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**ANALYSIS OF RENOGRAPHY FOR QUANTITATIVE
MEANS IN DIFFERENTIATING RENAL OBSTRUCTION**

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**Interdisciplinary Graduate School
NTU Institute for Health Technologies (HealthTech NTU)**

A thesis submitted to the Nanyang Technological University in
partial fulfillment of the requirement for the degree of
Doctor of Philosophy

2019

Statement of Originality

I hereby certify that the work embodied in this thesis is the result of original research, is free of plagiarised materials, and has not been submitted for a higher degree to any other University or Institution.

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Assoc. Prof. Ng Yin Kwee Eddie

Authorship Attribution Statement

This thesis contains material from 1 paper published in the following peer-reviewed journal where I was the first and corresponding author.

Chapter 7 is published as Suriyanto, Ng EYK, Say XJ, Ng CED, Yan XS, Kumar SD. Quantitative means for differentiating renal obstruction by analyzing renography by compartmental modeling of renal fluid flow rate. Nuclear Medicine Communication. 2016; 37(9): 904-910.

The contributions of the co-authors are as follows:

- I planned the project, carried out the initial work in checking and proving the model, liaised with collaborators, analysed the data, and prepared the manuscript.
- Dr. Ng Yin Kwee Eddie initiated the project with collaborators, provided guidance to me.
- Ms. Say Xian Jue took part in processing of data.
- Dr. David Eng Chee Ng provided clinical support and guidance.
- Dr. Xuexian Sean Yan provided clinical support and evaluation of samples.
- Dr. Dinesh Kumar Srinivasan provided feedback and revised the manuscript.

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SUMMARY

One of the causes of renal failure is due to the presence of an obstruction in the kidney. Standard evaluation of renal obstruction using renography is by visual interpretation in which diagnosis is decided based on the pattern of the graph. However, this method is highly subjective due to the intra-observer and inter-observer variability and may lead to inconclusive findings. The works in this thesis were carried out to search for objective methods in the assessment of renal obstruction through quantification of renogram and to develop robust systematic methods for clinical evaluation of renogram.

First, the existing quantitative parameters of renogram in the literature were studied. The reference ranges of the parameters for both unobstructed and obstructed classes were proposed which can be used to verify and justify the diagnosis of renal obstruction.

Secondly, a Baseline Screening System (BSS) that can exclude obstruction and avoid unnecessary administration of furosemide based on the first 10 min result of a renogram is proposed. It was developed using a logistic regression (LR) model and could be used to avoid unnecessary diuretic administration in more than 50% of the unobstructed samples.

When the BSS does not imply the absence of obstruction, the patient needs to continue the renography with the injection of diuretics. The result of the full scanning can be analyzed by using the proposed Basic Integrative System – Renal Obstruction (BISRO). BISRO could provide an accuracy of 84.38%, a

sensitivity of 90%, a specificity of 86.36%, and an area under the curve of receiver operating characteristics (AUC of ROC) of 0.86 in differentiating unobstructed and obstructed classes.

Next, a search for new quantitative parameters which can provide a higher accuracy of diagnosis and able in differentiating the severity of obstruction was carried out. The first parameter investigated was the ratio of urine outflow to renal volume (U/V_2). A compartmental modeling was applied to model the behavior of tracers flowing through a kidney and it led to the formation of this parameter. Other new feasible indices studied were the statistical parameters derived from renogram, i.e. the mean count value (MeanCV) and median count value (MedianCV). To optimize the performance of the parameters, they were modified by lengthening the renogram duration through extrapolation using curve fitting by a compartmental model solution. The best variants of MeanCV and MedianCV to be used as indicators of renal obstruction were MeanCV₅₀ and MedianCV₆₀.

Using these newly proposed parameters together with the existing parameters found in the literature, an Advanced Integrative System – Renal Obstruction (AISRO) is proposed. Among 140 machine learning classifiers developed, linear SVM-4 parameter model had the best performance on the validation set with overall accuracy of 94% and it was suggested as the model for AISRO.

The reference ranges of individual quantitative parameters proposed in this thesis can be used to justify the renal obstruction diagnosis in F+10 diuretic renography. The novel parameters proposed, i.e. U/V_2 , $MeanCV_{50}$, and $MedianCV_{60}$, can increase the accuracy in differentiating the severity of renal obstruction. The developed BSS may help clinicians in deciding the need for diuresis injection. For diagnosis of renal obstruction, BISRO may aid the clinicians in identifying the presence of an obstruction, while AISRO may provide information about the severity of obstruction.

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LIST OF ABBREVIATIONS

AISRO	Advanced Integrative System – Renal Obstruction
AUC	Area Under Curve
BMI	Body Mass Index
BSS	Baseline Screening System
BISRO	Basic Integrative System – Renal Obstruction
CAD	Computer Aided Diagnosis
CART	Classification and Regression Trees
DA	Discriminant Analysis
DEI	Diuresis Excretion Index
DRF	Differential Renal Function
DT	Decision Trees
EC	Ensemble Classifier
ECOC	Error Correcting Output Codes
FN	False negative
FP	False positive
FPR	False positive rate
LR	Logistic Regression
MeanCV _T	Mean count value of time activity curve with renogram duration of T min
MedianCV _T	Median count value of time activity curve with renogram duration of T min
MLC	Machine Learning Classification

MLR	Multinomial Logistic Regression
$NORA_T$	Residual renal activity at time equals to T min
$NORA_{post}$	Residual renal activity at post-void
PoVC	Post-void count
PRC	Precision Recall Curve
PrVC	Pre-void count
RBF	Radial Basis Function
RF	Random Forest
ROC	Receiver Operating Characteristics
RS	Random Subspace
SD	Standard deviation
SSE	Sum of squared error
SSR	Sum of squared regression
SST	Sum of squared total
SVM	Support Vector Machine
TAC	Time Activity Curve
TN	True negative
TP	True positive
TPR	True positive rate

LIST OF NOMENCLATURES

a	Coefficient of the a renogram function (count)
b	Coefficient of exponential component of a renogram function (1/s)
c	Coefficient of trigonometry component of a renogram function (1/s)
C	Concentration of a compartment (count/m ³)
G	Quantity (mass/number of count) of a compartment (count)
H	Body height (m)
k	Proportional constant in a compartmental model (1/s)
k_{SVM}	Constant of a SVM model
$LT_{1/2,dec}$	Lasix half time (s, but often expressed in min for renography)
n_C	Number of counts (count)
n_p	Number of predictors
N	Number of data points in a dataset
p	Probability value of a t -test
p_f	Pressure of fluid (Pa)
R^2	R-squared value
$R_{20/max}$	Ratio of the number of count at 20 min to the peak count
$R_{post/max}$	Ratio of the post-void count to the peak count
$R_{pre/max}$	Ratio of the pre-void count to the peak count
$R_{pre/post}$	Ratio of the post-void count to the pre-void count
T	Duration or time (s, but often expressed in min for renography)

$T_{1/2,dec}$	Time from the start of renogram to the time when the number of counts decays to half of the peak count (s, but often expressed in min for renography)
$T_{1/2,dec(fp)}$	Time from T_{max} to the time when the number of counts decays to half of the peak count (s, but often expressed in min for renography)
T_h	Threshold of probably for classification
T_{max}	Time to peak count (s, but often expressed in min for renography)
$T_{max/2}$	Time to half of peak count (s, but often expressed in min for renography)
u	Input function to a compartment (count/s)
U/V_2	Ratio of urine flow rate over the renal volume (1/s)
V	Volume of a compartment (m ³)
v	Velocity of the fluid (m/s)
W	Body weight (kg)
w	Weightage applied to feature
x	Variables or parameters input as features to a classifier
y	Label or the outcome class
δ	Impulse function as an input model
ρ	Density of the fluid (kg/m ³)

CHAPTER 1

INTRODUCTION

1.1 Background

The kidney is an essential organ for the maintenance of homeostatic functions such as regulation of electrolytes, acid-base balance, and blood pressure. Renal failure is a medical condition where the kidney fails to perform its job. Major causes of renal failures are circulatory aggravation that reduces renal perfusion, the presence of obstruction that blocks the flow of fluid in a kidney, and diseases related renal blood vessels or parenchyma [1]. Renal obstruction leads to renal function impairment due to an increase of pressure in the collecting system and a decrease of pressure in glomerular filtration unit [2]. If it is left untreated, the condition will worsen and lead to renal tissue atrophy. In the worse case, a prolonged renal obstruction may cause renal death. An early diagnosis of renal obstruction increases the chance of having a successful treatment.

In order to evaluate the drainage of a kidney, several techniques can be used. The current gold standard for diagnosis of renal obstruction is the Whitaker Test [3]. Roger H. Whitaker developed this method in 1972 based on the concept of dynamic-pressure flow. Through this test, the fluid pressure difference between a kidney and a bladder can be measured. Based on the recorded pressure difference, the renal obstruction status can be evaluated and classified into one of the diagnoses: unobstructed system, obstruction between the renal pelvis and bladder, hypertonic bladder, hypertonic bladder with separate upper

tract obstruction, or partially obstructed [4]. Whitaker Test is an invasive method that requires an anesthetic and can potentially cause renal damages, such as infection, sepsis, subcapsular or parenchymal hematoma, intraabdominal bleeding, and peripelvic urinoma [5-7]. Because of these, the Whitaker Test should only be used if a less invasive test shows an equivocal or negative result but loin pain still exists in the patient [8].

1.2 Motivation

Determining fluid flow condition in a kidney is important in the evaluation of renal obstruction status. Based on the evaluation, the physicians can choose appropriate follow-up actions. The gold standard, Whitaker Test, is not advisable to be used due to its invasive nature. Hence, a search for alternative assessment methods is essential. The assessment methods used in the diagnosis of obstruction have the ability to capture the dynamic condition of a kidney. A static imaging cannot provide accurate functional information about the obstruction of flow in a kidney. For example, the use of ultrasonography as a renal obstruction diagnosis method often failed to detect an initial state of renal obstruction [9]. Other static imaging methods, such as ultrasound, also could not conclude the functionality of a kidney. Obstruction of fluid flow in a kidney is a dynamic phenomenon where a dynamic imaging should be preferred [10]. In addition, the renal morphology is immature in infant and children and consequently, it is challenging to evaluate the presence of an obstruction through static imaging in these cases [11].

Renography is a dynamic renal imaging technique using radioisotopes. Renography was first introduced in 1956. It had the potential to be used in various applications such as in confirmation of a urinary tract obstruction, evaluation of obstruction severity, determination of renal function and postoperative follow-up of pyeloplasty [12]. From renography, the time activity curve (TAC) that shows the number of counts captured by a gamma camera over time can be obtained (Fig 1.1). The TAC is often used to evaluate renal function and diagnose the presence of an obstruction, if any. In the presence of a renal obstruction, the tracer is trapped in a kidney for a much longer duration than in an unobstructed kidney. If a kidney has blood flow but it is partially obstructed, the tracer transit time will be delayed. For a totally obstructed kidney, the contrast from a gamma camera will not pass beyond the obstruction. So the interpretation of TAC obtained from renography can be useful for the evaluation of renal obstruction status [13].

Figure 1.1 TAC (renogram) of a pair of kidneys. This figure was part of a renogram sample, which was obtained from Department of Nuclear Medicine and Molecular Imaging, Singapore General Hospital, Singapore (CIRB Ref: 2014/808/C).

The main methodology used clinically in the evaluation of renal obstruction through renogram is visual interpretation [14, 15]. Based on this method, the diagnosis is decided based on the pattern/shape of a renogram. It is a highly subjective method as the decision made depends on the experience of the reader. Furthermore, due to its subjective nature, the relative severity of two obstructed renograms cannot be differentiated. Consequently, the diagnosis solely based on a visual interpretation is often misleading [16]. In order to obtain an objective diagnosis, quantifiable parameters derived from a renogram should also be taken into consideration during the interpretation of the renogram. A

number of quantitative indices derived from renogram have been proposed as an objective means of diagnosis. However, none of them had been accepted clinically as gold standard due to their drawbacks, such as low accuracy, high false positive rate, lack of physical implication, and absence of accepted benchmark. Because of these reasons, the research work of this thesis was carried out to search for quantitative parameters of renogram that can produce a high accuracy of diagnosis and to create systems for the evaluation of renograms using those parameters.

1.3 Objectives

The main hypothesis of this thesis is ‘quantification of renograms can differentiate the severity level of renal obstruction and lead to an accurate and objective determination of functionality of a kidney’. Based on this hypothesis, 3 main objectives are developed:

- 1) To study existing methods in the quantification of renogram in order to determine parameters that can be used as features in diagnosis of renal obstruction

- a. To conduct a comprehensive literature review on existing parameters.

The existing parameters refer to the parameters obtained from the quantification of renogram, which were proposed by other researchers in the literature.

- b. To derive these existing parameters from renogram samples and to propose reference values of each parameter in both unobstructed and

obstructed classes. Some algorithms are written to derive the value of these parameters and statistical analysis is carried out.

- c. To identify the parameters that can be used as indicators of renal obstruction. This can be extended further to rank the parameters based on their ability in differentiating renal obstruction.
- 2) To develop new quantitative parameters for the evaluation of renograms in order to improve the objective means of renal obstruction diagnosis through renography
- a. To derive a physical parameter from renogram. This physical parameter is the normalized urine flow rate, which is obtained by the application of compartmental modeling on the renogram.
 - b. To derive statistical parameters from renogram. The potentiality of using basic statistical parameters as indicators of renal obstruction is explored.
 - c. To test the accuracy of these newly proposed parameters as indicators of renal obstruction. The parameters in differentiating the renal obstruction status into 3 classes are tested and ranked.
- 3) To build systems for the diagnosis of renal obstruction with high accuracy
- a. To develop a baseline screening system that can determine the need for diuretic. The baseline refers to the part of renogram before diuresis administration. It is an attempt to omit the need for diuretic in the

case where an unobstructed kidney can be confirmed earlier based on the baseline scanning.

- b. To create a basic integrative system for determining the presence or absence of an obstruction using the existing parameters in the literature. The number of parameters used is determined by the accuracy analysis. Then a logistic regression (LR) method is applied by integrating the parameter to create a basic system that can provide diagnose of renal obstruction.
- c. To create an advanced integrative system to evaluate the severity of obstruction using all available parameters. The advanced integrative system is created using both existing parameters and newly proposed parameters of this thesis. Several methods of machine learning classification are applied in order to find the best system that can produce a high accuracy in diagnosing of the severity of renal obstruction.

1.4 Scopes

In order to achieve the objectives, first, a literature search is carried out to study the quantitative parameters proposed by other researchers. Based on the searching outcome, the parameters and their modified forms are calculated from the renogram samples. Using these parameters, a baseline screening system for initial screening of renogram is constructed. The baseline screening system is an attempt to confirm unobstructed kidney in case of a healthy kidney earlier during

renography so the patient does not need to have diuretic administration. Next, a basic integrative system is developed to provide the diagnosis of renal obstruction in a complete diuretic renogram. To improve the accuracy and the ability of the system to differentiate the severity of obstruction, an investigation of new possible quantitative parameters of renogram is performed. The new parameters developed are the physical parameter that can be an indication of the fluid flow rate through a kidney and statistical parameters that can differentiate the severity of obstruction. After that, the new parameters are incorporated into existing parameters to create an advanced system that is not only able to diagnosis obstruction, but it also provides an insight into the severity of renal obstruction.

1.5 Report Outline

The contents of the thesis are presented as the following:

Chapter 1

The beginning of Chapter 1 provides a background on the renal obstruction and its diagnosis. It offers a broad perspective on the field explored in the research of this thesis. Then it explains the gap that exists and needs to be solved which then becomes the motivation to carry out the works of this thesis. Based on the motivation, the objectives of the thesis are listed down and the scopes of the project are determined. The end of the chapter presents a systematic outline of this report.

Chapter 2

Chapter 2 describes the results of a literature search. It starts with a more detail information about the anatomy and physiology of a kidney as well as the causes of obstruction in a kidney. After that, it presents the methods to diagnosis renal obstruction with emphasis on renography as a dynamic imaging method for diagnosis of renal obstruction. It explains briefly about the choice of radiopharmaceutical used, the application of diuretics and the visual interpretation of renograms for diagnosis. Next, it presents the existing efforts to derive quantifiable parameters from renogram and currently available decision support tool used in the diagnosis of renal obstruction through renography.

Chapter 3

This chapter describes the patients and methods. First, the statistics of the renogram samples are shown. Then the uses of the data in the analysis of each chapter are explained. In addition, this chapter reviews the analytical tools that are used to perform the analysis in the studies of this thesis, such as compartmental modeling, machine learning, and other statistical tools.

Chapter 4

Chapter 4 discusses existing quantitative parameters to be used as indicators of renal obstruction. The definitions of the parameters are presented. Based on these definitions, the parameters are calculated from the renogram samples. The reference ranges of these parameters in unobstructed and obstructed classes are

proposed. In addition, the effects of patient information (age and gender) on these parameters are analyzed.

Chapter 5

In this chapter, the process of developing a baseline screening system is presented. First, the parameters that are derivable from the baseline screening are proposed. Then, the ranking of these parameters based on the unpaired t-test results is shown. Finally, a baseline screening system in the form of LR is suggested. The recommended cut off point of the probability in determining the need of diuretic is also revealed so that the recall can be optimized while the precision is kept at an optimum level.

Chapter 6

Chapter 6 presents the formation of the proposed basic integrative system for diagnosis of renal obstruction using the basic parameters obtained from a literature search and their modified forms. The parameters are ranked based on their abilities in differentiating renal obstruction. The parameters that can create significant differences in separating the classes are then used to create 2 LR systems. The first system is used to diagnosis the absence or presence of an obstruction, while the second system is developed to determine the severity of obstruction. Lastly, the performances of both systems are evaluated.

Chapter 7

In chapter 7, the work on deriving a new physical parameter as an indicator of renal obstruction is presented. First, the application of compartmental analysis to

model the fluid flow behaviors in a kidney is shown. Based on this concept, a mathematical expression related to the fluid flow rate can be derived. This leads to the formation of a new index, which is the normalized urine flow rate of a kidney. After that, this newly proposed index is applied to the renogram samples to test its feasibility to be used as an indicator of renal obstruction. Then, reference ranges of the parameter for both unobstructed and obstructed classes are proposed based on the statistical analysis. The effects of age and gender on the values of the parameter in both classes are also evaluated.

Chapter 8

Chapter 8 proposes basic statistical parameters, the mean and median, as indicators of renal obstruction. The value of these parameters calculated from standard duration-renogram shows the potential of the parameters to be used for diagnosis. Next, modification of the parameters is presented in order to improve its ability in differentiating the severity of obstruction. The best setting in deriving these parameters is then proposed based on the *t*-tests and their accuracies for diagnosis. Lastly, the reference ranges of these parameters are presented and the effects of age and gender on the parameters are evaluated.

Chapter 9

Chapter 9 presents an advanced integrative system that can be used to differentiate the severity of obstruction. The suitable parameters to be used as features in developing the machine learning classification are determined. Next, 140 models are built using 14 different algorithms on 10 different numbers of

parameters. The performance of the models is then evaluated to obtain the best classifier to be proposed as the novel integrative system.

Chapter 10

Chapter 10 discusses all the results obtained in previous chapters. In addition, the novel contributions of this work are outlined here. Lastly, the possible future work directions are presented.

Chapter 11

Chapter 11 presents a summary and conclusion of the works done in this thesis.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

The purpose of this chapter is to provide an insight on renal obstruction and its diagnosis. It starts with an overview of kidney's anatomy and physiology. Next, the formation of obstruction in a kidney is briefly discussed. After that, the methods for diagnosis of renal obstruction are explained with more details on the renography technique, which is a noninvasive kidney imaging. Then, a survey on existing quantifiable parameters from renogram as well as the decision support tools used in the diagnosis of renal obstruction in the form of computer-aided diagnosis (CAD) are presented.

2.2 Brief Review on Anatomy and Physiology of Kidney

A pair of kidneys is located on the posterior right and left side of the abdominal cavity of a human body. Each of these bean-shaped organs consisted of a million functional units, called nephrons. Each nephron contains glomerulus and a complex tubular portion, which ends into a collecting duct system. This anatomy allows the kidney to work in 2 stages process. First, the fluid and waste product pass through glomerulus by filtration. Then in the second stage, the filtered fluid passes through the tubule where some minerals are sent back into the bloodstream. The final fluid outcome is removed from the body in form of urine [18, 19].

A kidney functions as a filtration system where the unwanted materials are removed from the bloodstream and passed to the bladder for storage and eventual elimination from the body. The blood vessel that delivers the blood into a kidney is a large renal artery, which is a direct branch of the lower portion of an aorta. After filtration, purified blood is returned into the circulatory system by the large renal vein, which empties into inferior vena cava. Based on its structure, the outer region of a kidney is known as the kidney cortex and the inner of it is the kidney medulla (Fig 2.1). After the blood is filtered in the glomerulus, the filtrate empties from the collecting ducts in the kidney cortex, passes through the kidney medulla, and then leaves the kidney medulla at the tip of a pyramid known as papilla. From there, the urine converges into the renal pelvis, which is a larger chamber for urine collections. Finally, the urine leaves a kidney through a ureter and is accumulated inside a bladder.

Figure 2.1 Anatomy of a human kidney (Source: <http://www.kidneycoach.com/>)

2.3 Renal Obstruction

A kidney plays an important role in the maintenance of human body homeostasis, including regulation acid-base balance, electrolyte concentration, extracellular fluid volume, and blood pressure [20]. The failure of a kidney in performing its function may happen due to the presence of an obstruction. Obstruction in a kidney that is longer than 6 weeks leads to hydronephrosis with major loss of functional renal parenchyma [21].

Renal obstruction can occur due to intrinsic and extrinsic causes [22-24]. In most cases of renal obstruction, the causes are intrinsic such as due to smooth muscle discontinuity, collagen replacement at the ureteropelvic junction, or scarring of ureteric valves that lead to stenosis. Renal obstruction can also happen due to external causes like the crossing of vessels or unusual angulation, congenital abnormalities of a kidney, scar formation due to previous surgery, or fibroepithelial polyps. There are a number of possible treatment of ureteropelvic junction obstruction, such as pyeloplasty, endopyelotomy, nephrectomy, and nephrostomy [25]. If a renal obstruction is left untreated, tissue atrophy can occur, which can lead to renal death. When that happens, the kidney has to be replaced through kidney transplant or the patient needs to attend regular hemodialysis.

This thesis deals with the development of quantitative means to differentiate renal obstruction status into 3 distinct classes: i) unobstructed, ii) slightly obstructed and iii) heavily obstructed. Unobstructed is the condition where a kidney is healthy without any blockage of fluid flow. Slightly obstructed

refers to the condition where there is a resistance to the fluid flow due to the presence of a partial obstruction in a kidney and heavily obstructed is the complete obstruction of the fluid flow where if it is left untreated, it may lead to a rapid loss of renal function [4, 17].

2.4 Renal Obstruction Diagnosis

2.4.1 Whitaker Test

Whitaker Test incorporates urodynamic study with antegrade pyelography to assess the fluid flow behavior of a kidney. It measures the pressure difference between the renal pelvis and the bladder. The principle behind this measurement is the Bernoulli's principle, which states that in a steady flow, the total sum of all energy in a fluid along a streamline is the same for all point in that streamline. The basic mathematical formulation of this principle used in Whitaker Test is shown in Equation (2.1). As renal obstruction is a dynamic phenomenon, the use of this dynamic expression gives a better diagnosis outcome [4].

$$p_{f1} - p_{f2} = \frac{\rho}{2}(v_2^2 - v_1^2) \quad (2.1)$$

where p_f represents fluid pressure, v represents the velocity of the fluid and ρ represent the density.

In the Whitaker Test, saline or diluted contrast media is injected into the body with a constant rate through percutaneous puncture of the renal pelvis. The fluid pressure difference is then measured based on the pressure of the renal pelvis and bladder recorded by transducers (Fig 2.2). Whitaker Test is an objective

diagnosis of renal obstruction, hence it does not subject to much debate. However, it has an unfavorable characteristic, which is its invasive nature.

Figure 2.2 Whitaker Test setup for measuring the pressure difference between renal pelvis and bladder as an indicator of renal obstruction (adapted from [4])

2.4.2 Renography

Renography is a renal imaging technique using radioisotope as a tracer (Fig 2.3). It allows observation of renal function over time and is a prospective tool for renal obstruction diagnosis [26-30]. Furthermore, this technique can potentially be used to differentiate the degree of obstruction, whether it is partially

obstructed or completely obstructed [31, 32]. It can also be used as a follow-up measure for assessing kidney condition after a surgery [33]. Research has shown that diagnosis using renography has a comparable accuracy as compare to that of the Whitaker Test [34]. The advantage of using renography over the Whitaker Test is it is a non-invasive test [35]. Moreover, the result can be obtained rapidly as compared to the Whitaker Test and it is highly reproducible. In addition, this imaging is not a surgical procedure like the Whitaker Test, hence it eliminates the high risk of infection and can be performed on an outpatient basis [7]. Renography is safe to be used to an infant as young as 1 month old and therefore, it is a favorable method to be used by pediatric practitioners [11]. Renography is highly advisable to be carried out on a patient with suspected renal obstruction before an invasive Whitaker Test was performed [36].

Figure 2.3 Renal imaging obtained in a renography. This figure was part of a renogram sample, which was obtained from Department of Nuclear Medicine and Molecular Imaging, Singapore General Hospital, Singapore (CIRB Ref: 2014/808/C).

Beside for diagnosis of renal obstruction, renography is also a prospective method in assessing renal transplantation, for both renal evaluation and transplant evaluation. For transplant evaluation, it assesses the obstruction in the

transplanted kidney and allows differentiation of acute tubular necrosis, acute or chronic rejection and nephrotoxicity [37, 38]. Renography also has a crucial role in the evaluation of renovascular hypertension, acute renal function reflux nephropathy, and detection of cortical scar formation [39].

In a renography, the radioisotope is injected into the body circulatory system through intravenous administration with the patient lying in supine position. Then the tracer is extracted by the kidney through blood filtration in either the glomeruli or renal tubules depending on the type of radioisotope used. The tracer passes through renal parenchyma and later is collected in a renal pelvis. Next, the tracer is transferred out of a kidney by a ureter [40]. The movement of the tracer through the renal system is tracked by a gamma camera placed posteriorly to the kidneys. It captures the radiation of gamma rays from the tracer. The gamma camera takes a dynamic series of image and it uses 10-s frames for 20-30 min duration. At the end of the imaging, time activity curve (TAC) can be obtained by specifying the regions of interest. The shape of a TAC is influenced by the functional level of a kidney and also the volume of the whole collecting system [41]. When the transit time of the tracer in a kidney increases, there can be a renal obstruction or dilation of a kidney. In order to differentiate these two conditions, diuretic or furosemide is applied. After administration of furosemide, if the renal outflow increases, the obstruction in the flow path can be excluded. On the other hand, if there is only a slight change in the kidney outflow after furosemide, there is a high chance that the flow in a kidney is obstructed.

Radioisotopes are injected in renography to provide information about the functionality of a kidney. Radioisotopes are atoms in an unstable state. It undergoes radioactive decay by releasing gamma rays and or subatomic particles in order to reach a more stable state. This emission can be used to obtain information about a human's internal anatomy and the functioning of an organ. Hence, radioisotopes have been extensively used in nuclear medicine for diagnosis, treatment and research purposes [42]. The earliest tracer used in renography were 123-I-orthoiodohippurate ($^{123}\text{I-OIH}$) and 131-I-orthoiodohippurate ($^{131}\text{I-OIH}$) [43, 44]. Both of these tracers were cleared mainly by proximal tubules while only a small portion was filtered by glomeruli. $^{123}\text{I-OIH}$ was used more often in the past because it had a lower radiation and provided better imaging properties than $^{131}\text{I-OIH}$ [45]. These iodine-based tracers were cyclotron-produced isotopes with a short half-life which could be challenging to be used in a number of stations where there were long distances between the cyclotron and the clinic [46]. Another commonly used radioisotope in the past was technetium 99m diaminotetraethyl pentaacetic acid ($^{99\text{m}}\text{Tc-DPTA}$). This tracer was cleared only by glomerular filtration and hence, it was used for the measurement of glomerular filtration rate [47]. However, the extraction fraction of $^{99\text{m}}\text{Tc-DPTA}$ was low where only around 20% of it was extracted by a kidney for each pass through the kidney [48]. Moreover, if a kidney had a poor glomerular filtration rate, the use of this tracer was not recommended. A study done using $^{99\text{m}}\text{Tc-DPTA}$ had shown that the imaging using this tracer might lead to high false positive diagnosis [49].

A more superior radioisotope that is widely used nowadays in renography is technetium 99m mercaptoacetyltriglycine ($^{99m}\text{Tc-MAG}_3$). It readily emits 140 KeV gamma rays, which can be detected by gamma cameras. $^{99m}\text{Tc-MAG}_3$ can be prepared easily using commercial equipment and produces high-quality scanning images [50]. The use of $^{99m}\text{Tc-MAG}_3$ was first investigated by Frizberg et al [51]. In their study, $^{99m}\text{Tc-MAG}_3$ was found to have a higher renal clearance than that of $^{131}\text{I-OIH}$. As compared to $^{123}\text{I-OIH}$, $^{99m}\text{Tc-MAG}_3$ could produce a superior image quality, had a better availability and required a lower cost. The image produced allows quantification of renal uptake that can be helpful in the structural and functional evaluation of a kidney. This better image quality can be generated due to better contrast images created by a higher count rate captured as $^{99m}\text{Tc-MAG}_3$ produces a lower radiation dose per imageable photon and a higher allowable dose of $^{99m}\text{Tc-MAG}_3$ can be injected into patient [52-57]. In addition, $^{99m}\text{Tc-MAG}_3$ has a high plasma protein binding and has a plasma clearance rate of 250-300 ml/min. The half-life of $^{99m}\text{Tc-MAG}_3$ is 6 hours. It indicates that 93.7% of this tracer decays in 24 hours. The short physical half-life makes it a suitable radiopharmaceutical in collecting data rapidly and keeping the radiation exposure low in a patient.

Clinically, there are a number of different settings of renography proposed. These differences lead to a difficulty in the interpretation of the result. Therefore, a standardization of controllable factors in renogram is required. Controllable factors include patient preparation, state of hydration, radioisotopes used, and

data acquisition method. The rest of the factors are uncontrollable, such as renal function, compliance of kidney, and volume dilution or mixed chamber effect. More detail information on the standard protocol in carrying renography, including hydration state, patient position, patient preparation, radioisotopes agent used, furosemide dosage and timing, and data acquisition method can be found in ref [58-62]. In addition, the use of a common software package, such as International Atomic Energy Agency software package [63, 64], can help standardization of renography.

From renography, a TAC can be generated. It represents the change in the number of radioisotope counts in a kidney over the duration of imaging. Generally, a renogram has 3 regions that depict 3 phases of radioisotopes movement through a kidney (Fig 2.4). These 3 regions are [40]:

- a. Region I is the perfusion phase. It is the first 40 seconds of a renogram. In this region, there is a rapid rise of tracer uptake by a kidney caused by the first passage of tracer from an aorta that just reaches the kidney through the circulation.
- b. Region II is the parenchymal phase. This region represents a kidney response to the input of the tracer. In this region, a decrease of tracer uptake rate can be noticed. This decreasing trend occurs due to the fall of tracer concentration in the blood as a majority of it has been filtered into the kidney. Moreover, some tracer has started to be transported out of a kidney.

- c. Region III is the drainage phase. This region indicates the efficiency of a kidney in excreting the tracer. In this phase, the number of tracers decreases in case of an unobstructed kidney, as it empties out of the kidney into a bladder through a ureter. In a slightly obstructed kidney, the count also decreases but at a much slower rate. The number of counts increases or keeps at a constant steady state amount in the case of a heavily obstructed kidney.

Figure 2.4 Three phases of radioisotopes movement observed from a TAC obtained from renography.

Visual interpretation is the main assessment methods used clinically in the evaluation of renal obstruction through renogram [14, 15]. Based on this method, there are 3 types of renogram curve. After reaching the peak count, if the number of counts drops significantly, most likely the kidney is unobstructed (Fig 2.5(a)). On the other hand, if the number of count keeps increasing with or without an obvious peak count, an obstruction may exist. In this case, a diuretic compound can be injected to further confirm the presence of an obstruction. After diuretic

administration, if the number of counts decreases, the kidney is most likely unobstructed and the delay of transit time is caused by dilation of a kidney. On the contrary, if the number of counts keeps increasing after diuretic, very likely the kidney is obstructed (Fig 2.5(b)). There is another possible situation appears on a renogram where the number of counts reaches a plateau or the pattern is in between the general pattern of unobstructed and obstructed kidney, which is hard for the reader to judge the presence of an obstruction (Fig 2.5(c)). This can happen due to a poor renal function or a poor renal response to furosemide. There can be special cases where the renography result is negative but the patient complains about the symptoms of obstruction. In this case, a follow-up renography or a Whitaker Test needs to be carried out [65].

Figure 2.5 Visual interpretation of renogram to evaluate renal obstruction status.

A number of quantifiable parameters have been previously proposed by other researches in the literature:

- Diuresis excretion index (DEI) [66]
- Differential renal function (DRF): relative uptake by each kidney [67]
- Half time ($T_{1/2,dec}$): time taken for the number of counts to fall to half of the maximum count [68].

- Lasix half time ($LT_{1/2,dec}$) [69]
- Normalized residual activity (NORA_T): ratio of the number of counts at T min to the number of counts at 2 min [70]
- Peak count ($n_{c,peak}$) [28]
- Ratio of number of counts at 20 min to peak count ($R_{20/max}$) [68]
- Ratio of post-void count to maximum count ($R_{post/max}$) [71]
- Ratio of pre-void count to post-void count ($R_{pre/post}$) [68]
- Ratio of pre-void count to maximum count ($R_{pre/max}$) [71]
- Time to half peak ($T_{max/2}$): time to reach 50% of peak count [72]
- Time to peak (T_{max}): time to peak count [73]

A summary of the studies that used these parameters was tabulated in Table 2.1. From this table, DRF, $T_{1/2,dec}$ and T_{max} were found to be the most commonly used quantifiable parameters from renogram. All of the parameters were further explored in Chapter 4 of this thesis.

Table 2.1 A summary of existing quantifiable parameters derived from renogram for diagnosis of renal obstruction

Year	Authors	Parameters												
		DEI	DRF	$T_{1/2,dec}$	$LT_{1/2,dec}$	NORA ₂₀	NORA _{post}	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	$T_{max/2}$	T_{max}
1978	O'Reilly et al [66]	✓												
1987	English et al [44]	✓		✓										
1988	Rafri et al [53]		✓											
1990	Hvid-Jacobsen et al [57]		✓											✓
1991	Gordon et al [49]		✓	✓										
1992	Conway [74]		✓	✓										
1992	Peters et al [62]		✓	✓					✓					
1992	Sarkar [16]			✓										
1993	Itoh et al [52]		✓	✓										✓
1993	Yung et al [75]			✓										
1994	Gonzalez et al [76]													✓
1994	Kingensmith et al [77]			✓										✓
1995	Russell et al [78]					✓								✓
1997	Anderson et al [79]										✓			
1998	Maghraby et al [38]			✓										

Year	Authors	Parameters												
		DEI	DRF	$T_{1/2,dec}$	$LT_{1/2,dec}$	NORA ₂₀	NORA _{post}	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	$T_{max/2}$	T_{max}
1999	Barbalias et al [80]			✓										✓
1999	Piepsz et al [81]		✓											
2000	Piepsz et al [70]					✓			✓					✓
2000	Stafianakis et al [32]		✓	✓					✓					✓
2001	Adeyoju et al [82]		✓											
2001	Gordon et al [67]		✓			✓								✓
2001	Rossleigh [83]													
2002	Clausen et al [84]		✓						✓					✓
2002	German et al [31]			✓										✓
2002	Gungor et al [85]		✓											
2002	Piepsz et al [86]		✓			✓								✓
2003	Donoso et al [72]					✓	✓						✓	✓
2003	Karam et al [69]				✓									
2003	Kuyvenhoven et al [87]					✓								✓
2005	Jung et al [88]			✓										✓
2005	Vlajkovic et al [89]		✓		✓									✓
2006	Esteves et al [68]			✓		✓			✓					✓

Year	Authors	Parameters												
		DEI	DRF	$T_{1/2,dec}$	$LT_{1/2,dec}$	NORA ₂₀	NORA _{post}	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	$T_{max/2}$	T_{max}
2006	Sheu et al [90]		✓	✓										
2007	Garcia et al [71]			✓								✓		
2008	Durand et al [91]					✓								
2008	Shulkin et al [35]			✓										
2010	Cecile et al [92]					✓	✓							
2010	Coffey [93]		✓											
2011	Bao et al [94]		✓	✓		✓			✓	✓	✓			✓
2011	Piepsz et al [69]					✓								
2011	Zaknum et al [64]		✓			✓				✓				✓
2012	Demirel et al [95]		✓											
2012	Ismaili et al [11]		✓	✓		✓								
2012	Tantawy et al [28]							✓						✓
2012	Taylor et al [61]			✓			✓			✓				✓
2013	Tartaglione et al [96]		✓		✓				✓					✓
2014	Beatovic et al [63]			✓		✓				✓				✓
2014	Nijran et al [73]		✓											✓
2014	Salih et al [97]			✓										

Year	Authors	Parameters												
		DEI	DRF	$T_{1/2,dec}$	$LT_{1/2,dec}$	NORA ₂₀	NORA _{post}	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	$T_{max/2}$	T_{max}
2014	Taylor [45]		✓	✓			✓		✓	✓				✓
2016	Wesolowski et al [98]		✓											
2017	Mititelu et al [99]		✓	✓					✓					✓

There are some limitations in using renography to diagnosis renal obstruction. First, it cannot be applied to a patient with an impaired renal function [100]. In the case of an impaired renal function, the kidney does not have a significant response to the diuretic agent. As a result, if the kidney is impaired and dilated but not obstructed, the prolonged in time-dependent parameters may be recorded and the outcome may suggest a false positive diagnosis. In a study done to compare the renography and Whitaker Test, it was shown that the disagreement in the diagnosis occurred in a patient with impaired renal function [101]. This indicated Whitaker Test was a better choice of diagnosis method for a patient with impaired renal function. Another source of false positive in predicting renal obstruction can be due to a high capacity of a system that causes poor renal washout. In the other word, the system is dilated and acts as a reservoir to store the fluid [102]. Bladder fullness can also be a source of a false positive. It may slow down the flow and lead to misdiagnosis [91, 103]. Technical errors, such as patient movement and incorrect selection of regions of interest, can also affect the interpretation of the results [104].

2.4.3 Decision support tool for diagnosis of renal obstruction

The use of an advanced computing system in providing support in the diagnosis of diseases has been a recent trend. CAD can assist physicians in the evaluation of clinical cases. It provides an objective input and can be useful in the training of young physicians. It also solves the issue of the lack of experts to

provide an accurate diagnosis. Following are some of the proposed CAD in interpreting renograms found in the literature.

In 2007, Binongo et al created a system for diagnosis of obstruction using classification and regression trees (CART) [105]. This system was developed using 20 quantitative parameters. The first basic system developed showed that $R_{post/max}$, $NORA_{post}$, and $R_{20/max}$ were the primary parameters used in deciding the diagnosis. To improve the system, the authors implemented a bagged system. The bagged system used $R_{post/max}$, DRF , and renal clearance frequently in the evaluation of renal obstruction.

In 2011, Bao et al proposed a predictive model for the prediction of the presence and absence of obstruction based on an LR model [94]. In their study, 19 quantitative parameters were analyzed in order to find the key variables that could be used for diagnosis. It was found the important parameters to be used to determine the absence of an obstruction were $R_{20/max}$, $R_{post/max}$, and T_{max} . To diagnose the presence of an obstruction, a different set of parameters were proposed to be used: $R_{20/max}$ and $T_{1/2,dec}$.

RENEX was an expert system created to diagnose renal obstruction proposed by Garcia et al in 2011 [106]. It was a decision support tool to assist physicians in the interpretation of diuretic renography [107]. It generated a prediction based on 60 logical sequences. These logical sequences were created using 47 quantitative parameters. These parameters were patient demographics (such as height, weight, age, sex, body surface area) and quantifiable parameters

from renogram (such as T_{max} , DRF). The diagnosis of renal obstruction was produced by an algorithm that combined the certainty level of each parameter based on a set of rules [108]. The individual parameter was converted into a certainty factor by using the parameter knowledge library. This library contained sigmoid-type curves of each parameter using the boundary conditions set by a panel of 3 experts who divided the curve into 5 regions; i.e. definitely not obstructed, probably not obstructed, equivocal, probably obstructed, and definitely obstructed.

In the following year in 2012, Garcia et al proposed an improved model of RENEX called iRENEX [109]. In iRENEX, 56 new logical sequences had been added. These additional rules were clinical data of patients, including the patient histories. In addition, iRENEX was able to provide reasoning of the conclusions as a part of the system [110]. A summary of research studies conducted using CAD in the interpretation of renogram was tabulated in Table 2.2.

Table 2.2 A summary of studies conducted to create CAD for diagnosis of renal obstruction through renography.

Model	System	Number of parameters	Diagnosis	Result
Binongo predictive model[105]	Classification and regression trees	20	Nonobstruction and possible obstruction	Misclassification rate of basic tree: 6.7% to 30.0% Misclassification of bagged tree: 10%
Bao predictive model [94]	Logistic regression	19	Excluding obstruction and determining obstruction	Exclude obstruction: AUC 0.93, sensitivity 85%, specificity 93% Determine obstruction: AUC 0.84, sensitivity 82%, specificity 83%
RENEX [106, 111]	Rules-knowledge based	47	Unobstructed, kidney, obstructed kidney, and equivocal	Agree with experts in 84% of unobstructed kidney, 92% of obstructed kidney, and 45% of obstructed kidney
iRENEX [109]	Rules-knowledge based	47 + patient histories	Unobstructed, kidney, obstructed kidney, and equivocal	Agree with experts in 92% of unobstructed kidney, 95% of obstructed kidney

CHAPTER 3

PATIENTS AND METHODS

3.1 Introduction

The purpose of this chapter is to provide the information about the dataset, which is the patient data. The use of the data in each of the subsequent chapter is specified here. This chapter also presents a review of the tools that are applied to the analysis of the data. It starts with a brief introduction on the compartmental analysis. Then, the use of machine learning classification (MLC) and its various models, such as support vector machine (SVM), decision tree (DT), discriminant analysis (DA), logistic regression (LR) and ensemble classifier (EC), are presented. The methods for evaluation of the performance of the developed classifier are also discussed. Finally, the mathematical tools used in this thesis, such as Laplace transform, goodness of fit and missing data handling are presented.

3.2 Patients

The renograms from 94 patients were obtained from the Department of Nuclear Medicine and Molecular Imaging, Singapore General Hospital, Singapore (full renogram samples can be found in Appendix A). These renograms were derived from diuresis renography where the diuretic was injected into the patients 10 min after injection of the radioisotope (F+10 protocol). The use of the renogram data for this study was approved by the Institutional Review Board (CIRB Ref: 2014/808/C) and the data were analyzed anonymously. For each

patient, the renograms from both right and left kidneys were acquired. After screening by certified nuclear medicine experts, 170 out of 188 renogram samples were available for analysis. The rest 18 samples were excluded as they were deemed to be nonfunctional kidneys based on the interpretation by the experts.

3.2.1 Patient Demographic

Gender

Among 94 patients' renography data, 47 patients were men, 36 patients were women, and no gender information was available in 11 patients. There were 65 renogram data from women (47 with diuretics and 18 without diuretics) and 85 renograms from men (75 with diuretics and 10 without diuretics).

Age

The ages of 83 patients were recorded and no age information was available in 11 patients. The overall mean of age was 44.43 ± 20.10 . The means of age in men and women patients were 41.09 ± 21.72 and 49.22 ± 17.11 respectively. Detail statistics of age could be seen in Table 3.1.

Table 3.1 Statistics of patients' age in different genders

Gender	No of patients	Mean	Standard deviation	Minimum	5 th Percentile	95 th Percentile	Maximum
Men	47	41.09	21.72	1.00	6.30	77.30	82.00
Women	36	49.22	17.11	20.00	20.75	75.25	77.00

Race

The ethnic data were available in 83 out of 94 patients. By using the main organizing framework of race in Singapore, which is based on Chinese-Malay-

Indian-Others model [112], there were 62 Chinese patients, 8 Malay patients, 6 Indian patients, and 7 other races patients. The distribution of races of the renogram samples was similar to the population trend of Singapore [113] in 2017 as shown in Table 3.2.

Table 3.2 Ethnic compositions of renogram samples

Race	Patient demographic (%)	Singapore demographic (%)
Chinese	74.7	74.3
Malay	7.23	13.4
Indian	9.6	9.0
Others	8.4	3.2

Body Mass Index

BMI is an index commonly used to determine the general health of a patient based on the ratio of weight and height. This index can be calculated using the Equation (3.1).

$$\text{BMI} = \frac{W}{H^2} \quad (3.1)$$

where W represents the body weight in kg and H represents the body height in m.

BMI values can be can be classified into 3 groups:

- Underweight: $\text{BMI} < 18.5$
- Normal (healthy) range: $18.5 \leq \text{BMI} \leq 25$
- Overweight: $\text{BMI} > 25$

A limited number of patients' height and weight records were found. There were 33 patients with both height and weight information retrieved and 8 patients with

only height records were found. Consequently, the BMI could only be derived on 60 renogram samples of 33 patients who had both height and weight data available. The BMI distributions of renogram samples in unobstructed and obstructed classes were tabulated in Table 3.3. BMI can be a risk indicator in developing weight-related health problem and renal disease is one of them. Overweight increased the risk of developing advanced chronic renal disease [114, 115]. From the Table 3.3, it could be observed that most patients with unobstructed kidney had normal weight, while most patients with obstructed kidney have either normal weight or overweight.

Table 3.3 BMI values of renogram samples

BMI group	Unobstructed kidney	Obstructed kidney	Total
Underweight	7	1	8
Normal weight	31	6	37
Overweight	7	8	15

3.2.2 Clinical evaluation

Certified nuclear medicine doctors determined the clinical diagnosis of renogram samples based on the patient information, history, renogram, and other diagnostic outcomes. These experts classified the renograms into three classes: - i) unobstructed, ii) slightly obstructed, and iii) heavily obstructed. Among 94 patients, diuretic was applied in 75 patients (132 renograms) and the rest of 19 patients (38 renograms) did not have the diuretic injection. Among 132 renograms with diuretics, the experts classified 90 of them as unobstructed kidneys, 17 of

them as slightly obstructed kidneys, and the rest 25 renograms as heavily obstructed kidneys. Among 38 renograms without diuretics, the experts evaluated 30 of them as unobstructed kidneys, 5 of them as slightly obstructed kidneys, and 3 of them as heavily obstructed kidneys.

3.2.3 Utilization of the renogram samples

A total of 170 re-digitized renogram samples (both with and without diuretics) were included in the works of this thesis. Most of the analysis used 132 renograms with diuretic, as the application with the diuretic was the standard protocol. The renograms with diuretic were used in Chapter 4 for setting the reference values of parameters, in Chapter 6 for creating the basic system to determine renal obstruction, in Chapter 7 for testing and validating the newly derived flow rate parameter, in Chapter 8 for evaluating the proposed statistical parameters, and in Chapter 9 for developing the advanced system to differentiate severity of renal obstruction. Full 170 renogram samples were used in Chapter 5 where a system to determine the need for diuretics was formed by using 132 diuretic renogram samples as a training dataset and 38 renograms without diuretic as a validating dataset. Fig 3.1 summarized the use of renogram samples in this thesis.

Figure 3.1 A summary chart of the utilization of renogram samples in the works of this thesis.

3.3 Compartmental Analysis

The compartmental analysis was developed in the 1920s for studying the metabolism of a tracer-labeled compound. It is a mathematical approach to describe the transfer of materials in a system by a flow of solute from one compartment to the next compartment. In the compartmental analysis, a complex physiological system is converted into a relatively simple mathematical model where the particles' movement from one spatial region to another one can be examined. A compartment refers to a discrete spatial and homogeneous region used to represent a system that is continuous and essentially nonhomogeneous. Each compartment can be modeled as a lumped parameter system. There must be an existing relationship between the compartments being modeled based on a

prior knowledge. The number of compartments used depends on the complexity of the components and characteristics of the system. The model developed has to be tested on actual data and be analyzed based on the real physical system. Compartmental analysis has been used in many diverse fields including pharmacokinetics, epidemiology, biomedicine, system theory, complexity theory, engineering, physics, information science and social science [116, 117].

The compartmental analysis is built based on five postulates:

- Postulate 1: Existence

Existence means the ability to represent a system as one or more compartments. The formation of compartments can be purely logical constructs and not related to direct anatomical structures.

- Postulate 2: Homogeneity

Upon entering into a compartment, all substances are assumed to be distributed uniformly and instantaneously mixed. This postulate indicates that any sample taken out of a compartment has the same properties and these properties can be used to characterize the whole compartment.

- Postulate 3: Conservation

The governing equations derived from the compartments are based on the conservation of mass.

- Postulate 4: Stationarity

Stationarity refers to the constant value of all intrinsic properties of a system, such as temperature, compartment volume, and rate constants,

while other extrinsic properties, such as concentration of a substance, are time-dependent variables.

- Postulate 5: Linearity

All fluid outflows from a compartment are assumed to be linearly proportional to the amount or concentration of that compartment. It indicates that all input flows are either proportional to the amount or concentration of the previous compartment or having a specific function that equates to a known real condition if they are at the entry point of a system. The flow can be expressed by a basic linear relationship: $F = k C$, where F represents the mass flow rate of substance, C represents the concentration of a substance in the compartment and k represents the flow rate coefficient of a substance.

To represent the real tracer administration into the body, there are several types of possible input models:

- Bolus injection

This model characterizes the tracer injection as a sudden addition of a solute into a compartment. It is also known as an instantaneous injection. Mathematically, a bolus injection model can be written as a change in the initial condition or as an impulse function, $\delta(t)$.

- Constant continuous infusion

A constant continuous infusion input can be used to represent a continuous addition of a solute into a compartment by an infusion pump

or an intravenous drip. Mathematically, a constant continuous infusion input can be written as a unit step function, $u(t)$.

- Encapsulated pill or hypodermic needle injection

An encapsulated pill or hypodermic needle injection delivers the tracer in a constant continuous input mode over a specified period of time.

Mathematically, this injection can be represented by a pulse function, $u(t) - u(t - t_1)$, where t_1 is the duration of the pulse

3.3.1 Single compartmental model

In a single compartmental model, a system is represented by a box, an input is represented by an arrow pointed toward the box, and an output is represented by an arrow pointed away from the box (Fig 3.2). It is the simplest model that uses only one compartment to allow assessment of the transport of material in and out of it. Based on the conservation of mass, the rate of change of the quantity of solute in the compartment can be written in a form of a differential equation where the accumulation of a salute in the compartment equals to the inflow minus the outflow of the salute.

Figure 3.2 Schematic diagram of a single compartmental model.

The governing equation of this model is:

$$\frac{dG}{dt} = u(T) - kG \quad (3.2)$$

where $G = CV$ and k is the proportionality constant.

3.3.2 Multi compartmental model

A real system is often complex and a multi-compartmental model can be applied to represent it. The number of compartments used depends on the analyzed system. A high number of compartments induces unnecessary complexity and difficulty in solving the problem. The mathematical expression of a multi-compartmental model is an expanded formula of a single compartmental model. The governing equation for each of the compartment can be written as shown in Equation (3.3).

$$\frac{dG_n}{dt} = k_{n1}G_1 + k_{n2}G_2 + \dots + k_{nn}G_n + u_n(t) \quad (3.3)$$

where subscript n is the compartment number.

3.4 Machine Learning Classification

MLC creates a model that generalizes the pattern of a training dataset and then uses the model to predict the state of a new dataset. MLC has been widely used across different fields, for examples in handwritten recognition, face detection, pharmaceutical data analysis, computational neuroscience, and bioinformatics [118]. The main goal of using MLC in this thesis is to construct a classifiers to be used as CAD systems for evaluation of renal obstruction. Tenfold cross-validation technique was incorporated in all applications of MLC in this

thesis [119]. In this technique, the input dataset is split into ten equal parts. Nine parts of the data are used as the training dataset to create a classifier and then the classifier is evaluated using the remaining one part that acts as the testing dataset. This process is repeated ten times using a different portion as the testing dataset. The performance of the model is assessed by the average performance of the ten folds.

3.4.1 Support vector machine

SVM was a supervised machine learning method developed in 1965 [120]. It is commonly used for binary classification. SVM was a data-mining tool, which was originally developed for pattern recognition problem. In SVM, a margin maximizing technique is used to separate the classes by creating a line or plane that maximizes the separation distance between the closest points of training datasets from 2 different classes [121-123]. In a two-dimension case, a separation line maximizes the distance between two lines (Fig 3.3) that touch the first data of two neighboring classes. After getting this solid middle line as the classification line, any future samples can be classified based on its location relative to this separation line. For a high dimension case, a hyperplane can be created to separate the sample into distinct classes. [124]. Mathematically, given the training data: $(y_1, x_1), \dots (y_n, x_n)$, where x represents the features and y represents the label, the hyperplane has a form as shown in Equation (3.4). $\mathbf{w}$ is a vector perpendicular to the hyperplane and k_{svm} is a constant coefficient.

$$(\mathbf{w} \cdot \mathbf{x}) + k_{svm} = 0 \quad (3.4)$$

Figure 3.3 A line or hyperplane is used to separate different classes in an SVM. It is an example of SVM classifier with 2 features. The X_1 and X_2 refer to two features, which can be any quantities depends on the problem to be solved.

If the original dataset is inseparable in its original input space, applying an appropriate kernel may solve the problem. Application of kernel changes the original data space into an alternative feature space where the data become separable. To do this, an appropriate kernel is chosen and applied to the dataset [125-127]. Some of the commonly used kernels are the linear kernel, quadratic kernel, cubic kernel, and Gaussian Radial Basis Function (RBF) kernels. In a multiclass classification, the most common method used is error-correcting output code (ECOC). ECOC means one class is selected as the positive class and the rest of the classes are grouped as a negative class at a time. For predicting the class of a new data point, the data point will go through a set of binary classifiers developed using a different class as the positive class. The class where the data point has the highest probability to be positive is selected as the final outcome.

3.4.2 Decision trees

DT classifies a sample by putting it through a series of tests. These tests are designed to be in a form of steps that works from a root node to intermediate nodes and finally reaches the leaf node (Fig 3.4). The root node is a starting node of a tree. Each node (except leaf nodes) splits the dataset based on one input variable or feature. So each of these nodes is labeled with its own input feature. Each branch then leads to a subordinate node or a final decision node. The final decision node where the connection ends is often known as the leaf node [128]. A DT can be created by splitting the nodes into subsets based on the dividing feature of the node. Each branch that comes from this node should have one or a range of the values of the tested features and it is a subset of its origin node. This process is repeated until the whole tree is created and it is termed as recursive partitioning. The division of the node stops when it reaches a certain set target limit, such as a certain limit of data per node or when the splitting no longer provides additional value to the prediction. In making a prediction for a query data point, the data point just has to travel down the tree based on the feature values of the point until the leaf node is reached. The leaf node serves as the prediction outcome [129].

Figure 3.4 Formation of a root node, intermediate nodes and leaf nodes of a DT.

3.3.3 Discriminant analysis

Discriminant analysis (DA) is a method derived based on the linear discriminant formulated by Ronald A. Fisher in 1936 [130]. This method tries to find linear combinations of features that represent the characteristics of different classes. DA model consists of the mean and variance of the variable for each class. These statistical properties are estimated from the data and used to provide the prediction of a new data point. In making the prediction, the probability of the new data point belongs to each class is calculated based on Bayes Theorem and the class with the highest probability will be the output class. DA is suitable to be used for a classification problem with an output in a categorical form [131, 132].

3.4.4 Logistic regression

LR is used to determine the probability of a binary response based on the input parameters. This probably is obtained from a logistic model, which is a linear combination of independent variables. David Cox develops this method in 1958 [133]. The LR can be generalized to form a model with more than two outcomes in

a form of a multinomial logistic regression (MLR) [134]. The MLR has a similar concept to an LR. The only difference is the output from an MLR is categorical as compared to binary form in an LR. The LR itself is not a classifier, but rather it is a model to calculate the probability of an output belongs to a class by using the input features. By choosing a cutoff value in separating the classes, LR can function as an MLC. The probability is derived by applying the logistic function as shown in Equation (3.5) to the linear combination of parameters in a form similar to a linear regression. This linear combination is the sum of all the multiplication of each parameter with their weightages. The weightage is estimated by finding the model that gives the least error through maximization of the likelihood function as expressed in Equation (3.6) [135, 136].

$$P(y = +1 | \mathbf{x}, \mathbf{w}) = \frac{1}{1 + e^{-\mathbf{w}^T \mathbf{h}(\mathbf{x})}} \quad (3.5)$$

$$l(\mathbf{w}) = \prod_{i=1}^N P(y_i | \mathbf{x}, \mathbf{w}) \quad (3.6)$$

where y is the outcome label, x is the parameter input as features, w is the weightage applied to individual feature, and N is the number of data point in a dataset

3.4.5 Ensemble Classifiers

EC combines a number of basic machine learning models in order to form an optimum solution [137, 138]. This integrative model usually provides better classification accuracy, reduces computation time and requires lesser memory.

Adaboost

The core principle of boosting is to repeatedly feed a sequence of weak learners. The Adaboost was developed by Yoav Freund and Rober Schapire in 1996 to improve the performance of weak learning algorithm [139]. The prediction is obtained by the sum of the total weight obtained through a voting scheme. The weights are obtained through iteration, wherein each iteration, the weights are modified. The modification is based on the data points in the training dataset that are incorrectly predicted. The weight of these data points are set higher while the rest of the data has a decrease in the weights [140].

Random forest

Random forest (RF) a method developed based on a bootstrap aggregating model proposed by Leo Breiman [141]. RF builds a number of DTs using random input variables. The purpose of using random input variables is to avoid the correlation between the trees. If there are strong input variables that serve as strong predictors in a model, these features will be selected by many of the small DTs and induce the correlation among the trees. The prediction of the class label for a query data point is based on the voting of all the DTs [142, 143].

Random Subspace

Random subspace (RS) has a similar concept to RF, except for in RS the features are randomly sampled [144]. Each basic classifier is constructed using a random subspace of the feature space. This is done to avoid creating a model that overly focused on the highly predictive feature. The final decision of the outcome is

decided based on the majority voting of all basic classifiers [145]. RS improves the accuracy and stability of the EC developed [146].

Table 3.4 Characteristics of Classifier Types [147]

MLC	Prediction speed	Memory usage	Results interpretability
SVM	Medium for linear. Slow for others	Medium	Easy for linear SVM. Hard for all other kernel types
DT	Fast	Small	Easy
DA	Fast	Small for linear, large for quadratic	Easy
LR	Fast	Medium	Easy
EC	Fast to medium depending on choice of algorithm	Small to large depending on choice of algorithm	Hard

Note:

- Speed: fast 0.01 s, medium 1 s, slow 100 s
- Memory: small 1 MB, medium 4 MB, large 100MB

3.4.6 Evaluation of a classifier

There are some evaluation metrics can be applied to assess the performance of an MLC:

Accuracy, Sensitivity, and Specificity

In MLC, the final output can be put in comparison to the real label using a confusion matrix (Fig 3.5). True positive (TP) is the number of cases correctly predicted as positive and true negative (TN) is the number of cases correctly predicted as negative. The number of cases where the true labels are positive but the model predicts them as negative is called false negative (FN). Similarly, the

number of cases where the true labels are negative but predicted as positive is called false positive (FP) [148].

		Predicted class	
		Positive	Negative
Actual class	Positive	True Positive (TP)	False Negative (FN)
	Negative	False Positive (FP)	True Negative (TN)

Figure 3.5 A confusion matrix used in assessing the performance of a classifier.

Accuracy, sensitivity, and specificity are 3 main parameters that commonly used to reflect the performance of an MLC model. Accuracy refers to the ability to predict the cases correctly. It is calculated by finding the proportion of TP and TN over all samples as stated in Equation (3.7). Sensitivity means the ability of a test to determine the positive case or disease case correctly. Sensitivity can be estimated by finding the ratio of TP over all real positive cases as shown in Equation (3.8). Specificity has a similar concept as sensitivity but it focuses on the negative case rather than the positive case. It determines the ability of a system to conclude the negative case or healthy case correctly. Mathematically, it can be obtained by dividing the TN over all real negative cases as shown in Equation (3.9) [148].

$$\text{Accuracy} = \frac{TP + TN}{TP + FN + FP + TN} \quad (3.7)$$

$$\text{Sensitivity} = \frac{TP}{TP + FN} \quad (3.8)$$

$$\text{Specificity} = \frac{TN}{TN + FP} \quad (3.9)$$

Receiver Operating Characteristic

Receiver Operating Characteristic (ROC) is a graph used to assess the performance of a binary classifier and it has been widely in the medical field [149]. ROC was introduced as an assessment tool in machine learning by KA Spackman in 1989 [150]. In the ROC curve, the true positive rate (TPR, Equation (3.10)) is plotted against the false positive rate (FPR, Equation (3.11)) as depicted in Fig 3.6. Each point of the curve represents a pair of TPR and FPR corresponding to a specific decision threshold. The area under the curve (AUC) of ROC is a measurement of how well a parameter can separate different classes. It can be calculated by using Equation (3.12). The AUC of ROC with a value closer to 1 indicates a high ability of the classifier in separating two classes. If the value of it is 0.5, means the performance of a classifier is the same as a random guessing. For the AUC of ROC lower than 0.5, it performs badly as it produces prediction worse than a random guessing. Hence, it is desirable to have a classifier with AUC of ROC closer to 1 [151].

Figure 3.6 ROC curve: true positive rate versus false positive rate.

$$\text{TPR} = \frac{\text{TP}}{\text{TP} + \text{FN}} \quad (3.10)$$

$$\text{FPR} = \frac{\text{FP}}{\text{TN} + \text{FP}} \quad (3.11)$$

$$\text{AUC} = \int_{-\infty}^{\infty} \text{TPR}(T_h) \text{FPR}'(T_h) dT_h \quad (3.12)$$

where T_h is the threshold of probability for classification

Precision and Recall

Another method for assessing the performance of a binary classifier is by evaluating its precision and recall [152]. Precision is the fraction of true positive cases among all cases predicted as positive. In the other words, precision tells the number of correctly predicted positive results among all returned results. Recall is the fraction of true positive cases among all actual positive cases. It is the probability that real positive cases are being predicted among all true positive data. Precision and recall are usually discussed as a pair, where a value of one measure is linked to a fixed value of another measure. Thus, precision-recall curve (PRC) is often plotted to show the relation between the precision and recall (Fig 3.7) [153].

Figure 3.7 PRC curve: precision versus recall.

Mathematically, precision and recall can be written as Equations (3.13) and (3.14) respectively.

$$\text{Precision} = \frac{TP}{TP + FP} \quad (3.13)$$

$$\text{Recall} = \frac{TP}{TP + FN} \quad (3.14)$$

3.5 Mathematical and Statistical Tool

3.5.1 Laplace transform

To solve the differential equation derived from the compartmental analysis, the Laplace transform was applied. The Laplace transform is a mathematical method used to derive an analytic solution of a complex differential equation. It transforms a differential equation into an algebraic equation that can be solved in a simpler manner. The solution of the algebraic equation is then transformed back to get the result of the actual differential equation through the application of the inverse Laplace transform. If a function is denoted as $f(t)$ for all $t \geq 0$, the Laplace transform of this function is an integral of the multiplication

of $f(T)$ and a transformation function from $T = 0$ to $T = \infty$ as shown in Equation (3.15) [154].

$$L\{F(T)\} = F(s) = \int_0^{\infty} e^{-st} f(T) dT \quad (3.15)$$

By using Equation (3.15), the Laplace transform of a first and second order of $f(T)$ could be obtained as shown in Equations (3.16) and (3.17) respectively (detailed derivation of them can be found in Appendix B Equations (B.1) and (B.2)).

Laplace transform of first derivative:

$$L(f') = sL(f) - f(0) \quad (3.16)$$

Laplace transform of second derivative:

$$L(f'') = s^2 L(f) - sf(0) - f'(0) \quad (3.17)$$

3.5.2 Goodness of fit

In this thesis, the solution of the two-compartmental model was fitted to the renogram sample. The goodness of fit was used to determine the best curve that matched with the clinical data and it was assessed using the R-square (R^2) method [155, 156]. R^2 is a measurement of how close the data are to the fitted line. It is also known as the coefficient of determination. R^2 describes how much the amount of variation of the data explained by the model. A higher value of R^2 indicates a better model in fitting the data. R^2 can be calculated by finding the ratio between the sum of squared regression (SSR) and the sum of squared total (SST) as shown in Equation (3.18). Sum of squared regression is the difference between SST (Equation (3.19)) and sum of squared error (SSE, Equation (3.20)).

$$R^2 = \frac{SSR}{SST} = 1 - \frac{SSE}{SST} \quad (3.18)$$

$$SST = \sum_{i=1}^n (y_i - \bar{y})^2 \quad (3.19)$$

$$SSE = \sum_{i=1}^n (y_i - f(x_i))^2 \quad (3.20)$$

3.5.3 Missing data handling

Having incomplete data in a clinical research is truly common, even in the strictest research protocol. There are few methods for handling an incomplete dataset [157, 158]:

- Complete-case analysis

Complete-case analysis/casewise deletion/listwise deletion is the deletion of samples that have a missing value, so only those with complete information are included in the study. This is a widely used method because of its simplicity. However, there is a loss of accuracy and it may induce bias in the result due to the reduction of sample size. This method can be applied to big size dataset where the deletion of a small portion of samples does not affect much on the accuracy of the analysis

- Available-case analysis

Available-case analysis/pairwise deletion limits the analysis of the available values of parameters through descriptive statistics for individual parameters or comparison between two parameters. The use of this

method indicates there is a variation in the number of cases used in different analysis

- Weighted complete-case analysis

Weighted complete-case analysis applies different weights to complete and incomplete cases for reducing the bias of the analysis

- Single imputation

The situation where the missing value is replaced by a reasonable value is called the single imputation. Several forms of single imputation are mean imputation, median imputation, regression imputation, stochastic regression imputation, hot deck imputation, cold deck imputation, last observation carried forward and worse case analysis.

In this thesis, if a complete-case analysis is applied, a big portion of the dataset will be removed which is not favorable. Hence, an available-case analysis was chosen. It was also suitable to be used in the analysis of the work here because most analyses were statistics evaluation between individual parameters. In addition, single imputation in the form of mean imputation was also applied to the selected parameters in the development of integrative systems for diagnosis of renal obstruction.

3.5.4 Statistical analysis

The t -test is applied to investigate if two datasets can be differentiated significantly from one another. In this thesis, this test was used to check if a parameter could be used to differentiate unobstructed and obstructed classes

significantly and or to differentiate slightly and heavily obstructed classes significantly. It was also used to examine if a parameter can be used to determine the needs for diuretic by confirming the absence of an obstruction in the early phase of scanning.

The p -value is the probability for a null hypothesis to be true which can be obtained from the t -test. The null hypothesis refers to the hypothesis where two datasets were assumed to be from the same population. Generally, the p -value less than 0.05 is considered to indicate a significant difference in separating two classes. The verbal interpretation of the p -value in this thesis followed the definition in the GraphPad software as indicated in Table 3.4 [159].

Table 3.5 The evaluation of p -value obtained from the t -test

p -value	Evaluation	Sign on graph
< 0.0001	Extremely significant	****
0.0001 to 0.001	Extremely significant	***
0.001 to 0.01	Very significant	**
0.01 to 0.05	Significant	*
≥ 0.05	Not significant	

In this thesis, the p -values were obtained from the t -tests to examine the ability of the parameter in differentiating the classes and were subsequently used in parameter ranking. A parameter with a lower p -value indicated a better performance in separating the classes and was assigned a higher rank. On the other hand, a parameter with a higher p -value was given a lower rank due to its relatively low ability in separating the classes for diagnosis.

3.6 Application of Software

The analysis of this thesis was mainly performed using MatLab R2017b (The Mathworks Inc., Natick, Massachusetts, USA). First, it was used in re-digitalization of renogram. Then, the derivations of parameters found in the literature and the newly proposed parameter were done through coding in MatLab. Curve fitting on renogram using the compartmental analysis solution was also carried out in MatLab by using the Curve Fitting function under the Math, Statistics and Optimization Category. The analysis of the performance of parameters in MatLab as well as creating an integrative system for diagnosis of renal obstruction were done by using the Classification Learner function under the Machine Learning Apps in MatLab.

Other software was also used in this thesis. GraphPad Prism 7 (GraphPad Software, La Jolla, California, USA) was used to perform *t*-tests analysis. Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA) was utilized for tabulation of the dataset and performing basic statistical analysis such as calculation of mean, standard deviation and percentile. It was also used in plotting the scatter plot, line and bar chart for visualization of the data. Microsoft Power (Microsoft Corporation, Redmond, Washington, USA) was used in creating charts or diagrams as well as graphs in explaining a concept.

CHAPTER 4

RESULTS 1

REFERENCE VALUES OF BASIC PARAMETERS IN F+10 DIURESIS RENOGRAPHY

4.1 Introduction

In diuretic renography, a diuretic is injected intravenously into the body to induce urine. Generally, diuretic can be administered 15 min before the injection of radioisotopes (F-15 protocol) [35, 58], injected together with the radioisotopes (F0 protocol) [3, 35], or injected 20 min or 30 min after the injection of radioisotopes (F+20 or F+30 protocol) [35, 58, 74]. The reference values of the basic quantifiable parameters of renogram to be used in evaluating the renal obstruction can be found in those established protocols.

The injection of diuretic a period after radioisotopes injection allows assessment of maximal distension of a kidney. If the diuretic is applied earlier before radioisotopes, the fluid distention in a kidney cannot be observed. On the other hand, diuretic administration 20 min after radioisotopes implies that the scanning period has to be lengthened. This may cause discomfort in patients and also cause disruption in the scanning process due to the need for voiding. Hence, a recent study has proposed an injection of furosemide 10 min after radioisotopes (F+10)[96] to be used in diuretic renography. Biggest challenges in applying F+10 are the lack of protocol and method to interpret the outcome. In order to assist the evaluation of renal obstruction in F+10 diuretic renography, Chapter 4

presents the reference values of quantitative parameters in both unobstructed and obstructed classes. First, this chapter discusses the exiting parameters proposed by other researchers in the literature. These parameters are: diuresis excretion index (DEI), differential renal function (DRF), clearance half time ($T_{1/2}$), Lasix half time ($LT_{1/2}$), normalized residual activity ($NORA_t$), peak count ($n_{c,peak}$), peak time (T_{max}), ratio of number of count at 20 min to peak count ($R_{20/max}$), ratio of post-void count to maximum count ($R_{post/max}$), ratio of post-void count to pre-void count ($R_{post/pre}$), ratio of pre-void count to maximum count ($R_{pre/max}$), and time to half peak time ($t_{peak/2}$). Then the values of these parameters were derived from the renogram samples. Next, the statistical studies of them are presented and the reference values of them are proposed. In addition, the effects of age and gender on each of the parameters are also discussed.

4.2 Diuresis Excretion Index

DEI was derived as an indicator to judge the degree of flow impedance [66]. This index was developed to assess the equivocal renograms by analyzing the effect of diuretic.

4.2.1 Derivation

This index was derived by calculating the change in slope of a renogram before and after furosemide administration (Fig 4.1). The reference point was the number of counts at the point where the effect of furosemide started to take place. The slope was then calculated by finding the change in the number of counts 3 min before and 3 min after this reference point which was written as

Equation (4.1). If there was no response in a kidney after diuretic, the DEI would have a value close to zero and the kidney was most likely obstructed.

Figure 4.1 The derivation of DEI.

$$\text{DEI} = \frac{2n_{c,f} - n_{c,-f} - n_{c,+f}}{n_{c,f}} \times 100\% \quad (4.1)$$

where, $n_{c,-f}$ is the number of counts at 3 min before diuretic, $n_{c,f}$ is the number of counts during diuretic, and $n_{c,+f}$ is the number of counts at 3 min after diuretic

4.2.2 Ranges of Values for Diagnosis

Based on the formula in Equation (4.1), the values of DEI were derived from 132 sample renograms (the full list could be found in Appendix C.1). The statistics of the DEI was computed and tabulated in Table 4.1. The means of DEI were $-14.08\% \pm 28.77\%$ in unobstructed kidneys and $3.45\% \pm 7.89\%$ in obstructed kidneys. An unpaired t -test showed an extremely significant difference between the 2 groups in terms of statistical mean. However, from their distributions (minimums, percentiles, and maximums), it could be observed that the unobstructed class had a wider distribution and the value range for the obstructed class was actually fall within the range of the unobstructed class.

Table 4.1 Statistics of DEI (in percentage) in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	90	-14.08	28.77	-90.88	-61.02	31.76	58.69
Obstructed	42	3.45	7.89	-19.48	-12.71	12.41	16.07

Note: Extremely significant difference ($p = 0.0002$) was found in DEI between unobstructed and obstructed kidneys

From the physical point of view, DEI was a parameter obtained by attaining the change of slope before and after the diuretic injection. A negative value of it indicated a steepening of decline slope as the outflow from a kidney increased while a positive value indicated accumulation of tracer in a kidney, as the outflow from a kidney was still low. In the other words, a positive value of it was a sign of an obstructed kidney and a negative value of it was a sign of an unobstructed kidney. However, from the data, an unobstructed kidney had a positive value as high as 58.69%, 3.7 times higher than the maximum value of the obstructed kidney data. This indicated that using DEI as an indicator of renal obstruction might lead to a high false negative rate.

The cutoff point of the ranges of DEI for differentiation of unobstructed and obstructed classes was proposed in Table 4.2. In a study done by English et al using F-15 protocol, it was shown that DEI greater than 45% indicated the absence of obstruction and DEI in between 35%-45% was equivocal [44]. This is different from the proposed values as shown in Table 4.2. It was expected that the cutoff point for DEI in differentiating obstruction and obstruction should be close to 0 because a positive change in slope was a sign of a renal obstruction and negative

change in slope was a sign of an absence of obstruction. Hence, the proposed cutoff value in Table 4.2 was a more rationale finding.

Table 4.2 Reference ranges of DEI for diagnosis of renal obstruction

Index value	Kidney status
$< -9.31\%$	Unobstructed
$\geq -9.31\%$	Obstructed

4.2.3 Effect of Age and Gender

The means of DEI were $-13.02\% \pm 29.81\%$ and $-14.30\% \pm 28.53\%$ in unobstructed kidneys of men and women gender groups respectively and $5.16\% \pm 5.46\%$ and $1.83\% \pm 9.71\%$ in obstructed kidneys of men and women groups respectively (Fig 4.2(a)). No significant difference was seen in DEI between men and women in both unobstructed ($p = 0.85$) and obstructed classes ($p = 0.20$). For different age groups, the means of DEI were $-11.06\% \pm 28.09\%$ and $-16.07\% \pm 30.55\%$ in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and $6.34\% \pm 6.27\%$ and $0.94\% \pm 8.57\%$ in obstructed kidneys of the younger and older populations respectively (Fig 4.2(b)). The splitting of renogram samples into 2 age groups was set with the cutoff point at 42 years old to ensure an equal number of samples in the groups. This value was also close to the splitting value of 40 years old use in the study by Esteves et al [68]. There was no significant difference between the younger and older populations in the unobstructed class ($p = 0.44$). A significant

difference in DEI was observed between the younger and older populations in the obstructed class ($p = 0.03$).

Figure 4.2 The distribution of DEI in different gender groups (a) and different age groups (b).

4.3 Differential Renal Function

DRF represented the ratio of the amount of radioisotope uptake by each kidney over the total injected amount of radioisotopes. It was one of the commonly used parameters in the evaluation of renal function through renography [98]. Although the measurement of DRF was usually done through the

application of static renal scintigraphy, measurement through dynamic renography could provide similar results [95].

4.3.1 Derivation

DRF was derived by comparing the total activity of the perfusion phase of a TAC between a pair of kidneys. In the other words, it was a comparison of the number of counts in the right and left kidneys for the purpose of assessing the contribution of each kidney. It could be calculated by measuring the integral of counts during the 1 to 2 min or 2 to 3 min after injection of tracer [81]. After the tracer was injected for 2 to 3 min, some of the tracers may have left the renal space and the measurement of relative function might not be accurate anymore. It was important to note that a significant error of this parameter might occur due to the extrarenal background that led to overestimation on the response of a poorer functioning kidney [160]. In addition, DRF was also affected by the selection of the regions of interest of images [85].

4.3.2 Ranges of Values for Diagnosis

DRF was recorded in 78 renograms obtained from Singapore General Hospital (the full list could be found in Appendix C.1). The statistics of the DRF was computed and tabulated in Table 4.3. The means of DRF were $54.38\% \pm 13.66\%$ in unobstructed kidneys and $48.66\% \pm 13.12\%$ in obstructed kidneys. An unpaired *t*-test showed no significant difference was found between the 2 groups in terms of statistical mean. Consequently, DRF might not be an effective indicator of renal obstruction and no reference ranges of DRF were proposed for the

diagnosis of obstruction. However, there were some protocols that proposed the ranges of it for interpretation of renogram. Gordon et al suggested in the interpretation of renography outcome, the normal values of DRF were between 45% and 55% [67]. Taylor further suggested more detailed ranges of DRF for diagnosis. He proposed that a relative uptake of 50%/50% to 56%/44% was deemed to be of normal kidneys. The borderline was a relative uptake of 57%/43% to 59%/41%. Any value of DRF equal to or greater than 60%/40% was a sign of abnormality in a kidney [48].

Table 4.3 Statistics of DRF (in percentage) in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	53	54.38	13.66	18.60	36.60	83.12	85.10
Obstructed	25	48.66	13.12	28.66	32.37	70.77	84.50

Note: No significant difference ($p = 0.08$) was found in DRF between unobstructed and

obstructed kidneys

4.3.3 Effect of Age and Gender

The means of DRF were $52.13\% \pm 12.32\%$ and $59.59\% \pm 15.54\%$ in unobstructed kidneys of men and women gender groups respectively and $51.39\% \pm 13.28\%$ and $45.18\% \pm 12.65\%$ for obstructed kidneys of men and women groups respectively (Fig 4.3(a)). For different age groups, the means of DRF were $52.61\% \pm 13.80\%$ and $56.37\% \pm 13.52\%$ in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and $45.46\% \pm 7.06\%$ and $50.80\% \pm 15.84\%$ in obstructed kidneys of the younger and older populations respectively (Fig 4.3(b)). No significant

difference was seen in DRF between men and women in both unobstructed ($p = 0.06$) and obstructed classes ($p = 0.25$). There was also no significant difference between the younger and older populations in the unobstructed ($p = 0.32$) and obstructed classes ($p = 0.33$). This result was comparable with a study done by Demirel et al [95] where it was found that no statistical difference in DRF in terms of age and sex. Similar result was also obtained by Esteves et al [68] where the DRF was tested between men and women and between two age group and no significant differences were found in all comparisons.

Figure 4.3 The distribution of DRF in different gender groups (a) and different age groups (b).

4.4 Half Time

$T_{1/2,dec}$ was the time taken for the number of counts to drop to half of its peak count. It was one of the popularized indices used as quantitative parameters in determining renal obstruction [47, 90, 161].

4.4.1 Derivation

$T_{1/2,dec}$ was a controversial parameter as there were several different methods to derive it [62]. As every center used their own definitions, there was still a lack of standardization on the means to derive it [67]. Generally, $T_{1/2,dec}$ could be described as the time where the activity reduced to 50% of the number of counts at a reference time, which was usually the T_{max} . It could be derived directly from renogram by searching the duration taken for the number of counts to drop to half of the peak count. The duration of time in $T_{1/2,dec}$ could be from the start of the renogram (Fig 4.4(a)) or from the peak time (Fig 4.4(b)). $T_{1/2,dec}$ could also be found by finding the half time of an exponential decay curve fitted on the renogram (Fig 4.4(c)&(d)).

Figure 4.4 Various definitions of $T_{1/2,dec}$ of a renogram.

4.4.2 Ranges of Values for Diagnosis

In this thesis, $T_{1/2,dec}$ was derived using both references from peak and exponential fitted curve (the full list could be found in Appendix C.1). The statistics of the $T_{1/2,dec}$ was computed and tabulated in Table 4.4. Firstly, using peak count as a reference, the means of $T_{1/2,dec}$ were 12.63 ± 5.28 min in unobstructed kidneys and 27.72 ± 3.12 min in obstructed kidneys. An unpaired t -test showed an extremely significant difference between the unobstructed and obstructed classes in terms of statistical mean of $T_{1/2,dec}$ derived using this method. Next, using the exponential fitted curve, the means of $T_{1/2,dec}$ were 9.10 ± 3.86 min in unobstructed kidneys and 88.74 ± 161.02 min in obstructed kidneys. An

unpaired t -test showed an extremely significant difference was found between the 2 classes in terms of statistical mean of $T_{1/2,dec}$ derived using this method.

Table 4.4 Statistics of $T_{1/2,dec}$ (in min) in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
<i>Using peak count as a reference</i>							
Unobstructed	90	12.63	5.28	5.92	6.89	22.95	31.57
Obstructed	7	27.72	3.12	23.93	24.17	31.61	32.00
<i>Using exponential fitted curve</i>							
Unobstructed	90	9.10	3.86	3.54	5.44	16.52	26.10
Obstructed	34	88.74	161.02	18.36	18.64	382.87	731.36

Note: Extremely significant differences ($p < 0.0001$) were found in $T_{1/2,dec}$ between unobstructed and obstructed kidneys for both derivation method using peak count as a reference and using exponential fitted curve.

Out of 42 available obstructed renogram samples, only 7 samples had the $T_{1/2,dec}$ value derived using peak count as a reference. It was because in most of the unobstructed cases, the $T_{1/2,dec}$ did not occur within the 25 min duration of renography. On the other hand, $T_{1/2,dec}$ derived using exponential fitted curve could be obtained in 34 out of 42 obstructed renogram samples, as the derived values derived could be beyond 25 min duration of renography. The results obtained from both methods could differentiate unobstructed and obstructed classes significantly. It was recommended to derive $T_{1/2,dec}$ using an exponential fitting to avoid having too many missing data in the dataset.

Table 4.5 showed the proposed ranges of $T_{1/2,dec}$ for diagnosis of renal obstruction using both derivation methods. The cutoff points for both methods were around 20 min. Thus, if the number of counts failed to drop to half of the

peak count within 20 min, there is a high possibility that an obstruction was present in a kidney. This result was in accordance to the general guideline of the use of $T_{1/2,dec}$ for diagnosis where the value of it greater than 20 min was an indication of obstruction [74]. Even though the value of $T_{1/2,dec}$ derived here was based on F+10 protocol, the cut off point of $T_{1/2,dec}$ for diagnosis of obstruction was similar to that proposed in F-15 and F0 protocols [35] as well as F+20 [31] where $T_{1/2,dec}$ greater than 20 was a sign of obstruction.

Table 4.5 Reference ranges of $T_{1/2,dec}$ for diagnosis of renal obstruction

Index value	Kidney status
<i>Using peak count as a reference</i>	
< 21.55 min	Unobstructed
≥ 21.55 min	Obstructed
<i>Using exponential fitted curve</i>	
< 19.77 min	Unobstructed
≥ 19.77 min	Obstructed

4.4.3 Effect of Age and Gender

Using T_{max} as a reference, the means of $T_{1/2,dec}$ were 12.55 ± 4.53 min and 13.32 ± 6.67 min in unobstructed kidneys of men and women gender groups respectively and 28.06 ± 3.89 min and 26.11 ± 1.98 min in obstructed kidneys of men and women groups respectively (Fig 4.5(a)). For different age groups, the means $T_{1/2,dec}$ were 12.62 ± 5.77 min and 13.02 ± 4.83 min in obstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 26.44 ± 3.69 min and 28.38 ± 3.28 min in

obstructed kidneys of the younger and older populations respectively (Fig 4.5(b)). No significant difference was seen in $T_{1/2,dec}$ between men and women in both unobstructed ($p = 0.53$) and obstructed classes ($p = 0.56$). There was also no significant difference between the younger and older populations in the unobstructed ($p = 0.73$) and obstructed classes ($p = 0.53$).

Figure 4.5 The distribution of $T_{1/2,dec}$ derived by using peak count as a reference in different gender groups (a) and different age groups (b).

Using exponential fitted curve, the means of $T_{1/2,dec}$ were 8.93 ± 3.39 min and 9.59 ± 4.91 min in unobstructed kidneys of men and women gender groups

respectively and 50.38 ± 35.84 min and 134.51 ± 233.85 min in obstructed kidneys of men and women groups respectively (Fig 4.6(a)). For different age groups, the means of $T_{1/2,dec}$ were 8.46 ± 3.60 min and 9.91 ± 4.21 min in unobstructed kidneys of the younger and older populations respectively and 129.31 ± 240.70 min and 60.20 ± 56.46 min in obstructed kidneys of the younger and older populations respectively (Fig 4.6(b)). No significant difference was seen in $T_{1/2,dec}$ between men and women in both unobstructed ($p = 0.47$) and obstructed classes ($p = 0.18$). There was also no significant difference between the younger and older populations in the unobstructed ($p = 0.09$) and obstructed classes ($p = 0.27$). Due to the curve fitting estimation of the $T_{1/2,dec}$, the maximum value of it for the obstructed kidney could reach as high as 731 min. In an obstructed kidney, the graph often reached plateau state, so the time required the number of counts to drop to half of the peak count could be extremely long. Consequently, as seen in Fig 4.6, the variation of the $T_{1/2,dec}$ was broad and reached a high value. In both methods, there was no significant difference of $T_{1/2,dec}$ in terms of different genders and age groups. The same result was also obtained by Esteves et al where it was found that the age and gender did not affect the range of $T_{1/2,dec}$ in a normal kidney [68].

Figure 4.6 The distribution of $T_{1/2,dec}$ derived by exponential fitted a renogram in different gender groups (a) and different age groups (b).

In spite of being a widely used parameter, $T_{1/2,dec}$ should never be used as the only parameter in the diagnosis of renal obstruction. In a work done by Sheu et al, a number of good functioning kidneys had shown to have prolonged retention of tracer [90]. Another study by Salih et al found that the mean value of $T_{1/2,dec}$ of a normal kidney could be similar to those of obstructed one [97]. In addition, a study done by Binongo et al to develop renal obstruction classifier

suggested that $T_{1/2,dec}$ was not a crucial parameter in the diagnosis of renal obstruction [12].

4.5 Lasix Half Time

$LT_{1/2,dec}$ was a similar parameter as $T_{1/2,dec}$ except the reference point for the half of the value was not peak count but it was the number of counts at the Lasix instead. In the other words, $LT_{1/2,dec}$ was the time taken from the diuretic administration to the time where the number of counts reduced to half of the number of counts when the furosemide was injected [91].

4.5.1 Derivation

Like $T_{1/2,dec}$, there was no standardization of the means to derive $LT_{1/2,dec}$. There were two commonly used methods to derive $LT_{1/2,dec}$. The first method was by finding the time where the activity reduced to 50% of the number of counts at the Lasix. The duration could be from the start of the renogram (Fig 4.7(a)) or from the Lasix time (Fig 4.7(b)). The second method was by doing exponential decay curve fitting on renogram and then calculating the half time of the curve. For this method, the duration could also be from the start of the renogram (Fig 4.7(c)) or from the Lasix time (Fig 4.7(d)).

Figure 4.7 Various definitions of $LT_{1/2,dec}$ of a renogram.

4.5.2 Ranges of Values for Diagnosis

In this thesis, $LT_{1/2,dec}$ was derived using both references from the peak and exponential fitted curve (the full list could be found in Appendix C.1). The statistics of the $LT_{1/2,dec}$ was computed and tabulated in Table 4.6. Firstly, using Lasix time as a reference, the means of $LT_{1/2,dec}$ were 18.56 ± 4.74 min in unobstructed kidneys and 29.89 ± 2.00 min in obstructed kidneys. An unpaired t -test showed an extremely significant difference between the unobstructed and obstructed classes in terms of statistical mean of $LT_{1/2,dec}$ derived using this method. Next, using the exponential fitted curve, the means of $LT_{1/2,dec}$ were 23.93 ± 12.02 min in unobstructed kidneys and 122.13 ± 242.04 min in

obstructed kidneys. An unpaired t -test showed an extremely significant difference was found between the 2 classes in terms of statistical mean of $LT_{1/2,dec}$ derived using this method.

Table 4.6 Statistics of $LT_{1/2,dec}$ (in min) in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
<i>Using Lasix timing as a reference</i>							
Unobstructed	86	18.56	4.74	12.75	13.2	28.59	31.90
Obstructed	4	29.89	2.00	27.28	27.63	31.80	32.00
<i>Using exponential fitted curve</i>							
Unobstructed	90	23.93	12.02	14.51	15.97	35.58	118.10
Obstructed	29	122.13	242.04	25.64	30.36	512.73	1208.22

Note: Extremely significant differences were found in $LT_{1/2,dec}$ between unobstructed and obstructed kidneys for both derivation methods using Lasix time as a reference ($p < 0.0001$) and using exponential fitted curve ($p = 0.0002$).

As can be seen from Table 4.6, the number of obstructed kidneys that had the value of $LT_{1/2,dec}$ obtained by finding the exact half value of the number of counts at Lasix time was only 4. Meanwhile, $LT_{1/2,dec}$ could be obtained in 29 renograms when it was calculated through an exponential fitted curve. This suggested that derivation using curve fitting could be better to avoid having a large number of missing data for diagnosis.

For the purpose of determining renal obstruction, based on the renogram samples, it was suggested that the cutoff point for $LT_{1/2,dec}$ derived by using Lasix time as a reference was 25.85 min while the cutoff point for $LT_{1/2,dec}$ derived by using exponential fitted curve was 53.58 min as stated in Table 4.7. The second method's cutoff point had a value double than that of the first method. By looking

at the sample size, the cutoff point derived from the first method would have a lower reliability as the obstructed class only had 4 data. Hence, it was recommended to evaluate the renal obstruction using the second method until a future research with a high number of renograms were carried out to set the reference ranges of $LT_{1/2,dec}$ derived using the Lasix time as a reference. The cutoff point of $LT_{1/2,dec}$ derived from exponential fitted curve was comparable with the cutoff point of $LT_{1/2,dec}$ proposed by Karam et al [69]. In there study, it was suggested that in F+30 renography, $LT_{1/2,dec}$ with a duration longer than 20 min from Lasix time was a sign of obstruction. As the Lasix time used in F+30 protocol was 30 min, the half time they suggested was 50 min if it was counted from the start of renogram.

Table 4.7 Reference ranges of $LT_{1/2,dec}$ for diagnosis of renal obstruction

Index value	Kidney status
<i>Using Lasix timing as a reference</i>	
< 25.85 min	Unobstructed
$\geq$ 25.85 min	Obstructed
<i>Using exponential fitted curve</i>	
< 53.58 min	Unobstructed
$\geq$ 53.58 min	Obstructed

4.5.3 Effect of Age and Gender

The effects of age and gender on $LT_{1/2,dec}$ derived by both methods were studied. Using Lasix time as a reference, both the effects of age and gender could only be investigated in the unobstructed class. For obstructed class, there was no

data available in woman group to study the effect of gender and there was only 1 data available in the older population group (≥ 42 years old) to study the effect of age. For an unobstructed class, the means of $LT_{1/2,dec}$ were 18.47 ± 4.54 min and 18.39 ± 5.17 min in men and women gender groups respectively (Fig 4.8(a)). For different age groups, the means of $LT_{1/2,dec}$ were 18.45 ± 4.75 min and 18.45 ± 4.78 min of the younger population (< 42 years old) and older population respectively (Fig 4.8(b)). Fig 4.8 shows that the distributions of $LT_{1/2,dec}$ between men and women as well as between younger and older populations are similar. No significant difference was seen in $LT_{1/2,dec}$ between men and women in both unobstructed ($p = 0.95$). There was also no significant difference between the younger and older populations ($p = 0.99$).

Figure 4.8 The distribution of $LT_{1/2,dec}$ derived by using Lasix time as a reference in different gender groups (a) and different age groups (b).

Using exponential fitted curve, the means of $LT_{1/2,dec}$ were 24.03 ± 14.36 min and 23.62 ± 7.00 min in unobstructed kidneys of men and women gender groups respectively and 106.13 ± 171.14 min and 157.77 ± 322.40 min in obstructed kidneys of men and women groups respectively (Fig 4.9(a)). For different age groups, the means of $LT_{1/2,dec}$ were 22.25 ± 6.85 min and 25.69 ± 16.34 min in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 145.55 ± 335.11 min and 120.29 ± 170.22 min in obstructed kidneys of the younger and older populations

respectively (Fig 4.9(b)). No significant difference was seen in $LT_{1/2,dec}$ between men and women in both unobstructed ($p = 0.89$) and obstructed classes ($p = 0.61$). There was also no significant difference between younger and older populations in the unobstructed ($p = 0.20$) and obstructed classes ($p = 0.92$). The standard deviation of $LT_{1/2}$ in an obstructed group was found to be broad due to the long duration for the number of counts to drop to half of the value at Lasix injection despite the diuretic injection.

Figure 4.9 The distribution of $LT_{1/2,dec}$ derived by exponential fitted a renogram in different gender groups (a) and different age groups (b).

4.6 Normalized Residual Activity

NORA represented the quantification of renal output from a renogram [162]. It indicated the amount of tracer remaining inside a kidney, which could be an indicator of the renal emptying process. It was independent of the functionality level of a kidney and was frequently used in the evaluation of renal obstruction.

4.6.1 Derivation

NORA was defined as the ratio of the number of counts at a specific point of time to the number of counts at 2 min. Mathematically, it could be written as seen in Equation (4.2). It was a versatile parameter as it could be defined at different reference timing and as a result, there was a lack of standardization of it. The most well-known type of NORA was $NORA_{20}$ which was the ratio of the count at 20 min to the count at 2 min [92], and it could be written as shown in Equation (4.3). In addition, NORA could also be derived based on post-void count number over the number of counts at 2 min [47], which was expressed as Equation (4.4).

$$NORA_T = \frac{n_{c,T}}{n_{c,2}} \quad (4.2)$$

$$NORA_{20} = \frac{n_{c,20}}{n_{c,2}} \quad (4.3)$$

$$NORA_{\text{post}} = \frac{n_{c,\text{post}}}{n_{c,2}} \quad (4.4)$$

4.6.2 Ranges of Values for Diagnosis

Both $NORA_{20}$ and $NORA_{\text{post}}$ were derived to analyze their ability in differentiating renal obstruction (the full list could be found in Appendix C.1). The statistics of both NORA were computed and tabulated in Table 4.8. Using the

number of counts at 20 min as the nominator in the ratio, the means of $NORA_{20}$ were 0.44 ± 0.32 in unobstructed kidneys and 1.44 ± 0.56 in obstructed kidneys. An unpaired t -test showed an extremely significant difference between the unobstructed and obstructed classes in terms of statistical mean of $NORA_{20}$. Next, the means of $NORA_{post}$ were 10.29 ± 13.39 in unobstructed kidneys and 60.89 ± 89.27 in obstructed kidneys. An unpaired t -test showed an extremely significant difference was found between the 2 classes in terms of statistical mean of $NORA_{post}$ derived using this method.

Table 4.8 Statistics of NORA in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
$NORA_{20}$							
Unobstructed	90	0.44	0.32	0.13	0.15	1.20	1.50
Obstructed	42	1.44	0.56	0.76	0.80	2.39	2.98
$NORA_{post}$							
Unobstructed	81	10.29	13.39	0.57	0.66	42.19	48.28
Obstructed	37	60.89	89.27	0.05	2.01	212.65	391.41

Note: Extremely significant differences were found between unobstructed and obstructed kidneys in both $NORA_{20}$ and $NORA_{post}$ ($p < 0.0001$).

The cutoff point of $NORA_{20}$ in differentiating renal obstruction was found to be 0.90 (Table 4.9). This cutoff point was similar to the one proposed by Piepsz et al [86]. In their study, they found the value of $NORA_{20}$ for normal cases was less than 1.0. Meanwhile, the cutoff point of $NORA_{post}$ was 36.63 in differentiating renal obstruction.

Table 4.9 Reference ranges of NORA for diagnosis of renal obstruction

Index value	Kidney status
NORA ₂₀	
< 0.90	Unobstructed
≥ 0.90	Obstructed
NORA _{post}	
< 36.63	Unobstructed
≥ 36.63	Obstructed

4.6.3 Effect of Age and Gender

Next, the effects of age and gender on NORA₂₀ and NORA_{post} were investigated. The means of NORA₂₀ were 0.44 ± 0.30 and 0.47 ± 0.36 in the unobstructed kidneys of men and women gender groups respectively and 1.59 ± 0.64 and 1.28 ± 0.43 in obstructed kidneys of men and women groups respectively (Fig 4.10(a)). No significant difference was seen in NORA₂₀ between men and women in both unobstructed ($p = 0.71$) and obstructed classes ($p = 0.08$). No significant difference of NORA₂₀ between genders was also found by Esteves et al [125]. For different age groups, the means of NORA₂₀ were 0.44 ± 0.38 and 0.45 ± 0.25 in unobstructed kidney of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 1.54 ± 0.56 and 1.34 ± 0.56 in obstructed kidney of the younger and older populations respectively (Fig 4.10(b)). There was no significant difference between younger and older populations in the unobstructed ($p = 0.91$) and obstructed classes ($p =$

0.28). No influence of age on $NORA_{20}$ in unobstructed class was also deduced in a study done by Piepsz et al [86].

Figure 4.10 The distribution of $NORA_{20}$ in different gender groups (a) and different age groups (b).

For $NORA_{post}$, the means were 9.07 ± 12.47 and 12.59 ± 14.95 in unobstructed kidneys of men and women gender groups respectively and 54.72 ± 84.94 and 66.74 ± 95.12 in obstructed kidneys of men and women groups respectively (Fig 4.11(a)). No significant difference was seen in $NORA_{post}$ between men and women in both unobstructed ($p = 0.26$) and obstructed classes ($p = 0.69$). For different age groups, the means of $NORA_{post}$ were $8.40 \pm$

11.93 and 12.42 ± 14.74 in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 70.56 ± 81.31 and 52.67 ± 96.83 in obstructed kidneys of the younger and older populations respectively (Fig 4.11(b)). There was no significant difference between the younger and older populations in the unobstructed ($p = 0.18$) and obstructed classes ($p = 0.55$).

Figure 4.11 The distribution of $NORA_{post}$ in different gender groups (a) and different age groups (b).

4.7 Peak Count

The $n_{c,peak}$ could be found by recording the peak activity of a TAC. The main issue in using peak count was its value was highly dependent on the amount of radioisotopes injected. This amount might be different depending on the protocol implemented in each clinic. While other parameters could be normalized by peak count, the peak count could not be normalized by itself. Modification of it, such as $NORA_{peak}$, could be one of the solutions to use peak information as an indicator of renal obstruction.

The $n_{c,peak}$ was recorded in Appendix C.2. The statistics of $n_{c,peak}$ were computed and tabulated in Table 4.10. Using the means $n_{c,peak}$ were 9847 ± 7807 in unobstructed kidneys and 7595 ± 7591 in obstructed kidneys. This parameter had a wide range of distribution due to the inconsistency of the radioisotopes input amount. The minimum value of $n_{c,peak}$ reached as low as 400 while the maximum reached as high as 32165 within the same class. This showed that this parameter was not a suitable indicator of renal obstruction. Its p -value was found to be larger than 0.05, which further verified that it was not a viable parameter in differentiating renal obstruction.

Table 4.10 Statistics of $n_{c,peak}$ in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	90	9847	7807	400	709	21852	32165
Obstructed	42	7597	7591	350	553	23074	28037

Note: No significant differences were found between unobstructed and obstructed kidneys in $n_{c,peak}$ ($p = 0.12$).

4.8 Ratio of Number of Count at 20 min to Peak Count

The $R_{20/max}$ was a simple ratio that provided information about the renal outflow in relative to the peak activity. In a healthy kidney, the number of counts decreased rapidly right after peak activity to a lower number of counts. In this situation, $R_{20/max}$ had a small value. If the $R_{20/max}$ was close to 1, it was a sign of obstruction because TAC was in a plateau condition where there was a delayed washout [48]. Thus, this parameter was a potential indicator of renal function.

4.8.1 Derivation

$R_{20/max}$ was defined as the ratio of the number of counts at 20 min to the number of counts at peak of a renogram. Mathematically, it could be written as seen in Equation (4.5).

$$R_{20/max} = \frac{n_{c,20}}{n_{c,max}} \quad (4.5)$$

4.8.2 Ranges of Values for Diagnosis

Using Equation (4.5), $R_{20/max}$ of the renogram samples were derived (the full list could be found in Appendix C.2). To study the ranges of values of $R_{20/max}$ in both unobstructed and obstructed classes, a statistical analysis was carried out. The statistics of $R_{20/max}$ were computed and tabulated in Table 4.11. The means $R_{20/max}$ were 0.29 ± 0.15 in unobstructed kidneys and 0.82 ± 0.13 in obstructed kidneys. An unpaired t -test showed an extremely significant difference between the unobstructed and obstructed classes in terms of statistical mean of $R_{20/max}$. A study done by Clausen et al showed that the mean of $R_{20/max}$ in healthy renal

donor was 0.22, which was close but slightly lower than the mean of $R_{20/max}$ for an unobstructed class derived from renogram samples of this thesis [120].

Table 4.11 Statistics of $R_{20/max}$ in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	90	0.29	0.15	0.10	0.13	0.63	0.67
Obstructed	37	0.82	0.13	0.54	0.58	0.97	0.99

Note: Extremely significant differences were found between unobstructed and obstructed kidneys in $R_{20/max}$ ($p < 0.0001$).

To use this parameter in differentiating renal obstruction, the cutoff point between the unobstructed and obstructed classes was 0.57 (Table 4.12).

Table 4.12 Reference ranges of $R_{20/max}$ for diagnosis of renal obstruction

Index value	Kidney status
< 0.57	Unobstructed
≥ 0.57	Obstructed

4.8.3 Effect of Age and Gender

By dividing the renogram samples into gender groups, the means $R_{20/max}$ were 0.29 ± 0.14 and 0.30 ± 0.17 in unobstructed kidneys of men and women gender groups respectively and 0.84 ± 0.13 and 0.81 ± 0.14 in obstructed kidneys of men and women groups respectively (Fig 4.12(a)). No significant difference was seen in $R_{20/max}$ between men and women in both unobstructed ($p = 0.60$) and obstructed classes ($p = 0.40$). This was consistent with a study done by Clausen et al [84] that found a similar outcome. For different age groups, the means $R_{20/max}$ were 0.28 ± 0.17 and 0.30 ± 0.13 in the unobstructed kidney

of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 0.85 ± 0.12 and 0.80 ± 0.14 in obstructed kidneys of the younger and older populations respectively (Fig 4.12(b)). There was no significant difference between younger and older populations in the unobstructed ($p = 0.48$) and obstructed classes ($p = 0.32$). No significant difference due to the different age population was also observed in a study done by Esteves et al [3].

Figure 4.12 The distribution of $R_{20/max}$ in different gender groups (a) and different age groups (b)

4.9 Ratio of Post-Void Count to Maximum Count

$R_{post/max}$ presumed to be a more robust measurement of renal drainage as compared to half time according to Taylor [45]. Bao et al [94] and Garcial et al [71] found that this ratio was a crucial parameter in determining the absence of an obstruction in a renogram without the diuretic.

4.9.1 Derivation

$R_{post/max}$ was defined as the ratio of the number of counts obtained from a post-void image to the number of counts at peak of a renogram. Mathematically, it could be written as seen in Equation (4.6).

$$R_{post/max} = \frac{n_{c,post}}{n_{c,max}} \quad (4.6)$$

4.9.2 Ranges of Values for Diagnosis

The full list of derived $R_{post/max}$ could be found in Appendix C.2. The statistics of $R_{post/max}$ were computed and tabulated in Table 4.13 to determine its ability in differentiating renal obstruction. The means of $R_{post/max}$ were 7.50 ± 9.49 in unobstructed kidneys and 35.09 ± 48.30 in obstructed kidneys. An unpaired t -test showed an extremely significant difference between the unobstructed and obstructed classes in terms of statistical mean of $R_{post/max}$ ($p < 0.0001$).

Table 4.13 Statistics of $R_{post/max}$ in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	81	7.50	9.49	0.42	0.52	26.96	38.91
Obstructed	37	35.09	48.30	0.03	1.42	143.36	175.90

Note: Extremely significant differences were found between unobstructed and obstructed kidneys in $R_{post/max}$ ($p < 0.0001$).

To use this parameter for differentiating renal obstruction, the cutoff point to separate the unobstructed and obstructed classes was 24.74 (Table 4.14).

Table 4.14 Reference ranges of $R_{post/max}$ for diagnosis of renal obstruction

Index value	Kidney status
< 24.74	Unobstructed
≥ 24.74	Obstructed

4.9.3 Effect of Age and Gender

By dividing the renogram samples into gender groups, the means of $R_{20/max}$ were 6.86 ± 9.34 and 8.72 ± 9.82 in unobstructed kidneys of men and women gender groups respectively and 29.08 ± 45.57 and 40.78 ± 51.32 in obstructed kidney of men and women groups respectively (Fig 4.13(a)). No significant difference was seen in $R_{20/max}$ between men and women in both unobstructed ($p = 0.41$) and obstructed classes ($p = 0.47$). This was consistent with studies done by Clausen et al [84] and Esteves et al [68]. For different age groups, the means of $R_{20/max}$ were 6.20 ± 8.39 and 8.98 ± 10.52 in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 43.34 ± 49.63 and 28.08 ± 47.26 in

obstructed kidneys of the younger and older populations respectively (Fig 4.13(b)). There was no significant difference between younger and older populations in the unobstructed ($p = 0.19$) and obstructed classes ($p = 0.35$).

Figure 4.13 The distribution of $R_{post/max}$ in different gender groups (a) and different age groups (b).

4.10 Ratio of Pre-void Count to Post-void Count

The ratio of pre-void count (PrVC) and post-void count (PoVC) could provide information about the bladder condition. When the bladder was full, a

false positive outcome could be obtained from evaluation of renogram. Thus, it could be beneficial to incorporate this ratio in the evaluation of renal obstruction.

4.10.1 Derivation

$R_{pre/post}$ was defined as the ratio of the number of counts obtained from a pre-void image to the number of counts obtained from a post-void image. Mathematically, it could be written as seen in Equation (4.7).

$$R_{pre/post} = \frac{n_{c,pre}}{n_{c,post}} \quad (4.7)$$

4.10.2 Ranges of Values for Diagnosis

To test the ability of $R_{pre/post}$ in the evaluation of renal obstruction, the value of this parameter was derived from available renogram samples (the full list could be found in Appendix C.2). The statistics of both $R_{pre/post}$ were computed and tabulated in Table 4.15. The means of $R_{pre/post}$ were 1.89 ± 2.69 in unobstructed kidneys and 1.52 ± 0.95 in obstructed kidneys. An unpaired t -test showed no significant difference between the unobstructed and obstructed classes in terms of statistical mean of $R_{pre/post}$. Hence, this parameter was not suitable to be used as a sole parameter in determining renal obstruction and no further analysis on the effect of age and gender was carried out.

Table 4.15 Statistics of $R_{pre/post}$ in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	81	1.89	2.69	1.01	1.09	3.03	25.3
Obstructed	37	1.52	0.95	0.85	0.91	3.57	5.37

Note: No significant differences were found between unobstructed and obstructed kidneys in $R_{pre/post}$ ($p = 0.41$).

4.11 Ratio of Pre-void Count to Maximum Count

$R_{pre/max}$ was another parameter obtained by using a pre-void image. It was an important parameter in evaluating the presence of obstruction according to Garcia et al [71]. However, the value of this parameter was dependent on a duration of renography. If the duration is 20 min, this parameter is the same as $R_{20/max}$.

4.11.1 Derivation

$R_{pre/max}$ could be derived similar to the $R_{post/max}$. Instead of using the number of counts from a post-void image, the number of counts used in $R_{pre/max}$ was the count number obtained from a pre-void image. In the other words, $R_{pre/max}$ was the ratio of the number of counts obtained from a pre-void image to the number of counts at peak of a renogram. Mathematically, it could be written as seen in Equation (4.8).

$$R_{pre/max} = \frac{n_{c,pre}}{n_{c,max}} \quad (4.8)$$

4.11.2 Ranges of Values for Diagnosis

The statistics of $R_{pre/max}$ were computed and tabulated in Table 4.16 to determine its ability in differentiating renal obstruction (the full list of derived $R_{pre/max}$ could be found in Appendix C.2). The means of $R_{pre/max}$ were 7.50 ± 9.49 in unobstructed kidneys and 35.09 ± 48.30 in obstructed kidneys. An unpaired t -test showed an extremely significant difference between the unobstructed and obstructed classes in terms of statistical mean of $R_{pre/max}$.

Table 4.16 Statistics of $R_{pre/max}$ in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	81	18.11	67.08	0.64	0.88	42.14	602.25
Obstructed	37	42.84	52.12	0.03	4.13	139.42	165.90

Note: Extremely significant differences were found between unobstructed and obstructed kidneys in $R_{pre/max}$ ($p < 0.0001$).

To use this parameter for differentiating renal obstruction, the cutoff point in differentiating unobstructed and obstructed classes was 24.74 (Table 4.17).

Table 4.17 Reference ranges of $R_{pre/max}$ for diagnosis of renal obstruction

Index value	Kidney status
< 4.29	Unobstructed
≥ 4.29	Obstructed

4.11.3 Effect of Age and Gender

Next, the effects of age and gender on $R_{pre/max}$ were explored. The means of $R_{pre/max}$ were 21.04 ± 82.44 and 12.56 ± 13.95 in unobstructed kidneys in men and women gender groups respectively and 35.64 ± 51.04 and

49.67 ± 53.58 in obstructed kidneys in men and women groups respectively (Fig 4.14(a)). No significant difference was seen in $R_{pre/max}$ between men and women in both unobstructed ($p = 0.59$) and obstructed classes ($p = 0.42$). For different age groups, the means $R_{pre/max}$ were 9.62 ± 11.81 and 27.71 ± 96.91 in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 53.97 ± 55.62 and 33.38 ± 48.34 in obstructed kidneys of the younger and older populations respectively (Fig 4.14(b)). There was no significant difference between the younger and older populations in the unobstructed ($p = 0.23$) and obstructed classes ($p = 0.24$).

Figure 4.14 The distribution of $R_{pre/max}$ in different gender groups (a) and different age groups (b).

4.12 Time to Half of Peak

$T_{max/2}$ referred to the time taken for the number of counts to reach half of the number of counts at peak during the perfusion phase of a renogram. This parameter represented the condition where the uptake rate of the tracer by a kidney was around the maximum rate. Intuitively, $T_{max/2}$ could be an indicator of renal function, but its ability to predict renal obstruction needed to be further examined.

4.12.1 Derivation

$T_{max/2}$ was the time required for the number of counts to reach half of the maximum count. It could be derived by recording the peak count of a renogram and then determining the time needed to reach of half of the peak count value. This parameter was versatile as a lot of slightly different version can be used, such as $T_{2max/3}$ [38] and $T_{3max/4}$ [49, 79].

4.12.2 Ranges of Values for Diagnosis

The ranges of $T_{max/2}$ of unobstructed and obstructed classes were suggested in Table 4.18. Based on the derived value listed in Appendix C.2, the means of $T_{max/2}$ were 1.21 ± 0.40 min in unobstructed kidneys and 1.51 ± 0.94 min in obstructed kidneys. An unpaired t -test showed a significant difference between the unobstructed and obstructed classes in terms of statistical mean of $T_{max/2}$.

Table 4.18 Statistics of $T_{max/2}$ (in min) in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	90	1.21	0.40	0.52	0.67	1.96	2.37
Obstructed	42	1.51	0.94	0.35	0.50	3.38	4.32

Note: Significant differences ($p = 0.011$) were found in $T_{max/2}$ between unobstructed and obstructed kidneys

Table 4.19 showed the proposed ranges of $T_{max/2}$ for diagnosis of renal obstruction using both derivation methods. The cutoff point was around 1.36 min. As the means of $T_{max/2}$ for two classes were close, this parameter was very sensitive to the imaging setup. A slightly different protocol used, for example early

or a slight delay in image scanning, might lead to either false positive or false negative diagnosis. Hence, if this parameter was chosen as an indicator of obstruction, extra care was needed to ensure the precise timing was recorded.

Table 4.19 Reference ranges of $T_{max/2}$ for diagnosis of renal obstruction

Index value	Kidney status
< 1.36 min	Unobstructed
$\geq$ 1.36 min	Obstructed

4.12.3 Effect of Age and Gender

Next, the effect of age and gender on the $T_{max/2}$ was examined. The means of $T_{max/2}$ were 1.24 ± 0.42 min and 1.18 ± 0.39 min in unobstructed kidneys of men and women gender groups respectively and 1.78 ± 1.11 min and 1.20 ± 0.68 min in obstructed kidneys of men and women groups respectively (Fig 4.15(a)). No significant difference was seen in $T_{max/2}$ between men and women in both unobstructed ($p = 0.53$) and obstructed classes ($p = 0.06$). For different age groups, the means of $T_{max/2}$ were 1.23 ± 0.47 min and 1.22 ± 0.34 min in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 1.62 ± 0.97 min and 1.37 ± 0.95 min in obstructed kidneys of the younger and older populations respectively (Fig 4.15(b)). There was a also significant difference between the younger and older populations in unobstructed ($p = 0.94$) and obstructed classes ($p = 0.43$).

Figure 4.15 The distribution of $T_{max/2}$ in different gender groups (a) and different age groups (b).

4.13 Time to Peak

T_{max} was the amount of time required to reach peak number of counts in a renogram. It represented the condition where the tracer uptake by a kidney is equal to the tracer output of a kidney. It was one of the commonly used parameters in evaluating renal obstruction. Russell et al suggested T_{max} was a simple parameter that could be used to evaluate renal transit time [78].

4.13.1 Derivation

T_{max} could be obtained by finding the duration from the start point of renogram to the point where the number of counts reached the maximum value. Shorter T_{max} indicated good functionality of a kidney, while lengthened T_{max} could be a sign of abnormality in a kidney. It was important to note even though prolonged T_{max} might indicate a kidney was obstructed, it could also be a sign of dehydration or impaired renal function [61].

4.13.2 Ranges of Values for Diagnosis

To propose the range of T_{max} in both unobstructed and obstructed kidneys, the T_{max} of the renogram samples were first recorded (the full list could be found in Appendix C.2). Then, the ranges of T_{max} of unobstructed and obstructed classes were suggested as seen in Table 4.20. The means of T_{max} were 5.08 ± 2.95 min in unobstructed kidneys and 15.94 ± 9.75 min in obstructed kidneys. An unpaired t -test showed an extremely significant difference between the unobstructed and obstructed classes in terms of statistical mean of T_{max} .

Table 4.20 Statistics of T_{max} (in min) in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	90	5.08	2.95	2.32	2.74	12.07	14.22
Obstructed	42	15.94	9.75	3.02	4.14	30.99	32.00

Note: Extremely significant differences ($p < 0.0001$) were found in T_{max} between unobstructed and obstructed kidneys

The proposed ranges of T_{max} statistics in Table 4.20 was based on renogram samples obtain from F+10 protocol and might not be valid to be used

for other protocol as the peak of renogram was dependent on the timing of diuretic administration. A study done by Donoso et al showed that there was a significant difference in the mean of T_{max} produced from F0 and F+20 protocols [72].

For the purpose of using T_{max} as a single index for diagnosis, the cutoff point in differentiating unobstructed and obstructed classes was 9.98 min (Table 4.21). In the absence of a renal obstruction, the T_{max} had to be lower than this cutoff value. In F+10 protocol, this cutoff would happen before administration of diuretics. The value this parameter could be checked within the first 10 min of renography. Thus, it had the potential to be used as a parameter to determine the need for diuretic as an unobstructed kidney could be confirmed based on the evaluation of this parameter before the diuretic was injected.

Table 4.21 Reference ranges of T_{max} for diagnosis of renal obstruction

Index value	Kidney status
< 9.98 min	Unobstructed
$\geq$ 9.98 min	Obstructed

4.13.3 Effect of Age and Gender

Next, the effect of age and gender on the T_{max} was examined. The means T_{max} were 5.17 ± 2.96 min and 5.06 ± 3.01 min for an unobstructed kidney in men and women gender group respectively and 15.98 ± 9.86 min and 16.69 ± 10.53 min for an obstructed kidney in men and women groups respectively (Fig 4.16(a)). For different age groups, the means T_{max} were 5.45 ± 3.49 min and

4.79 ± 2.23 min in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 17.56 ± 9.77 min and 15.24 ± 10.45 min in obstructed kidneys of the younger and older populations respectively (Fig 4.16(b)). No significant difference was seen in T_{max} between men and women in both unobstructed ($p = 0.87$) and obstructed classes ($p = 0.83$). There was also significant difference between the younger and older populations in unobstructed ($p = 0.31$) and obstructed classes ($p = 0.49$). These results were in agreement with a study done by Clausen et al who found that there were not significant influences of gender and age on the T_{max} [84].

Figure 4.16 The distribution of T_{max} in different gender groups (a) and different age groups (b)

4.14 Summary

In this chapter, the existing parameters in the literature were explored. These parameters were DEI , DRF , $T_{1/2,dec}$, $LT_{1/2,dec}$, $NORA$, $n_{c,peak}$, $R_{20/max}$, $R_{post/max}$, $R_{pre/post}$, $R_{pre/max}$, $T_{max/2}$, and T_{max} . No reference ranges of these parameters for F+10 protocol was found in the literature. Hence, the statistics of these parameters in both unobstructed and obstructed classes were evaluated in this chapter. The cutoff points of these parameters to be used as an individual

index in the interpretation of renogram were proposed here. The effects of age and gender were also evaluated and it was found that in general, these parameters were not significantly influenced by both age and gender.

CHAPTER 5

RESULTS 2

BASELINE SCREENING SYSTEM: THE NEED FOR DIURETICS

5.1 Introduction

Administering diuretic during renography is a common practice in renography. The purpose of diuretic injection is to avoid a false positive diagnosis of renal obstruction caused by a dilation of a kidney. However, using a diuretic does induce some possible side effects to the body. The diuretic injection can potentially be omitted if the absence of obstruction can be confirmed in the early stage of scanning. Thus, this chapter explores the idea of determining the need for diuretic based on initial scanning before diuretic is applied.

Firstly, a brief explanation of diuretic and its protocols in renography are presented. Next, a set of quantifiable parameters based on the first 10 min of the renograms is evaluated. The parameters are ranked and used to create an LR model as a Baseline Screening System (BSS). The cutoff point of the probability in deciding the need for diuretic was determined based PRC analysis.

5.2 Diuretic in Renography

Diuretic, which is also called as Lasix or furosemide, induces urine in a healthy kidney. It can increase the accuracy in the interpretation of renogram because it reduces false positive diagnosis caused by a renal dilation [163]. In the case where a kidney is dilated and causes a reservoir effect, the application of diuretics causes the number of counts drops momentarily right after injection

(Fig 5.1(a)). On the other hand, if an obstruction is present, the number of counts does not decrease or may even keep increasing after the injection of diuretics (Fig 5.1(b)). However, there are a number of drawbacks regarding the application of diuretics. Injecting diuretics requires additional intravenous injection with an exception in the F0 protocol where it is injected together with radioisotopes. A diuretic may induce a number of side effects such as hypotension, allergic reaction and cause ototoxicity as well as nephrotoxicity [164-166].

Figure 5.1 The use of furosemide to differentiate unobstructed (a) and obstructed kidneys (b).

A baseline scan of a renogram refers to the scanning result before a diuretic is injected. If a baseline scan can be used to predict a kidney is unobstructed with a high accuracy, the administration of diuretic can potentially be omitted [47]. When the tracer passes through a kidney promptly as observed from a renogram, the decision to remove diuretic injection may be made by on-spot evaluation of baseline scans by experts [14]. However, the evaluation by experts is highly subjective depends on their experience. Furthermore, most

physicians only have limited exposure to renogram as low volume of studies were performed per clinic which lead to a low confidence level to this subjective interpretation. Hence, no clear guideline on the evaluation of the need for diuretic could be found in any renography protocols.

There are several distinctive protocols regarding the timing of furosemide administration. Diuretics can be injected, before, during, or after radioisotopes injection. Commonly used protocols are an injection of furosemide 15 min before radioisotopes (F-15) [167], injection at the same time as radioisotopes (F0) [89], injection 10 min, 20 min or 30 min after radioisotopes (F+10, F+20, or F+30) [168]. As a result of this variation in diuretic administration, the evaluation of renal obstruction is more accurate by following their respective guidelines.

Each of the different protocols has its own advantages. The F-15 protocol reduces the incidence of equivocal results in the diagnosis [167]. In addition, F-15 measures a renal function during the steady state of the maximum urinary flow rate while other protocols that injected diuretic during or after radioisotopes injection record the renal count when there is continuous change in the urinary flow rate as affected by the diuretic injection. This observation of the number of counts during peak flow can help the evaluation of kidney with decreased function [16]. The shortcoming of F-15 is the recorded renogram may lose information about the compliance of a kidney.

F0 offers ease of administration as the diuretic is injected together with the radioisotopes. F0 is suggested to be used in a known hydronephrosis case as

the presence of dilation may not be observed [161]. F0 has an advantage of having a lower disruption rate as compared to other diuretic timing protocols as a less bladder distention occurs [169]. Furthermore, it allows a shorter acquisition time that reduces discomfort in the patients due to immobilization and also removes the need of repeated venous puncture [82, 89].

Injection of diuretic after radioisotopes, such as in F+10, F+20, or F+30, is used with a rationale that early injection of furosemide before the kidney is full of the tracers may generate false positive interpretation due to a delay in clearance as the kidney is still in the filling-up process [16]. Besides, by applying furosemide a period after radioisotopes injection, the maximal distension in the kidney can be assessed. Most of the protocols recommend the use of this method as it is believed to be superior in differentiating renal obstruction [17]. In addition, using F+10, F+20 or F+30 allows the evaluation of baseline scanning, which potentially can omit the need for diuretic if a kidney can be confirmed to be unobstructed before the diuretic is injected. Among these protocols, F+10 is the shortest duration renography, which can reduce bladder filling and avoid disruption during the procedure due to voiding [96]. The renogram samples used in this thesis were obtained from F+10 diuresis renography.

5.3 Derivation of Parameters

The first step to develop an objective means of deciding the need for diuretic during renography in a F+10 renography was to derive quantifiable parameters of renogram within the first 10 min of TAC.

5.3.1 Normalized residual activity

$NORA_T$ was a parameter obtained by calculating the ratio of the number of counts at a time T to the number of counts at 3 min. It was very versatile as it can be defined at any specific time. For first 10 min of renogram before diuretic, 8 possible NORAs were derived and evaluated:

- $NORA_3$
- $NORA_4$
- $NORA_5$
- $NORA_6$
- $NORA_7$
- $NORA_8$
- $NORA_9$
- $NORA_{10}$

The full derived values for all the 8 variants NORAs could be found in Appendix C.3. After obtaining all the values, unpaired t -tests were carried out to check the ability of each parameter in differentiating unobstructed or obstructed classes. The p -values obtained for each parameter were plotted as a scatter plot as shown in Fig 5.2. All parameters were found to be able to significantly differentiate renal obstruction with $p < 0.05$ except $NORA_4$ which had $p = 0.28$. The lowest the p -value the better means of 2 classes being separated as distinct groups. Among these 8 NORAs, the best parameter to be used to confirm unobstructed condition earlier before diuretic was $NORA_{10}$.

Figure 5.2 NORAs derived from the first 10 min of renograms with their p -values obtained from t -tests in separating unobstructed and obstructed classes.

5.3.2 Time to peak and its variants

The time taken for the number of counts to reach its peak in a renogram had been widely used as an indicator of obstruction [73]. A longer T_{max} could be an indicator of a slow outflow rate of a kidney and an obstruction might be present. Other variants could also be formed using a similar concept of T_{max} . To search for best variation of T_{max} , 10 parameters derived were evaluated:

- $T_{max/10}$
- $T_{5max/10}$
- $T_{9max/10}$
- $T_{2max/10}$
- $T_{6max/10}$
- T_{max}
- $T_{3max/10}$
- $T_{7max/10}$
- $T_{4max/10}$
- $T_{8max/10}$

The derived values for all these 10 parameters could be found in Appendix C.4. Next, the unpaired t -tests were carried out to check the ability of the

parameters in differentiating renal obstruction. Based on the obtained p -values, only the means of last 4 parameters ($T_{7max/10}$, $T_{8max/10}$, $T_{9max/10}$, and T_{max}) had significant differences in separating unobstructed and obstructed groups with p -value being less than 0.05 (Fig 5.3). Out of these 4 parameters, the one that could best separate the classes was T_{max} .

Figure 5.3 T_{max} and its variations derived from the first 10 min of renogram with their p -values obtained from t -tests in separating unobstructed and obstructed classes.

5.3.3 Mean count value

The basic statistical parameter, mean value, had the potential to be used in differentiating renal obstruction. However, no research had been done to explore this parameter. The proof of the potentiality of using mean count value (MeanCV) could be found in Chapter 8. Here, the ability of MeanCV in the determination of the need for diuretic was evaluated. Ten possible variants of

MeanCV with different duration start from 1 min of renogram to 10 min of renogram were derived:

- MeanCV₁
- MeanCV₂
- MeanCV₃
- MeanCV₄
- MeanCV₅
- MeanCV₆
- MeanCV₇
- MeanCV₈
- MeanCV₉
- MeanCV₁₀

The renogram samples were normalized over the peak count and then the values of ten variants of MeanCV were derived and analyzed (the full list could be found in Appendix C.5). Unpaired *t*-tests have been carried out to test the performance of these parameters. The parameters, which were found to have a *p*-value lesser than 0.05 were MeanCV₁, MeanCV₄, MeanCV₅, MeanCV₈, MeanCV₉, and MeanCV₁₀. From the Fig 5.4, it could be observed that the last 3 parameters had better *p*-values and MeanCV₁₀ performed the best in separating unobstructed and obstructed classes.

Figure 5.4 MeanCVs derived from the first 10 min of renogram with their p -values obtained from t -tests in separating unobstructed and obstructed classes.

5.3.4 Median count value

Similar to MeanCV, a median count value (MedianCV) was another parameter never been explored in the literature. Its feasibility to be used as an indicator in determining renal obstruction was analyzed in Chapter 8. Here, 10 variations of MedianCV were derived based on 10 different durations of renogram, started from 1 min until 10 min. These 10 MedianCVs were:

- MedianCV₁
- MedianCV₂
- MedianCV₃
- MedianCV₄
- MedianCV₅
- MedianCV₆
- MedianCV₇
- MedianCV₈
- MedianCV₉
- MedianCV₁₀

Using normalized renogram samples, the values of these parameters were derived (the full list could be found in Appendix C.6). Fig 5.5 showed a scatter plot of the p -values of each of these parameters based on unpaired t -tests results. The means of parameters that could separate the unobstructed and obstructed classes significantly were found to be MedianCV₁, MedianCV₄, MedianCV₅, MedianCV₈, MedianCV₉, and MedianCV₁₀. Among the variants of MedianCV, the parameter that could best differentiate renal obstruction was MedianCV₁₀.

Figure 5.5 MedianCVs derived from the first 10 min of renogram with their p -values obtained from t -tests in separating unobstructed and obstructed classes.

5.3.5 Ranking of parameters

After obtaining the best parameters in each group of parameters, the p -values of them were used as a reference to rank the parameters. From Table 5.1, it could be observed that T_{max} was the best parameter to be used for diagnosis of renal obstruction based on baseline renograms.

Table 5.1 Ranking of parameter for BSS

Parameter	<i>p</i> -value	Rank
T_{max}	3.58×10^{-14}	1
NORA ₁₀	1.38×10^{-13}	2
MeanCV ₁₀	5.84×10^{-13}	3
MedianCV ₁₀	6.62×10^{-13}	4

In order to form an integrative system for diagnosis of renal obstruction using the combination of these parameters, the number of parameters to be used, which should be kept low and provided a high accuracy of diagnosis, had to be determined. To do that, LR model was applied to obtain the accuracy of diagnosis renal obstruction using 1 parameter (first rank parameter), 2 parameters (first and second rank parameters), 3 parameters (top 3 parameters), and all 4 parameters. The results were plotted as shown in Fig 5.6. As the number of parameters used increased, the accuracy of diagnosis increased. The highest accuracy obtained was 84.70% by using all 4 parameters. Hence, it was recommended to use all 4 parameters in developing an integrative model.

Figure 5.6 The accuracies in differentiating renal obstructing using LR classifiers developed by using different numbers of parameters.

5.4 Development of an Integrative System for Determining Need for Diuretic

The analysis so far was carried out as an effort to determine the parameters that could be used to create a model that provided a prediction of whether diuretic was required to be injected into the patient based on baseline scanning results. It was found that T_{max} , $NORA_{10}$, $MeanCV_{10}$, and $MeanCV_{10}$ could be used to separate the unobstructed and obstructed classes.

5.4.1 Formation of a logistic regression model as BSS

BSS was developed by combining these top 4 parameters using an LR model. The LR model was chosen because it could be implemented easily in a clinic that already had the renography instruments. The LR was created using 132 diuretic renography samples as the training dataset. The mathematical expression of BSS was built with 10 folds validation technique in MATLAB R2017b and was shown in Equation (5.1).

$$\ln\left(\frac{P(\text{no})}{P(\text{yes})}\right) = 55.03 - 0.04T_{max} - 7.57\text{NORA}_{10} - 114.10\text{MeanCV}_{10} + 52.20\text{MedianCV}_{10} \quad (5.1)$$

This model could provide a prompt decision on whether the diuretic was required in renography. By inputting the value of these 4 parameters to Equation 5.1, the physicians would be able to obtain the probability of 'no' and 'yes'. A higher probability of 'no' than 'yes' meant no diuretic was required as a kidney could be confirmed as unobstructed. On the other hand, a higher probability of 'yes' than 'no' meant diuretic was required as no decision could be made based on the first 10 min of the scanning.

5.4.2 Improving the accuracy of BSS by analyzing PRC

In order to avoid missing any positive case of obstruction, the cutoff point to make the decision based on the LR equation shown in Equation 5.1 was adjusted. This adjustment was decided based on the PRC of the model. First, the precisions and recalls of the model at different thresholds of probability were calculated. Then these pairs of precision-recall were plotted as shown in Fig 5.7.

Figure 5.7 PRC of BSS obtained by applying different thresholds of probability in providing the prediction of the need for diuretic.

To avoid having a false negative, the recall of the model needed to be kept at a value of 1. At the recall of 1, the best obtainable precision would be 0.59 which could be attained by setting the cutoff point for the probability of 'yes' at 1.23%. Any probability of 'yes' larger than this value would need to have diuretics injection while the probability of 'yes' smaller or equal to this value could be confirmed as unobstructed and did not need to proceed with diuretic injection or could even end the renography process.

5.4.3 Validation of BSS

To assess the performance of BSS in deciding the need for diuretic, 38 renogram samples without diuretics, which were not used in developing the LR model, were used as the validation dataset. The clinical evaluations of these samples were provided by nuclear medicine experts based on renogram, patient information, and history, as well as other scanning results. BSS was applied to

these renograms and the predictions were put in comparison to their clinical diagnosis in the confusion matrix in Table 5.2.

Table 5.2 Confusion matrix to assess the performance of BSS

Confusion Matrix		Prediction	
		No diuretic	Yes diuretic
Clinical interpretation	Unobstructed	21	8
	Obstructed	0	9

From the results, 21 out of 29 unobstructed kidneys were predicted as unobstructed by BSS. In the other words, more than two third of unobstructed samples could be confirmed solely based on the first 10 min of renogram using BSS. The rest of the 17 samples needed to have the diuretic injection. Out of them, 9 were really obstructed and 8 were unobstructed.

5.5 Summary

In this chapter, an attempted to develop a system for determining the need for diuretic in renography was carried out. A total of 38 parameters were analyzed. Similar parameters were grouped together and the best parameter in each group was tabulated and ranked based on the p -values. The most important parameter in separating the unobstructed and obstructed classes was found to be T_{max} . It was followed by $NORA_{10}$, $MeanCV_{10}$, and $MeanCV_{10}$ at the second, third and fourth place. BSS, an integrative system that combined these 4 parameters was created. The cutoff point of the probability of ‘yes’ in BSS was set to be 1.23% where any renogram that had a value of this probability lower or equal to this

cutoff could have omission of diuretic. In the verification of the performance of BSS, it was found that two third of the unobstructed samples in the validation dataset could be confirmed by BSS and could have omission of the diuretic injection. For the renogram samples in the validation dataset that were predicted as necessary to have a diuretic test, half of them were really obstructed based on the evaluation by the nuclear medicine experts. Thus, BSS was extremely useful to reduce the unnecessary injection of diuretics to the patients with unobstructed kidneys. For the patients that needed to proceed with diuretic injection, their full scanning renograms could be evaluated by using the proposed system in the next Chapter 6.

CHAPTER 6

RESULTS 3

BASIC INTEGRATIVE SYSTEM FOR DIAGNOSIS OF RENAL OBSTRUCTION

6.1 Introduction

Rather than using individual parameters in the diagnosis of renal obstruction, the combination of the parameters may provide better insight on the kidney functionality. By developing an LR model, a diagnosis system can be obtained where the parameters are integrated with weightage on each parameter. The objective of this chapter is to derive an LR model that can be used as a Basic Integrative System for Renal Obstruction (BISRO).

To develop BISRO, first, the parameters that are derivable from 25 min F+10 diuretic renograms were computed. Within similar parameters, the best performance parameter was determined based on their p -values in separating two distinct groups. Then parameters were ranked and used to create LR models for separating 2 classes (unobstructed and obstructed kidneys) and 3 classes (unobstructed, slightly obstructed and heavily obstructed kidneys). There were 132 renogram samples available for the analysis; 100 of them were used to create the LR models. The rest 32 samples were used in the last step to verify the performances of the models in differentiating kidney obstruction.

6.2 Derivation of Parameters

There were 59 parameters derivable from a full 25 min renogram. The parameters with their variances were grouped together and the best parameters among them were determined based on unpaired t -tests results.

6.2.1 Diuresis excretion index

DEI was used to assess renal obstruction by looking at the diuretic effect on a kidney. It measured the change of renogram slope before and after diuretic injection. The value of DEI on the renogram samples had been computed in Chapter 4. Unpaired t -tests were applied to evaluate the performance of this parameter as an indicator of renal obstruction. The p -value in separating unobstructed and obstructed classes was less than 0.05 and the p -value in further separating obstructed classes into slightly and heavily obstructed classes was 0.45. This parameter could separate the samples into 2 classes but not into 3 classes.

6.2.2 Differential renal function

DRF could be obtained by finding the ratio of the number of counts in a kidney in relative to the kidney at the other side. This value was highly dependent on the functionality of each kidney. Thus, it would not be an accurate parameter in determining renal obstruction. If both kidneys were obstructed, one of them could have a higher value of DRF because of the differences in the degree of obstruction. In addition, an unpaired t -test showed no significant difference was found between the unobstructed and obstructed classes in terms of statistical mean of DRF.

6.2.3 Half time and its variants

$T_{1/2,dec}$ referred to the time taken for the number of counts to drop to half of its peak value. Renogram with a shorter $T_{1/2,dec}$ could be an indicator of a smooth flow inside a kidney as the tracer could flow out of the kidney promptly. On the other hand, a longer $T_{1/2,dec}$ could be a sign that the tracer flow was blocked inside a kidney. Following were the derived $T_{1/2,dec}$ and several of its variants (the full derived values of these parameters could found in Appendix C.7):

- $T_{1/2,dec}$ or • $T_{6/10,dec}$ • $T_{8/10,dec}$
- $T_{5/10,dec}$ • $T_{7/10,dec}$ • $T_{9/10,dec}$

The parameters that determined time taken to reach the number of counts lower than that of the $T_{1/2,dec}$, such as $T_{1/10,dec}$, $T_{2/10,dec}$, $T_{3/10,dec}$, and $T_{4/10,dec}$, were not included because in most renograms, the number of counts never dropped to a level lower than half of the peak count especially in slightly or heavily obstructed kidney. Hence, these parameters could not be calculated in a lot of renogram samples or the number of derived values was too small for a statistical analysis.

After obtaining the values of these parameters, unpaired t -tests were done to assess their ability in differentiating the severity of renal obstruction. The results in form of p -values were plotted as shown in Fig 6.1. All of the parameters could separate the unobstructed and obstructed classes significantly with $p < 0.05$. The best parameter to be used to separate these 2 classes was $T_{7/10,dec}$. For a further division of obstructed into slightly and heavily obstructed classes, only 2

parameters, $T_{7/10,dec}$ and $T_{9/10,dec}$, could perform this separation with $p < 0.05$.

The best parameter that allowed determining the severity of obstruction was $T_{9/10,dec}$ that had a lower p -value between these 2 parameters.

Figure 6.1 The p -values of $T_{1/2,dec}$ and its variations derived from 25 min of renogram. Blue square markers represent the p -values for differentiating unobstructed and obstructed classes and red dot markers represent the p -values for further differentiation of obstructed class into slightly and heavily obstructed classes.

As described in Chapter 4, there were various ways to define $T_{1/2,dec}$. The above $T_{1/2,dec}$ and its variants were derived as the duration from the start of renogram to the time where the number of counts reached a certain fraction of the maximum value. Another way to define $T_{1/2,dec}$ was the duration between the T_{max} and time where the number of counts dropped to half of T_{max} . To distinguish this second approach from the previous $T_{1/2,dec}$, the half time

obtained from the second approach was denoted as $T_{1/2,dec(fp)}$. Using this second definition, the following parameters were calculated (the full derived values were shown in Appendix C.8):

- $T_{1/2,dec(fp)}$ or $T_{5/10,dec(fp)}$
- $T_{6/10,dec(fp)}$
- $T_{7/10,dec(fp)}$
- $T_{8/10,dec(fp)}$
- $T_{9/10,dec(fp)}$

Similar to the analysis of $T_{1/2,dec}$, t -tests were applied to $T_{1/2,dec(fp)}$ and its variants. The results were presented as a scatter plot as shown in Fig 6.2. The p -values of all 5 parameters were found to be lower than 0.05 in differentiating slightly and heavily obstructed classes, which meant they could separate the absence and presence of obstruction significantly. The parameter chosen to be used to determine renal obstruction was $T_{7/10,dec(fp)}$, which had the lowest p -value. The only parameter that could differentiate slightly and heavily obstructed kidneys significantly was $T_{1/2,dec(fp)}$.

Figure 6.2 The p -values of $T_{1/2,dec}(fp)$ and its variations derived from 25 min of renogram. Blue square markers represent the p -values for differentiating unobstructed and obstructed classes and red dot markers represent the p -values for further differentiation of obstructed class into slightly and heavily obstructed classes.

6.2.4 Lasix half time and its variants

$LT_{1/2,dec}$ was the time taken for the number of counts to fall to half of the value when the diuretic was injected. If the number of counts could drop to half of the value when the diuretic was injected in a short duration, it could mean the diuretic successfully induced fluid flow in a dilated kidney and the kidney was actually unobstructed. Similar to $T_{1/2,dec}$, there were several possible variants of $LT_{1/2,dec}$ could be derived from the renogram samples:

- $LT_{1/2,dec}$ or $LT_{5/10,dec}$
- $LT_{6/10,dec}$
- $LT_{7/10,dec}$
- $LT_{8/10,dec}$

- $LT_{9/10,dec}$

The values of these parameters in each renogram samples were calculated (the full list of the derived value could be found in Appendix C.9). The number of counts after diuretic injection was rarely dropped to more than that of $LT_{1/2,dec}$ within the rest of the scanning time after diuretic injection. Thus, $LT_{1/10,dec}$, $LT_{2/10,dec}$, $LT_{3/10,dec}$, and $LT_{4/10,dec}$ were hardly available in actually renography and were excluded from the analysis here.

Next, an assessment of the performances of using these parameters in differentiating renal obstruction was carried out by the application of unpaired t -tests. The p -values obtained were plotted in Fig 6.3. The means of $LT_{1/2,dec}$ and its variants were found to be able to differentiate unobstructed and obstructed classes. The best parameter among them was $LT_{9/10,dec}$, which had the lowest p -value. For further separation of obstructed class into unobstructed classes, the evaluations were done on all these 5 parameters, except $LT_{1/2,dec}$, as there was not sufficient data on $LT_{1/2,dec}$ of obstructed kidneys. Among the rest of the 4 parameters, the one that could differentiate slightly and heavily obstructed classes was $LT_{9/10,dec}$ and the rest of the parameters did not have a p -value lower than 0.05.

Figure 6.3 The p -values of $LT_{1/2,dec}$ and its variations derived from 25 min of renogram. Blue square markers represent the p -values for differentiating unobstructed and obstructed classes and red dot markers represent the p -values for further differentiation of obstructed class into slightly and heavily obstructed classes.

6.2.5 Normalized residual activity

$NORA_T$ was a normalized number of counts at time T to the number of counts at 2 min. The most common type of NORA used in literature was $NORA_{20}$. In this thesis, all formed of derivable NORA from 25 min renogram were assessed, i.e. from the $NORA_3$ (a ratio of number of counts at 3 min to the number of counts at 2 min) to $NORA_{25}$ (a ratio of number of counts at 25 min to the number of counts at 2 min). Following was the list of derived NORAs (the full list of the values calculated from all samples was tabulated in Appendices C.10-C.12):

• NORA ₃	• NORA ₁₁	• NORA ₁₉
• NORA ₄	• NORA ₁₂	• NORA ₂₀
• NORA ₅	• NORA ₁₃	• NORA ₂₁
• NORA ₆	• NORA ₁₄	• NORA ₂₂
• NORA ₇	• NORA ₁₅	• NORA ₂₃
• NORA ₈	• NORA ₁₆	• NORA ₂₄
• NORA ₉	• NORA ₁₇	• NORA ₂₅
• NORA ₁₀	• NORA ₁₈	

Unpaired *t*-tests were conducted on all of these parameters and the results were shown in Fig 6.4. Almost all of the parameters could differentiate the presence and absence of obstruction significantly. It could be observed from the Fig 6.4 that the parameters derived from a longer timing were able to separate the classes better. The only parameter that could not differentiate the presence of renal obstruction was NORA₄. For differentiating the severity of obstruction in slightly and heavily obstruction, 5 out of these 23 parameters could perform the task with a *p*-value lower than 0.05; i.e. NORA₆, NORA₂₂, NORA₂₃, NORA₂₄, and NORA₂₅. Among all these NORAs, the NORA₂₅ was the best parameter in differentiating unobstructed and obstructed as well as slightly and heavily obstructed.

Figure 6.4 p -values of NORAs derived from 25 min of renogram. Blue square markers represent the p -values for differentiating unobstructed and obstructed classes and red dot markers represent the p -values for further differentiation of obstructed class into slightly and heavily obstructed classes.

6.2.6 Time to peak and its variations

A set of these parameters was derived based on first 10 min of renogram for developing BSS in chapter 5. Using a similar concept, this set of parameters was derived from the full 25 min renogram. The parameters computed were:

- $T_{max/10}$
- $T_{5max/10}$
- $T_{9max/10}$
- $T_{2max/10}$
- $T_{6max/10}$
- T_{max}
- $T_{3max/10}$
- $T_{7max/10}$
- $T_{4max/10}$
- $T_{8max/10}$

The derived values of these parameters in renogram samples could be found in Appendix C.13. The p -values of these parameters obtained from unpaired t -tests were plotted in Fig 6.5. It was found that the parameters

$T_{6max/10}$ to T_{max} could separate the unobstructed and obstructed classes significantly. Within these 5 parameters, the one with the lowest p -value was $T_{9max/10}$. In differentiating the severity of obstruction, the last 3 parameters, $T_{8max/10}$, $T_{9max/10}$, and T_{max} , could separate the obstruction status into slightly and heavily obstructed groups significantly. The best parameter with the lowest p -value was T_{max} .

Figure 6.5 The p -values of T_{max} and its variants derived from 25 min of renogram. Blue square markers represent the p -values for differentiating unobstructed and obstructed classes and red dot markers represent the p -values for further differentiation of obstructed class into slightly and heavily obstructed classes.

6.2.7 Parameters related pre-void and post-void images

Pre-void and post-void images were usually taken as part of a renography procedure. These images provided information about kidney condition before and after voiding. It could be used to assess bladder condition as a full bladder might induce a false positive of diagnosis. The values of pre-void count (PrVC) and post-

void count (PoVC) of the renogram samples were tabulated in Appendix C.14. The mean of PrVC was able to differentiate unobstructed and obstructed classes ($p < 0.05$) but could not further divide the obstructed class into slightly and heavily obstructed ($p = 0.13$). On the other hand, the mean of PoVC had the ability to separate unobstructed and obstructed classes ($p < 0.05$) as well as slightly and heavily obstructed classes ($p = 0.02$).

To find the relative function before and after voiding, the ratio of PrVC to PoVC, $R_{pre/post}$, could be derived. No significant difference was found in the value of $R_{pre/post}$ between unobstructed and obstructed kidneys ($p = 0.41$). Other parameters that could be derived by using PrVC and PoVC were the normalization of them with respect to the maximum count. The $R_{pre/max}$ had a p -value less than 0.05 in the comparison of unobstructed and obstructed classes and $p = 0.11$ in the comparison between slightly and heavily obstructed classes. It indicated that $R_{pre/max}$ could perform well in determining the presence of obstructed but not in determining the severity of obstruction. A similar observation was found in $R_{post/max}$. It could differentiate unobstructed and obstructed classes ($p < 0.05$) but could not determine the severity of obstruction ($p = 0.07$). The form of NORA related to PoVC, $NORA_{post}$, was also assessed. This parameter had the potential to be used in the diagnosis of renal obstruction as it could differentiate both unobstructed and obstructed classes ($p < 0.05$), as well as slightly and heavily obstructed classes ($p < 0.05$). Fig 6.6 summarized the performance of the parameters related to pre-void and post-void images.

Figure 6.6 The p -values of parameters related to pre-void and post-void image derived from 25 min of renogram. Blue square markers represent the p -values for differentiating unobstructed and obstructed classes and red dot markers represent the p -values for further differentiation of obstructed class into slightly and heavily obstructed classes.

6.2.8 Other quantifiable parameters from renogram

There were other parameters derivable from renogram, which could also be the choices of parameters to develop BISRO, i.e. $R_{20/max}$, Lasix time to peak (LT_{max}), and peak count ($n_{c,peak}$) (the full list of the derived values of these parameters could be found in Appendix C.14). The p -values of these parameters were plotted in Fig 6.7. $R_{20/max}$ and LT_{max} had a p -value less than 0.05 in both separation of unobstructed and obstructed classes and separation of slightly and heavily obstructed classes. As the T_{max} was an important parameter in the diagnosis of renal obstruction, $n_{c,peak}$ could be a potential parameter for diagnosis of renal obstruction. Unfortunately, for separating the renal obstruction

status, this parameter had p -values larger than 0.05. Hence, $n_{c,peak}$ was not a suitable parameter to be used in developing BISRO.

Figure 6.7 The p -values of $R_{20/max}$, LT_{max} , and $n_{c,peak}$ derived from 25 min of renogram. Blue square markers represent the p -values for differentiating unobstructed and obstructed classes and red dot markers represent the p -values for further differentiation of obstructed class into slightly and heavily obstructed classes.

6.2.9 Ranking of parameters for developing a system that differentiates unobstructed and obstructed classes (2 classes)

Next, the p -values of all distinct parameters were compiled. For the parameter with a number of variants, only the best parameters among them were included. The p -values of them were used as references to rank the parameters and the ranking could be seen in Table 6.1. Among these parameters, the highest rank parameter was $NORA_{25}$. The last 3 parameters of the list could not be used

because the means of them were not able to differentiate between unobstructed and obstructed classes significantly.

Table 6.1 Ranking of parameters for developing a system that differentiate unobstructed and obstructed classes

Parameter	<i>p</i> -value	Rank
NORA ₂₅	2.62×10^{-29}	1
$R_{20/max}$	2.58×10^{-28}	2
$T_{7/10,dec}$	3.22×10^{-27}	3
$T_{7/10,dec(fp)}$	1.65×10^{-26}	4
$LT_{9/10,dec}$	1.04×10^{-16}	5
LT_{max}	1.40×10^{-14}	6
PoVC	3.03×10^{-14}	7
$T_{9max/10}$	1.28×10^{-13}	8
NORA _{post}	1.15×10^{-12}	9
$R_{post/max}$	2.45×10^{-6}	10
PrVC	1.24×10^{-5}	11
DEI	1.68×10^{-4}	12
$R_{pre/max}$	4.96×10^{-2}	13
DRF	6.26×10^{-2}	14
$n_{c,peak}$	1.22×10^{-1}	15
$R_{pre/post}$	4.12×10^{-1}	16

The number of parameters required to form an integrative system was decided by judging at the accuracy of diagnosis obtained from LR classifiers, which were built using different numbers of parameters starting from 1 to 14. The results were plotted as shown in Fig 6.8. Initially, as the number of parameters used increased, the overall accuracy of diagnosis increased. After a while, the

overall accuracy reached a plateau with any additional parameters included in the system did not affect the accuracy of diagnosis. As the number of parameters kept increasing, the overall accuracies started to drop due to too many parameters used that caused over-fitting of the system. So to integrate the parameters to form an LR model to differentiate a renal status into 2 classes; i) unobstructed, and ii) obstructed, 4 parameters should be integrated.

Figure 6.8 The overall accuracies of LR classifiers in differentiating renal obstruction status into 2 classes developed using different numbers of parameters.

6.2.10 Ranking of parameters for developing a system that differentiates unobstructed, slightly obstructed and heavily obstructed classes (3 classes)

Applying similar steps to the ranking of parameters for a system with 2 classes, parameters used to develop a system to differentiate renal obstruction status into 3 classes (unobstructed, slightly obstructed, and heavily obstructed) were ranked based on their p -values. There were two p -values evaluated for the means of each parameter. The first one was obtained by comparing the unobstructed and obstructed classes. The parameters must be able to determine

the presence or absence of obstruction before further they were further examined on their ability in determining the severity of obstruction. The second p -value was derived from the comparison of slightly and heavily obstructed classes. The ranking of parameters was determined based on this second p -value with a precondition that their first p -values must have a value smaller than 0.05. The compilation of the parameters with their p -values and ranks could be seen in Table 6.2. The top 9 of the parameters had both p -value that could differentiate the severity of obstruction, with the best parameter being LT_{max} that had the lowest p -value in separating slightly and heavily obstructed. Four parameters at rank 10 to 13 could determine the presence of an obstruction but failed to differentiate slightly and heavily obstructed kidneys. Last 3 parameters in the rank could not be used for diagnosis of renal obstruction as they have p -values larger than 0.05.

Table 6.2 Ranking of parameters for developing a system that can differentiate unobstructed, slightly obstructed, and heavily obstructed classes

Parameter	<i>p</i> -value (U vs O)	<i>p</i> -value (S vs H)	Rank
LT_{max}	1.40×10^{-14}	7.38×10^{-6}	1
T_{max}	1.76×10^{-7}	3.22×10^{-5}	2
$T_{9/10,dec}$	9.30×10^{-19}	3.84×10^{-3}	3
$LT_{9/10,dec}$	1.04×10^{-16}	5.31×10^{-3}	4
NORA ₂₅	2.62×10^{-29}	1.64×10^{-2}	5
$R_{20/max}$	2.58×10^{-28}	2.17×10^{-2}	6
PoVC	3.03×10^{-14}	2.37×10^{-2}	7
$T_{5/10,dec(fp)}$	1.05×10^{-13}	2.54×10^{-2}	8
NORA _{post}	1.15×10^{-12}	2.56×10^{-2}	9
$R_{post/max}$	2.45×10^{-6}	7.64×10^{-2}	10
$R_{pre/max}$	4.96×10^{-2}	1.14×10^{-1}	11
PrVC	1.24×10^{-5}	1.32×10^{-1}	12
DEI	1.68×10^{-4}	4.58×10^{-1}	13
DRF	6.26×10^{-2}	3.51×10^{-2}	14
$n_{c,peak}$	1.22×10^{-1}	6.18×10^{-1}	15
$R_{pre/post}$	4.12×10^{-1}	7.08×10^{-1}	16

Note: U: unobstructed; O: obstructed, S: slightly obstructed, H: heavily obstructed

After determining the ranking of parameters, the next step was to find out the numbers of parameters needed to create an MLR model. By using different numbers of parameters start from 1 parameter until all 9 potential parameters, the MLR classifiers were created. The overall accuracies calculated were plotted as shown in Fig 6.9. From the figure, it could be observed that the overall accuracies had an increasing trend up to the use of 5 parameters. Using more

than 5 parameters did not increase the overall accuracy of the model. Thus, for separating renal obstruction status into 3 classes, it was suggested to integrate the first 5 parameters.

Figure 6.9 The overall accuracies of MLR classifiers in differentiating renal obstruction status into 3 classes developed using different numbers of parameters.

6.3 Development of an Integrative System for Differentiating Renal Obstruction Status into 2 Classes

From section 6.2.9, it was found that 4 parameters should be used to develop the model for differentiating unobstructed and obstructed classes. These parameters were $NORA_{25}$, $R_{20/max}$, $T_{7/10,dec}$, and $T_{7/10,dec(fp)}$. Next, a model that could assist physicians in the diagnosis of renal obstruction clinically was developed.

6.3.1 Formation of a logistic regression model

An LR model was chosen as the system for diagnosis because it could be easily implemented where the clinicians would only need to input the value of the parameters into the equation. This prediction could be obtained using the existing renography instruments without a necessity to obtain new instruments. The LR model was built in MATLAB R2017b with 10 folds validation. The values of 4 chosen parameters derived from 100 25-min F+10 diuresis renograms were input as the features. The final expression of the LR equation obtained was shown in Equation (6.1).

$$\ln \left(\frac{P(\text{unobstructed})}{P(\text{obstructed})} \right) = 16.97 + 1.73\text{NORA}_{25} - 47.15R_{20/\max} + 0.86T_{7/10,dec} - 0.59T_{7/10,dec(fp)} \quad (6.1)$$

By using Equation (6.1), the probability of a renogram belonged to the unobstructed and obstructed class could be calculated. The highest probability would be the final decision of the model. Based on the training dataset, this model had an accuracy of 94.00%, a sensitivity of 90.63%, a specificity of 95.59% and an AUC of ROC of 0.95 as shown in the confusion matrix in Table 6.3.

Table 6.3 Confusion matrix to assess the developed LR model in differentiating renal obstruction status into 2 classes on the training dataset

Confusion Matrix		Prediction	
		Unobstructed	Obstructed
Clinical interpretation	Unobstructed	65	3
	Obstructed	3	29

6.3.2 Validation of model

Next, the accuracy of the developed model was tested using the 32 sample renograms as the validation dataset, which were not part of the samples that were used in building the model. First, the prediction of the renal obstruction status of these renograms was determined by the application of the model. Then it was compared with the clinical evaluations of the samples by certified nuclear medicine experts. The comparison was shown in a confusion matrix in Table 6.4. Based on the testing on validation dataset, the application of the model had an accuracy of 84.38%, a sensitivity of 90.00%, a specificity of 86.36% and an AUC of ROC of 0.86.

Table 6.4 Confusion matrix to assess the developed LR model in differentiating renal obstruction status into 2 classes on the validation dataset

Confusion Matrix		Prediction	
		Unobstructed	Obstructed
Clinical interpretation	Unobstructed	19	3
	Obstructed	1	9

6.4 Development of an Integrative System for Differentiating Renal Obstruction Status into 3 Classes

For differentiating renal obstruction status into unobstructed, slightly obstructed and heavily obstructed, 5 parameters should be used as suggested in the section 6.2.10. These parameters were LT_{max} , T_{max} , $T_{9/10,dec}$, $LT_{9/10,dec}$, and $NORA_{25}$. The values of these 5 parameters were calculated on 132 25-min F+10

diuresis renograms. 100 of them were used as a training dataset and the rest 32 of the samples were used as a validation dataset.

6.4.1 Formation of a logistic regression model

The model was built in MATLAB R2017b with 10 folds validation. The 5 chosen parameters were served as the feature. As an LR model was meant to create a binary classifier, MLR was applied. In MLR, there were 2 equations derived to predict diagnosis as shown in Equations (6.2) and (6.3).

$$\ln \left(\frac{P(\text{unobstructed})}{P(\text{heavily obstructed})} \right) = 20.18 - 1.19LT_{max} + 0.32T_{max} - 0.02T_{9/10,dec} - 0.79LT_{9/10,dec} - 10.73NORA_{25} \quad (6.2)$$

$$\ln \left(\frac{P(\text{slightly obstructed})}{P(\text{heavily obstructed})} \right) = 6.17 - 0.95LT_{max} - 0.17T_{max} + 0.04T_{9/10,dec} - 0.24LT_{9/10,dec} + 1.26NORA_{25} \quad (6.3)$$

The first equation was used to find the ratio of the probability of being an unobstructed kidney and the probability of being a heavily obstructed kidney and the second equation was used to find the ratio of the probability of being a slightly obstructed kidney and the probability of being a heavily obstructed kidney. The total probability of these 3 conditions was equal to 1. The class with the highest probability would be the outcome diagnosis of a renogram. Based on the training dataset, this model had an overall accuracy of 95.00% as shown in the confusion matrix in Table 6.5.

Table 6.5 Confusion matrix to assess the developed LR model in differentiating renal obstruction status into 3 classes on the training dataset

Confusion Matrix		Prediction		
		Unobstructed	Slightly obstructed	Heavily obstructed
Clinical interpretation	Unobstructed	67	1	0
	Slightly obstructed	1	11	1
	Heavily obstructed	1	1	17

6.4.2 Validation of model

The model for differentiating renal obstruction status into 3 classes was further verified using the validation dataset. First, by applying the model, the prediction of the samples could be obtained. Then it was compared with the clinical evaluations by certified nuclear medicine experts. The comparison was shown in a confusion matrix in Table 6.6. Based on the testing on validation dataset, the application of the developed MLR model had an overall accuracy of 71.88%.

Table 6.6 Confusion matrix to assess the developed LR model in differentiating renal obstruction status into 3 classes on the validation dataset

Confusion Matrix		Prediction		
		Unobstructed	Slightly Obstructed	Heavily Obstructed
Clinical interpretation	Unobstructed	18	2	2
	Slightly Obstructed	0	1	3
	Heavily Obstructed	0	2	4

6.5 Summary

This chapter described the development of 2 systems created in differentiating renal obstruction. A total of 59 parameters were evaluated on their ability to differentiate both unobstructed and obstructed classes as well as slightly and heavily obstructed classes. The first model was built for differentiating renal obstructed status into 2 classes. It used top 4 parameters, which were $NORA_{25}$, $R_{20/max}$, $T_{7/10,dec}$, and $T_{7/10,dec(fp)}$. Using these parameters as features, an integrative system was developed using an LR. This system had an accuracy of 84.38%, a sensitivity of 90.00%, a specificity of 86.36%, and an AUC of ROC of 0.86 based on the testing of validation dataset. This system was proposed as the Basic Integrative System – Renal Obstruction (BISRO). BISRO could provide a simple and fast evaluation of the presence or absence of an obstruction. The second system was created for the purpose of differentiating renal obstruction into 3 classes. Five parameters with highest p -values in separating slightly and heavily obstructed class were used as input features to create an MLR model. The application of this second system on the validation dataset showed an overall accuracy of 71.88%.

CHAPTER 7
RESULT 4
SEARCHING OF NEW PARAMETER:
NORMALIZED URINE FLOW RATE
AS A PHYSICAL PARAMETER OF RENAL OBSTRUCTION

7.1 Introduction

In the previous chapters, an analysis was done by the utilization of quantifiable parameters that existed in the literature. The uses of these parameters were suggested in the protocols proposed by several authors [35, 58, 67]. However, none of them has become a gold standard for diagnosis of renal obstruction. Low accuracy, high false positive rate, lack of physical implication, and absence of accepted benchmarks are some of the drawbacks. In addition, as shown in Chapter 6, the integrative system that takes into account the combination of them still does not be able to produce high accuracy diagnosis in differentiating renal status based on the severity of obstruction. Thus, a search for better quantitative parameters of renogram that can produce a high accuracy of diagnosis is crucial.

Chapter 7 explores the possibility to derive a parameter that can represent the physical flow rate in a kidney. In the presence of an obstruction, the flow rate in a kidney is expected to be lower than the flow rate in a healthy kidney. The new novel parameter is derived through the application of compartmental analysis to model the fluid transfer phenomena in a kidney. This model is a modified version of an initial model reported in a study by Loh et al [170]. The solution of the

model describes the renogram trend and the proposed parameter U/V_2 can be derived from this solution. The feasibility of using U/V_2 is then evaluated and presented. The reference values of U/V_2 for normal and disease ranges are proposed. In addition, the effects of age and gender on the parameter are assessed at the end of this chapter.

7.2 Compartmental Analysis to Model Renography

7.2.1 Two-compartmental model of the fluid flow path in renography

A two-compartmental model was applied to model the radioisotope flow in renography from the input into a body to the output from a kidney. These two compartments were illustrated in Fig 7.1. Two control volumes were used in the model; the first compartment represented the body (blood circulation), which received radioisotopes from an intravenous injection and passed on this tracer to a kidney and the second compartment represent the kidney that filtered the radioisotopes from the blood and removed it in form of urine into a urinary bladder.

Figure 7.1 Separation of two control volumes in analyzing tracer flow in a renography.

7.2.2 Governing equations derived from the compartmental model

Differential equations could be derived based on the conservation of mass from each of the control volume shown in Fig 7.1. The differential equation described the rate of change of mass (in this case the rate change of tracer count) accumulated in a compartment as a function of inflows and outflows. The rate of change of the number of counts in the first compartment was equal to the difference between the tracer input through injection and the tracer flow rate in the blood that would be filtered by a kidney, which could be written as Equation (7.1). The rate of change of the number of counts in the second compartment was equal to the difference between an input of tracer by filtration of blood and an output from a kidney in form of urine, which could be written as Equation (7.2).

$$\frac{dG_1}{dt} = -FC_1 + I(T) \quad (7.1)$$

$$\frac{dG_2}{dt} = FC_1 - C_2U(T) \quad (7.2)$$

where $G_1 = C_1V_1$ expressed the quantity of tracer in the first compartment and $G_2 = C_2V_2$ expressed the quantity of tracer in the second compartment.

As the kidney compliance was negligible, the volumes of chambers 1 and 2 were approximated to be constant. The Equations (7.1) and (7.2) could be written as Equations (7.3) and (7.4) respectively.

$$\begin{aligned} \frac{d(C_1V_1)}{dt} &= -FC_1 + I(T) \\ \frac{V_1dC_1}{dt} &= -FC_1 + I(T) \end{aligned} \quad (7.3)$$

$$\begin{aligned}\frac{d(C_2V_2)}{dt} &= FC_1 - UC_2 \\ \frac{V_2 dC_2}{dt} &= FC_1 - UC_2\end{aligned}\tag{7.4}$$

7.2.3 Solving the differential equations of the compartmental model

In order to obtain the rate of change of tracer concentration in a kidney, the Equations (7.3) and (7.4) were processed using algebraic rearrangement followed by Laplace transform. First, Equation (7.4) was differentiated with an assumption that the blood flow rate was constant. The differentiated equation was shown in Equation (7.5).

$$\frac{V_2 d^2 C_2}{dt^2} = F \frac{dC_1}{dt} - U \frac{dC_2}{dt}\tag{7.5}$$

To combine Equation (7.3) and (7.5), the Equation (7.3) was rearranged into a form shown in Equation (7.6).

$$\frac{dC_1}{dt} = \frac{I(T) - FC_1}{V_1}\tag{7.6}$$

Then it was substituted into Equation (7.5) and after simplification it became Equation (7.7).

$$\begin{aligned}\frac{V_2 d^2 C_2}{dt^2} &= F \left(\frac{I(T) - FC_1}{V_1} \right) - U \frac{dC_2}{dt} \\ \frac{V_2 d^2 C_2}{dt^2} &= F \left(\frac{I}{V_1} - \frac{FC_1}{V_1} \right) - U \frac{dC_2}{dt}\end{aligned}\tag{7.7}$$

Next, Equation (7.4) was rearranged into Equation (7.8) to be inserted into Equation (7.7).

$$FC_1 = \frac{V_2 dC_2}{dt} + UC_2\tag{7.8}$$

By, substituting it into Equation (7.8), Equation (7.9) was obtained.

$$\begin{aligned}\frac{V_2 d^2 C_2}{dt^2} &= F \left(\frac{I}{V_1} - \frac{V_2 \frac{dC_2}{dt} + UC_2}{V_1} \right) - U \frac{dC_2}{dt} \\ \frac{V_2 d^2 C_2}{dt^2} &= \left(\frac{F}{V_1} \right) I - \left(\frac{F}{V_1} \right) \left(V_2 \frac{dC_2}{dt} + UC_2 \right) - U \frac{dC_2}{dt} \\ \frac{V_2 d^2 C_2}{dt^2} &= \left(\frac{F}{V_1} \right) I - \frac{dC_2}{dt} \left(\frac{FV_2}{V_1} + U \right) - \left(\frac{FU}{V_1} \right) C_2\end{aligned}\quad (7.9)$$

A linear second order differential equation was derived from the two-compartmental model as presented in equation (7.9). To simplify this equation, Newton's notations for differentiation were applied where $\dot{C}$ was used to represent $\frac{dC_2}{dt}$ and $\ddot{C}$ was used to represent $\frac{d^2 C_2}{dt^2}$. As the Equation (7.9) only left with concentration of second compartment C_2 , which was the focus of the derivation, from this step onwards the C_2 was written as simply C . Based on this notation, Equation (7.9) could be rewritten as Equation (7.10).

$$V_2 \ddot{C} = \left(\frac{F}{V_1} \right) I - \dot{C} \left(\frac{FV_2}{V_1} + U \right) - \left(\frac{FU}{V_1} \right) C \quad (7.10)$$

The indices showed in the following Equations (7.11) and (7.12) were used to further reduce the complexity of Equation (7.10) into a form written in Equation (7.13)

$$\beta = \left(\frac{FV_2}{V_1} + U \right) \quad (7.11)$$

$$\gamma = \left(\frac{FU}{V_1} \right) \quad (7.12)$$

$$V_2 \ddot{C} + \beta \dot{C} + \gamma C = \left(\frac{F}{V_1} \right) I \quad (7.13)$$

The equation (7.13) was a standard form of a linear second order ordinary differential equation. The solution of this differential equation could be obtained by applying Laplace transform. The input function was modeled as a bolus injection where the tracer was injected at certain dose in infinitesimal time. Using bolus injection as input function was also suggested by Coffey in his study attempted to model the renography using one-compartmental model [171]. The bolus injection could be written as an impulse function $\delta(t)$ and the Laplace transform of it was 1. Then using the Laplace transform in Equations (3.16) and (3.17), the Equation (7.13) could be transformed into Equation (7.14).

$$\begin{aligned}
 L\{V_2\ddot{C} + \beta\dot{C} + \gamma C\} &= L\left\{\left(\frac{F}{V_1}\right)I\right\} \\
 V_2[s^2C(s) - sC(0) - \dot{C}(0)] + \beta[sC(s) - C(0)] \\
 + \gamma C(0) &= \frac{F}{V_1}
 \end{aligned}
 \tag{7.14}$$

As there was no tracer inside the body before renography, the initial conditions were set to be zero, where $C(0) = 0$ and $\dot{C}(0) = 0$. Substituting these initial conditions and doing some rearrangement, the equation for the concentration of tracer could be obtained as written in Equation (7.15).

$$\begin{aligned}
 (V_2s^2 + \beta s + \gamma)C(s) &= \frac{F}{V_1} \\
 C(s) &= \left(\frac{F}{V_1}\right) \frac{1}{V_2s^2 + \beta s + \gamma} \\
 C(s) &= \left(\frac{F}{V_1V_2}\right) \frac{1}{s^2 + \frac{\beta}{V_2}s + \frac{\gamma}{V_2}}
 \end{aligned}
 \tag{7.15}$$

The behavior of a system could be determined based on its characteristic equation. The concentration function in Equation (7.15) has a characteristic equation expressed in Equation (7.16).

$$s^2 + \frac{\beta}{V_2}s + \frac{\gamma}{V_2} = 0 \quad (7.16)$$

Based on Equation (7.16), there would be 3 possible response functions of a tracer flow. It could be under-damped, over-damped, or critically damped depending on the square root of the characteristic equation, Equation (7.17).

$$s = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

$$s = \frac{-\frac{\beta}{V_2} \pm \sqrt{\left(\frac{\beta}{V_2}\right)^2 - 4(1)\left(\frac{\gamma}{V_2}\right)}}{2(1)}$$

$$s = -\frac{\beta}{2V_2} \pm \sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}} \quad (7.17)$$

7.2.3 Classification of physiological behaviors of a kidney

Based on the solution of the compartmental modeling of a kidney, the physiological behaviors of a kidney could be classified into 3 conditions: under-damped, over-damped and critically damped.

Condition 1: Under-damped behavior

The under-damped behavior happened when:

$$\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2} < 0$$

There were two square roots of the characteristic equation as shown in Equations (7.18a) and (7.18b).

$$s_1 = -\frac{\beta}{2V_2} + i \sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}} \quad (7.18a)$$

$$s_2 = -\frac{\beta}{2V_2} - i \sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}} \quad (7.18b)$$

These 2 equations were substituted back to factorize Equation (7.15) and modify it into a concentration function for an under-damped behavior as presented in Equation (7.19).

$$\begin{aligned} C(s) &= \left(\frac{F}{V_1 V_2} \right) \frac{1}{(s - s_1)(s - s_2)} \\ C(s) &= \left(\frac{F}{V_1 V_2} \right) \frac{1}{\left(s - \left(-\frac{\beta}{2V_2} + i \sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}} \right) \right) \left(s - \left(-\frac{\beta}{2V_2} - i \sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}} \right) \right)} \\ C(s) &= \left(\frac{F}{V_1 V_2} \right) \frac{1}{\left(s + \frac{\beta}{2V_2} \right)^2 - \left(i \sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}} \right)^2} \\ C(s) &= \left(\frac{F}{V_1 V_2} \right) \frac{1}{\left(s + \frac{\beta}{2V_2} \right)^2 + \left(\sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}} \right)^2} \end{aligned} \quad (7.19)$$

After getting the expression of $C(s)$, it had to be transformed back to $C(T)$ in order to obtain the solution in the original space. Using the inverse Laplace transform formula presented in Equation (7.20) (detailed derivation of this

Equation could be found in Appendix C Equation (C.3), the expression of C in T space could be derived as shown in Equation (7.21).

$$L^{-1}\left(\frac{1}{(s+a)^2 + \omega^2}\right) = \frac{e^{-aT} \sin \omega T}{\omega} \quad (7.20)$$

$$C(T) = \left(\frac{F}{V_1 V_2}\right) \frac{1}{\sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}}} e^{-\frac{\beta}{2V_2}T} \sin\left(\sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}} T\right) \quad (7.21)$$

By multiplying the volume to the concentration, a mathematical expression for the number of tracers that could represent a renogram in an under-damped condition could be written as Equation (7.22).

$$G_2(T) = C(T)V_2$$

$$G_2(T) = V_2 \left(\frac{F}{V_1 V_2}\right) \frac{1}{\sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}}} e^{-\frac{\beta}{2V_2}T} \sin\left(\sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}} T\right)$$

$$G_2(T) = a_1 e^{-bT} \sin c_1 T \quad (7.22)$$

where

$$a_1 = \frac{F}{V_1 c_1} \quad (7.23)$$

$$b = \frac{\beta}{2V_2} \quad (7.24)$$

$$c_1 = \sqrt{\frac{\gamma}{V_2} - \frac{\beta^2}{4V_2^2}} \quad (7.25)$$

The coefficients a_1 , b , and c_1 showed in Equations (7.23), (7.24), and (7.25) could be determined through curve fitting of a renogram using the under-damped solution, Equation (7.22).

Condition 2: Over-damped behavior

The over-damped behavior happened when:

$$\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2} > 0$$

There were two square roots of the characteristic equation as shown in Equations (7.26a) and (7.26b).

$$s_1 = -\frac{\beta}{2V_2} + \sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}} \quad (7.26a)$$

$$s_2 = -\frac{\beta}{2V_2} - \sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}} \quad (7.26b)$$

These 2 equations were substituted back to factorize Equation (7.15) and modify it into a concentration function for an over-damped behavior as presented in Equation (7.27).

$$\begin{aligned} C(s) &= \left(\frac{F}{V_1 V_2} \right) \frac{1}{(s - s_1)(s - s_2)} \\ C(s) &= \left(\frac{F}{V_1 V_2} \right) \frac{1}{\left(s - \left(-\frac{\beta}{2V_2} + \sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}} \right) \right) \left(s - \left(-\frac{\beta}{2V_2} - \sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}} \right) \right)} \end{aligned}$$

$$C(s) = \left(\frac{F}{V_1 V_2} \right) \frac{1}{\left(s + \frac{\beta}{2V_2} \right)^2 - \left(\sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}} \right)^2} \quad (7.27)$$

After getting the expression of $C(s)$, it had to be transformed back to $C(T)$ in order to obtain the solution in the original space. Using the inverse Laplace transform formula presented in Equation (7.28) (detailed derivation of this Equation could be found in Appendix C Equation (C.4), the expression of C in T space could be derived as shown in Equation (7.29).

$$L^{-1}\left(\frac{1}{(s+a)^2 - \omega^2}\right) = \frac{e^{-aT} \sinh \omega T}{\omega} \quad (7.28)$$

$$C(T) = \left(\frac{F}{V_1 V_2} \right) \frac{1}{\sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}}} e^{-\frac{\beta}{2V_2}T} \sinh \left(\sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}} T \right) \quad (7.29)$$

By multiplying the volume to the concentration, a mathematical expression for the number of tracers that could represent a renogram in an over-damped condition could be written as Equation (7.30).

$$G_2(T) = C(T)V_2$$

$$G_2(T) = V_2 \left(\frac{F}{V_1 V_2} \right) \frac{1}{\sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}}} e^{-\frac{\beta}{2V_2}T} \sinh \left(\sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}} T \right)$$

$$G_2(T) = a_2 e^{-bT} \sinh c_2 T \quad (7.30)$$

where

$$a_2 = \frac{F}{V_1 c_2} \quad (7.31)$$

$$b = \frac{\beta}{2V_2} \quad (7.32)$$

$$c_2 = \sqrt{\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2}} \quad (7.33)$$

The coefficients a_2 , b , and c_2 showed in Equations (7.31), (7.32), and (7.33) could be determined through curve fitting of a renogram using the over-damped solution, Equation (7.30).

Condition 3: Critically damped behavior

The critically damped behavior happened when:

$$\frac{\beta^2}{4V_2^2} - \frac{\gamma}{V_2} = 0$$

There were two square roots of the characteristic equation as shown in Equations (7.34)

$$s_1 = s_2 = -\frac{\beta}{2V_2} \quad (7.34)$$

These 2 equations were substituted back to factorize Equation (7.15) and modify it into a concentration function for a critically damped behavior as presented in Equation (7.35).

$$C(s) = \left(\frac{F}{V_1 V_2}\right) \frac{1}{(s - s_1)(s - s_2)}$$

$$C(s) = \left(\frac{F}{V_1 V_2}\right) \frac{1}{\left(s - \left(-\frac{\beta}{2V_2}\right)\right)^2} \quad (7.35)$$

After getting the expression of $C(s)$, it had to be transformed back to $C(T)$ in order to obtain the solution in the original space. Using the inverse Laplace

transform formula presented in Equation (7.36) (detailed derivation of this Equation could be found in Appendix C Equation (C.5), the expression of C in T space could be derived as shown in Equation (7.37).

$$L^{-1}\left(\frac{1}{(s-a)^2}\right) = Te^{aT} \quad (7.36)$$

$$C(T) = \left(\frac{F}{V_1 V_2}\right) Te^{-\frac{\beta}{2V_2}T} \quad (7.37)$$

By multiplying the volume to the concentration, a mathematical expression for the number of tracers that could represent a renogram in a critically damped condition could be written as Equation (7.38).

$$\begin{aligned} G_2(T) &= C(T)V_2 \\ G_2(T) &= V_2 \left(\frac{F}{V_1 V_2}\right) Te^{-\frac{\beta}{2V_2}T} \\ G_2(T) &= aTe^{-bT} \end{aligned} \quad (7.38)$$

where

$$a_3 = \frac{F}{V_1} \quad (7.39)$$

$$b = \frac{\beta}{2V_2} \quad (7.40)$$

The coefficients a_3 and b showed in Equations (7.39), and (7.40) could be determined through curve fitting of a renogram using the critically damped solution, Equation (7.38).

7.3 Application of Compartmental Analysis Solutions on Renograms

The renogram samples obtained from a hospital were re-digitalized and normalized in the MATLAB. The curve fitting function in MATLAB was applied to fit the solutions of the compartmental analysis to these renograms. For each kidney, 3 possible conditions were applied in order to determine which solutions could match a renogram well. Using the sample ID no 1 as an example, the curve fitting using different conditions were fitted into the renogram as illustrated in Fig 7.2.

Figure 7.2 Curve fitting of 3 different solutions of compartmental modeling on a renogram sample: (a) under-damped condition, (b) over-damped condition, and (c) critically damped condition.

By comparing these 3 plots through visual interpretation, the over-damped solution seemed to fit the best. To have a more objective way of determining the best-fit curve, the goodness of fit, R^2 was applied. A higher the value of R^2 indicated a better fitting of the model on a renogram. The goodness of fit was evaluated in renogram samples of patient 1-10 (20 kidneys) and the results were tabulated in Table 7.1. Table 7.1 showed the best condition to represent the real renogram based on the errors analysis was the over-damped solution in all the samples.

Table 7.1 The best model solution to fit renograms based on R^2

Patient ID No	Kidney	Condition	R^2	Best fit curve
1	Right	Under-damped	0.549	Over-damped
		Over-damped	0.878	
		Critically damped	0.601	
	Left	Under-damped	0.888	
		Over-damped	0.970	
		Critically damped	0.884	
2	Right	Under-damped	0.933	Over-damped
		Over-damped	0.946	
		Critically damped	0.937	
	Left	Under-damped	0.949	
		Over-damped	0.956	
		Critically damped	0.949	
3	Right	Under-damped	0.296	Over-damped
		Over-damped	0.800	
		Critically damped	0.334	
	Left	Under-damped	0.027	
		Over-damped		

		Over-damped	0.775	
		Critically damped	0.047	
		Under-damped	0.585	
4	Right	Over-damped	0.940	Over-damped
		Critically damped	0.796	
		Under-damped	0.945	
	Left	Over-damped	0.957	Over-damped
		Critically damped	0.946	
		Under-damped	0.708	
5	Right	Over-damped	0.927	Over-damped
		Critically damped	0.709	
		Under-damped	0.694	
	Left	Over-damped	0.971	Over-damped
		Critically damped	0.694	
		Under-damped	0.674	
6	Right	Over-damped	0.946	Over-damped
		Critically damped	0.762	
		Under-damped	0.683	
	Left	Over-damped	0.889	Over-damped
		Critically damped	0.747	
		Under-damped	0.425	
7	Right	Over-damped	0.974	Over-damped
		Critically damped	0.426	
		Under-damped	0.318	
	Left	Over-damped	0.920	Over-damped
		Critically damped	0.878	
		Under-damped	0.860	
8	Right	Over-damped	0.906	Over-damped
		Critically damped	0.871	
		Under-damped	0.083	
	Left	Under-damped	0.083	Over-damped

9	Right	Over-damped	0.852	Over-damped
		Critically damped	0.084	
		Under-damped	0.868	
		Over-damped	0.925	
		Critically damped	0.879	
		Under-damped	0.753	
	Left	Over-damped	0.956	Over-damped
		Critically damped	0.753	
		Under-damped	0.756	
		Over-damped	0.917	
10	Right	Critically damped	0.818	Over-damped
		Under-damped	0.562	
		Over-damped	0.952	
	Left	Critically damped	0.563	Over-damped
		Under-damped	0.562	

7.4 Derivation of Physical Parameter: U/V_2

From the curve fitting process, the coefficients of the compartmental analysis solution could be obtained. Next, using these coefficients, a new parameter proposed to be an index in differentiating renal obstruction could be derived. The parameter was a normalized urine flow rate with respect to the volume of the compartment, U/V_2 .

7.4.1 Formulation of urine volumetric flow rate

To compute the U/V_2 , some algebraic rearrangements were carried out. As presented in section 7.3, the best condition to fit a renogram was found to be over-damped. The expression of the compartmental solution for an over-damped system was shown in Equation (7.30). The coefficients a_2 , b , and c_2 were obtained

from the curve fitting (the full list of the values of these coefficients could be found in Appendix C.15). Combining Equations (7.32) and (7.33), Equation (7.41) was formed.

$$c_2^2 = b^2 - \frac{\gamma}{V_2} \quad (7.41)$$

After that, Equation (7.12) could be substituted into Equation (7.41).

$$c_2^2 = b^2 - \frac{FU}{V_1 V_2}$$

$$c_2 = \frac{b^2}{c_2} - \left(\frac{F}{V_1 c_2} \right) \frac{U}{V_2} \quad (7.42)$$

Finally, by substituting Equation (7.31) into Equation (7.42), the expression U/V_2 as a function of a_2 , b , and c_2 was obtained as written in Equation (7.43).

$$c_2 = \frac{b^2}{c_2} - a_2 \frac{U}{V_2}$$

$$\frac{U}{V_2} = \frac{b^2 - c_2^2}{a_2 c_2} \quad (7.43)$$

7.4.2 Evaluation of U/V_2 as a potential parameter in differentiating renal obstruction

By using Equation (7.43), the values of U/V_2 on all renogram samples were derived (the full list can be seen in Appendix C.15). The potentiality of using this parameter as an indicator of renal obstructed was evaluated by comparing the trend of U/V_2 and the diagnosis of renograms by certified nuclear medicine experts as shown in Fig 7.3. Intuitively, a high value of U/V_2 indicated a faster flow rate and it signified an unobstructed or less obstructed kidney. On the other hand, a low value of the parameter indicated a slower flow rate, which implied a

presence of an obstruction in a renal flow. From Fig 7.3, it could be observed that higher values of U/V_2 corresponded to the diagnosis of being unobstructed kidneys, intermediate values corresponded to the diagnosis of being slightly obstructed kidneys and lower values were associated with the diagnosis of being heavily obstructed kidneys. Thus, this flow parameter developed from the compartmental analysis indeed represented the transport phenomena of the injected radioisotopes and it could be used as an index to differentiate the severity of renal obstruction.

Figure 7.3 The distribution of U/V_2 calculated from renogram samples. The shape of the points indicates the diagnosis obtained from certified nuclear medicine experts. Red triangles represent unobstructed kidneys, yellow squares represent slightly obstructed kidneys and green diamonds represent heavily obstructed kidneys. The bar shows the range of U/V_2 .

7.5 Ranges of U/V_2 Values for Diagnosis

To study the ranges of U/V_2 values in both unobstructed and obstructed classes, a statistical analysis was carried out. The statistics of U/V_2 were computed and tabulated in Table 7.2. The means of U/V_2 were $1.24 \times 10^{-3} \pm 4.07 \times 10^{-4}$ 1/s in unobstructed kidneys and $1.44 \times 10^{-4} \pm 2.81 \times 10^{-4}$ 1/s in obstructed

kidneys. An unpaired t -test showed an extremely significant difference between the unobstructed and obstructed classes in terms of statistical mean of U/V_2 .

Table 7.2 Statistics of U/V_2 (in 1/s) in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
Unobstructed	90	1.24×10^{-3}	4.07×10^{-4}	4.89×10^{-4}	6.42×10^{-4}	1.90×10^{-3}	2.09×10^{-3}
Obstructed	42	1.44×10^{-4}	2.81×10^{-4}	-5.70×10^{-4}	-2.86×10^{-4}	4.89×10^{-4}	5.52×10^{-4}

Note: Extremely significant differences were found between unobstructed and obstructed kidneys in U/V_2 ($p < 0.0001$).

To simply determine the presence or absence of renal obstruction, the value of the parameter for separating the unobstructed and obstruction classes was 6.30×10^{-4} 1/s (Table 7.3).

Table 7.3 Reference ranges of U/V_2 (in 1/s) for diagnosis of renal obstruction

Index value	Kidney status
$> 6.30 \times 10^{-4}$	Unobstructed
$\leq 6.30 \times 10^{-4}$	Obstructed

The confusion matrix obtained by using the proposed cutoff point in Table 7.3 in the diagnosis on the renogram samples was tabulated in Table 7.4. The reference ranges successfully diagnosed the presence of an obstruction in all obstructed kidneys (42/42) while it was able to determine 96% (86/90) of unobstructed kidneys.

Table 7.4 Confusion matrix to assess the performance of the proposed reference ranges of U/V_2 in the diagnosis of renal obstruction on sample renograms

Confusion Matrix		Prediction	
		Unobstructed	Obstructed
Clinical interpretation	Unobstructed	86	4
	Obstructed	0	42

7.6 Effect of Age and Gender on U/V_2

By dividing the renogram samples into gender groups, the means of U/V_2 were $1.22 \times 10^{-3} \pm 3.61 \times 10^{-4}$ 1/s and $1.25 \times 10^{-3} \pm 4.92 \times 10^{-4}$ 1/s in unobstructed kidneys of men and women gender groups respectively and $1.37 \times 10^{-4} \pm 2.86 \times 10^{-4}$ 1/s and $1.19 \times 10^{-4} \pm 2.92 \times 10^{-4}$ 1/s in obstructed kidneys of men and women groups respectively (Fig 7.4(a)). No significant difference was seen in U/V_2 between men and women in both unobstructed ($p = 0.75$) and obstructed classes ($p = 0.85$). For different age groups, the means of U/V_2 were $8.78 \times 10^{-4} \pm 6.49 \times 10^{-4}$ 1/s and $7.29 \times 10^{-4} \pm 6.33 \times 10^{-4}$ 1/s in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and $1.13 \times 10^{-3} \pm 4.58 \times 10^{-4}$ 1/s and $8.25 \times 10^{-4} \pm 7.35 \times 10^{-4}$ 1/s in obstructed kidney of the younger and older populations respectively (Fig 7.4(b)). There was no significant difference between the younger and older populations in the unobstructed ($p = 0.29$) and obstructed classes ($p = 0.13$).

Figure 7.4 The distribution of U/V_2 in different gender groups (a) and different age groups (b).

7.7 Summary

The aim of this chapter was to derive a parameter that could represent the physical flow rate in a kidney. In order to achieve that, first, a two-compartmental analysis was applied to model the radioisotope flow in the body. From this modeling, a linear second order differential equation was obtained. The solution obtained from the equation through the application of Laplace transform showed that there were 3 possible conditions of the flow in a kidney: under-damped,

over-damped, and critically damped. The over-damped condition was found to be the best solution to fit a renogram. By applying the over-damped solution to a renogram, a volumetric flow rate parameter was obtained. It was a normalized urine flow rate over the volume of a kidney U/V_2 , which was the proposed parameter to be a new novel indicator of renal obstruction. From the distribution of U/V_2 derived from all renograms, it was found that a high value of it indicated the absence of an obstruction and in contrast, a low value of it indicated the presence of an obstruction. The cutoff point in separating unobstructed and obstructed classes was found to be 6.3×10^{-4} 1/s. In addition, the effect of age and gender were evaluated and it was found that U/V_2 was not significantly influenced by both age and gender.

CHAPTER 8
RESULT 5
SEARCHING OF NEW PARAMETER:
MEAN COUNT VALUE AND MEDIAN COUNT VALUE
AS STATISTICAL PARAMETERS OF RENAL OBSTRUCTION

8.1 Introduction

In Chapter 7, a physical parameter U/V_2 was proposed to be a new indicator of renal obstruction. As a continuation of the effort in finding new quantifiable parameters from renogram, Chapter 8 presents important yet simple statistical parameters which are also promising indicators of renal obstruction. These parameters are the mean count value (MeanCV) and median count value (MedianCV). They are easy to be derived but never explored in any studies in the literature. The MeanCVs and MedianCVs of standard 25-min renograms are derived and evaluated. To improve the performance of these parameters, a compartmental model is applied to extrapolate the renogram. From the extended renogram, variants of both MeanCV and MedianCV are derived and the best parameters for each of them are deduced. Then reference values of the best MeanCV and MedianCV for normal and disease ranges are presented. In addition, the effects of age and gender on them are assessed at the end of this chapter.

8.2 Derivation of Statistical Parameters: Basic MeanCV and MedianCV

Basic MeanCV and MedianCV referred to the MeanCV₂₅ and MedianCV₂₅ calculated from standard 25 min F+10 renogram. The parameters were computed from 132 re-digitalized renograms (the full list of the computed values could be found in Appendix C.16). The calculated values were laid out as scatter plots and marked according to their diagnosis by certified nuclear medicine doctors as shown in Fig 8.1. As demonstrated in scatter plots, the Basic MeanCV (Fig 8.1(a)) and Median CV (Fig 8.1(b)) could successfully separate the samples into unobstructed and obstructed classes. The scatter plots clearly indicated the potentiality of using these parameters as indices in differentiating renal obstruction. However, in determining the severity of obstruction, both of the parameters could not differentiate the slightly and heavily obstructed classes.

Figure 8.1 The scatter plots of MeanCV₂₅ (a) and MedianCV₂₅ (b) derived from renograms. The color and shape of points represent their clinical diagnosis; i.e. green triangles represent unobstructed kidneys, blue diamonds represent slightly obstructed kidneys, and red squares represent heavily obstructed kidneys.

8.3 Optimization of MeanCV and MedianCV

8.3.1 Compartmental modeling for extrapolation of renograms

To improve the accuracies of basic MeanCV and MedianCV in predicting the severity of renal obstruction, modification of the means in deriving both parameters was carried out. It was done by application of the over-damped solution derived from compartmental analysis in Chapter 7. Equation (7.30) was used to curve-fit all renogram samples. The best-fitted curve of each renogram was used to derive modified MeanCV and MedianCV for a duration longer than 25 min.

Using the curve-fitting solution, the number of counts of a renogram was estimated for 10 different durations of renogram, from a duration of 10 min up to 100 min with a step increase of 10 min. The MeanCV and MedianCV were

calculated for each of the duration (the full list of the derived variants of MeanCV and MedianCV were tabulated in Appendices C.17 and C.18 respectively). Then, these parameters were tested on their ability to create significant differences in separating renogram samples into 3 classes. The derived MeanCVs and MedianCVs of different durations were plotted as scatter plots in Fig 8.2(a) and (b) respectively. For MeanCV, different classes of renal obstruction could not be separated among the renogram samples with a duration of 10 min (Fig 8.2(a)). Different classes started to differentiate from each other and cluster into three separate regions as duration increased beyond 10 min. These plots signified that the MeanCV could be an effective indicator of renal obstruction when it was derived from a renogram with a longer duration. Similarly, the MedianCV calculated from renograms with a longer duration performed better in separating the samples into different classes based on the severity of renal obstruction (Fig 8.2(b)).

Figure 8.2 The scatter plots of extended MeanCVs (a) and MedianCVs (b) derived from 132 renograms for 10 different durations; i.e. starting from 10 to 100 min.

The MedianCV tended to have a value close to 0 for an unobstructed kidney and a value close to 1 for a heavily obstructed kidney. On the other hand, the MeanCV had more variation of its value in both unobstructed and heavily obstructed kidneys. Consequently, the MedianCV could create a diagnosis of renal obstruction with a high level of confidence as compared to MeanCV. However, as a tradeoff, the MedianCV could not indicate the severity level of renal obstruction clearly as the values were clustered closely together for each of the classes. Hence, the MeanCV could provide a better insight into the relative severity level of renal obstruction.

8.3.2 Performance evaluation of the variants of MeanCV and MedianCV

Next, the ability of the extended MeanCVs derived from renogram with different durations in differentiating the severity of obstruction was studied by using unpaired *t*-tests. The *t*-tests were carried out in two stages – (1) the first stage was to check if the parameter could separate unobstructed and obstructed classes significantly and (2) the second stage was to further split the obstructed classes into slightly and heavily obstructed classes. The results of the unpaired *t*-tests on MeanCVs derived from different durations of renogram were plotted in Fig 8.3(a). Similarly, unpaired *t*-tests were also applied on the MedianCVs to determine the duration of renogram to derive this parameter that could separate the classes. The results were plotted in Fig 8.3(b).

(a) Mean count value

Figure 8.3 Unpaired t-tests applied on MeanCVs (a) and MedianCVs (b) in order to examine the durations of renogram to derive these parameters that can differentiate renal obstruction into 3 classes significantly.

Based on unpaired t -tests results (Fig 8.3(a)), the MeanCV was able to differentiate unobstructed and obstructed classes significantly in renograms with a duration of 20 min and longer, and it was able to differentiate slightly and heavily obstructed classes in renograms with duration of 30 min and longer. Using the same analysis, the duration of renogram for deriving MedianCV that could separate the samples into three renal obstruction classes was determined. Results showed that renograms with a duration of 10 min or longer were able to be used to derive MedianCV that could separate unobstructed and obstructed classes significantly and renograms with a duration of 30 min or longer could be used to derive MedianCV that could further separate the samples into slightly and heavily obstructed classes significantly (Fig 8.3(b)).

8.3.3 Selection of the best variants of MeanCV and MedianCV

Next, MLC was applied to determine the best variants of MeanCV and MedianCV as indicators of renal obstruction. It predicted the renal obstruction status of the renograms based on a train model developed using the parameter. By comparing the prediction with the true diagnosis, the accuracies of each classifier and their ROC curves were obtained. The overall accuracies and AUCs of ROC of the MeanCV and MedianCV derived from renograms with duration of 10 to 100 min were plotted in Fig 8.4. The trend of the overall accuracies of the classifiers developed using MeanCV as a renal obstruction indicator was shown in Fig 8.4(a) left panel. Data suggested that the curve increased initially and after reaching a certain point, it stayed in a steady state where there were only slight

changes in the overall accuracy as the duration of renogram increased. This plateau started around MeanCV₅₀. The AUCs of ROC also improved as the duration of renogram was extended and reached steady states around MeanCV₄₀ as illustrated in Fig 8.4(a) right panel. Based on these observations, the recommended duration of renogram for deriving MeanCV as an indicator of renal obstruction was 50 min. Similar trends were observed for the overall accuracies and AUCs of ROC of classifiers developed using MedianCV as shown in Fig 8.4(b). The accuracy reached a plateau at MedianCV₆₀ while the ROC showed no improvement after the MedianCV₄₀. Based on these observations, in order to use MedianCV as an indicator of renal obstruction, the recommended duration of renogram for deriving MedianCV was 60 min.

Figure 8.4 Overall accuracies and AUCs of ROC of the classifiers developed using MeanCV (a) and MedianCV (b) derived from renograms with duration of 10 to 100 min. AUCs of ROC are based on 3 scenarios; i.e. a blue circle-dot line consists of AUCs of ROC of classifiers where the unobstructed class is set as the positive class, a red diamond-dot line consists of AUCs of ROC of classifiers where the slightly obstructed class is set as the positive class, and a green triangle-dot line consists of AUCs of ROC of classifier where the heavily obstructed class is set as the positive class.

8.4 Ranges of MeanCV₅₀ and MedianCV₆₀ Values for Diagnosis

The statistics of the proposed statistical parameters were computed and tabulated in Table 8.1. The means of MeanCV₅₀ were 0.29 ± 0.10 in unobstructed kidneys and 0.74 ± 0.13 in obstructed kidneys. An unpaired *t*-test showed an extremely significant difference between the unobstructed and obstructed classes

in terms of statistical mean of MeanCV₅₀. Next, the means of MedianCV₆₀ were 0.12 ± 0.10 in unobstructed kidneys and 0.73 ± 0.20 in obstructed kidneys. An unpaired *t*-test showed an extremely significant difference was found between the 2 groups in terms of statistical mean of MedianCV₆₀.

Table 8.1 Statistics of MeanCV₅₀ and MedianCV₆₀ in normal and obstructed kidneys

Renal status	No of renogram	Mean	SD	Min	5 th Percentile	95 th Percentile	Max
MeanCV ₅₀							
Unobstructed	90	0.29	0.10	0.16	0.18	0.48	0.56
Obstructed	42	0.74	0.13	0.51	0.55	0.90	0.92
MedianCV ₆₀							
Unobstructed	90	0.12	0.10	0.01	0.02	0.33	0.45
Obstructed	42	0.73	0.20	0.38	0.44	1.00	1.00

Note: Extremely significant differences were found in both MeanCV₅₀ and Median CV₆₀ between unobstructed and obstructed kidneys ($p < 0.0001$).

For the purpose of determining renal obstruction, based on renogram samples, it was suggested that the cutoff point of MeanCV₅₀ was 0.50. Meanwhile, the cutoff point of MedianCV₆₀ was 0.35 in differentiating renal obstruction (Table 8.2).

Table 8.2 Reference ranges of MeanCV₅₀ and MedianCV₆₀ for diagnosis of renal obstruction

Index value	Kidney status
MeanCV ₅₀	
< 0.50	Unobstructed
≥ 0.50	Obstructed
MedianCV ₆₀	
< 0.35	Unobstructed
≥ 0.35	Obstructed

The confusion matrix obtained by using the proposed cutoff point in Table 8.2 in predicting the diagnosis of renogram samples was tabulated in Table 8.3. The reference ranges of MeanCV₅₀ successfully diagnosed the presence of an obstruction in all obstructed kidneys (42/42) while it was able to determine 98% (88/90) of unobstructed kidneys. Meanwhile, the reference ranges of MedianCV₆₀ were also 100% (42/42) accurately diagnosed the presence of an obstruction in all obstructed kidneys and it had an accuracy of 97% (87/90) in determining unobstructed kidneys.

Table 8.3 Confusion matrix to assess the performance of the proposed reference ranges of MeanCV₅₀ and MedianCV₆₀ in the diagnosis of renal obstruction on sample renograms

Confusion Matrix		Prediction			
		MeanCV ₅₀		MedianCV ₆₀	
		Unobstructed	Obstructed	Unobstructed	Unobstructed
Clinical interpretation	Unobstructed	88	2	87	3
	Obstructed	0	42	0	42

8.5 Effect of Age and Gender on MeanCV₅₀ and MedianCV₆₀

Next, the effects of age and gender on MeanCV₅₀ and MedianCV₆₀ were investigated. The means of MeanCV₅₀ were 0.29 ± 0.09 and 0.30 ± 0.12 in unobstructed kidneys of men and women gender groups respectively and 0.75 ± 0.13 and 0.75 ± 0.12 in obstructed kidneys of men and women groups respectively (Fig 8.5(a)). No significant difference was seen in MeanCV₅₀ between men and women in both unobstructed ($p = 0.70$) and obstructed classes ($p = 0.95$). For different age groups, the means of MeanCV₅₀ were 0.29 ± 0.10 and 0.31 ± 0.09 in unobstructed kidneys of the younger population (< 42 years old) and older population (≥ 42 years old) respectively and 0.76 ± 0.13 and 0.74 ± 0.13 in obstructed kidneys of the younger and older populations respectively (Fig 8.5(b)). There was no significant difference between the younger and older populations in the unobstructed ($p = 0.33$) and obstructed classes ($p = 0.77$).

Figure 8.5 The distribution of MeanCV₅₀ in different gender groups (a) and different age groups (b).

For MedianCV₆₀, the means were 0.12 ± 0.09 and 0.14 ± 0.13 in unobstructed kidneys of men and women gender groups respectively and 0.74 ± 0.22 and 0.73 ± 0.20 in obstructed kidneys of men and women groups respectively (Fig 8.6(a)). No significant difference was seen in MedianCV₆₀ between men and women in both unobstructed ($p = 0.75$) and obstructed classes ($p = 0.15$). For different age groups, the means of MedianCV₆₀ were 0.11 ± 0.11 and 0.14 ± 0.10 in unobstructed kidneys of the younger population

(< 42 years old) and older population (≥ 42 years old) respectively and 0.75 ± 0.21 and 0.73 ± 0.20 in obstructed kidney of the younger and older populations respectively (Fig 8.6(b)). There was no significant difference between the younger and older populations in the unobstructed ($p = 0.34$) and obstructed classes ($p = 0.81$).

Figure 8.6 The distribution of MedianCV₆₀ in different gender groups (a) and different age groups (b).

8.6 Summary

In addition to the new parameter U/V_2 proposed in Chapter 7, in Chapter 8, two more parameters were introduced, the MeanCV₅₀ and MedianCV₆₀. The basic MeanCV and MedianCV derived from basic protocol showed their potential in diagnosis of renal obstruction, but they were unable to differentiate the severity of obstruction. By lengthening the duration of renogram through extrapolation using compartmental model, the variants of MeanCV and MedianCV could be derived. From the optimization study, the MeanCV₅₀ and MedianCV₆₀ were found to be the best variants for MeanCV and MedianCV. These parameters could separate unobstructed and obstructed classes as well as further separate the obstructed classes into slightly and heavily obstructed classes. The cutoff points in separating unobstructed and obstructed classes were found to be 0.50 and 0.35 for MeanCV₅₀ and MedianCV₆₀ respectively. At the end of the chapter, the effects of age and gender were evaluated and it was found that both MeanCV₅₀ and MedianCV₆₀ were not significantly influenced by both age and gender.

CHAPTER 9

RESULTS 6

ADVANCED INTEGRATIVE SYSTEM FOR DIFFERENTIATING THE SEVERITY OF OBSTRUCTION

9.1 Introduction

BISRO was developed in Chapter 6 for assisting the diagnosis of renal obstruction. This system can distinguish unobstructed and obstructed classes. However, it has a lower accuracy in differentiating slightly and heavily obstructed classes. Determining the severity of renal obstruction can be useful for the physicians in preparing a treatment plan for a patient. According to the severity of obstruction, there are a number of possible treatments of renal obstruction, such as pyeloplasty, endopyelotomy, nephrectomy, and nephrostomy [25]. Hence, there is a need to develop a more advanced diagnosis system that can provide objective information about the severity of renal obstruction.

In Chapter 9, development of Advanced Integrative System – Renal Obstruction (AISRO) is presented. AISRO is created by using both existing parameters in the literature as well as the newly proposed parameters in this thesis: U/V_2 , MeanCV_{50} , and MedianCV_{60} . These parameters are the parameters that are able to distinguish the severity of renal obstruction with p -values lower than 0.05. The parameters are ranked based on their p -values obtained from unpaired t -tests. Using different numbers of parameters, a set of MLC was created using different algorithms. The overall accuracies of all classifiers are then

compared. It is found that linear SVM developed using the top 4 parameters can produce the highest accuracy and this model is proposed to be used as AISRO.

9.2 Ranking of parameters for AISRO

There were 17 potential distinct parameters analyzed to be used in the development of AISRO. Fourteen of them were the existing parameters derived in Chapter 6. In addition, three more parameters were added, which were the proposed new parameters proposed in Chapter 7 and 8: U/V_2 , MeanCV_{50} , and MedianCV_{60} . Following was the list of the 17 parameters:

• DEI	• PoVC	• LT_{max}
• DRF	• $R_{post/max}$	• $n_{c,peak}$
• NORA_{25}	• $R_{pre/post}$	• U/V_2
• T_{max}	• $R_{pre/max}$	• MeanCV_{50}
• $T_{5/10,dec(fp)}$	• NORA_{post}	• MedianCV_{60}
• PrVC	• $R_{20/max}$	

Before assessing the ability in differentiating severity (slightly or heavily) of renal obstruction, a check on the ability of the parameters in distinguishing unobstructed and obstructed kidneys was carried out. The p -values obtained from the t -tests in separating unobstructed and obstructed classes were tabulated in Table 9.1. From the table, it could be observed that the last 3 parameters: DRF, $n_{c,peak}$, and $R_{pre/post}$ could not separate unobstructed and obstructed classes. Hence, the 14 parameters left to be used in further processing.

Table 9.1 Assessing the ability of the parameters in differentiating unobstructed and obstructed classes using the p -values obtained from the t -tests

Parameter	p -value
MedianCV ₆₀	7.44×10^{-47}
MeanCV ₅₀	3.50×10^{-46}
U/V_2	7.31×10^{-32}
NORA ₂₅	2.62×10^{-29}
$R_{20/max}$	2.58×10^{-28}
LT_{max}	1.40×10^{-14}
PoVC	3.03×10^{-14}
$T_{5/10,dec(fp)}$	1.05×10^{-13}
NORA _{post}	1.15×10^{-12}
T_{max}	1.76×10^{-7}
$R_{post/max}$	2.45×10^{-6}
PrVC	1.24×10^{-5}
DEI	1.68×10^{-4}
$R_{pre/max}$	4.96×10^{-2}
DRF	6.26×10^{-2}
$n_{c,peak}$	1.22×10^{-1}
$R_{pre/post}$	4.12×10^{-1}

Next, the ability of the parameters in differentiating slightly and heavily obstructed was assessed using unpaired t -tests. At the same time, the parameters were rank based on their p -values. The results were shown in Table 9.2. Among 14 parameters, the last 4 parameters in the rank could not separate slightly and heavily obstructed classes. Therefore, the final 10 parameters were used as features in developing MLC as AISRO.

Table 9.2 Assessing the ability of the parameters in differentiating slightly obstructed and heavily obstructed classes using the p -values obtained from the t -tests

Parameter	p -value	Rank
MedianCV ₆₀	5.44×10^{-9}	1
MeanCV ₅₀	6.58×10^{-9}	2
U/V_2	7.72×10^{-8}	3
LT_{max}	7.38×10^{-6}	4
T_{max}	3.22×10^{-5}	5
NORA ₂₅	1.64×10^{-2}	6
$R_{20/max}$	2.17×10^{-2}	7
PoVC	2.37×10^{-2}	8
$T_{5/10,dec(fp)}$	2.54×10^{-2}	9
NORA _{post}	2.56×10^{-2}	10
$R_{post/max}$	7.64×10^{-2}	11
$R_{pre/max}$	1.14×10^{-1}	12
PrVC	1.32×10^{-1}	13
DEI	4.58×10^{-1}	14

9.3 Development of an Advanced Integrative System for Differentiating Renal Obstruction Status into 3 Classes

Ten potential features were used to develop MLC. Various MLC models were developed using different methods, including support vector machine (SVM), decision tree (DT), discriminant analysis (DA), logistic regression (LR) and ensemble classifier (EC). For each of the methods, 10 models were developed using different numbers of parameters as features, start from 1 parameter to 10

parameters. Ten-fold cross-validation method was applied in the development of all models. There were 132 renogram samples available for the analysis; 100 of them were used in building the model. The rest 32 samples were used in the last step to verify the performance of these models in differentiating kidney obstruction.

9.3.1 Machine learning classification

In order to find the best MLC to be used as the classifier for AISRO, 14 machine learning methods were implemented and evaluated:

a. DT: course tree

It used few nodes to make coarse distinctions between classes. The maximum number of splits for the DT is set as 4.

b. DT: medium tree

It used a moderate number of nodes to make finer distinctions between classes. The maximum number of splits for the DT is set as 20.

c. DT: fine tree

It used a high number of nodes to create the finest distinctions between classes. The maximum number of splits is set as 100.

d. DA: linear discriminant

In this discriminant analysis, different classes were separated by linear boundaries.

e. DA: quadratic discriminant

In this discriminant analysis, different classes were separated by nonlinear (quadratic) boundaries.

f. SVM: linear SVM

It created a hyperplane in the form of a linear equation to separate the classes.

g. SMV: quadratic SVM

It created a hyperplane in the form of a quadratic equation to separate the classes.

h. SVM: cubic SVM

It created a hyperplane in the form of a cubic equation to separate the classes.

i. SVM: coarse Gaussian SVM

It created a fine distinction between classes using RBF kernel with kernel scale to $\sqrt{n_p}/4$.

j. SVM: medium Gaussian SVM

It created a fine distinction between classes using RBF kernel with kernel scale to $\sqrt{n_p}$.

k. SVM: fine Gaussian SVM

It created a fine distinction between classes using RBF kernel with kernel scale to $4\sqrt{n_p}$.

l. EC: boosted trees

It developed a superior classifier by application of AdaBoost method to DT.

m. EC: bagged trees

It developed a superior classifier by application of RF method to DT.

n. EC: subspace discriminant

It developed a superior classifier by application of subspace method to DA.

9.3.2 Formation of MLC models

The fourteen MLC methods in section 9.3.1 were applied in building the models. Ten parameters in Table 9.2 were input as the features of the classifier. For each method, 10 models were developed using different numbers of features in order to determine the best classifier. The training dataset for all models was formed by using 100 renogram samples. The MLC models were built in MATLAB 2017b with 10-fold validation and the overall accuracies of all models were tabulated in Table 9.3. Among 140 models built, the model with the highest overall accuracies was quadratic SVM-10 parameters model.

Table 9.3 The accuracies of 14 different MLC developed using 1 to 10 parameters

Classifier model		Number of parameter									
		1	2	3	4	5	6	7	8	9	10
DT	Coarse tree	91%	91%	89%	90%	91%	91%	91%	89%	89%	89%
	Medium tree	91%	91%	89%	90%	91%	91%	91%	89%	90%	91%
	Fine tree	91%	91%	89%	90%	91%	91%	91%	89%	90%	91%
DA	Linear discriminant	91%	90%	91%	92%	93%	91%	92%	90%	93%	92%
	Quadratic discriminant	91%	89%	89%	89%	89%	90%	92%	91%	91%	91%
SVM	Linear SVM	91%	92%	93%	94%	94%	92%	93%	93%	93%	94%
	Quadratic SVM	88%	93%	91%	91%	90%	90%	88%	92%	91%	95%
	Cubic SVM	88%	91%	86%	89%	90%	89%	90%	90%	89%	92%
	Coarse Gaussian SVM	91%	90%	92%	93%	92%	92%	93%	94%	94%	94%
	Medium Gaussian SVM	89%	89%	90%	92%	92%	91%	92%	89%	88%	87%
	Fine Gaussian SVM	91%	89%	88%	87%	75%	68%	68%	68%	68%	68%
EC	Boosted tree	68%	68%	68%	68%	68%	68%	68%	68%	68%	68%
	Bagged tree	92%	94%	89%	91%	91%	91%	91%	90%	94%	93%
	Subspace discriminant	91%	92%	93%	92%	93%	93%	91%	90%	90%	90%
Note: cell color		61-70%	71-80%	81-90	91-100 %	best					

9.3.3 Validation of models

The highest accuracy model for differentiating renal obstruction status into 3 classes, which was the quadratic SVM-10 parameters model, was validated

using the validation dataset. By applying the model, the predictions of the 32 renogram samples were obtained. Then the predictions were put in comparison with the clinical evaluation of the samples by certified nuclear medicine experts as tabulated in Table 9.4. This model could provide 95% accuracy in confirming the absence of obstruction (21/22) and 90% accuracy in confirming the presence of an obstruction (9/10). In determining the severity of obstruction, the model diagnosed the slightly obstructed class with an accuracy of 50% (2/4) and heavily obstructed classes with an accuracy of 83% (5/6). The model had an overall accuracy of 88% (28/32) in the diagnosis of the validation dataset.

Quadratic SVM-10 parameters model seemed to be the best model with an overall accuracy of 95% on training dataset shown in Table 9.4. However, 10 parameters were required to build the model. There were a number of other models developed using fewer parameters and provided an overall accuracy with just 1% lower than that of quadratic SVM-10 parameters model. These models were linear SVM-4 parameters, coarse Gaussian SVM-8 parameters, and bagged tree EC-2 parameters. The overall accuracies of the models were also included in Table 9.4. The highest overall accuracy on validation dataset was 94% obtained from the application of linear SVM-4 parameters and coarse Gaussian SVM-8 parameters models. As linear SVM-4 parameter model required less parameter, it was suggested as the MLC model for AISRO. Even though it had lower accuracy in training dataset as compared to quadratic SVM-10 parameters model, it provided a much higher accuracy in the validation dataset. Linear SVM-4 parameter model

had an accuracy of 95% (21/22) in confirming the absence of an obstruction and an accuracy of 100% (10/10) in confirming the presence of an obstruction. It meant no obstruction case was missed out from the being diagnosed. In determining the severity of obstruction, the model 100% (4/4) accurately grouped the slightly obstructed kidneys and had an accuracy of 83% (5/6) in the diagnosis of a heavily obstructed kidney.

Table 9.4 Combined confusion matrices of several high accuracy models to differentiate renal obstruction status into 3 classes on the validation dataset

Model	Clinical interpretation	Prediction			Overall Accuracy
		Unobstructed	Slightly obstructed	Heavily obstructed	
(95% training accuracy) Quadratic SVM-10 parameters	Unobstructed	21	1	0	88%
	Slightly obstructed	1	2	1	
	Heavily obstructed	0	1	5	
(94% training accuracy) Linear SVM-4 parameters or coarse Gaussian SVM-8 parameters	Unobstructed	21	1	0	94%
	Slightly obstructed	0	4	0	
	Heavily obstructed	0	1	5	
(94% training accuracy) Bagged tree EC-2 parameters	Unobstructed	21	1	0	84%
	Slightly obstructed	2	2	0	
	Heavily obstructed	0	2	4	

9.4 Summary

The last chapter for the results presented the development of a system created to determine the severity of obstruction. The parameters included were existing parameter in the literature as well as the new parameter proposed in this thesis. Using these as features for developing machine learning, 140 models were built using 14 different MLC models with 10 different numbers of parameters. Among them, linear SVM-4 parameter model had the best performance on the validation set by using only the top 4 parameters and it was suggested as the model for AISRO.

CHAPTER 10

DISCUSSION

10.1 Introduction

This chapter provides the discussion of the results obtained from Chapter 4 to 9. The performance of the proposed parameters and systems are discussed in comparison with the findings in the literature. Next, research contributions of this thesis are elaborated. Lastly, the recommendations for future works are presented in this chapter.

10.2 Discussion

Renography is a commonly used renal imaging method to evaluate the presence of an obstruction in a kidney. It offers a non-invasive assessment as compared to the invasive Whitaker Test, which is the gold standard for diagnosis of renal obstruction. The interpretation of renograms in the clinic is majority done through visual interpretation, which is a highly subjective method. This thesis aims to quantify the renograms in order to obtain parameters that can differentiate renal obstruction and to develop systems that can provide an accurate and objective interpretation of renogram. In order to achieve the aims, first, a literature search was conducted to find the existing parameters proposed by other researchers. Then, these parameters were derived and the statistics of them were analyzed to form the reference values and ranges for diagnosis. Next, new parameters obtained from the quantification of renogram were proposed and tested. The parameters were the physical parameter U/V_2 and statistical

parameter MeanCV and MedianCV. The last objective was to build systems for the diagnosis of renal obstruction, which were the BSS, BISRO, and AISRO.

10.2.1 Reference values of parameters for F+10 diuresis renography

The protocols found in the literature offered guidelines in evaluating the possible quantifiable parameters from renogram for F-15, F0, F+20 and F+30 [35, 58, 74]. F+10 was a more recent diuresis renography protocol and there was still no reference value in evaluating renal obstruction by using parameters derived from it. In Chapter 4, the previously proposed parameters in the literature were derived on renogram samples. After that, the statistics of the parameters were calculated in order to determine the proposed ranges of values for both unobstructed and obstructed classes. The abilities of the parameters in separating these classes were also tested by using unpaired t -tests. The summary of the reference ranges and cutoff points in separating unobstructed and obstructed classes were tabulated in Table 10.1. In order to have a comprehensive reference source, in addition to the parameters explored in Chapter 4, the newly proposed parameters of this thesis were also included in the summary of Table 10.1, i.e. the U/V_2 proposed in Chapter 7, and MeanCV₅₀ and MedianCV₆₀ in Chapter 8.

Table 10.1 The summary of reference values for unobstructed and obstructed classes in F+10 diuresis renography and the proposed cutoff values to differentiate these classes

Parameter	Mean $\pm$ SD		<i>p</i> -value	Cutoff point
	Unobstructed	Obstructed		
DEI (%)	-14.08 ± 28.77	3.45 ± 7.89	0.0002	-9.31
DRF (%)	54.38 ± 13.66	48.66 ± 13.12	0.08	NA
$T_{1/2,dec}$ (min) ^a	12.63 ± 5.28	27.72 ± 3.12	< 0.0001	21.55
$T_{1/2,dec}$ (min) ^b	9.10 ± 3.86	88.74 ± 161.02	< 0.0001	19.77
$LT_{1/2,dec}$ (min) ^c	18.56 ± 4.74	29.89 ± 2.00	< 0.0001	25.85
$LT_{1/2,dec}$ (min) ^d	23.93 ± 12.02	122.13 ± 242.04	0.0002	53.58
NORA ₂₀	0.44 ± 0.32	1.44 ± 0.56	< 0.0001	0.90
NORA _{post}	10.29 ± 13.39	60.89 ± 89.27	< 0.0001	36.63
$n_{c,peak}$	9847 ± 7807	7597 ± 7591	0.12	NA
$R_{20/max}$	0.29 ± 0.15	0.82 ± 0.13	< 0.0001	0.57
$R_{post/max}$	7.50 ± 9.49	35.09 ± 48.30	< 0.0001	24.74
$R_{pre/post}$	1.89 ± 2.69	1.52 ± 0.95	0.41	NA
$R_{pre/max}$	1.89 ± 2.69	1.52 ± 0.95	< 0.0001	4.29
$T_{max/2}$ (min)	1.21 ± 0.40	1.51 ± 0.94	< 0.0001	1.36
T_{max} (min)	5.08 ± 2.95	35.09 ± 48.30	< 0.0001	9.98
U/V_2 (1/s)	$1.24 \times 10^{-3} \pm 4.07 \times 10^{-4}$	$1.44 \times 10^{-4} \pm 2.81 \times 10^{-4}$	< 0.0001	6.30×10^{-4}
MeanCV ₅₀	0.29 ± 0.10	0.74 ± 0.13	< 0.0001	0.50
MedianCV ₆₀	0.12 ± 0.10	0.73 ± 0.20	< 0.0001	0.35

^a $T_{1/2,dec}$ derived using peak count as reference count value

^b $T_{1/2,dec}$ derived using exponential fitted curve

^c $LT_{1/2,dec}$ derived using Lasix time as reference count value

^d $LT_{1/2,dec}$ derived using exponential fitted curve

Note: Cutoff points were only available for the parameters with significant difference between unobstructed and obstructed classes

The effects of age and gender were also tested on all of these parameters. No significant difference was found between men and women as well as between younger and older populations in all parameters, with an exception for DEI, where there was a significant difference between the younger and older populations of the obstructed class with $p = 0.03$. However, the finding needed to be further verified in a future study as the sample size available to obtain this result was small with 18 DEI values available in the younger population and 20 DEI values in the older population of the obstructed class.

The finding that age and gender had little or no effect on the renogram interpretation was in agreement with a number of studies that showed no significant effect of age or gender on the quantitative parameters in both unobstructed and obstructed classes [77, 86]. In addition, the influence of additional clinical information about the patient on the interpretation of renography was also studied by Taylor et al [172]. Their study showed that clinical information did not change the diagnosis and had little impact on renogram interpretation.

10.2.2 Baseline Screening System

The administration of diuretic was part of standard protocols in renography for diagnosis of renal obstruction [35, 74]. The purpose of it was to reduce a false positive diagnosis due to the reservoir effect of a dilated kidney. However, this injection might induce side effects including fever, diarrhea, and vomiting. If the absence of obstruction could be confirmed early, the injection of

diuretic could be omitted and the unnecessary discomfort in patients could be avoided. Chapter 5 attempted to develop BSS as a means to determine whether diuretic injection was needed during renography. It was a system that integrated 4 parameters that could differentiate renal obstruction. These 4 parameters were T_{max} , $NORA_{10}$, $MeanCV_{10}$, and $MeanCV_{10}$. T_{max} was found to be the top parameter that could provide an evaluation of renal obstruction based on the first 10 min of renograms. It was a parameter that could represent the flow efficiency of a kidney as it expressed the renal transit time [78].

In the assessment of the BSS performance on the validation dataset, which had a disease prevalence of 21%, the system was able to give a suggestion that omitted diuretic injection on 55% of the renogram samples that are indeed unobstructed kidneys. Kuyvenhoven et al proposed a means to eliminate the need for diuretic based on the baseline scanning by using 3 parameters: T_{max} , $NORA_{20}$ and output efficiency [87]. Based on their method, the decision on diuretic administration was made by assessing individual parameters with reference to the cutoff points. This method could be ambiguous when different parameters gave different outcomes of diagnosis. The author tested this method on a validation dataset that had a disease prevalence of 18% and it was found around 20% of the sample could have omission of diuretic injection. BSS performed better in confirming unobstructed kidneys as compared to their method. Furthermore, it was a more superior integrative method that could avoid ambiguous diagnosis by assessing individual parameters.

10.2.3 Basic Integrative System – Renal Obstruction

When the BSS decision was to proceed with diuretics, the complete 25 min renograms could be evaluated by using BISRO. BISRO was a system created using the LR model for differentiating unobstructed and obstructed classes as proposed in Chapter 6. To develop BISRO, 4 out of 59 parameters were selected to build an LR equation. These 4 parameters were $NORA_{25}$, $R_{20/max}$, $T_{7/10,dec}$, and $T_{7/10,dec(fp)}$. Among them, the top parameter was $NORA_{25}$. $NORA_{20}$ was a parameter explored in a number of studies recently and believed to be an indicator of renal clearance [68, 92]. In this chapter, the variations of NORA were evaluated from $NORA_3$ to $NORA_{25}$. It was found that the longer timing to derive NORA, the better the derived parameter in differentiating renal obstruction. In the renogram samples of this work, $NORA_{25}$ was found to be the best variant of NORA instead of $NORA_{20}$.

The developed BISRO had an accuracy of 94.00%, a sensitivity of 90.63%, a specificity of 95.59% and an AUC of ROC of 0.95. This model was further verified by testing on the validation dataset and the results had an accuracy of 84.38%, a sensitivity of 90.00%, a specificity of 86.36% and an AUC of ROC of 0.86. The performance of BISRO was compared to another proposed model by Bao et al [94] which was created for the same purpose to diagnose renal obstruction. Both models were created using the LR algorithm. Bao et al model was created by selecting 2 out of 19 parameters, while BISRO was created by selecting 4 out of 59 parameters. The crucial parameters in Bao et al model such as $R_{20/max}$, $R_{post/max}$,

$T_{1/2}$, and T_{max} were included in BISRO's choices of parameters, while Bao et al did not include other important parameters such as NORA. The performance comparisons of both models were shown in Table 10.2. For the training of the model, BISRO showed a better performance of having a higher AUC, sensitivity, and specificity. In the verification of the model, BISRO had slightly higher AUC than Bao et al model. Bao et al model had a higher specificity than BISRO, which meant their model could predict unobstructed kidney well. However, it had a lower sensitivity as compared to BISRO, which indicated that their model could not confirm obstructed as good as BISRO. The objective of the diagnosis was to determine the presence of obstruction and any false negative diagnosis would be costly as it caused a delay for a patient to receive an appropriate treatment. Hence, a higher sensitivity in BISRO was preferred. Nevertheless, Bao et al model had a higher number of validation data as compared to BISRO. Hence, the performance of BISRO needed to be further verified in a higher number of renogram samples as the dataset.

Table 10.2 Comparison of proposed BISRO and Bao et al model created for differentiating unobstructed and obstructed kidneys

Dataset	Performance	Bao et al model [94]	BISRO (Chapter 6)
Training	AUC	0.89	0.95
	Sensitivity	85%	90%
	Specificity	95%	96%
Validation	AUC	0.84	0.86
	Sensitivity	78%	90%
	Specificity	95%	86%

Besides the development of BISRO, there was another model built in Chapter 6. This second model was created using MLR for differentiating the renal obstruction status into 3 classes. To build it, 5 out of 59 parameters were used. The final model was in form of 2 equations where the first one provided the ratio between the probability of being an unobstructed kidney and the probability of being a heavily obstructed kidney and the second equation was to find the ratio between the probability of being a slightly obstructed kidney and the probability of being a heavily obstructed kidney. Based on the training dataset, this model had an overall accuracy of 95.00%. However, when the model was tested on the validation dataset, the overall accuracy of the model dropped to 71.88%, which meant a high percentage of misclassification could occur in using this model. As an alternative, AISRO, which was also developed for the classification of renal obstruction status into 3 classes, was developed in Chapter 9.

10.2.4 New parameter for diagnosis of renal obstruction: U/V_2

Until today, there is still no quantifiable parameter from renogram accepted as a gold standard for diagnosis of renal obstruction. In Chapter 7, a new parameter, which represented physical flow rate in a kidney was proposed. The parameter was U/V_2 , which was an index that represented how many substances flowed through a kidney per second on the basis of the capacity of the kidney.

This parameter was derived based on the compartmental analysis applied to renography. The application of the compartmental model in evaluating renal functionality was first proposed by Barbalias et al [80]. In their study six-compartmental model was used to model renogram for the purpose of differentiating parenchymatic dysfunction and pelvocalyceal obstruction. The authors suggested that the application of compartmental analysis could provide quantitative parameters that might facilitate diagnosis of renal status.

The application of 6 compartments might over-complicated the system, laborious to derive an analytical solution and difficult to interpret the meaning of the solution. The works done using a single compartmental modeling had been carried out by Coffey JP [171]. His study showed that a single compartment model might allow the assessment of obstruction in a kidney. In this study, a two-compartmental model was shown to be sufficient to derive a meaningful and significant parameter. From the compartmental modeling applied, a second-order differential equation was obtained and the solution led to 3 possible conditions of flow: under-damped, over-damped and critically damp. By assessing the goodness

of fit of the model on actual renograms, it was found that over-damped was the best condition to fit renogram. This outcome was expected because theoretically, an under-damped model indicated an oscillation movement of fluid through the kidney before reaching a steady state, which was unlikely to occur in a kidney. A critically damped model represented the fastest possible condition for fluid to be filtered out of a kidney, which could only occur in a completely perfect kidney without any defect. The over-damped condition represented fluid flow that was slightly slower than the critically damped condition, and this should be the case for the human kidneys. The finding that over-damped was the best condition to use was in agreement with a study done by Loh et al where two-compartmental modeling was first tested to be applied on renograms [170]. By using a set of coefficients obtained from the curve fitting, U/V_2 could be derived. It was found that as the value of U/V_2 decreases, the kidney status shifts from unobstructed to slightly obstructed and then to heavily obstructed.

10.2.5 New parameters for diagnosis of renal obstruction: MeanCV₅₀ and MedianCV₆₀

Besides proposing the physical parameter U/V_2 as an indicator of renal obstruction, two statistical parameters were proposed in Chapter 8, which were the MeanCV₅₀ and MedianCV₆₀. Initial feasibility study of MeanCV₂₅ and MedianCV₂₅ showed the potential in using them in separating unobstructed and obstructed classes. However, both parameters failed to differentiate the slightly and heavily obstructed classes. If the duration of imaging is extended, the derived

value of MeanCV and MedianCV from a lengthened renogram might be able to differentiate the severity of renal obstruction. It is based on the fact that in a prolonged renogram of an unobstructed kidney, the number of counts would keep at a low level as the radioisotope had been washing out of the kidney, which further lowered the value of MeanCV and MedianCV. On the other hand, in a prolonged renogram of an obstructed kidney, the number of counts would either keep increasing or only has a slight fall due to the obstruction in the kidney, which might increase the values MeanCV and MedianCV. Consequently, by lengthening the renogram, different renal obstruction classes may be further separated from each other.

However, practically, conducting diuresis a renography clinically with a duration longer than 30 min was not recommended due to the physical discomfort in patients who have to maintain the same body posture for a long imaging process. One of the solutions to it was to predict the renogram trend beyond its original imaging result. It could be done by applying the compartmental model solution derived in Chapter 7 and used the best-fit curve to predict the renogram trend. By doing so, a renogram with duration beyond 30 min could be estimated and used to derive the variants of MeanCV and MedianCV.

MeanCV₅₀ and MedianCV₆₀ were selected to be the best parameters among the variants of MeanCV and MedianCV derived from extrapolated renogram with duration of 10 min to 100 min. A value of either of these parameters closer to 0 meant there was a substantial fall in the number of counts

due to the tracer washout from a kidney. It indicated a good clearance of radioisotopes and the kidney was unlikely to be obstructed. On the other hand, a value closer to 1 happened when the curve of renogram increased over time or stay plateau at a high number of count throughout the scanning process. It indicated the presence of blockage in the flow path, as the radioisotope was not able to flow out of a kidney.

In Table 2.1 presented in Chapter 2, $T_{1/2,dec}$ and T_{max} were found to be the parameters started to be used as indicators of renal obstruction from the early development of renography until today. Besides, $R_{20/max}$ and $NORA_{20}$ were the parameters that gained popularity in recent years. The proposed $MeanCV_{50}$ and $MedianCV_{60}$ together with the U/V_2 were put in comparison with these 4 parameters as tabulated in Table 10.3 in terms of their performance in differentiating unobstructed and obstructed classes as well as differentiating slightly and heavily obstructed classes. The lower a p -value was, the better the parameter was and p -value lesser than 0.05 was generally accepted as having a significant difference in separating 2 classes. All 7 parameters could be used to separate unobstructed and obstructed classes ($p < 0.0001$) with an extremely significant difference. Among them, the top 3 parameters were the 3 proposed parameters: $MedianCV_{60}$, $MeanCV_{50}$, and U/V_2 . For differentiating slightly and heavily obstructed classes, $NORA_{20}$ and $T_{1/2,dec}$ were not able to perform the task as their p -values were larger than 0.05. For the rest of 5 parameters, the top 3 parameters were also $MedianCV_{60}$, $MeanCV_{50}$, and U/V_2 .

Table 10.3 Comparison of new proposed parameters U/V_2 , MeanCV_{50} , and MedianCV_{60} and the existing commonly used parameters in the literature $T_{1/2,dec}$, T_{max} , $R_{20/max}$, and NORA_{20}

Parameter	<i>p</i> -value (U vs O)	Rank	Parameter	<i>p</i> -value (S vs H)	Rank
MedianCV_{60}	7.44×10^{-47}	1	MedianCV_{60}	5.44×10^{-9}	1
MeanCV_{50}	3.50×10^{-46}	2	MeanCV_{50}	6.58×10^{-9}	2
U/V_2	7.31×10^{-32}	3	U/V_2	7.72×10^{-8}	3
$R_{20/max}$	2.58×10^{-28}	4	T_{max}	3.22×10^{-5}	4
NORA_{20}	1.41×10^{-25}	5	$R_{20/max}$	2.17×10^{-2}	5
$T_{1/2,dec}$	4.47×10^{-11}	6	NORA_{20}	5.78×10^{-2}	6
T_{max}	1.76×10^{-7}	7	$T_{1/2,dec}$	1.50×10^{-1}	7

Note: U: unobstructed, O: obstructed, S: slightly obstructed, and H: heavily obstructed.

MedianCV_{60} , MeanCV_{50} , and U/V_2 were quantifiable parameters from renogram that could provide a better assessment of renal obstruction. These parameters could potentially be used to form a sophisticated system for diagnosis of renal obstruction by incorporating them together with other existing parameters in the literature. They could also be added to an existing diagnosis system to improve its performance.

10.2.6 Advanced Integrative System – Renal Obstruction

AISRO was an integrative system created for determining the severity of renal obstruction. The existing parameters used in the development of BISRO as well as newly proposed parameters of this thesis were analyzed to be used as features for AISRO. Top 10 parameters were found to be able to differentiate both unobstructed and obstructed as well as slightly and heavily obstructed. These

parameters were: MedianCV₆₀, MeanCV₅₀, U/V_2 , LT_{max} , T_{max} , NORA₂₅, $R_{20/max}$, PoVC, $T_{5/10,dec(fp)}$, and NORA_{post}.

In order to find the best MLC model for AISRO, 14 different MLC methods were applied. For each method, 10 different models were built using 10 different numbers of parameters, start from using the top 1 parameter up to using all top 10 parameters. The model with the best accuracy on training dataset was found to be quadratic SVM-10 parameters model, which could correctly classify 95 out of 100 renogram samples. However, the overall accuracy of this model dropped to 88% during the validation of the model. Some other models used fewer parameter were found to have slightly lower accuracy on training dataset than quadratic SVM-10 parameters model. During the validation, some of these models outperformed the quadratic SVM-10 parameters model. This could be a sign of over-fitting in the quadratic SVM-10 parameters model. It was found that linear SVM-4 parameters model was able to classify 94 out of 100 renogram samples on training dataset, and had a higher accuracy during testing on validation dataset where it had an overall accuracy of 94%. Hence, linear SVM-4 parameters was proposed as the model for the integrative system AISRO.

The performance of AISRO was found to be comparable with more complex systems found in the literature: RENEX [111] and iRENEX [109]. The comparison between the performance of RENEX and the AISRO was shown in Table 10.4. RENEX made a decision based on 47 quantitative parameters while AISRO created diagnosis by integrating only 4 quantitative parameters. In Table

10.4, AISRO was more superior in confirming an unobstructed kidney. It also had double accuracy in predicting slightly obstructed kidney. However, it had a slightly lower accuracy in the diagnosis of the heavily obstructed kidney. Another similar system, iRENEX, was compared to AISRO in Table 10.5. iRENEX was a system similar to RENEX with additional of patients' history to be taken into consideration in making a decision. It could be seen that AISRO outperformed iRENEX in predicting renal obstruction status. It was important to take note that the performance of RENEX and iRENEX was evaluated in much larger renogram samples as compared to that of AISRO. So, more renogram samples were required to further validate the performance of AISRO.

Table 10.4 Comparison of proposed RENEX and AISRO in differentiating renal obstruction status into 3 classes

Renal status	Agreement with Experts	
	RENEX [111]	AISRO (Chapter 9)
Unobstructed	84%	95%
Slightly obstructed*	45%	100%
Heavily obstructed**	92%	83%

*In RENEX study was termed as equivocal

** In RENEX study was termed as obstructed

Table 10.5 Comparison of proposed iRENEX and AISRO in differentiating unobstructed and obstructed kidneys

Renal status	Agreement with Experts	
	iRENEX [109]	AISRO (Chapter 9)
Unobstructed	92%	95%
Obstructed	95%	100%

A summary of all results of the thesis for diagnosis of renal obstruction was illustrated in a flowchart shown in Fig 10.1. This flowchart proposed a means to interpret a renogram based on the quantifiable parameters from the renogram as well as the implementation of integrative systems in differentiating renal obstruction. When the renography is conducted, the need of diuretics can be determined 10 mins after radioisotopes injection using the BSS proposed in Chapter 5. Positive result of BSS indicates a kidney is suspected to be obstructed while negative result indicates a kidney is unobstructed. For the sample with positive result of BSS, diuretics have to be injected and a full diuretic renography was carried out. A number of quantifiable parameters can be derived from a complete renogram and each of them can be interpreted based on the range proposed in Chapter 4. The presence or absence of obstruction can be confirmed by using BISRO proposed in Chapter 6. BISRO can give prediction of whether a kidney is obstructed, but it cannot provide information on the severity of obstruction. If the severity of obstruction has to be determined in order to have a more personalized treatment plan, AISRO, which is proposed in Chapter 9, can be used. AISRO is developed not only with the existing parameters found in the

literature, it also incorporates new parameters proposed in Chapter 7: U/V_2 and Chapter 8: MeanCV₅₀, and MedianCV₆₀.

Figure 10.1 A flowchart to summarize the results of the thesis as a framework to be used in the interpretation of a renogram.

10.3 Novel Research Contribution

The major contributions of this thesis work are as follows:

- The reference values of 18 quantifiable parameters (DEI , DRF , $T_{1/2,dec}$ using T_{max} , $T_{1/2,dec}$ using exponential fitting, $LT_{1/2,dec}$ using Lasix time, $LT_{1/2,dec}$ using exponential fitting, $NORA_{20}$, $NORA_{post}$, $n_{c,peak}$, $R_{20/max}$, $R_{post/max}$, $R_{pre/post}$, $R_{pre/max}$, $T_{max/2}$, T_{max} , U/V_2 , MeanCV₅₀, and MedianCV₆₀) from renogram were derived specifically for F+10 diuresis

renography protocol. These ranges may assist the interpretation of renogram clinically.

- b. The cutoff points of each quantifiable parameter, which can be used as the benchmarks in the diagnosis of renal obstruction, were proposed. This can be used to verify the decision on the final diagnosis of renal obstruction by assessing the parameters individually.
- c. An integrated system, BSS, to determine the need of diuresis in F+10 renography was proposed. BSS can be used as initial renal obstruction screening system in renography. If the system concludes that diuretic is not needed, it also means that the kidney can be confirmed as unobstructed based on the baseline scanning.
- d. BISRO was a new system suggested for differentiating renal obstruction status into 2 classes: unobstructed and obstructed. BISRO integrated 4 parameters selected from 59 quantifiable indices from renogram in a form of LR model. It is easy to be applied and can provide a fast and accurate diagnosis of obstruction clinically.
- e. A new physical parameter U/V_2 was proposed as an indicator of renal obstruction. It represented the fluid outflow rate from a kidney. U/V_2 has the ability to differentiate the severity of renal obstruction.
- f. New statistical parameter MeanCV₅₀, and MedianCV₆₀ were proposed to be used in differentiating the severity of renal obstruction. These

parameters could outperform existing popularized parameter such as

$T_{1/2,dec}$ and T_{max} .

- g. To differentiate the severity of renal obstruction, AISRO was created. AISRO integrated 4 parameters in a form of linear SVM model. The diagnosis provided by AISRO can assist physicians in planning a more personalized plan for treatment.

10.4 Limitations of the Present Work

Following are the limitations of the works presented in this thesis:

- a. Majority of the renogram samples were used as the training dataset to form classifiers and only a small number of renogram samples available to be used as the validation dataset. By having more data, the accuracy of the developed models can be further improved and verified.
- b. Imbalance in the number of available healthy and disease renogram samples. Out of a total of 170 renograms, 120 were unobstructed kidneys and 50 were obstructed kidneys (22 were slightly obstructed and 28 were heavily obstructed). This imbalance of data may lead to bias towards the majority class and a lower accuracy in predicting the minority class.
- c. Missing patient information. There was some missing information in the clinical data retrieved from the hospital, including missing data on age and gender of few patients. Consequently, the effect of age and gender on certain parameters, such as $T_{1/2,dec}$ in the obstructed class, could not be studied due to a low number of data available.

- d. The renogram samples obtained from the hospital were in a picture format (PDF). To study them, re-digitalization was carried out by replotting them into MatLab. This replotting process might induce a small error in the data. Having and analyzing raw renogram samples directly from scanning outcomes could eliminate this possible source of error.
- e. Intraobserver and interobserver variability in providing clinical evaluation of renogram by nuclear medicine doctors. The diagnosis of renogram was provided by doctors based on the patient information, renogram, and other data. This interpretation may subject to the availability of the information during the decision making process and the expertise of the doctors.

10.5 Recommendations for Future Work

Following are the recommendations for possible future works as an expansion of the works in this thesis:

- a. To fine-tune the proposed reference value of the parameters for F+10 protocol in both unobstructed and obstructed classes, a larger sample size can be gathered. The cutoff point of an individual parameter for differentiating unobstructed and obstructed can also be adjusted to improve its accuracy.
- b. The proposed BSS has the potentiality to be used not only for F+10 renography but also in other protocol where the diuretic is injected after radioisotope injection, such as in F+20 and F+30 renography. BSS is an

integrative system created based on parameters obtained within 10 min of renogram where the diuretic is not applied yet, hence the same system may also be applied directly without the need to modify it in F+20 and F+30 renography where the diuretic is injected at a much later time than F+10. By using BSS, a fraction of the unobstructed kidneys can be confirmed earlier. Thus, future works can be done to verify the performance of BSS on F+20 and F+30 renography.

- c. BISRO, which is an integrative system for diagnosis can be improved by refining the coefficient of its LR model through larger training dataset. In addition, more samples could also be used as a validation dataset to verify the performance of this system
- d. The parameters U/V_2 , MeanCV_{50} , and MedianCV_{60} were tested in this thesis to be indicators of renal obstruction based on F+10 renography. The parameters can be further explored to be used in other protocol of renography, such as F-15, F0, F+20, and F+30. The reference values for each of the parameters can also be set for each of the protocols so these new parameters can gain further acceptance to be used clinically.
- e. The advance integrative system AISRO needs to be further validated. In this work 100 renogram samples were used to build it and 32 samples left to be used as a validation dataset. Besides, the renal obstruction status of a kidney can also be further divided into more classes, for example using stage 1 to stage 4, so a more personalized treatment plan can be made.

- f. After fine-tuning and validating the models by using of a larger dataset, the models can be incorporated into the existing computing system of the renography equipment in the hospitals. Software, which provides a prediction on renal obstruction status based on the renogram, can be developed. The software should be able to extract the raw time-activity curve from the renogram and derive all the quantifiable parameters. If the software can be run in real-time, BSS model can be implemented to determine the need for diuretics 10 mins after the injection of radioisotopes. Once a full diuretic renogram is completed, the results can be analysis by the software through either BISRO or AISRO model and outcome of the software will be a predicted renal obstruction status, which can be used by physicians in deciding a suitable treatment plan for the patients.
- g. The approaches used in this thesis can be replicated to create reference values, to search for crucial parameters, and to build integrative systems for diagnosis of other renal status through renography. For example, quantitative parameters can be derived and integrated to create a system for evaluation of renal transplant dysfunction. The approaches can also be used to develop a system for the diagnosis of renal artery stenosis in captopril renography.

CHAPTER 11

CONCLUSION

A kidney has a crucial role in the maintenance of homeostatic functions. The presence of an obstruction in the renal flow lead to tissue atrophy and may eventually cause renal death. The current gold standard in confirming renal obstruction is the Whitaker Test. However, it is seldom being carried out clinically due to its invasive nature. Dynamic renal imaging using renography offers an effective alternative that is non-invasive. However, the interpretation of renogram is still a contested topic. The main method to evaluate renal obstruction through renogram is by a visual interpretation, which is really subjective and dependent on the reader's experience. A more objective method using quantifiable parameters from renogram can be a solution as an effective means for diagnosis of renal obstruction. It can improve the reliability in the evaluation of renal obstruction through renography and avoid experience dependency in the interpretation.

The first objective of this thesis was to study existing parameters in literature. In this study, 15 parameters were derived and evaluated. The statistics of them were calculated for both unobstructed and obstructed classes. They could serve as the reference value in evaluating renal obstruction for an individual parameter. Their abilities to separate the 2 classes were also tested. Among the parameters $NORA_{25}$, $R_{20/max}$, and $T_{7/10,dec}$ were the top 3 parameters that could differentiate unobstructed and obstructed classes. For further separating into 3 renal obstruction statuses, the top 3 parameters were found to be LT_{max} , T_{max} ,

and $T_{9/10,dec}$. In addition, the effects of age and gender on the parameters were evaluated and it was found that these 2 factors had little or no effect on renogram interpretation.

The second objective of this thesis was to develop new parameters to be used as indicators of renal obstruction. There were 3 new quantitative parameters proposed in this thesis. The first one was a physical parameter derived from compartmental analysis U/V_2 . U/V_2 represented the normalized substance flow rate out of a kidney. A higher value of it was a sign of the absence of obstruction, while a lower value of it was an indication of the impedance of flow rate due to the presence of an obstruction. The second and third parameters were the MeanCV and MedianCV. Basic MeanCV and MedianCV calculated from standard duration renography could not differentiate the severity of obstructed. Thus, these parameters were modified to improve their performance through implementation of a compartmental model to extrapolate the renogram. The MeanCV₅₀ and MedianCV₆₀ were found to be the best variants of MeanCV and MedianCV to be used in determining renal obstruction.

The last objective of this thesis was to build a system for diagnosis of renal obstruction. To begin with, BSS was developed as a system that could determine the need for diuretic. By implementing BSS, more than 50% of the unobstructed kidneys could be confirmed earlier and omitted from having a diuretic injection. For those who needed to go through full diuretic renography, the renal obstruction could be assessed by either using BISRO or AISRO. BISRO was a simple

system that could be implemented easily clinically. This proposed system could provide information whether there was an obstruction in a kidney with an accuracy of 84%. When there was a need to determine the severity of obstruction, AISRO could be applied. AISRO was a proposed system that could determine if the sample was an unobstructed, slightly obstructed or heavily obstructed kidney with an accuracy of 94%.

As technology advances rapidly in the past decades, the medical knowledge and imaging technique also expands in a fast rate. Physicians often require to gain a high volume of knowledge with limited training time. This increases the likelihood of physician errors in the diagnosis. High intelligence system in computer-assisted diagnosis like the one proposed in this thesis can assist physicians in the interpretation of image to confirm the diagnosis and determine an appropriate treatment plan. The use of these diagnosis systems is helpful in assisting the evaluation renogram, reducing the intraobserver and interobserver variability, and producing fast diagnosis with a high degree of accuracy. The results obtained can enhance the physician's confidence in the diagnosis. Furthermore, the proposed diagnosis system can solve the issue of lack of nuclear medicine experts in developing countries.

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LIST OF PUBLICATIONS

Published work:

- Suriyanto, Ng EYK, Say XJ, Ng CED, Yan XS, Kumar SD. Quantitative means for differentiating renal obstruction by analyzing renography by compartmental modeling of renal fluid flow rate. Nuclear Medicine Communication. 2016; 37(9): 904-910.

Prepared to be submitted:

- ^{99m}Tc -MAG₃ diuresis renography in differentiating renal obstruction: Using statistical parameters as new quantifiable indices

Plan to prepare for submission:

- Reference values of quantifiable parameters from renogram for F+10 diuretic renography
- Baseline screening system for F+10 diuretic renography: the need of diuresis
- Integrating parameters to form systems for diagnosis of renal obstruction using diuretic renography

APPENDIX A RENOGRAM SAMPLES

Patient 001

Patient 003

Patient 005

Patient 002

Patient 004

Patient 006

Patient 007

Patient 010

Patient 013

Patient 008

Patient 011

Patient 014

Patient 009

Patient 012

Patient 015

Patient 016

Patient 019

Patient 022

Patient 017

Patient 020

Patient 023

Patient 018

Patient 021

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Patient 085

Patient 080

Patient 083

Patient 086

Patient 081

Patient 084

Patient 087

Patient 088

Patient 091

Patient 094

Patient 089

Patient 092

Patient 090

Patient 093

APPENDIX B

LAPLACE TRANSFORM

Laplace transform of the first derivative:

$$\begin{aligned}
 L(f') &= \int_0^{\infty} e^{-sT} f'(T) dT \\
 L(f') &= [e^{-sT} f(T)] \Big|_0^{\infty} + s \int_0^{\infty} e^{-sT} f(T) dT \\
 L(f') &= sL(f) - f(0)
 \end{aligned} \tag{B.1}$$

Laplace transform of the second derivative:

$$\begin{aligned}
 L(f'') &= sL(f') - f'(0) \\
 L(f'') &= s[sL(f) - f(0)] - f'(0) \\
 L(f'') &= s^2 L(f) - sf(0) - f'(0)
 \end{aligned} \tag{B.2}$$

Laplace transform of $F(T) = \frac{e^{-aT} \sin \omega T}{\omega}$

$$\begin{aligned}
 L\{F(T)\} &= \int_0^{\infty} e^{-sT} f(T) dT \\
 L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) &= \int_0^{\infty} e^{-st} \frac{e^{-aT} \sin \omega T}{\omega} dT \\
 L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) &= \int_0^{\infty} \frac{e^{-(s+a)T} \sin \omega T}{\omega} dT \\
 L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) &= -\frac{1}{(s+a)} \int_0^{\infty} \frac{\sin \omega T}{\omega} d(e^{-(s+a)T}) \\
 L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) &= 0 + \frac{\omega}{(s+a)} \int_0^{\infty} \frac{e^{-(s+a)T} \cos \omega T}{\omega} dT \\
 L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) &= -\frac{\omega}{(s+a)^2} \int_0^{\infty} \frac{\cos \omega T}{\omega} d(e^{-(s+a)T})
 \end{aligned}$$

$$\begin{aligned}
 L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) &= \frac{1}{(s+a)^2} - \frac{\omega^2}{(s+a)^2} \int_0^\infty \frac{e^{-(s+a)T} \sin \omega T}{\omega} dT \\
 L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) &= \frac{1}{(s+a)^2} - \frac{\omega^2}{(s+a)^2} L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) \\
 \left(1 + \frac{\omega^2}{(s+a)^2}\right) L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) &= \frac{1}{(s+a)^2} \\
 L\left(\frac{e^{-aT} \sin \omega T}{\omega}\right) &= \frac{1}{(s+a)^2 + \omega^2} \tag{B.3}
 \end{aligned}$$

Laplace transform of $F(T) = \frac{e^{-aT} \sinh \omega T}{\omega}$

$$\begin{aligned}
 L\{F(T)\} &= \int_0^\infty e^{-sT} f(T) dT \\
 L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) &= \int_0^\infty e^{-sT} \frac{e^{-aT} \sinh \omega T}{\omega} dT \\
 L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) &= \int_0^\infty \frac{e^{-(s+a)T} \sinh \omega T}{\omega} dT \\
 L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) &= -\frac{1}{(s+a)} \int_0^\infty \frac{\sinh \omega T}{\omega} d(e^{-(s+a)T}) \\
 L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) &= 0 + \frac{\omega}{(s+a)} \int_0^\infty \frac{e^{-(s+a)T} \cosh \omega T}{\omega} dT \\
 L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) &= -\frac{\omega}{(s+a)^2} \int_0^\infty \frac{\cosh \omega T}{\omega} d(e^{-(s+a)T}) \\
 L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) &= \frac{1}{(s+a)^2} + \frac{\omega^2}{(s+a)^2} \int_0^\infty \frac{e^{-(s+a)T} \sinh \omega T}{\omega} dT \\
 L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) &= \frac{1}{(s+a)^2} + \frac{\omega^2}{(s+a)^2} L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) \\
 \left(1 - \frac{\omega^2}{(s+a)^2}\right) L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) &= \frac{1}{(s+a)^2}
 \end{aligned}$$

$$L\left(\frac{e^{-aT} \sinh \omega T}{\omega}\right) = \frac{1}{(s+a)^2 - \omega^2} \quad (\text{B.4})$$

Laplace transform of $F(T) = Te^{aT}$

$$L\{F(T)\} = \int_0^{\infty} e^{-sT} f(T) dT$$

$$L(Te^{aT}) = \int_0^{\infty} e^{-sT} Te^{aT} dT$$

$$L(Te^{aT}) = \int_0^{\infty} e^{-(s-a)T} T dT$$

$$L(Te^{aT}) = -\frac{1}{(s-a)} \int_0^{\infty} T d(e^{-(s-a)T})$$

$$L(Te^{aT}) = 0 + \frac{1}{(s-a)} \int_0^{\infty} e^{-(s-a)T} dT$$

$$L(Te^{aT}) = \frac{1}{(s-a)^2} \quad (\text{B.5})$$

APPENDIX C

QUANTITATIVE PARAMETERS DERIVED FROM RENOGRAM SAMPLES

Table C.1 Derived Basic Parameters – Part 1

Reno ID	Parameter							
	DEI	DRF	$T_{1/2,dec}$ (real)	$T_{1/2,dec}$ (exp)	$LT_{1/2,dec}$ (real)	$LT_{1/2,dec}$ (exp)	NORA ₂₀	NORA _{post}
1	11.488			168.219			2.199	
2	-10.350		10.033	11.940	28.667	36.389	0.383	
3	-0.760		18.883	9.717	18.883	19.708	0.825	
4	-8.781		29.583	18.611	29.583	33.570	1.533	
5	-59.969		7.017	5.214	13.217	20.397	0.153	
6	-17.577		9.233	8.876	20.017	21.658	0.286	
7	-14.209		8.517	7.830	21.700	25.592	0.322	
8	4.583			32.815		43.034	0.920	
9	4.676			24.133		34.412	1.196	
10	-34.901		7.583	7.014	17.650	23.180	0.210	
11	-5.557	46.72	8.883	6.564	17.467	20.403	0.311	14056.07
12	4.932	53.28	16.400	11.501	20.050	21.163	0.625	24035.26
13	3.584	46.14	8.917	8.022	18.833	22.354	0.303	15650.53
14	33.556	53.86	15.117	10.381	16.717	18.789	0.412	20959.45
15	2.266	40.68		38.251		56.882	1.458	127401.78
16	-25.499	59.32	7.350	8.100	19.800	29.637	0.237	7622.58
17	1.623			89.917			1.706	293681.03
18	-85.319		8.283	5.948	13.083	16.575	0.132	7272.82
19	12.357	64.7		24.074		35.778	1.583	487.48
20	2.058	72.29	25.617	20.471	32.000	35.749	0.817	36706.83
21	5.366	40.94	22.350	12.038	22.583	21.763	1.252	34161.19
22	-14.180	59.06	12.250	8.143	16.300	19.662	0.383	16165.93
23	3.011	50.5	12.667	6.454	13.983	16.084	0.233	25183.21
24	9.862	49.5	23.933	18.655	27.283	25.643	0.796	72886.27
25	18.349	40.05	16.150	8.469	16.267	18.488	0.635	38729.72
26	-14.526	59.95	12.017	6.309	13.883	16.160	0.277	14808.89
27	5.005	50.44		52.887		103.386	1.422	43535.79
28	3.616	49.56	32.000	34.593		53.661	0.782	16483.13
29	12.987	44.1	30.683	18.361	30.683	30.262	1.463	101244.97
30	-56.195	55.9	10.233	7.245	15.133	22.780	0.362	24266.23
31	16.066			53.785		56.302	0.904	45392.33
32	-6.065						1.010	61747.99
33	18.739		21.833	8.959	21.833	20.934	1.368	38620.53
34	7.179			22.304		80.002	2.061	81514.81
35	7.202			69.752			2.982	290756.71
36	33.272		15.683	7.107	15.683	17.199	0.676	66258.00
37	-23.885	49.2	13.333	7.002	13.850	17.956	0.438	31788.32
38	-28.546	50.8	13.367	8.384	13.733	20.331	0.517	23499.26
39	-10.308	53.29	8.133	5.681	16.167	19.961	0.180	11836.02
40	2.689	46.71		731.358		1208.220	1.382	136910.65
41	-39.707	51.82	9.967	5.804	14.417	17.938	0.245	19131.35
42	11.462	48.18		31.297		77.980	2.254	263066.39

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter							
	DEI	DRF	$T_{1/2,dec}$ (real)	$T_{1/2,dec}$ (exp)	$LT_{1/2,dec}$ (real)	$LT_{1/2,dec}$ (exp)	NORA ₂₀	NORA _{post}
43	-18.854		8.150	7.981	21.683	26.299	0.254	15389.14
44	12.002			33.885		43.683	1.150	117774.59
45	-16.012	49.73	9.367	7.632	17.483	23.891	0.310	21428.70
46	7.375	50.27	31.567	21.349	31.567	31.532	1.306	111546.08
47	29.906	85.1	15.000	9.087	15.617	18.967	0.536	45777.80
48	8.587	84.5		154.341		666.739	1.317	36785.20
49	10.210		24.717	20.344		30.514	0.860	34271.04
50	-25.938		12.483	8.960	14.750	20.934	0.325	20742.29
51	22.448	58.9	6.733	5.410	14.283	14.507	0.146	9109.40
52	5.704	41.1	24.150	12.129	24.600	25.267	1.504	46941.27
53	-43.912	18.6	9.917	5.319	16.133	18.692	0.242	
54	10.218	41.4					2.402	
55	3.627	58.03	12.083	6.412	17.133	15.392	0.215	14678.38
56	12.418	41.97		24.543		44.777	2.625	127884.27
57	-29.896	68.58	7.833	6.630	16.467	25.116	0.204	12366.50
58	3.475	31.42		34.019		43.006	1.116	25649.67
59	-38.317	45.61	9.300	8.541	23.567	27.973	0.361	16281.00
60	-40.697	54.39	9.050	8.992	25.200	30.166	0.379	18877.97
61	5.526	53.89	18.883	7.545	18.900	17.515	0.868	43959.43
62	3.580	46.11	12.067	6.268	14.167	15.433	0.267	22212.33
63	-39.287		8.383	7.604	16.683	23.782	0.265	25376.61
64	-18.690	84.16	7.300	6.696	16.717	23.326	0.201	15406.08
65	-53.556	60.8	8.150	7.284	22.650	27.060	0.278	14344.88
66	4.759	39.2		71.713		112.734	0.854	35577.44
67	-28.008		7.033	6.057	16.117	21.641	0.173	32712.55
68	0.216	42.04					1.488	220265.30
69	21.651	57.96	21.050	9.130	21.050	20.798	1.141	105229.57
70	3.167	37.4		658.093			1.835	294258.30
71	9.659	62.6		28.419		38.155	1.103	97926.84
72	11.437	49	19.983	11.090	19.983	21.034	0.841	72753.58
73	-24.639	51	8.800	6.835	18.400	20.718	0.230	16796.84
74	-50.897		11.017	6.510	13.117	20.704	0.215	12637.78
75	-35.580		6.217	6.204	28.683	25.681	0.165	7766.80
76	-12.918	36.15		37.909		281.728	1.098	13116.49
77	-13.155	63.85		44.418		66.165	0.760	19511.06
78	-11.299		15.183	11.099	21.917	22.625	0.707	83171.25
79	-29.960		11.417	6.613	13.200	16.139	0.189	8034.76
80	2.243						2.102	155389.70
81	-32.093		12.300	13.728	28.367	34.328	0.442	27013.50
82	-6.029						1.396	179155.84
83	-12.958		7.183	15.464		47.345	0.366	42351.95
84	-18.576		5.917	5.755	18.100	21.943	0.164	14018.83
85	7.079		12.717	8.412	14.650	20.223	0.397	16876.87
86	19.689		14.533	9.331	15.883	18.967	0.505	46412.43
87	-9.333		12.250	12.160	26.767	28.700	0.387	21635.97
88	4.627		14.633	11.690	19.983	21.900	0.424	21609.51
89	-7.715		9.533	8.443	16.950	20.552	0.257	14937.09
90	-19.479			28.494		37.357	1.005	81889.98
91	-23.607	81.6	12.233	10.913	20.300	27.288	0.413	43104.59
92	-8.955	59.7	13.000	6.934	14.317	15.885	0.321	
93	6.271	40.3	23.433	10.438	23.433	21.507	1.377	
94	10.799	28.66		234.678			1.231	35192.83
95	-14.244	71.34	25.933	26.103		53.616	0.571	25015.00

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter							
	DEI	DRF	$T_{1/2,dec}$ (real)	$T_{1/2,dec}$ (exp)	$LT_{1/2,dec}$ (real)	$LT_{1/2,dec}$ (exp)	NORA ₂₀	NORA _{post}
96	2.013	61.75		35.755		55.364	1.069	32745.62
97	-7.514	38.25					1.186	115079.41
98	-45.574	58.7	7.267	5.322	14.217	22.093	0.144	14509.82
99	-61.872	41.3	6.783	5.488	14.967	22.641	0.151	8754.59
100	36.755	25.27	15.733	8.713	15.850	17.708	0.492	18970.42
101	9.845	74.73	15.400	20.068		40.330	0.567	44884.93
102	-0.127	83.45	7.533	9.158	25.583	26.377	0.291	15619.83
103	2.184	44.04		49.191		111.491	2.145	64678.81
104	-4.414	55.96	21.667	15.570	23.567	24.884	0.802	19139.47
105	6.174	48.66	10.717	7.061	15.733	17.143	0.238	7695.82
106	28.551	51.34	21.867	10.535	21.867	21.300	1.123	31562.67
107	58.688		15.383	3.541	15.383	14.663	0.348	53080.00
108	-36.826		8.617	6.058	16.517	21.265	0.220	20087.27
109	-21.769	51.57	9.417	6.665	15.100	19.590	0.255	19159.98
110	0.627	48.43		47.946		48.402	1.220	92524.97
111	3.405						1.921	234848.31
112	1.612		27.517	22.871		32.557	0.873	61389.57
113	-35.684	52.7	11.750	6.697	13.467	16.572	0.210	9385.99
114	-17.666	47.3	16.833	13.700	23.433	25.732	0.541	24584.02
115	0.369	82.9	14.817	11.901	17.783	22.649	0.555	60793.97
116	36.221	31.43	25.817	15.542	25.817	25.797	1.145	15798.83
117	-1.454	68.57	18.183	17.296	31.900	33.626	0.606	13981.94
118	-87.660	51.3	12.067	8.082	12.800	21.054	0.401	17534.65
119	10.224	48.7					2.060	192698.03
120	-42.987		9.983	20.219		118.104	0.633	31153.81
121	-90.876		11.433	6.226	12.750	18.687	0.241	11858.60
122	-52.674		8.300	6.398	14.283	21.069	0.215	13066.36
123	-63.720		8.083	8.277	25.050	34.088	0.199	5204.10
124	4.010		13.983	11.484	18.767	23.352	0.420	25936.50
125	-34.299		7.033	7.918	29.533	34.592	0.243	13814.29
126	-28.939		12.917	9.026	13.367	18.813	0.372	16195.11
127	12.137		14.267	9.121	15.017	19.053	0.494	36050.15
128	-35.378		10.217	7.807	16.533	25.359	0.316	41188.67
129	-13.652	52.12	6.517	6.258	17.567	19.753	0.143	11631.77
130	19.709	47.88	15.817	9.244	16.167	17.525	0.479	48985.89
131	-4.123			41.061		54.205	1.160	117230.40
132	0.612		9.617	6.559	14.033	17.171	0.186	15917.70

Table C.2 Derived Basic Parameters – Part 2

Reno ID	Parameter						
	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	$t_{peak/2}$	T_{max}
1	2400	0.927				2.733	16.700
2	7000	0.355				0.900	2.767
3	6720	0.465				1.583	10.300
4	3360	0.741				2.117	15.717
5	12608	0.131				0.917	2.883
6	9800	0.237				0.800	2.950
7	18788	0.232				1.083	3.750
8	9000	0.702				0.917	4.733
9	6500	0.785				1.117	11.500
10	12000	0.175				1.000	2.917
11	12223	0.181	0.682	1.700	1.160	1.733	4.117
12	14380	0.351	0.945	1.841	1.741	1.817	4.183
13	10700	0.215	1.040	1.188	1.235	1.283	3.933
14	12200	0.291	1.231	1.084	1.334	1.400	4.000
15	10150	0.879	7.591	0.881	6.691	1.383	15.550
16	10672	0.192	0.582	3.032	1.764	0.917	3.250
17	1100	0.896	140.461	0.912	128.170	1.783	27.867
18	900	0.115	7.073	1.393	9.857	0.667	2.700
19	9447	0.796	0.026	0.943	0.025	1.950	13.433
20	6547	0.544	3.741	1.120	4.189	0.767	7.217
21	16412	0.617	1.028	2.428	2.495	2.033	9.433
22	16788	0.263	0.663	1.922	1.275	1.267	4.017
23	18945	0.166	0.950	2.517	2.391	1.183	4.550
24	17577	0.603	3.152	1.236	3.897	1.133	4.783
25	14953	0.347	1.426	1.636	2.332	1.783	9.650
26	18487	0.182	0.521	1.685	0.878	1.367	4.317
27	3772	0.985	8.010	1.004	8.040	0.650	18.133
28	2925	0.671	4.869	1.026	4.998	0.517	3.017
29	13195	0.812	4.282	1.080	4.623	1.733	11.800
30	14078	0.232	1.115	1.299	1.449	1.517	4.100
31	550	0.728	66.531	1.445	96.149	0.383	11.183
32	350	0.886	154.934	1.004	155.534	0.350	28.583
33	800	0.649	23.016	1.445	33.248	2.217	12.750
34	550	0.987	71.091	1.498	106.476	2.417	20.867
35	1900	0.967	49.832	2.132	106.239	4.317	22.067
36	1490	0.353	23.290	1.218	28.371	1.833	10.667
37	11025	0.269	1.778	1.622	2.884	1.500	7.717
38	11224	0.327	1.328	1.799	2.388	1.233	7.633
39	12161	0.134	0.728	1.429	1.040	1.233	3.783
40	11560	0.942	8.108	0.914	7.413	1.183	6.033
41	15517	0.168	0.844	1.240	1.047	1.200	4.683
42	23207	0.963	4.865	1.157	5.628	2.717	18.600
43	850	0.207	14.791	1.664	24.605	0.950	2.983
44	950	0.749	81.075	1.096	88.898	1.150	12.017
45	12897	0.213	1.147	1.414	1.622	1.317	3.900
46	17322	0.661	3.266	1.442	4.711	1.917	9.317
47	26152	0.304	0.997	1.202	1.198	1.667	6.650
48	25421	0.938	1.039	5.372	5.579	1.317	14.150
49	920	0.576	25.000	2.961	74.022	1.000	6.167
50	1010	0.272	17.228	1.799	30.990	0.517	3.517

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter						
	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	$t_{peak/2}$	T_{max}
51	15679	0.103	0.415	1.677	0.695	1.333	3.833
52	17624	0.668	1.186	3.641	4.318	2.367	14.217
53	15527	0.166				1.283	4.733
54	20556	0.864				3.600	31.000
55	22094	0.135	0.419	1.518	0.637	1.450	4.650
56	28037	0.943	1.649	3.746	6.177	3.417	14.333
57	21557	0.167	0.471	2.617	1.233	1.050	3.100
58	11936	0.783	1.515	3.532	5.351	1.167	5.833
59	6627	0.253	1.739	1.121	1.950	1.233	4.000
60	7721	0.266	1.718	1.069	1.837	1.083	3.833
61	22251	0.454	1.039	1.366	1.419	1.883	9.917
62	14693	0.177	1.011	1.228	1.242	1.333	4.550
63	1190	0.211	17.011	1.119	19.040	0.883	3.150
64	17063	0.164	0.736	1.777	1.308	0.950	3.167
65	12621	0.228	0.935	1.585	1.482	0.950	3.183
66	7811	0.736	3.943	1.627	6.414	0.867	3.117
67	2600	0.145	10.610	1.497	15.884	0.817	2.883
68	14336	0.952	9.854	0.917	9.033	0.800	31.750
69	24583	0.566	2.135	1.259	2.687	2.000	13.517
70	14819	0.962	10.434	0.853	8.901	1.650	28.000
71	18597	0.756	3.622	1.363	4.935	0.983	9.367
72	20666	0.500	2.105	1.207	2.540	1.583	10.200
73	15168	0.187	0.903	1.365	1.233	1.000	3.417
74	1010	0.169	9.844	1.851	18.222	0.950	3.483
75	700	0.151	10.184	1.576	16.046	0.817	2.717
76	1056	0.955	10.778	1.205	12.989	0.500	24.517
77	2012	0.632	8.080	1.049	8.479	0.617	6.117
78	32165	0.419	1.537	1.373	2.110	1.533	5.717
79	700	0.159	9.709	1.655	16.071	0.883	2.950
80	850	0.921	80.608	1.680	135.395	2.667	30.800
81	700	0.383	33.591	1.632	54.807	0.550	3.533
82	900	0.926	132.166	0.924	122.132	0.600	29.783
83	990	0.333	38.910	1.262	49.108	0.600	2.450
84	1290	0.144	9.527	1.297	12.353	0.683	2.917
85	400	0.259	27.588	1.095	30.195	1.167	4.767
86	1100	0.325	27.301	1.072	29.259	1.350	5.950
87	800	0.340	23.804	25.300	602.245	0.567	2.700
88	1000	0.323	16.515	1.516	25.040	1.033	3.883
89	880	0.213	14.113	1.251	17.658	0.967	2.767
90	1050	0.575	44.881	1.685	75.621	1.567	10.233
91	14388	0.307	2.245	1.103	2.476	1.283	3.600
92	15530	0.212				1.483	4.483
93	14550	0.654				2.083	11.450
94	1972	0.869	12.624	1.120	14.142	0.650	26.117
95	3954	0.491	5.457	1.085	5.922	0.717	3.367
96	8308	0.708	2.622	2.181	5.720	1.267	4.967
97	5001	0.832	16.180	1.295	20.954	0.800	32.000
98	20451	0.120	0.591	1.436	0.849	0.983	3.067
99	14103	0.127	0.528	1.540	0.813	1.050	2.867
100	6515	0.354	2.112	1.300	2.745	1.233	7.567
101	17015	0.425	1.995	1.526	3.044	1.417	3.600
102	17051	0.251	0.791	1.759	1.391	0.917	3.250
103	5407	0.949	5.337	1.358	7.249	2.600	16.583

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter						
	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	$t_{peak/2}$	T_{max}
104	4679	0.524	2.680	1.254	3.361	1.217	5.317
105	12303	0.183	0.488	2.103	1.026	1.033	3.317
106	19912	0.579	0.822	3.579	2.941	1.883	12.750
107	1150	0.197	26.232	1.094	28.698	1.600	12.583
108	1350	0.164	11.183	1.593	17.813	0.950	4.133
109	9933	0.168	1.278	1.174	1.500	1.500	4.167
110	9468	0.806	6.483	1.189	7.708	1.383	4.267
111	600	0.856	175.898	0.941	165.433	2.333	30.700
112	630	0.595	66.779	1.168	78.022	1.250	4.133
113	11094	0.180	0.730	1.630	1.190	0.983	3.500
114	10258	0.453	2.018	1.478	2.983	0.900	3.750
115	19547	0.378	2.128	1.144	2.435	1.200	5.083
116	2356	0.649	3.822	1.357	5.186	1.600	11.067
117	3855	0.445	2.674	1.615	4.319	1.017	3.833
118	7888	0.282	1.572	1.323	2.079	1.233	4.767
119	13009	0.945	6.818	1.231	8.394	2.317	28.367
120	880	0.421	23.834	1.941	46.269	1.150	3.917
121	720	0.173	11.856	1.726	20.465	1.183	4.200
122	1050	0.179	10.363	1.614	16.729	0.917	2.900
123	740	0.175	6.181	4.163	25.731	0.733	3.300
124	1150	0.351	18.904	1.631	30.834	0.750	3.650
125	1100	0.218	11.286	1.651	18.630	0.683	2.767
126	580	0.280	21.121	1.797	37.957	1.317	3.467
127	1010	0.372	26.963	1.563	42.144	1.017	7.000
128	1300	0.236	23.720	1.280	30.358	0.767	3.900
129	13593	0.139	0.838	1.431	1.198	0.833	2.317
130	17402	0.313	1.843	1.012	1.865	1.350	5.250
131	1320	0.824	63.448	1.190	75.520	0.833	7.367
132	1300	0.162	10.685	1.238	13.228	0.800	3.117

Table C.3 Derived NORA Analyzed for Developing BSS

Reno ID	Parameter							
	NORA ₃	NORA ₄	NORA ₅	NORA ₆	NORA ₇	NORA ₈	NORA ₉	NORA ₁₀
1	1.303	1.553	1.561	1.618	1.779	1.886	1.877	1.927
2	1.078	0.999	0.872	0.805	0.725	0.683	0.572	0.542
3	1.241	1.364	1.502	1.634	1.656	1.642	1.648	1.707
4	1.231	1.285	1.472	1.608	1.678	1.782	1.774	1.936
5	1.157	0.994	0.821	0.698	0.589	0.530	0.470	0.411
6	1.206	1.075	0.916	0.762	0.675	0.641	0.609	0.571
7	1.286	1.375	1.254	1.032	0.873	0.766	0.678	0.610
8	1.208	1.285	1.292	1.295	1.281	1.213	1.231	1.213
9	1.153	1.221	1.315	1.372	1.408	1.456	1.509	1.506
10	1.198	1.095	0.897	0.732	0.650	0.562	0.514	0.473
11	1.453	1.713	1.610	1.388	1.142	0.975	0.846	0.748
12	1.497	1.774	1.743	1.671	1.497	1.397	1.306	1.237
13	1.308	1.409	1.220	1.031	0.895	0.780	0.701	0.631
14	1.335	1.415	1.280	1.178	1.108	1.079	1.044	1.008
15	1.181	1.283	1.319	1.402	1.421	1.478	1.518	1.550
16	1.220	1.134	0.897	0.766	0.649	0.581	0.532	0.480
17	1.155	1.277	1.358	1.420	1.492	1.532	1.568	1.610
18	1.116	0.936	0.759	0.673	0.626	0.578	0.538	0.502
19	1.220	1.415	1.541	1.613	1.678	1.732	1.767	1.887
20	1.206	1.356	1.460	1.467	1.499	1.469	1.418	1.338
21	1.246	1.510	1.668	1.748	1.841	1.938	2.007	1.989
22	1.257	1.453	1.403	1.320	1.210	1.093	1.020	0.909
23	1.329	1.386	1.378	1.312	1.251	1.168	1.091	0.988
24	1.229	1.307	1.315	1.299	1.278	1.259	1.244	1.186
25	1.304	1.501	1.589	1.653	1.681	1.758	1.794	1.797
26	1.298	1.496	1.485	1.297	1.172	1.060	0.996	0.919
27	1.103	1.145	1.249	1.259	1.289	1.328	1.319	1.363
28	1.162	1.125	1.057	1.040	1.068	1.024	0.978	0.965
29	1.274	1.393	1.506	1.561	1.507	1.666	1.698	1.747
30	1.400	1.554	1.483	1.280	0.995	0.995	0.894	0.802
31	1.084	1.111	1.129	1.107	1.112	1.109	1.119	1.148
32	1.037	0.911	0.897	0.818	0.857	0.829	0.859	0.904
33	1.174	1.323	1.432	1.586	1.679	1.778	1.859	1.924
34	1.117	1.252	1.355	1.425	1.535	1.570	1.674	1.718
35	1.239	1.472	1.683	1.828	1.991	2.128	2.278	2.386
36	1.237	1.441	1.570	1.653	1.679	1.774	1.847	1.891
37	1.278	1.459	1.556	1.552	1.604	1.621	1.532	1.436
38	1.263	1.416	1.471	1.476	1.563	1.579	1.544	1.403
39	1.321	1.315	1.096	0.929	0.768	0.683	0.605	0.490
40	1.284	1.394	1.466	1.465	1.394	1.374	1.423	1.392
41	1.279	1.430	1.457	1.314	1.103	0.843	0.807	0.731
42	1.256	1.449	1.555	1.677	1.698	1.763	1.824	1.879
43	1.229	1.118	0.945	0.825	0.736	0.629	0.554	0.495
44	1.200	1.301	1.344	1.418	1.415	1.418	1.453	1.460

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter							
	NORA ₃	NORA ₄	NORA ₅	NORA ₆	NORA ₇	NORA ₈	NORA ₉	NORA ₁₀
45	1.306	1.452	1.261	1.112	0.951	0.839	0.773	0.668
46	1.311	1.451	1.560	1.658	1.761	1.863	1.948	1.935
47	1.347	1.593	1.706	1.757	1.757	1.704	1.689	1.600
48	1.239	1.366	1.314	1.251	1.213	1.158	1.185	1.171
49	1.155	1.318	1.401	1.479	1.490	1.439	1.398	1.325
50	1.135	1.182	1.153	1.080	1.007	0.952	0.900	0.828
51	1.267	1.400	1.236	0.879	0.688	0.661	0.655	0.681
52	1.271	1.450	1.642	1.729	1.886	1.936	1.997	2.087
53	1.253	1.408	1.437	1.420	1.270	1.115	1.023	0.706
54	1.234	1.453	1.613	1.792	1.919	2.008	2.097	1.909
55	1.322	1.509	1.537	1.375	1.200	1.013	0.952	0.893
56	1.292	1.537	1.805	2.024	2.166	2.293	2.403	2.511
57	1.221	1.140	0.969	0.802	0.693	0.599	0.521	0.478
58	1.193	1.291	1.377	1.424	1.394	1.395	1.393	1.378
59	1.281	1.426	1.316	1.129	0.962	0.826	0.739	0.640
60	1.279	1.426	1.326	1.093	0.969	0.808	0.719	0.646
61	1.274	1.487	1.668	1.784	1.848	1.868	1.900	1.910
62	1.305	1.487	1.482	1.372	1.239	0.855	0.878	0.947
63	1.238	1.192	1.007	0.816	0.710	0.647	0.592	0.566
64	1.219	1.116	0.902	0.749	0.648	0.563	0.523	0.462
65	1.204	1.167	0.978	0.832	0.698	0.626	0.538	0.462
66	1.156	1.086	0.984	0.964	0.936	0.913	0.920	0.913
67	1.183	0.978	0.793	0.684	0.605	0.537	0.476	0.421
68	1.137	1.165	1.202	1.176	1.250	1.280	1.299	1.331
69	1.246	1.395	1.542	1.612	1.710	1.768	1.827	1.891
70	1.155	1.237	1.279	1.318	1.326	1.410	1.493	1.501
71	1.191	1.273	1.318	1.359	1.386	1.421	1.446	1.437
72	1.264	1.382	1.491	1.547	1.574	1.623	1.637	1.678
73	1.210	1.194	1.026	0.887	0.751	0.676	0.602	0.539
74	1.256	1.262	1.191	1.048	0.972	0.865	0.761	0.679
75	1.042	0.852	0.691	0.573	0.499	0.417	0.379	0.333
76	1.063	1.117	1.043	1.055	0.981	0.857	0.864	1.006
77	1.008	1.066	1.040	1.181	1.031	1.043	1.122	1.027
78	1.298	1.519	1.653	1.679	1.557	1.352	1.213	1.107
79	1.186	1.143	1.040	0.923	0.847	0.764	0.741	0.696
80	1.208	1.367	1.506	1.512	1.604	1.665	1.722	1.779
81	1.125	1.121	1.043	0.943	0.913	0.843	0.798	0.762
82	1.078	1.119	1.162	1.190	1.234	1.229	1.294	1.305
83	1.079	0.834	0.686	0.631	0.557	0.513	0.512	0.482
84	1.130	0.927	0.705	0.565	0.473	0.404	0.378	0.339
85	1.245	1.441	1.532	1.395	1.239	1.139	1.033	1.001
86	1.241	1.437	1.523	1.552	1.502	1.458	1.421	1.350
87	1.132	1.072	0.954	0.857	0.803	0.755	0.714	0.640
88	1.255	1.299	1.230	1.101	1.012	0.929	0.898	0.845
89	1.205	0.965	0.902	0.767	0.719	0.642	0.637	0.593
90	1.166	1.346	1.439	1.500	1.584	1.616	1.690	1.679

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter							
	NORA ₃	NORA ₄	NORA ₅	NORA ₆	NORA ₇	NORA ₈	NORA ₉	NORA ₁₀
91	1.306	1.323	1.230	1.100	1.010	0.946	0.877	0.819
92	1.309	1.483	1.491	1.443	1.359	1.275	1.204	1.146
93	1.280	1.437	1.615	1.723	1.790	1.876	1.961	2.041
94	1.114	1.162	1.273	1.045	1.257	1.293	1.185	1.187
95	1.145	1.029	1.007	0.956	0.858	0.926	0.846	0.806
96	1.281	1.437	1.510	1.505	1.492	1.405	1.401	1.341
97	1.160	1.196	1.203	1.140	1.114	1.037	1.021	0.978
98	1.204	1.087	0.907	0.744	0.632	0.546	0.483	0.439
99	1.179	0.977	0.800	0.668	0.573	0.493	0.449	0.400
100	1.224	1.309	1.309	1.374	1.370	1.370	1.321	1.279
101	1.273	1.319	1.154	1.061	0.976	0.936	0.866	0.833
102	1.157	1.053	0.843	0.709	0.613	0.549	0.501	0.451
103	1.201	1.307	1.464	1.554	1.653	1.783	1.799	1.907
104	1.248	1.425	1.522	1.505	1.487	1.511	1.471	1.480
105	1.271	1.266	1.122	0.982	0.909	0.802	0.786	0.704
106	1.229	1.401	1.490	1.611	1.688	1.719	1.806	1.856
107	1.249	1.435	1.588	1.661	1.711	1.720	1.736	1.720
108	1.240	1.341	1.213	1.044	0.876	0.733	0.651	0.540
109	1.356	1.516	1.347	1.137	0.979	0.856	0.781	0.715
110	1.298	1.493	1.483	1.451	1.407	1.417	1.411	1.389
111	1.175	1.254	1.310	1.329	1.350	1.425	1.445	1.437
112	1.231	1.464	1.435	1.440	1.400	1.387	1.356	1.222
113	1.158	1.148	1.066	0.966	0.920	0.861	0.782	0.727
114	1.137	1.191	1.156	1.124	1.088	1.032	0.989	0.909
115	1.239	1.405	1.466	1.305	1.291	1.270	1.218	1.188
116	1.278	1.448	1.557	1.681	1.715	1.571	1.597	1.484
117	1.238	1.347	1.357	1.250	1.230	1.180	1.149	1.035
118	1.213	1.303	1.421	1.307	1.283	1.124	1.129	1.084
119	1.190	1.283	1.397	1.418	1.453	1.520	1.564	1.597
120	1.337	1.486	1.398	1.123	1.004	0.831	0.815	0.753
121	1.280	1.383	1.349	1.210	1.079	1.003	0.896	0.822
122	1.204	1.149	0.950	0.800	0.706	0.625	0.576	0.529
123	1.131	1.027	0.875	0.745	0.672	0.585	0.530	0.475
124	1.167	1.195	1.173	1.101	1.020	0.967	0.907	0.867
125	1.092	0.949	0.764	0.670	0.564	0.504	0.456	0.414
126	1.284	1.309	1.258	1.282	1.187	1.118	1.100	1.075
127	1.232	1.316	1.316	1.300	1.329	1.286	1.287	1.194
128	1.242	1.333	1.256	1.156	1.020	0.844	0.760	0.683
129	0.918	0.732	0.640	0.562	0.479	0.438	0.389	0.352
130	1.305	1.459	1.525	1.513	1.501	1.492	1.446	1.412
131	1.149	1.190	1.268	1.310	1.366	1.389	1.368	1.343
132	1.149	1.030	0.894	0.789	0.720	0.641	0.593	0.543
133	1.014	0.878	0.778	0.690	0.619	0.590	0.514	0.496
134	1.058	0.924	0.792	0.728	0.638	0.579	0.511	0.454
135	1.266	1.373	1.463	1.547	1.526	1.565	1.628	1.651
136	1.247	1.295	1.131	0.994	0.825	0.817	0.837	0.822

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter							
	NORA ₃	NORA ₄	NORA ₅	NORA ₆	NORA ₇	NORA ₈	NORA ₉	NORA ₁₀
137	1.010	0.801	0.659	0.556	0.477	0.444	0.408	0.350
138	1.094	0.993	0.897	0.788	0.722	0.656	0.597	0.515
139	1.157	1.076	1.000	0.962	0.926	0.896	0.886	0.868
140	1.216	1.148	1.017	0.928	0.796	0.685	0.594	0.516
141	1.219	1.414	1.477	1.497	1.469	1.347	1.280	1.244
142	1.021	0.861	0.701	0.595	0.514	0.434	0.411	0.364
143	1.261	1.464	1.631	1.713	1.728	1.694	1.615	1.460
144	1.232	1.407	1.437	1.321	1.244	1.189	1.037	0.874
145	1.329	1.565	1.610	1.632	1.426	1.290	1.193	1.113
146	1.248	1.491	1.690	1.659	1.734	1.540	1.515	1.351
147	1.149	1.023	0.913	0.835	0.779	0.702	0.635	0.588
148	1.170	1.034	0.918	0.799	0.732	0.662	0.586	0.554
149	1.216	1.326	1.239	1.027	0.810	0.729	0.605	0.495
150	1.196	1.183	1.154	1.046	0.781	0.747	0.607	0.511
151	1.149	1.082	0.933	0.816	0.724	0.660	0.599	0.550
152	1.317	1.555	1.716	1.909	2.063	2.159	2.212	2.305
153	1.312	1.403	1.319	1.203	1.084	0.965	0.874	0.792
154	1.267	1.470	1.508	1.499	1.516	1.462	1.410	1.381
155	1.202	1.065	0.859	0.673	0.582	0.499	0.444	0.405
156	1.240	1.216	1.078	0.862	0.718	0.622	0.544	0.496
157	1.301	1.408	1.241	0.930	0.850	0.781	0.590	0.459
158	1.247	1.369	1.344	1.305	1.147	1.013	0.658	0.382
159	1.260	1.342	1.355	1.320	1.261	1.218	1.191	1.122
160	1.042	0.860	0.718	0.655	0.594	0.528	0.487	0.443
161	1.222	1.317	1.237	1.200	1.176	1.039	0.987	0.909
162	1.178	1.166	1.119	1.073	1.022	0.961	0.904	0.890
163	1.198	1.293	1.257	1.222	1.153	1.001	0.975	0.957
164	1.234	1.339	1.391	1.413	1.398	1.257	1.234	1.221
165	1.405	1.639	1.709	1.714	1.731	1.681	1.624	1.561
166	1.263	1.242	1.074	0.877	0.711	0.647	0.599	0.535
167	1.219	1.142	0.957	0.798	0.680	0.643	0.634	0.576
168	1.230	1.271	1.112	0.957	0.841	0.735	0.700	0.680
169	1.157	1.237	1.259	1.282	1.292	1.293	1.265	1.222
170	1.143	1.246	1.323	1.365	1.422	1.463	1.443	1.468

Table C.4 Derived T_{max} and Its Variants Analyzed for Developing BSS

Reno ID	Parameter									
	$T_{max/10}$	$T_{2max/1}$	$T_{3max/1}$	$T_{4max/1}$	$T_{5max/1}$	$T_{6max/1}$	$T_{7max/1}$	$T_{8max/1}$	$T_{9max/1}$	T_{max}
1	0.200	0.450	0.700	1.017	1.750	2.667	3.117	5.167	6.500	10.000
2	0.233	0.417	0.567	0.700	0.900	1.083	1.300	1.600	1.933	2.767
3	0.117	0.300	0.450	0.683	1.400	2.083	2.667	4.067	5.183	10.000
4	0.117	0.433	0.617	1.083	1.833	2.633	4.167	5.417	7.600	9.967
5	0.100	0.367	0.517	0.733	0.917	1.200	1.400	1.750	2.083	2.883
6	0.067	0.333	0.500	0.650	0.800	1.133	1.517	1.833	2.233	2.950
7	0.350	0.550	0.700	0.883	1.083	1.483	1.900	2.333	2.783	3.750
8	0.317	0.517	0.667	0.800	0.917	1.133	1.533	2.233	2.800	4.733
9	0.317	0.483	0.683	0.833	1.083	1.617	2.183	3.850	5.867	8.950
10	0.417	0.533	0.700	0.850	1.000	1.233	1.517	1.867	2.250	2.917
11	0.917	1.100	1.333	1.533	1.733	2.033	2.367	2.783	3.217	4.117
12	0.950	1.167	1.400	1.583	1.817	2.100	2.433	2.783	3.283	4.183
13	0.550	0.717	0.900	1.083	1.283	1.667	1.950	2.383	2.767	3.933
14	0.950	1.167	1.400	1.583	1.817	2.100	2.433	2.783	3.283	4.183
15	0.350	0.517	0.717	0.917	1.250	1.750	2.467	3.383	5.883	10.000
16	0.383	0.533	0.667	0.800	0.917	1.167	1.517	1.933	2.333	3.250
17	0.117	0.217	0.333	0.683	1.167	1.833	2.833	4.233	6.200	10.000
18	0.233	0.250	0.283	0.417	0.667	0.900	1.267	1.650	2.100	2.700
19	0.550	0.783	0.933	1.133	1.733	2.483	3.400	4.800	7.317	10.000
20	0.183	0.333	0.433	0.567	0.767	1.533	2.167	2.950	3.950	7.217
21	0.533	0.750	0.933	1.333	2.033	2.833	3.700	4.567	6.783	9.433
22	0.567	0.783	0.950	1.050	1.267	1.567	2.050	2.533	3.167	4.017
23	0.417	0.650	0.817	0.933	1.183	1.550	1.917	2.450	2.800	4.550
24	0.417	0.617	0.700	0.900	1.133	1.433	1.717	2.217	2.717	4.783
25	0.433	0.633	0.900	1.283	1.783	2.267	2.900	3.800	5.867	9.650
26	0.483	0.717	0.817	1.067	1.367	1.800	2.200	2.633	3.217	4.317
27	0.100	0.200	0.300	0.467	0.600	0.700	1.583	2.950	4.833	9.633
28	0.100	0.217	0.300	0.417	0.517	0.600	0.717	1.200	2.100	3.017
29	0.550	0.733	0.933	1.250	1.650	2.100	2.750	4.017	6.300	10.000
30	0.550	0.733	0.917	1.167	1.517	1.783	2.167	2.567	2.983	4.100
31	0.150	0.317	0.400	0.367	0.383	0.417	1.083	1.517	2.567	10.000
32	0.267	0.300	0.317	0.333	0.350	0.383	0.400	0.750	1.450	3.050
33	0.183	0.367	0.517	0.983	1.850	2.867	4.417	5.700	7.383	10.000
34	0.350	0.417	0.433	0.517	1.217	2.350	3.700	5.167	7.783	10.000
35	0.350	0.700	1.250	1.867	2.767	3.800	4.933	6.250	8.217	10.000
36	0.517	0.617	0.883	1.283	1.817	2.467	3.333	4.450	7.117	10.000
37	0.450	0.633	0.800	1.150	1.500	1.883	2.367	3.150	4.017	7.717
38	0.400	0.583	0.750	0.883	1.233	1.800	2.450	3.000	4.083	7.633
39	0.500	0.700	0.900	1.100	1.233	1.533	1.783	2.183	2.650	3.783
40	0.500	0.700	0.867	1.050	1.183	1.583	2.050	2.500	3.167	6.033
41	0.333	0.467	0.717	0.900	1.200	1.583	2.100	2.533	3.200	4.683
42	0.400	0.600	0.817	1.167	1.767	2.533	3.250	4.433	6.417	10.000
43	0.117	0.233	0.350	0.450	0.950	1.283	1.517	1.917	2.350	2.983
44	0.333	0.350	0.450	0.667	1.017	1.533	2.083	2.833	4.200	9.350

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	$T_{max/10}$	$T_{2max/1}$	$T_{3max/1}$	$T_{4max/1}$	$T_{5max/1}$	$T_{6max/1}$	$T_{7max/1}$	$T_{8max/1}$	$T_{9max/1}$	T_{max}
45	0.450	0.667	0.850	0.983	1.317	1.683	2.050	2.500	3.000	3.900
46	0.550	0.800	1.033	1.333	1.917	2.550	3.450	5.183	7.167	9.317
47	0.367	0.650	0.933	1.333	1.667	2.183	2.733	3.200	3.950	6.650
48	0.333	0.550	0.683	0.867	1.300	1.500	1.900	2.400	2.933	3.900
49	0.117	0.217	0.333	0.433	1.000	1.533	2.183	3.233	4.350	6.167
50	0.183	0.233	0.333	0.317	0.517	0.817	1.300	1.733	2.317	3.517
51	0.267	0.500	0.717	0.983	1.333	1.617	1.933	2.367	2.983	3.833
52	0.400	0.733	1.050	1.567	2.133	2.917	4.083	5.200	6.933	10.000
53	0.283	0.467	0.667	0.883	1.283	1.600	2.067	2.650	3.250	4.733
54	0.467	0.750	1.067	1.550	2.300	3.150	4.250	5.550	7.150	9.483
55	0.467	0.683	0.883	1.117	1.433	1.850	2.350	2.850	3.500	4.650
56	0.517	0.817	1.300	2.000	2.800	3.867	4.800	5.900	7.733	10.000
57	0.383	0.550	0.717	0.833	1.050	1.250	1.533	1.900	2.267	3.100
58	0.467	0.617	0.767	0.950	1.167	1.483	1.967	2.633	3.883	5.833
59	0.500	0.633	0.817	1.000	1.233	1.633	1.983	2.417	3.000	4.000
60	0.483	0.683	0.767	0.967	1.083	1.350	1.967	2.450	3.017	3.833
61	0.417	0.633	0.917	1.317	1.883	2.450	3.250	4.200	5.367	9.917
62	0.317	0.533	0.717	0.933	1.333	1.667	2.133	2.617	3.233	4.550
63	0.267	0.333	0.383	0.567	0.883	1.183	1.633	2.017	2.450	3.150
64	0.300	0.467	0.633	0.783	0.950	1.350	1.583	1.950	2.433	3.167
65	0.267	0.417	0.600	0.750	0.950	1.267	1.567	1.850	2.450	3.183
66	0.233	0.467	0.600	0.733	0.867	1.100	1.383	1.750	2.200	3.117
67	0.417	0.517	0.567	0.683	0.817	0.950	1.333	1.817	2.250	2.883
68	0.267	0.350	0.467	0.583	0.683	0.833	1.683	2.567	5.183	9.900
69	0.350	0.500	0.800	1.200	1.800	2.450	3.400	4.733	6.900	10.000
70	0.217	0.283	0.433	0.500	0.783	1.483	2.267	3.617	7.267	9.467
71	0.267	0.433	0.600	0.717	0.983	1.417	2.067	2.817	4.883	9.367
72	0.400	0.600	0.833	1.133	1.583	2.000	2.667	3.783	5.450	10.000
73	0.300	0.483	0.650	0.817	1.000	1.350	1.650	1.917	2.500	3.417
74	0.367	0.483	0.600	0.700	0.950	1.400	1.667	2.117	2.450	3.483
75	0.367	0.467	0.550	0.667	0.817	0.950	1.233	1.600	1.933	2.717
76	0.133	0.183	0.283	0.367	0.500	0.633	0.700	1.450	1.883	4.050
77	0.200	0.267	0.383	0.567	0.617	0.783	1.150	1.650	5.267	6.117
78	0.717	0.900	1.050	1.267	1.533	2.050	2.600	3.183	3.983	5.717
79	0.250	0.383	0.500	0.583	0.883	1.150	1.517	1.800	2.283	2.950
80	0.250	0.400	0.517	0.600	1.333	2.233	3.217	4.600	6.967	10.000
81	0.333	0.383	0.417	0.467	0.550	0.750	1.333	1.750	2.083	3.533
82	0.333	0.383	0.467	0.433	0.533	0.617	1.400	2.533	5.617	10.000
83	0.350	0.333	0.400	0.450	0.600	0.900	1.200	1.467	1.867	2.450
84	0.333	0.383	0.433	0.483	0.683	0.900	1.233	1.633	2.250	2.917
85	0.317	0.400	0.483	0.817	1.167	1.617	2.217	2.850	3.700	4.767
86	0.367	0.417	0.600	0.817	1.350	1.800	2.400	2.983	3.617	5.950
87	0.333	0.367	0.417	0.483	0.567	0.967	1.333	1.683	2.100	2.700
88	0.283	0.383	0.467	0.600	1.033	1.333	1.733	2.233	2.650	3.883
89	0.300	0.350	0.467	0.583	0.967	1.283	1.533	1.867	2.333	2.767
90	0.050	0.083	0.750	0.917	1.450	2.033	3.117	4.250	6.233	9.683
91	0.633	0.900	0.967	1.117	1.283	1.500	1.850	2.167	2.567	3.600

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	$T_{max/10}$	$T_{2max/1}$	$T_{3max/1}$	$T_{4max/1}$	$T_{5max/1}$	$T_{6max/1}$	$T_{7max/1}$	$T_{8max/1}$	$T_{9max/1}$	T_{max}
92	0.417	0.617	0.833	1.083	1.483	1.750	2.100	2.633	3.183	4.483
93	0.533	0.800	1.017	1.450	2.017	2.700	3.900	5.133	7.450	10.000
94	0.167	0.267	0.300	0.483	0.600	0.733	1.217	6.067	4.133	8.400
95	0.233	0.350	0.400	0.583	0.717	0.917	1.333	1.700	2.383	3.367
96	0.267	0.317	0.600	0.850	1.267	1.700	2.183	2.650	3.367	4.967
97	0.233	0.283	0.367	0.483	0.600	0.817	1.217	1.817	2.433	4.600
98	0.400	0.550	0.700	0.867	0.983	1.300	1.533	1.867	2.317	3.067
99	0.317	0.483	0.750	0.883	1.050	1.250	1.517	1.833	2.217	2.867
100	0.617	0.783	0.883	1.083	1.233	1.517	1.900	2.383	3.200	7.567
101	0.800	0.817	1.167	1.150	1.417	1.600	1.800	2.217	2.617	3.600
102	0.317	0.450	0.550	0.667	0.917	1.133	1.400	1.783	2.217	3.250
103	0.250	0.433	0.683	1.117	1.717	2.733	4.183	5.633	7.533	10.000
104	0.267	0.417	0.667	0.800	1.217	1.683	2.267	2.917	3.667	5.317
105	0.433	0.583	0.717	0.867	1.033	1.400	1.800	2.067	2.483	3.317
106	0.517	0.717	0.967	1.267	1.767	2.450	3.383	4.933	6.700	10.000
107	0.383	0.550	0.583	0.950	1.533	2.167	2.833	3.733	4.767	7.767
108	0.450	0.567	0.583	0.733	0.950	1.317	1.767	2.167	2.783	4.133
109	0.750	0.917	1.100	1.217	1.500	1.733	2.133	2.517	3.017	4.167
110	0.700	0.900	1.067	1.167	1.383	1.717	2.200	2.700	3.167	4.267
111	0.400	0.450	0.500	0.583	1.200	1.700	2.133	3.167	7.517	9.733
112	0.417	0.500	0.583	0.817	1.250	1.550	2.050	2.550	3.450	4.133
113	0.183	0.433	0.600	0.767	0.983	1.167	1.450	1.750	2.167	3.500
114	0.167	0.383	0.567	0.717	0.900	1.150	1.483	1.817	2.383	3.750
115	0.267	0.517	0.683	0.867	1.183	1.600	2.100	2.683	3.317	5.083
116	0.200	0.450	0.600	0.833	1.567	2.133	2.817	3.483	5.000	6.467
117	0.317	0.433	0.633	0.800	1.017	1.233	1.783	2.283	2.900	3.833
118	0.433	0.633	0.817	0.983	1.233	1.517	1.983	2.533	3.583	4.767
119	0.517	0.717	0.883	1.167	1.500	1.850	2.450	3.883	6.350	10.000
120	0.350	0.417	0.533	0.900	1.133	1.500	2.067	2.600	3.033	3.917
121	0.300	0.367	0.400	0.817	1.183	1.450	1.883	2.333	2.850	4.200
122	0.350	0.417	0.433	0.617	0.917	1.233	1.567	1.850	2.283	2.900
123	0.150	0.250	0.333	0.483	0.733	1.033	1.433	1.667	2.167	3.300
124	0.383	0.417	0.433	0.467	0.750	1.033	1.300	1.817	2.267	3.650
125	0.400	0.417	0.433	0.467	0.683	0.883	1.250	1.583	2.000	2.767
126	0.600	0.633	0.800	1.067	1.317	1.550	1.867	2.133	2.600	3.467
127	0.583	0.600	0.650	0.817	1.017	1.450	1.817	2.217	2.700	7.000
128	0.300	0.333	0.350	0.483	0.767	1.350	1.583	2.250	2.783	3.900
129	0.283	0.417	0.517	0.733	0.833	0.983	1.233	1.433	1.733	2.317
130	0.383	0.600	0.750	0.983	1.350	1.800	2.267	2.667	3.433	5.250
131	0.533	0.567	0.617	0.700	0.833	1.400	1.917	2.800	4.917	7.367
132	0.483	0.567	0.617	0.717	0.800	0.983	1.200	1.583	2.183	3.117
133	0.283	0.367	0.450	0.567	0.667	0.783	0.883	1.050	1.467	2.650
134	0.317	0.417	0.550	0.667	0.733	0.833	0.967	1.183	1.717	2.717
135	0.167	0.400	0.600	0.817	1.317	1.967	2.617	3.483	5.167	9.667
136	0.267	0.517	0.650	0.800	1.000	1.267	1.683	2.117	2.533	3.583
137	0.167	0.367	0.483	0.600	0.750	0.983	1.167	1.417	1.617	2.650

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	$T_{max/10}$	$T_{2max/1}$	$T_{3max/1}$	$T_{4max/1}$	$T_{5max/1}$	$T_{6max/1}$	$T_{7max/1}$	$T_{8max/1}$	$T_{9max/1}$	T_{max}
138	0.217	0.400	0.550	0.667	0.800	1.033	1.267	1.567	1.950	2.683
139	0.433	0.617	0.750	0.883	1.033	1.283	1.517	1.733	2.100	2.933
140	0.467	0.667	0.850	0.967	1.167	1.450	1.667	1.983	2.483	3.283
141	0.350	0.550	0.683	0.850	1.117	1.650	2.133	2.867	3.550	5.933
142	0.317	0.500	0.650	0.783	0.900	1.000	1.150	1.383	1.733	2.633
143	0.283	0.567	0.750	1.017	1.517	2.117	2.700	3.717	4.433	6.850
144	0.383	0.450	0.567	0.733	1.083	1.500	2.033	2.633	3.333	4.717
145	0.450	0.667	0.800	1.083	1.467	1.950	2.383	2.950	3.583	5.883
146	0.433	0.667	0.867	1.200	1.633	2.200	2.933	3.617	4.483	7.467
147	0.100	0.217	0.300	0.367	0.567	0.750	1.183	1.550	2.150	3.083
148	0.200	0.267	0.367	0.433	0.700	0.817	1.333	1.783	2.267	2.650
149	0.083	0.167	0.317	0.517	0.817	1.233	1.733	2.233	2.917	3.900
150	0.233	0.267	0.417	0.533	0.783	1.117	1.483	1.933	2.400	3.533
151	0.417	0.583	0.750	0.883	1.000	1.217	1.483	1.750	2.133	2.800
152	0.567	0.867	1.233	1.783	2.417	3.233	4.267	5.567	7.050	10.000
153	0.633	0.817	0.983	1.133	1.350	1.667	1.967	2.300	2.750	4.300
154	0.650	0.867	1.017	1.183	1.417	1.750	2.183	2.717	3.400	6.600
155	0.383	0.583	0.700	0.867	0.967	1.283	1.583	1.900	2.350	3.117
156	0.350	0.567	0.717	0.850	1.017	1.233	1.633	2.050	2.533	3.317
157	0.450	0.650	0.800	0.967	1.217	1.550	1.917	2.483	2.850	4.017
158	0.367	0.600	0.783	0.883	1.167	1.450	1.817	2.450	2.933	4.183
159	0.517	0.700	0.783	0.950	1.150	1.450	1.850	2.250	2.767	4.800
160	0.517	0.667	0.783	0.850	0.967	1.133	1.283	1.517	1.900	2.533
161	0.400	0.450	0.467	0.517	0.867	1.233	1.650	2.200	2.850	3.950
162	0.467	0.483	0.517	0.567	0.650	0.850	1.183	1.583	2.250	3.733
163	0.400	0.517	0.550	0.800	1.150	1.383	1.717	2.300	2.867	3.817
164	0.417	0.483	0.567	0.583	0.917	1.433	2.067	2.600	3.467	6.383
165	0.617	0.850	1.067	1.250	1.650	2.033	2.417	2.933	3.550	6.900
166	0.600	0.783	0.933	1.083	1.200	1.383	1.667	2.017	2.350	3.117
167	0.500	0.617	0.767	0.900	1.000	1.267	1.617	1.950	2.400	3.167
168	0.483	0.633	0.767	0.950	1.050	1.350	1.733	2.150	2.650	3.617
169	0.150	0.183	0.233	0.333	0.583	1.083	1.717	2.183	3.067	7.167
170	0.217	0.233	0.383	0.550	0.933	1.633	2.200	3.400	5.500	9.500

Table C.5 Derived MeanCV Analyzed for Developing BSS

Reno ID	Parameter									
	Mean CV ₁	Mean CV ₂	Mean CV ₃	Mean CV ₄	Mean CV ₅	Mean CV ₆	Mean CV ₇	Mean CV ₈	Mean CV ₉	Mean CV ₁₀
1	0.218	0.342	0.421	0.503	0.568	0.608	0.648	0.686	0.719	0.744
2	0.263	0.511	0.667	0.745	0.766	0.767	0.758	0.746	0.727	0.706
3	0.291	0.403	0.492	0.560	0.612	0.665	0.707	0.740	0.765	0.786
4	0.235	0.344	0.423	0.483	0.531	0.577	0.615	0.649	0.680	0.707
5	0.286	0.498	0.654	0.722	0.733	0.717	0.695	0.668	0.641	0.614
6	0.312	0.505	0.651	0.724	0.745	0.735	0.716	0.694	0.675	0.656
7	0.196	0.398	0.543	0.653	0.710	0.729	0.722	0.705	0.683	0.661
8	0.227	0.454	0.585	0.678	0.741	0.781	0.811	0.827	0.839	0.849
9	0.214	0.394	0.505	0.574	0.628	0.670	0.707	0.737	0.765	0.788
10	0.194	0.441	0.607	0.696	0.721	0.713	0.693	0.670	0.645	0.622
11	0.039	0.212	0.383	0.523	0.613	0.657	0.668	0.660	0.646	0.627
12	0.029	0.191	0.365	0.508	0.604	0.664	0.694	0.708	0.713	0.713
13	0.127	0.338	0.501	0.620	0.684	0.703	0.699	0.685	0.667	0.647
14	0.029	0.191	0.365	0.508	0.604	0.664	0.694	0.708	0.713	0.713
15	0.197	0.373	0.483	0.563	0.618	0.661	0.696	0.727	0.753	0.777
16	0.215	0.451	0.606	0.698	0.719	0.712	0.692	0.667	0.643	0.620
17	0.319	0.434	0.512	0.573	0.622	0.663	0.698	0.729	0.754	0.778
18	0.367	0.561	0.695	0.746	0.745	0.724	0.701	0.678	0.657	0.636
19	0.110	0.286	0.389	0.468	0.530	0.582	0.623	0.658	0.688	0.715
20	0.316	0.458	0.550	0.628	0.690	0.739	0.774	0.800	0.819	0.829
21	0.121	0.270	0.367	0.443	0.513	0.567	0.613	0.653	0.688	0.719
22	0.108	0.337	0.487	0.601	0.677	0.721	0.742	0.749	0.745	0.737
23	0.161	0.370	0.521	0.634	0.705	0.747	0.771	0.782	0.784	0.779
24	0.182	0.401	0.552	0.656	0.724	0.768	0.798	0.819	0.833	0.841
25	0.139	0.289	0.405	0.496	0.566	0.620	0.661	0.696	0.726	0.753
26	0.134	0.331	0.475	0.589	0.669	0.711	0.722	0.724	0.718	0.709
27	0.407	0.546	0.619	0.670	0.710	0.745	0.771	0.794	0.814	0.831
28	0.465	0.642	0.741	0.801	0.828	0.838	0.851	0.857	0.856	0.854
29	0.118	0.287	0.412	0.505	0.572	0.622	0.660	0.691	0.721	0.748
30	0.116	0.310	0.467	0.591	0.670	0.707	0.710	0.701	0.690	0.675
31	0.470	0.627	0.719	0.778	0.818	0.843	0.861	0.874	0.885	0.896
32	0.525	0.710	0.799	0.833	0.845	0.843	0.840	0.835	0.832	0.832
33	0.252	0.356	0.427	0.483	0.529	0.571	0.610	0.646	0.680	0.710
34	0.269	0.401	0.473	0.525	0.571	0.613	0.647	0.680	0.709	0.737
35	0.141	0.242	0.320	0.383	0.439	0.488	0.534	0.575	0.614	0.650
36	0.125	0.282	0.387	0.471	0.536	0.589	0.631	0.667	0.699	0.727
37	0.155	0.327	0.455	0.551	0.628	0.680	0.721	0.755	0.779	0.792
38	0.181	0.364	0.480	0.575	0.642	0.689	0.728	0.762	0.787	0.803
39	0.127	0.356	0.526	0.643	0.694	0.704	0.693	0.673	0.651	0.627
40	0.132	0.349	0.496	0.602	0.678	0.730	0.765	0.787	0.806	0.821
41	0.208	0.391	0.523	0.625	0.698	0.740	0.753	0.739	0.718	0.699
42	0.163	0.310	0.406	0.486	0.549	0.601	0.644	0.678	0.709	0.736
43	0.339	0.512	0.652	0.727	0.748	0.741	0.724	0.702	0.678	0.653

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Mean CV ₁	Mean CV ₂	Mean CV ₃	Mean CV ₄	Mean CV ₅	Mean CV ₆	Mean CV ₇	Mean CV ₈	Mean CV ₉	Mean CV ₁₀
44	0.260	0.425	0.536	0.617	0.674	0.718	0.753	0.780	0.803	0.822
45	0.147	0.349	0.498	0.615	0.678	0.702	0.701	0.690	0.675	0.656
46	0.106	0.264	0.374	0.456	0.517	0.566	0.609	0.647	0.683	0.713
47	0.152	0.302	0.422	0.527	0.610	0.673	0.719	0.752	0.775	0.791
48	0.214	0.399	0.540	0.647	0.714	0.752	0.773	0.785	0.793	0.799
49	0.354	0.474	0.557	0.626	0.684	0.730	0.768	0.795	0.811	0.821
50	0.409	0.575	0.687	0.762	0.804	0.825	0.832	0.830	0.825	0.813
51	0.208	0.382	0.528	0.640	0.700	0.711	0.686	0.660	0.639	0.623
52	0.142	0.264	0.359	0.434	0.494	0.547	0.592	0.633	0.668	0.699
53	0.216	0.390	0.519	0.620	0.693	0.740	0.768	0.772	0.769	0.752
54	0.125	0.256	0.345	0.418	0.478	0.531	0.579	0.621	0.658	0.689
55	0.138	0.324	0.459	0.568	0.650	0.695	0.709	0.706	0.695	0.683
56	0.105	0.217	0.298	0.365	0.425	0.481	0.532	0.576	0.616	0.653
57	0.193	0.432	0.600	0.694	0.727	0.725	0.708	0.685	0.660	0.635
58	0.166	0.379	0.512	0.602	0.670	0.723	0.761	0.788	0.808	0.826
59	0.150	0.357	0.507	0.622	0.690	0.718	0.719	0.707	0.689	0.669
60	0.154	0.381	0.524	0.634	0.702	0.726	0.724	0.711	0.691	0.670
61	0.146	0.289	0.393	0.476	0.547	0.607	0.656	0.695	0.728	0.754
62	0.189	0.371	0.505	0.613	0.689	0.732	0.751	0.741	0.722	0.711
63	0.295	0.484	0.625	0.715	0.749	0.744	0.725	0.702	0.679	0.657
64	0.224	0.443	0.601	0.693	0.719	0.711	0.690	0.664	0.639	0.616
65	0.246	0.462	0.611	0.706	0.737	0.736	0.720	0.697	0.672	0.645
66	0.258	0.493	0.643	0.725	0.760	0.772	0.779	0.781	0.782	0.782
67	0.241	0.484	0.635	0.706	0.713	0.699	0.676	0.651	0.626	0.601
68	0.321	0.503	0.601	0.670	0.714	0.744	0.767	0.790	0.809	0.827
69	0.171	0.310	0.408	0.481	0.541	0.590	0.630	0.667	0.699	0.727
70	0.320	0.460	0.548	0.609	0.653	0.688	0.715	0.740	0.764	0.787
71	0.247	0.427	0.538	0.615	0.670	0.712	0.745	0.772	0.795	0.815
72	0.159	0.321	0.440	0.526	0.592	0.644	0.685	0.718	0.746	0.770
73	0.219	0.438	0.592	0.692	0.733	0.738	0.727	0.710	0.688	0.666
74	0.222	0.431	0.587	0.688	0.744	0.767	0.770	0.763	0.749	0.730
75	0.255	0.512	0.664	0.711	0.711	0.690	0.660	0.629	0.601	0.573
76	0.464	0.645	0.740	0.792	0.824	0.846	0.860	0.857	0.848	0.851
77	0.361	0.562	0.650	0.708	0.742	0.774	0.799	0.809	0.819	0.828
78	0.070	0.266	0.404	0.513	0.600	0.665	0.707	0.726	0.729	0.725
79	0.288	0.495	0.643	0.728	0.764	0.770	0.767	0.756	0.742	0.727
80	0.268	0.391	0.469	0.531	0.585	0.627	0.662	0.696	0.723	0.750
81	0.347	0.544	0.681	0.756	0.790	0.802	0.804	0.797	0.787	0.776
82	0.373	0.544	0.629	0.681	0.722	0.753	0.775	0.797	0.817	0.834
83	0.327	0.558	0.693	0.733	0.725	0.705	0.679	0.654	0.635	0.617
84	0.310	0.538	0.674	0.733	0.729	0.699	0.663	0.627	0.596	0.567
85	0.238	0.402	0.518	0.610	0.685	0.729	0.749	0.751	0.747	0.738
86	0.210	0.372	0.490	0.585	0.658	0.713	0.751	0.776	0.791	0.801
87	0.323	0.534	0.680	0.753	0.782	0.784	0.775	0.764	0.751	0.736
88	0.270	0.452	0.588	0.687	0.743	0.769	0.773	0.768	0.760	0.749
89	0.271	0.475	0.629	0.701	0.716	0.710	0.696	0.680	0.663	0.647

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Mean CV ₁	Mean CV ₂	Mean CV ₃	Mean CV ₄	Mean CV ₅	Mean CV ₆	Mean CV ₇	Mean CV ₈	Mean CV ₉	Mean CV ₁₀
90	0.338	0.424	0.497	0.559	0.611	0.655	0.693	0.727	0.754	0.777
91	0.090	0.332	0.515	0.634	0.696	0.724	0.732	0.733	0.727	0.717
92	0.155	0.336	0.483	0.596	0.675	0.725	0.754	0.769	0.775	0.776
93	0.107	0.255	0.361	0.437	0.499	0.552	0.597	0.635	0.668	0.699
94	0.391	0.553	0.638	0.694	0.745	0.760	0.778	0.800	0.819	0.827
95	0.317	0.532	0.662	0.739	0.767	0.775	0.776	0.776	0.774	0.767
96	0.235	0.396	0.519	0.617	0.689	0.739	0.776	0.797	0.812	0.821
97	0.358	0.553	0.670	0.748	0.797	0.826	0.842	0.848	0.848	0.846
98	0.189	0.435	0.602	0.691	0.717	0.711	0.691	0.665	0.639	0.613
99	0.196	0.440	0.609	0.685	0.698	0.685	0.661	0.635	0.608	0.583
100	0.111	0.343	0.500	0.605	0.673	0.722	0.761	0.790	0.810	0.822
101	0.059	0.296	0.487	0.613	0.674	0.700	0.708	0.709	0.705	0.698
102	0.245	0.482	0.637	0.721	0.738	0.726	0.703	0.678	0.652	0.628
103	0.204	0.333	0.415	0.477	0.526	0.571	0.610	0.646	0.679	0.708
104	0.225	0.394	0.508	0.602	0.674	0.727	0.763	0.790	0.811	0.826
105	0.176	0.403	0.566	0.672	0.720	0.734	0.732	0.724	0.711	0.699
106	0.118	0.279	0.387	0.468	0.530	0.582	0.626	0.663	0.695	0.723
107	0.193	0.344	0.446	0.527	0.597	0.654	0.698	0.735	0.763	0.785
108	0.200	0.418	0.563	0.664	0.722	0.741	0.736	0.721	0.697	0.672
109	0.057	0.278	0.448	0.577	0.653	0.680	0.681	0.671	0.657	0.641
110	0.066	0.291	0.449	0.570	0.654	0.706	0.741	0.765	0.784	0.798
111	0.250	0.404	0.513	0.590	0.641	0.677	0.707	0.731	0.755	0.776
112	0.201	0.385	0.517	0.619	0.693	0.740	0.773	0.795	0.809	0.817
113	0.253	0.479	0.634	0.724	0.769	0.786	0.790	0.786	0.778	0.764
114	0.271	0.487	0.626	0.716	0.769	0.800	0.819	0.828	0.830	0.826
115	0.210	0.392	0.518	0.617	0.689	0.733	0.753	0.769	0.777	0.782
116	0.232	0.362	0.459	0.543	0.608	0.663	0.710	0.741	0.759	0.773
117	0.230	0.434	0.566	0.668	0.732	0.768	0.788	0.800	0.805	0.804
118	0.159	0.370	0.510	0.605	0.677	0.724	0.750	0.761	0.765	0.766
119	0.130	0.312	0.441	0.525	0.588	0.636	0.674	0.706	0.735	0.760
120	0.217	0.401	0.534	0.635	0.698	0.716	0.714	0.699	0.684	0.666
121	0.249	0.425	0.560	0.661	0.726	0.758	0.767	0.764	0.754	0.741
122	0.262	0.472	0.626	0.714	0.742	0.740	0.724	0.703	0.680	0.657
123	0.351	0.543	0.676	0.747	0.761	0.753	0.734	0.711	0.685	0.661
124	0.303	0.516	0.651	0.737	0.788	0.815	0.825	0.825	0.820	0.812
125	0.309	0.539	0.682	0.740	0.743	0.726	0.701	0.672	0.644	0.619
126	0.132	0.352	0.527	0.642	0.707	0.748	0.773	0.783	0.787	0.791
127	0.167	0.393	0.546	0.653	0.720	0.761	0.793	0.818	0.833	0.843
128	0.304	0.478	0.601	0.695	0.751	0.775	0.778	0.768	0.749	0.727
129	0.267	0.536	0.680	0.706	0.699	0.680	0.655	0.629	0.604	0.579
130	0.170	0.350	0.484	0.590	0.667	0.722	0.759	0.786	0.805	0.818
131	0.208	0.414	0.534	0.611	0.664	0.706	0.741	0.772	0.795	0.813
132	0.212	0.489	0.645	0.723	0.744	0.741	0.728	0.711	0.691	0.672
133	0.348	0.622	0.745	0.790	0.793	0.780	0.759	0.739	0.716	0.694
134	0.296	0.576	0.710	0.766	0.770	0.761	0.744	0.722	0.698	0.674
135	0.248	0.389	0.488	0.566	0.621	0.669	0.705	0.734	0.761	0.784

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Mean CV ₁	Mean CV ₂	Mean CV ₃	Mean CV ₄	Mean CV ₅	Mean CV ₆	Mean CV ₇	Mean CV ₈	Mean CV ₉	Mean CV ₁₀
136	0.227	0.439	0.587	0.687	0.737	0.749	0.742	0.728	0.718	0.709
137	0.313	0.568	0.706	0.743	0.732	0.706	0.674	0.644	0.617	0.592
138	0.286	0.528	0.676	0.746	0.766	0.763	0.752	0.736	0.717	0.695
139	0.168	0.429	0.605	0.695	0.734	0.752	0.761	0.765	0.765	0.765
140	0.147	0.387	0.559	0.662	0.701	0.715	0.711	0.696	0.675	0.652
141	0.203	0.388	0.510	0.605	0.676	0.730	0.767	0.788	0.798	0.801
142	0.237	0.527	0.679	0.728	0.729	0.709	0.684	0.653	0.625	0.599
143	0.195	0.346	0.450	0.533	0.607	0.667	0.714	0.748	0.772	0.783
144	0.238	0.420	0.538	0.633	0.705	0.747	0.766	0.776	0.776	0.764
145	0.150	0.326	0.457	0.563	0.646	0.702	0.732	0.744	0.744	0.740
146	0.144	0.306	0.416	0.508	0.587	0.649	0.695	0.728	0.742	0.752
147	0.425	0.603	0.721	0.778	0.790	0.783	0.771	0.751	0.732	0.712
148	0.367	0.556	0.688	0.752	0.766	0.759	0.742	0.723	0.701	0.679
149	0.356	0.502	0.615	0.702	0.751	0.768	0.756	0.730	0.705	0.676
150	0.337	0.518	0.646	0.729	0.764	0.787	0.779	0.753	0.730	0.702
151	0.183	0.443	0.615	0.707	0.738	0.741	0.731	0.714	0.695	0.676
152	0.098	0.223	0.317	0.395	0.459	0.514	0.563	0.608	0.645	0.679
153	0.089	0.315	0.489	0.610	0.683	0.719	0.731	0.730	0.721	0.708
154	0.080	0.296	0.449	0.564	0.648	0.705	0.747	0.776	0.793	0.806
155	0.194	0.434	0.598	0.688	0.710	0.695	0.670	0.642	0.613	0.587
156	0.190	0.424	0.580	0.680	0.725	0.731	0.714	0.691	0.664	0.638
157	0.158	0.369	0.517	0.630	0.697	0.703	0.691	0.680	0.657	0.629
158	0.180	0.393	0.535	0.642	0.711	0.755	0.774	0.776	0.759	0.719
159	0.140	0.373	0.531	0.639	0.710	0.756	0.782	0.798	0.808	0.812
160	0.159	0.461	0.634	0.695	0.701	0.689	0.673	0.653	0.632	0.612
161	0.285	0.472	0.598	0.685	0.739	0.770	0.785	0.791	0.790	0.782
162	0.275	0.521	0.658	0.740	0.784	0.811	0.820	0.819	0.815	0.806
163	0.214	0.419	0.558	0.660	0.722	0.760	0.781	0.788	0.785	0.781
164	0.239	0.422	0.541	0.630	0.691	0.739	0.774	0.792	0.803	0.807
165	0.090	0.272	0.417	0.535	0.621	0.683	0.726	0.758	0.779	0.793
166	0.106	0.363	0.548	0.660	0.711	0.720	0.705	0.684	0.663	0.641
167	0.160	0.413	0.580	0.679	0.715	0.712	0.695	0.675	0.657	0.641
168	0.156	0.396	0.552	0.660	0.713	0.727	0.722	0.707	0.690	0.674
169	0.412	0.542	0.640	0.711	0.760	0.795	0.822	0.844	0.860	0.868
170	0.315	0.450	0.543	0.608	0.661	0.701	0.735	0.763	0.787	0.806

Table C.6 Derived MedianCV Analyzed for Developing BSS

Reno ID	Parameter									
	Median CV ₁	Median CV ₂	Median CV ₃	Median CV ₄	Median CV ₅	Median CV ₆	Median CV ₇	Median CV ₈	Median CV ₉	Median CV ₁₀
1	0.219	0.397	0.475	0.519	0.568	0.678	0.757	0.799	0.804	0.817
2	0.241	0.567	0.777	0.925	0.865	0.835	0.799	0.770	0.748	0.715
3	0.314	0.463	0.512	0.588	0.680	0.728	0.768	0.798	0.808	0.880
4	0.254	0.385	0.456	0.519	0.587	0.638	0.664	0.670	0.728	0.762
5	0.288	0.539	0.719	0.856	0.808	0.755	0.710	0.661	0.613	0.588
6	0.298	0.560	0.694	0.832	0.835	0.786	0.734	0.693	0.647	0.620
7	0.163	0.473	0.604	0.721	0.835	0.830	0.778	0.733	0.697	0.657
8	0.193	0.554	0.694	0.765	0.851	0.924	0.959	0.952	0.939	0.940
9	0.207	0.473	0.569	0.666	0.734	0.764	0.777	0.810	0.842	0.872
10	0.171	0.507	0.698	0.839	0.826	0.778	0.731	0.679	0.629	0.591
11	0.030	0.128	0.384	0.593	0.725	0.824	0.778	0.725	0.688	0.639
12	0.009	0.119	0.384	0.566	0.720	0.843	0.870	0.840	0.808	0.787
13	0.071	0.361	0.558	0.711	0.818	0.806	0.765	0.721	0.679	0.645
14	0.009	0.119	0.384	0.566	0.720	0.843	0.870	0.840	0.808	0.787
15	0.180	0.425	0.547	0.647	0.705	0.764	0.809	0.828	0.838	0.851
16	0.183	0.512	0.694	0.815	0.806	0.750	0.722	0.683	0.641	0.600
17	0.367	0.486	0.547	0.622	0.668	0.718	0.757	0.793	0.818	0.843
18	0.454	0.621	0.765	0.839	0.793	0.753	0.708	0.654	0.619	0.594
19	0.074	0.335	0.475	0.531	0.601	0.647	0.711	0.749	0.780	0.817
20	0.351	0.554	0.594	0.667	0.725	0.804	0.864	0.904	0.941	0.926
21	0.090	0.318	0.429	0.494	0.563	0.614	0.670	0.745	0.795	0.823
22	0.071	0.330	0.588	0.689	0.786	0.865	0.867	0.840	0.821	0.795
23	0.132	0.421	0.585	0.715	0.812	0.938	0.918	0.899	0.878	0.851
24	0.151	0.452	0.628	0.760	0.857	0.933	0.969	0.967	0.964	0.949
25	0.116	0.338	0.431	0.550	0.637	0.716	0.773	0.823	0.848	0.870
26	0.103	0.368	0.530	0.657	0.774	0.853	0.805	0.774	0.770	0.754
27	0.444	0.647	0.690	0.730	0.765	0.805	0.829	0.835	0.862	0.912
28	0.487	0.780	0.822	0.864	0.918	0.898	0.914	0.910	0.902	0.893
29	0.084	0.334	0.456	0.575	0.662	0.732	0.788	0.798	0.846	0.861
30	0.082	0.347	0.494	0.647	0.772	0.855	0.807	0.749	0.690	0.651
31	0.643	0.715	0.804	0.872	0.891	0.943	0.954	0.958	0.962	0.963
32	0.745	0.814	0.908	0.925	0.904	0.882	0.872	0.859	0.843	0.838
33	0.280	0.401	0.465	0.522	0.569	0.611	0.646	0.688	0.709	0.745
34	0.387	0.486	0.531	0.582	0.617	0.650	0.685	0.730	0.751	0.789
35	0.144	0.262	0.348	0.420	0.478	0.521	0.579	0.618	0.661	0.706
36	0.074	0.345	0.435	0.531	0.604	0.656	0.725	0.762	0.806	0.832
37	0.150	0.359	0.501	0.617	0.715	0.787	0.838	0.898	0.932	0.927
38	0.148	0.457	0.550	0.634	0.712	0.801	0.864	0.896	0.912	0.917
39	0.101	0.357	0.597	0.748	0.838	0.791	0.751	0.711	0.666	0.622
40	0.099	0.389	0.569	0.685	0.799	0.877	0.924	0.935	0.939	0.944
41	0.220	0.438	0.571	0.685	0.793	0.875	0.851	0.817	0.771	0.715
42	0.156	0.353	0.461	0.534	0.597	0.670	0.725	0.772	0.803	0.828
43	0.421	0.528	0.688	0.817	0.817	0.787	0.749	0.705	0.672	0.622

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Median CV ₁	Median CV ₂	Median CV ₃	Median CV ₄	Median CV ₅	Median CV ₆	Median CV ₇	Median CV ₈	Median CV ₉	Median CV ₁₀
44	0.320	0.497	0.595	0.681	0.762	0.815	0.860	0.884	0.905	0.912
45	0.115	0.403	0.556	0.691	0.800	0.819	0.776	0.734	0.691	0.660
46	0.084	0.281	0.436	0.507	0.589	0.665	0.704	0.735	0.758	0.790
47	0.140	0.322	0.466	0.570	0.660	0.767	0.845	0.905	0.950	0.941
48	0.180	0.454	0.593	0.737	0.828	0.909	0.903	0.891	0.875	0.867
49	0.460	0.499	0.594	0.671	0.724	0.775	0.836	0.883	0.914	0.917
50	0.508	0.620	0.748	0.839	0.923	0.926	0.906	0.884	0.877	0.839
51	0.188	0.411	0.551	0.714	0.829	0.805	0.743	0.671	0.594	0.530
52	0.145	0.294	0.371	0.481	0.554	0.611	0.664	0.696	0.735	0.788
53	0.237	0.430	0.565	0.688	0.785	0.862	0.907	0.863	0.819	0.794
54	0.121	0.283	0.390	0.469	0.528	0.579	0.639	0.680	0.720	0.754
55	0.122	0.373	0.516	0.631	0.728	0.830	0.805	0.769	0.741	0.699
56	0.092	0.249	0.335	0.400	0.461	0.516	0.563	0.614	0.669	0.720
57	0.173	0.486	0.687	0.821	0.843	0.802	0.751	0.706	0.662	0.622
58	0.132	0.445	0.603	0.705	0.776	0.839	0.871	0.908	0.949	0.967
59	0.103	0.403	0.564	0.708	0.818	0.845	0.801	0.753	0.713	0.678
60	0.113	0.423	0.622	0.703	0.815	0.829	0.788	0.750	0.711	0.689
61	0.132	0.334	0.430	0.526	0.606	0.668	0.726	0.780	0.835	0.873
62	0.178	0.421	0.566	0.669	0.779	0.867	0.869	0.840	0.793	0.732
63	0.351	0.548	0.679	0.798	0.861	0.797	0.745	0.705	0.655	0.638
64	0.213	0.516	0.664	0.813	0.823	0.764	0.706	0.668	0.619	0.581
65	0.236	0.533	0.669	0.823	0.844	0.808	0.764	0.713	0.678	0.629
66	0.218	0.556	0.736	0.866	0.893	0.852	0.838	0.831	0.824	0.811
67	0.175	0.618	0.735	0.831	0.776	0.737	0.692	0.654	0.631	0.587
68	0.342	0.643	0.680	0.752	0.794	0.856	0.876	0.882	0.885	0.887
69	0.198	0.362	0.453	0.531	0.611	0.660	0.704	0.739	0.781	0.816
70	0.400	0.533	0.603	0.664	0.728	0.766	0.795	0.821	0.825	0.848
71	0.223	0.505	0.613	0.688	0.763	0.819	0.851	0.874	0.892	0.905
72	0.151	0.366	0.473	0.599	0.676	0.757	0.775	0.825	0.851	0.889
73	0.207	0.501	0.647	0.816	0.851	0.825	0.782	0.736	0.705	0.647
74	0.206	0.508	0.637	0.787	0.914	0.896	0.838	0.804	0.784	0.767
75	0.219	0.609	0.765	0.805	0.776	0.733	0.685	0.632	0.598	0.539
76	0.511	0.755	0.832	0.895	0.920	0.930	0.935	0.926	0.912	0.907
77	0.371	0.665	0.781	0.818	0.828	0.848	0.867	0.875	0.880	0.883
78	0.030	0.255	0.488	0.595	0.683	0.771	0.842	0.850	0.819	0.788
79	0.318	0.545	0.695	0.846	0.882	0.868	0.798	0.776	0.770	0.738
80	0.283	0.476	0.516	0.565	0.624	0.680	0.714	0.769	0.785	0.832
81	0.442	0.649	0.733	0.871	0.915	0.897	0.871	0.829	0.819	0.811
82	0.425	0.696	0.714	0.767	0.797	0.827	0.833	0.859	0.886	0.897
83	0.444	0.623	0.807	0.818	0.772	0.723	0.676	0.623	0.615	0.583
84	0.405	0.635	0.769	0.847	0.790	0.745	0.679	0.623	0.578	0.519
85	0.304	0.456	0.569	0.654	0.768	0.815	0.862	0.809	0.789	0.761
86	0.249	0.459	0.540	0.647	0.722	0.802	0.876	0.926	0.916	0.908
87	0.434	0.609	0.749	0.880	0.899	0.849	0.816	0.787	0.750	0.716
88	0.321	0.494	0.635	0.765	0.871	0.898	0.847	0.812	0.790	0.768
89	0.353	0.518	0.692	0.807	0.785	0.754	0.731	0.688	0.642	0.619

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Median CV ₁	Median CV ₂	Median CV ₃	Median CV ₄	Median CV ₅	Median CV ₆	Median CV ₇	Median CV ₈	Median CV ₉	Median CV ₁₀
90	0.371	0.431	0.507	0.593	0.644	0.688	0.749	0.794	0.820	0.853
91	0.042	0.341	0.598	0.749	0.882	0.872	0.840	0.805	0.773	0.752
92	0.140	0.377	0.505	0.664	0.785	0.867	0.916	0.889	0.879	0.847
93	0.091	0.288	0.410	0.492	0.581	0.628	0.662	0.705	0.744	0.792
94	0.439	0.671	0.719	0.759	0.809	0.809	0.826	0.846	0.861	0.869
95	0.339	0.637	0.754	0.863	0.879	0.863	0.823	0.814	0.800	0.794
96	0.264	0.445	0.563	0.665	0.778	0.851	0.911	0.929	0.932	0.928
97	0.398	0.662	0.756	0.831	0.910	0.947	0.939	0.936	0.917	0.895
98	0.164	0.507	0.696	0.833	0.830	0.778	0.729	0.684	0.635	0.594
99	0.211	0.480	0.694	0.832	0.784	0.723	0.681	0.639	0.590	0.552
100	0.066	0.339	0.590	0.725	0.816	0.884	0.918	0.944	0.948	0.945
101	0.020	0.247	0.559	0.756	0.870	0.843	0.813	0.785	0.754	0.733
102	0.236	0.551	0.720	0.863	0.823	0.771	0.721	0.686	0.647	0.597
103	0.221	0.368	0.469	0.528	0.580	0.630	0.667	0.686	0.723	0.768
104	0.235	0.445	0.572	0.655	0.741	0.819	0.882	0.932	0.959	0.959
105	0.121	0.492	0.637	0.780	0.873	0.835	0.795	0.759	0.723	0.708
106	0.090	0.322	0.446	0.541	0.606	0.664	0.714	0.756	0.783	0.803
107	0.156	0.412	0.496	0.578	0.653	0.721	0.766	0.830	0.876	0.915
108	0.119	0.516	0.640	0.752	0.863	0.835	0.810	0.772	0.727	0.673
109	0.016	0.240	0.511	0.663	0.798	0.802	0.762	0.723	0.676	0.649
110	0.015	0.244	0.540	0.663	0.772	0.863	0.931	0.932	0.934	0.932
111	0.302	0.479	0.562	0.660	0.741	0.772	0.822	0.840	0.846	0.852
112	0.215	0.444	0.586	0.685	0.794	0.847	0.909	0.940	0.932	0.926
113	0.230	0.504	0.716	0.863	0.927	0.900	0.874	0.833	0.816	0.801
114	0.250	0.538	0.703	0.842	0.914	0.943	0.943	0.933	0.912	0.896
115	0.195	0.454	0.572	0.684	0.776	0.848	0.866	0.873	0.866	0.858
116	0.251	0.441	0.486	0.580	0.649	0.741	0.801	0.837	0.868	0.876
117	0.248	0.500	0.640	0.738	0.828	0.911	0.916	0.904	0.890	0.873
118	0.130	0.407	0.598	0.707	0.796	0.854	0.896	0.873	0.851	0.819
119	0.096	0.337	0.501	0.628	0.707	0.745	0.784	0.803	0.836	0.875
120	0.276	0.467	0.597	0.675	0.791	0.784	0.766	0.731	0.693	0.671
121	0.345	0.465	0.604	0.720	0.832	0.894	0.845	0.832	0.788	0.771
122	0.377	0.542	0.680	0.833	0.839	0.801	0.773	0.715	0.665	0.638
123	0.428	0.593	0.732	0.879	0.844	0.790	0.757	0.723	0.672	0.634
124	0.418	0.597	0.740	0.838	0.934	0.950	0.927	0.899	0.869	0.847
125	0.415	0.637	0.773	0.867	0.818	0.768	0.706	0.672	0.639	0.606
126	0.042	0.372	0.584	0.756	0.875	0.943	0.934	0.917	0.885	0.849
127	0.029	0.494	0.610	0.755	0.854	0.929	0.961	0.975	0.969	0.962
128	0.406	0.551	0.664	0.749	0.859	0.873	0.861	0.819	0.772	0.757
129	0.279	0.612	0.818	0.790	0.729	0.695	0.662	0.621	0.590	0.556
130	0.159	0.407	0.534	0.655	0.744	0.858	0.909	0.953	0.949	0.944
131	0.059	0.554	0.618	0.714	0.777	0.817	0.845	0.857	0.879	0.901
132	0.064	0.607	0.779	0.873	0.848	0.813	0.777	0.732	0.699	0.676
133	0.325	0.779	0.909	0.919	0.874	0.838	0.803	0.761	0.718	0.683
134	0.253	0.713	0.871	0.904	0.868	0.810	0.769	0.739	0.712	0.686
135	0.247	0.462	0.534	0.608	0.680	0.767	0.802	0.830	0.830	0.886

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Median CV ₁	Median CV ₂	Median CV ₃	Median CV ₄	Median CV ₅	Median CV ₆	Median CV ₇	Median CV ₈	Median CV ₉	Median CV ₁₀
136	0.189	0.500	0.659	0.774	0.875	0.836	0.796	0.763	0.729	0.684
137	0.319	0.605	0.841	0.852	0.786	0.720	0.669	0.622	0.575	0.540
138	0.259	0.581	0.767	0.900	0.864	0.834	0.797	0.753	0.716	0.702
139	0.120	0.487	0.697	0.868	0.887	0.863	0.848	0.836	0.818	0.806
140	0.120	0.417	0.635	0.811	0.843	0.813	0.787	0.757	0.721	0.677
141	0.170	0.482	0.572	0.672	0.763	0.816	0.893	0.921	0.897	0.879
142	0.196	0.599	0.839	0.862	0.818	0.761	0.711	0.651	0.610	0.563
143	0.180	0.397	0.497	0.581	0.657	0.730	0.777	0.847	0.905	0.897
144	0.230	0.486	0.599	0.695	0.768	0.859	0.875	0.861	0.845	0.831
145	0.144	0.377	0.509	0.612	0.719	0.806	0.869	0.852	0.817	0.790
146	0.121	0.351	0.467	0.572	0.637	0.712	0.781	0.849	0.849	0.850
147	0.484	0.683	0.791	0.873	0.858	0.829	0.793	0.740	0.726	0.705
148	0.429	0.660	0.747	0.847	0.830	0.802	0.762	0.733	0.699	0.669
149	0.395	0.558	0.640	0.752	0.851	0.851	0.801	0.755	0.707	0.672
150	0.382	0.566	0.711	0.807	0.870	0.883	0.850	0.817	0.785	0.721
151	0.152	0.501	0.706	0.874	0.866	0.826	0.787	0.740	0.709	0.678
152	0.084	0.251	0.344	0.436	0.512	0.573	0.630	0.677	0.718	0.745
153	0.039	0.318	0.544	0.714	0.842	0.885	0.849	0.816	0.788	0.753
154	0.020	0.293	0.524	0.660	0.763	0.835	0.913	0.964	0.940	0.929
155	0.155	0.528	0.687	0.833	0.813	0.747	0.693	0.639	0.587	0.545
156	0.161	0.490	0.656	0.789	0.870	0.819	0.781	0.725	0.666	0.616
157	0.124	0.413	0.593	0.712	0.805	0.767	0.715	0.673	0.641	0.614
158	0.135	0.451	0.614	0.732	0.817	0.912	0.896	0.860	0.832	0.800
159	0.092	0.424	0.623	0.741	0.853	0.928	0.934	0.927	0.919	0.901
160	0.089	0.524	0.786	0.851	0.787	0.745	0.696	0.645	0.620	0.597
161	0.389	0.564	0.660	0.764	0.855	0.914	0.889	0.877	0.865	0.832
162	0.196	0.651	0.789	0.840	0.937	0.943	0.931	0.893	0.871	0.853
163	0.237	0.451	0.627	0.765	0.826	0.916	0.916	0.890	0.869	0.844
164	0.255	0.530	0.612	0.693	0.786	0.855	0.903	0.912	0.902	0.885
165	0.064	0.269	0.462	0.580	0.714	0.812	0.893	0.945	0.951	0.937
166	0.053	0.346	0.655	0.796	0.881	0.828	0.775	0.723	0.679	0.618
167	0.108	0.491	0.680	0.814	0.840	0.789	0.729	0.685	0.655	0.617
168	0.113	0.487	0.640	0.776	0.864	0.816	0.785	0.747	0.716	0.683
169	0.492	0.580	0.669	0.774	0.831	0.893	0.922	0.947	0.959	0.954
170	0.381	0.514	0.579	0.672	0.736	0.766	0.808	0.834	0.882	0.885

Table C.7 Derived $T_{1/2,dec}$ and Its Variants Analyzed for Developing BISRO and AISRO

Reno ID	Parameter				
	$T_{5/10,dec}$	$T_{6/10,dec}$	$T_{7/10,dec}$	$T_{8/10,dec}$	$T_{9/10,dec}$
1					28.133
2	10.033	8.233	6.533	5.083	4.150
3	18.883	16.950	14.600	12.583	11.883
4	29.583	26.467	25.000	18.467	17.267
5	7.017	5.983	5.017	4.317	3.717
6	9.233	6.617	5.417	4.717	3.883
7	8.517	7.333	6.367	5.650	5.000
8		27.967	20.317	15.550	10.917
9		28.617	22.417	19.083	14.033
10	7.583	6.083	5.300	4.600	4.033
11	8.883	7.583	6.700	6.017	5.333
12	16.400	14.100	9.783	7.467	6.283
13	8.917	7.417	6.233	5.467	4.767
14	15.117	14.217	10.850	6.500	5.017
15			30.717	28.200	18.917
16	7.350	6.183	5.317	4.483	4.050
17					
18	8.283	5.667	4.800	4.083	3.533
19		27.967	23.483	19.217	16.950
20	25.617	14.450	13.700	12.400	9.900
21	22.350	20.117	18.967	15.950	13.500
22	12.250	10.433	9.000	7.467	6.117
23	12.667	11.400	10.083	8.567	6.783
24	23.933	20.050	17.567	15.283	9.883
25	16.150	15.300	14.567	13.767	11.350
26	12.017	10.033	7.950	6.267	5.650
27				31.633	25.633
28	32.000	25.900	14.883	10.933	7.250
29	30.683	25.583	24.517	20.550	15.733
30	10.233	8.600	6.617	6.133	5.533
31			27.500	14.033	13.183
32					29.700
33	21.833	20.500	19.450	17.633	14.383
34			31.000	25.717	22.383
35					30.767
36	15.683	15.233	14.750	14.100	12.800
37	13.333	12.600	12.017	10.683	9.717
38	13.367	12.817	12.350	10.533	9.917
39	8.133	6.817	5.917	5.117	4.483
40					31.933
41	9.967	7.683	7.200	6.783	5.967
42			31.417	26.067	21.100
43	8.150	6.967	5.550	4.683	4.067
44			26.100	17.683	14.633
45	9.367	7.617	6.417	5.767	4.717
46	31.567	23.117	18.100	15.683	13.433
47	15.000	14.083	13.583	12.683	10.467
48					29.500
49	24.717	19.033	16.283	14.067	11.267

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter				
	$T_{5/10,dec}$	$T_{6/10,dec}$	$T_{7/10,dec}$	$T_{8/10,dec}$	$T_{9/10,dec}$
50	12.483	11.350	9.717	7.900	6.017
51	6.733	6.100	5.800	5.417	4.833
52	24.150	20.467	19.467	17.517	16.217
53	9.917	9.483	9.000	7.450	6.850
54					
55	12.083	8.867	7.350	6.433	5.683
56		30.350	26.650	26.200	23.167
57	7.833	6.617	5.617	4.933	4.200
58		25.767	23.683	18.983	11.583
59	9.300	7.767	6.650	5.933	5.183
60	9.050	7.617	6.733	5.817	5.200
61	18.883	16.983	15.317	13.517	12.617
62	12.067	9.367	7.417	7.067	6.150
63	8.383	6.617	5.717	4.983	4.500
64	7.300	6.083	5.217	4.650	4.067
65	8.150	6.700	5.717	5.000	4.283
66			27.317	7.433	4.567
67	7.033	5.850	4.800	4.067	3.567
68					
69	21.050	19.200	17.567	16.400	15.200
70					
71		31.567	24.933	17.550	15.050
72	19.983	15.550	14.583	13.533	11.517
73	8.800	7.350	6.200	5.250	4.533
74	11.017	8.950	7.750	6.167	5.417
75	6.217	5.433	4.583	3.650	3.433
76		29.433	29.667	26.117	27.267
77		32.000	23.600	11.883	9.633
78	15.183	11.533	9.283	7.983	7.100
79	11.417	9.250	7.317	5.300	4.517
80					
81	12.300	11.283	8.667	6.933	5.017
82					
83	7.183	5.683	4.467	3.667	3.317
84	5.917	5.033	4.567	4.033	3.667
85	12.717	11.350	8.633	7.050	6.050
86	14.533	13.767	13.150	10.983	8.417
87	12.250	9.433	7.417	5.483	4.617
88	14.633	12.100	8.250	6.517	5.583
89	9.533	6.717	5.400	3.967	3.683
90		17.050	13.617	12.600	11.933
91	12.233	10.167	8.067	6.250	5.200
92	13.000	12.117	10.767	8.950	6.967
93	23.433	21.283	19.100	17.550	15.700
94					31.650
95	25.933	12.583	10.467	5.583	3.950
96		29.717	23.650	13.117	9.450
97					
98	7.267	6.200	5.367	4.633	4.000
99	6.783	5.633	4.817	4.233	3.600
100	15.733	14.917	14.300	13.550	12.650
101	15.400	11.767	8.083	5.900	4.733
102	7.533	6.083	5.217	4.517	4.000

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter				
	$T_{5/10,dec}$	$T_{6/10,dec}$	$T_{7/10,dec}$	$T_{8/10,dec}$	$T_{9/10,dec}$
103				31.500	24.000
104	21.667	16.867	14.083	12.717	11.817
105	10.717	9.500	7.000	5.500	4.617
106	21.867	18.767	16.800	15.417	14.183
107	15.383	15.133	14.717	14.400	13.800
108	8.617	7.650	6.567	5.817	5.050
109	9.417	7.517	6.433	5.550	4.917
110			28.950	21.733	17.317
111					
112	27.517	19.833	17.517	14.083	9.350
113	11.750	10.617	8.650	6.800	5.183
114	16.833	12.533	11.033	9.367	7.250
115	14.817	13.133	12.017	10.117	5.900
116	25.817	21.583	15.617	15.117	14.333
117	18.183	14.200	11.233	9.383	7.017
118	12.067	10.983	10.417	7.850	7.017
119					
120	9.983	7.433	6.500	5.317	5.167
121	11.433	9.933	8.200	6.733	5.733
122	8.300	6.817	5.733	4.867	4.200
123	8.083	6.717	5.633	4.567	3.983
124	13.983	12.767	10.517	8.250	6.250
125	7.033	5.983	4.817	4.250	3.600
126	12.917	12.383	11.733	10.100	6.900
127	14.267	13.483	13.000	12.400	10.117
128	10.217	8.450	7.517	6.400	5.350
129	6.517	5.350	4.167	3.383	2.967
130	15.817	14.833	13.950	12.533	10.467
131		30.867	27.100	21.633	12.317
132	9.617	7.433	5.700	4.733	3.933

Table C.8 Derived $T_{1/2,dec(fp)}$ and Its Variants Analyzed for Developing BISRO and AISRO

Reno ID	Parameter				
	$T_{5/10,dec(fp)}$	$T_{6/10,dec(fp)}$	$T_{7/10,dec(fp)}$	$T_{8/10,dec(fp)}$	$T_{9/10,dec(fp)}$
1					11.433
2	7.267	5.467	3.767	2.317	1.383
3	8.583	6.650	4.300	2.283	1.583
4	13.867	10.750	9.283	2.750	1.550
5	4.133	3.100	2.133	1.433	0.833
6	6.283	3.667	2.467	1.767	0.933
7	4.767	3.583	2.617	1.900	1.250
8		23.233	15.583	10.817	6.183
9		17.117	10.917	7.583	2.533
10	4.667	3.167	2.383	1.683	1.117
11	4.767	3.467	2.583	1.900	1.217
12	12.217	9.917	5.600	3.283	2.100
13	4.983	3.483	2.300	1.533	0.833
14	11.117	10.217	6.850	2.500	1.017
15			15.167	12.650	3.367
16	4.100	2.933	2.067	1.233	0.800
17					
18	5.583	2.967	2.100	1.383	0.833
19		14.533	10.050	5.783	3.517
20	18.400	7.233	6.483	5.183	2.683
21	12.917	10.683	9.533	6.517	4.067
22	8.233	6.417	4.983	3.450	2.100
23	8.117	6.850	5.533	4.017	2.233
24	19.150	15.267	12.783	10.500	5.100
25	6.500	5.650	4.917	4.117	1.700
26	7.700	5.717	3.633	1.950	1.333
27				13.500	7.500
28	28.983	22.883	11.867	7.917	4.233
29	18.883	13.783	12.717	8.750	3.933
30	6.133	4.500	2.517	2.033	1.433
31			16.317	2.850	2.000
32					1.117
33	9.083	7.750	6.700	4.883	1.633
34			10.133	4.850	1.517
35					8.700
36	5.017	4.567	4.083	3.433	2.133
37	5.617	4.883	4.300	2.967	2.000
38	5.733	5.183	4.717	2.900	2.283
39	4.350	3.033	2.133	1.333	0.700
40					25.900
41	5.283	3.000	2.517	2.100	1.283
42			12.817	7.467	2.500
43	5.167	3.983	2.567	1.700	1.083
44			14.083	5.667	2.617
45	5.467	3.717	2.517	1.867	0.817
46	22.250	13.800	8.783	6.367	4.117
47	8.350	7.433	6.933	6.033	3.817
48					15.350
49	18.550	12.867	10.117	7.900	5.100

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter				
	$T_{5/10,dec(fp)}$	$T_{6/10,dec(fp)}$	$T_{7/10,dec(fp)}$	$T_{8/10,dec(fp)}$	$T_{9/10,dec(fp)}$
50	8.967	7.833	6.200	4.383	2.500
51	2.900	2.267	1.967	1.583	1.000
52	9.933	6.250	5.250	3.300	2.000
53	5.183	4.750	4.267	2.717	2.117
54					
55	7.433	4.217	2.700	1.783	1.033
56		16.017	12.317	11.867	8.833
57	4.733	3.517	2.517	1.833	1.100
58		19.933	17.850	13.150	5.750
59	5.300	3.767	2.650	1.933	1.183
60	5.217	3.783	2.900	1.983	1.367
61	8.967	7.067	5.400	3.600	2.700
62	7.517	4.817	2.867	2.517	1.600
63	5.233	3.467	2.567	1.833	1.350
64	4.133	2.917	2.050	1.483	0.900
65	4.967	3.517	2.533	1.817	1.100
66			24.200	4.317	1.450
67	4.150	2.967	1.917	1.183	0.683
68					
69	7.533	5.683	4.050	2.883	1.683
70					
71		22.200	15.567	8.183	5.683
72	9.783	5.350	4.383	3.333	1.317
73	5.383	3.933	2.783	1.833	1.117
74	7.533	5.467	4.267	2.683	1.933
75	3.500	2.717	1.867	0.933	0.717
76		4.917	5.150	1.600	2.750
77		25.883	17.483	5.767	3.517
78	9.467	5.817	3.567	2.267	1.383
79	8.467	6.300	4.367	2.350	1.567
80					
81	8.767	7.750	5.133	3.400	1.483
82					
83	4.733	3.233	2.017	1.217	0.867
84	3.000	2.117	1.650	1.117	0.750
85	7.950	6.583	3.867	2.283	1.283
86	8.583	7.817	7.200	5.033	2.467
87	9.550	6.733	4.717	2.783	1.917
88	10.750	8.217	4.367	2.633	1.700
89	6.767	3.950	2.633	1.200	0.917
90		6.817	3.383	2.367	1.700
91	8.633	6.567	4.467	2.650	1.600
92	8.517	7.633	6.283	4.467	2.483
93	11.983	9.833	7.650	6.100	4.250
94					5.533
95	22.567	9.217	7.100	2.217	0.583
96		24.750	18.683	8.150	4.483
97					
98	4.200	3.133	2.300	1.567	0.933
99	3.917	2.767	1.950	1.367	0.733
100	8.167	7.350	6.733	5.983	5.083
101	11.800	8.167	4.483	2.300	1.133
102	4.283	2.833	1.967	1.267	0.750

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter				
	$T_{5/10,dec(fp)}$	$T_{6/10,dec(fp)}$	$T_{7/10,dec(fp)}$	$T_{8/10,dec(fp)}$	$T_{9/10,dec(fp)}$
103				14.917	7.417
104	16.350	11.550	8.767	7.400	6.500
105	7.400	6.183	3.683	2.183	1.300
106	9.117	6.017	4.050	2.667	1.433
107	2.800	2.550	2.133	1.817	1.217
108	4.483	3.517	2.433	1.683	0.917
109	5.250	3.350	2.267	1.383	0.750
110			24.683	17.467	13.050
111					
112	23.383	15.700	13.383	9.950	5.217
113	8.250	7.117	5.150	3.300	1.683
114	13.083	8.783	7.283	5.617	3.500
115	9.733	8.050	6.933	5.033	0.817
116	14.750	10.517	4.550	4.050	3.267
117	14.350	10.367	7.400	5.550	3.183
118	7.300	6.217	5.650	3.083	2.250
119					
120	6.067	3.517	2.583	1.400	1.250
121	7.233	5.733	4.000	2.533	1.533
122	5.400	3.917	2.833	1.967	1.300
123	4.783	3.417	2.333	1.267	0.683
124	10.333	9.117	6.867	4.600	2.600
125	4.267	3.217	2.050	1.483	0.833
126	9.450	8.917	8.267	6.633	3.433
127	7.267	6.483	6.000	5.400	3.117
128	6.317	4.550	3.617	2.500	1.450
129	4.200	3.033	1.850	1.067	0.650
130	10.567	9.583	8.700	7.283	5.217
131		23.500	19.733	14.267	4.950
132	6.500	4.317	2.583	1.617	0.817

Table C.9 Derived $LT_{1/2,dec}$ and Its Variants Analyzed for Developing BISRO and AISRO

Reno ID	Parameter				
	$LT_{5/10,dec}$	$LT_{6/10,dec}$	$LT_{7/10,dec}$	$LT_{8/10,dec}$	$LT_{9/10,dec}$
1				10.000	10.633
2	28.667	26.683	18.467	12.783	11.850
3	18.883	16.950	14.600	12.583	11.883
4	29.583	26.467	25.000	18.467	13.133
5	13.217	12.500	11.683	11.300	11.000
6	20.017	17.000	14.183	12.633	11.633
7	21.700	14.483	13.267	12.200	10.933
8			29.267	17.750	14.350
9		28.617	22.417	19.083	14.033
10	17.650	16.550	12.950	11.717	10.850
11	17.467	14.667	13.583	12.350	11.233
12	20.050	18.267	16.617	15.300	13.050
13	18.833	15.867	14.533	13.200	11.383
14	16.717	15.650	15.117	14.450	13.767
15			30.717	25.383	18.917
16	19.800	16.583	13.283	12.317	11.167
17				12.217	19.483
18	13.083	12.667	12.350	11.650	10.683
19		27.967	23.483	19.217	16.950
20	32.000	26.067	14.283	13.167	12.400
21	22.583	20.233	19.183	17.000	13.933
22	16.300	14.150	13.033	12.267	11.217
23	13.983	13.333	12.733	12.050	10.983
24	27.283	22.583	19.517	17.117	15.167
25	16.267	15.400	14.683	13.983	12.317
26	13.883	13.217	12.583	12.117	11.783
27				31.633	25.633
28			29.450	19.817	13.450
29	30.683	25.583	24.517	20.550	15.733
30	15.133	12.583	11.783	11.250	10.783
31			27.500	14.033	13.183
32				13.333	22.517
33	21.833	20.500	19.450	17.633	14.383
34			31.000	25.717	13.533
35				10.517	13.850
36	15.683	15.233	14.767	14.100	12.800
37	13.850	13.100	12.533	11.983	10.850
38	13.733	13.100	12.767	12.317	10.633
39	16.167	14.383	13.167	12.433	10.933
40					32.000
41	14.417	13.083	12.517	11.950	11.217
42			31.417	26.067	21.100
43	21.683	17.000	14.067	12.550	11.350
44			26.100	17.683	14.650
45	17.483	14.617	13.050	12.233	10.850
46	31.567	23.917	18.767	16.183	13.917
47	15.617	14.517	13.850	13.417	12.400
48				10.000	29.500
49		30.833	18.017	15.433	13.550

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter				
	<i>LT</i> _{5/10,dec}	<i>LT</i> _{6/10,dec}	<i>LT</i> _{7/10,dec}	<i>LT</i> _{8/10,dec}	<i>LT</i> _{9/10,dec}
50	14.750	13.267	12.633	11.933	11.033
51	14.283	13.833	13.400	12.100	11.300
52	24.600	20.483	19.467	17.517	16.217
53	16.133	14.017	12.083	10.400	10.133
54			10.450	12.700	21.800
55	17.133	16.033	15.267	13.783	12.067
56		30.350	26.650	26.200	23.167
57	16.467	14.983	12.633	11.983	10.967
58		25.933	24.217	21.567	14.533
59	23.567	18.667	13.583	11.467	10.633
60	25.200	19.583	12.717	11.683	10.817
61	18.900	17.000	15.333	13.533	12.617
62	14.167	13.600	12.867	12.017	11.667
63	16.683	13.500	12.267	11.950	11.500
64	16.717	15.333	13.067	11.917	11.317
65	22.650	20.067	12.467	11.750	11.250
66				29.383	26.217
67	16.117	14.550	12.600	11.667	10.567
68				10.433	13.083
69	21.050	19.200	17.567	16.400	15.200
70				10.233	14.650
71		31.583	24.967	17.583	15.067
72	19.983	15.550	14.583	13.533	11.517
73	18.400	14.250	12.750	11.917	10.733
74	13.117	12.833	12.633	12.233	11.233
75	28.683	14.467	12.783	12.017	11.500
76		29.433	29.183	26.117	20.567
77			32.000	17.483	15.417
78	21.917	20.883	17.450	13.733	11.750
79	13.200	12.967	12.750	12.533	11.150
80				10.850	16.917
81	28.367	18.283	12.717	12.067	11.350
82				13.983	15.700
83		30.050	24.183	13.917	12.067
84	18.100	16.283	14.133	12.000	11.233
85	14.650	13.700	13.267	12.483	10.783
86	15.883	14.267	13.717	13.183	11.583
87	26.767	20.050	16.233	13.033	11.783
88	19.983	18.333	17.000	14.433	13.200
89	16.950	15.333	13.250	12.867	11.267
90		17.050	13.617	12.600	11.933
91	20.300	14.083	12.933	12.333	11.633
92	14.317	13.467	12.700	12.067	11.050
93	23.433	21.283	19.100	17.550	15.700
94			10.783	13.183	31.650
95		31.900	27.667	13.100	12.417
96		31.317	29.217	19.233	13.083
97			11.750	18.650	24.167
98	14.217	12.783	11.983	11.417	10.800
99	14.967	12.683	11.917	11.400	10.867
100	15.850	15.000	14.383	13.667	12.833
101		30.367	17.700	15.283	13.533
102	25.583	20.817	15.983	13.683	11.567

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter				
	$LT_{5/10,dec}$	$LT_{6/10,dec}$	$LT_{7/10,dec}$	$LT_{8/10,dec}$	$LT_{9/10,dec}$
103				31.500	10.867
104	23.567	17.333	14.500	13.050	12.050
105	15.733	13.817	13.383	12.500	11.350
106	21.867	18.767	16.800	15.417	14.183
107	15.383	15.133	14.717	14.400	13.800
108	16.517	14.100	12.667	12.267	11.500
109	15.100	13.483	12.733	12.117	11.217
110			31.367	22.833	18.117
111		10.150	11.183	15.883	23.650
112		27.683	20.783	18.317	15.100
113	13.467	12.900	12.383	11.767	11.067
114	23.433	18.500	15.800	12.367	11.400
115	17.783	15.000	13.550	12.800	11.417
116	25.817	21.583	15.617	15.117	14.333
117	31.900	26.650	15.833	14.067	11.367
118	12.800	12.267	11.883	10.883	10.500
119			10.000	11.233	16.567
120			17.450	18.533	11.117
121	12.750	12.283	11.917	11.550	10.867
122	14.283	12.650	11.883	11.500	10.817
123	25.050	13.200	12.333	11.417	11.033
124	18.767	15.283	13.900	13.033	11.967
125	29.533	13.867	12.800	12.300	11.583
126	13.367	13.033	12.533	12.150	11.567
127	15.017	13.967	13.333	12.883	12.367
128	16.533	13.550	12.533	11.733	11.083
129	17.567	14.400	13.133	11.917	11.367
130	16.167	15.283	14.467	13.550	11.767
131			29.250	23.567	13.567
132	14.033	13.300	13.033	12.700	11.733

Table C.10 Derived NORA₃ – NORA₁₁ Analyzed for Developing BISRO and AISRO

Reno ID	Parameter								
	NORA ₃	NORA ₄	NORA ₅	NORA ₆	NORA ₇	NORA ₈	NORA ₉	NORA ₁₀	NORA ₁₁
1	1.303	1.553	1.561	1.618	1.779	1.886	1.877	1.927	2.209
2	1.078	0.999	0.872	0.805	0.725	0.683	0.572	0.542	0.505
3	1.241	1.364	1.502	1.634	1.656	1.642	1.648	1.707	1.760
4	1.231	1.285	1.472	1.608	1.678	1.782	1.774	1.936	1.969
5	1.157	0.994	0.821	0.698	0.589	0.530	0.470	0.411	0.372
6	1.206	1.075	0.916	0.762	0.675	0.641	0.609	0.571	0.545
7	1.286	1.375	1.254	1.032	0.873	0.766	0.678	0.610	0.540
8	1.208	1.285	1.292	1.295	1.281	1.213	1.231	1.213	1.174
9	1.153	1.221	1.315	1.372	1.408	1.456	1.509	1.506	1.505
10	1.198	1.095	0.897	0.732	0.650	0.562	0.514	0.473	0.419
11	1.453	1.713	1.610	1.388	1.142	0.975	0.846	0.748	0.690
12	1.497	1.774	1.743	1.671	1.497	1.397	1.306	1.237	1.196
13	1.308	1.409	1.220	1.031	0.895	0.780	0.701	0.631	0.586
14	1.335	1.415	1.280	1.178	1.108	1.079	1.044	1.008	0.977
15	1.181	1.283	1.319	1.402	1.421	1.478	1.518	1.550	1.576
16	1.220	1.134	0.897	0.766	0.649	0.581	0.532	0.480	0.437
17	1.155	1.277	1.358	1.420	1.492	1.532	1.568	1.610	1.646
18	1.116	0.936	0.759	0.673	0.626	0.578	0.538	0.502	0.438
19	1.220	1.415	1.541	1.613	1.678	1.732	1.767	1.887	1.962
20	1.206	1.356	1.460	1.467	1.499	1.469	1.418	1.338	1.329
21	1.246	1.510	1.668	1.748	1.841	1.938	2.007	1.989	1.942
22	1.257	1.453	1.403	1.320	1.210	1.093	1.020	0.909	0.845
23	1.329	1.386	1.378	1.312	1.251	1.168	1.091	0.988	0.889
24	1.229	1.307	1.315	1.299	1.278	1.259	1.244	1.186	1.180
25	1.304	1.501	1.589	1.653	1.681	1.758	1.794	1.797	1.672
26	1.298	1.496	1.485	1.297	1.172	1.060	0.996	0.919	0.889
27	1.103	1.145	1.249	1.259	1.289	1.328	1.319	1.363	1.401
28	1.162	1.125	1.057	1.040	1.068	1.024	0.978	0.965	0.933
29	1.274	1.393	1.506	1.561	1.507	1.666	1.698	1.747	1.782
30	1.400	1.554	1.483	1.280	0.995	0.995	0.894	0.802	0.684
31	1.084	1.111	1.129	1.107	1.112	1.109	1.119	1.148	1.217
32	1.037	0.911	0.897	0.818	0.857	0.829	0.859	0.904	0.940
33	1.174	1.323	1.432	1.586	1.679	1.778	1.859	1.924	1.970
34	1.117	1.252	1.355	1.425	1.535	1.570	1.674	1.718	1.844
35	1.239	1.472	1.683	1.828	1.991	2.128	2.278	2.386	2.480
36	1.237	1.441	1.570	1.653	1.679	1.774	1.847	1.891	1.820
37	1.278	1.459	1.556	1.552	1.604	1.621	1.532	1.436	1.283
38	1.263	1.416	1.471	1.476	1.563	1.579	1.544	1.403	1.216
39	1.321	1.315	1.096	0.929	0.768	0.683	0.605	0.490	0.437
40	1.284	1.394	1.466	1.465	1.394	1.374	1.423	1.392	1.387
41	1.279	1.430	1.457	1.314	1.103	0.843	0.807	0.731	0.671
42	1.256	1.449	1.555	1.677	1.698	1.763	1.824	1.879	1.979

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter								
	NORA ₃	NORA ₄	NORA ₅	NORA ₆	NORA ₇	NORA ₈	NORA ₉	NORA ₁₀	NORA ₁₁
43	1.229	1.118	0.945	0.825	0.736	0.629	0.554	0.495	0.462
44	1.200	1.301	1.344	1.418	1.415	1.418	1.453	1.460	1.432
45	1.306	1.452	1.261	1.112	0.951	0.839	0.773	0.668	0.592
46	1.311	1.451	1.560	1.658	1.761	1.863	1.948	1.935	1.814
47	1.347	1.593	1.706	1.757	1.757	1.704	1.689	1.600	1.561
48	1.239	1.366	1.314	1.251	1.213	1.158	1.185	1.171	1.227
49	1.155	1.318	1.401	1.479	1.490	1.439	1.398	1.325	1.363
50	1.135	1.182	1.153	1.080	1.007	0.952	0.900	0.828	0.749
51	1.267	1.400	1.236	0.879	0.688	0.661	0.655	0.681	0.633
52	1.271	1.450	1.642	1.729	1.886	1.936	1.997	2.087	2.127
53	1.253	1.408	1.437	1.420	1.270	1.115	1.023	0.706	0.523
54	1.234	1.453	1.613	1.792	1.919	2.008	2.097	1.909	2.140
55	1.322	1.509	1.537	1.375	1.200	1.013	0.952	0.893	0.861
56	1.292	1.537	1.805	2.024	2.166	2.293	2.403	2.511	2.579
57	1.221	1.140	0.969	0.802	0.693	0.599	0.521	0.478	0.429
58	1.193	1.291	1.377	1.424	1.394	1.395	1.393	1.378	1.274
59	1.281	1.426	1.316	1.129	0.962	0.826	0.739	0.640	0.545
60	1.279	1.426	1.326	1.093	0.969	0.808	0.719	0.646	0.568
61	1.274	1.487	1.668	1.784	1.848	1.868	1.900	1.910	1.873
62	1.305	1.487	1.482	1.372	1.239	0.855	0.878	0.947	0.953
63	1.238	1.192	1.007	0.816	0.710	0.647	0.592	0.566	0.530
64	1.219	1.116	0.902	0.749	0.648	0.563	0.523	0.462	0.429
65	1.204	1.167	0.978	0.832	0.698	0.626	0.538	0.462	0.427
66	1.156	1.086	0.984	0.964	0.936	0.913	0.920	0.913	0.892
67	1.183	0.978	0.793	0.684	0.605	0.537	0.476	0.421	0.361
68	1.137	1.165	1.202	1.176	1.250	1.280	1.299	1.331	1.344
69	1.246	1.395	1.542	1.612	1.710	1.768	1.827	1.891	1.938
70	1.155	1.237	1.279	1.318	1.326	1.410	1.493	1.501	1.578
71	1.191	1.273	1.318	1.359	1.386	1.421	1.446	1.437	1.451
72	1.264	1.382	1.491	1.547	1.574	1.623	1.637	1.678	1.609
73	1.210	1.194	1.026	0.887	0.751	0.676	0.602	0.539	0.474
74	1.256	1.262	1.191	1.048	0.972	0.865	0.761	0.679	0.640
75	1.042	0.852	0.691	0.573	0.499	0.417	0.379	0.333	0.307
76	1.063	1.117	1.043	1.055	0.981	0.857	0.864	1.006	0.973
77	1.008	1.066	1.040	1.181	1.031	1.043	1.122	1.027	0.968
78	1.298	1.519	1.653	1.679	1.557	1.352	1.213	1.107	1.052
79	1.186	1.143	1.040	0.923	0.847	0.764	0.741	0.696	0.637
80	1.208	1.367	1.506	1.512	1.604	1.665	1.722	1.779	1.811
81	1.125	1.121	1.043	0.943	0.913	0.843	0.798	0.762	0.702
82	1.078	1.119	1.162	1.190	1.234	1.229	1.294	1.305	1.335
83	1.079	0.834	0.686	0.631	0.557	0.513	0.512	0.482	0.473
84	1.130	0.927	0.705	0.565	0.473	0.404	0.378	0.339	0.311
85	1.245	1.441	1.532	1.395	1.239	1.139	1.033	1.001	0.907
86	1.241	1.437	1.523	1.552	1.502	1.458	1.421	1.350	1.242
87	1.132	1.072	0.954	0.857	0.803	0.755	0.714	0.640	0.623
88	1.255	1.299	1.230	1.101	1.012	0.929	0.898	0.845	0.824
89	1.205	0.965	0.902	0.767	0.719	0.642	0.637	0.593	0.537

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter								
	NORA ₃	NORA ₄	NORA ₅	NORA ₆	NORA ₇	NORA ₈	NORA ₉	NORA ₁₀	NORA ₁₁
90	1.166	1.346	1.439	1.500	1.584	1.616	1.690	1.679	1.693
91	1.306	1.323	1.230	1.100	1.010	0.946	0.877	0.819	0.775
92	1.309	1.483	1.491	1.443	1.359	1.275	1.204	1.146	1.039
93	1.280	1.437	1.615	1.723	1.790	1.876	1.961	2.041	2.086
94	1.114	1.162	1.273	1.045	1.257	1.293	1.185	1.187	1.113
95	1.145	1.029	1.007	0.956	0.858	0.926	0.846	0.806	0.837
96	1.281	1.437	1.510	1.505	1.492	1.405	1.401	1.341	1.318
97	1.160	1.196	1.203	1.140	1.114	1.037	1.021	0.978	0.989
98	1.204	1.087	0.907	0.744	0.632	0.546	0.483	0.439	0.380
99	1.179	0.977	0.800	0.668	0.573	0.493	0.449	0.400	0.350
100	1.224	1.309	1.309	1.374	1.370	1.370	1.321	1.279	1.344
101	1.273	1.319	1.154	1.061	0.976	0.936	0.866	0.833	0.838
102	1.157	1.053	0.843	0.709	0.613	0.549	0.501	0.451	0.431
103	1.201	1.307	1.464	1.554	1.653	1.783	1.799	1.907	2.044
104	1.248	1.425	1.522	1.505	1.487	1.511	1.471	1.480	1.465
105	1.271	1.266	1.122	0.982	0.909	0.802	0.786	0.704	0.643
106	1.229	1.401	1.490	1.611	1.688	1.719	1.806	1.856	1.879
107	1.249	1.435	1.588	1.661	1.711	1.720	1.736	1.720	1.720
108	1.240	1.341	1.213	1.044	0.876	0.733	0.651	0.540	0.506
109	1.356	1.516	1.347	1.137	0.979	0.856	0.781	0.715	0.658
110	1.298	1.493	1.483	1.451	1.407	1.417	1.411	1.389	1.442
111	1.175	1.254	1.310	1.329	1.350	1.425	1.445	1.437	1.563
112	1.231	1.464	1.435	1.440	1.400	1.387	1.356	1.222	1.216
113	1.158	1.148	1.066	0.966	0.920	0.861	0.782	0.727	0.661
114	1.137	1.191	1.156	1.124	1.088	1.032	0.989	0.909	0.840
115	1.239	1.405	1.466	1.305	1.291	1.270	1.218	1.188	1.104
116	1.278	1.448	1.557	1.681	1.715	1.571	1.597	1.484	1.762
117	1.238	1.347	1.357	1.250	1.230	1.180	1.149	1.035	0.984
118	1.213	1.303	1.421	1.307	1.283	1.124	1.129	1.084	0.854
119	1.190	1.283	1.397	1.418	1.453	1.520	1.564	1.597	1.711
120	1.337	1.486	1.398	1.123	1.004	0.831	0.815	0.753	0.725
121	1.280	1.383	1.349	1.210	1.079	1.003	0.896	0.822	0.720
122	1.204	1.149	0.950	0.800	0.706	0.625	0.576	0.529	0.462
123	1.131	1.027	0.875	0.745	0.672	0.585	0.530	0.475	0.431
124	1.167	1.195	1.173	1.101	1.020	0.967	0.907	0.867	0.829
125	1.092	0.949	0.764	0.670	0.564	0.504	0.456	0.414	0.386
126	1.284	1.309	1.258	1.282	1.187	1.118	1.100	1.075	1.036
127	1.232	1.316	1.316	1.300	1.329	1.286	1.287	1.194	1.191
128	1.242	1.333	1.256	1.156	1.020	0.844	0.760	0.683	0.616
129	0.918	0.732	0.640	0.562	0.479	0.438	0.389	0.352	0.332
130	1.305	1.459	1.525	1.513	1.501	1.492	1.446	1.412	1.325
131	1.149	1.190	1.268	1.310	1.366	1.389	1.368	1.343	1.300
132	1.149	1.030	0.894	0.789	0.720	0.641	0.593	0.543	0.525

Table C.11 Derived NORA₁₂ – NORA₂₀ Analyzed for Developing BISRO and AISRO

Reno ID	Parameter								
	NORA ₁₂	NORA ₁₃	NORA ₁₄	NORA ₁₅	NORA ₁₆	NORA ₁₇	NORA ₁₈	NORA ₁₉	NORA ₂₀
1	2.037	2.172	2.281	2.262	2.161	2.363	2.256	2.346	2.199
2	0.467	0.424	0.389	0.384	0.348	0.385	0.386	0.368	0.383
3	1.552	1.386	1.283	1.200	1.070	1.062	0.947	0.877	0.825
4	1.953	1.856	1.996	2.001	1.952	1.912	1.713	1.573	1.533
5	0.268	0.222	0.202	0.184	0.164	0.161	0.149	0.166	0.153
6	0.495	0.436	0.403	0.372	0.377	0.343	0.323	0.292	0.286
7	0.497	0.448	0.392	0.358	0.350	0.351	0.342	0.327	0.322
8	1.133	1.154	1.113	1.073	1.045	0.980	0.965	0.945	0.920
9	1.500	1.461	1.378	1.271	1.346	1.288	1.240	1.223	1.196
10	0.362	0.331	0.310	0.293	0.304	0.262	0.232	0.221	0.210
11	0.617	0.563	0.492	0.441	0.410	0.382	0.355	0.351	0.311
12	1.167	1.116	1.079	1.024	0.940	0.839	0.765	0.699	0.625
13	0.538	0.512	0.472	0.418	0.374	0.338	0.332	0.311	0.303
14	0.947	0.941	0.883	0.727	0.560	0.496	0.465	0.448	0.412
15	1.599	1.620	1.631	1.637	1.656	1.615	1.570	1.483	1.458
16	0.397	0.347	0.309	0.300	0.303	0.280	0.265	0.255	0.237
17	1.611	1.643	1.643	1.667	1.647	1.670	1.692	1.712	1.706
18	0.376	0.256	0.232	0.233	0.228	0.210	0.167	0.140	0.132
19	1.955	1.972	1.947	1.881	1.808	1.787	1.725	1.607	1.583
20	1.247	1.106	0.996	0.887	0.852	0.835	0.842	0.848	0.817
21	1.899	1.854	1.785	1.708	1.623	1.591	1.512	1.420	1.252
22	0.751	0.645	0.552	0.508	0.468	0.440	0.425	0.405	0.383
23	0.796	0.648	0.494	0.352	0.285	0.260	0.256	0.240	0.233
24	1.166	1.158	1.126	1.077	1.016	0.962	0.897	0.851	0.796
25	1.631	1.504	1.435	1.182	0.938	0.792	0.696	0.661	0.635
26	0.771	0.587	0.439	0.369	0.339	0.315	0.298	0.281	0.277
27	1.412	1.418	1.400	1.402	1.399	1.423	1.438	1.411	1.422
28	0.915	0.910	0.849	0.819	0.824	0.783	0.795	0.715	0.782
29	1.798	1.780	1.779	1.722	1.582	1.547	1.530	1.507	1.463
30	0.536	0.464	0.431	0.406	0.387	0.377	0.398	0.378	0.362
31	1.170	1.132	1.003	0.914	0.934	0.903	0.927	0.898	0.904
32	0.935	0.918	0.911	0.980	0.983	0.990	0.977	1.027	1.010
33	2.066	2.068	1.996	1.870	1.820	1.723	1.646	1.547	1.368
34	1.802	1.900	1.924	1.924	1.946	1.908	2.034	2.050	2.061
35	2.612	2.709	2.800	2.796	2.836	2.869	2.933	2.966	2.982
36	1.777	1.670	1.554	1.269	0.886	0.769	0.746	0.697	0.676
37	1.147	0.882	0.690	0.578	0.536	0.445	0.473	0.438	0.438
38	1.218	0.863	0.647	0.610	0.568	0.539	0.530	0.529	0.517
39	0.405	0.352	0.314	0.279	0.250	0.227	0.206	0.203	0.180
40	1.398	1.404	1.374	1.362	1.380	1.390	1.387	1.377	1.382
41	0.579	0.446	0.383	0.329	0.337	0.312	0.280	0.252	0.245
42	2.073	2.179	2.228	2.144	2.229	2.322	2.337	2.316	2.254

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter								
	NORA ₁₂	NORA ₁₃	NORA ₁₄	NORA ₁₅	NORA ₁₆	NORA ₁₇	NORA ₁₈	NORA ₁₉	NORA ₂₀
43	0.423	0.371	0.349	0.333	0.315	0.297	0.280	0.258	0.254
44	1.533	1.480	1.409	1.360	1.319	1.253	1.197	1.152	1.150
45	0.553	0.471	0.428	0.379	0.348	0.330	0.316	0.315	0.310
46	1.840	1.814	1.734	1.636	1.560	1.469	1.391	1.352	1.306
47	1.498	1.374	1.077	0.882	0.736	0.669	0.580	0.539	0.536
48	1.234	1.324	1.402	1.367	1.366	1.326	1.301	1.308	1.317
49	1.326	1.266	1.205	1.115	1.079	0.985	0.955	0.898	0.860
50	0.654	0.540	0.442	0.401	0.387	0.389	0.366	0.341	0.325
51	0.557	0.506	0.380	0.305	0.218	0.175	0.157	0.159	0.146
52	2.052	2.138	2.227	2.168	2.072	1.900	1.737	1.640	1.504
53	0.496	0.437	0.422	0.380	0.365	0.320	0.288	0.292	0.242
54	2.145	2.231	2.271	2.293	2.333	2.380	2.403	2.423	2.402
55	0.816	0.729	0.699	0.644	0.542	0.450	0.367	0.279	0.215
56	2.645	2.667	2.773	2.696	2.482	2.637	2.589	2.592	2.625
57	0.382	0.315	0.300	0.286	0.246	0.229	0.215	0.205	0.204
58	1.297	1.306	1.276	1.219	1.190	1.155	1.146	1.139	1.116
59	0.473	0.437	0.443	0.435	0.406	0.401	0.406	0.374	0.361
60	0.495	0.444	0.428	0.435	0.423	0.407	0.415	0.398	0.379
61	1.835	1.632	1.479	1.380	1.260	1.147	1.051	0.948	0.868
62	0.772	0.648	0.505	0.380	0.321	0.301	0.295	0.285	0.267
63	0.448	0.360	0.330	0.305	0.294	0.280	0.280	0.273	0.265
64	0.363	0.324	0.309	0.286	0.248	0.225	0.213	0.209	0.201
65	0.355	0.297	0.292	0.308	0.290	0.300	0.298	0.296	0.278
66	0.934	0.894	0.871	0.859	0.833	0.853	0.844	0.862	0.854
67	0.324	0.279	0.250	0.243	0.216	0.200	0.193	0.185	0.173
68	1.386	1.406	1.417	1.468	1.477	1.467	1.478	1.500	1.488
69	1.966	2.001	2.010	1.854	1.683	1.515	1.359	1.232	1.141
70	1.591	1.638	1.695	1.729	1.725	1.770	1.817	1.816	1.835
71	1.403	1.418	1.413	1.319	1.264	1.180	1.144	1.121	1.103
72	1.457	1.403	1.289	1.108	0.968	0.939	0.920	0.866	0.841
73	0.418	0.373	0.347	0.301	0.300	0.296	0.279	0.242	0.230
74	0.571	0.365	0.262	0.256	0.227	0.223	0.222	0.209	0.215
75	0.272	0.219	0.229	0.185	0.183	0.193	0.180	0.173	0.165
76	1.009	0.897	0.964	0.847	0.911	0.937	0.995	1.009	1.098
77	0.966	0.920	0.893	0.919	0.932	0.812	0.859	0.939	0.760
78	0.975	0.919	0.878	0.849	0.837	0.790	0.765	0.736	0.707
79	0.577	0.411	0.290	0.250	0.238	0.222	0.207	0.194	0.189
80	1.875	1.910	1.949	1.965	1.998	2.061	2.071	2.108	2.102
81	0.626	0.525	0.490	0.456	0.453	0.454	0.443	0.451	0.442
82	1.292	1.300	1.266	1.294	1.375	1.342	1.390	1.416	1.396
83	0.445	0.404	0.389	0.389	0.377	0.375	0.366	0.359	0.366
84	0.278	0.251	0.248	0.236	0.210	0.190	0.168	0.161	0.164
85	0.844	0.760	0.557	0.477	0.461	0.434	0.437	0.427	0.397
86	1.223	1.116	0.887	0.741	0.661	0.629	0.558	0.530	0.505
87	0.568	0.516	0.451	0.442	0.436	0.445	0.420	0.403	0.387
88	0.797	0.763	0.711	0.638	0.645	0.594	0.511	0.470	0.424
89	0.507	0.455	0.383	0.354	0.344	0.296	0.292	0.276	0.257

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter								
	NORA ₁₂	NORA ₁₃	NORA ₁₄	NORA ₁₅	NORA ₁₆	NORA ₁₇	NORA ₁₈	NORA ₁₉	NORA ₂₀
90	1.549	1.252	1.170	1.100	1.065	1.056	1.016	1.015	1.005
91	0.704	0.566	0.497	0.473	0.444	0.438	0.423	0.418	0.413
92	0.929	0.760	0.604	0.505	0.439	0.393	0.357	0.322	0.321
93	2.101	2.017	1.980	1.978	1.861	1.734	1.611	1.496	1.377
94	1.204	1.222	1.252	1.210	1.094	1.043	1.281	1.304	1.231
95	0.783	0.672	0.577	0.587	0.633	0.572	0.596	0.587	0.571
96	1.284	1.224	1.108	1.076	1.077	1.087	1.092	1.073	1.069
97	1.007	0.969	0.967	1.005	1.032	1.060	1.096	1.150	1.186
98	0.307	0.254	0.224	0.202	0.184	0.176	0.163	0.158	0.144
99	0.275	0.228	0.215	0.200	0.195	0.179	0.171	0.164	0.151
100	1.343	1.189	1.033	0.817	0.659	0.577	0.560	0.523	0.492
101	0.788	0.777	0.722	0.683	0.646	0.609	0.583	0.573	0.567
102	0.402	0.383	0.355	0.339	0.315	0.287	0.280	0.279	0.291
103	2.097	2.106	2.208	2.232	2.255	2.252	2.200	2.216	2.145
104	1.349	1.192	1.078	1.005	0.954	0.913	0.845	0.838	0.802
105	0.590	0.536	0.406	0.401	0.334	0.309	0.291	0.253	0.238
106	1.914	1.938	1.774	1.622	1.465	1.339	1.237	1.158	1.123
107	1.756	1.688	1.558	1.132	0.668	0.437	0.388	0.365	0.348
108	0.444	0.348	0.324	0.319	0.283	0.258	0.245	0.227	0.220
109	0.589	0.475	0.399	0.358	0.335	0.314	0.288	0.268	0.255
110	1.440	1.407	1.338	1.339	1.415	1.366	1.316	1.275	1.220
111	1.586	1.651	1.729	1.697	1.803	1.745	1.778	1.799	1.921
112	1.199	1.172	1.203	1.109	1.104	1.081	1.036	0.913	0.873
113	0.554	0.423	0.314	0.287	0.265	0.252	0.247	0.223	0.210
114	0.773	0.706	0.691	0.669	0.628	0.589	0.559	0.535	0.541
115	1.031	0.915	0.780	0.715	0.634	0.609	0.591	0.568	0.555
116	1.700	1.622	1.673	1.468	1.173	1.068	1.089	1.085	1.145
117	0.898	0.868	0.839	0.777	0.715	0.705	0.686	0.656	0.606
118	0.740	0.522	0.443	0.443	0.415	0.437	0.424	0.411	0.401
119	1.801	1.849	1.902	1.920	1.914	2.012	1.996	1.982	2.060
120	0.650	0.563	0.568	0.558	0.606	0.577	0.608	0.628	0.633
121	0.557	0.384	0.352	0.298	0.296	0.289	0.258	0.257	0.241
122	0.364	0.311	0.283	0.254	0.257	0.234	0.225	0.216	0.215
123	0.359	0.287	0.289	0.292	0.282	0.284	0.250	0.207	0.199
124	0.779	0.696	0.599	0.535	0.498	0.460	0.438	0.434	0.420
125	0.343	0.275	0.243	0.229	0.230	0.215	0.225	0.224	0.243
126	0.890	0.653	0.499	0.412	0.416	0.372	0.407	0.398	0.372
127	1.122	0.935	0.715	0.602	0.553	0.547	0.519	0.532	0.494
128	0.526	0.440	0.389	0.360	0.352	0.351	0.314	0.325	0.316
129	0.275	0.253	0.220	0.192	0.188	0.185	0.159	0.152	0.143
130	1.259	1.193	1.067	0.896	0.737	0.622	0.544	0.503	0.479
131	1.272	1.218	1.177	1.135	1.143	1.153	1.160	1.143	1.160
132	0.476	0.390	0.273	0.250	0.229	0.214	0.214	0.184	0.186

Table C.12 Derived NORA₂₁ – NORA₂₅ Analyzed for Developing BISRO and AISRO

Reno ID	Parameter				
	NORA ₂₁	NORA ₂₂	NORA ₂₃	NORA ₂₄	NORA ₂₅
1	2.304	2.330	2.274	2.299	2.246
2	0.350	0.352	0.347	0.334	0.318
3	0.706	0.722	0.691	0.639	0.633
4	1.677	1.590	1.490	1.375	1.446
5	0.143	0.145	0.143	0.133	0.134
6	0.275	0.273	0.252	0.256	0.245
7	0.309	0.295	0.291	0.289	0.277
8	0.893	0.888	0.884	0.874	0.849
9	1.131	1.083	1.048	1.037	1.007
10	0.203	0.203	0.202	0.195	0.188
11	0.304	0.290	0.285	0.266	0.260
12	0.585	0.553	0.538	0.529	0.491
13	0.290	0.287	0.282	0.261	0.257
14	0.403	0.400	0.380	0.356	0.341
15	1.389	1.335	1.355	1.344	1.306
16	0.219	0.215	0.205	0.201	0.206
17	1.743	1.755	1.779	1.796	1.860
18	0.129	0.118	0.113	0.108	0.104
19	1.512	1.449	1.433	1.340	1.328
20	0.853	0.795	0.777	0.771	0.770
21	1.107	1.043	0.954	0.885	0.823
22	0.355	0.339	0.318	0.317	0.310
23	0.225	0.220	0.218	0.223	0.219
24	0.756	0.729	0.700	0.657	0.637
25	0.625	0.623	0.585	0.563	0.560
26	0.238	0.239	0.216	0.211	0.192
27	1.355	1.373	1.345	1.338	1.316
28	0.744	0.748	0.726	0.738	0.712
29	1.420	1.393	1.366	1.322	1.184
30	0.343	0.318	0.316	0.315	0.292
31	0.902	0.854	0.885	0.894	0.906
32	0.990	1.025	1.029	1.072	1.081
33	1.177	1.026	0.928	0.839	0.790
34	2.086	1.944	1.806	1.767	1.679
35	3.039	3.065	3.035	2.995	2.980
36	0.656	0.620	0.591	0.556	0.552
37	0.427	0.419	0.446	0.446	0.415
38	0.492	0.533	0.519	0.485	0.484
39	0.192	0.169	0.173	0.175	0.149
40	1.382	1.374	1.381	1.361	1.350
41	0.232	0.224	0.209	0.192	0.182
42	2.142	2.030	1.967	1.928	1.888
43	0.242	0.246	0.232	0.229	0.223

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter				
	NORA ₁₂	NORA ₁₃	NORA ₁₄	NORA ₁₅	NORA ₁₆
44	1.117	1.107	1.092	1.108	1.101
45	0.300	0.280	0.273	0.265	0.256
46	1.266	1.236	1.194	1.159	1.157
47	0.497	0.473	0.469	0.446	0.437
48	1.324	1.313	1.318	1.317	1.316
49	0.835	0.813	0.801	0.785	0.760
50	0.307	0.303	0.286	0.283	0.284
51	0.103	0.108	0.100	0.112	0.101
52	1.314	1.248	1.190	1.147	1.147
53	0.226	0.218	0.207	0.197	0.177
54	2.469	2.517	2.527	2.577	2.602
55	0.175	0.154	0.143	0.139	0.137
56	2.596	2.560	2.509	2.465	2.443
57	0.207	0.199	0.185	0.180	0.176
58	1.105	1.090	1.035	0.974	0.909
59	0.358	0.349	0.341	0.307	0.297
60	0.366	0.357	0.331	0.340	0.324
61	0.772	0.704	0.634	0.544	0.474
62	0.256	0.225	0.209	0.189	0.180
63	0.265	0.266	0.258	0.240	0.229
64	0.199	0.201	0.195	0.179	0.177
65	0.263	0.251	0.219	0.219	0.226
66	0.875	0.820	0.802	0.805	0.815
67	0.172	0.168	0.166	0.159	0.153
68	1.477	1.493	1.505	1.505	1.512
69	1.016	0.950	0.872	0.827	0.794
70	1.814	1.851	1.877	1.866	1.879
71	1.108	1.103	1.073	1.052	1.018
72	0.792	0.760	0.722	0.701	0.671
73	0.226	0.213	0.211	0.187	0.187
74	0.209	0.200	0.201	0.216	0.233
75	0.168	0.146	0.157	0.130	0.125
76	0.953	0.851	0.956	0.937	1.033
77	0.893	0.816	0.783	0.858	0.784
78	0.652	0.547	0.483	0.452	0.462
79	0.173	0.164	0.161	0.171	0.170
80	2.107	2.147	2.157	2.174	2.179
81	0.413	0.422	0.394	0.378	0.386
82	1.426	1.400	1.389	1.417	1.401
83	0.363	0.326	0.351	0.342	0.329
84	0.159	0.155	0.152	0.138	0.138
85	0.378	0.375	0.379	0.362	0.326
86	0.503	0.470	0.475	0.457	0.429
87	0.383	0.384	0.364	0.360	0.346
88	0.423	0.460	0.395	0.374	0.352
89	0.245	0.259	0.245	0.223	0.214
90	0.993	1.003	0.994	0.986	0.991

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter				
	NORA ₁₂	NORA ₁₃	NORA ₁₄	NORA ₁₅	NORA ₁₆
91	0.395	0.418	0.397	0.389	0.380
92	0.288	0.282	0.278	0.258	0.243
93	1.313	1.197	1.099	1.002	0.914
94	1.327	1.364	1.394	1.339	1.360
95	0.621	0.583	0.576	0.625	0.564
96	1.061	1.070	1.070	1.044	1.038
97	1.207	1.247	1.298	1.297	1.197
98	0.139	0.138	0.133	0.123	0.128
99	0.147	0.136	0.132	0.135	0.129
100	0.461	0.456	0.435	0.416	0.392
101	0.568	0.579	0.577	0.591	0.612
102	0.266	0.249	0.236	0.242	0.228
103	2.128	2.078	2.096	2.036	1.998
104	0.788	0.754	0.763	0.746	0.698
105	0.233	0.201	0.206	0.183	0.161
106	1.035	0.954	0.903	0.866	0.817
107	0.325	0.311	0.310	0.302	0.303
108	0.203	0.202	0.200	0.190	0.197
109	0.252	0.258	0.250	0.245	0.224
110	1.214	1.219	1.157	1.126	1.091
111	1.889	1.968	1.999	2.034	2.015
112	0.850	0.842	0.807	0.815	0.786
113	0.191	0.182	0.177	0.174	0.158
114	0.508	0.494	0.473	0.444	0.451
115	0.541	0.523	0.520	0.482	0.477
116	0.964	1.094	0.995	0.992	0.891
117	0.680	0.610	0.593	0.568	0.604
118	0.402	0.374	0.359	0.343	0.321
119	2.126	2.159	2.156	2.158	2.145
120	0.556	0.630	0.658	0.629	0.605
121	0.240	0.249	0.238	0.236	0.227
122	0.191	0.200	0.192	0.180	0.174
123	0.214	0.216	0.206	0.221	0.239
124	0.411	0.383	0.397	0.381	0.369
125	0.224	0.227	0.218	0.216	0.216
126	0.349	0.350	0.356	0.305	0.316
127	0.471	0.459	0.436	0.401	0.402
128	0.317	0.298	0.301	0.296	0.283
129	0.141	0.122	0.125	0.125	0.104
130	0.471	0.455	0.433	0.413	0.408
131	1.155	1.121	1.106	1.069	1.036
132	0.166	0.157	0.144	0.146	0.142

Table C.13 Derived T_{max} and Its Variants Analyzed for Developing BISRO and AISRO

Reno ID	Parameter									
	$T_{max/10}$	$T_{2max/10}$	$T_{3max/10}$	$T_{4max/10}$	$T_{5max/10}$	$T_{6max/10}$	$T_{7max/10}$	$T_{8max/10}$	$T_{9max/10}$	T_{max}
1	0.233	0.417	0.567	0.700	0.900	1.083	1.300	1.600	1.933	2.767
2	0.117	0.300	0.483	0.700	1.583	2.233	2.983	4.783	5.433	10.300
3	0.100	0.367	0.517	0.733	0.917	1.200	1.400	1.750	2.083	2.883
4	0.067	0.333	0.500	0.650	0.800	1.133	1.517	1.833	2.233	2.950
5	0.350	0.550	0.700	0.883	1.083	1.483	1.900	2.333	2.783	3.750
6	0.417	0.533	0.700	0.850	1.000	1.233	1.517	1.867	2.250	2.917
7	0.917	1.100	1.333	1.533	1.733	2.033	2.367	2.783	3.217	4.117
8	0.950	1.167	1.400	1.583	1.817	2.100	2.433	2.783	3.283	4.183
9	0.550	0.717	0.900	1.083	1.283	1.667	1.950	2.383	2.767	3.933
10	0.633	0.850	1.067	1.200	1.400	1.567	1.967	2.267	2.717	4.000
11	0.383	0.533	0.667	0.800	0.917	1.167	1.517	1.933	2.333	3.250
12	0.233	0.250	0.283	0.417	0.667	0.900	1.267	1.650	2.100	2.700
13	0.533	0.750	0.933	1.333	2.033	2.833	3.700	4.567	6.783	9.433
14	0.567	0.783	0.950	1.050	1.267	1.567	2.050	2.533	3.167	4.017
15	0.417	0.650	0.817	0.933	1.183	1.550	1.917	2.450	2.800	4.550
16	0.433	0.633	0.900	1.283	1.783	2.267	2.900	3.800	5.867	9.650
17	0.483	0.717	0.817	1.067	1.367	1.800	2.200	2.633	3.217	4.317
18	0.550	0.733	0.917	1.167	1.517	1.783	2.167	2.567	2.983	4.100
19	0.200	0.367	0.517	1.300	2.217	3.583	5.400	7.033	9.517	12.750
20	0.517	0.617	0.883	1.317	1.833	2.517	3.367	4.550	7.417	10.667
21	0.450	0.633	0.800	1.150	1.500	1.883	2.367	3.150	4.017	7.717
22	0.400	0.583	0.750	0.883	1.233	1.800	2.450	3.000	4.083	7.633
23	0.500	0.700	0.900	1.100	1.233	1.533	1.783	2.183	2.650	3.783
24	0.333	0.467	0.717	0.900	1.200	1.583	2.100	2.533	3.200	4.683
25	0.117	0.233	0.350	0.450	0.950	1.283	1.517	1.917	2.350	2.983
26	0.450	0.667	0.850	1.000	1.317	1.683	2.050	2.500	3.000	3.900
27	0.550	0.800	1.033	1.333	1.917	2.550	3.450	5.183	7.167	9.317
28	0.367	0.650	0.933	1.333	1.667	2.183	2.733	3.200	3.950	6.650
29	0.183	0.233	0.333	0.317	0.517	0.817	1.300	1.733	2.317	3.517
30	0.267	0.500	0.717	0.983	1.333	1.617	1.950	2.367	2.983	3.833
31	0.433	0.767	1.217	1.650	2.367	3.350	4.667	6.533	9.517	14.217
32	0.283	0.467	0.667	0.883	1.283	1.600	2.067	2.650	3.250	4.733
33	0.467	0.683	0.883	1.117	1.450	1.850	2.350	2.850	3.500	4.650
34	0.383	0.550	0.717	0.833	1.050	1.250	1.533	1.900	2.267	3.100
35	0.500	0.633	0.817	1.000	1.233	1.633	1.983	2.417	3.000	4.000
36	0.483	0.683	0.767	0.967	1.083	1.350	1.967	2.450	3.017	3.833
37	0.417	0.633	0.917	1.317	1.883	2.450	3.250	4.200	5.367	9.917
38	0.317	0.533	0.717	0.933	1.333	1.667	2.133	2.617	3.233	4.550
39	0.267	0.333	0.383	0.567	0.883	1.183	1.633	2.017	2.450	3.150
40	0.300	0.467	0.633	0.783	0.950	1.350	1.583	1.950	2.433	3.167
41	0.267	0.417	0.600	0.750	0.950	1.267	1.567	1.850	2.450	3.183
42	0.417	0.517	0.567	0.683	0.817	0.950	1.333	1.817	2.250	2.883

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	$T_{max/10}$	$T_{2max/10}$	$T_{3max/10}$	$T_{4max/10}$	$T_{5max/10}$	$T_{6max/10}$	$T_{7max/10}$	$T_{8max/10}$	$T_{9max/10}$	T_{max}
43	0.367	0.550	0.867	1.333	2.000	2.783	4.083	6.000	8.633	13.517
44	0.400	0.600	0.833	1.133	1.583	2.017	2.683	3.800	5.483	10.200
45	0.300	0.483	0.650	0.817	1.000	1.350	1.650	1.917	2.500	3.417
46	0.367	0.483	0.600	0.700	0.950	1.400	1.667	2.117	2.450	3.483
47	0.367	0.467	0.550	0.667	0.817	0.950	1.233	1.600	1.933	2.717
48	0.717	0.900	1.050	1.267	1.533	2.050	2.600	3.183	3.983	5.717
49	0.250	0.383	0.500	0.583	0.883	1.150	1.517	1.800	2.283	2.950
50	0.333	0.383	0.417	0.467	0.550	0.750	1.333	1.750	2.083	3.533
51	0.350	0.333	0.400	0.450	0.600	0.900	1.200	1.467	1.867	2.450
52	0.333	0.383	0.433	0.483	0.683	0.900	1.233	1.633	2.267	2.917
53	0.317	0.400	0.483	0.817	1.167	1.617	2.217	2.850	3.700	4.767
54	0.367	0.417	0.600	0.817	1.350	1.800	2.400	2.983	3.617	5.950
55	0.333	0.367	0.417	0.483	0.567	0.967	1.333	1.683	2.100	2.700
56	0.283	0.383	0.467	0.600	1.033	1.333	1.733	2.233	2.650	3.883
57	0.300	0.350	0.467	0.583	0.967	1.283	1.533	1.867	2.333	2.767
58	0.633	0.900	0.967	1.117	1.283	1.500	1.850	2.167	2.567	3.600
59	0.417	0.617	0.833	1.083	1.483	1.750	2.100	2.633	3.183	4.483
60	0.550	0.800	1.050	1.517	2.083	2.867	4.183	5.650	8.433	11.450
61	0.233	0.350	0.400	0.583	0.717	0.917	1.333	1.700	2.400	3.367
62	0.400	0.550	0.700	0.867	0.983	1.300	1.533	1.867	2.317	3.067
63	0.317	0.483	0.750	0.883	1.050	1.250	1.517	1.833	2.217	2.867
64	0.617	0.783	0.883	1.083	1.233	1.517	1.900	2.383	3.200	7.567
65	0.800	0.817	1.167	1.150	1.417	1.600	1.800	2.217	2.617	3.600
66	0.317	0.450	0.550	0.667	0.917	1.133	1.400	1.783	2.217	3.250
67	0.267	0.417	0.667	0.800	1.217	1.683	2.267	2.917	3.667	5.317
68	0.433	0.583	0.717	0.867	1.033	1.400	1.800	2.067	2.483	3.317
69	0.517	0.750	0.983	1.367	1.883	2.667	3.767	5.383	8.350	12.750
70	0.383	0.550	0.583	0.967	1.600	2.233	2.917	3.883	5.000	12.583
71	0.450	0.567	0.583	0.733	0.950	1.317	1.767	2.167	2.783	4.133
72	0.750	0.917	1.100	1.217	1.500	1.733	2.133	2.517	3.017	4.167
73	0.183	0.433	0.600	0.767	0.983	1.167	1.450	1.750	2.167	3.500
74	0.167	0.383	0.567	0.717	0.900	1.150	1.483	1.817	2.383	3.750
75	0.267	0.517	0.683	0.867	1.200	1.600	2.100	2.683	3.317	5.083
76	0.200	0.450	0.633	0.850	1.600	2.217	2.883	3.667	8.633	11.067
77	0.317	0.433	0.633	0.800	1.017	1.233	1.783	2.283	2.900	3.833
78	0.433	0.633	0.817	0.983	1.233	1.517	1.983	2.533	3.583	4.767
79	0.350	0.417	0.533	0.900	1.150	1.500	2.067	2.600	3.050	3.917
80	0.300	0.367	0.400	0.817	1.183	1.450	1.883	2.333	2.850	4.200
81	0.350	0.417	0.433	0.617	0.917	1.233	1.567	1.850	2.283	2.900
82	0.150	0.250	0.333	0.483	0.733	1.050	1.433	1.667	2.167	3.300
83	0.383	0.417	0.433	0.467	0.750	1.033	1.300	1.817	2.267	3.650
84	0.400	0.417	0.433	0.467	0.683	0.883	1.250	1.583	2.000	2.767
85	0.600	0.633	0.800	1.067	1.317	1.550	1.867	2.133	2.600	3.467
86	0.583	0.600	0.650	0.817	1.017	1.450	1.817	2.217	2.700	7.000
87	0.300	0.333	0.350	0.483	0.767	1.350	1.583	2.250	2.800	3.900
88	0.283	0.417	0.517	0.733	0.833	0.983	1.233	1.433	1.733	2.317

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	$T_{max/10}$	$T_{2max/10}$	$T_{3max/10}$	$T_{4max/10}$	$T_{5max/10}$	$T_{6max/10}$	$T_{7max/10}$	$T_{8max/10}$	$T_{9max/10}$	T_{max}
89	0.383	0.600	0.750	0.983	1.350	1.800	2.267	2.667	3.433	5.250
90	0.483	0.567	0.617	0.717	0.800	0.983	1.200	1.583	2.183	3.117
91	0.133	0.433	0.667	1.300	2.117	3.017	4.833	6.800	13.133	15.717
92	0.317	0.517	0.667	0.800	0.917	1.133	1.533	2.233	2.800	4.733
93	0.317	0.500	0.683	0.833	1.117	1.650	2.217	3.967	5.983	11.500
94	0.550	0.800	0.950	1.217	1.950	2.833	3.767	5.367	9.300	13.433
95	0.183	0.333	0.433	0.567	0.767	1.533	2.167	2.950	3.950	7.217
96	0.417	0.617	0.700	0.900	1.133	1.433	1.717	2.217	2.717	4.783
97	0.550	0.750	0.950	1.317	1.733	2.183	2.933	4.267	7.533	11.800
98	0.117	0.217	0.333	0.433	1.000	1.533	2.183	3.233	4.350	6.167
99	0.550	0.850	1.483	2.367	3.417	4.467	5.617	7.450	9.917	14.333
100	0.267	0.433	0.600	0.717	0.983	1.417	2.067	2.817	4.883	9.367
101	0.200	0.267	0.383	0.567	0.617	0.783	1.150	1.650	5.267	6.117
102	0.050	0.083	0.750	0.950	1.567	2.317	3.300	4.617	6.517	10.233
103	0.267	0.317	0.600	0.850	1.267	1.700	2.183	2.650	3.367	4.967
104	0.267	0.550	0.950	1.550	2.600	4.333	6.183	8.833	10.867	16.583
105	0.700	0.900	1.067	1.167	1.383	1.717	2.200	2.700	3.167	4.267
106	0.417	0.500	0.583	0.817	1.250	1.550	2.050	2.550	3.450	4.133
107	0.533	0.567	0.617	0.700	0.833	1.400	1.917	2.800	4.917	7.367
108	0.233	0.567	0.917	1.650	2.733	3.333	6.167	9.850	10.633	16.700
109	0.367	0.550	0.767	1.017	1.383	1.967	2.883	5.100	8.750	15.550
110	0.133	0.250	0.417	0.950	1.783	2.900	4.683	7.483	19.500	27.867
111	0.100	0.217	0.317	0.483	0.650	0.783	2.083	4.133	7.217	18.133
112	0.100	0.217	0.300	0.417	0.517	0.600	0.717	1.200	2.100	3.017
113	0.167	0.333	0.400	0.367	0.383	0.850	0.550	1.917	6.883	11.183
114	0.283	0.300	0.317	0.333	0.350	0.367	0.600	9.933	21.350	28.583
115	0.383	0.400	0.483	1.000	2.417	3.983	6.417	8.967	13.533	20.867
116	0.450	0.950	1.783	2.967	4.317	6.083	8.283	10.533	13.850	22.067
117	0.500	0.700	0.867	1.050	1.183	1.583	2.050	2.500	3.167	6.033
118	0.417	0.717	1.067	1.750	2.717	3.717	5.550	9.933	12.267	18.600
119	0.333	0.350	0.483	0.733	1.150	1.667	2.233	3.067	5.533	12.017
120	0.333	0.567	0.700	0.883	1.317	1.517	1.950	2.467	5.717	14.150
121	0.500	0.900	1.500	2.450	3.600	5.283	9.883	12.700	21.800	31.000
122	0.467	0.617	0.767	0.950	1.167	1.483	1.967	2.633	3.883	5.833
123	0.233	0.467	0.600	0.733	0.867	1.100	1.383	1.750	2.200	3.117
124	0.283	0.383	0.517	0.667	0.800	1.700	2.750	6.983	13.100	31.750
125	0.250	0.367	0.483	0.817	1.650	2.800	7.083	10.233	15.700	28.000
126	0.133	0.183	0.300	0.367	0.500	0.650	0.717	12.733	4.900	24.517
127	0.300	0.467	0.567	1.467	2.667	4.017	6.933	11.200	16.933	30.800
128	0.350	0.400	0.483	0.517	0.600	1.267	2.583	6.800	23.500	29.783
129	0.167	0.267	0.350	0.500	0.650	0.850	1.933	13.183	7.250	26.117
130	0.250	0.333	0.467	0.567	0.800	1.250	11.750	5.950	24.167	32.000
131	0.417	0.483	0.667	1.633	2.333	6.333	11.183	15.883	23.650	30.700
132	0.583	0.833	1.200	1.700	2.317	4.317	8.050	11.233	16.567	28.367

Table C.14 Other Quantitative Parameters from Renogram for Developing BISRO and AISRO

Reno ID	Parameter								
	PrVC	PoVC	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	LT_{max}	$NORA_{post}$
1			2400	0.927				0.000	
2			7000	0.355				0.300	
3			6720	0.465				0.000	
4			3360	0.741				0.000	
5			12608	0.131				0.000	
6			9800	0.237				0.000	
7	14181	8341	18788	0.232				0.000	
8	25029	13596	9000	0.702				0.000	
9	13216	11128	6500	0.785				0.000	
10	16274	15016	12000	0.175				0.383	
11	18827	6209	12223	0.181	0.682	1.700	1.160	0.000	14056.07
12	8871	6366	14380	0.351	0.945	1.841	1.741	0.000	24035.26
13	40952	16865	10700	0.215	1.040	1.188	1.235	0.000	15650.53
14	21402	11135	12200	0.291	1.231	1.084	1.334	0.000	20959.45
15	45300	18000	10150	0.879	7.591	0.881	6.691	0.000	127401.78
16	34867	21317	10672	0.192	0.582	3.032	1.764	0.000	7622.58
17	16223	9630	1100	0.896	140.461	0.912	128.170	0.000	293681.03
18	20400	15700	900	0.115	7.073	1.393	9.857	0.000	7272.82
19	26598	18413	9447	0.796	0.026	0.943	0.025	2.750	487.48
20	42273	34702	6547	0.544	3.741	1.120	4.189	0.667	36706.83
21	31800	19600	16412	0.617	1.028	2.428	2.495	0.000	34161.19
22	26800	14900	16788	0.263	0.663	1.922	1.275	0.000	16165.93
23	12643	8849	18945	0.166	0.950	2.517	2.391	0.000	25183.21
24	16243	13104	17577	0.603	3.152	1.236	3.897	0.000	72886.27
25	20914	12572	14953	0.347	1.426	1.636	2.332	0.000	38729.72
26	20917	14795	18487	0.182	0.521	1.685	0.878	0.000	14808.89
27	81598	56580	3772	0.985	8.010	1.004	8.040	0.000	43535.79
28	31343	26072	2925	0.671	4.869	1.026	4.998	0.000	16483.13
29	31300	17400	13195	0.812	4.282	1.080	4.623	0.000	101244.97
30	10900	6500	14078	0.232	1.115	1.299	1.449	0.100	24266.23
31	76100	20900	550	0.728	66.531	1.445	96.149	4.217	45392.33
32			350	0.886	154.934	1.004	155.534	0.000	61747.99
33	14064	9262	800	0.649	23.016	1.445	33.248	0.000	38620.53
34	26585	10157	550	0.987	71.091	1.498	106.476	0.000	81514.81
35	12922	11527	1900	0.967	49.832	2.132	106.239	0.000	290756.71
36	14184	13268	1490	0.353	23.290	1.218	28.371	0.000	66258.00
37	31565	23109	11025	0.269	1.778	1.622	2.884	0.000	31788.32
38	18244	14854	11224	0.327	1.328	1.799	2.388	0.367	23499.26
39	22658	20243	12161	0.134	0.728	1.429	1.040	0.000	11836.02
40	22320	12559	11560	0.942	8.108	0.914	7.413	0.000	136910.65
41	18700	11800	15517	0.168	0.844	1.240	1.047	0.000	19131.35
42	41298	27585	23207	0.963	4.865	1.157	5.628	0.000	263066.39
43	66058	52480	850	0.207	14.791	1.664	24.605	3.517	15389.14
44	52500	43500	950	0.749	81.075	1.096	88.898	0.200	117774.59
45	18700	13700	12897	0.213	1.147	1.414	1.622	0.000	21428.70
46	18404	9942	17322	0.661	3.266	1.442	4.711	0.000	111546.08
47	11232	7129	26152	0.304	0.997	1.202	1.198	0.000	45777.80
48	67873	49448	25421	0.938	1.039	5.372	5.579	0.000	36785.20
49	11250	6796	920	0.576	25.000	2.961	74.022	0.000	34271.04

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter								
	PrVC	PoVC	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	LT_{max}	NORA _{post}
50	38365	23514	1010	0.272	17.228	1.799	30.990	0.150	20742.29
51	48617	38521	15679	0.103	0.415	1.677	0.695	0.383	9109.40
52	15936	12290	17624	0.668	1.186	3.641	4.318	0.150	46941.27
53	12078	11035	15527	0.166				0.083	
54	32185	30031	20556	0.864				0.000	
55	481796	19043	22094	0.135	0.419	1.518	0.637	0.000	14678.38
56	25040	16515	28037	0.943	1.649	3.746	6.177	0.083	127884.27
57	15539	12419	21557	0.167	0.471	2.617	1.233	0.000	12366.50
58	35625	32302	11936	0.783	1.515	3.532	5.351	0.000	25649.67
59			6627	0.253	1.739	1.121	1.950	0.000	16281.00
60			7721	0.266	1.718	1.069	1.837	1.450	18877.97
61	23414	21578	22251	0.454	1.039	1.366	1.419	1.033	43959.43
62	17354	12089	14693	0.177	1.011	1.228	1.242	0.000	22212.33
63	11463	7443	1190	0.211	17.011	1.119	19.040	0.000	25376.61
64	17884	13757	17063	0.164	0.736	1.777	1.308	1.650	15406.08
65	51798	33943	12621	0.228	0.935	1.585	1.482	0.800	14344.88
66	23716	13479	7811	0.736	3.943	1.627	6.414	0.000	35577.44
67	15726	12542	2600	0.145	10.610	1.497	15.884	0.000	32712.55
68	12628	6004	14336	0.952	9.854	0.917	9.033	0.000	220265.30
69	58559	16360	24583	0.566	2.135	1.259	2.687	2.750	105229.57
70	33003	30167	14819	0.962	10.434	0.853	8.901	2.583	294258.30
71	24047	15097	18597	0.756	3.622	1.363	4.935	0.000	97926.84
72	14904	12694	20666	0.500	2.105	1.207	2.540	0.000	72753.58
73	13200	8100	15168	0.187	0.903	1.365	1.233	0.000	16796.84
74	30600	20700	1010	0.169	9.844	1.851	18.222	0.000	12637.78
75	47600	41600	700	0.151	10.184	1.576	16.046	0.000	7766.80
76	12218	9004	1056	0.955	10.778	1.205	12.989	1.067	13116.49
77	16649	10310	2012	0.632	8.080	1.049	8.479	0.000	19511.06
78	16400	12400	32165	0.419	1.537	1.373	2.110	0.000	83171.25
79	40717	20974	700	0.159	9.709	1.655	16.071	0.000	8034.76
80	14735	8536	850	0.921	80.608	1.680	135.395	0.000	155389.70
81	17565	10881	700	0.383	33.591	1.632	54.807	0.150	27013.50
82	19041	4574	900	0.926	132.166	0.924	122.132	0.000	179155.84
83	35459	21740	990	0.333	38.910	1.262	49.108	0.000	42351.95
84	20493	12415	1290	0.144	9.527	1.297	12.353	0.000	14018.83
85	22015	12250	400	0.259	27.588	1.095	30.195	0.000	16876.87
86	42565	27233	1100	0.325	27.301	1.072	29.259	0.333	46412.43
87	39466	30836	800	0.340	23.804	25.300	602.245	0.000	21635.97
88	16289	11386	1000	0.323	16.515	1.516	25.040	0.000	21609.51
89	32463	32066	880	0.213	14.113	1.251	17.658	0.000	14937.09
90	17197	13891	1050	0.575	44.881	1.685	75.621	0.000	81889.98
91			14388	0.307	2.245	1.103	2.476	5.717	43104.59
92			15530	0.212				0.000	
93			14550	0.654				1.500	
94	232	246	1972	0.869	12.624	1.120	14.142	3.433	35192.83
95	27427	24490	3954	0.491	5.457	1.085	5.922	0.000	25015.00
96	68500	55400	8308	0.708	2.622	2.181	5.720	0.000	32745.62
97	61000	56500	5001	0.832	16.180	1.295	20.954	1.800	115079.41
98	68100	23000	20451	0.120	0.591	1.436	0.849	0.950	14509.82
99	173183	46231	14103	0.127	0.528	1.540	0.813	4.333	8754.59
100	91781	67362	6515	0.354	2.112	1.300	2.745	0.667	18970.42
101	17059	16257	17015	0.425	1.995	1.526	3.044	0.283	44884.93
102	79402	47125	17051	0.251	0.791	1.759	1.391	0.233	15619.83

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter								
	PrVC	PoVC	$n_{c,peak}$	$R_{20/max}$	$R_{post/max}$	$R_{pre/post}$	$R_{pre/max}$	LT_{max}	$NORA_{post}$
103	47518	21784	5407	0.949	5.337	1.358	7.249	0.283	64678.81
104	39196	28857	4679	0.524	2.680	1.254	3.361	6.583	19139.47
105	72982	61380	12303	0.183	0.488	2.103	1.026	0.733	7695.82
106	49154	42071	19912	0.579	0.822	3.579	2.941	0.550	31562.67
107	99687	83751	1150	0.197	26.232	1.094	28.698	0.000	53080.00
108			1350	0.164	11.183	1.593	17.813	6.700	20087.27
109	67910	77048	9933	0.168	1.278	1.174	1.500	5.550	19159.98
110	140987	154507	9468	0.806	6.483	1.189	7.708	17.867	92524.97
111	30328	30212	600	0.856	175.898	0.941	165.433	8.133	234848.31
112	14619	14243	630	0.595	66.779	1.168	78.022	0.000	61389.57
113	52882	36592	11094	0.180	0.730	1.630	1.190	1.183	9385.99
114	54437	54227	10258	0.453	2.018	1.478	2.983	18.583	24584.02
115	58562	39100	19547	0.378	2.128	1.144	2.435	10.867	60793.97
116	201855	94680	2356	0.649	3.822	1.357	5.186	12.067	15798.83
117	85700	93726	3855	0.445	2.674	1.615	4.319	3.100	13981.94
118	130599	112892	7888	0.282	1.572	1.323	2.079	8.600	17534.65
119	84453	77021	13009	0.945	6.818	1.231	8.394	2.017	192698.03
120	141830	26403	880	0.421	23.834	1.941	46.269	4.150	31153.81
121			720	0.173	11.856	1.726	20.465	21.000	11858.60
122	63867	18083	1050	0.179	10.363	1.614	16.729	0.000	13066.36
123	50100	30800	740	0.175	6.181	4.163	25.731	2.100	5204.10
124	129495	141265	1150	0.351	18.904	1.631	30.834	21.750	25936.50
125	131909	154620	1100	0.218	11.286	1.651	18.630	18.000	13814.29
126	13716	11382	580	0.280	21.121	1.797	37.957	14.517	16195.11
127	115086	68517	1010	0.372	26.963	1.563	42.144	20.800	36050.15
128	109919	118949	1300	0.236	23.720	1.280	30.358	19.783	41188.67
129	27888	24894	13593	0.139	0.838	1.431	1.198	16.117	11631.77
130	104791	80914	17402	0.313	1.843	1.012	1.865	22.000	48985.89
131	99260	105539	1320	0.824	63.448	1.190	75.520	20.700	117230.40
132	109200	88700	1300	0.162	10.685	1.238	13.228	18.367	15917.70

Table C.15 Coefficients a_2 , b , and c_2 Obtained from Curve Fitting of Renograms and Derived U/V_2

Reno ID	Parameter				Reno ID	Parameter			
	a_2	b	c_2	U/V_2		a_2	b	c_2	U/V_2
1	2.38	7.37E-03	6.19E-03	1.09E-03	43	109.40	1.88E-03	4.43E-05	7.26E-04
2	4.64	2.67E-03	1.40E-03	7.93E-04	44	4.22	2.74E-03	1.59E-03	7.43E-04
3	3.82	6.30E-03	3.58E-03	1.97E-03	45	3.09	5.97E-03	4.04E-03	1.54E-03
4	2.35	7.94E-03	6.57E-03	1.29E-03	46	4.30	4.84E-03	2.63E-03	1.46E-03
5	2.96	5.96E-03	4.20E-03	1.44E-03	47	2.72	7.82E-03	5.67E-03	1.88E-03
6	3.06	6.51E-03	4.40E-03	1.71E-03	48	3.53	3.37E-03	2.08E-03	9.57E-04
7	7.27	3.68E-03	1.04E-03	1.66E-03	49	3.52	5.76E-03	3.79E-03	1.41E-03
8	4.54	2.95E-03	1.46E-03	9.96E-04	50	2.26	8.26E-03	7.35E-03	8.51E-04
9	3.03	5.05E-03	3.30E-03	1.46E-03	51	1.86	1.13E-02	1.04E-02	1.02E-03
10	3.65	3.79E-03	2.37E-03	1.02E-03	52	3.20	7.88E-03	5.22E-03	2.09E-03
11	2.74	6.92E-03	5.04E-03	1.63E-03	53	3.21	4.77E-03	3.29E-03	1.14E-03
12	2.90	8.08E-03	5.95E-03	1.72E-03	54	4.51	3.35E-03	1.85E-03	9.36E-04
13	61.57	1.93E-03	8.23E-05	7.30E-04	55	2.34	7.97E-03	6.91E-03	9.83E-04
14	3.79	4.24E-03	2.53E-03	1.21E-03	56	2.62	5.71E-03	4.64E-03	9.16E-04
15	14.56	3.51E-03	6.17E-04	1.33E-03	57	2.46	7.35E-03	5.85E-03	1.38E-03
16	8.59	2.46E-03	7.26E-04	8.89E-04	58	2.84	4.74E-03	3.47E-03	1.05E-03
17	11.75	3.61E-03	7.31E-04	1.45E-03	59	43.04	3.26E-03	1.96E-04	1.25E-03
18	3.59	4.62E-03	2.72E-03	1.43E-03	60	100.70	1.80E-03	4.69E-05	6.89E-04
19	192.30	1.79E-03	2.32E-05	7.18E-04	61	1.97	8.84E-03	8.33E-03	5.29E-04
20	124.30	2.31E-03	4.64E-05	9.21E-04	62	5.68	5.32E-03	2.10E-03	2.01E-03
21	6.98	3.06E-03	1.10E-03	1.06E-03	63	3.91	6.07E-03	3.31E-03	2.00E-03
22	3.87	3.56E-03	2.16E-03	9.62E-04	64	6.90	2.76E-03	1.09E-03	8.56E-04
23	4.70	5.04E-03	2.32E-03	1.84E-03	65	2.22	4.91E-03	4.19E-03	7.05E-04
24	4.85	4.67E-03	2.21E-03	1.58E-03	66	2.56	7.32E-03	5.70E-03	1.44E-03
25	2.41	8.60E-03	7.07E-03	1.41E-03	67	3.11	3.61E-03	2.77E-03	6.25E-04
26	2.92	5.44E-03	3.71E-03	1.47E-03	68	3.80	4.83E-03	2.84E-03	1.41E-03
27	2.95	2.55E-03	1.93E-03	4.89E-04	69	73.32	1.88E-03	6.62E-05	7.25E-04
28	5.81	2.85E-03	1.22E-03	9.36E-04	70	205.60	2.63E-03	3.43E-05	9.77E-04
29	2.89	6.93E-03	5.58E-03	1.05E-03	71	4.34	5.07E-03	2.62E-03	1.65E-03
30	7.21	4.40E-03	1.34E-03	1.81E-03	72	5.72	4.03E-03	1.52E-03	1.60E-03
31	63.98	1.64E-03	6.46E-05	6.50E-04	73	4.29	4.95E-03	2.83E-03	1.35E-03
32	10.58	3.90E-03	8.87E-04	1.53E-03	74	2.66	5.75E-03	4.84E-03	7.48E-04
33	9.99	3.60E-03	8.31E-04	1.47E-03	75	3.05	4.25E-03	3.14E-03	8.63E-04
34	4.59	5.33E-03	2.61E-03	1.80E-03	76	2.91	3.10E-03	2.42E-03	5.36E-04
35	3.10	4.92E-03	3.26E-03	1.35E-03	77	2.39	5.45E-03	4.75E-03	6.36E-04
36	3.13	5.01E-03	3.33E-03	1.35E-03	78	4.05	4.08E-03	2.35E-03	1.17E-03
37	69.23	2.26E-03	8.65E-05	8.55E-04	79	1.96	7.29E-03	6.52E-03	8.25E-04
38	5.75	3.97E-03	1.62E-03	1.40E-03	80	4.75	4.59E-03	2.31E-03	1.44E-03
39	2.72	6.75E-03	5.12E-03	1.39E-03	81	3.09	6.47E-03	4.47E-03	1.59E-03
40	4.17	5.64E-03	3.00E-03	1.83E-03	82	2.49	8.60E-03	6.99E-03	1.44E-03
41	3.00	6.46E-03	4.54E-03	1.56E-03	83	2.74	6.18E-03	5.09E-03	8.80E-04
42	3.25	6.48E-03	4.12E-03	1.87E-03	84	2.45	8.45E-03	6.75E-03	1.56E-03

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter				Reno ID	Parameter			
	a_2	b	c_2	U/V_2		a_2	b	c_2	U/V_2
85	4.12	4.03E-03	2.39E-03	1.07E-03	109	2.17	3.43E-03	3.24E-03	1.83E-04
86	4.07	3.64E-03	2.28E-03	8.67E-04	110	1.46	5.80E-03	5.98E-03	-2.37E-04
87	2.99	6.04E-03	4.41E-03	1.28E-03	111	1.81	9.59E-03	9.60E-03	-1.21E-05
88	2.78	8.05E-03	5.81E-03	1.91E-03	112	2.02	1.21E-02	1.18E-02	3.32E-04
89	6.82	2.92E-03	1.14E-03	9.28E-04	113	1.90	1.40E-02	1.38E-02	1.80E-04
90	3.33	6.10E-03	4.04E-03	1.56E-03	114	1.52	1.70E-02	1.72E-02	-1.57E-04
91	3.92	1.80E-03	1.09E-03	4.79E-04	115	2.94	1.51E-03	1.15E-03	2.79E-04
92	2.28	5.48E-03	5.10E-03	3.43E-04	116	2.26	1.23E-03	1.14E-03	8.27E-05
93	2.59	3.41E-03	2.97E-03	3.72E-04	117	2.04	4.37E-03	4.31E-03	6.11E-05
94	2.95	2.20E-03	1.70E-03	3.89E-04	118	2.44	1.81E-03	1.56E-03	2.25E-04
95	2.34	5.40E-03	4.82E-03	5.31E-04	119	2.26	4.26E-03	3.96E-03	2.75E-04
96	2.99	3.92E-03	3.18E-03	5.52E-04	120	1.85	5.71E-03	5.70E-03	4.33E-06
97	3.42	2.21E-03	1.58E-03	4.50E-04	121	1.37	2.64E-03	2.84E-03	-2.87E-04
98	2.56	4.21E-03	3.63E-03	4.89E-04	122	2.42	3.99E-03	3.62E-03	3.25E-04
99	6.54	1.30E-03	5.02E-04	4.37E-04	123	1.83	8.16E-03	7.97E-03	2.10E-04
100	2.39	4.27E-03	3.92E-03	3.05E-04	124	1.58	7.24E-03	7.38E-03	-1.67E-04
101	1.97	8.61E-03	8.34E-03	2.70E-04	125	1.42	6.02E-03	6.22E-03	-2.81E-04
102	2.26	4.25E-03	3.78E-03	4.38E-04	126	1.80	1.33E-02	1.32E-02	7.80E-05
103	2.21	4.82E-03	4.47E-03	3.29E-04	127	1.39	4.24E-03	4.45E-03	-3.00E-04
104	2.32	1.77E-03	1.61E-03	1.53E-04	128	1.55	8.53E-03	8.66E-03	-1.73E-04
105	2.45	3.48E-03	3.15E-03	2.86E-04	129	1.60	1.10E-02	1.11E-02	-1.12E-04
106	2.54	4.34E-03	3.76E-03	4.88E-04	130	1.40	1.13E-02	1.15E-02	-1.98E-04
107	2.20	4.61E-03	4.34E-03	2.58E-04	131	1.12	6.25E-03	6.58E-03	-5.70E-04
108	1.83	2.85E-03	2.87E-03	-1.20E-05	132	1.45	3.11E-03	3.30E-03	-2.62E-04

Table C.16 Derived Basic MeanCV and MedianCV

Ren o ID	Parameter		Ren o ID	Parameter		Ren o ID	Parameter	
	MeanCV	MedianCV		MeanCV	MedianCV		MeanCV	MedianCV
	25	25		25	25		25	25
1	0.807	0.903	45	0.417	0.312	89	0.426	0.367
2	0.499	0.382	46	0.736	0.749	90	0.700	0.630
3	0.661	0.669	47	0.597	0.554	91	0.506	0.388
4	0.772	0.795	48	0.873	0.932	92	0.507	0.430
5	0.344	0.198	49	0.738	0.740	93	0.734	0.778
6	0.439	0.357	50	0.537	0.461	94	0.835	0.861
7	0.424	0.309	51	0.364	0.343	95	0.634	0.569
8	0.801	0.825	52	0.721	0.767	96	0.774	0.720
9	0.809	0.834	53	0.438	0.297	97	0.752	0.757
10	0.384	0.274	54	0.721	0.790	98	0.345	0.208
11	0.397	0.294	55	0.441	0.449	99	0.333	0.192
12	0.565	0.586	56	0.795	0.901	100	0.650	0.688
13	0.422	0.347	57	0.382	0.254	101	0.574	0.542
14	0.549	0.615	58	0.821	0.847	102	0.413	0.325
15	0.838	0.883	59	0.438	0.310	103	0.806	0.911
16	0.388	0.276	60	0.443	0.305	104	0.710	0.671
17	0.797	0.859	61	0.663	0.679	105	0.441	0.382
18	0.366	0.243	62	0.449	0.396	106	0.700	0.724
19	0.787	0.818	63	0.415	0.292	107	0.587	0.641
20	0.704	0.627	64	0.373	0.263	108	0.398	0.254
21	0.719	0.785	65	0.403	0.251	109	0.399	0.278
22	0.496	0.397	66	0.755	0.753	110	0.835	0.900
23	0.481	0.407	67	0.353	0.233	111	0.691	0.729
24	0.760	0.819	68	0.841	0.897	112	0.742	0.770
25	0.622	0.639	69	0.703	0.739	113	0.463	0.343
26	0.441	0.337	70	0.800	0.839	114	0.637	0.581
27	0.894	0.943	71	0.830	0.856	115	0.596	0.539
28	0.757	0.752	72	0.676	0.664	116	0.734	0.722
29	0.811	0.845	73	0.411	0.303	117	0.643	0.619
30	0.431	0.289	74	0.434	0.274	118	0.510	0.341
31	0.803	0.780	75	0.338	0.213	119	0.767	0.827
32	0.826	0.843	76	0.827	0.835	120	0.511	0.423
33	0.703	0.751	77	0.771	0.779	121	0.444	0.278
34	0.793	0.866	78	0.560	0.519	122	0.394	0.260
35	0.757	0.863	79	0.436	0.335	123	0.408	0.268
36	0.611	0.615	80	0.767	0.825	124	0.587	0.542
37	0.552	0.447	81	0.560	0.452	125	0.385	0.249
38	0.579	0.470	82	0.830	0.861	126	0.541	0.394
39	0.366	0.248	83	0.456	0.367	127	0.631	0.572
40	0.893	0.942	84	0.333	0.220	128	0.461	0.334
41	0.420	0.293	85	0.500	0.434	129	0.342	0.248
42	0.784	0.839	86	0.600	0.551	130	0.622	0.644
43	0.412	0.307	87	0.528	0.449	131	0.822	0.823
44	0.812	0.840	88	0.562	0.550	132	0.404	0.312

Table C.17 Derived Variants of MeanCV

Reno ID	Parameter									
	Mean CV ₁₀	Mean CV ₂₀	Mean CV ₃₀	Mean CV ₄₀	Mean CV ₅₀	Mean CV ₆₀	Mean CV ₇₀	Mean CV ₈₀	Mean CV ₉₀	Mean CV ₁₀₀
1	0.659	0.787	0.835	0.860	0.876	0.888	0.898	0.906	0.913	0.919
2	0.706	0.563	0.445	0.359	0.297	0.252	0.218	0.191	0.170	0.153
3	0.757	0.720	0.596	0.489	0.407	0.345	0.298	0.262	0.233	0.210
4	0.665	0.772	0.733	0.660	0.586	0.520	0.464	0.416	0.376	0.342
5	0.618	0.400	0.279	0.211	0.169	0.141	0.121	0.106	0.094	0.085
6	0.664	0.508	0.390	0.309	0.253	0.213	0.184	0.161	0.143	0.129
7	0.670	0.493	0.366	0.284	0.230	0.192	0.165	0.144	0.128	0.116
8	0.841	0.827	0.768	0.705	0.647	0.594	0.546	0.504	0.467	0.433
9	0.803	0.832	0.775	0.708	0.644	0.586	0.535	0.490	0.450	0.415
10	0.633	0.438	0.315	0.241	0.194	0.162	0.139	0.122	0.108	0.097
11	0.613	0.457	0.329	0.251	0.201	0.168	0.144	0.126	0.112	0.101
12	0.701	0.628	0.500	0.401	0.329	0.277	0.238	0.209	0.186	0.167
13	0.637	0.482	0.360	0.280	0.227	0.190	0.163	0.143	0.127	0.114
14	0.744	0.627	0.492	0.392	0.322	0.271	0.233	0.205	0.182	0.164
15	0.756	0.831	0.825	0.800	0.769	0.736	0.704	0.673	0.644	0.616
16	0.629	0.447	0.327	0.252	0.203	0.170	0.146	0.128	0.114	0.102
17	0.668	0.763	0.826	0.870	0.896	0.913	0.926	0.935	0.942	0.948
18	0.647	0.438	0.314	0.240	0.193	0.161	0.138	0.121	0.107	0.097
19	0.704	0.797	0.762	0.701	0.637	0.579	0.526	0.480	0.439	0.404
20	0.796	0.745	0.659	0.580	0.513	0.456	0.408	0.367	0.333	0.304
21	0.731	0.765	0.654	0.539	0.447	0.377	0.325	0.285	0.254	0.228
22	0.725	0.571	0.432	0.338	0.274	0.230	0.197	0.173	0.153	0.138
23	0.762	0.573	0.412	0.313	0.251	0.210	0.180	0.157	0.140	0.126
24	0.853	0.811	0.706	0.610	0.529	0.462	0.408	0.364	0.328	0.297
25	0.753	0.706	0.567	0.453	0.370	0.311	0.267	0.234	0.208	0.187
26	0.707	0.525	0.376	0.286	0.229	0.191	0.164	0.143	0.127	0.115
27	0.830	0.872	0.889	0.898	0.905	0.911	0.916	0.920	0.925	0.929
28	0.843	0.797	0.736	0.678	0.626	0.578	0.535	0.497	0.463	0.432
29	0.745	0.821	0.765	0.686	0.610	0.543	0.486	0.437	0.396	0.361
30	0.666	0.501	0.370	0.287	0.231	0.194	0.166	0.145	0.129	0.116
31	0.847	0.832	0.800	0.767	0.734	0.702	0.672	0.643	0.616	0.591
32	0.751	0.800	0.837	0.872	0.898	0.915	0.927	0.936	0.943	0.949
33	0.676	0.734	0.643	0.538	0.450	0.382	0.330	0.290	0.258	0.232
34	0.588	0.754	0.780	0.758	0.719	0.675	0.631	0.589	0.551	0.515
35	0.498	0.698	0.784	0.820	0.833	0.834	0.829	0.819	0.808	0.795
36	0.727	0.690	0.554	0.440	0.359	0.301	0.258	0.226	0.201	0.181
37	0.769	0.649	0.495	0.386	0.313	0.262	0.224	0.196	0.175	0.157
38	0.761	0.653	0.516	0.413	0.340	0.286	0.247	0.216	0.192	0.173
39	0.631	0.425	0.298	0.226	0.181	0.151	0.129	0.113	0.101	0.091
40	0.808	0.887	0.901	0.900	0.893	0.883	0.872	0.859	0.847	0.834
41	0.688	0.484	0.345	0.262	0.211	0.176	0.151	0.132	0.117	0.105
42	0.607	0.754	0.778	0.762	0.732	0.698	0.663	0.629	0.596	0.565
43	0.659	0.486	0.366	0.287	0.233	0.196	0.168	0.147	0.131	0.118

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Mean CV ₁₀	Mean CV ₂₀	Mean CV ₃₀	Mean CV ₄₀	Mean CV ₅₀	Mean CV ₆₀	Mean CV ₇₀	Mean CV ₈₀	Mean CV ₉₀	Mean CV ₁₀₀
44	0.807	0.834	0.797	0.748	0.699	0.653	0.610	0.570	0.534	0.501
45	0.642	0.481	0.358	0.279	0.226	0.189	0.162	0.142	0.126	0.114
46	0.720	0.766	0.705	0.629	0.559	0.497	0.445	0.401	0.363	0.331
47	0.767	0.685	0.541	0.430	0.352	0.295	0.254	0.222	0.198	0.178
48	0.787	0.854	0.875	0.886	0.891	0.895	0.897	0.898	0.899	0.899
49	0.810	0.785	0.703	0.623	0.552	0.492	0.441	0.397	0.361	0.329
50	0.798	0.620	0.479	0.381	0.312	0.263	0.227	0.199	0.177	0.159
51	0.639	0.436	0.304	0.230	0.184	0.153	0.132	0.115	0.102	0.092
52	0.661	0.749	0.678	0.579	0.491	0.419	0.363	0.319	0.285	0.256
53	0.709	0.506	0.358	0.271	0.217	0.181	0.155	0.136	0.121	0.109
54	0.529	0.673	0.759	0.819	0.855	0.880	0.897	0.910	0.920	0.928
55	0.689	0.515	0.370	0.282	0.226	0.188	0.162	0.141	0.126	0.113
56	0.600	0.766	0.767	0.711	0.640	0.572	0.511	0.458	0.414	0.376
57	0.654	0.436	0.305	0.231	0.185	0.154	0.132	0.116	0.103	0.093
58	0.822	0.843	0.793	0.733	0.675	0.622	0.573	0.530	0.491	0.456
59	0.667	0.513	0.387	0.302	0.245	0.206	0.177	0.155	0.138	0.124
60	0.674	0.515	0.387	0.302	0.245	0.205	0.176	0.154	0.137	0.124
61	0.766	0.734	0.593	0.473	0.386	0.324	0.278	0.244	0.217	0.195
62	0.716	0.533	0.386	0.295	0.237	0.198	0.170	0.148	0.132	0.119
63	0.676	0.501	0.375	0.293	0.237	0.199	0.171	0.150	0.133	0.120
64	0.643	0.427	0.299	0.227	0.182	0.152	0.130	0.114	0.101	0.091
65	0.661	0.470	0.343	0.264	0.213	0.178	0.153	0.134	0.119	0.107
66	0.771	0.772	0.745	0.713	0.680	0.648	0.618	0.590	0.563	0.538
67	0.614	0.412	0.292	0.222	0.178	0.149	0.128	0.112	0.099	0.089
68	0.730	0.809	0.860	0.895	0.916	0.930	0.940	0.948	0.953	0.958
69	0.712	0.754	0.650	0.538	0.448	0.379	0.327	0.286	0.255	0.229
70	0.659	0.756	0.824	0.868	0.895	0.912	0.925	0.934	0.941	0.947
71	0.835	0.854	0.805	0.748	0.691	0.639	0.592	0.549	0.510	0.476
72	0.772	0.740	0.620	0.513	0.429	0.366	0.317	0.279	0.249	0.224
73	0.660	0.474	0.346	0.267	0.215	0.180	0.154	0.135	0.120	0.108
74	0.717	0.514	0.371	0.284	0.228	0.190	0.163	0.143	0.127	0.114
75	0.594	0.402	0.287	0.220	0.177	0.147	0.126	0.111	0.098	0.088
76	0.824	0.834	0.826	0.814	0.800	0.786	0.771	0.757	0.743	0.729
77	0.815	0.798	0.754	0.708	0.664	0.622	0.584	0.549	0.517	0.487
78	0.709	0.628	0.506	0.410	0.339	0.287	0.247	0.217	0.193	0.174
79	0.725	0.520	0.379	0.291	0.235	0.196	0.168	0.147	0.131	0.118
80	0.607	0.723	0.800	0.850	0.880	0.900	0.914	0.925	0.933	0.940
81	0.750	0.628	0.517	0.430	0.364	0.313	0.273	0.241	0.216	0.195
82	0.732	0.803	0.852	0.889	0.911	0.926	0.936	0.944	0.951	0.956
83	0.643	0.528	0.432	0.359	0.303	0.260	0.227	0.201	0.179	0.162
84	0.594	0.378	0.263	0.199	0.159	0.133	0.114	0.100	0.088	0.080
85	0.732	0.582	0.448	0.354	0.289	0.243	0.209	0.183	0.163	0.147
86	0.795	0.684	0.537	0.428	0.350	0.295	0.254	0.222	0.198	0.178
87	0.731	0.593	0.476	0.388	0.324	0.276	0.239	0.211	0.188	0.169
88	0.754	0.630	0.509	0.416	0.348	0.296	0.257	0.226	0.202	0.182
89	0.654	0.491	0.371	0.292	0.238	0.200	0.172	0.151	0.134	0.121

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Mean CV ₁₀	Mean CV ₂₀	Mean CV ₃₀	Mean CV ₄₀	Mean CV ₅₀	Mean CV ₆₀	Mean CV ₇₀	Mean CV ₈₀	Mean CV ₉₀	Mean CV ₁₀₀
90	0.752	0.747	0.686	0.621	0.561	0.508	0.462	0.421	0.386	0.356
91	0.709	0.587	0.464	0.374	0.309	0.261	0.225	0.198	0.176	0.159
92	0.770	0.598	0.434	0.331	0.265	0.221	0.190	0.166	0.148	0.133
93	0.712	0.770	0.673	0.562	0.470	0.399	0.344	0.302	0.269	0.242
94	0.759	0.812	0.845	0.875	0.900	0.916	0.928	0.937	0.944	0.950
95	0.754	0.691	0.615	0.547	0.488	0.437	0.395	0.358	0.327	0.299
96	0.799	0.803	0.754	0.698	0.645	0.595	0.551	0.511	0.474	0.442
97	0.680	0.738	0.780	0.821	0.856	0.880	0.897	0.910	0.920	0.928
98	0.625	0.400	0.275	0.207	0.166	0.138	0.119	0.104	0.092	0.083
99	0.608	0.395	0.275	0.208	0.166	0.139	0.119	0.104	0.093	0.083
100	0.827	0.746	0.590	0.469	0.383	0.322	0.277	0.242	0.215	0.194
101	0.699	0.641	0.554	0.477	0.414	0.362	0.320	0.285	0.257	0.233
102	0.655	0.483	0.361	0.282	0.229	0.192	0.165	0.144	0.128	0.116
103	0.606	0.769	0.810	0.811	0.796	0.774	0.749	0.723	0.697	0.672
104	0.823	0.775	0.664	0.565	0.484	0.420	0.368	0.327	0.293	0.265
105	0.700	0.516	0.378	0.291	0.235	0.196	0.168	0.147	0.131	0.118
106	0.713	0.756	0.652	0.540	0.449	0.380	0.327	0.287	0.255	0.230
107	0.796	0.701	0.540	0.421	0.340	0.284	0.244	0.213	0.190	0.171
108	0.671	0.464	0.330	0.251	0.201	0.168	0.144	0.126	0.112	0.101
109	0.651	0.475	0.341	0.260	0.209	0.174	0.149	0.130	0.116	0.104
110	0.806	0.854	0.818	0.766	0.712	0.662	0.615	0.573	0.534	0.499
111	0.544	0.646	0.735	0.801	0.841	0.867	0.886	0.900	0.912	0.920
112	0.813	0.785	0.703	0.623	0.552	0.492	0.441	0.398	0.361	0.330
113	0.759	0.548	0.398	0.305	0.246	0.205	0.176	0.154	0.137	0.123
114	0.815	0.704	0.584	0.488	0.414	0.356	0.310	0.274	0.245	0.222
115	0.770	0.667	0.542	0.444	0.370	0.315	0.273	0.240	0.214	0.193
116	0.770	0.773	0.691	0.605	0.531	0.468	0.416	0.372	0.336	0.305
117	0.777	0.707	0.610	0.526	0.456	0.400	0.353	0.315	0.284	0.258
118	0.746	0.590	0.446	0.349	0.283	0.237	0.204	0.178	0.158	0.143
119	0.583	0.720	0.802	0.852	0.881	0.901	0.915	0.926	0.934	0.941
120	0.667	0.582	0.493	0.419	0.361	0.314	0.276	0.246	0.221	0.200
121	0.728	0.524	0.377	0.288	0.232	0.193	0.166	0.145	0.129	0.116
122	0.662	0.465	0.337	0.259	0.209	0.174	0.149	0.131	0.116	0.105
123	0.665	0.485	0.363	0.283	0.230	0.193	0.166	0.145	0.129	0.116
124	0.804	0.663	0.533	0.435	0.363	0.309	0.268	0.235	0.210	0.189
125	0.634	0.456	0.337	0.262	0.212	0.178	0.153	0.134	0.119	0.107
126	0.785	0.631	0.482	0.378	0.308	0.258	0.222	0.194	0.173	0.155
127	0.833	0.716	0.568	0.456	0.376	0.317	0.273	0.240	0.213	0.192
128	0.717	0.539	0.405	0.316	0.257	0.215	0.185	0.162	0.144	0.130
129	0.598	0.400	0.284	0.216	0.174	0.145	0.124	0.109	0.097	0.087
130	0.818	0.713	0.555	0.437	0.356	0.298	0.256	0.224	0.199	0.179
131	0.810	0.835	0.799	0.754	0.708	0.664	0.623	0.585	0.550	0.518
132	0.680	0.478	0.345	0.265	0.213	0.178	0.153	0.134	0.119	0.107

Table C.18 Derived Variants of MedianCV

Reno ID	Parameter									
	Median CV ₁₀	Median CV ₂₀	Median CV ₃₀	Median CV ₄₀	Median CV ₅₀	Median CV ₆₀	Median CV ₇₀	Median CV ₈₀	Median CV ₉₀	Median CV ₁₀₀
1	0.753	0.891	0.918	0.926	0.930	0.933	0.936	0.939	0.942	0.945
2	0.739	0.549	0.395	0.282	0.199	0.141	0.099	0.070	0.049	0.035
3	0.890	0.757	0.595	0.442	0.318	0.224	0.156	0.108	0.075	0.051
4	0.761	0.857	0.772	0.675	0.578	0.486	0.405	0.334	0.274	0.224
5	0.641	0.339	0.158	0.071	0.032	0.014	0.006	0.003	0.001	0.001
6	0.690	0.485	0.329	0.221	0.147	0.098	0.065	0.043	0.029	0.019
7	0.705	0.468	0.288	0.173	0.103	0.061	0.036	0.021	0.013	0.007
8	0.935	0.857	0.776	0.699	0.627	0.563	0.505	0.452	0.405	0.362
9	0.940	0.882	0.794	0.707	0.626	0.553	0.487	0.428	0.377	0.330
10	0.658	0.396	0.219	0.119	0.064	0.034	0.018	0.010	0.005	0.003
11	0.665	0.453	0.260	0.133	0.064	0.030	0.014	0.006	0.003	0.001
12	0.801	0.653	0.483	0.336	0.225	0.148	0.096	0.062	0.040	0.025
13	0.679	0.468	0.294	0.179	0.108	0.064	0.038	0.023	0.013	0.008
14	0.821	0.639	0.455	0.310	0.207	0.137	0.090	0.059	0.039	0.025
15	0.876	0.902	0.862	0.820	0.779	0.739	0.700	0.663	0.628	0.594
16	0.654	0.411	0.242	0.140	0.080	0.046	0.026	0.015	0.008	0.005
17	0.750	0.813	0.858	0.904	0.953	1.000	1.000	1.000	1.000	1.000
18	0.664	0.382	0.208	0.112	0.060	0.032	0.017	0.009	0.005	0.002
19	0.812	0.875	0.799	0.715	0.632	0.554	0.484	0.421	0.365	0.316
20	0.873	0.764	0.654	0.556	0.470	0.397	0.335	0.282	0.237	0.199
21	0.853	0.822	0.676	0.520	0.379	0.264	0.178	0.116	0.074	0.047
22	0.785	0.570	0.372	0.232	0.142	0.086	0.052	0.031	0.019	0.011
23	0.831	0.572	0.329	0.167	0.079	0.035	0.016	0.007	0.003	0.001
24	0.973	0.845	0.705	0.578	0.470	0.381	0.308	0.248	0.200	0.160
25	0.888	0.743	0.562	0.394	0.261	0.166	0.103	0.063	0.038	0.023
26	0.768	0.521	0.294	0.147	0.068	0.030	0.013	0.006	0.002	0.001
27	0.906	0.912	0.915	0.918	0.921	0.924	0.927	0.930	0.933	0.936
28	0.883	0.807	0.735	0.668	0.606	0.550	0.499	0.453	0.410	0.372
29	0.862	0.893	0.797	0.692	0.591	0.499	0.419	0.351	0.292	0.243
30	0.713	0.489	0.300	0.176	0.101	0.058	0.033	0.019	0.010	0.006
31	0.888	0.847	0.807	0.768	0.730	0.695	0.661	0.628	0.597	0.568
32	0.789	0.818	0.848	0.879	0.911	0.944	0.979	1.000	1.000	1.000
33	0.783	0.796	0.670	0.533	0.403	0.292	0.204	0.139	0.093	0.061
34	0.658	0.888	0.852	0.801	0.744	0.686	0.628	0.573	0.522	0.474
35	0.547	0.800	0.910	0.924	0.908	0.891	0.873	0.854	0.835	0.816
36	0.866	0.729	0.553	0.386	0.252	0.156	0.093	0.054	0.031	0.017
37	0.863	0.669	0.457	0.287	0.171	0.098	0.056	0.031	0.018	0.010
38	0.847	0.670	0.484	0.334	0.225	0.150	0.100	0.066	0.043	0.029
39	0.665	0.385	0.189	0.087	0.039	0.017	0.008	0.003	0.002	0.001
40	0.928	0.961	0.946	0.931	0.915	0.899	0.884	0.868	0.853	0.838
41	0.731	0.457	0.244	0.122	0.060	0.029	0.014	0.007	0.003	0.002
42	0.686	0.880	0.844	0.802	0.756	0.710	0.665	0.621	0.580	0.540
43	0.680	0.454	0.293	0.187	0.119	0.075	0.048	0.030	0.019	0.012

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Median CV ₁₀	Median CV ₂₀	Median CV ₃₀	Median CV ₄₀	Median CV ₅₀	Median CV ₆₀	Median CV ₇₀	Median CV ₈₀	Median CV ₉₀	Median CV ₁₀₀
44	0.936	0.881	0.817	0.754	0.693	0.637	0.585	0.536	0.492	0.451
45	0.680	0.462	0.290	0.177	0.106	0.064	0.038	0.023	0.014	0.008
46	0.840	0.823	0.728	0.628	0.535	0.452	0.380	0.319	0.267	0.223
47	0.878	0.713	0.521	0.355	0.231	0.147	0.092	0.057	0.035	0.022
48	0.893	0.920	0.919	0.918	0.917	0.916	0.915	0.914	0.913	0.912
49	0.917	0.816	0.706	0.604	0.514	0.436	0.368	0.311	0.263	0.222
50	0.837	0.599	0.411	0.279	0.188	0.126	0.084	0.056	0.038	0.025
51	0.680	0.406	0.197	0.086	0.036	0.015	0.006	0.002	0.001	0.000
52	0.758	0.823	0.712	0.585	0.461	0.349	0.256	0.183	0.128	0.088
53	0.762	0.491	0.259	0.121	0.053	0.022	0.009	0.004	0.002	0.001
54	0.597	0.750	0.819	0.875	0.931	0.990	1.000	1.000	1.000	1.000
55	0.749	0.512	0.293	0.149	0.071	0.032	0.015	0.006	0.003	0.001
56	0.669	0.896	0.829	0.746	0.655	0.564	0.477	0.397	0.327	0.266
57	0.686	0.388	0.188	0.086	0.038	0.017	0.008	0.003	0.001	0.001
58	0.957	0.889	0.811	0.734	0.662	0.596	0.535	0.481	0.431	0.387
59	0.712	0.503	0.325	0.203	0.125	0.077	0.047	0.029	0.017	0.011
60	0.719	0.503	0.322	0.200	0.122	0.075	0.045	0.027	0.017	0.010
61	0.911	0.777	0.595	0.420	0.277	0.174	0.105	0.062	0.036	0.020
62	0.773	0.524	0.304	0.162	0.083	0.042	0.021	0.010	0.005	0.003
63	0.707	0.473	0.300	0.187	0.116	0.071	0.044	0.027	0.016	0.010
64	0.673	0.377	0.183	0.085	0.039	0.018	0.008	0.004	0.002	0.001
65	0.690	0.434	0.254	0.145	0.082	0.046	0.026	0.015	0.008	0.005
66	0.837	0.797	0.756	0.716	0.678	0.642	0.607	0.574	0.543	0.513
67	0.637	0.362	0.187	0.094	0.047	0.023	0.011	0.006	0.003	0.001
68	0.810	0.853	0.888	0.924	0.962	1.000	1.000	1.000	1.000	1.000
69	0.828	0.813	0.674	0.525	0.387	0.274	0.187	0.124	0.080	0.051
70	0.737	0.802	0.853	0.906	0.963	1.000	1.000	1.000	1.000	1.000
71	0.964	0.898	0.822	0.749	0.680	0.616	0.557	0.504	0.455	0.411
72	0.908	0.778	0.619	0.470	0.347	0.252	0.182	0.130	0.093	0.066
73	0.692	0.443	0.261	0.150	0.085	0.048	0.027	0.015	0.009	0.005
74	0.761	0.488	0.275	0.147	0.077	0.040	0.021	0.011	0.006	0.003
75	0.611	0.351	0.190	0.101	0.053	0.028	0.015	0.008	0.004	0.002
76	0.872	0.855	0.838	0.821	0.805	0.789	0.772	0.757	0.741	0.726
77	0.875	0.818	0.760	0.706	0.654	0.606	0.561	0.520	0.481	0.445
78	0.798	0.649	0.485	0.347	0.243	0.168	0.115	0.079	0.054	0.037
79	0.762	0.486	0.283	0.161	0.090	0.050	0.028	0.015	0.009	0.005
80	0.688	0.784	0.840	0.895	0.955	1.000	1.000	1.000	1.000	1.000
81	0.786	0.621	0.482	0.372	0.285	0.218	0.167	0.128	0.097	0.074
82	0.803	0.840	0.875	0.911	0.949	0.988	1.000	1.000	1.000	1.000
83	0.663	0.517	0.399	0.306	0.234	0.178	0.136	0.104	0.079	0.060
84	0.604	0.304	0.141	0.065	0.029	0.013	0.006	0.003	0.001	0.001
85	0.786	0.577	0.392	0.258	0.168	0.109	0.070	0.045	0.029	0.019
86	0.889	0.704	0.504	0.342	0.226	0.147	0.095	0.061	0.039	0.025
87	0.765	0.581	0.431	0.317	0.232	0.169	0.124	0.090	0.065	0.048
88	0.807	0.630	0.471	0.347	0.255	0.186	0.135	0.098	0.071	0.052
89	0.681	0.465	0.305	0.197	0.127	0.081	0.052	0.033	0.021	0.013

Appendix C: Quantitative Parameters Derived from Renogram Samples

Reno ID	Parameter									
	Median CV ₁₀	Median CV ₂₀	Median CV ₃₀	Median CV ₄₀	Median CV ₅₀	Median CV ₆₀	Median CV ₇₀	Median CV ₈₀	Median CV ₉₀	Median CV ₁₀₀
90	0.858	0.781	0.694	0.612	0.538	0.471	0.412	0.360	0.314	0.274
91	0.766	0.589	0.424	0.298	0.207	0.143	0.099	0.068	0.047	0.032
92	0.847	0.605	0.364	0.193	0.094	0.043	0.019	0.008	0.004	0.002
93	0.824	0.834	0.700	0.555	0.418	0.302	0.211	0.143	0.095	0.062
94	0.818	0.842	0.865	0.888	0.913	0.938	0.963	0.990	1.000	1.000
95	0.797	0.698	0.606	0.524	0.453	0.390	0.336	0.289	0.249	0.214
96	0.905	0.839	0.766	0.696	0.631	0.571	0.517	0.467	0.421	0.380
97	0.731	0.763	0.796	0.830	0.865	0.903	0.941	0.982	1.000	1.000
98	0.655	0.342	0.146	0.058	0.022	0.009	0.003	0.001	0.000	0.000
99	0.632	0.337	0.157	0.070	0.031	0.014	0.006	0.003	0.001	0.000
100	0.959	0.782	0.574	0.391	0.254	0.160	0.099	0.061	0.037	0.023
101	0.768	0.657	0.544	0.446	0.363	0.295	0.239	0.194	0.156	0.126
102	0.681	0.453	0.288	0.180	0.112	0.069	0.043	0.026	0.016	0.010
103	0.682	0.896	0.894	0.864	0.831	0.797	0.763	0.730	0.697	0.666
104	0.936	0.805	0.659	0.527	0.417	0.328	0.257	0.201	0.157	0.122
105	0.746	0.497	0.296	0.169	0.094	0.052	0.029	0.016	0.009	0.005
106	0.830	0.815	0.676	0.526	0.388	0.274	0.187	0.124	0.081	0.052
107	0.915	0.732	0.516	0.329	0.194	0.109	0.059	0.031	0.016	0.008
108	0.709	0.429	0.225	0.112	0.055	0.026	0.013	0.006	0.003	0.001
109	0.700	0.464	0.259	0.132	0.065	0.031	0.015	0.007	0.003	0.002
110	0.939	0.912	0.844	0.774	0.707	0.645	0.587	0.534	0.485	0.441
111	0.603	0.678	0.748	0.825	0.910	1.000	1.000	1.000	1.000	1.000
112	0.917	0.815	0.705	0.603	0.513	0.436	0.369	0.312	0.264	0.223
113	0.805	0.522	0.299	0.164	0.089	0.047	0.025	0.013	0.007	0.004
114	0.876	0.709	0.555	0.429	0.330	0.253	0.194	0.148	0.113	0.086
115	0.846	0.679	0.513	0.378	0.275	0.199	0.143	0.103	0.074	0.053
116	0.907	0.816	0.701	0.590	0.490	0.405	0.334	0.274	0.225	0.184
117	0.846	0.721	0.597	0.490	0.400	0.326	0.265	0.215	0.175	0.142
118	0.809	0.591	0.387	0.241	0.147	0.088	0.053	0.032	0.019	0.011
119	0.661	0.797	0.859	0.913	0.969	1.000	1.000	1.000	1.000	1.000
120	0.707	0.584	0.473	0.380	0.305	0.244	0.195	0.155	0.124	0.099
121	0.776	0.501	0.281	0.148	0.076	0.039	0.020	0.010	0.005	0.003
122	0.690	0.426	0.243	0.136	0.075	0.041	0.023	0.012	0.007	0.004
123	0.685	0.450	0.285	0.178	0.111	0.069	0.043	0.027	0.016	0.010
124	0.854	0.659	0.489	0.359	0.261	0.190	0.137	0.099	0.072	0.052
125	0.652	0.418	0.257	0.157	0.095	0.057	0.034	0.021	0.012	0.007
126	0.855	0.634	0.425	0.271	0.170	0.105	0.065	0.040	0.024	0.015
127	0.927	0.734	0.534	0.372	0.254	0.171	0.115	0.077	0.051	0.034
128	0.755	0.516	0.330	0.207	0.129	0.080	0.049	0.030	0.019	0.011
129	0.612	0.343	0.181	0.094	0.048	0.025	0.013	0.007	0.003	0.002
130	0.930	0.741	0.527	0.346	0.217	0.132	0.079	0.047	0.028	0.016
131	0.931	0.878	0.819	0.760	0.704	0.651	0.602	0.556	0.513	0.473
132	0.711	0.438	0.248	0.136	0.074	0.040	0.022	0.012	0.006	0.003