way analysis of variance to assess differences of interpretation time and McNemar's test was used to assess differences of sensitivity and specificity.

(Strahle et al., 2017) tried to reduce the cost and increase the efficiency by developing a systematic process at defining the appropriate type and number of acquisitions for breast MRI. They evaluated a full diagnostic protocol (FDP) breast MRI and used the information to develop an abbreviated protocol for breast cancer screening. The purpose of the study was maximizing lesion detection while reducing the cost. The statistical population was all women who obtained their mammograms between 2009 and 2011 at a community hospital. T-test and Wilcoxon test were used to compare the stats for a given acquisition.

(Kuhl et al., 2014) has shown that the usage of the abbreviated protocol is a suitable option in women with the high risk of breast cancer. The authors demonstrated that studies the abbreviated protocol does not compromise the sensitivity and specificity relative to the conventional complete protocol. (Oldrini, Derraz, Salleron, Marchal, & Henrot, 2018) compared the diagnostic accuracy of the complete protocol to an abbreviated protocol with the usage of the breast imaging reporting and data system classification for the interpretation time of breast MRIs regardless of the indication for examination. They also studied between-reader variability and influence of reader expertise on diagnostic accuracy.

To minimize and eliminate long term disability of patients who have suffered an ischemic stroke, Intravenous tissue plasminogen activator (IV-tPA) has been widely used in North America. Nevertheless, studies have shown that this treatment may increase the cost of tPA, hospitalization, and post-IV-tPA in the health care system. Head CT and comprehensive brain MRI have been used to choose patients eligible for IV-tPA. (Paolini et al., 2013) studied the evaluation of rapid Brain Attack Team (BAT) MRI as a clinical tool in selecting patients for IV-tPA administration with an unclear diagnosis or inconsistent stroke-like symptoms.

The existing gaps in the literature

1. There is no prior study that investigates the relation between the incidence of MS with the referring physician specialization. In particular, among studies that conduct comparative cost analysis in the content of MS MRI protocols, none has investigated more complicated scenarios such as the one that choice of MRI procedure depends on the referral pattern.

2. Only a handful of studies compare the cost of different MRI protocols from the perspective of patients.

3. Mapping different MRI procedures and calculating the throughput of the system have only been investigated in a few studies.

4. There is no prior study on conducting comparative cost analysis on different PC MRI procedures and consequently mapping those protocols.

Chapter 3

Definition of the disease and Diagnostic procedure

This chapter explains the characteristic of MS and PC, followed by elaborating on different MRI tests designated for their diagnostics.

3.1 Multiple sclerosis (MS)

MS is a progressive disease that potentially debilitates the central nervous system and causes damage to the myelin, the protective layer around the nerves as it is shown in Figure 3.1 (Ropper et al., 2014). This brain disorder causes symptoms such as visual impairment, loss of coordination and balance, severe fatigue, bladder dysfunction, stroke, numbness, weakness, and also mood change. The nature of symptoms varies and may be characterized by periods of relapse. In most countries like Canada, MS is usually diagnosed before the age of 50. Most of the household residents with the age of 15 or more reporting MS had been diagnosed at ages 20 to 49 (95% CI: 75.9 to 86.5). The average age for people to have their first symptoms experience was 32 with a diagnosis about five years later by age 37 (Gilmour, Ramage-Morin, & Wong, 2018).

The lives of most of the people diagnosed with MS is significantly affected by the disease. About two-thirds of them reported that MS changed their life fairly, quite a bit, or extremely. The remaining third stated that their lives are only slightly affected. Although 57% of MS patients

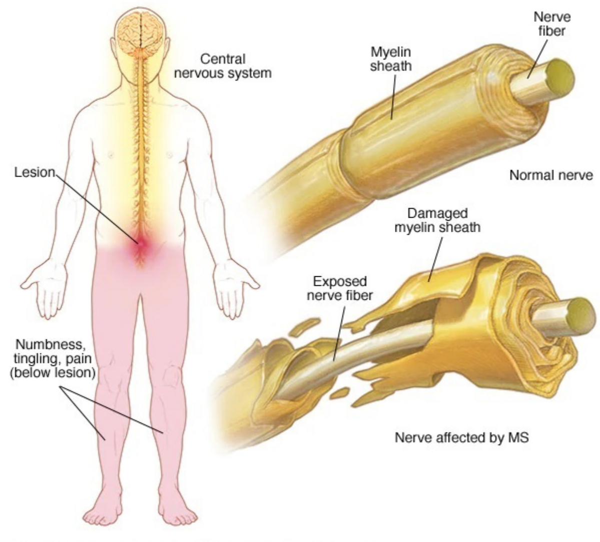

Figure 3.1: Myelin damage and the nervous system (Ropper et al., 2014)

may walk without help, about one third (31%) needs a wheelchair, a mechanical aid like a cane or walker, or another person's support, 12% could not walk at all. Only More than half (53%) are usually pain-free, but the rest reported pain that prevented multiple activities (21%) or some activities (25%). Almost two-third (62%) have trouble sleeping at night. About a third reported that MS prevented driving (30%) or endangered their educational opportunities (32%). More than half (58%) have experienced at least some restrictions on job opportunities; 44% described these limitations as ”very little” or ”severe.” 43% also reported that MS had a negative impact on their social interactions. For example, they feel embarrassed or perceived that others feel uncomfortable or avoid them (Gilmour et al., 2018).

3.1.1 MRI procedure for the diagnostic MS

MS usually has a non-specific neurological impairment with a critical period: the gap between the symptoms of diagnosis and the diagnosis is longer for those who show signs at an earlier age. The gap is reported as 5.4 years as compared with 2.6 years for men. However, in 2010, McDonald's MRI Criteria were revised to detect MS with a single contrast-enhanced (C+) MRI scan in the appropriate clinical setting. Accordingly, the recommended MRI protocol currently includes at

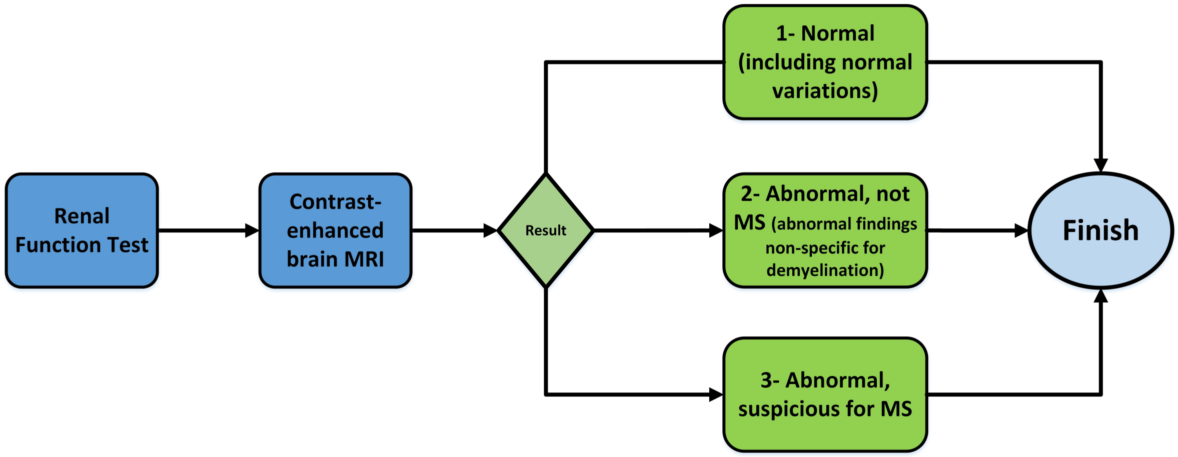

Figure 3.2: C+ MRI for diagnosing MS

least 3-dimensional (3D) T1 weighted, 3D T2 fluid attenuated inversion-recovery (FLAIR), 3D T2 weighted, and pre- and post-single-dose, gadolinium T1 weighted imaging (Polman et al., 2011).

The objective of C+ MRI test is to detect and restrict the brain for any abnormality related to MS. For this test, patients are required two visits to the hospital, one for the renal function testing and one for the MRI examination. The renal function test is a requirement prior to IV contrast injection. C+ MRI is summarized in Figure 3.2. C+ brain MRI is a reliable test to diagnose MS. However, it has some drawbacks including long time, high cost, and contrast injection which brings some discomfort and stress to patients. MRI imaging results are divided based on final reports' conclusion/impression into three ordinal categories:

1) Normal (including normal variations): no indication of demyelination

2) Abnormal, not MS: abnormal findings, non-specific to demyelination or non-specific findings unrelated to symptoms (incidental findings)

3) Abnormal, suspicious for MS: findings suspicious or typical to demyelinating disease.

It should be noted that categories 2 and 3 do not mean excluding or establishing a diagnosis of MS; they rather indicate the need for further investigation. A binary "result" is then defined by classifying the first two categories (Normal and Abnormal, not MS) as Negative and the third category (Abnormal, suspicious for MS) as Positive.

There is an increasing body of evidence supporting use of targeted, focused, and abbreviated

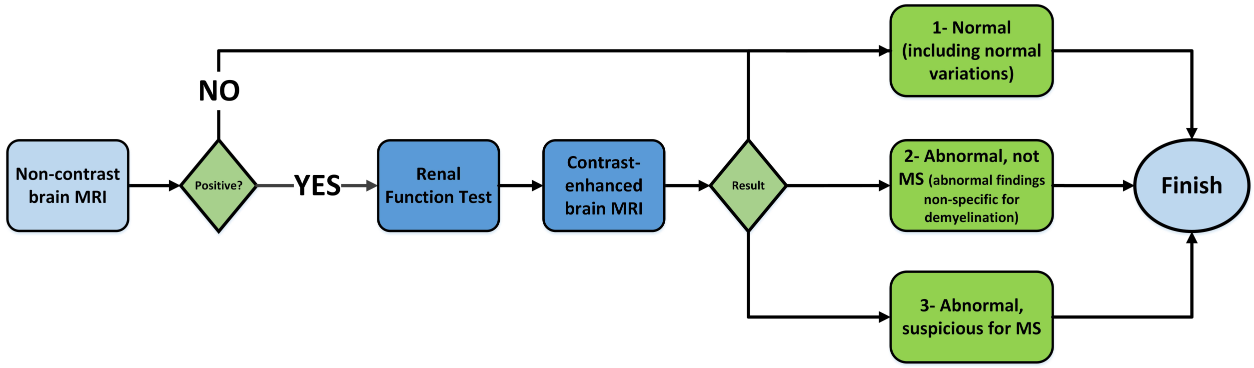

Figure 3.3: Two-tiered MRI for diagnosing MS

MRI protocols in various patient sub-populations based on patient characteristics or disposition (e.g. outpatients with headache, suspected stroke in emergency room). This decision was later reinforced by publication of the first article on two-tiered MRI approach in 2014 and has remained in place ever since (Sharma et al., 2014).

This approach was proposed to reduce the negative affects of C+ brain MRI on healthcare service and patients experience. In this approach, all patient would undergo an abbreviated non-contrast brain MRI (C-). If MRI result is negative, MS imaging would be considered complete in a single hospital visit. If MRI result is positive, patients would enter C+ MRI for an additional two hospital visits. The two-tiered MRI procedure is illustrated in Figure 3.3.

3.2 Prostate Cancer

With life time risk of 2.8 %, the prostate cancer (PC) is rare before age 50 years old and the majority of death (around 70%) is related to age 75 or older (Moyer, 2012). PC begins when cells in the prostate gland start to grow uncontrollably. Prostate is an organ in the men's reproductive system. Most of the semen that carries the sperm is made by prostate. It is located under the bladder and surrounds the upper part of the urethra, the organ that carries urine from the bladder. The prostate is splitted into four zones as depicted in Figure 3.4 (Sathianathen et al., 2018):

1. The anterior fibromuscular stroma
2. The transition zone (TZ) with 20 % of occurrence of cancers

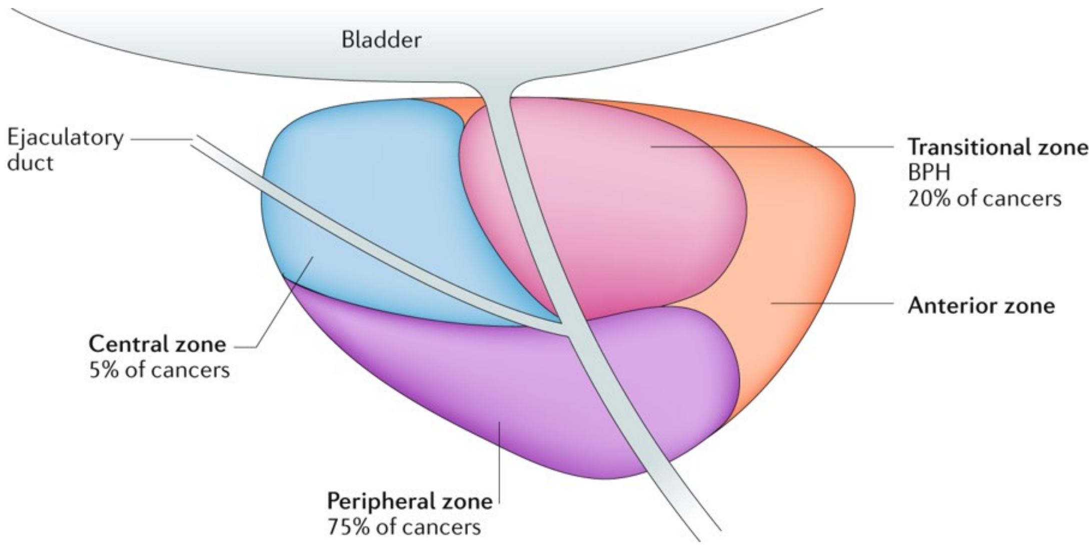

Figure 3.4: Prostate Zones (Sathianathen et al., 2018)

3. The central zone (CZ) with 5 % of occurrence of cancers
4. The outer peripheral zone (PZ) with 75 % of occurrence of cancers

Cancers detected in the CZ are rare, and the cancers that occur in the CZ are usually subsequent to invasion by PZ tumors. According to (Moyer, 2012), patients after screening usually are categorized into three cases:

1. The patients with high chance of death without the results of early screening
2. The patients with low chance of death without the results of early testing
3. The patients with decreasing chance of death due to results of screening

3.2.1 MRI procedure for diagnostic PC

One popular screening or testing method for diagnosing the prostate cancer is prostate specific antigen (PSA). The first objective of PSA is to group men undergoing treatment to reduce their mortality rate. Evidences prove that most PSA testing results are correlated with Benign cancer in which the tumor is not progressive and the cancer is not a threat to the patient (Merrill & Stephenson, 2000).

Statistical evidences reveals that false positive is a big portion of the results of PSA tests (about 80 % of false positive rate). Aside the negative psychological impacts on patients, patients with false positive are more likely to have biopsy that is an invasive part of treatment and causes reported fever, bleeding, and infections that are considered as “moderate or major problems” (Rosario et al., 2012).

To reduce the effects of unnecessary biopsies and overtreatment, the technique in magnetic resonance imaging, or multi-parametric MRI (MpMRI) is utilized. MpMRI increases the diagnostic capabilities that leads to less biopsies and consequently less side effects. MpMRI combines anatomic T2W, diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) MRI to improve diagnostic capabilities for addressing central challenges in prostate cancer which is critical for reducing mortality. T2W images are used to discern prostatic zonal anatomy, assess abnormalities within the gland, and to evaluate for seminal vesicle invasion, EPE, and nodal involvement. Diffusion-weighted imaging (DWI) reflects the random motion of water molecules and is a key component of the prostate mpMRI exam. It should include an apparent diffusion coefficient (ADC) map and high b-value images. The ADC map is a display of ADC values for each voxel in an image. DCE MRI is defined as the acquisition of rapid T1W gradient echo scans before, during and after the intravenous administration of a low molecular weight gadolinium based contrast agent (GBCA). T1W images are primarily used to determine the presence of hemorrhages and designed to plot the gland (Weinreb et al., 2016).

The contrast injection is a part of DCE examination. Prostate cancer is usually multifocal. The largest tumor focus usually yields the highest Gleason score and is most likely to contribute to extra prostatic extension (EPE) and positive surgical margins.

In 2012, European Society of Urogenital Radiology (ESUR) introduced a pipeline called PI-RADS version 1 for scoring system that organizes diagnostic procedure. Later on, due to fast growing progress the PIRADS v2 was developed.

The objective of MpMRI test is to detect and restrict the area for abnormally related to prostate cancer. Accordingly, PI-RADS v2 categorizes the lesion of interest into the following five groups:

PI-RADS 1 – Very low (clinically significant cancer is highly unlikely to be present)

PI-RADS 2 – Low (clinically significant cancer is unlikely to be present)

PI-RADS 3 – Intermediate (the presence of clinically significant cancer is equivocal)

PI-RADS 4 – High (clinically significant cancer is likely to be present)

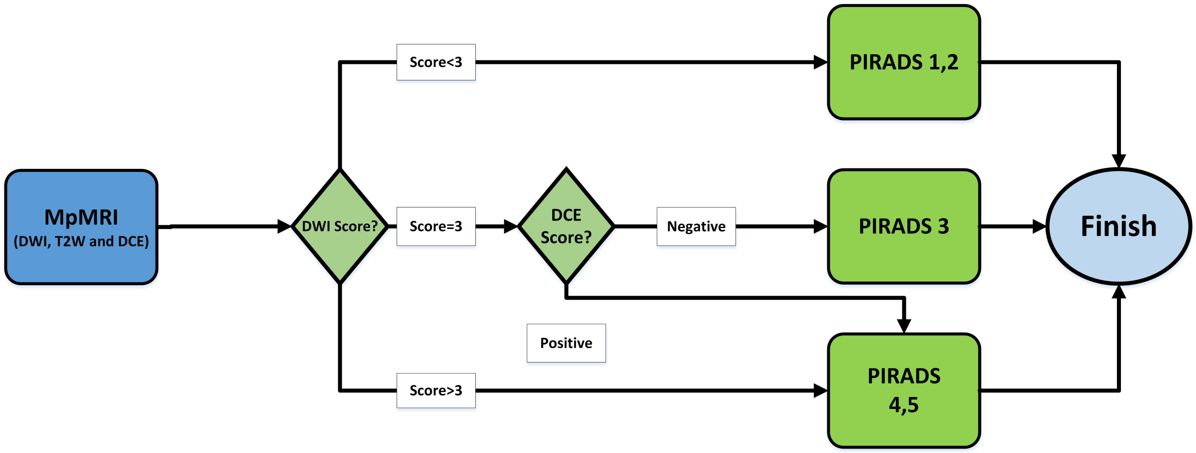

Figure 3.5: MpMRI, PIRADS v2 classification flow diagram for PZ

DWI	T2W	DCE	PIRADS
1	Any	Any	**1**
2	Any	Any	**2**
3	Any	-	**3**
3	Any	+	**4**
4	Any	Any	**4**
5	Any	Any	**5**

Table 3.1: PIRADS v2 Scoring table for MpMRI for PZ

PI-RADS 5 – Very high (clinically significant cancer is highly likely to be present)

The MpMRI results should be interpreted independently and biopsy should be considered only for PIRADS 4 and 5 and not for PIRADS 1 and 2. Figure 3.5 determines the pipeline for diagnosing. In case that the score of DWI is 3, the score of DCE acts the main role. A positive DCE may leads to score the PIRADS from 3 to 4 (Weinreb et al., 2016) as in it shown in Table 3.1. In this case, the final decision of any further treatment is reserved to the specialist due to the complexity of results and the decision making process.

MpMRI is the most comprehensive method used in diagnosis for prostate cancer and is the standard procedure for staging the PC. However it has some drawbacks including high cost, long time and use of contrast injection for DCE which causes some discomforts for patients. Therefore, Biparametric MRI or BpMRI is utilized for overcome these limitations. The BpMRI contains T2W and DWI. The major different between MpMRI and BpMRI is that the DCE which is omitted in BpMRI. Elimination of DCE removes the injection of IV contrast from procedure. Injection of IV contrast agent is costly and leads to patient dissatisfaction. As a result, BpMRI provide the same services with lower cost and higher satisfaction. However, when it comes to DWI score 3; BpMRI is unable to lead to the best PIRADS score (Scialpi et al., 2017).

Chapter 4

Statistical test of dependency between the result of brain MRI and referring physician specialization

In this chapter we explain the statistical test we exploited for testing one hypothesis in this thesis. A statistical test attempts to answer a specific claim about a population parameter based on the sample data. The intention is to conclude whether there is enough evidence to ”reject” a conjecture or hypothesis about the process. Alternatively, it may be a disappointing result, indicating we may not yet have enough data to ”prove” a statement by rejecting the null hypothesis.

4.1 Hypothesis

The very first step of performing a hypothesis test is to define the null and alternative hypotheses. The null hypothesis is often an initial claim that is based on prior analyses or specialized knowledge. The alternative hypothesis declares that a population parameter is smaller, larger, or different than the hypothesized value in the null hypothesis. Accordingly, our null and alternative hypothesis are defined as follows:

- *The incidence of multiple sclerosis (MS) diagnosis based on MRI* ***does not differ*** *between* *patients referred by neurologists and non-neurologists in a community-based practice in a large metropolitan area in Canada.*

- *The incidence of multiple sclerosis diagnosis based on MRI **differs** between patients referred by neurologists and non-neurologists in a community-based practice in a large metropolitan area in Canada.*

4.2 Variables

Next step is to define the type of data and variables. In general, the data in statistical tests categorized into three groups:

1. **Measurement variables**: These variables can be measured like length, pH, and bone density.

2. **Nominal variables**: are also called attribute variables. These variables classify observations into a small number of categories. An individual observation of a nominal variable is a name, not a number. Examples of nominal variables include sex (the possible values are male or female), type of disease, and blood type.

3. **Ranked variables**: also called ordinal variables are those kinds of variables that categorizes data base on the rank or order, even though the exact values are unknown.

Our sample data comes from the healthcare perform center, which is used as a sample to represents the population of Canada. Based on the null and alternative hypothesis, our variables are referring physician specialization (neurologist or non-neurologist) and the test result (positive or negative). Accordingly, the type of variables this thesis is nominal; This leads to a 2x2 contingency table (Table 4.1).

4.3 Fisher's exact test

Based on our data and size of the sample (less than 1000) the suitable test of dependent for the data and variables is Two-tailed Fisher's exact test of independence. Fisher's Exact test is a test of significance which is used in the place of chi-square test in 2 by 2 tables, especially in cases of small samples. a two-tailed test is a method in which the critical area of a distribution is two-sided and

Variable X (test result)

Variable Y (referral pattern)		Positive	Negative	Total
	neurologist	a	b	a+b
	non-neurologist	c	d	c+d
	Total	a+c	b+d	N=a+b+c+d

Table 4.1: Fisher's exact test 2 by 2

the test verifies whether or not a sample is greater than or less than a certain range of values.

Fisher's exact test tests the probability of getting a contingincy table that is as strong due to the chance of sampling. There are certain assumptions on which the Fisher's exact test is based. The sample assumed to be random. It is also assumed that the value of each sample is independent from other samples value. In other words, the value of one sample does not get affected by the value of others. Another assumption is mutual exclusively between observations. Accordingly, in our test, all of the assumptions are met. The contingency Table 4.1 shows the data set for 2x2 variables.

Fisher's exact test obtains the probability of the combination of the frequencies that are actually collected. It also includes the finding of the probability of every possible combination, which designates more evidence of association. This probability (p-value) is calculated as follows:

$p = [(a + b)! (c + d)! (a + c)! (b + d)!] / a! b! c! d! N!$

In this formula, the a, b, c and d are the individual frequencies of the 2x2 contingency table, and N is the total frequency.

Significance level

In this study, we consider the significance level for the statistical hypothesis test as 0.05. If the p-value is less than 0.05, we have enough evidence to reject the null hypothesis; otherwise the null hypothesis cannot be rejected. Any change in the significance level requires strong and justifiable reason. With a significance level of 0.05, there is a 5 percent chance of rejecting the null hypothesis, even if it is true. This is called a "Type I error" or "false positive". If there is a deviation from the null hypothesis, and the test fails to reject it, that is called a "Type II error" or "false negative".

	positive	negative	Total
Neurologists	9	43	52
non-neurologists	21	270	281
Total	30	313	343

Table 4.2: MS incidence data set

We collected the data from Picture Archive and Storage System (PACS) to scan and identify non-contrast (C-) and contrast-enhanced (C+) MRI of brain related to MS as well as test referring physician. Out of 343 test results we collected, a total number of 291 patients were referred by non-neurologists. 21 reports of non-neurologists were positive, and 270 were negative accordingly. 52 patients were referred by neurologists, in which 9 reports were positive, and 43 were negative.

The p-value in our experiment was calculated as 0.029, which means there is a significance difference between the test results of patients referred by neurologists and non-neurologists. Table 4.2 summarizes the results. These results indicate that devising an MRI protocol of MS diagnostics based on referring physician specialization could lead to different results in the term of cost, efficiency, and throughput.

Chapter 5

Comparison of different MS diagnostic procedures

5.1 Two-tiered MRI policy with respect to referring physician specialization

Brain MRI examinations can be ordered without a pre-authorization or referral from a neurologist in our community-based practice in (Canada, blinded). Shortly after the release of revised 2010 McDonald's criteria (Polman et al., 2011), an increase in the number of brain MRI requests was seen, which explicitly required the contrast of IV and the application of McDonald's criteria. Brain MRI can be performed without using the IV contrast, which is a non-sensitive white-water-borne protein-free protocol. Within a year of accomplishing this particular process, a useful review of the MRI segment of the brain to rule-out MS was conducted. A meagre percentage of abnormal (positive) scans in MRIs was seen that are used to evaluate MS in patients undergoing neurological work. The Brain MRI without contrast (C-), denoted as scenario 2 in this study, needs fewer resources (machine time, technician time, material) and less costly, but it is not accurate as full Brain MRI with the injection of contrast (C+). We call the C+ protocol as scenario 1 in this study.

Accordingly, we adopted a two-tiered policy where a non-contrast short protocol sensitive to white matter lesions (C- brain MRI) is used to screen the patients referred by non-neurologists in the hope of maintaining accuracy and reducing the cost and increasing efficiency. We call this approach as scenario 3. In this approach patients referred by a neurologist would undergo an abbreviated non-contrast brain MRI (C-). If MRI result is negative, MS imaging would be considered complete in a single hospital visit. If MRI result is positive, patients would enter C+ MRI for an additional two hospital visits. Patients referred by neurologists, however, would enter C+ MRI directly. This approach is shown in Figure 5.1.

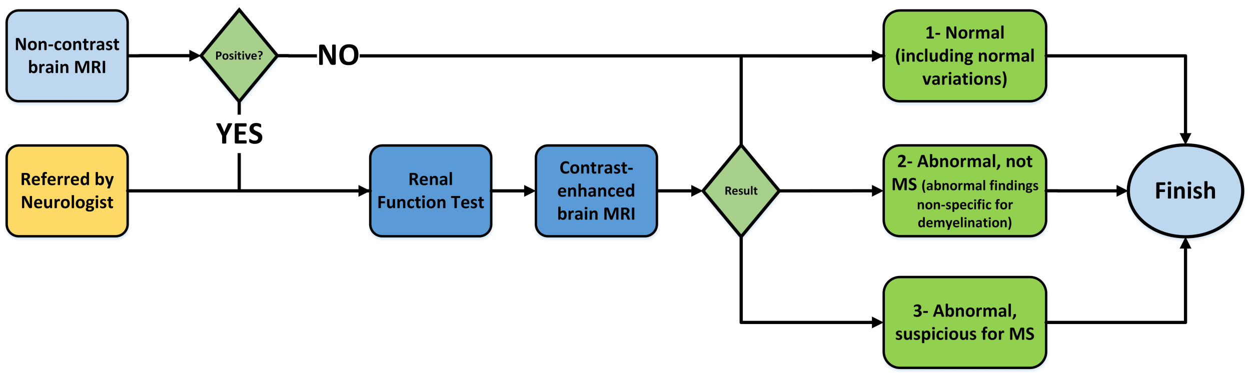

Figure 5.1: Two-tiered MRI with respect to referring physician specialization for diagnosing MS

5.2 Time-driven activity-based costing in Healthcare

In order to compare the cost of different MRI approaches, we used time-driven activity-based costing (TDABC) approach. Activity-based Costing (ABC) is the fundamental element of TDABC which is an excellent way to identify and allocates the costs of overhead activities, and then assign those costs to products. The ABC System identifies the relationship between costs, overhead activities, and completed products, and through this relationship, allocates indirect costs to products that are less arbitrary. However, some costs are difficult to calculate when using this cost accounting method. Indirect costs, such as wages for personnel and administrators ,are difficult to assign to a product. Hence, this method has found its way to the manufacturing sector.

The foundation of ABC system of cost accounting is on activities; activity can be an event, unit of work, or task with a definite purpose, such as designing products, setting up machines for production, or operating machines (Turney, 1992) & (Cooper & Kaplan, 1991).

ABC is challenging to implement due to high costs incurred by interviews and surveys required to setup the initial ABC model. It also suffers from subjective and costly-to-validate time allocations, as well as the problem of maintaining and updating the model as the cost of processes and resources change overtime. Further, once the initial model is made, model updates need to be reviewed through a new round of surveys and interviews to reflect changes in the company's procedures (Kaplan & Anderson, 2003).

Time-driven ABC addresses all of the above limitations. It is easier, less expensive and faster to implement, and allows driver costs to be based on practical capability of supplied resources. Time-driven ABC estimation requires only two parameters: the unit cost of supply and the expected time for a transaction or an activity.

TDABC method uses an estimate of the time required each time the activity is performed. This one-time estimate replaces the interview process with people to learn how much time they spend on all activities in a dictionary. Time estimation can be achieved by direct observation or interviews. High precision is not required at this stage; a general estimation is sufficient (Kaplan & Anderson, 2007).

TDABC in healthcare is primarily used to estimate the cost of clinical practices and visits in order to inform operational improvement and compare them with reimbursement tariffs. TDABC programs varied, but in general, it involves the following the seven-steps model reflected (Keel, Savage, Rafiq, & Mazzocato, 2017):

Step 1. Select the medical condition

Step 2. Describe the care delivery value chain

Step 3. Develop process maps for each activity in patient care delivery

Step 4. Obtain time estimations for each process

Step 5. Measure the cost of providing patient care resources

Step 6. Measure the capacity of each resource and calculate the capacity cost rate

Step 7. Calculate the total cost of patient care

The purpose of this study is to provide the best quality care to the patient at the lowest overall cost in brain MRI for diagnosing MS. Not every TDABC is the same, nor all of its terms apply to every project. We defined the steps of this study inspired by TDABC approach. The main difference of this study with TDABC method, is the scale of the project. In the majority of studies on the application of the TDABC in a healthcare project, medical condition is in the center of attention and all the values are defined to optimize the procedure of curing that medical condition. However, the purpose of our study is to provide -or maintain- the best quality at the lowest cost in the procedure of diagnosing the disease. Therefore, some steps of TDABC approach, such as describing the care delivery value chain, which starts from monitoring and preventing and continues to intervene and recovering, are not take into consider action.

5.3 Data collection

In this study, we defined and later collected five types of data, including patient-related data, MRI protocol's data, MRI results, cost and, adverse events' data. With accessing this data, we are able to map different MRI diagnostic procedures and compare them in term of different performance indicators. The detailed description of each type of data along with its features and the method of data collection are provided in the following sections.

5.3.1 Patient

With the absence of searchable radiology or hospital information system (RIS, HIS), to acquire patients' data for diagnosing MS, Picture Archive and Storage System (PACS) was used to scan and identify all the patients with either non-contrast (C-) or contrast-enhanced (C+) MRI of brain. All patients with results containing any or combination of ”rule out”, ”Multiple Sclerosis”, ”MS”, ”demyelination”, ”demyelinating disease” and, ”McDonald's criteria” were counted as inclusion criteria. Exclusion criteria split into 4 categories:

1. Patients with a previous/known diagnosis of MS (either first scan or follow-up)

2. Patients with prior abnormal CT scan suspicious for demyelinating disease based on history or radiology report.

3. Patients with a test history containing any or combination of ”follow-up, Headache / Migraine, Lesion, Vertigo, Ataxia, Dizziness, Tremors, Nausea, TIA, Stroke, Syncope, Memory loss, Dementia, Alzheimer's, Cognitive, Decline, Deterioration”, without keywords included in inclusion criteria.

4. Patients with brain MRIs performed with specific protocols (identifiable on PACS, e.g. MRI IACs, C- MRA).

Data related to patients as gender and age were also collected. MRI services are not offered to patients younger than 18 years old or younger in this hospital.

5.3.2 MRI protocol

All data related to brain MRI protocol, such as the number of sequences in each protocol and presence or absence of IV contrast were collected. Base on protocol exam card, an average scan per sequence time were calculated. Manual extraction of pre-exam scan times based on individual exam time-stamps on PACS was hardly possible; therefore, we did not obtain it. Two MRI technologists with more than 7 years of MRI scanning experience in the hospital estimated the average MRI room time. Referring physician specialization's data were collected using the online physician directory of Collège des Médecins du Québec. Clinical referrals were sorted into two categories: neurologists and non-neurologist.

5.3.3 MRI results

To obtain the MRI results, a master student in Industrial Engineering was trained by a radiologist with 6 years of mixed academic and community practice experience to search in the PACS and obtain and evaluate clinical information for all inclusion and exclusion criteria and also evaluate the finalized report. Any inconclusive report was reviewed and classified by the radiologist.

5.3.4 Cost

From healthcare system perspective, all costs related to the protocol, such as MRI operational cost, including salaries (technologists, secretary), service contract, contrast administration cost, costs associated with renal function tests before contrast administration and radiologist professional fees, were obtained. From the patient's perspective, the costs were parking expenses and loss of productivity for half a day for each test. No other costs are incurred by the patients during visits due to 100% insurance coverage in Canada.

5.3.5 Adverse events

An effort was made to account for patient experience given the invasive nature of both venipuncture and IV contrast administration. We collectively termed these complications as ”adverse events” leading to a less than satisfactory patient experience. The true incidence of venipuncture complications is not known given retrospective nature of the study. Patient records for documentation of contrast reactions were also not studied, nor a measure of patient experience such as satisfaction surveys. We ignored patient dissatisfaction from staying longer in the magnet bore during C+ MRI, and rare (0.05%) (AmericanCollegeOfRadiology et al., 2015) contrast extravasation.

Non-tangible expenses such as radiologist interpretation time, loss of time or personal productivity to patients as well as discomfort and complications due to phlebotomy IV contrast administration were considered but could not be translated to financial value reliably.

5.4 Comparison Parameters

After mapping different approaches and obtaining data related to them, defining parameters for comparison is the next step. With proper parameters that can be measured and compared, the protocols would be ready to analyze. Parameters can be categorized as cost (system and patient's perspective), service performance, and service value. Hence, these parameters were defined, calculated and compared as:

1. (Health) System cost: This is the cost of MRI utilization plus renal testing. System cost is the main portion of expenses as all the costs in public health care are covered by health insurance. System costs are classified into two subgroups:

a. System cost per completed MRI workup no matter what the results are.

b. System cost per positive MRI.

2. Total patient cost: This is the cost of parking and loss of productivity for half a day (per test) for patients. As we mentioned before, in Canada, due to 100 % insurance coverage, patients would not pay for medical tests. We consider the following subgroups for patient cost:

a. Patient cost per completed MRI workup

b. Patient cost per positive MRI

3. (Health) Service Performance: The service performance is measured in terms of the following parameters:

a. Throughput: Time required to complete MRI workup (target outcome)

b. Number of callbacks

c. Number of estimated adverse events

d. Percentage of patients with less than satisfactory MRI experience after complete MRI workup for all patients

e. The number needed to harm (NNH): this number is an epidemiological measure that indicates the harm or adverse effects. It indicates how many people should be exposed to the risk factor in a given period in order to cause harm an average of one person who otherwise would not have been harmed. It is defined as the inverse of the absolute risk increase and calculated as 1/(EER-CER), where EER is the incidence in the treated (exposed) group, and CER is the incidence in control (unexposed) group. Intuitively, lower the number needed to harm means worse risk factor, and when it is equal to 1, it means that every exposed person is harmed (Porta, 2014).

The MS scenario 2 (abbreviated protocol) will be considered as the control groups given their lowest rate of adverse events. Two sets of NNHs will be calculated: Once calculating adverse events for both venipuncture and contrast and once calculating only contrast complications. The reason for the latter is to assess the significance of taking venipuncture complications into account, not previously addressed in MRI economics literature to the best of our knowledge.

4. MRI Service Value:

a. Value is defined using Baldor's formula as (Quality x Service)/(Cost x Time)

i. Quality is defined as the diagnostic outcome of individual MRIs and is considered constant between all MRI scenarios (similar accuracy of MRI interpretation by the radiologists). Service is defined as the inverse rate of adverse events.

ii. Cost is defined as the total of system and patient's costs.

iv. Time is the same as throughput

b. Service value will be calculated for and compared between different MRI scenarios.

5.5 Results

A total of 4812 C- and C+ MRIs were identified in the initial PACS query. 343 cases were relevant to our study with a mean age of 42.3 (age range 18-85). A total number of 291 patients were referred by non-neurologists. 21 reports of non-neurologists were positive, and 270 were negative accordingly. 52 patients were referred by neurologists, in which 9 reports were positive, and 43 were negative.

All studies were performed on a 1.5T Siemens Avanto magnet (Siemens AG, Munich, Germany). Table 5.1 shows the C- and C+ protocol sequences and average scan time and average room time based on MRI technologist estimate. Total room time compared to acquisition time is longer for C+ versus C- MRI (13 vs. 8.5 min) due to the additional time required to establish IV access.

MRI C- Sequences	Time (mm:ss)	MRI C+ Sequences*	Time (mm:ss)
Localizer	00:27	Localizer	00:27
Ax FLAIR	02:44	Sag FLAIR	04:00
Sag Proton Density	02:44	Ax FLAIR	03:04
		Ax T1 Pre	01:19
		Contrast Injection	00:30
		Ax T2	01:18
		Ax GRE	01:52
		DWI	01:52
		SAG MPRAGE	05:27
		Ax T1 Post	02:03
Acquisition Time C-	06:29	**Acquisition Time C+**	21:52
Room Time C-	15	**Room Time C+**	35

Table 5.1: C+ and C- MRI Protocols, acquisition and room times

From a total of 104 referring clinicians, 13 were neurologists (12.5 %) and 91 non-neurologists (87.5 %). Of the non-neurologists, 68 were General Practitioners (GPs) and 23 non-neurologist specialists [(internal medicine (n=11), general and specialized surgery (n=4), anesthesiology (n=1), ophthalmology (n=1), emergency medicine (n=1), Physical medicine and rehabilitation (n=2), Rheumatology (n=1), Hematology (n=1), Anesthesiology (n=1)].

MRI accessibility

At our hospital, similar to most MRI services, we are unable to offer C- and C+ exams equally throughout the day since C+ MRIs require presence of a licensed individual. At this hospital C+ MRIs are only performed from 7:30am to 2:30pm (7 hours), with the remaining 8 hours limited to C- MRIs. In one workday (7h x 60min / 35min =) only 12 C+ MRIs can be performed, while the number of C- MRIs can reach (15h x 60min / 15min =) 60. Combining the two studies will allow 12 C+ MRIs and an additional (8h x 60min / 15min =) 32 C- MRIs, for a total number of 44 patients per day.

Table 5.2 shows the time to complete the diagnostic services required for this patient cohort, longest in scenario #1. Scenario #2 is most efficient, rendering the service in 8.21 days, while it takes 3.48 times longer for scenario #1 to complete the service.

N = 343	Scenario 1	Scenario 2	Scenario 3
Time required for Initial C+ MRIs	*343/12* = 28.6	*0*	*52/12* = 4.3
Time required for Initial C- MRIs	0	*343/60* = 5.71	*291/60* = 4.85
Time required for Call Back C+ MRIs	0	30/60 = 0.5	21/60 = 0.35
Total Time (days)	28.6	8.21	9.5

Table 5.2: Time required to complete MRI workup for all patients referred to rule out MS

For simplicity, this is calculated with the conservative assumption that the callback protocol is the same as the initial C+ study (35 min room time) and therefore underestimates the efficiency of scenario #2. Practices can further shorten the acquisition time for callback C+ MRIs by acquiring only the ”missing” sequences, increasing the efficiency of scenarios #2 and #3.

5.5.1 Adverse events

In absence of objective data in our patient cohort, we used the literature to estimate the prevalence of adverse events related to IV contrast and venipuncture. The latest edition (V10.3, 2018) of ACR manual on contrast media [10] reports that “adverse event rate for Gadolinium based contrast agents (GBCAs) administered at clinical doses (0.1–0.2 mmol/kg for most) ranges from 0.07 % to 2.4 %". We used the arbitrary average of the range extremes for an estimate complication rate of [(0.07+2.4) / 2 =] 1.2 %. We noted and did not choose the much lower rates of adverse reactions had been reported for ProHance and MultiHance (0.003 %) from the EuroCMR Registry (Bruder et al., 2011) as they pertained to a potentially different population.

Venipuncture adverse events, in light of paucity of literature on this topic, were estimated from a 1992 study (Dale & Howanitz, 1996), the 1991 report of "College of American Pathologists Q-Probe study of patient satisfaction and complications" (Howanitz, Cembrowski, & Bachner, 1991) and its 1996 update (Dale & Howanitz, 1996). In the latter two reports, patient dissatisfaction were mainly due to post-venipuncture bruising or need for more than one needle stick. Bruise rates in these studies were 12.3 %, 16.6 % and 12.9 %, respectively, averaged to [(12.3+16.6+12.9) / 3 =] 14 %. The rate for more than one needle stick was 3 % in the 1995 report, and not specified in the other studies. The cumulative adverse event rate for venipuncture was calculated as (14 + 3 =) 17 %. We do note that these two rates are definitely not additive (patients requiring more attempts are more likely to get bruises), however, this overestimation may be balanced by ignoring less common complication rates, such as "serious complications" in 3.4 % (Dale & Howanitz, 1996) and syncope in less than 1 % (Organization et al., 2010).

Therefore, a C+ MRI would expose the patient to 17 % adverse events during renal testing venipuncture and (17 % + 1.2 % =) 18.2 % adverse events due to second venipuncture and contrast.

5.5.2 Cost

System's expenses

In absence of established MRI price/cost data, three sources were considered:

1) Price in Montreal's private MRI clinics.

2) Direct Pay Fee charged by our public hospital to individuals who do not have public health insurance.

3) Cost in public hospital for patients with health insurance according to MRI operational budget of the department, calculated as below:

a. Annual MRI operational cost: $ 1,569,274

b. Annual MRI operation: 3900 hours (15 hours/day, 5 days/week)

c. MRI operation cost per hour: $ 402.38 and per minute: $ 6.71

As most MRI services are offered in the public hospitals to insured patients, the last estimate were used for cost analysis. Other expenses include:

1) Contrast cost [one bottle of IV contrast ($ 15) plus phlebotomy ($ 2.17 = needle $ 1.15 + IV line cap $ 0.88 + dressing $ 0.14)]: $ 17.17.

2) Renal function test: $ 3.23.

3) Radiologist professional fees: $ 105.

Patient's expenses

Based on average daily income of $ 221.5 (252 work days/year, average annual salary of $ 55820 in city of (Blinded), each hospital visit incurs a half day income loss of $ 110.8, in agreement with estimates in a recent similar study (Pahwa et al., 2017). Parking fee is $ 20 per hospital visit.

Non-tangible costs include patient anxiety due to call back. The call backs are always performed within a week, so the delay in diagnosis is considered negligible. All costs related to patients and system are summarized in Table 5.3.

5.5.3 Decision tree results

As we mentioned earlier, three scenarios were included in this study: 1) The patient would undergo a contrast-enhanced brain MRI (hereafter referred to as C+). This will require two visits to the hospital: one for renal function testing and one for the MRI examination. The results of renal functions test are not available the same day at this hospital for outpatients. Figure 5.2 shows the total cost of 343 patients, and adverse patient experience for the renal function test and C+ MRI test. The total system cost in Scenario 1 for 343 patients is 123,514.30 $. Total patient cost is 89,728.80 $. The total portion of adverse patient experience is 35 %. Table 5.4 summarizes all the costs related to each visit in scenario 1. The system cost per MRI in this scenario is 360.10 $ as well as the patient cost is 261.60 $.

[1] Radiologist professional fee is waived for the recall exam

	C- MRI	C+ MRI
Price in private MRI clinics	**$675.00**	**$800.00**
Exam cost	$675.00	$800.00
Contrast Cost	Included	Included
Radiologist Professional Fee	Included	Included
Direct Pay at Hospital (no insurance)	**$433.20**	**$433.20**
Exam cost	$328.20	$328.20
Contrast Cost	Included	Included
Radiologist Professional Fee	$105.00	$105.00
Cost to public hospital for insured patient		
First Visit		
Exam Cost ($6.71/min)	**$205.60**	**$356.87**
Contrast Cost	$100.60	$234.70
Radiologist Professional Fee	$0.00	$17.17
Callback	$105.00	$105.00
Exam Cost ($6.71/min)		
Contrast Cost	**NA**	**$251.87**
Radiologist Professional Fee	NA	$234.70
Renal Function Test Cost	NA	$17.17
Patient Costs	NA	0*
Parking, Renal Test		
Half day income loss, Renal Test	**$0.00**	**$3.23**
Parking, MRI Exam		
Half day income loss, MRI Exam	**$130.80**	**$261.60**

Table 5.3: System and patient costs[1]

2) The patient would undergo an abbreviated non-contrast brain MRI (hereafter referred to as C-). If MRI result is negative, MS imaging would be considered complete in a single hospital visit. If MRI result is positive, patients would enter scenario #1 for an additional two hospital visits. Figure 5.3 shows the total cost of 343 patients, and adverse patient experience for C- MRI test, the renal function test, and C+ MRI test. The total system cost in Scenario 2 for 343 patients is 78,173.80 $ .The total patient cost is 52,712.40 $. The total portion of adverse patient experience is 3.09 %. Table 5.5 summarizes all the costs related to each visit in scenario 2. The system cost per MRI in this scenario is 227.91 $ as well as the patient cost is 153.68 $.

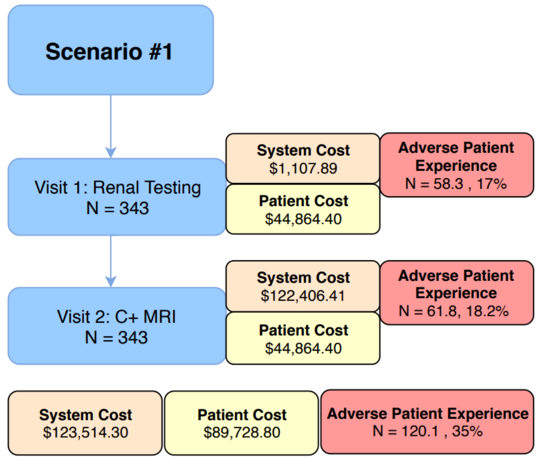

Figure 5.2: Scenario #1

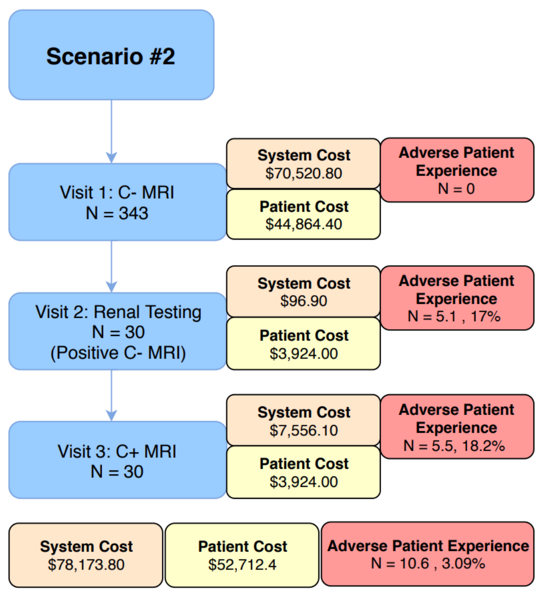

Figure 5.3: Scenario 2

Hospital Visit	#1	#1	#2	#2	#3	#3	
	N=	Cost	N=	Cost	N=	Cost	**Total**
C- MRI	0	0	0	0	0	0	**System**
C+ MRI	0	0	343	$122,406.41	0	0	$123,514.30
Renal Test	343	$1,107.89	0	0	0	0	**Patient**
Patient Parking & Income Loss	343	$44,864.40	343	$44,864.40	0	0	$89,728.80
						System Cost per MRI	$360.10
						Patient expense per MRI	$261.60

Table 5.4: Scenario 1 Cost

Hospital Visit	#1	#1	#2	#2	#3	#3	
	N=	Cost	N=	Cost	N=		**Total**
C- MRI	343	$70,520.80	0	0	0	0	**System**
C+ MRI	0	0	0	0	30	$7,556.10	$79,624.90
Renal Test	0	0	30	$1,548.00	0	0	**Patient**
Patient Parking & Income Loss	343	$44,864.40	30	$3,924.00	30	$3,924.00	$52,712.40
						System Cost per MRI	$227.91
						Patient expense per MRI	$153.68

Table 5.5: Scenario 2 Cost

3) Patients referred by a neurologist would enter scenario 1, patients referred by non-neurologists would follow scenario 2. Figure 5.4 shows the total cost of 343 patients, and adverse patient experience for C- MRI test, the renal function test, and C+ MRI test. The total system cost in Scenario 2 for 343 patients is 83,911.90 $ .The total patient cost is 54,412.80 $. The total portion of adverse patient experience is 7.5 %. Table 5.6 summarizes all the costs related to each visit in scenario 2. The system cost per MRI in this scenario is 244.64 $ as well as the patient cost is 158.64 $.

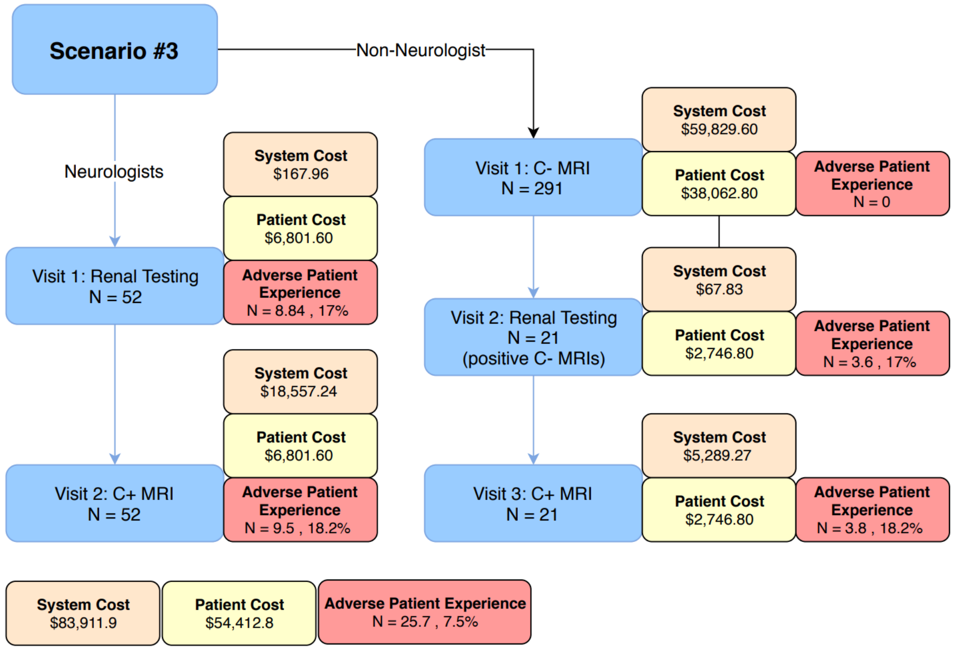

Figure 5.4: Scenario 3

Hospital Visit	#1	#1	#2	#2	#3	#3	
	N=	Cost	N=	Cost	N=		Total
C- MRI	**291**	$59,829.60	0	0	0	0	**System**
C+ MRI	0	$0.00	**52**	$18,557.24	**21**	$5,289.27	$87,442.91
Renal Test	**52**	$2,683.20	**21**	$1,083.60	0	0	**Patient**
Patient Parking & Income Loss	343	$44,864.40	73	$9,548.40	21	$2,746.80	$57,159.60
System Cost per MRI							$244.64
Patient expense per MRI							$158.64

Table 5.6: Scenario 3 Cost

5.6 Discussion

Decision Tree Analysis

The Institute for Healthcare Improvement (IHI) Triple Aim initiative is a structure that defines an approach in order to optimize health system performance. The so-called ”Triple Aim” seeks to:

1) improve patient experience (including quality and satisfaction),

2) improve the population’s health, and

3) reduce per capita cost of healthcare.

We will compare the three MRI scenarios with these aims that we will call IHI’s Aim 1, Aim 2, Aim 3 for the sake of simplicity.

The MS MRI scenario 2: imposes the least direct expense on patients and has the least number of adverse effects but the highest callback. It is likely that venipuncture- and contrast-related complications adversely affect patient experience more than call back anxiety. Nevertheless, we ascribed them equal weight towards the total number of unpleasant experiences. Scenario 2 remains the lowest among the three scenarios, meeting IHI’s Aim 1. With the lowest number of adverse events, it meets IHI’s Aim 2 compared to other scenarios. It is the most cost-effective strategy, meeting IHI’s Aim 3.

The current standard of practice (scenario 1) imposes the highest cost on both the health system (+ 58%) and patients (+ 70%), while suffering from the least efficient throughput, inflicting a tremendous number of adverse events (11.3 times higher than scenario 2), has the lowest number (worst) needed to harm and offers the least service value (table 5.7). Hence, it does not meet any of IHI’s Aims.

	Scenario 1	Scenario 2	Scenario 3
Quality (arbitrary)	100	100	100
Service	2.85 (1 / 35%)	32.36 (1 / 3.09%)	13.33 (1 / 3.09%)
Cost ($)	621.70 (360.10 + 261.60)	381.59 (227.91 + 153.68)	403.28 (244.64 + 158.64)
Time (days)	28.6	8.21	9.5
Value	0.02	1.03	0.35
Added Value (arbitrary)	Current practice	1.02	0.33
Relative Value	Current practice	64.44	21.71

Table 5.7: Comparison of MRI Service Value in different scenarios

The performance of scenario 3 is in between the other two scenarios, pretty close to Scenario 1. We considered this scenario since patients referred by neurologists are expected to have the highest pre-test probability of having MS, and we postulated that the rate of positive MRI results in these patients would affect the performance of each scenario.

In our population of 17% MRI positive in patients referred by neurologists, scenario 2 is still the most cost-effective option compared to other scenarios. Nevertheless, with a different positive rate for neurologists patients, scenario 3 could be more cost-effective. Given the extreme 100% positive MRI rate in neurologists patients in Scenario 2, it is necessary to callback all these patients, and each neurologists patient will have to receive both C- and C + MRI, affecting all measured variables negatively.

It has been shown that the participation of academic neuroradiologists in the utilization management program results in a reduction of 20% in additional studies using appropriate criteria. Scenario 2 is similar to a series of interventions in a program without pre-authorization programs not only on eligibility criteria but also on the economics of MRI technology (a.k.a. MR economics) (Bell, 1996). In a follow-up study in 2016, Friedman and Smith reported that radiologist involvement had a significant impact on a collaborative utilization management program. The highest impact was related to family practice (42.7%), internal medicine (41.8%), and neurology (33.4%), which constituted 104/92 (88.8%) of the referring clinician referred to this study (68, 11, 13 sequentially). They concluded that this outcome was independent of the provider's expertise. On the other hand, Scenario 3 shows that considering the expertise of the service provider has a significant impact on the service parameters.

This is the first important conclusion of our study: that expertise of the referring clinician, by affecting the likelihood of a positive pre-test result, can serve as a decision node for two- or multi-tiered protocols. To the best of our knowledge, this effect has not been described in the literature before.

The Patient Perspective

We have already noted that Scenario 1 imposes the highest direct costs to patients and the highest rate of adverse events, albeit without any callback. Callbacks are considered undesirable for two reasons: 1) by most imaging facilities, they are considered to disrupt workflow, and 2) they are associated with patient anxiety as well as discomfort and dissatisfaction.

We calculated that scenario 1 would require 3.11 times more time to complete the diagnostic services needed for this patient group (Table 5.9). This means that in multi-tiered approaches,

	Events (E)	Non-events (N)	Subjects (S)	Event rate (ER)	
Experiment (E)	EE	EN	EE + EN	EER = EE / ES	**NNH**
Control (C)	CE	CN	CE + CN	CER = CE / CS	1 / (EER − CER)
			Venipuncture +Contrast		
Scenario #1	120.1	222.9	343	35%	**3.13**
Scenario #2	10.6	332.4	343	3.09%	N/A: Control
Scenario #3	25.7	317.3	343	7.5%	**22.72**
			Contrast Only		
Scenario #1 (343 C+ MRIs)	4.1	338.9	343	1.2%	91.32
Scenario #2 (30 C+ MRIs)	0.4	342.6	343	0.1%	N/A: Control
Scenario #3 (73 C+ MRIs)	0.9	342.1	343	0.3%	664.7

Table 5.9: Number needed to harm, using scenario 2 as the control group

callback should not be dismissed or minimized, but optimized.

N = 343	Scenario 1	Scenario 2	Scenario 3
System cost	$123,514.30	$79,624.90	$87,442.91
System cost per completed MRI workup	$360.10	$227.91	$244.64
System cost per positive MRI	$4,117.14	$2,605.79	$2,797.06
Patient cost	$89,728.80	$52,712.40	$57,159.60
Patient cost per completed MRI workup	$261.60	$153.68	$158.64
Patient cost per positive MRI	$2,990.96	$1,757.08	$1813.76
Service Performance			
Throughput (days)	28.6	8.21	9.5
Number of call backs (anxiety and inconvenience)	0	30	21
Number of estimated adverse events	120.1	10.6	25.7
Number (and rate) of unpleasant experiences (Adverse events + call backs)	120.1	40.6	46.7
Number needed to harm (NNH)	3.13	N/A: Control	22.72
Relative Value	Current practice	64.44	21.71

Table 5.8: Summary of cost, service performance, patient experience and value analysis Coloured numbers in parentheses in scenarios 1 and 3 cells represents comparison to scenario 2

Phlebotomy is an underestimated procedure: Table 5.8 illustrates the number needed to plummets falls from 91.32 to 3.13 when considering venipuncture complications.

Chapter 6

Comparison of different PC diagnostic procedures

In this chapter, we first introduce a two-tiered MRI scenario for diagnosing PC. Then, we compare two scenarios base on cost and efficiency.

6.1 Two-tiered MpMRI policy

In order to overcome the limits of BpMRI and the cost and dissatisfaction rate of MpMRI (chapter 3), a two-tiered MpMRI was introduced. In this procedure, all patients take a BpMRI. Patients with PIDADS score (DWI) of 1, 2, 4 and 5 do not need to come back for further MRI tests due to the certainty of the results for these scores. However, all patients with a DWI score of 3 need to come back for another test, which would be MpMRI to determine their PIRADS score. The proposed Two-tiered MpMRI is shown in Figure 6.1.

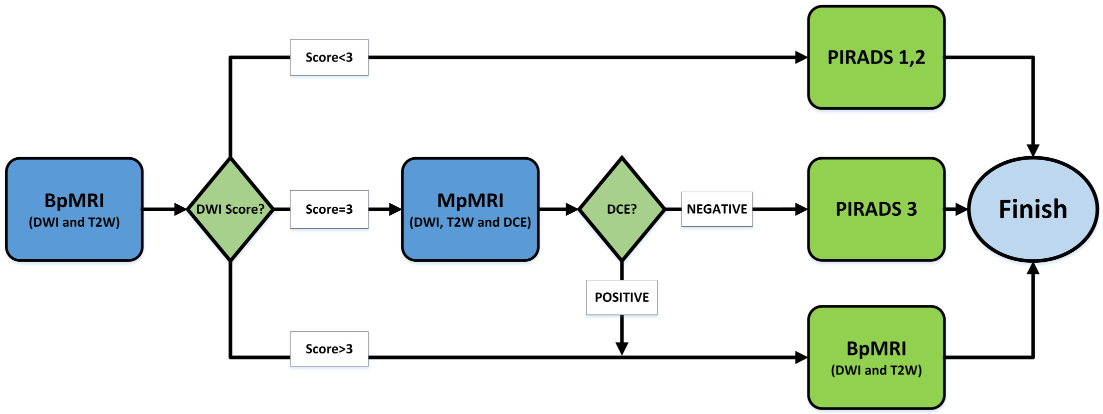

Figure 6.1: Two-tiered MpMRI, PIRADS v2 classification flow diagram for PZ

6.2 Data collection

Similar to the MS MRI study (chapter 5), we defined and later collected five types of data, including patient-related data, MRI protocol's data, MRI results, cost and, adverse events' data. With accessing this data, we can map the PC diagnostic procedures for different approaches and compare them through different parameters. We explain each type of data, its features and the method of a data collection below.

6.2.1 Patient

Patients' data is abstracted from the electronic medical record (EMR) for all patients included in this study by a trained researcher. The researcher reviewed the MRI reports and isolated the portion related to PC disease and assigned Prostate Imaging Reporting and Data System (PI-RADS) categories. Patients' age, allocated MRI time, overall PIRATES results, TZ score, PZ score, DWI score for PZ and Referring MD are collected. The patients' results were categorized as positive and negative groups. A positive category means the findings on the MpMRI report were a likely cause of PC based on PIRATES V2 (Scores 3, 4 and 5). All patients with overall PIRATES score of 1 and 2 are categorized as negative. Patients with positive results are considered to have the disease and patients with negative results are assumed to be disease-free as it is shown in Table 6.1.

Category	PIRADS Score	Disease or disease-free
1	1 and 2	Disease-free -
2	3, 4 and 5	Have disease +
exclusion	N/A	N/A

Table 6.1: Definition of having disease and disease-free based on PIRADS score

6.2.2 MRI protocol

All data related to PC MRI protocol such as the pre-tests need to be performed, presence or absence of IV contrast and, the sequences of the tests were collected. Due to the lack of information, we were unable to estimate the scanning time of BpMRI and MpMRI.

6.2.3 MRI results

To obtain the MRI results, a Master's student in Industrial Engineering was trained by a radiologist with 6 years of mixed academic and community practice experience (blinded) to search in the PACS and obtain and evaluate clinical information for all inclusion and exclusion criteria and also evaluate the finalized report. Any inconclusive report was reviewed and classified by the radiologist.

6.2.4 Cost

Similar to previous chapter, the main perspectives are the healthcare system and patient. From the healthcare system perspective, all costs related to the protocol, such as MRI operational cost including salaries (technologists, secretary), service contract, contrast administration cost, costs associated with renal function tests before contrast administration and professional radiologist fees, were obtained. From the patient's perspective, the costs were parking expenses and loss of productivity for half a day for each test. No other costs are incurred by the patients during visits due to 100% insurance coverage in Canada.

6.2.5 Adverse events

The nature of adverse events is identical with adverse events in chapter 5.

6.3 Comparison Parameters

After mapping MRI protocols (Chapter 3) and obtaining data related to them, modeling parameters for comparison is the next step. With proper parameters that can be measured and compared, the protocols would be ready to analyze. Parameters can be categorized as cost (system and patient's perspective), service performance, and service value. These parameters are defined as follows:

1. (Health) System cost: This is the cost of MRI utilization plus renal testing. System cost is the main portion of expenses as all the costs in public health care are covered by health insurance. Subgroups:

a. System cost per completed MRI workup no matter what the results are.

b. System cost per positive MRI.

2. Total patient cost: This is the cost of parking and loss of productivity for half a day (per test) for patients. As we mentioned before, in Canada, due to 100 % insurance coverage, patients would not pay for medical tests. These costs are classified into two subgroups:

a. Patient cost per completed MRI workup

b. Patient cost per positive MRI

3. (Health) Service Performance:

a. Number of callbacks

b. Number of estimated adverse events

c. Percentage of patients with less than satisfactory MRI experience after complete MRI workup for all patients

d. The number needed to harm (NNH)[1]

4. MRI Service Value:

a. Value is defined using Baldor's formula as (Quality x Service)/(Cost x Time)

[1]Defined in chapter 5

i. Quality is defined as the diagnostic outcome of individual MRIs and is considered constant between all MRI scenarios (similar accuracy of MRI interpretation by the radiologists). Service is defined as the inverse rate of adverse events.

ii. Cost is defined as the multiplication of system and patient costs.

iv. Time is the same as throughput (it is constant for PC)

b. Service value will be calculated for and compared between scenarios.

6.4 Results

A total number of 145 patients were studied, including 10 cases of PIRADS 5, 13 cases of PIRADS 4, and 6 cases of PIRADS 3. Among those with PIRADS 4, there were 2 cases with DWI score of 3 and their overall PIRADS score was upgraded to 4 based on positive DCE. All other 116 cases were negative with PIRADS 2. We had no cases with negative results and PIRADS 1.

According to the data, 80 % of cases were directly negative (PIRADS score 1 or 2), 14.5 % are directly positive (PIRADS score 4 or 5) and 5.5 % are results with DWI score of 3. Among those cases with PIRADS 3, 25 % upgraded to PIRADS 4 based on the DCE positive results as it is illustrated in Figure 6.2. All studies were performed on a 1.5T Siemens Avanto magnet (Siemens AG, Munich, Germany).

6.4.1 Adverse events

The nature of adverse events in MpMRI is similar to Brain MRI (renal function test adverse events and contrast injection adverse events). Therefore, a MpMRI would expose the patient to 17 % adverse events during renal testing venipuncture and (17 % + 1.2 % =) 18.2 % adverse events due to second venipuncture and contrast.

6.4.2 Cost

All the costs related to the healthcare system and patients are similar to MS MRI costs. Table 6.2 shows these these costs.

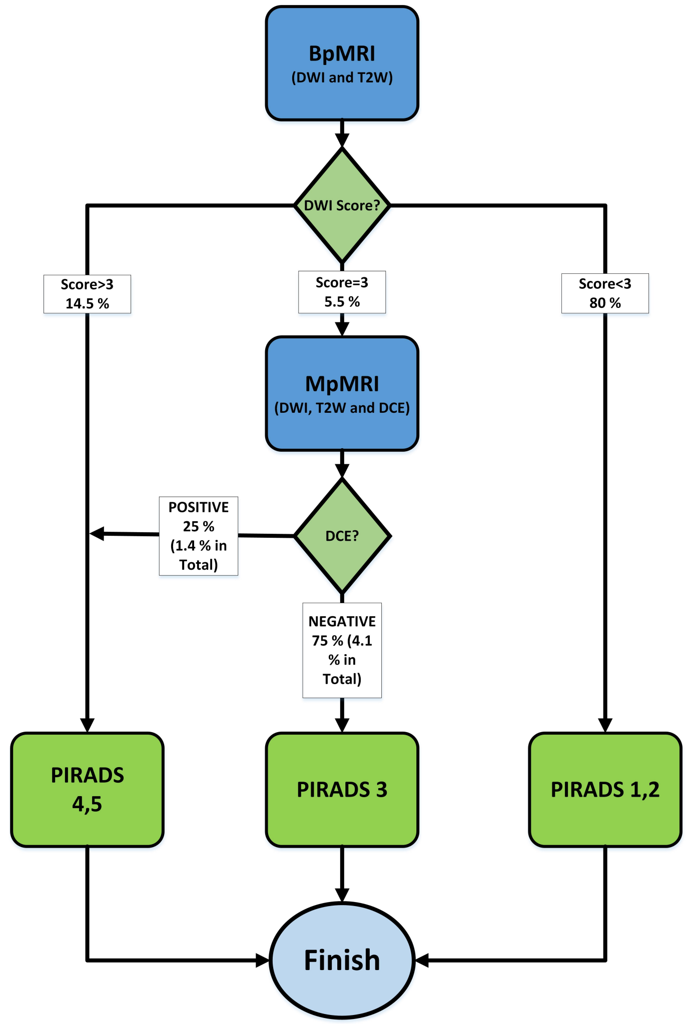

Figure 6.2: Two-tiered MpMRI, PIRADS v2 classification flow diagram for PZ with the rate of each result score

System's expenses

In absence of established MRI price/cost data, three sources were considered:

1) Price in Montreal's private MRI clinics.

2) Direct Pay Fee charged by our public hospital to individuals who do not have public health insurance.

3) Cost in public hospital for patients with health insurance according to MRI operational budget of the department, calculated as below:

a. Annual MRI operational cost: $ 1,569,274

b. Annual MRI operation: 3900 hours (15 hours/day, 5 days/week)

c. MRI operation cost per hour: $ 402.38 and per minute: $ 6.71

As most MRI services are offered in the public hospitals to insured patients, the last estimate were used for cost analysis. Other expenses include:

1) Contrast cost [one bottle of IV contrast ($ 15) plus phlebotomy ($ 2.17 = needle $ 1.15 + IV line cap $ 0.88 + dressing $ 0.14)]: $ 17.17.

2) Renal function test: $ 3.23.

3) Radiologist professional fees: $ 105.

Patient's expenses

Based on average daily income of $ 221.5 (252 work days/year, average annual salary of $ 55820 in city of (Blinded), each hospital visit incurs a half day income loss of $ 110.8, in agreement with estimates in a recent similar study (Pahwa et al., 2017). Parking fee is $ 20 per hospital visit.

Non-tangible costs include patient anxiety due to call back. The call backs are always performed within a week, so the delay in diagnosis is considered negligible.

6.4.3 Decision tree results

Two scenarios have been taken into consiteration as follows:

Scenario 1: 145 patients would visit the hospital twice. The first visit is for renal function testing, and the second visit is for MpMRI. There is no callbacks required. Figure 6.3 shows the total cost of 145 patients, and adverse patient experience for the renal function test and MpMRI test. The total system cost in Scenario 1 for 145 patients is 52,214.50 $. Total patient cost is 37,932 $. The total portion of adverse patient experience is 35.2 %. Table 6.3 summarizes all the costs related to each visit in scenario 1. The system cost per MRI in this scenario is 360.10 $, where as the patient cost is 261.60 $.

Scenario 2: 145 patients would visit the hospital once to undergo BpMRI. 116 with negative MRI complete their workup (PIRADS 1 & 2). 21 with positive MRI also complete their workup (PIRADS 4 & 5). 8 patients with PIRADS 3 would visit the hospital twice more. The first visit

[1] Radiologist professional fee is waived for the recall exam

	BpMRI	MpMRI
Price in private MRI clinics	**$675.00**	**$800.00**
Exam cost	$675.00	$800.00
Contrast Cost	Included	Included
Radiologist Professional Fee	Included	Included
Direct Pay at Hospital (no insurance)	**$433.20**	**$433.20**
Exam cost	$328.20	$328.20
Contrast Cost	Included	Included
Radiologist Professional Fee	$105.00	$105.00
Cost to public hospital for insured patient		
First Visit		
Exam Cost ($6.71/min)	**$205.60**	**$356.87**
Contrast Cost	$100.60	$234.70
Radiologist Professional Fee	$0.00	$17.17
Callback	$105.00	$105.00
Exam Cost ($6.71/min)		
Contrast Cost	**NA**	**$251.87**
Radiologist Professional Fee	NA	$234.70
Renal Function Test Cost	NA	$17.17
Patient Costs	NA	0*
Parking, Renal Test		
Half day income loss, Renal Test	**$0.00**	**$3.23**
Parking, MRI Exam		
Half day income loss, MRI Exam	**$130.80**	**$261.60**

Table 6.2: System and patient costs

is for renal function testing, and the second visit is for MpMRI. Figure 6.4 shows the total cost of 145 patients, and adverse patient experience for the renal function test and MpMRI test. The total system cost in Scenario 1 for 145 patients is 31,852.80 $. Total patient cost is 21,058.80 $. The total portion of adverse patient experience is 1.94 %. Table 6.4 summarizes all costs related to each visit in scenario 2. The system cost per MRI in this scenario is 219.67 $ as well as the patient cost is 145.23 $.

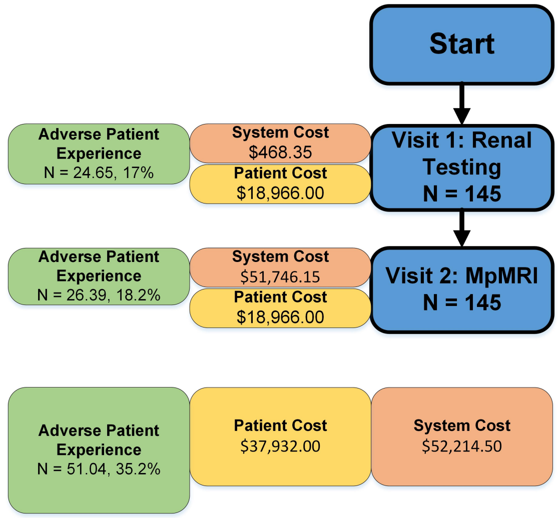

Figure 6.3: Scenario #1 decision tree

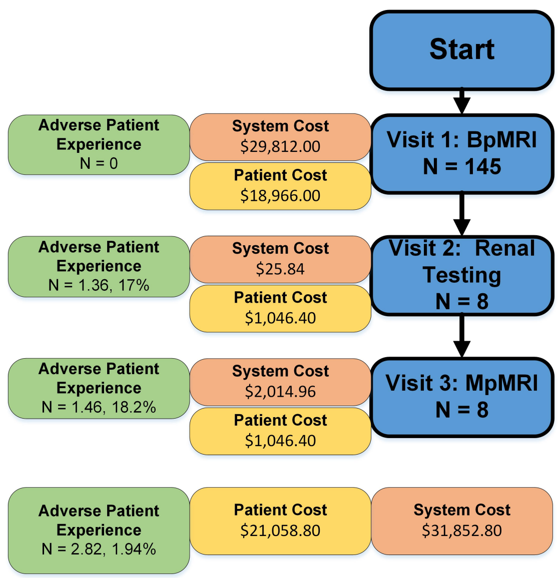

Figure 6.4: Scenario 2 decision tree

Hospital visit	#1 Number	#1 Cost	#2 Number	#2 Cost	#3 Number	#3 Cost	Total cost
BpMRI	0	0	0	0	0	0	**system**
MpMRI	0	0	145	$51,746.15	0	0	$52,214.50
Renal Test	145	$468.35	0	0	0	0	**patient**
Patient Parking & Income loss	145	$18,966.00	145	$18,966.00	0	0	$37,932.00
						system cost per MRI	$360.10
						Patient expense per MRI	$261.60

Table 6.3: Scenario #1 cost

Hospital visit	#1 Number	#1 Cost	#2 Number	#2 Cost	#3 Number	#3 Cost	Total cost
BpMRI	145	$29,812.00	0	0	0	0	**system**
MpMRI	0	0	0	$0.00	8	$2,014.96	$31,852.80
Renal Test	0	0.00	8	$25.84	0	0	**patient**
Patient Parking & Income loss	145	$18,966.00	8	$1,046.40	8	$1,046.40	$21,058.80
						system cost per MRI	$219.67
						Patient expense per MRI	$145.23

Table 6.4: Scenario 2 cost

We also compare the two MRI scenarios with three IHI's aims:

1) improve patient experience (including quality and satisfaction),

2) improve the population's health, and

3) reduce per capita cost of healthcare.

The PC MRI scenario 2: has the least number of adverse effects but the highest callback. As we discussed in chapter 5, the contrast-related complication negatively affects patient experience more than call back anxiety. Scenario 2 imposes the least direct expense on patients. Scenario 2 remains the lowest among the two scenarios, meeting IHI's Aim 1. With the lowest number of adverse events, it meets IHI's Aim 2 compared to the other scenario. It is the most cost-effective strategy, meeting IHI's Aim 3.

The current standard of practice (scenario 1) imposes the highest cost on both the health system (+ 63%) and patients (+ 80%), while suffering from inflicting a tremendous number of adverse events (18 times higher than scenario 2), has the lowest number (worst) needed to harm and offers (table 6.6) the least service value (table 6.7). It does not meet any of IHI's Aims.

N=145	Scenario 1	Scenario 2
System cost	$52,214.50	$31,852.80
System cost per completed MRI workup	$360.10	$219.67
System cost per positive MRI	$1,800.50	$1,098.37
Patient cost	$37,932.00	$21,058.80
Patient cost per completed MRI workup	$261.60	$145.23
Patient cost per positive MRI	$1,308.00	$726.17
Service Performance		
Number of call backs (anxiety and inconvenience)	0	8
Number of estimated adverse events	51.04	2.82
Number (and rate) of unpleasant experiences (Adverse events + call backs)	51.04	10.82
Number needed to harm (NNH)	3.01	N/A
Relative Value	current practice	61.00

Table 6.5: Summary of cost, service performance, patient experience and value analysis

NNH	Events (E)	Non-Events (N)	Subjects (S)	Event rate (ER)	
Experiment (E)	EE	EN	EE + EN	EER = EE / ES	NNH
Control (C)	CE	CN	CE + CN	CER = CE / CS	1 / (EER - CER)
Venipuncture + Contrast					
Scenario 1	51.04	93.96	145	35.20%	3.27
Scenario 2	6.69	138.31	145	4.61%	N/A
Contrast only					
Scenario 1	1.74	143.26	145	1.20%	95.90
Scenario 2	0.23	144.77	145	0.16%	N/A

Table 6.6: Number needed to harm, using scenario #2 as the control group

MRI Service Value	Scenario 1	Scenario 2
Quality (arbitrary)	100	100
Service	2.84	21.68
Cost ($)	$621.70	$404.11
Value	0.01	0.05
Added Value	current practice	0.05
Relative value	current practice	61.00

Table 6.7: MRI Service Value

The Patient Perspective

We have already noted that Scenario 1 imposes the highest direct costs to patients and the highest rate of adverse events, albeit without any callback. However, the average number of visits in scenario 1 is 2 visits and in scenario 2 is 1.11 visits which is less than scenario 1. Callbacks are considered undesirable for two reasons: 1) by most imaging facilities, they are considered to disrupt workflow, and 2) they are associated with patient anxiety as well as discomfort and dissatisfaction.

Chapter 7

Conclusion and future work direction

This chapter concludes the thesis by providing a summary of key findings and contributions in the thesis. Some future directions of research are also provided.

7.1 Summary of Contributions

The main contributions of the thesis can be summarized as follows.

1. Dependency between the result of brain MRI and referring physician specialization: by exploiting Fisher's exact test, the result obtained was that there is a significance difference between the test results of patients referred by neurologists and non-neurologists.

2. Mapping MS and PC MRI procedures: throughout our study, we mapped MS and PC MRI procedures. All data related to costs, specialist and machine, and materials needed for these procedures were collected. We used this information to compare different scenarios in terms of cost, efficiency, throughput, and number of adverse events. These maps can be used later for further research in the field of diagnostic procedures.

3. Comparison of different MS MRI approaches: a new approach was proposed which respects referring physician specialization was proposed. We compared three different MRI procedures in terms of IHI's aims. The current practice of diagnosing MS shows to be missing all IHI's aims compare to other approaches. The two-tiered scenario showed to be promising in all IHI's aims. It decreased the per capita cost of MRI procedure, increased patients' experience and improved the population's health. Although the third scenario, which was based on referring physician specialization, could not provide the best performance and cost-efficiency, under different circumstances (i.e. the higher rate of positive results for neurologist patients), it could be the best option.

4. Comparison of different PC diagnostic procedures: we compared two MRI procedures for diagnosing PC; MpMRI and two-tiered MpMRI. In this part of the project, we compared these approaches in terms of 3 IHI aims. As a result, two-tiered MpMRI turned out to be the best option in all IHI's aims. Two-tiered MpMRI showed to be cost-efficient and reduced the number of callbacks and venipuncture, contrast complication, and consequently. reduces patients' anxiety and dissatisfaction.

5. Improving utilization and healthcare service: by adopting two-tiered scenario for both studies (MS and PC) we reduced patients' throughput and waiting time. We also reduced the number of sequences which leads to higher radiology efficiency, resulting in less busy physicians, more accessible radiologist, and faster report turn-around time.

7.2 Future Work

The existing study can be extended into the following directions:

- The two-tiered procedure with respect to referring physician specialization can be used for PC diagnostic procedure as well. However, the setting might be different, but it worth to try.
- More complicated classification models shall be tried out. In this thesis, we studied the two-tiered method and two-tiered with respect to referring physician specialization. There are other scenarios for multi-tiered that could be further investigated.
- Implementing the same method on other disease diagnostic procedures. There is an infinite number of diseases that are diagnosed with full MRI procedures. The two-tiered or multi-tiered MRI procedure can be investigated for those diseases as well (Oldrini et al., 2018) & (Paolini et al., 2013).

- Sample size computation is an essential aspect of comparison analytics. Increasing the number of sample size could lead to more reliable and valid results.

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