UNIVERSITY OF LIVERPOOL

Intelligent System for the Personalised Management and Treatment of Hydrocephalus

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor in Philosophy

by

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Abstract

Hydrocephalus is a neurological disease that manifests itself in an elevated fluid pressure within the brain, and if left untreated, may be fatal. The percentage of people suffering from hydrocephalus is increasing rapidly, but treatment is often less than satisfactory. Currently hydrocephalus is treated using shunt implants, which consist of a mechanical valve and tubes that regulate the pressure of cerebrospinal fluid (CSF) by draining excess fluid into the abdomen.

It is desirable to have a hydrocephalus shunting valve that responds dynamically to the changing needs of the patient, opening and closing according to a dynamic physiological pattern, rather than simply to the hydrostatic pressure across the valve. Such a valve would by necessity be mechatronic, electronically controlled by software.

This work proposes an intelligent system that would upgrade the current mechanical shunt systems to an intelligent level, autonomously managing high ICP hydrocephalus to give the patient real-time monitoring and managing, autonomously treating hydrocephalus (controlled arrest of hydrocephalus) to give patient real-time therapy, and personalising the management and treatment by incorporating the patient feedback and ICP readings in the therapy. The best approach that could provide these features is a multi-agent paradigm.

A model of the intracranial hydrodynamics for a high ICP hydrocephalus patient is developed, in order to interactively investigate the influence of varying the shunting system parameters on the intracranial hydrodynamics. Furthermore, different valve types are modelled and their performance are investigated based on a novel multi-dimensional Figure of Merit (FoM), that is specially developed to evaluate the management and treatment of hydrocephalus.

An algorithm is proposed to help in developing a valve schedule that dynamically changes based on each patient's intracranial pressure data and the derived FoM, thus providing the physician with an easy tool that facilitates the use of the mechatronic valve.

Different parameters that characterise the mechatronic valve behaviour are identified and investigated for better understanding of the effect of mechatronic shunting management and treatment on the intracranial hydrodynamics of high ICP hydrocephalus patients,. Furthermore, to optimise the gain of such an investigation, the relations among valve parameters, schedule parameters and initial ICP values were modelled.

A new technique is introduced to determine the actual degree of shunt dependence. In addition, three novel enhancements are investigated to actively establish shunt independence (controlled arrest of hydrocephalus). The change in the intracranial hydrodynamics as a result of weaning process is mathematically modelled and simulated to provide an interactive environment for testing the above enhancements. The aggregation of the above work has provided an infrastructure for developing the personalised shunting system based on a multiagent approach. Belief, Desire, and Intention (BDI) and Blackboard architectures are implemented. The design of an intelligent system for the personalised management and treatment of hydrocephalus is then accomplished. The intelligent software of the system is implemented using a Java-based interpreter for an extended version of AgentSpeak called Jason.

With such a system, the hospitalisation periods and patient suffering and inconvenience are reduced, the quality of treatment is improved and better understanding of intracranial hydrodynamics may be established thanks to the valuable resource of ICP data.

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Abbreviations

ABP	Arterial Blood Pressure
ASTM	American Society for Testing and Materials
BDI	Belief Desire Intention
CSF	Cerebro Spinal Fluid
CT	Computerised Tomography
FoM	Figure of Merit
FV	Flow Velocity
ICP	Intra Cranial Pressure
IM	Intracranial Media
MR	Magnetic Resonance
PPLL	Pulsed Phase Lock Loop
RAM	Random Access Memory
RF	Radio Frequency

This thesis is dedicated to my husband Abdel Rahman who has been a great source of motivation and inspiration, and supported me all the way since the beginning of my studies. Also, this thesis is dedicated to my daughters Hala, Sara and Mira who offered me unconditional love and support throughout the course of this thesis.

Chapter 1

Introduction

Personalised healthcare is primarily concerned with the devolution of patient monitoring and treatment from the hospital to the home. Solutions, such as body-worn sensors for clinical and healthcare monitoring, improve the quality of life by offering patients greater independence. Such solutions can go beyond monitoring to active intervention and treatment based on sensory measurement and patient feedback, effectively taking healthcare out of the hospital environment. Such personalised healthcare solutions play an increasingly important role in delivering high quality and cost-effective healthcare.

The realisation of truly autonomous systems for the personalised treatment of physiological disorders such as hydrocephalus is closer than ever. This thesis is concerned with the possibilities that current technology offers in the area of intelligent and personalised hydrocephalus implants that seek to autonomously manage the symptoms and treat the causes in a manner specifically tuned to the individual high pressure hydrocephalus patient.

1.1 Overview

The human brain is surrounded by a fluid called the cerebrospinal fluid (CSF), that protects it from physical injury, keeps its tissue moist and transports the products of metabolism. This fluid is constantly produced in the choroid plexus and drained through granulations near the sagittal sinus. If the rate of CSF absorption or drainage is consistently less than the rate of production (for a variety of reasons), the ventricles expand causing the brain to become compressed, leading to the disorder known as hydrocephalus [9], whereby for non-infants, an increase in intracranial pressure (ICP), leading to the occlusion of circulation and cell death. This can lead to one of the three types of hydrocephalus; communicating, non-communicating and normal pressure hydrocephalus [1]. Hydrocephalus is thus the accumulation of CSF in the brain due to the malfunction of the natural drainage system.

Nowadays shunts are used to treat hydrocephalus patients, whereby excess fluid is drained to keep the ICP within the physiological ranges. The shunts consist of a mechanical valve that passively opens and closes according to the differential pressure across it.

The passive operation of these shunts causes many problems. Over-drainage and under-drainage are typical drawbacks of such shunts, where CSF is either drained in excess or less than needed, which could cause dramatic effects on the patient such as brain damage. Difficulty in diagnosing over/under-drainage can make treatment of this complication particularly frustrating for patients and their families. The only explained reason for such drawbacks is the inability of such shunts to autonomously respond to the dynamic environment [75].

Beside their documented drawbacks [10, 94], these shunts do not suit many of hydrocephalus patients. This can be realised from the considerable high shunt revision and failure rates: between 30% and 40% of all CSF shunts placed in pediatric patients fail within the first year [3, 84, 85, 115] and it is not uncommon for patients to have multiple shunt revisions within their lifetime.

Nevertheless, most patients seem to be only partially shunt-dependent, *i.e.* their natural drainage system is partially malfunctioning; the degree of shunt-dependence may range from 1% to 100% thus draining 30-50% of CSF production might be sufficient to keep the ICP within physiological ranges and only a few need full drainage [10]. Thus current shunts do not help in revealing the degree of dependence, but on the contrary, they tend to encourage the patients to become fully shunt dependent. Research has shown however, that in some cases, the shunt dependence could be reduced to less than 1% [10] which even allows for the eventual removal of the shunt [10, 107].

Furthermore, shunt designers have recently modified the goals of the shunt to have the option of (re-)establishing shunt independence step by step [10]. This means that the statement of Hemmer "once a shunt, always a shunt" may no longer be true, as the next generation of shunts should be able to achieve a controlled arrest of hydrocephalus in the long run.

Another thing that current shunts lack is personalised treatment. Despite the fact that the intracranial hydrodynamics not only differs between different patients, but also for the same patient (this varies with age, health, lifestyle and other factors), current shunts are used for all hydrocephalus patients without taking into consideration any of these factors. Whereas, considering factors such as degree of shunt dependance and treatment satisfaction in the treatment delivered by shunts would have provided the patient with the treatment that suits him/her [75].

One of the recent advances in the treatment of hydrocephalus is the invention of a mechatronic valve in 2005 [74]. The desirability of such a valve lies in the potential of having shunts that not only control hydrocephalus symptoms but also seek to treat it. In contrast to current valves, such a valve could be regulated based on a schedule not on the differential pressure across the valve. This valve would allow improved adaptation to the situation existing in a hydrocephalus patient [73]. Prudent exploitation of such a mechatronic valve would open the door for different shunting systems to be developed.

The effectiveness of such a valve is highly dependent on selecting an appropriate valve schedule that delivers personal dynamic treatment for every individual patient. Providing such a schedule is likely to be one of the obstacles facing the implementation of the mechatronic valve. The software that controls the valve can be a simple schedule or advanced intelligent software that monitors and analyses the ICP and responds accordingly.

An intelligent system (*e.g.* [75]) can be used to autonomously regulate the mechatronic valve according to certain valve schedule and update it based on the intracranial pressure when such data is available. In such a system, ICP readings and other sensory inputs such as patient feedback, would help in tuning the treatment and enabling the intervention of the medical practitioner to update and manually adapt the schedule.

The use of such a valve in a closed loop shunting system in conjunction with a pressure sensor would allow the valve to respond to actual intracranial pressure in the ventricles instead of a pressure at distance from the ventricles (differential pressure across the valve) as the case in current valves. Also the mechatronic valve could add a new option for hydrocephalus shunts that is aiming to treat hydrocephalus not only managing it. This could be achieved by establishing either a controlled arrest of the shunt dependence or at least reducing the shunt dependence.

1.2 Problem Definition

Shunt insertion explicitly changes the CSF dynamics in patients with hydrocephalus, causing many to improve clinically. However, the relationship between a changed hydrodynamic state and improved clinical performance is not fully known. Therefore, further research in this area is an important challenge, where development of better methods for assessment of CSF dynamic parameters as well as studies on relationships between CSF dynamics and outcome after shunting is targeted.

All reasons mentioned in previous section and more urged the need for a shunt that responds to the dynamic needs of the patient and at the same time that can achieve a progressive removal of the shunt. In order to have such shunt, a mechatronic valve which is electrically controlled by software is needed.

To address the lack of personalised treatment, the difficulty in diagnosing shunt faults, the high rate of shunt revisions, the high shunt dependence, and the lack of full understanding of shunt effect on the intracranial hydrodynamics, a personalised hydrocephalus shunting system needs to be developed. By having such system, the hospitalisation periods and patient suffering and inconvenience are reduced, the quality of treatment is improved and better understanding of intracranial hydrodynamics is established thanks to the valuable resource of ICP data.

This research proposes a personalised intelligent system that would autonomously manage and treat hydrocephalus by controlling the CSF flow and enabling the patient to play a vital role in the treatment process. This objective would be achieved by implementing a multi-agent approach to develop a system that would provide personalised, reactive, pro-active, goal-driven and distributed treatment for hydrocephalus. The short term goal of the intelligent system would be to maintain ICP within acceptable limits and eliminate symptoms. The long term goal, on the other hand, would be to reduce (if not eliminate) shunt dependence. Patients with high pressure hydrocephalus are specifically addressed in this research.

Intracranial hydrodynamics has been simulated for high pressure hydrocephalus conditions. Furthermore, three different valve types are simulated and their performance are compared based on a novel multi-dimensional figure of merit. A multi-dimensional Figure of Merit (FoM) has been derived to evaluate high pressure hydrocephalus management and treatment. The figure of merit incorporated six dimensions that cover some of the key factors of the high pressure hydrocephalus management and treatment evaluation. This allows for the interactive investigation of the influence of varying shunting system's parameters on the intracranial hydrodynamics.

An algorithm was proposed to help in developing a schedule for the mechatronic valve that dynamically change based on the patients' own intracranial pressure data and a novel figure of merit, thus providing the physician with an easy tool that facilitate the use of the mechatronic valve. The algorithm was implemented in software. Real ICP data for hydrocephalus patients (before shunting) were used to test this algorithm and the resulted schedules along with the resulted intracranial pressure data have illustrated the effectiveness of the algorithm in providing a schedule that maintain ICP within the normal limits.

Different parameters that characterise the mechatronic valve behaviour were identified and investigated to help in understanding the effect of using such type of valves on the intracranial hydrodynamics. As a result these parameters would facilitate the process of selecting a personalised schedule that respond to the patients' needs. To optimise the gain of such investigation, the relations among valve parameters, schedule parameters and initial ICP values were modelled. Such models would be valuable assets and considered as rules of thumb for an implanted shunting system that would autonomously modify the valve schedule based on these rules. As an outcome of this investigation, vital parameters were identified and used as an inputs for the schedule selection, modification and weaning processes.

Arresting shunt dependence (weaning) is the goal of the future shunts, therefore weaning was investigated. A new technique is introduced to determine the actual shunt dependence and then singling out shunt independence in an attempt of progressively shunt removing thus minimising the risks. In addition, three novel enhancements are investigated to actively establish shunt independence (controlled arrest of hydrocephalus). Where the change in the intracranial hydrodynamics as a result of weaning process was mathematically modelled and simulated to provide an interactive environment for testing the above enhancements.

Different architectures were used to design the Multi-agent system to find the best architecture that suits the application. BDI and Blackboard architectures were implemented. In which different types of agents are used. The design of an intelligent system for personalised management and treatment of hydrocephalus was accomplished. A systematic process (Prometheus methodology [80]) was used to design the agent system. The intelligent software of the system is implemented using a Java-based interpreter for an extended version of AgentSpeak called Jason [12].

1.3 Objectives

This research aims to design and build an intelligent system that would upgrade the current mechanical shunt systems to an intelligent level allowing them to:

- autonomously manage high pressure hydrocephalus symptoms,
- autonomously treat high pressure hydrocephalus (reduce shunt dependency) to give patient real-time therapy,
- personalise the management and treatment of the high pressure hydrocephalus through involving the patient's real-time feedback and ICP readings in the therapy.

1.4 Contribution

The original contribution of this research can be summarised as follows.

1. The novelty in this work is the idea of implementing multi-agent approach in managing an implantable shunting system that utilise real-time ICP readings in addition to patient input as a direct feedback to instantaneously and even autonomously manage the shunt. Thus enabling real-time reconfiguration of the shunt parameters based on the real-time feedback to manage the valve, capture actual shunt dependence and progressively reducing it.
2. Deriving a novel multi-dimensional figure of merit for evaluating the performance of hydrocephalus management and treatment. Its dimensions are useful whether interpreted individually or as an overall average.
3. Proposing an algorithm for selecting a personalised valve schedule that maintains ICP within the normal range and at the same time minimises the valve open duration in order to avoid developing shunt dependence.
4. Proposing a novel technique in capturing patient's actual shunt dependency and proposing enhancements on the shunt wean for mechatronic shunting systems. Thus, it enables progressive shunt removal.

5. Mathematically modelling the patient's adaptation and the corresponding change in the intracranial parameters as a result of weaning process. Such a model provides a dynamic environment for testing the weaning techniques.

1.5 List of Publications

The following publications have arisen as a direct result of the author's research.

1. L. Momani, W. Al-Nuaimy, M. Al-Jumaily and C. Mallucci. A Mechatronic Valve in the Management of Hydrocephalus: Methods and Performance, Medical and Biological Engineering and Computing Journal (under review)

2. L. Momani, A. Alkharabsheh, N. Al-Zubi, and W. Al-Nuaimy. Reduction of Mechatronic Shunt Dependence for Hydrocephalus Patients, in *4th Annual Symposium of the Benelux Chapter of the IEEE Eng Med Biol Soc. (EMBS)*, University of Twente, the Netherlands, Nov 2009.

3. L. Momani, A. Alkharabsheh, and W. Al-Nuaimy. Intelligent and Personalised Hydrocephalus Treatment and Management, in *Biomedical Engineering*, , Carlos Alexandre Barros de Mello (Ed.), 2009, ISBN: 978-953-307-013-1, INTECH, Available from: http://sciyo.com/articles/show/title/intelligent-and-personalised-hydrocephalus-treatment-and-management

4. L. Momani, A. Alkharabsheh, N. Al-Zubi, and W. Al-Nuaimy. Instantiating a Mechatronic Valve Schedule for a Hydrocephalus Shunt, in *Conf Proc IEEE Eng Med Biol Soc.*, Minnesota, USA, pp. 749-752, Sep 2009.

5. L. Momani, A. Alkharabsheh and W. Al-Nuaimy. Design of an Intelligent and Personalised Shunting System for Hydrocephalus, in *Proceedings of IEEE Eng Med Biol Soc.*, Vancouver, Canada, pp. 779-782, Aug 2008.

6. L. Momani, W. Al-Nuaimy, M. Al-Jumaily, C. Mallucci, A. Al-Kharabsheh and Y. Huang. Simulation of a Smart Hydrocephalus Shunting System, in *35th Annual Meeting of the International Society for Pediatric Neurosurgery*, Liverpool, UK, Sep 2007.

7. L. Momani, W. Al-Nuaimy, M. Al-Jumaily, C. Mallucci, A. Al-Kharabsheh and Y. Huang. Simulation of a "Blind" Mechatronic Valve for a Hydrocephalus Shunt, in *Hydrocephalus Workshop* - Rhodes, Greece, May 2007.

8. L. Momani and W. Al-Nuaimy. Electronic Shunt System for Hydrocephalus, in *Postgraduate Researchers in Science / Medicine (PRISM) Conference*, St Martin's College, Lancaster, UK, Jul 2006.

The following publications are the results of the research group work, where the author appears as a co-author,

1. A. Alkharabsheh, L. Momani, N. Al-Zubi, and W. Al-Nuaimy. A Real-Time Self diagnosis Method for a Hydrocephalus Shunting System, in *4th Annual Symposium of the Benelux Chapter of the IEEE Eng Med Biol Soc. (EMBS)*, University of Twente, The Netherlands, Nov 2009.

2. N. Al-Zubi, L. Momani, A. Alkharabsheh, and W. Al-Nuaimy. Multivariate Analysis of Intracranial Pressure (ICP) Signal Using Principal Component Analysis, in *Proceedings of the IEEE Eng Med Biol Soc.*, Minnesota, USA, pp. 4670-4673, Sep 2009.

3. A. Alkharabsheh, L. Momani, N. Al-Zubi, and W. Al-Nuaimy. A Bidirectional Wireless Management Protocol for Mechatronic Shunting System, in *4th International Conference on Broadband Communication, Information Technology and Biomedical Applications*, Wroclaw, Jul 2009.

4. N. Al-Zubi, A. Alkharabsheh, L. Momani and W. Al-Nuaimy. Distributed Multi-agent Approach for Hydrocephalus treatment and management Using Electronic Shunting, in *HEALTHINF*, Portugal, pp. 503-507, Jan 2009.

5. A. Alkharabsheh, L. Momani, N. Al-Zubi and W. Al-Nuaimy. An Intelligent Implantable Wireless Shunting System for Hydrocephalus Patients, in *Proceedings of 13th International Conference on Biomedical Engineering*, Suntec, Singapore, pp. 210-215, Dec 2008.

6. M. Al-Jumaily, W. Al-Nuaimy, C. Mallucci, L. Momani and Y. Huang. Wireless Programmable CSF Shunt System for the Treatment of Hydrocephalus, in *34th Annual Meeting of the International Society for Pediatric Neurosurgery*, Taipei, Taiwan, Sep 2006.

1.6 Thesis Structure

This thesis consists of eight chapters. In Chapter 2, hydrocephalus is reviewed, along with current treatment approaches and their drawbacks. Chapter 3 introduces the proposed intelligent shunting system. In Chapter 4, the intracranial model is outlined for a patient with hydrocephalus. In addition, a novel FoM to qualify the management and treatment delivered by a shunt driven by a mechatronic valve is introduced. Treatment personalisation is investigated in Chapter 5. In Chapter 6, different approaches to capture and reduce shunt dependence are proposed. In Chapter 7, all the findings from previous chapters are embedded into a multi-agent system that performs the proposed tasks autonomously. This is followed by discussion of the main conclusions and outlining future prospects in the final chapter.

Chapter 2

Hydrocephalus

Hydrocephalus is neurological disorder caused by blockage or reabsorption difficulty that upsets the natural balance of production and absorption of cerebrospinal fluid (CSF) in the brain, resulting in a build-up of the fluid in the ventricles of the brain, which leads to an increase in the intracranial pressure (ICP). To understand this disorder, a brief background is explored in this chapter about hydrocephalus. It also introduces intracranial pressure and a short review about current methods used in ICP measurements. Current treatment is explored, where shunt components, types, related patents and drawbacks are viewed. Shunts in the literature and recent advances are summerised, followed by a discussion of the main conclusions.

2.1 Intracranial Pressure

Intracranial Pressure (ICP) is defined as the pressure within the cranium and thus in the brain tissue and cerebrospinal fluid (CSF); this pressure is exerted on the brain's intracranial blood circulation vessels. ICP is a dynamic phenomenon constantly fluctuating in response to activities such as exercise, coughing, straining, arterial pulsation, and respiratory cycle. ICP is measured in millimeters of mercury (mmHg) and, at rest, is normally 7-15 mmHg for a supine adult, and becomes negative (averaging -10 mmHg) in the vertical position [103]. Changes in ICP are attributed to volume changes in one or more of the constituents contained in the cranium.

Elevated intracranial pressure (ICP) is a major factor associated with morbidity and mortality in patients with neurological disorders such as head trauma, cerebral stroke, hydrocephalus and brain tumor. The care of hydrocephalus patients can be improved with continuous ICP monitoring. Conventional methods for ICP monitoring are currently limited to patients with severe neurological conditions because of their invasive nature. This is because invasive intracranial pressure (ICP) sensors are potentially dangerous for neurosurgical patients.

2.1.1 Measurement of ICP

The assessment of intracranial pressure (ICP) generally requires invasive methods, nevertheless, there are considerable work on developing non invasive methods. Below are some examples on these methods. Schmidt *et al.* [95] have introduced a mathematical model allowed the non-invasive estimation of ICP (nICP) from arterial blood pressure (ABP) and blood flow velocity (FV). Selected hemodynamic parameters, calculated from the cerebral blood FV and the ABP curves, were used to express the relationship between ABP input and ICP output by linear transformation rules. In several clinical studies the accuracy and possible benefits of this method of non-invasive ICP (nICP) assessment were investigated and the results demonstrated that the nICP assessment model constitutes a reliable method to monitor ICP and may therefore provide various useful clinical applications.

Shimazu *et al.* have developed a new cerebrospinal fluid shunt device to measure intracranial pressure (ICP) indirectly by the collapsing method. Indirect ICP is determined from the pressure fluctuation corresponding to a sudden collapse and reformation of thin silicone rubber domes [99, 100].

Furthermore, changes in dural thickness were measured to estimate intracranial pressure. The dural thickness on magnetic resonance imaging with contrast enhancement was compared by Kuchiwaki *et al.* [58] in a hydrocephalic patient before and after shunt operation. Dural thickness measurements obtained ultrasonographically in the supine position were similar to direct measurements of thickness. Tranquart *et al.* [111] have also investigated a transcranial Doppler sonography of the changes in cerebral blood flow velocity in basilar artery in hydrocephalic adult rabbits related to the modification of intracranial pressure (ICP). Their study suggested that in patients with hydrocephalus, transcranial doppler ultrasound could be used as a non-invasive method of measuring ICP.

Some researchers paid excessive effort on developing an implantable miniature ICP sensors. Some of these sensors are piezoresistive pressure sensors on the basis of semiconductor microcrystals and laser recrystallised SOI layers (*e.g.* [31]). Other researchers, like Zoghi and Rastergar proposed the development of an implantable miniature intracranial pressure (ICP) sensor based on a transmissive optical approach [27, 125, 126]. They have investigated two transport mechanisms, one using a fiber optic approach and the other a telemetric approach, each of which would be used depending on the desired application of intracranial pressure monitoring. Zoghi [126] introduced a novel optical fiber intracranial pressure (ICP) sensor system that uses a reflective fiber optic displacement sensor to measure hydrostatic pressure. This sensing technique exhibits a high degree of sensitivity and linearity, and is less susceptible to environmental perturbations than current intensity modulating techniques. Experimental results are presented for measurements taken with and without an anti-reflection (AR) coating on the fiber tip facing the sensor mirror. These measurements indicate an improved dynamic range of operation for this sensor.

The evolution of innovative new acoustic signal processing algorithms and digital signal processing architectures, is implemented in different medical electronics applications. Ultrasound techniques were also used for non-invasive measuring of ICP directly or indirectly through measuring other parameters such as monitoring density variation of the brain (*e.g.* [35, 88, 102, 104]). Pulsed phase lock loop technique (PPLL) was used in measuring ICP in different ways. Some examples are illustrated below.

An ultrasonic device have been developed to monitor intracranial pressure waveforms non-invasively using pulsed phase lock loop (PPLL) technique. The PPLL device records slight movement of the skull associated with ICP pulsations. In conclusion, PPLL technology enables in vivo evaluation of ICP dynamics non-invasively in clinical settings [112].

Ragauskas *et al.* [83] have investigated the peculiarities of the ultrasound pulse propagation through human extra/intracranial media by mathematical simulation and to confirm the simulation results experimentally by proving the suitability of the ultrasonic time-of-flight measurement method for human intracranial media (IM) physiological non-invasive monitoring. They applied the models for developing of a new non-invasive sonographic intracranial pressure (ICP) monitor (Vittamed). And their study has shown the possibility of achieving clinically acceptable accuracy of the long term non-invasive ICP monitoring of head injured patients in intensive care units.

An innovative methods and technology was presented for non-invasive intracranial hemodynamics monitoring based on the measurement of brain parenchyma acoustic properties. The clinical investigation of new technology showed the similarity between the invasively recorded intracranial pressure (ICP) and non-invasively recorded intracranial blood volume pulse waves, slow waves and slow trends under intensive care unit conditions [89].

Telemtric non-invasive ICP measurement is of great benefit for patients with chronic hydrocephalus, and could also be implemented in fields where disposable telemetric sensors are needed. The measurement of intracranial pressure has become very popular, largely due to the increase in available microsystem components. -Flick had shown how a fully implantable stand-by device for measuring intracranial pressure and temperature under normal conditions can be implemented, consisting of a sensor element combined with a transcutaneous telemetric interface [37].

Wang *et al.* [118] have implemented a telemetry microsystem, including multiple sensors, integrated instrumentation and a wireless interface. They have employed a methodology akin to that for System-on-Chip microelectronics to design an integrated circuit instrument containing several "intellectual property" blocks that will enable convenient reuse of modules in future projects. Trials in animal cases were carried out to show that the transmitter was as effective as a conventional RF device whilst consuming less power. A microcontroller with embedded software and RAM was implemented to provide greater control and flexibility.

Lin *et al.* have introduced a new method for ICP non-invasive monitoring using near-infrared light is proposed. Both theoretical and experimental studies have shown that correlation analysis applied to ICP, cerebrospinal fluid (CSF) and near-infrared diffuse reflection light from the brain tissue provides a possibility for non-invasive ICP detection [60].

Fontanelle pressures correlated well with invasively determined cerebrospinal fluid (CSF) pressures in a group of neonates and infants with hydrocephalus. Pairaudeau *et al.* have developed a fontanometer based on the strain-gauge principle that can be zeroed *in vivo* and has the additional advantage of a fast response time and allows reliable measurements of spontaneous pulsations and induced changes in CSF pressure. Unlike previously reported devices, the accuracy of this transducer was shown to be independent of external forces [81].

2.2 Hydrocephalus

The human brain is surrounded by a fluid called the cerebrospinal fluid (CSF), that protects it from physical injury, keeps its tissue moist and transports the products of metabolism. This fluid is constantly produced in the parenchyma at rate of approximately 20ml.h^{-1} and drained through granulations near the sagittal sinus. Figure 2.1 illustrates the parts of the brain. In a healthy person, a balance exists between the production and resorption of cerebrospinal fluid. If the amount of CSF produced exceeds the amount absorbed (for a variety of reasons), the ventricles expand causing the brain to become compressed, leading to the disorder known as hydrocephalus [9], as shown in Figure 2.2, which might lead to the occlusion of circulation and cell death.

Hydrocephalus refers to a condition whereby the volume of the "water" (hydro) in the "head" (cephalus) continually increases. This can lead to one of the two types of hydrocephalus: communicating and noncommunicating [1]. This leads to an elevation of the pressure exerted by the cranium on the brain tissue, cerebrospinal fluid, and the brain's circulating blood volume, referred to as intracranial pressure (ICP), and manifests itself in symptoms such as headache, vomiting, nausea or

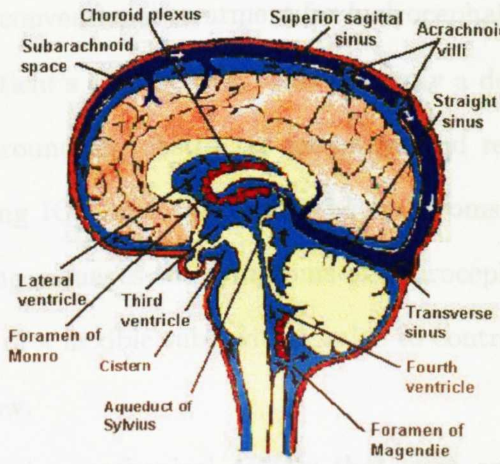


FIGURE 2.1: Brain parts [91].

coma. ICP is a dynamic phenomenon constantly fluctuating in response to activities such as exercise, coughing, straining, arterial pulsation, and respiratory cycle. Hydrocephalic patients may experience pressures of up to 120 mmHg. If left untreated, elevated ICP may lead to serious problems in the brain. There is no alternative in most cases to the implantation of a drainage system, known as a shunt.

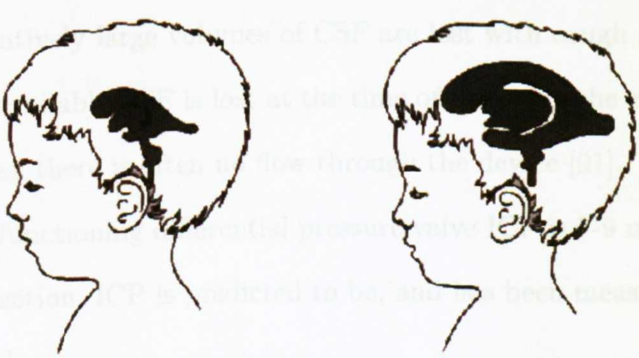


FIGURE 2.2: Schematic drawing of the ventricles in (a) normal and (b) hydrocephalus cases.

2.3 Current Treatment

Since the 1960s the conventional treatment for hydrocephalus is to insert a shunting device in the patient's CSF system. This is simply a device which diverts the accumulated CSF around the obstructed pathways and returns it to the bloodstream, thus reducing ICP, and alleviating the symptoms of hydrocephalus. In other words, shunting manages the symptoms of hydrocephalus but do not treat it. A shunt consists of a flexible tube with a valve to control the rate of drainage and prevent back-flow.

These valves are passive mechanical devices that open and close depending on either the differential pressure or flow. Although there are various valve technologies and approaches, they all essentially do the same thing, which is to attempt to passively control the symptoms of hydrocephalus by assisting the body's natural drainage system. The valve is usually chosen by the surgeon on the grounds of experience, cost and personal preference. Low pressure standard and flow regulated valves are frequently used to treat hydrocephalus. In the low pressure standard valve, the CSF that flows through the shunt is irrevocably lost with each ICP pulsation. Relatively large volumes of CSF are lost with cough and straining and essentially all available CSF is lost at the time of assuming the erect position. For much of the day there is often no flow through the device [91].

In a normally functioning differential pressure valve ICP is 7-9 mmHg recumbent. In the erect position, ICP is predicted to be, and has been measured to be -1.5 to -2.2 mmHg [91].

2.3.1 Shunt Principle

Most shunts currently available respond to differences in pressure between the ventricle cavity which they drain and the cavity to which the shunt drains to (so called pressure differential valved shunts). There are many standard differential pressure valved shunts currently available with only slight differences between them. There is no evidence that any one company's design is better than another [78].

2.3.2 Shunt Components

A shunt consists of at least 3 elements: proximal catheter, valve and distal catheter. Proximal catheter is the upper end of the shunt that is placed in the brain's fluid chambers. Distal catheter is the ending point of the shunt that drains CSF to one of several body cavities and shunts are categorised based on the distal cavity: right atrium of the heart via the jugular vein (ventriculoatrial shunt), abdominal cavity (ventriculopleural shunt), peritoneal cavity (ventriculoperitoneal shunt), chest cavity and recently major blood sinuses [33] (*e.g.*, the sagittal sinus) draining blood from the brain. Nowadays, peritoneal cavity is the most common distal site for shunt placement (ventriculoperitoneal shunt). It is a large cavity, more than capable of handling any amount of CSF delivered by the shunt in all but the most unusual cases. Valve is used to regulate the flow of the CSF between the proximal and distal catheters.

2.3.3 Valves for CSF Shunts

The current treatment of hydrocephalus relies on implantable shunts which employ passive, pressure operated, mechanical valves. These valves and their associated components must be selected by the surgeon so that the rate of flow through the shunt at the desired maximum pressure is in balance with the given rate of cerebrospinal fluid accumulation. Difficulties with the biomechanics and confounding by the changes in the condition of the patient with time lead to a high rate of complications in hydrocephalus shunting.

A valve opens and permits flow when a certain pressure level is exceeded. Below that pressure the valve is closed. The opening pressure refers to the pressure level at which the valve opens, whereas the closing pressure is defined as the pressure level when the valve closes during decrease of pressure. Silicone material is easy to deform, has a non-perfect elasticity and may have adhesive properties. The mechanical behavior of the material is the reason for differences between opening and closing pressures. The shape of the silicone material tends to adapt slowly to altered flow conditions. As a result there is a bad reproducibility (hysteresis) of flow-pressure relationship when comparing the curves resulting from a low to a high flow and reverse [71].

2.3.3.1 Valve Categories

Commercially available valves are categorised as low, medium, or high pressure, depending on their response to the pressure differential between upper and lower ends of the shunt. Theoretically, a low pressure shunt drains at pressure of 0 mmHg, a medium pressure one at 4.4 mmHg, and a high pressure one at 8.8 mmHg. However, while these figures may be roughly correct when the patient is recumbent, there is a complete change in the upright position. The result is the pressures within the head drop into the negative range as CSF is sucked out of the head by siphoning and over-drainage of the ventricles can occur. This is true regardless of which type of simple pressure differential valve is utilised. There is no physiological correlation between the type of valve, the intracranial pressure, and the outcome of surgery. Nor is there at this time any convincing evidence that one pressure setting is universally better than another [78].

2.3.3.2 Valve Types Used for Hydrocephalus

There are several different types of hydrocephalus valves depending on the mechanical principle and componenets.

- Ball and spring valve: The mechanical principle of this type of valve is a metallic spring exerting force on a ball which is located at a conical orifice that can be occluded by the ball. The ball used to be made of metal, but currently it is made of industrial corrundum (saphire or ruby). The hydrodynamic characteristics of this valve depend on tension and deformability of the spring on one hand and of the cone shape and diameter on the other hand. Because silicone rubber is not used in this valve, there are no problems like hysteresis and 'drift'. This valve incorporates an 'on/off' principle, leading to a high flow immediately after the opening of the valve which might bring an increased risk of overdrainage, *e.g.* Hakim valve [71].

- Diaphragm valves: The principle of this type is based on a mobile and flexible silicone membrane which moves in response to pressure differences, leading to a circular flow pattern. The hydrodynamics of this valve depend on elasticity, tension and thickness of the membrane as well as on shape and size of the orifice in the valve. There is a risk that the membrane may collapse at excessive pressure differences. Another problem is the non-linear increase in resistance of the membrane with enlargement of its surface which may lead to overdrainage. Because the valve is made of silicone, basic problems as hysteresis and drift may arise, *e.g.* PS medical, Pudenz and Accu-flo [71].

- Complex valves: A tight conical cylinder is inserted into a ring which is attached to a pressure-sensitive silicone membrane. The inner diameter of the ring is slightly larger than the outer diameter of the conical cylinder. The distance between cylinder and ring varies with the pressure, leaving more or less space for the passage of CSF. The system is vulnerable and sensitive to increased proximal pressure. The membrane is easily damaged, and the ring or cylinder may dislocate [71].

- Slit valves: These valves consist of a 'slit' in a silicone layer. The principle is based on memory properties of silicone: after deformation the material will resume its original shape, which may take a variable time in the range of seconds to days. There are two types of slit valves: proximal and distal slit valves. The proximal valves consist of either a side slit at the lower catheter-end, or they may have one or multiple slits at the upper end [71].

- Programmable (Adjustable) valve: These valves can be programmed to change the opening pressure of the valve non-invasively between a range of pressures. Adjustable hydrocephalus shunts are very popular in management of hydrocephalus. They are supposed to help in minimizing number of revisions. Drawback of almost all constructions is that they may be accidentally readjusted in relatively weak magnetic field (around 30-40 milli Tesla) [5].

Some of the commercially available valve types are summarised in in Appendix A (Table A.1).

2.3.3.3 Magnetic-Proof

It has been found that external household magnets can change the pressure settings of programmable shunt valves. Liu *et al.* have compared two popular, adjustable, shunt valves used to regulate the cerebrospinal fluid of hydrocephalus patients: the Codman Hakim Programmable Valve (CHPV), and the PS Medical STRATA

Valve. They measured the threshold magnetic fields required to change the settings of these two valves at different initial settings. Both types were susceptible to setting changes, with the actual threshold magnetic field strength needed depending on the valve setting and also having some valve variability. The magnetic fields required to increase the valve settings were similar for the two valves, but the fields required for reducing the settings were lower for the STRATA valve than for the CHPV [62].

The MR-compatibility of medical implants and devices becomes more and more important with the increasing number of high-field MR-scanners employed. Patients with hydrocephalus need frequent follow-up MR-examinations to assure correct functioning of a shunt. Lindner *et al.* have tested three types of gravitational valves: the Paedi GAV, the Dual Switch and the proGAV (Miethke Company, Berlin). In sum, there is strong evidence for maintenance of function of these valves after exposure to 3T [61].

As for the system being magnetic-proof to 1.5T or 3T, it has been proven that the existing shunt systems are not affected by 1.5T since it is the minimum recommended by the ASTM standards. There is also a study that shows that most of the valves used in the shunt systems are not affected by 3T. Except for the programmable valves, the study could not confirm they are 3T magnetic-proof [61, 62].

2.3.4 Shunts in Literature

Tremendous efforts are ongoing to develop comprehensive shunts that drain CSF and at the same time non-invasively monitor ICP. A novel cerebrospinal fluid (CSF) shunt system was reported for the hydrocephalus patients. The CSF shunt system consists of a micro telemetry pressure sensor, an electromagnetic micropump and a controller. The pressure sensor has a flexible p+ diaphragm and a planar copper coil that construct an LC resonant circuit. The cerebrospinal pressure is measured from the phase shift at the resonance frequency. The micropump consists of an actuator diaphragm and a pair of passive valves. Each device is fabricated by micromachining technology and tested to obtain the characteristic. The feasibility of the proposed shunt system is evaluated with the in vitro performance test [123].

Bosio had introduced two new solutions for cerebrospinal fluid valve shunts : the first based on the principle of multihole flow and the second - mechanically less complex - based on the action of elastic elements on a ball-cone valve in relation to constant pressure [14].

Kim *et al.* proposed implanting a micropump for cerebrospinal fluid shunt in hydrocephalus patients. The micropump consist of a corrugated parylene diaphragm and a set of nozzle and diffuser. The electromagnetic force drives the diaphragm. The static or dynamic characteristics of the fabricated devices have been obtained experimentally [53].

2.3.5 Relevant Patents

The following patents have the potential of adding new perspectives to the current treatment of hydrocephalus.

- Hydrocephalus valve

  In 2005, Meithke [74] claimed patent to a hydrocephalus valve with an electric actuating system. This valve would allow improved adaptation to the situation existing in a patient in the case of a hydrocephalus valve with an electric actuating system comprising a control system opening and closing the hydrocephalus valve. The valve would present new perspectives for diagnosis and therapy of hydrocephalus. He proposed to operate this valve without recourse to a pressure transducer. The device would be programmed by a physician, who determines at what time the shunt is open. The size of the device is similar to pacemakers and would be implanted in the chest of the patients. The advantages of the new device might be counterbalanced by the drawbacks like the big housing needed or the new risks [73].

- Intracranial monitoring and therapy delivery control device, system and method

  In 2001, Miesel *et al.* had invented an implantable medical device having an hermetically sealed enclosure housing electrical and electronic circuitry and a battery for powering such circuitry is connected to an intracranial lead or pigtail which measures or senses intracranial physiologic signals such as intracranial fluid pressure and/or temperature. The implantable medical device is preferably implanted subcutaneously beneath a patient's skin and telemeters stored data or real-time-sensed data to an external device which may be configured to combine barometric pressure data with intracranial pressure data to derive intracranial gauge pressure. The implantable medical device and its associated lead reduce the risk of intracranial infections [72].

- Pressure sensor controlled valve

  A sensor-valve was invented by Cosman in 1988. It is an element in a fluid shunting system such as used in hydrocephalus and controls the flow of fluid in the shunt system according to the difference in pressure at some point inside the valve and the pressure in a bodily region outside and near to the valve. This is accomplished by means of a flexible diaphragm portion of the valve which communicates with the shunt fluid pressure on one side and the bodily region pressure on the other, the pressure difference causing the diaphragm to move and thus change the degree of opening of the valve fluid passage aperture. This would, for example, enable maintaining the difference between ventricular fluid pressure and pressure at the brain's surface at some desired value in the situation of an implanted hydrocephalus shunt valve system [22].

2.4 Major Drawbacks of Current Shunts

Despite shunting developments, shunting can have complications, different types of shunts seemingly associated with different types of complications. Shunt complications can be very serious and become life threatening if not discovered and treated early. However, due to their passive mode of operation, shunt malfunctions are generally not detected before they manifest clinically. These can be divided into issues of under-drainage, over-drainage and infection. Over-drainage and under-drainage are typical drawbacks of such shunts, where CSF is either drained in excess or less than needed, which could cause dramatic effects on the patient such as brain damage. The common cause for these two drawbacks might be an inappropriate opening/closing of the valve in respect of the duration or the timing. In other words, valve open for too short/too long periods or it does not open/close at the right timing.

Under-drainage is usually due to blockage of the upper or lower tubes of the shunt by in-growing tissue, though it can also be caused by the shunt breaking or its parts becoming disconnected from each other. The rate of blockage can be as high as 20% in the first year after insertion, decreasing to approximately 5% per year [16]. And the clinical presentation of shunt blockage is usually dominated by signs of raised pressure as the brain fluid (CSF) builds up. As ICP is not readily measurable, interferences must be drawn from the symptoms presented.

Sometimes the symptoms come on quickly over hour or days, but occasionally they may develop over many weeks with intermittent headache, and tiredness, change in behaviour or deterioration in schoolwork. Diagnosing shunt blockage is not always straightforward. In fact, parents can be as successful at diagnosing shunt blockage as general practitioner and paediatrician. Whilst additional investigations such as CT scans, X-rays and a shunt taps may help, a definitive diagnosis is sometimes only possible through surgery [9].

In the case of over-drainage (siphoning effect), the shunt allows CSF to drain from the ventricles more quickly than it is produced, which may be induced by the siphoning effect of hydrostatic pressure created by elevation of the ventricular catheter with respect to the distal catheter, (*i.e.*, when the patient sits, stands, or is held erect). If this happens suddenly, then the ventricles in the brain collapse, tearing delicate blood vessels on the outside of the brain and causing a haemorrhage. This can be trivial or it can cause symptoms similar to those of a stroke. If the over-drainage is more gradual, the ventricles collapse gradually to become slit-like. This often interferes with shunt function causing the opposite problem, high CSF pressure, to reappear. The symptoms of over-drainage can be very similar to those of under-drainage though there are important differences.

Studies have shown that the siphoning effect is minimized by the anti-siphon device which closes when the pressure inside the unit becomes negative relative to ambient pressure, yet will reopen to allow the flow of cerebrospinal fluid to resume before the intraventricular pressure becomes excessive [47], but this does not always work. A 'programmable' or adjustable shunt is intended to allow adjustment of the working pressure of the valve without operation. But the adjustable valve is no less prone to over-drainage than any other and it cannot be used to treat this condition [16].

Difficulty in diagnosing over-/under-drainage can make treatment of this complication particularly frustrating for patients and their families. It may be necessary to monitor ICP, often over 24 hours. This can be done using an external pressure monitor in the scalp connected to a recorder. Early ICP monitoring is recommended when the clinician is unable to assess the neurological examination accurately. The main concerns are the risks of infection, bleeding, device accuracy and drift of measurement over time. Thus to avoid these risks, a research work is undergoing to develop implanted pressure sensors for short and long term monitoring interrogated by telemetry [46].

One of the obvious reasons for such drawbacks is the inability of such shunts to autonomously respond to the dynamic environment. Inaccuracies and long term drift are also considered among the drawbacks of such shunts. This is mainly due to the fact that these shunts are (typically, but not always) regulated according to the differential pressure across the valves, which differs from intracranial pressure in the brain.

Beside their documented drawbacks such as overflow, underflow, inaccuracy, and long-term-drift [10, 94], these shunts do not suit many of hydrocephalus patients this can be realised from the considerable high shunt revision and failure rates, *i.e.* between 30% and 40% of all cerebrospinal fluid (CSF) shunts placed in pediatric patients fail within 1 year [3, 84, 85, 115] and it is not uncommon for patients to have multiple shunt revisions within their lifetime.

Nevertheless, most patients seems to be only partially shunt-dependent, *i.e.* their natural drainage system is partially malfunctioning (blocked). The blockage degree varies and accordingly the patient's degree of shunt dependence can be varied. The degree of shunt-dependence may range from minimal to fully shunt dependent thus draining 30-50% of CSF production are sufficient to keep the ICP within physiological ranges. Only a few need full drainage [10]. Thus the current shunts do not help in revealing the degree of dependence, but on the contrary, they tend to encourage the patients to become fully shunt dependent. Whereas in some cases, the shunt dependence could be reduced to less than 1% [10] which even allows the eventual removal of the shunt [10, 107].

Furthermore, the shunt designers have recently modified the goals of the shunt to have the option of re-establishing shunt independence step by step [10]. This means that the statement of Hemmer "once a shunt, always a shunt" may no longer be true, as the next generation of shunts should be able to achieve a controlled arrest of hydrocephalus in the long run.

Another thing that current shunts lack is personalisation. Since they are used for all hydrocephalus patients without taking into consideration factors such as degree of shunt dependance, treatment satisfaction, that would provide the patient with the treatment that suits him [75].

One of the reasons that cause faults in the current shunts is the dynamic behaviour of intracranial hydrodynamics which not only differs within different patients, but also for the same patient this varies with age, health, lifestyle and other factors.

2.5 Recent Advances

In order to achieve such a system, a mechatronic valve is needed which is electrically controlled via software. In this shunting system, the patient could play a vital role in feeding back his/her dissatisfaction, *i.e.* due to symptoms, regarding the treatment.

The intervention of a mechatronic valve provides the opportunity for different shunting systems to be developed. This type of valve can be controlled by software that can vary in its complexity and intelligence. The controlling methods could vary from a simple program that lacks any intelligence to very sophisticated and intelligent program.

Despite ICP monitoring currently being an invasive procedure, patients with hydrocephalus may need repeated episodes of monitoring months or years apart. This is a result of problems arising in which ICP readings are needed for diagnosis. The invasive nature of ICP monitoring has motivated researchers, as a result, a telemetric implantable pressure sensor for short- and long-term monitoring of ICP with high accuracy is developed [46]. Such a sensor was mainly used for monitoring ICP wirelessly by the physician who could manually adjust the valve settings accordingly.

Recently, a group in Transonic Systems Incorporation has been developing a flowmetre for hydrocephalus patients. It consists of transcutaneously powered flow probe module integrated with standard shunt tubing exterior to the skull. This module will measure dynamic shunt volumetric flow by sending transit-time ultrasonic pulses through the tubing wall. This extra-luminar design ensures that transducers never contact CSF, and that the module can be integrated with existing shunt systems [28].

Such advancements have made developing a pesonalised hydrocephalus management and treatment achievable.

2.6 Conclusions

Reviewing hydrocephalus, current treatment and their drawbacks underscored the need for a shunt that responds to the dynamic needs of the patient while simultaneously bringing about a controlled arrest of the patient's shunt dependence.

The intervention of a mechatronic valve and an implantable pressure sensor could lead to the development of a new generation of 'smart' hydrocephalus shunts that provide feedback from intracranial pressure measurements to control flow through the valve. This shunting system would not only autonomously respond to the patient needs but also overcome the main drawbacks associated with current shunts. It is envisioned that in the new design the passive opening of the shunt valve will be replaced by direct pressure detection using a pressure sensor, a control module, and an electronically operated valve. With this design the surgeon could select diverse pressure/flow characteristics to match the individual patient, tune the device to accommodate changes in the patient, and monitor the ICP signal externally.

Chapter 3

Intelligent and Personalised Shunting[1]

Patients with hydrocephalus may need repeated episodes of ICP monitoring months or years apart. Since ICP monitoring is currently an invasive (and hence risky) process, this motivated researchers to develop a telemetric implantable pressure sensor for short- and long-term monitoring of ICP with high accuracy.

In this research, an electronic valve and an implanted pressure sensor are integrated into intelligent and personalised telemetric system that continuously and autonomously monitors the ICP, regulates the valve based on patient's ICP data and assesses its performance without the need for returning to physician every time this has been done. This would help the physician in maintaining the system and save both time and effort. Furthermore, it would service the patient 24 hours a day even while out of the hospital.

In this chapter, the intelligent and personalised shunts in the literature are briefly reviewed. Next, the proposed approach is introduced. The two main roles of proposed system are explained and illustrated through a walkthrough. Also the

[1]Part of this chapter has been published under the title "Intelligent and Personalised Hydrocephalus Treatment and Management", in *Biomedical Engineering*, , Carlos Alexandre Barros de Mello (Ed.), 2009, ISBN: 978-953-307-013-1, INTECH.

advantages and limitations of such a system are explored. This is followed by the conclusions of the chapter.

3.1 Intelligent and Personalised Shunts in the Literature

The idea of developing a personalised hydrocephalus shunting system as described above is novel since the only way personalised hydrocephalus treatment was handled in the literature is through implementing programmable hydrocephalus valves in which differential pressure settings of the valve can be varied according to the patient case and it is decided by the surgeon.

On the other hand, the idea of intelligent shunt or so called 'smart' shunt was evolving around developing an implantable pressure sensor with a transceiver that wirelessly conveys pressure readings to a physician, whom modifies the valve settings accordingly. Follows a brief summary of the related literature.

Zoghi and Rastergar [125] proposed the development of an implantable miniature intracranial pressure (ICP) sensor based on a transmissive optical approach. The proposed sensor will be composed of a pressure-sensing membrane, an optical transmitter and receiver, and a signal transport mechanism. They have investigated two transport mechanisms, one using a fiber optic approach and the other a telemetric approach, each of which would be used depending on the desired application of intracranial pressure monitoring [125, 126]. Once implanted, this sensor could not only be used to continuously monitor ICP but could also be used in the development of a new generation of 'smart' hydrocephalus shunts to provide feedback from intracranial pressure measurements to control flow through the valve. They envisioned that in the new design the passive opening of the shunt valve will be replaced by direct pressure detection using the proposed sensor, a control module, and an electronically operated valve. With this design the surgeon could select diverse pressure/flow characteristics to match the individual patient, to tune the device to accommodate changes in the patient, and to monitor the ICP signal externally [125].

Cote *et al.* [23] have designed, built and tested a nonlinear closed-loop control system with flat pressure-versus-flow characteristics that is aimed at regulating intracranial pressure (ICP) by adjusting the volume of cerebral spinal fluid (CSF). The control system design allows both the pressure setpoint and hysteresis to be adjusted to overcome the difficulties inherent in differential pressure-activated, fixed resistance, open-loop shunts.

Johannessen *et al.* [118] have implemented a telemetry microsystem, including multiple sensors, integrated instrumentation and a wireless interface. They have employed a methodology similar to that for System-on-Chip microelectronics to design an integrated circuit instrument containing several "intellectual property" blocks. The present system was optimised for low-power and included mixed-signal sensor circuits, a programmable digital system, a feedback clock control loop and RF circuits. A base station was built in order to retrieve the data from the microsystem in real-time. The base station was designed to be adaptive and timing tolerant since the microsystem design was simplified to reduce power consumption and size. Trials in animal carcasses were carried out to show that the transmitter was as effective as a conventional RF device whilst consuming less power .

A miniature telemetric pressure-measuring system was presented by Chatzandroulis *et al* [17]. The system uses passive telemetry to transfer power to the transponder and pressure data to the remote base unit. A novel capacitive-type pressure sensor based on an SiGeB diaphragm is used as a sensing element. The merits of combining a capacitive pressure sensor and passive telemetry lies in the inherent low-power consumption of the sensor and the continuous availability of power through induction. The pressure sensor is connected to an integrated interface circuit, which includes a capacitance to frequency converter and an internal voltage regulator to suppress supply voltage fluctuations on the transponder side. In addition, the sensor and accompanying interface circuit take up very little space so as to be suitable for implantation.

A wireless, externally powered, implantable device for monitoring of intracranial pressure has been developed by Manwaring *et al* [67]. The implantable device is based on low power microprocessor and small dimension pressure transducer conveniently packaged in a biofriendly material. An external interrogator powers and communicates with the subcutaneously implanted device. The developed intracranial pressure monitor system eliminates the need for the battery power supply, and thus avoids the hazards associated with potential leaking of the batteries. Another advantage of the system is its wireless mode of operation. By keeping the interrogator in the close proximity of the patient skull, for example in the patient's pillow, the system can be used for continuous monitoring of the intracranial pressure, even while the patient sleeps. A natural extension of the system is to connect the interrogator to a phone line or data network, the ultimate goal being to enable remote monitoring, logging, and analysis of the intracranial pressure.

Flick *et al.* [37] showed how a fully implantable stand-by device for measuring intracranial pressure and temperature under normal conditions can be implemented, consisting of a sensor element combined with a transcutaneous telemetric interface. One of the main points is automatic event recognition, used as a switch between the sampling rates in order to capture special signal component in an emergency situation. Therefore, a signal processing and waveform analysis is exigent, first to control the measured signal online on the portable unit, and second to process the data offline on the stationary unit.

3.2 Proposed Approach

An intelligent shunting system is proposed that would autonomously manage the CSF flow, personalise the management of CSF flow through involving real-time intracranial pressure readings and patient's feedback, and responding to them. It also would autonomously manage and personalise the treatment of hydrocephalus, thus providing treatment that is personalised, goal-driven and reactive as well as pro-active, which gradually reduce shunt dependence and progressively establish a controlled arrest of the shunt. In addition, it would be able to monitor performance of its components, thus minimising the shunt revisions, provide distant hydrocephalus service and clinical practice (*e.g.* telementoring), establish hydrocephalus database (*e.g.* computer based patient records) and exchange hydrocephalus management and treatment information (*e.g.* share the medical experience) by regularly reporting the patient's record to the physician.

All these qualities can only be attained by a multi-agent approach [75]. This would also involve replacing a passive valve (commonly used in hydrocephalus shunts) with a mechatronic valve [73] controlled by an intelligent microcontroller that wirelessly communicates through a transceiver with a separate smart hand-held device. The system is illustrated in Figure 3.1.

This shunting system consists of two subsystems: implantable and external (patient device). The implanted subsystem would mainly consist of ultra low power commercial microcontroller [108], mechatronic valve, pressure sensor [46] and low

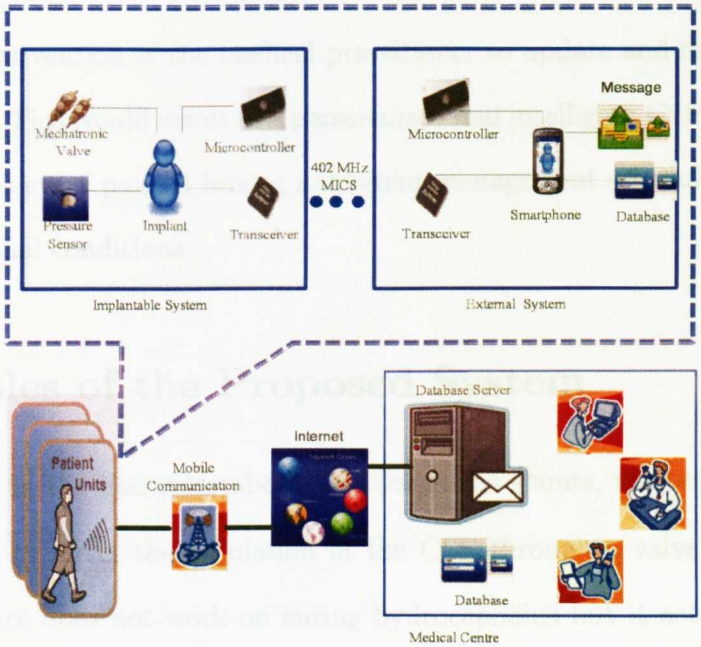


FIGURE 3.1: Schematic diagram of the intelligent and personalised shunting system.

power transceiver [124]. This implantable shunting system would wirelessly communicate with a hand-held smartphone operated by the patient, or on the patient's behalf by a clinician or guardian. This device would have a graphical user interface and an RF interface to communicate with the user and the implantable wireless shunt respectively.

This system would also enable a physician to monitor and modify the management and treatment parameters wirelessly, thus reducing, if not eliminating, the need for shunt revision operations. Once implanted, such a system could not only lead to better management and treatment of the hydrocephalus (especially the complicated cases), but also allow the dynamics of this disease and the effect of shunting to be understood in greater depth.

An intelligent system, *e.g.* [75], can be used to autonomously regulate the mechatronic valve according to a time-based schedule and update it based on the intracranial pressure that is measured when needed. In such a system, ICP readings and other sensory inputs such as patient feedback would help in autonomously tuning the management and treatment of hydrocephalus. At the same time, enabling the intervention of the medical practitioner to update and manually adapt the schedule. This would result in a personalised and intelligent CSF management, which leads to every patient having a different management schedule according to his/her personal conditions.

3.3 Roles of the Proposed System

Even though in the literature about hydrocephalus shunts, the term 'treatment' was reserved to mean the regulation of the CSF through a valve, nevertheless, such procedure does not work on curing hydrocephalus but it actually manages hydrocephalus to keep it under control. For this reason, in this work, the term 'management' will refer to this approach for symptom management, while the term 'treatment' will be reserved to mean treating hydrocephalus underlying causes towards reduction of dependence on shunt.

The intelligent shunting system will perform two main roles; management of hydrocephalus (*i.e.* symptoms) and shunt faults, and treatment of hydrocephalus.

3.3.1 Management

This involves managing both hydrocephalus and the shunting system. The former is mainly regulating the valve in order to maintain ICP within the normal range. Unlike current shunts, this regulation will be personalised based on patient feedback and ICP readings. This can be summarised in monitoring the success of management and its optimisation, adapting the management to the individual and actual conditions, responding to symptoms delivered via patient feedback and capturing real shunt dependence. On the other hand the latter covers the shunt self monitoring, diagnosing and fault detection.

- Managing hydrocephalus: Similar to any other shunt, the proposed shunt will aim to control ICP within the normal physiological limits. To achieve this, the following tasks are performed:

    1. Monitoring ICP, the success of management and its optimisation: The shunt will routinely collect ICP readings measured by the implanted sensor, analyse them internally to check the extent to which the current schedule succeeded in maintaining pressure within normal range. In addition, a figure of merit is calculated to help in evaluating the performance of management (*i.e.* current schedule) and in selecting a schedule that best suit the situation. The novelty of such function would be in it is ability to collect ICP data while the valve is closed, thus providing a valuable record of ICP for un-shunted case with no need to perform any additional invasive operation. Such traces are considered valuable in understanding patient-specific cases and the effect of applying different schedules, since currently physician do not perform ICP monitoring before shunting unless all other methods did not work out in diagnosing hydrocephalus due to the risks of such procedure.

    2. Adapting the management to the individual and actual conditions: to successfully manage hydrocephalus, it should adapt the schedule to the needs of the specific-patient and arising circumstances. If a problem arises in the measured ICP (*e.g.* ICP is high), the system would respond dynamically and instantaneously by updating the valve schedule.

    3. Responding to symptoms delivered via patient feedback: Nowadays, reoccurrence of symptoms in shunted patient is usually dealt by externally

monitor the ICP. Such procedure is invasive and accompanied by many risks and complications. That is why intracranial monitoring usually is the last option for un-shunted patient unless it is vital to diagnose hydrocephalus in some cases. In this system, patient feedback would be logged into the patient device to represent the type of symptom and its severity. As a result of receiving such feedback, the shunting system will investigate the cause of the symptom by checking the normality of ICP and perform self-checking for any faults in the system. And later draw a conclusion whether the cause of the symptom was due to abnormality in ICP or not. In the case of any abnormality, it will respond by either modifying the valve schedule to accommodate the symptom or alerting the physician in case of fault possibility.

The availability of such option in the proposed shunting system, spares patient from unnecessary pain, suffering and risks accompanied with the current diagnosis method. And on the contrary to current methods, this option will provide an instant diagnosing while the patient is living his/her normal life, thus no need to wait for an appointment or being hospitalised

4. Capturing real shunt dependence: Knowing that patients seem to be only partially shunt-dependent, the current shunts do not help in revealing the degree of dependence, but on the contrary, they tend to encourage the patients to become fully shunt dependent. Proposed shunting system can help in revealing the actual shunt dependence.

- Managing the Shunting System: It is important that the system functions properly so that a reasonable intracranial pressure is maintained. Currently, shunt faults are the leading cause of shunt revisions. The main shunt faults are blockage and disconnection. In an effort to detect these faults in early stages, thus avoiding any further patient inconveniences that could arise if left undetected, the proposed shunting system will perform the following preventive procedure.

1. Self monitoring: routinely check up if the ICP data changes in responsive manner to the valve states.
2. Self diagnosis: use novel fault detection measures, which are based on ICP data and valve status, to find any possibility of occurrence of any fault, determine its type (*e.g.* shunt blockage/disconnection/breakage or sensor dislocation/drift), and its degree.

3.3.2 Treatment

The goal of shunting has evolved over time since it was first introduced. The shunt nowadays is expected to provide an option of establishing gradual shunt arrest [10]. It is also the dream of any hydrocephalus shunted patient to regain his/her independence of the shunt and mainly rely on his/her reconditioned natural drainage system.

The capability of the proposed system to be wirelessly reprogrammed without the need for surgery and its ability to monitor the change in the intracranial hydrodynamics are essential in facilitating the shunt arrest process.

At the stage when the shunting system is fully in control of the intracranial hydrodynamics and the patient's real shunt dependence is captured, the objective will be modified to be reducing shunt dependence and progressively arresting the use of the shunt. The author refers to this latter process as weaning.

The weaning process will help the patient to either adapt gradually to higher levels of ICP or reactivate the natural drainage to take part of the drainage process.

Weaning will be implemented over stages. The length of each stage will vary based on patient response and capability to accommodate such change. For each weaning stage, the effect of modifying weaning parameters will be evaluated by routinely collecting ICP readings and patient feedback.

3.4 Advantages and Limitations

The advantages of the proposed shunting system are identified and the limitations facing implementing such system are explored below.

3.4.1 Advantages

The potential advantages of implementing such a shunting system are various and clear. One of its main advantages is personalising the management and treatment, *i.e.* being responsive to patients' needs and circumstances. In addition, it will provide autonomous management and treatment, *i.e.* most of the times functions without supervision or intervention. At the same time provides the option for the physician to wirelessly access, modify and replace the current shunt parameters. Such system has the potential to progressively achieving shunt removal.

The collective results of the above advantages are reduction of patient suffering (*e.g.* hospitalisation, invasive diagnosis of symptoms, waiting for appointment) and improving the quality of shunting.

Furthermore, the collected ICP data for patients at different valve status will be valuable assets for better understanding of hydrocephalus, intracranial hydrodynamics and the effect of shunting on them. Thus might lead to a qualitative jump in this field.

3.4.2 Limitations

Implementing such a system is not problem free, and is expected to encounter different implementing limitations. Ironically, the main obstacle would be the physicians' and patients' mentality. It will not be easy to convince either of them to use such intelligent shunting, as new technology it will be faced with doubt and considered as a threat for both of them.

Some examples of implementation problems would be inaccuracy or breakage of ICP sensor, intermittent problems (*e.g.* not responding) in the mechatronic valve, technical issues, and potential faults. On the other hand, such problems are expected in any mechanical systems.

Some short term obstacles (that would be resolved with the rapid continuous development in high-technology components) are power limitations, implantable memory limitations and product size limitations.

3.5 Walkthrough

A quick walkthrough of the proposed shunting system is summarised. It illustrates the shunt functions through an example of one day in the life of shunted hydrocephalus patient.

Once implanted, the system will attempt to initialise itself by first collecting ICP data for 24 hours and then instantiate an initial personalised 24 sub-schedules based on hourly derived parameters (*e.g.* average ICP and rate of change in ICP) from the collected data. Starting from the first day, the implanted shunt will perform its routine tasks; ICP monitoring, valve regulating according to the schedule, self diagnosis, and daily backup of the results.

In case the patient logged his/her feedback on his/her patient device (PD), the intelligent agent on PD starts to investigate the cause of the feedback and request ICP data to be collected from the implanted shunt. It also would check its database if any similar feedback that might have occurred previously at the time of the day or if such symptom is recently reoccurring.

By receiving the ICP data, the external shunting system (PD) performs analysis and calculates some derived parameters to check if the cause for such symptoms is due ICP abnormality or shunt fault. If the results of the analysis indicated that the cause of the symptom is not due to ICP abnormality or shunt fault, then a message will show up on the PD display to reassure the patient that the symptom is not ICP-related. The feedback, its time along with the ICP data and the decision made are saved to be uploaded at a later time to patient's personal record in the central database at the hospital. On the other hand, if the results showed that the cause is due to ICP abnormality, then the intelligent system will work on modifying the schedule at that hour and track its effect for the next couple of days. A message will also show up informing the patient that the problem has been handled.

The implanted shunt will regularly regulate the valve according to a time-based schedule and at the same time will perform a check up on the ICP and the shunt itself. To do this, it will collect ICP data while the valve is open and closed. It will check if these data is within the acceptable limits and if not, it will alert the PD to perform modification on the schedule. The patient device will also calculate some derived parameter to detect any possibility of fault occurrence in the shunt. In case any fault is detected, then it will inform the physician through web communication, in order to take some procedures in early stage to spare the patient from unnecessary pain and suffering.

Intelligent shunting system will work as a personal physician that accompanies patient 24 hours a day, thus the patient no longer has to wait for an appointment or stay in the hospital every time he/she had a symptom. The ICP and shunt can be checked in minutes anywhere and anytime while the patient having his/her normal life.

With time, the shunt will recognise any progress, *i.e.* patient did not experience any symptoms for long period of time, thus the shunt will decide after consulting the physician to start reducing shunt dependence (shunt weaning process). Patient will be asked to play a vital role at this stage, by giving his/her feedback whenever he/she has symptoms, to tune and personalise the weaning process.

3.6 Conclusions

The realisation of truly autonomous shunting systems for personalised hydrocephalus management and treatment requires the use of implanted mechatronic valve, pressure sensor, smart hand held device, improved algorithms to analyse the inputs (*e.g.* ICP readings and patient feedback) and extract relevant information from raw data, and rule-based decisions controlled by the local intelligence. Such shunting system would give hydrocephalus patients the freedom to go anywhere they like while receiving medical services and health care in a timely fashion. Visits of patients to hospitals or the doctor will be reduced to a necessary minimum, while increasing the quality of care that is provided.

Implementing a CSF management system that delivers an intelligent personalised treatment that has self auditing ability would be a big step towards reducing the drawbacks of the current systems and improving the quality of management and treatment that not only manages the disease but try to cure it. In addition, it will tremendously help in understanding hydrocephalus and the intracranial hydrodynamics. The proposed system is still experimental and is not yet being used clinically. However, its potential interest for improving the quality of treatment delivered to hydrocephalus patients is clear.

In order to develop an intelligent agent based shunting system, some obstacles were faced. Lack of ICP data and good understanding of intracranial hydrodynamics, *e.g.* the effect of shunting and weaning on the intracranial hydrodynamics, are considered two of the main obstacles for this research. These obstacle directed the path of this work. In an effort to overcome such obstacles, a dynamic environment is developed that mimic the intracranial hydrodynamics of hydrocephalus patient. Such environment would work as test bed for intelligent shunt in order to optimise it.

Chapter 4

Hydrocephalus Intracranial Hydrodynamics Model

An intelligent shunting system is seen as the future in hydrocephalus management and treatment, and toward this end, suitably-programmed mechatronic valves would mimic normal physiology and overcome many of the problems associated with current mechanical valves. CSF dynamic models and feasibility studies are necessary to enable the advent of such devices. In order to evaluate and predict the performance of different shunting systems, a model of intracranial hydrodynamics and the shunting systems were conceptualised and simulated mathematically and numerically.

In this chapter the mathematical models for the intracranial hydrodynamics are reviewed and the proposed intracranial hydrodynamics model are introduced. Furthermore, three different valve types are simulated and compared based on a novel multi-dimensional figure of merit. In addition, the need for 'intelligence' to control the mechatronic valve is demonstrated.

4.1 Review of Mathematical Models of Intracranial Hydrodynamics

Great efforts have been invested in the last two decades to develop mathematical models for intracranial hydrodynamics under various conditions (*e.g.* [19, 94, 113, 116]). The main goal for such research has been to achieve a better understanding of the physiological view of the brain with a hope of finding a cure or at least treatment for many physiological disorders of the brain. Some of these models [7, 25, 113] were derived based on electrical circuits, while others (such as in [116]) employed general techniques based on control theory. In addition, neural network was also employed to establish a patient's intracranial pressure model *e.g.* [98]. One of the most cited and used models is the mathematical model derived by Ursino [113] in 1988, where he presented equations that are able to mimic the behavior of the of the intracranial arterial vascular bed, intracranial venous vascular bed, cerebrospinal fluid absorption and production processes, and the constancy of overall intracranial volume. What follows is a review of intracranial hydrodynamics models.

A common assumption (*e.g.* [7, 116]) has been that the space inside the skull bone, is a closed cavity, which can be divided into three volumes: that of the CSF, of the blood and of the tissue. Based on this assumption, three mass balance equation may be derived which is known as the "Monro-Kellie doctrine":

$$V_{total} = V_{CSF} + V_{blood} + V_{tissue} \tag{4.1}$$

where V_{CSF} is defined as the net excess CSF produced, that is, the total produced less the amount absorbed through natural drainage or shunt.

A general equation for the CSF volume can be derived [30],

$$V_{CSF}(t) = \int \left(V_{produced}^{\cdot}(t) - V_{resorbed}^{\cdot}(t) - V_{shunt}^{\cdot}(t)\right) dt \tag{4.2}$$

where $V_{produced}^{\cdot}(t)$, $V_{resorbed}^{\cdot}(t)$ and $V_{shunt}^{\cdot}(t)$ are the CSF production, resorption flow rates and shunt drain flow rate, respectively.

CSF is produced by a fluid exchange between the blood and CSF compartment where CSF is transferred out of the arterial blood to the plexus choroideus. The amount is proportional to the pressure difference between the arterial blood pressure (ABP) and ICP as follows [94, 116],

$$V_{produced}^{\cdot}(t) = k_{prod} \cdot \left(ABP_{plex}(t) - ICP(t)\right) \tag{4.3}$$

where $ABP_{plex}(t)$ is the arterial blood pressure, $ICP(t)$ is the intracranial pressure and k_{prod} is a production constant which is equal to the inverse of the CSF formation resistance.

As for the arterial blood pressure, Schley *et al.* [94] have simply modelled it as variations with amplitude A and frequency ω, through

$$ABP(t) = A_o + A\exp(i\omega t) + \text{complex conjugate} \tag{4.4}$$

The addition of the complex conjugate ensures that $ABP(t)$ is real, but it can be dropped for simplicity since it may be incorporated into the results at any stage [94].

Anderson [7] has also modeled $ABP(t)$ through the following relation:

$$ABP(t) = 17.5\sin\left(2\pi t - \frac{\pi}{2}\right) - 12.5\sin(4\pi t) + 16000 \tag{4.5}$$

The CSF resorption takes place in the granulationes arachnoideales, where it is transferred from the CSF compartment into the sinus sagittalis. Resorption only starts when ICP is above a certain pressure threshold (R_G). Starting from that point, the resorption rate is proportional to the difference between ICP and venous pressure (VBP) as follows [94, 116],

$$\dot{V}_{resorbed}(t) = \begin{cases} 0 & \text{if } ICP < R_G, \\ k_{res} \cdot \Big(ICP(t) - VBP(t)\Big) & \text{otherwise} \end{cases} \tag{4.6}$$

where k_{res} is a constant proportional to the inverse of the CSF resorption (outflow) resistance, R_G is a resorption threshold pressure and $VBP(t)$ is the venous blood pressure and it is usually assumed to be constant of value around 4 mmHg.

The flow through the shunt will be the same in all its components (catheter, valve and tubing) since the system is non-compliant, and may of course be zero if the valve is closed [94]. Different types of valve have a variety of flow rate responses depending upon the valve mechanism involved, *e.g.* highly nonlinear, quasi-linear. But the majority exhibit a quasi-linear response, *i.e.* nonlinear for only very low flow rates. The shunt drain flow rate can be calculated by,

$$\dot{V}_{shunt}(t) = \begin{cases} 0 & \text{if valve is closed,} \\ \frac{ICP(t) - ICP_o}{R_v} & \text{if valve is open} \end{cases} \tag{4.7}$$

where ICP_o is the pressure at which the valve opens, and R_v is the valve resistance.

As for the volume of the blood, it is simply the sum of the arterial and venous blood volumes as follows [7, 113],

$$V_{blood}(t) = V_a(t) + V_v(t) \tag{4.8}$$

where V_a and V_v are arterial and venous blood volumes, respectively. The arterial and venous blood flow rates can be calculated as follows,

$$\frac{dV_a(t)}{dt} = C_{ai}\frac{d\big(ABP(t) - ICP(t)\big)}{dt} \tag{4.9}$$

$$\frac{dV_v(t)}{dt} = C_{vi}\frac{d\big(VBP(t) - ICP(t)\big)}{dt} \tag{4.10}$$

Taking the derivative of Equation (8) with respect to time, the resulting relationship would be,

$$\frac{dV_{blood}(t)}{dt} = C_{ai}\frac{d\big(ABP(t) - ICP(t)\big)}{dt} + C_{vi}\frac{d\big(VBP(t) - ICP(t)\big)}{dt} \tag{4.11}$$

where C_{ai} and C_{vi} are the intracranial arterial and intracranial venous compliances, respectively.

The last part of Equation 5.5 is the volume of tissue. Some researchers had assumed it is constant [116], whereas others had derived the following Equation for it [7],

$$\frac{dV_{tissue}(t)}{dt} = -C_{tiss}\frac{d\big(ICP(t)\big)}{dt} \tag{4.12}$$

where C_{tiss} is the cerebral tissue compliance.

To see the effect of the intracranial volume changes on the ICP, a constitutive equation linking this volume to ICP is needed. The relation between the total volume and the intracranial pressure is complex. Some researchers (*e.g.* [94]) have assumed, for simplicity, a linear relationship for values not too far from the optimal range:

$$V_{total}(t) = V_o + k\Big(ICP(t) - ABP(t)\Big) \tag{4.13}$$

Others (*e.g.* [116]) have fitted the moderate ICP values into an exponential relation with the total volume,

$$ICP(t) = P_o + k_{elast} \exp\Big(aV_{total}(t)\Big) \tag{4.14}$$

where k_{elast} is the elastance coefficient of the intracranial venous compartment.

4.2 Intracranial Hydrodynamics Model

Tremendous effort is ongoing to understand the behavior of intracranial hydrodynamics since such understanding would facilitate solving many longstanding problems such as hydrocephalus. Developing a comprehensive model that mimic the behavior of the hydrodynamics in case of hydrocephalus patients (non shunted and shunted) is an important milestone in understanding hydrocephalus and in evaluating current and future treatments.

To evaluate the suitability of different shunting methods, an environment of intracranial hydrodynamics should be simulated. Different models have been used to simulate the intracranial hydrodynamics.

In this chapter, mathematical equations (from [94], [30], [116], and [113]) were utilised to simulate the intracranial hydrodynamics. In addition, mathematical models for the different shunting systems (*i.e.* standard valve, closed loop shunt and scheduled shunt) were developed. For all these types of shunts, the value of CSF flow through the valve (when open) depends on the differential pressure across it. But the mechanism of opening the valve varies between the different types of shunting regimes.

Standard valve opens when the differential pressure across the valves exceeds the rated opening pressure. In a closed loop shunt, on the other hand, the valve is made to open according to the intracranial pressure inside the ventricles that is read by a pressure sensor. The scheduled shunt opens according to a fixed schedule regardless of the intracranial or differential pressure.

The overall model is illustrated in Figure 4.1, and the output ICP waveform for this model in case of hydrocephalus is demonstrated in Figure 4.5(a). The hydrocephalus was simulated by increasing the resorption resistance (R_{res}) and threshold pressure (R_G) at the absorption site of CSF. Since the failure of the sagittal sinus, which is where the CSF is absorbed into the venous system, is thought to be the cause of most cases of hydrocephalus. R_G was increased since the natural drainage system starts absorbing the CSF only if the ICP became larger than this threshold pressure. So very large value of R_{res} and R_G means total failure of the drainage system (no resorption of CSF), and this leads to almost full dependance on the shunt, *i.e.* introducing the case of hydrocephalus.

This model would be used to assess and investigate the performance of different

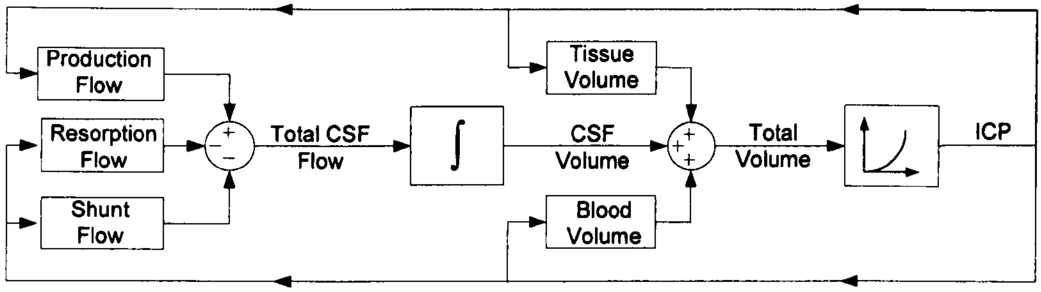


FIGURE 4.1: The overall model of the hydrodynamics of the intracranial system. The model was build based on the mathematical models outlined in Equations 5.5-4.14.

shunting methods based on a novel figure of merit. The Simulink models are illustrated in more details in Appendix B.

In this model, $ICP(t)$ is regarded as the actual intracranial pressure inside the ventricles that is read by the implanted pressure sensor, and $P_t(t)$ is the differential pressure across the valve that is calculated by,

$$P_t(t) = ICP(t) + P_h(t) + P_d(t) \tag{4.15}$$

where P_h is hydrostatic pressure and P_d is drainage distal pressure.

The modelled shunting systems are described in details below.

4.2.1 Existing Shunts

There are many different types of valve on the market, and these have a variety of flow rate responses to pressure differences. In order to circumvent the complexity problem for the flow characteristics, it has been assumed that the valve has a quasi-linear behaviour. In addition, the outlet pressure of the valve is assumed to be atmospheric since drainage into the heart occurs at close to atmospheric pressure while pressure in abdomen is less constant. Pressure is measured relative to the atmospheric pressure, so the atmospheric pressure is taken to be zero [94]. In a low pressure standard valve (commonly used), there is a resistance R_v to flow when the valve is open, above some rated opening pressure P_{open}. It is assumed that the opening and closing pressures of the valve are equal.

The CSF flow for a low pressure standard valve is given by,

$$\text{Valve Flow} = \begin{cases} 0 & P_t(t) < P_{open}, \\ \frac{P_t(t) - P_{open}}{R_v} & P_t(t) \geq P_{open} \end{cases} \tag{4.16}$$

where P_{open} is the opening pressure of the standard valve, and R_v is the resistance of the standard valve.

4.2.2 Closed-Loop Shunt

A closed-loop shunt would comprise of a mechatronic valve, a microcontroller and a pressure sensor which are illustrated in the block diagram in Figure 4.2(a). The function of the sensor would be to provide the microcontroller with ICP readings that are measured in the ventricles of the brain. Subsequently, the microcontroller would process these readings to obtain the correct decision about whether to open or close the valve. In other words, the valve would open only when there is a clinical need for opening (when ICP exceeds the acceptable upper pressure limit). The mathematical model for this type of shunt is shown below,

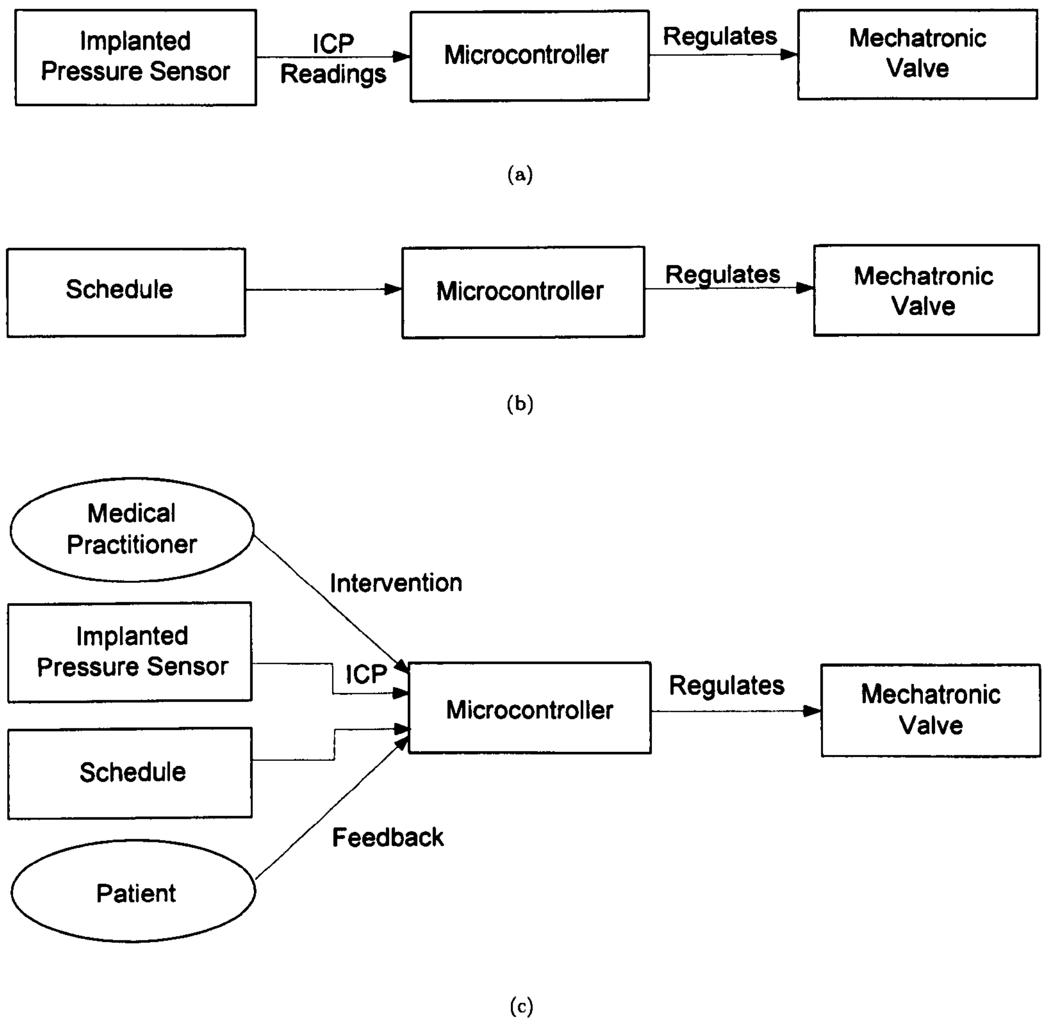


FIGURE 4.2: Different systems controlling the mechatronic valve: (a) closed-loop shunt, (b) scheduled shunt, and (c) intelligent shunt.

$$\text{Valve Flow} = \begin{cases} 0 & ICP(t) < P_{UL}, \\ \frac{P_t(t)}{R_v} & ICP(t) > P_{UL} \end{cases} \tag{4.17}$$

where P_{UL} is the acceptable upper pressure limit, and R_v is the resistance of the mechatronic valve.

4.2.3 Scheduled Shunt

This shunt consists only of a mechatronic valve and microcontroller, as illustrated in Figure 4.2(b). This time the valve is controlled by a fixed schedule. The valve would open at specific times for certain periods irrespective of ICP. In practise, this schedule would be synthesised by analysing the medical records of the patient, personal information, *e.g.* age, occupation, and other medical attributes.

The mathematical model for this type of shunts is,

$$\text{Flow} = \begin{cases} 0 & S(t) = \text{closed}, \\ \frac{P_t(t)}{R_v} & S(t) = \text{open} \end{cases} \tag{4.18}$$

where $S(t)$ is the valve status, taking the value of either open or closed as a function of time, and R_v is the resistance of the mechatronic valve.

4.3 Figure of Merit

In this section, a multi-dimensional numerical figure of merit (FoM) is proposed to enable the performance of different shunting approaches to be quantified and investigated . Later it can be used to evaluate the performance of the intelligent shunting management and treatment of hydrocephalus.

The objective of any FoM is to quantify the performance of a system. The need to numerically quantify performance arises from the fact that in cases such as this, there is no single "best" solution. The judgement of which hydrocephalus management is better may become subjective where large volumes of data must be compared. It is therefore desirable that certain characteristics of the hydrocephalus management and treatment be represented as a number or a set of numbers to reduce both subjectivity and bias.

The evaluation of performance of different hydrocephalus management and treatment schemes is dependent on a variety of factors. Some of the key factors in the evaluation are:

- Windowed mean ICP values.
- Percentage of time ICP is within the normal range.
- Degree of over/under-drainage.
- Percentage of time during which the valve is open.
- "Improvement" in ICP levels attained due to the treatment.
- Degree of shunt dependence.

As these are indicators often cited by experts investigating shunt performance, it is only logical that any candidate FoM would incorporate one or more of the above factors.

A multi-dimensional FoM is proposed that varies with the intracranial dynamics. It would incorporate the following proposed dimensions,

$$\overline{\text{FoM}} = \text{Average of} \begin{cases} FoM_1 & \text{Normality} \\ FoM_2 & \text{Maintainability} \\ FoM_3 & \text{Over/under-drainage} \\ FoM_4 & \text{Open duration} \\ FoM_5 & \text{Improvement} \\ FoM_6 & \text{Effective opening period} \\ FoM_7 & \text{Degree of shunt dependency} \end{cases}$$

1. **Normality Measure**

FoM_1 is a simple indicator of the normality of the ICP values. It measures whether the mean ICP is within the physiological limits, *i.e.* upper and lower limits. These limits vary with the posture of the patient, *i.e.* erect and recumbent postures.

$$FoM_1 = \left(\frac{P_{\mathrm{UL}} - \overline{ICP}}{|P_{\mathrm{UL}}|}\right) \cdot \left(\frac{\overline{ICP} - P_{\mathrm{LL}}}{|P_{\mathrm{LL}}|}\right) \tag{4.19}$$

$$\overline{ICP} = \frac{\sum_{i=1}^{N} ICP_i}{N}$$

where $\overline{ICP}$ is the mean ICP in Δt period, ICP_i is the real-time ICP, N is the number of ICP readings, and P_{UL} and P_{LL} are the upper and the lower limits of the normal ICP range, respectively.

The system should attempt to maintain FoM_1 as high as possible at all times, where positive value for FoM_1 indicates that $\overline{\mathrm{ICP}}$ was kept within the physiological limits, while negative value means that $\overline{\mathrm{ICP}}$ was out of these limits.

2. **Maintainability Measure**

This dimension measures the fraction of time for which ICP was maintained within normal limits over any given observation window.

$$FoM_2 = \frac{\sum_{i=1}^{n} \Delta t_i}{\Delta T} \tag{4.20}$$

where Δt_i is the interval of time at which ICP was maintained within the normal range, and ΔT is the sample interval.

Ideally, it would be desired that FoM_2 be very close to 1, indicating that the ICP was maintained (either natuarally or by means of the shunt) within the physiological limits for the whole sample interval. The minimum value for FoM_2 is 0, indicating that the ICP was constantly outside the normal range for the whole sample interval.

3. **Over-/Under-Drainage Measure**

Over-drainage occurs when the shunt allows CSF to drain from the ventricles more quickly than it is produced. In the case of under-drainage, CSF is not removed quickly enough and the symptoms of hydrocephalus return. These are two of the commonest shunt problems. Thus the third dimension reflects the degree of over-/underdrainage over the total time period that the valve is open.

$$FoM_3 = 1 - \frac{\sum_{i=1}^{n} \triangle t_i}{\triangle T_o} \qquad (4.21)$$

where $\triangle t_i$ is the time interval during which over-/under-drainage occurred while valve is open (*i.e.* ICP is out the normal range), and $\triangle T$ is the total open time.

As FoM_3 gets smaller, this means that the intracranial hydrodynamics are suffering from over/under-drainage for longer time, and vice versa. A maximum of one can be reached, indicating no over-/underdrainage had been detected over the sample time. On the other hand, a minimum of zero would indicate constant over- or under-drainage.

4. **Opening Duration Measure**

This measures the level of optimisation in the opening of the valve, based on the premise that the valve should not be open for longer than necessary to regulate ICP.

The measure of valve opening duration is given by FoM_4,

$$FoM_4 = 1 - \frac{\Delta t_i}{\Delta T} \tag{4.22}$$

where Δt_i is total time during which the valve is open, and ΔT is the sample interval.

The longer the valve is closed, the closer to unity FoM_4 is. FoM_4 values vary between 0 (valve is open all the time) and 1 (valve is closed all the time).

5. **Effective Opening Duration Measure**

When a valve is opened, the ICP value keeps decreasing till either the differential pressure becomes zero or the valve is instructed to close. The effect of opening the valve, *i.e.* maintain ICP within normal range, continues for a period of time even after closing the valve. So the subsequent interval following the opening period starting with the time at which the valve is closed until the time at which the ICP crosses the upper limit of the normal physiological range, is referred to here as the "effective opening duration", as illustrated in Figure 4.3.

It is the subsequent interval following the opening period (while valve is closed) during which ICP maintained within normal range as a result of the previous opening period.

To measure this dimension, the following relation is used,

$$FoM_5 = \frac{T_e}{T_o + T_e} \tag{4.23}$$

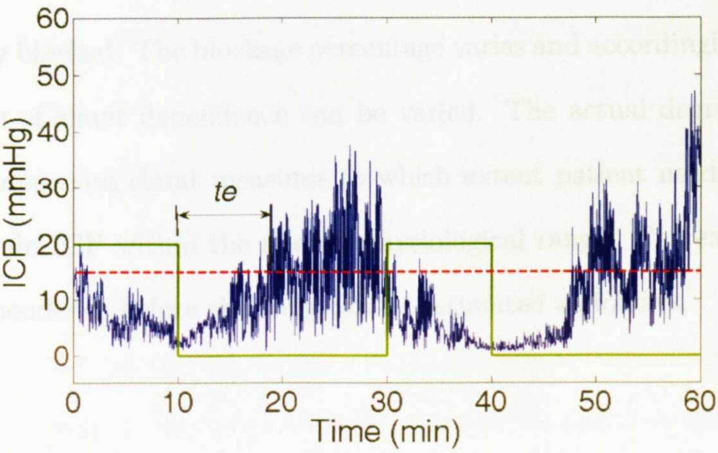


FIGURE 4.3: Illustration of the effective time.

where T_e is the effective opening duration and T_o is the actual opening duration.

The increase of FoM_5 indicates that the tested shunting system has good influence in keeping ICP within normal range even when the valve is closed.

6. **Improvement Measure**

This dimension measures the improvement due to implementing a shunting system. And since "improvement" is highly subjective aspect, the effect of the management or treatment would be measured by inspecting the mean ICP before and after shunting or modifying the management/treatment.

$$FoM_6 = \frac{\overline{ICP}_{\text{before}} - \overline{ICP}_{\text{after}}}{\overline{ICP}_{\text{before}}} \tag{4.24}$$

The results of FoM_6 can be interpreted as its value increases, the treatment is more effective in reducing ICP.

7. **Degree of Shunt Dependence Measure**

It is known that the natural drainage in most hydrocephalus patients is not totally blocked. The blockage percentage varies and accordingly the patient's degree of shunt dependence can be varied. The actual degree of patient's dependence on shunt measures to which extent patient needs the shunt to maintain ICP within the normal physiological range. The expected degree of dependence before shunting can be estimated as follows,

$$\text{Expected degree of dependence} = \frac{f_{\text{normal}} - f_{\text{hydrocephalus}}}{f_{\text{normal}}} \tag{4.25}$$

where f_{normal} is the natural drainage flow in a healthy person, and $f_{\text{hydrocephalus}}$ is the natural drainage flow in case of hydrocephalus for this specific patient.

The degree of dependence is expected to vary for a specific patient based on the type of the implemented shunting system. FoM_7 measures the increase in dependence due to changing shunting parameters as follows,

$$FoM_7 = \frac{f_{\text{after}} - f_{\text{before}}}{f_{\text{before}}} \tag{4.26}$$

where f_{before} and f_{after} are the natural drainage flow in the patient before and after shunting, respectively.

As the value of FoM_7 increases this means that management has less effect on increasing the degree of dependence.

There is almost inverse relation between valve flow and the natural drainage flow. As the valve flow increases, ICP decreases, thus ICP will not exceed the natural pressure threshold (R_G). As a result the natural drainage will not be activated. For this reason, valve flow can be used as a rough indicator of shunt dependence. Specially because the natural drainage flow in most cases is unknown and difficult to be measured. In this work, thanks to the proposed model, the natural drainage flow can measured directly for the numerical simulations. Then the shunt dependence measure based on natural drainage flow is compared with the one based on the valve flow to evaluate the correctness of our assumption, as a result both of them gave same indication. Expected degree of dependence based on valve flow can be expressed as follows.

$$FoM_7 = \frac{f_{\text{vbefore}} - f_{\text{vafter}}}{f_{\text{vbefore}}} \tag{4.27}$$

where f_{vbefore} and f_{vafter} are the CSF flow through a valve in a patient before and after shunting/modifying shunting parameters, respectively.

The expected relations between the different FoM dimensions and the total open duration are illustrated in Figure 4.4. The total open duration is the open duration per drainage period multiplied by the number of drainage periods for specific interval of time. Knowing that d_1 and d_2 are the values of total open durations at which the average ICP values are at the upper (UL) and lower (LL) normal limits, respectively. And d_{opt} the value of total open duration that corresponds to the maximum FoM value.

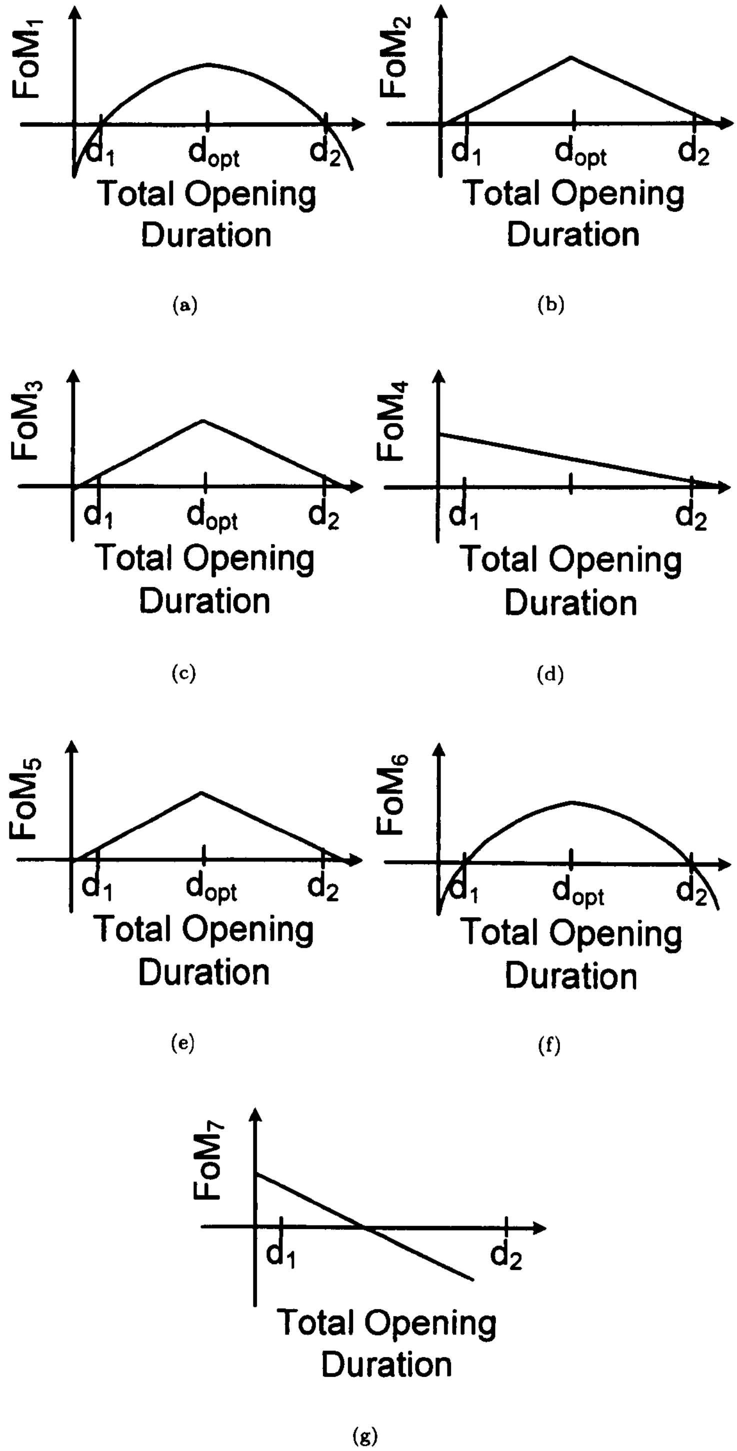


FIGURE 4.4: The expected relations between the dimensions of FoM and total opening duration; (a) FoM_1, (b) FoM_2, (c) FoM_3, (d) FoM_4, (e) FoM_5 (f) FoM_6, and (g) FoM_7.

4.4 Performance of Different Shunting Systems

Figure 4.5(a) shows the ICP waveforms for a case of simulated hydrocephalus before adding any shunt; the elevated mean ICP is clear. The resulting ICP waveforms after adding different shunting systems and their corresponding valve status or schedules representing the response of each shunt, are illustrated in Figures 4.5 to 4.8 over a 3-hour period.

4.4.1 Standard Valve

It can be seen from Figure 4.5(b) that the standard valve is open during almost the whole simulation period, reducing the mean ICP to be within the acceptable normal range (*i.e.* upper and lower limits of 15 and -5 mmHg). But the average ICP level is 1.81; this is lower than expected for a healthy person [6]. The opening pressure and the resistance for the simulated valve is shown in Appendix C (Table C.1). It can also be noticed that the effective opening duration is wasted due to the short closing periods. Another thing is that the patient appears to be fully dependent on the shunt in draining CSF, *i.e.* the partially functional natural drainage will no longer be active since the continuous opening of the valve will maintain the ICP below the natural drainage threshold (R_G). This can be clearly visualised from Figure 4.6(b) that shows the absence of any natural absorption flow in the case of standard valve compared to the case with no shunt in Figure 4.5(a).

4.4.2 Closed Loop Shunt

The resulting ICP waveform after adding such a shunt, shown in Figure 4.5, illustrates how this type of shunt has succeeded in keeping the ICP within normal range of a healthy person (*i.e.* ICP for healthy adult should be around 4 to 12 mmHg) since the upper acceptable limit for this shunt was considered 10mmHg.

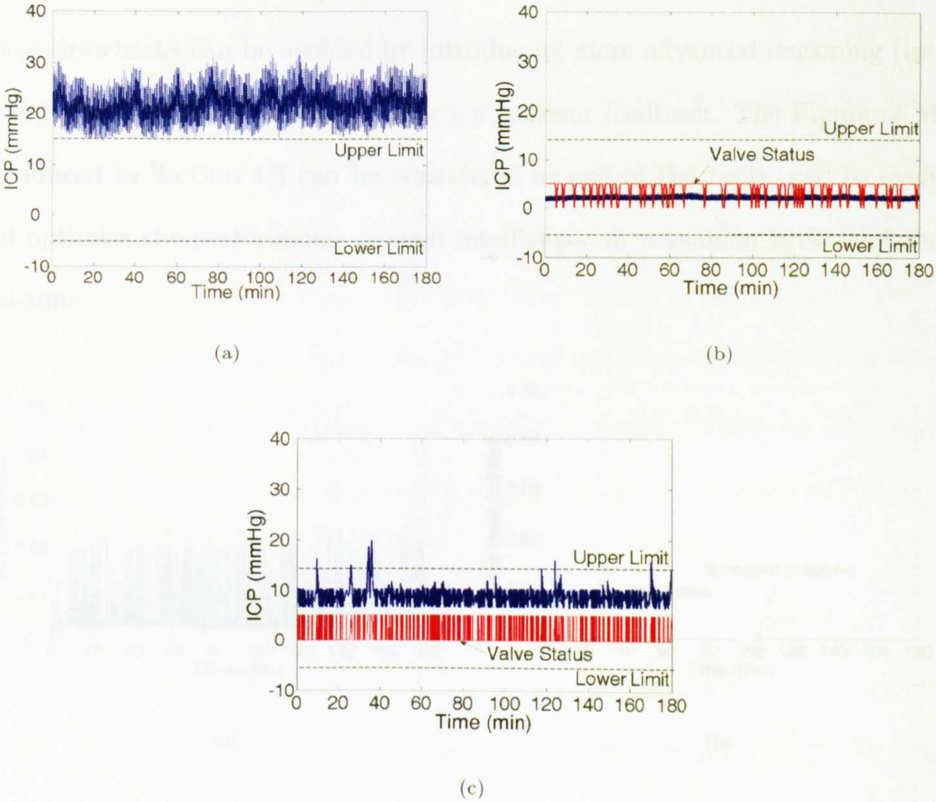


FIGURE 4.5: Simulated ICP waveforms for different shunting systems: (a) hydrocephalus (no shunt), (b) standard low pressure valve and (c) closed loop shunt.

The closed loop shunt gave better results than the standard shunt in respect of degree of shunt dependence (as shown in Figure 4.6(c)), closing duration and effective open duration. Although such a shunting system could be theoretically successful, its practical feasibility would be limited by the current technology. For example, current implantable pressure sensors are inaccurate in the long-term, and implantable batteries have short life due to size limitations. But the price for that was having high opening frequency (approximately 2.5Hz) compared even to a standard valve (typically 1/40 Hz) which can lead to a shorter life for the mechanical parts of the valve and for the battery. This high opening frequency is due to the simple reasoning logic employed, which is incapable of deciding whether there is a genuine need to open or close the valve.

These drawbacks can be avoided by introducing more advanced reasoning (intelligence) with additional sensory inputs *e.g.* patient feedback. The Figure of Merit introduced in Section 4.3 can be considered as one of the tools used to evaluate and optimise the performance of such intelligence in managing hydrocephalus in real-time.

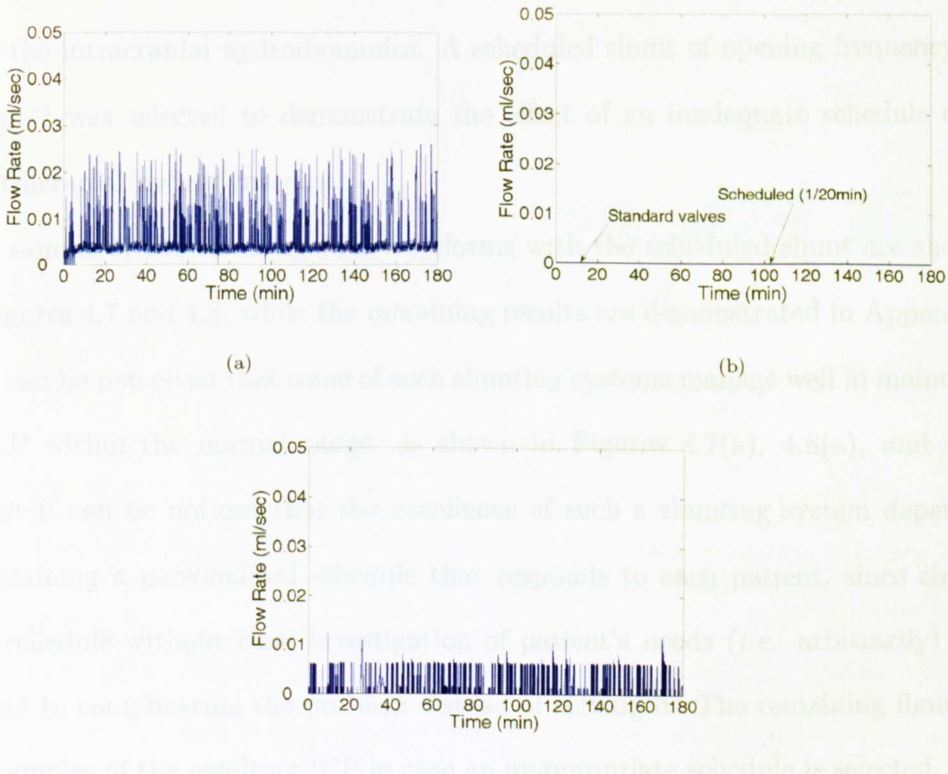


FIGURE 4.6: Simulated natural CSF absorption flow for different shunting systems: (a) No shunt, (b) Standard valve, and (c) Closed loop shunt.

4.4.3 Scheduled Shunt

The performance of such shunt is dependant on the opening duration and frequency, thus it was simulated at different opening durations (5, 10, and 15 minutes) and frequencies (1/20, 1/30, 1/40 and 1/80 min^{-1}) in order to investigate the effect of varying schedule parameters on its performance to eventually select the optimum schedule for the simulated case. The frequencies started with the 1/20 min^{-1} to mimic an output behaviour close to that of the standard mechanical valves, then increased gradually to see the effect of such increase on the behaviour of the intracranial hydrodynamics. A scheduled shunt of opening frequency 1/80 min^{-1} was selected to demonstrate the effect of an inadequate schedule on the intracranial hydrodynamics.

A sample of the resulting ICP waveforms with the scheduled shunt are shown in Figures 4.7 and 4.8, while the remaining results are demonstrated in Appendix D. It can be perceived that some of such shunting systems manage well in maintaining ICP within the normal range, as shown in Figures 4.7(a), 4.8(a), and 4.8(b). But it can be noticed that the excellence of such a shunting system depends on obtaining a personalised schedule that responds to each patient, since choosing a schedule without close investigation of patient's needs (*i.e.* arbitrarily) would lead to complicating the problem instead of solving it. The remaining figures are examples of the resulting ICP in case an inappropriate schedule is selected. It can be seen in these figures that the high ICP was not reduced to within the normal range *i.e.* the system is experiencing under-drainage. At the same time, over-drainage could have been experienced if the valve is opened for longer time or while ICP is low. In addition, we should not forget that the intracranial hydrodynamics for each patient are not stable and change over time. This means that this time-triggered shunt would not respond to the dynamic changes but would rather open whether or not there is a need for opening.

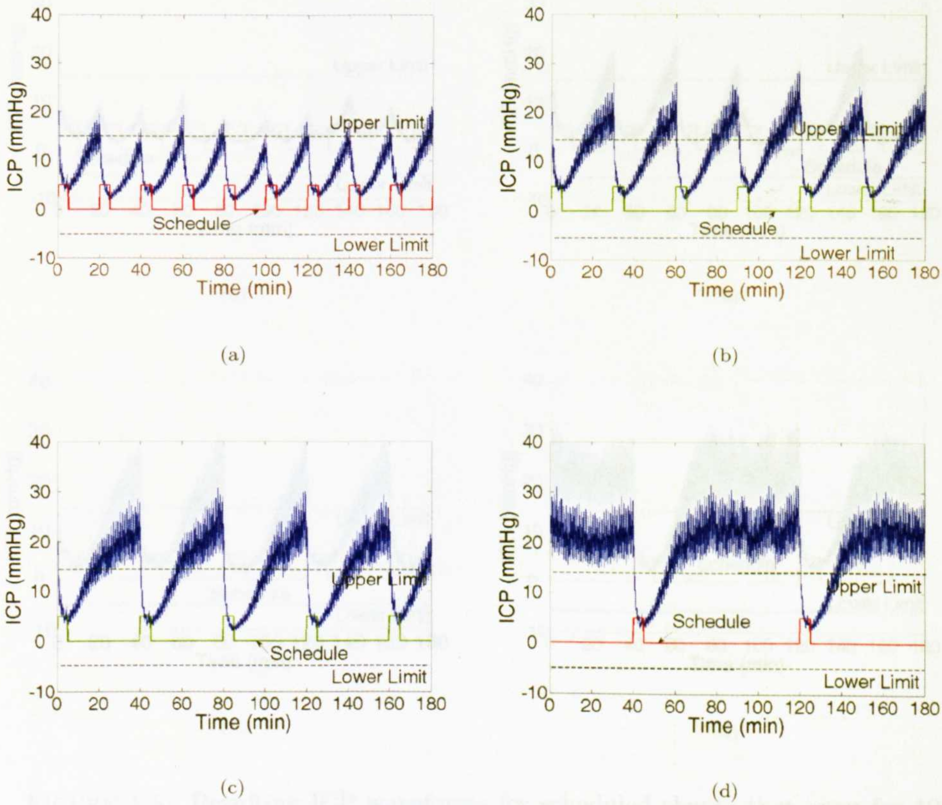


FIGURE 4.7: Simulated ICP waveforms for scheduled shunts that open for 5 minutes every: (a) 20min, (b) 30min, (c) 40min, and (d) 80min.

Comparing the different scheduled shunting systems based on the figures of merit, it has been observed that (as shown in Figure 4.9) as the open duration per drainage period increases, normality (FoM_1), maintainability (FoM_2), underdrainage (FoM_3), and improvement (FoM_6) measures increase at different rates and paths till a duration threshold is reached after which these measures are expected to decrease. The value of this threshold varies with the opening frequency and FoM dimension. Increasing the opening frequency has the same effect on the previous FoM dimensions as increasing the opening duration, as shown in the corresponding Figure D.2 in Appendix D. In general the simulated shunts did not experience over-drainage but most of them had problems of underdrainage.

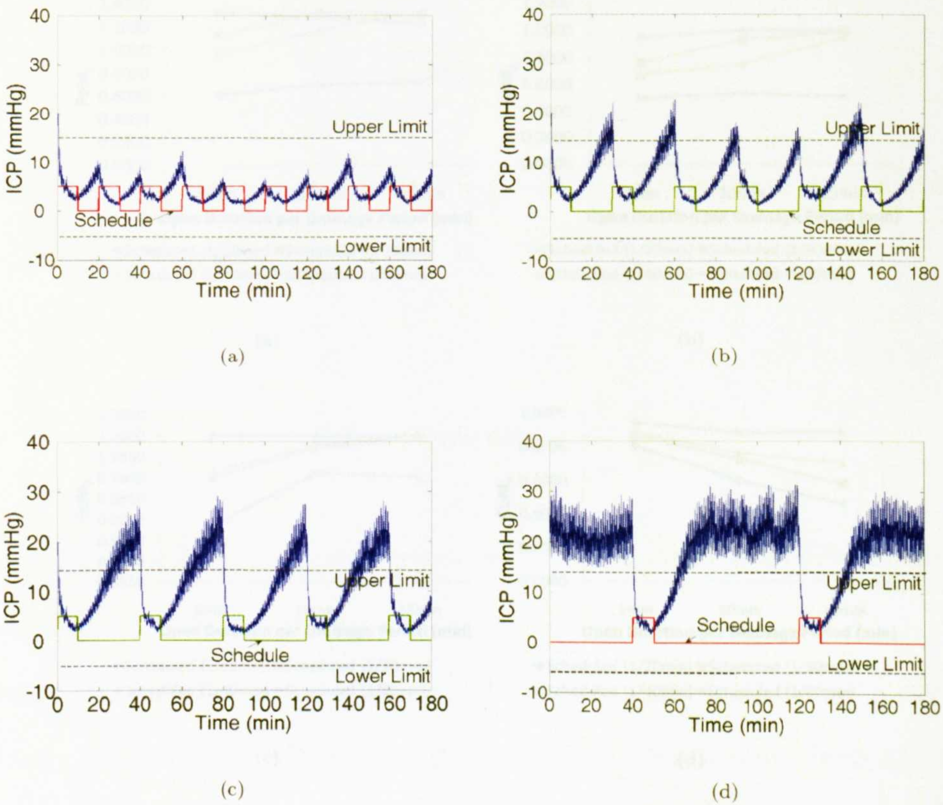


FIGURE 4.8: Resulting ICP waveforms for scheduled shunts that open for 10 minutes every: (a) 20min, (b) 30min, (c) 40min, and (d) 80min.

On the other hand, when the open duration or open frequency increases, the figures for open duration (FoM_4), effective open duration (FoM_5), and degree of shunt independence (FoM_7) decrease as shown in Figures 4.9(d), 4.9(e), and 4.9(g). The effective opening duration can be increased by increasing the opening duration or frequency or both. From this one can conclude that increasing the open duration will not effectively improve the performance, instead increasing the frequency to certain limit and maintaining the open duration would result in more effective management and treatment.

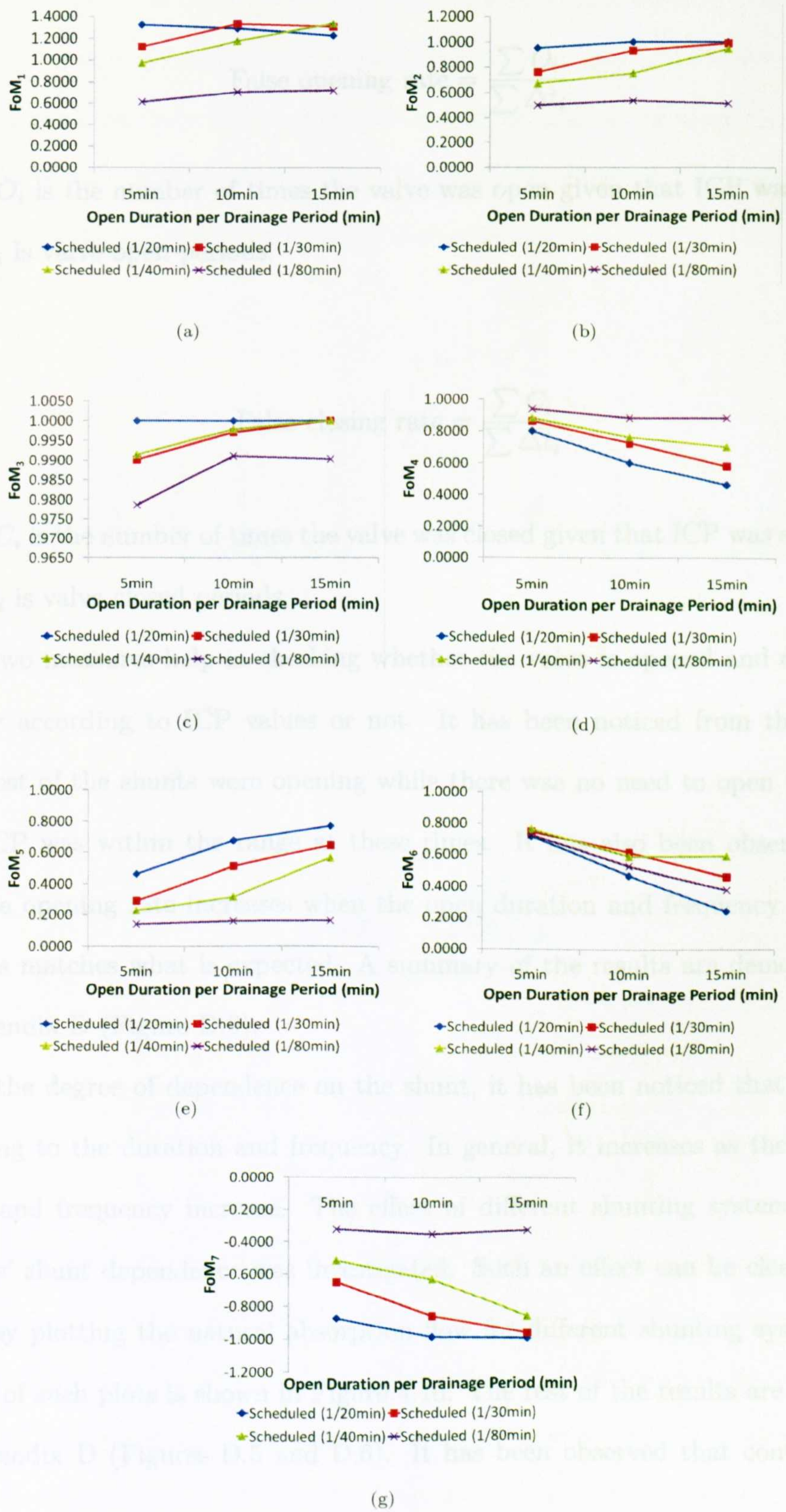


FIGURE 4.9: The figure of merits versus duration: (a) FoM_1, (b) FoM_2, (c) FoM_3, (d) FoM_4, (e) FoM_5 (f) FoM_6, and (g) FoM_7.

Also the false opening and closing rates for the whole testing period has been calculated as follows;

$$\text{False opening rate} = \frac{\sum O_i}{\sum \Delta t_i} \tag{4.28}$$

where, O_i is the number of times the valve was open given that ICP was normal and Δt_i is valve open periods.

$$\text{False closing rate} = \frac{\sum C_i}{\sum \Delta t_i} \tag{4.29}$$

where, C_i is the number of times the valve was closed given that ICP was abnormal and Δt_i is valve closed periods.

These two measures help in checking whether the valve is opened and closed efficiently according to ICP values or not. It has been noticed from the results that most of the shunts were opening while there was no need to open the valve since ICP was within the range at these times. It has also been observed that the false opening rate increases when the open duration and frequency increase, and this matches what is expected. A summary of the results are demonstrated in Appendix D (Figure D.3).

As for the degree of dependence on the shunt, it has been noticed that it varies according to the duration and frequency. In general, it increases as the opening period and frequency increase. The effect of different shunting systems on the patients' shunt dependence was investigated. Such an effect can be clearly visualised by plotting the natural absorption flow for different shunting systems. A sample of such plots is shown in Figure 4.10. The rest of the results are included in Appendix D (Figures D.5 and D.6). It has been observed that continuously opening the valve, as the case in the standard valve and scheduled 1/20 min^{-1} shunt, encourages the laziness of the natural drainage system and convert it from probably being partially functioning (partially dependant on the shunt) into fully shunt dependant. Whereas in the closed loop and the other scheduled valves, the natural drainage is functioning to different degrees.

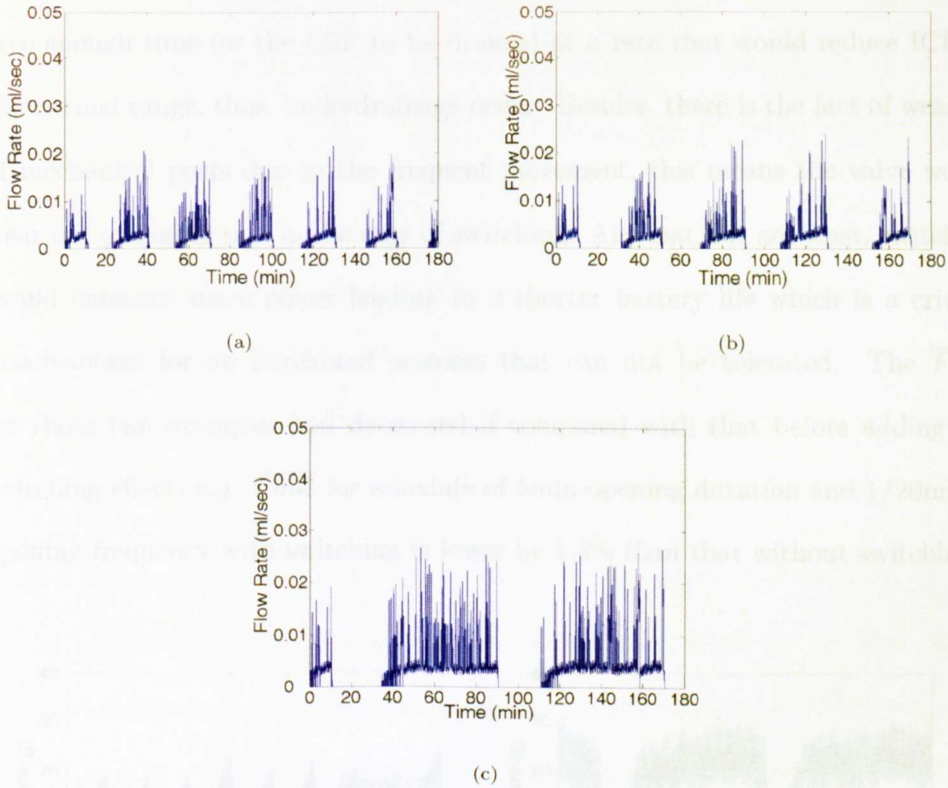


FIGURE 4.10: Simulated natural CSF absorption flow for scheduled shunting systems that alternate between states for 10min every: (a) 20 min, (b) 30 min, (c) 40 min, and (d) 80 min.

A switching effect was investigated to test whether opening and closing the valve more frequently during the opening period would be more effective in achieving the goal of the shunting system. The purpose of switching is to reduce the overflow that would happen if the valve remained open continuously for a long time or if the valve opened while ICP was low. Figure 4.11 shows examples of the ICP waveform after adding a switching effect. During the opening period the valve alternate between states for 1 minute every 2 minutes.

For the cases studied, switching slightly reduced the degree of shunt dependence, reduced the total opening duration while increasing the effective opening duration. On the other hand, it has been noticed that ICP could not be reduced to within the normal range. This is due to the too short opening durations which did not give enough time for the CSF to be drained at a rate that would reduce ICP to the normal range, thus, underdrainage occur. Besides, there is the fact of wearing of mechanical parts due to the frequent movement, this means the valve would wear out at higher rate in the case of switching. And last but not least, switching would consume more power leading to a shorter battery life which is a critical disadvantage for an implanted systems that can not be tolerated. The $\overline{FoM}$ for those two examples had decreased if compared with that before adding the switching effect, *e.g.* $\overline{FoM}$ for schedule of 5min opening duration and $1/20\text{min}^{-1}$ opening frequency with switching is lower by 1.4% than that without switching.

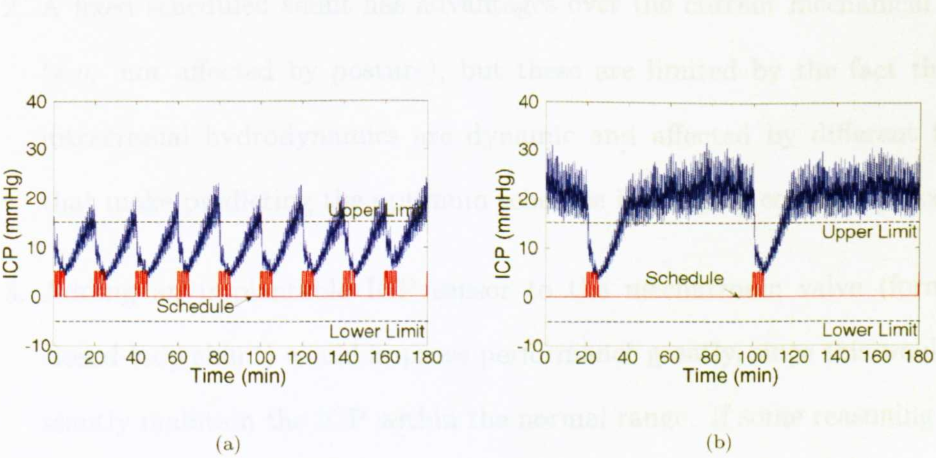


FIGURE 4.11: Simulated ICP waveforms after adding switching effect for scheduled shunts that alternate between states for 5 minutes (switches every 1 min) every: (a) 20min, and (b) 80min.

To choose the optimum shunt among of the simulated ones, the overall figure of merit, $\overline{FoM}$ for all shunts had been calculated by taking the average of the seven dimensions. The closed loop shunt scored the highest $\overline{FoM}$ (0.7808) followed by the scheduled shunt of 5min opening duration and 1/20min^{-1} opening frequency with $\overline{FoM}$ equals 0.6263.

4.5 Conclusions

In this chapter, different paradigms to regulate CSF flow were modelled and investigated, where the human intracranial hydrodynamics were modeled to serve a test environment. As a result of this investigation, the following conclusions can be drawn:

1. Despite of the tremendous achievement of current valves (standard low/medium pressure) in managing and treating hydrocephalus, in order to overcome some of the most frustrating problems it is proposed that future treatment approaches shift from passive mechanical to active mechatronic valves.

2. A fixed scheduled shunt has advantages over the current mechanical valves (*e.g.* not affected by posture), but these are limited by the fact that the intracranial hydrodynamics are dynamic and affected by different factors that make predicting the optimum schedule is a highly complex process.

3. Adding an implantable ICP sensor to the mechatronic valve (forming a closed-loop shunt) would improve performance greatly, since this would constantly maintain the ICP within the normal range. If some reasoning about the ICP value is applied, this shunt performance would resemble to a large extent the natural drainage system. This approach is not without disadvantages however.

4. Exploring the previous options for controlling the mechatronic valve revealed the need for further investigation to develop a shunting system that would deliver an intelligent and personalised treatment for hydrocephalus patients. This shunting system should integrate the schedule and the closed loop shunting systems and incorporate some sort of intelligence that would enable it to respond dynamically to the changes in the environment. At the same time, it should manage treatment without the need of continuous ICP monitoring. For this reason, another sensory input, *e.g.* patient feedback and medical practitioner intervention, can be added to improve the quality of the treatment. A block diagram that illustrates this type of shunting system is shown in Figure 4.2(c).

For a scheduled shunt to be efficient, it should be carefully selected. This urges the need to develop an algorithm that autonomously select schedule parameters based on patient's personal data. Such algorithm will be explored in details in the following chapter.

Chapter 5

Hydrocephalus Management Personalisation[2]

Despite the success of conventional devices in managing CSF in hydrocephalus patients, they have been plagued with a number of problems. One of the non documented problems is the inability of such devices to autonomously and spontaneously adapt to patients' needs that has lead to frequent hospital visits and shunt revisions.

Thus it is desirable to have a shunt valve that responds dynamically to the changing needs of the patient, opening and closing according to a dynamic physiological pattern, rather than simply to the hydrostatic pressure across the valve. Such a valve, as mentioned previously, would by necessity be mechatronic, electronically controlled by software. This software can be a simple schedule or advanced intelligent software that monitors, analyses the intracranial pressure and responds accordingly.

Scheduled shunt can perform effectively in maintaining ICP normal under the condition of smartly selecting its schedule in a way that would suit the individual

[2]Part of this chapter has been published under the title "Instantiating a Mechatronic Valve Schedule for a Hydrocephalus", in Conf Proc IEEE Eng Med Biol Soc., Minnesota, USA, pp.749-752 , 2009.

patient. This chapter will show author's efforts in personalising the mechatronic valve schedule.

5.1 Introduction

The only way the personalized hydrocephalus treatment was handled in the literature is through implementing programable shunts in which differential pressure of the valve can be varied according to the patient case and it is decided by the surgeon.

With the advent of the programmable valve system, neurosurgeons can pre-select one of different pressure settings. After implantation, the valve can be adjusted non-invasively to adapt to changes in patient condition. That means surgeons are able to make pressure adjustments to help control intracranial pressure and ventricle size at any time.

The intervention of a mechatronic valve provides the opportunity for different shunting systems to be developed. This type of valve can be controlled by software, that can vary in its complexity and intelligence. The following software systems can be developed to regulate the opening and closing of such a valve. The first option would be a scheduled program, as the one introduced by Miethke [73], that consist of the opening and closing times of the valve for a period of 24 hours. This schedule repeats itself daily. The second option would be a closed loop shunt whereby the readings of an implanted ICP sensor governs the opening/closing of the valve according to the "acceptable" ICP limits. In other words, the valve would only open when the ICP reading exceeds these pre-configured limits. The idea of using a pressure sensor integrated into a shunt system for monitoring ICP and interrogated by telemetry is not novel idea [38, 48, 72], where ICP readings used as a measure to monitor the performance of the implanted shunt. Whereas, utilising these readings as a feedback to instantaneously and even autonomously regulate the shunt is not yet available. Thus the third option would be adding an element of intelligence and personalisation to the above by enabling real-time reconfiguration of the shunt parameters based on different sensory inputs, and in the long run reduce or eliminate shunt dependence.

5.2 Hydrocephalus Management Using Mechatronic Valve

One of the recent advances in the management of hydrocephalus is the invention of a mechatronic valve. The desirability of such valve lies in the potential of having shunt that not only control hydrocephalus but also seeks to treat it. In contrast to current valves, such a valve is regulated based on a time based schedule not on the differential pressure across the valve. Thus the effectiveness of such valve is highly dependant on selecting an appropriate valve schedule that delivers personal treatment for every individual patient. Providing such a schedule is likely to be one of the obstacles facing the implementation of the mechatronic valve.

The mechatronic valve compromises an electrical switching valve which can be adjusted by the electrical actuating system between an open and a closed positions, wherein the switching valve is stable at these positions when the electrical actuating system is not activated, such that no energy is required to maintain the closed and open positions [74].

The mechatronic valve consists of a spherical valve body which in the closed position rests in a sealing manner on a valve aperture and in the open position rests in a recess laterally adjacent to the valve aperture. Figure 5.1 shows a schematic longitudinal sectional view of a bi-stable mechatronic valve [74]. An electronic system is supplied with power by a battery. Depending on switching direction, a current is applied to a coil, so a magnetic field is generated which moves a slide. The slide can adopt two different rest states, which are secured by spring. The spring would secure the seat of a sphere even in the case of vibrations and keep the force to displace the sphere small. The valve outlet is a hole that has a diameter around 1 mm, corresponding to the internal diameter of a typical drainage tube. The sphere is preferably produced from a hard and light material (*e.g.* aluminum oxide ceramic) and it should has a diameter that is three times greater than the hole of the valve outlet. Thus if it is pushed over the hole, then the drainage would be closed. And if pushed into the position of the blind hole, then the total cross-section of the hole is exposed, thus minimising the danger of blockage. The position of the slide can be continuously detected by a detector [74].

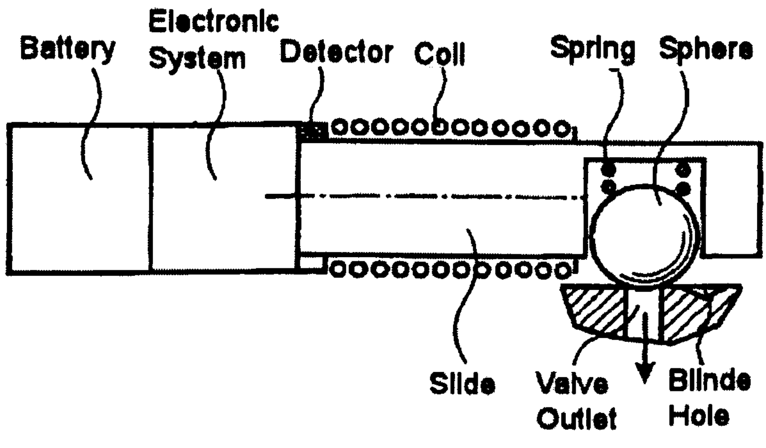


FIGURE 5.1: A schematic longitudinal sectional view of a bi-stable mechatronic valve [74].

The slide of the mechatronic valve is controlled by a time based schedule. The schedule would be simply the distribution of the valve status (open/close) over time. Such schedule would incur many disadvantages *e.g.* over-/under-drainage, if its selection is arbitrary. In order to optimise the usefulness of such a valve, its schedule should be selected in way that delivers a personalised treatment for each specific patient. Achieving such a goal is not an easy task due to the dynamic behaviour of intracranial pressure that not only varies among patients but also within individual patient with time. There are two extremes for schedule alternatives. One is a dynamic schedule that responds to the instantaneous intracranial pressure which requires an implanted pressure sensor, *i.e.* closed loop shunting system. The other extreme is a fixed schedule that has a fixed open frequency over 24 hours. This alternative lacks flexibility and ignores the intracranial dynamic behaviour while the first is impractical.

A schedule structure is proposed that offers a compromise between the two schedule extremes. Thus to facilitate the process of schedule selection and to add some degree of flexibility, a 24-hours schedule, shown in Figure 5.2, is divided into 24 one hour sub-schedules. Each sub-schedule is identified by three parameters; the targeted hour (hr), open duration (d_{ON}) and closed duration (d_{OFF}) for that specific hour.

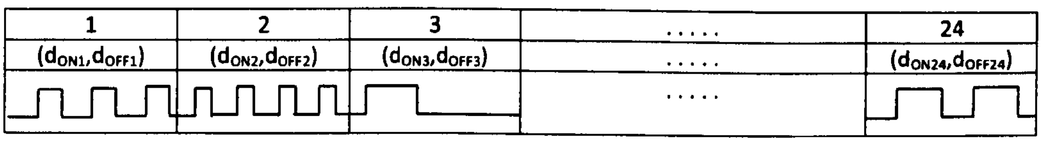


FIGURE 5.2: A 24-hour schedule structure.

An investigation has been done to decide which of the following options to be implemented in designing a valve schedule,

1. Opening the valve for d_{tot} once per hour, as shown in Figure 5.3(a).

2. Distributing d_{tot} over the hour, thus opening the valve for a duration of d_{ON} every period of T_o, where d_{ON} equals $\frac{d_{tot}}{n}$ and n is the number of drainage periods per hour and equals $(n) = \frac{60}{T_o}$ as shown in Figure 5.3(b).

3. In addition to the schedule in (1) and (2), a switching effect is added, *i.e.* alternating between closing and opening valve status within opening periods as in Figure 5.3(c).

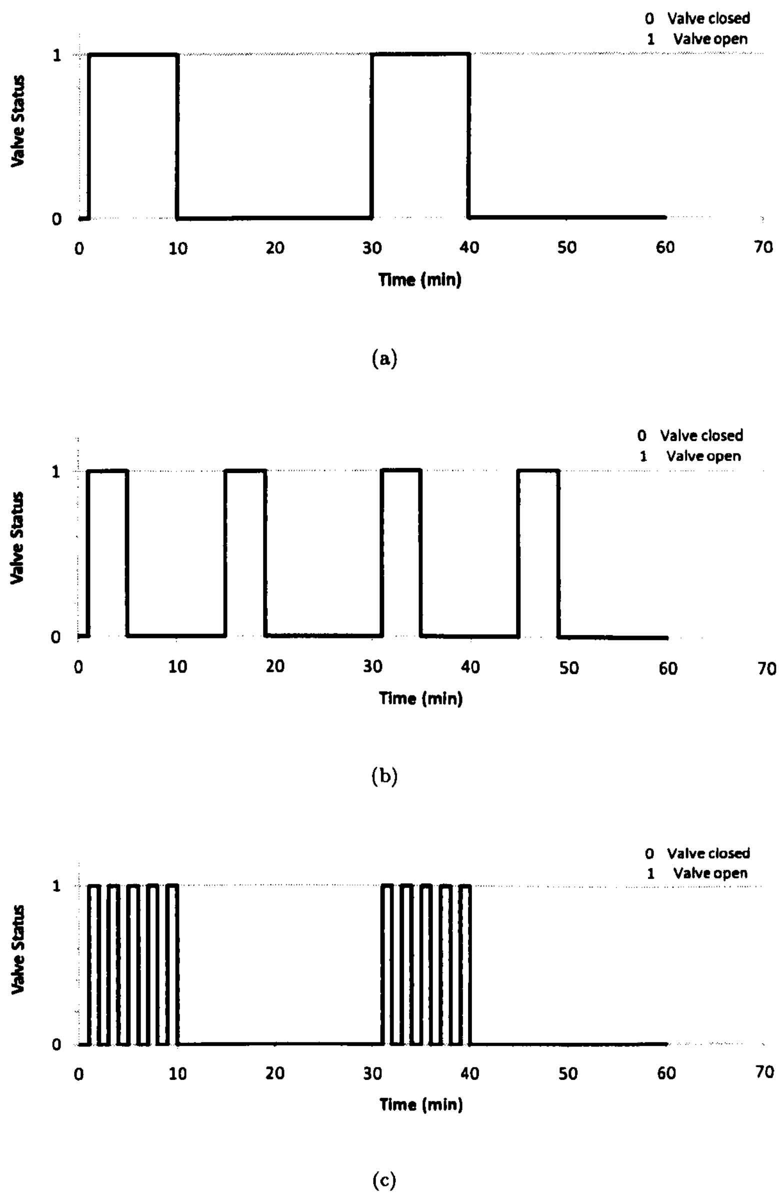


FIGURE 5.3: Different techniques in implementing valve schedules. (a) Variable total open duration per hour with one drainage period, (b) Same as in option (a) but with switching, and (c) Variable total open duration per hour with variable number of drainage periods.

As a result of the numerical simulations, the second option was more effective in maintaining ICP within normal range. At the same time, this technique keeps the total opening duration per hour constant irrespective of the opening rate thus not increasing shunt dependence. In the following sections, this option is applied.

Management and treatment in the proposed shunting system is presented by a time-based valve schedule, thus dynamically modifying the schedule, would mean changing the applied management. Management would be modified in order to adapt to the individual patient and actual conditions. This modification is accomplished based on real-time inputs (*e.g.* symptoms delivered via patient feedback and internally measured ICP) and derived parameters such as rate of ICP change, effective opening time and figure of merits. When updating the schedule, the modification is only applied on the targeted sub-schedule (hour).

The system acquires knowledge directly and wirelessly from the patient's satisfaction input (feedback), to make decision regarding modifying the schedule or it just records and saves patient's satisfaction for future interpretation.

Once the shunting system is implanted, the system is initially programmed by taking into consideration the empirical data of patient's history, *e.g.* ICP data, personal information, medical history, family history.

In long run, the system become stable and reaches a state in which it personalise the patient and it deals smartly and dynamically with any changes with no need for help. As a result, these personalised schedules can be categorised according to hydrocephalus patient types so as to develop an optimum schedule for each patient's category that can be used, in future, as the initial schedule when implanting the shunt.

Personalising the management of a mechatronic shunt will involve two main tasks; instantiating a personalised initial valve schedule and personalise its modification.

5.3 Instantiating a Personalised Initial Schedule

In this section, an algorithm is proposed to help in initialising a valve schedule based on the patients' own intracranial pressure data and the novel figure of merit, thus providing the physician with an easy tool that facilitate the use of the mechatronic valve. The algorithm was implemented in $MATLAB^{TM}$ and $Simulink^{TM}$. A model that mimics real ICP data for three hydrocephalus patients (before shunting) was used to test this algorithm and the resulted schedules along with the resulted intracranial pressure traces have illustrated the effectiveness of the algorithm in providing schedule that maintain ICP within the normal limits.

5.3.1 Schedule Design

The valve schedule can be personalised to the needs of the patient through utilising the patients' intracranial pressure readings whether it was taken by an external or implanted pressure sensor. An algorithm is proposed to derive such a schedule. Facing the fact that part of the algorithm will be implanted inside the body of the patient, urged the need for simple algorithm that perform its tasks in very short time. This scheduling algorithm is intended to facilitate the modification of a mechatronic valve schedule in order to be responsive to the dynamic intracranial pressure behavior, especially when it is used within an intelligent shunting system [4, 75]. The scheduling algorithm is illustrated in Figure 5.4. It derives the open duration and open period for each hour (subschedule) based on the corresponding available pressure data of 24 hours sample. The effect of implementing each subschedule on this specific patient is evaluated though numerical simulations that predict ICP in response to the subschedule. Then a FoM is used to evaluate the performance of different alternatives. As a result a subschedule is chosen that corresponds to the maximum FoM value. The components of the algorithm are described in more details in the following sections.

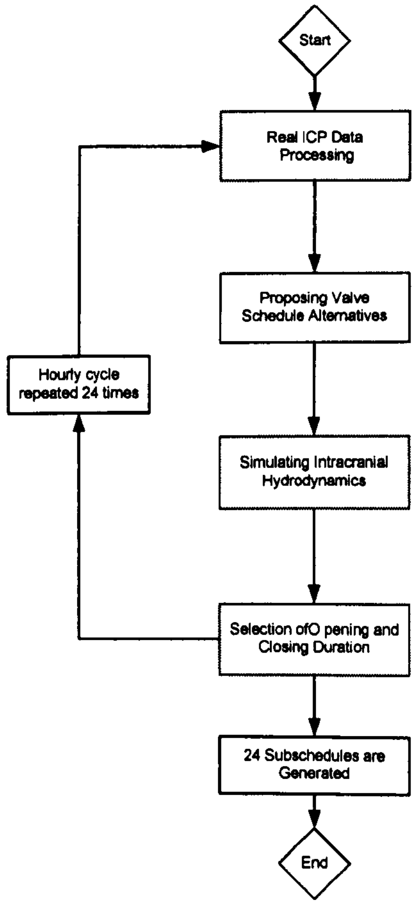


FIGURE 5.4: A general scheduling algorithm.

5.3.1.1 Management of Real ICP Data

A 24-hour ICP trace is collected for the patient as part of the hydrocephalus diagnosis process (*i.e.* before shunting) and is used to derive a personalised valve schedule for him/her. The objective of this step is to instantiate alternatives for the open periods and durations based on the available real data. According to the proposed algorithm, this data is filtered to obtain the variation of average ICP with time. Then the data is divided into one hour samples of a total of 24 samples. The average pressure (ICP_{avg}) is then determined for each sample. Based on this pressure, maximum and minimum total opening durations for each hour ($\triangle t_{min}$ and $\triangle t_{max}$) are calculated. These are the intervals the valve needs to be open in order to reduce ICP_{avg} to the upper and lower normal limits, respectively. The rate of ICP changes for the cases of open and closed valve are estimated, whereas the natural increase/decrease is derived from the real ICP data. The rate of ICP drainage ($\frac{\delta ICP}{\delta t}$), which is pressure dependent, is estimated using numerical simulation for the mechatronic valve. By assuming that the rate of ICP drainage while the valve is open is constant and is not dependent on pressure, the values of $\triangle t_{\mathtt{min}}$ and $\triangle t_{\mathtt{max}}$ can be estimated as follows,

$$\triangle t_{\mathtt{min}} = \frac{ICP_{\mathtt{avg}} - P_{\mathrm{UL}}}{\frac{\delta ICP}{\delta t}} \tag{5.1}$$

$$\triangle t_{\mathtt{max}} = \frac{ICP_{\mathtt{avg}} - P_{\mathrm{LL}}}{\frac{\delta ICP}{\delta t}} \tag{5.2}$$

where $\frac{\delta ICP}{\delta t}$ is the drop in ICP with time when the mechatronic valve is opened, and P_{UL} and P_{LL} are the upper and lower normal limits for ICP, respectively. Thus, the total open duration $d_{\mathtt{tot}}$ for the hour under investigation could take any value between $\triangle t_{\mathtt{min}}$ and $\triangle t_{\mathtt{max}}$ to ensure that the resulting ICP would be between the normal limits, *i.e.* no over/under-drainage occurs.

For each alternative of the total open duration (d_{tot}), ten alternatives for the number of drainage periods per hour (n) are tested, where the open duration

(d_{ON}) (in minutes) for each period is calculated as follows, then it is rounded to the closet integer,

$$d_{ON} = \frac{d_{\mathtt{tot}}}{n}, n = 1, 2, .., 10 \tag{5.3}$$

$$p_{ON} = \frac{60}{n}, n = 1, 2, .., 10 \tag{5.4}$$

n could take the value of zero if there was no need to open the valve *i.e.* ICP is already within the normal limits.

Each of these subschedules is studied individually within a simulated intracranial environment to investigate and monitor its effect on maintaining ICP within normal limits and evaluating its performance as described in the following sections.

5.3.1.2 Simulation of Intracranial Hydrodynamics

Mathematical models ([94], [30], [116], and [113]) were utilised to simulate the intracranial hydrodynamics with a mechatronic valve. To enhance the personalising aspect of the treatment, $Simulink^{TM}$ model was used to implement these equations and at the same time to reproduce the available specific patient's real ICP data. Then the model is used to predict the intracranial hydrodynamics in response to each of the subschedules individually for that specific patient.

5.3.1.3 Performance Evaluation

Based on the output of the simulation for each subschedule alternative, the FoM, described in Chapter 4, is calculated to evaluate the performance of the mechatronic valve under the specified subschedule.

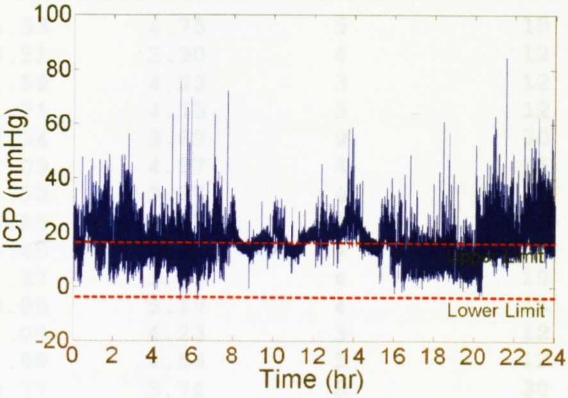
For each hour, the subschedule with the highest FoM among the subschedule alternatives is selected to be part of the final schedule.

5.3.2 Results

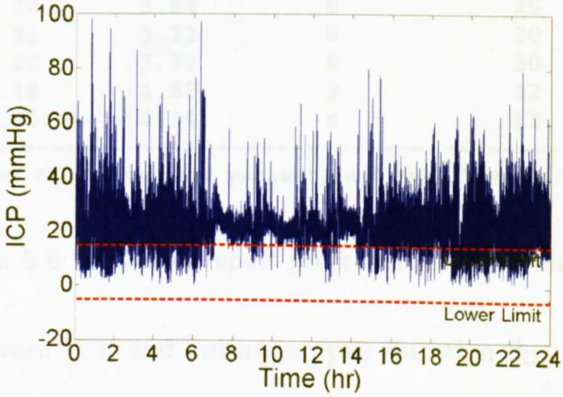
All simulations have been performed for a total of 24 hours, where $Matlab^{TM}$ was used to implement the algorithm while $Simulink^{TM}$ was used for implementing the schedule alternatives on an intracranial hydrodynamics model. The duration of operation required to run such algorithm using $Matlab^{TM}$ was considerably short (around 0.14 seconds per hour) due to the simplicity of the algorithm.

The algorithm was tested by applying it on real ICP data for a group of three hydrocephalus patients. Simulation is done for each hour of the 24 hour separately. Figure 5.5(a) shows real ICP data for one of the hydrocephalus patients, while Figure 5.5(b) shows the reproduced ICP for this patient before treatment. Figure 5.5(c) presents the predicted ICP after adding a mechatronic valve equipped with a personalised schedule that has scored the highest FoM for this specific patient.

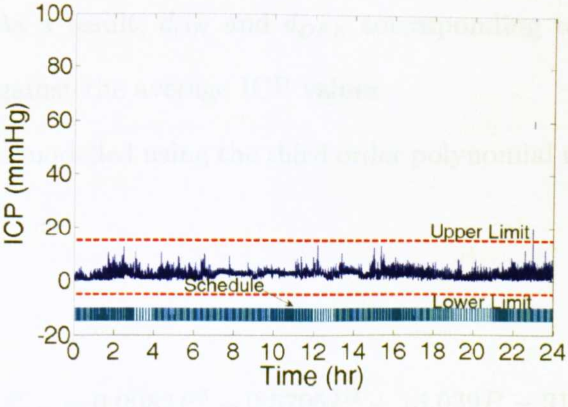
Figure 5.6 shows a sample report generated as an outcome of the algorithm after being automated by $Matlab^{TM}$ and $Simulink^{TM}$. It contains the resultant 24-hour schedule, average ICP before (ICP_b) and after (ICP_a) applying the subschedule for each hour. It also contains the open duration (d_{ON}), closed duration (d_{OFF}) and the maximum FoM value for each hour on which the selection was based.



(a)



(b)



(c)

FIGURE 5.5: ICP traces for hydrocephalus patient. (a) Real ICP, (b) reproduced ICP before adding a personalised scheduled shunt, and (c) predicted ICP after adding a personalised scheduled shunt.

Initial Schedule Design Results
Output Summary

Hour	Mean ICP_b*	Mean ICP_a*	d_{ON}	d_{OFF}	FoM
1	35.33	4.75	5	15	0.7345
2	23.51	3.30	4	12	0.7273
3	21.59	4.23	3	12	0.7326
4	21.71	4.73	3	12	0.7301
5	22.34	3.69	9	30	0.7274
6	22.09	4.97	4	15	0.7256
7	21.58	3.77	4	15	0.7273
8	20.80	4.07	4	15	0.7275
9	24.45	5.37	4	15	0.7233
10	21.37	3.93	4	15	0.7291
11	23.88	5.19	4	15	0.7250
12	21.05	4.23	3	12	0.7297
13	21.88	4.56	3	12	0.7289
14	20.77	3.74	8	30	0.7279
15	24.97	5.16	4	15	0.7284
17	22.35	4.90	3	12	0.7255
18	21.65	4.73	3	12	0.7270
19	21.59	4.23	4	15	0.7273
20	23.22	3.84	6	20	0.7249
21	19.51	3.32	8	30	0.7267
22	22.20	3.72	9	30	0.7233
23	21.18	4.52	3	12	0.7276
24	21.90	4.34	4	15	0.7269

* Mean ICP_b is for the un-shunted patient, and Mean ICP_a is for shunted patient.

FIGURE 5.6: A sample report generated for one of the patients.

The relation between ICP and optimum open duration d_{ON} and closed duration d_{OFF} (that has maximum FoM) was investigated. Numerical simulations were performed for each hour at different average ICP values and the FoM was calculated for each trial. As a result, d_{ON} and d_{OFF} corresponding to the maximum FoM was projected against the average ICP values.

This relation was modelled using the third order polynomial minimum square error fit, as below:

$$d^*_{ON} = 0.0082P^3 - 0.5705P^2 + 13.039P - 91.2460 \tag{5.5}$$

$$d^{*}_{OFF} = 0.0346P^3 - 2.3399P^2 + 51.7150P - 356.1000 \tag{5.6}$$

where P is the average intracranial pressure before applying a scheduled shunt. The above algorithm can help in designing a personalised schedule that has optimum performance based on a figure of merit. The optimisation process can be carried out subsequently to update and further personalise the schedule whenever new real ICP data is provided.

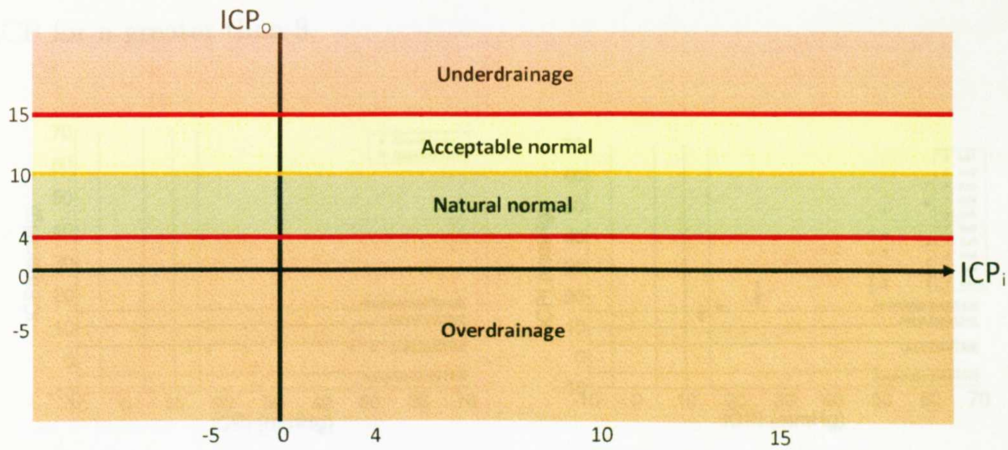
Future enhancements would include incorporating more parameters in developing the initial valve schedule, *e.g.* regular day in the patient life (patient sleeping and working times, type of work, sitting or standing, etc) and other parameters derived from ICP traces, would enhance the performance of initial schedules.

5.3.3 Instantiating a Fixed Initial Valve Schedule

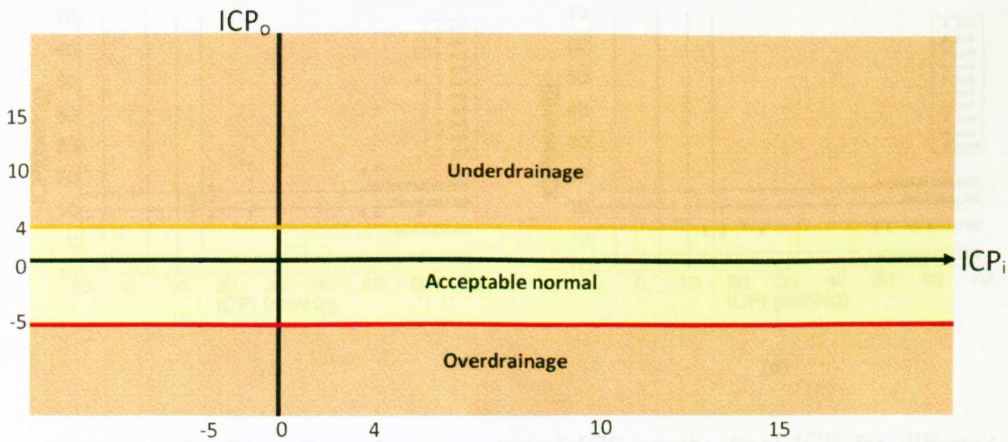
Another alternative for an initial schedule, is a general fixed schedule that is instantiated based on three criteria; intracranial pressure, effective duration time, and figure of merit.

5.3.3.1 ICP Criterion

ICP was calculated for different shunting systems to explore the efficiency of these systems in maintaining ICP either within acceptable normal ranges (4 to 15 mmHg for recumbent posture and -5 to 4 mmHg for erect posture) "acceptable zone" or at tighten range that represent the normal ICP range for a healthy person (4 to 10 mmHg in recumbent posture) "good zone", as shown in Figure 5.7. Each zone has its unique interpretation. In attempt to force the shunting systems to replicate the effect of normal drainage system (that corresponds to the patient's posture) then the target range would be "good zone". Two ICP-related parameters were calculated the average ICP over an hour with and without shunt and average ICP at the start ($ICP_{initial}$) and end (ICP_{final}) of a specific hour. The effect of the initial value of ICP on the performance of the shunt in maintaining final ICP within the "good zone" were investigated.



(a)



(b)

FIGURE 5.7: ICP zones and their interpretation for (a) recumbent posture, and (b) erect posture.

A sample of the results are shown in Figure 5.8. It can be noticed that the standard and closed loop shunts were able to maintain the final ICP within the "accepted zone" regardless of the initial ICP, but only closed loop shunt maintained it within the targeted limits. While not all the scheduled shunts were able to achieve this target. Only schedules with open duration above 25 min for any number of drainage periods succeeded in maintaining ICP within the acceptable limits but falling out the "good zone". Nevertheless, applying the golden rule to minimise the open duration, d_{tot} should equal 15 or 20 min to be able to normalise ICP for n greater than 3.

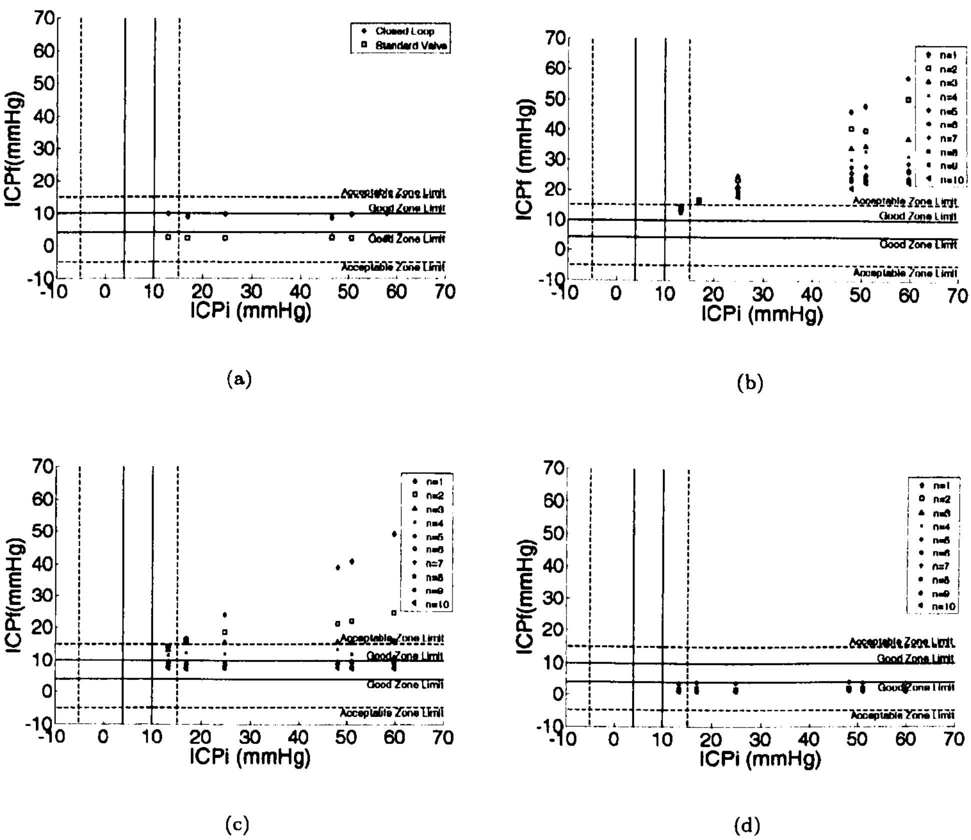


FIGURE 5.8: The effect of varying initial ICP on the final ICP for different shunts (a) standard and closed loop shunt, scheduled shunt at (b) d_{tot}=5min, (c) d_{tot}=15min, and (d) d_{tot}=35min.

Also to reflect the degree of improvement induced due to the applied treatment, average ICP with no shunt versus average ICP with shunt over a specific hour was explored. A sample of such graphs are shown in Figure 5.9. Those graphs indicated that both standard and closed loop shunt succeeded in maintaining any ICP after shunting within "good zone". By looking at the scheduled shunts results, it can be concluded that only few schedules succeeded in reaching the targeted zone. Those has little in common. They characterised by having a total open duration equal or greater than 15 for n equal or greater than 3. In order to minimise open duration and number of drainage periods thus reducing wear and save power, the best schedule that satisfy this condition and at the same time effective enough to keep ICP within the "good zone" is $d_{tot} = 15$ and $n = 4$. It has also been observed that the average ICP after shunting decreases with the increase in the total open duration (d_{tot}) whereas number of drainage periods (n) has a minor effect on it.

5.3.3.2 Total Effective Opening Duration Criterion

Total effective opening duration (t_e) increases with the increase of n, but the rate of the increase in t_e varies as shown in Figure 5.10(b). Thus, it can be considered that there is no significant effect on total t_e as n increases above 4. And since increasing n would be at the cost of power and wear rate, the best choice for n according to this relation would be 4 or less.

On the other hand, total t_e has a parabolic relation with d_{tot}, as shown in Figure 5.10(a), where the maximum total t_e varies with n. It can be noticed that as n increases, maximum total t_e increases and the corresponding d_{tot} decreases till n reaches 4 after which the maximum total t_e always corresponds to d_{tot} equals 15min. As a result of observations, the best range for open duration is [15,30]. But since the golden rule of the mechatronic valve is to minimise the open duration,

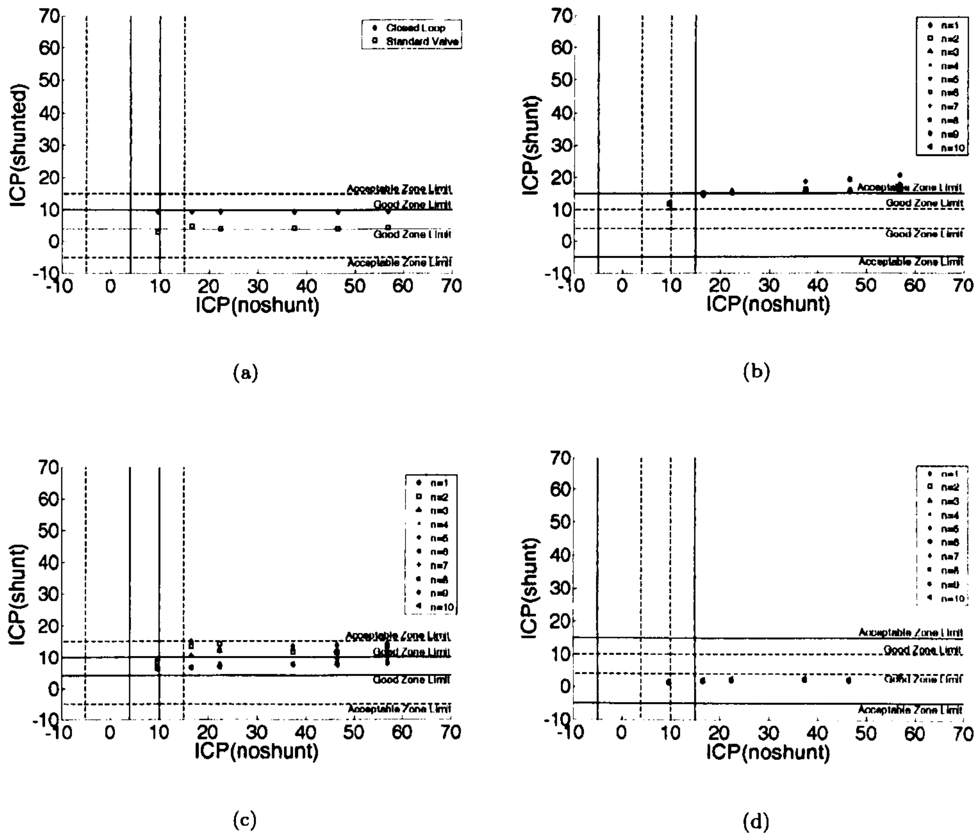


FIGURE 5.9: The effect of different shunting systems on average ICP per hour for various ICP before shunting (a) standard and closed loop shunt, scheduled shunt at (b) d_{tot} =5min, (c) d_{tot} =15min, and (d) d_{tot} =35min.

then the best option would be d_{tot} equals 15min. It is obvious from Figure 5.10(c) that the initial ICP value does not affect the total t_e.

5.3.3.3 FoM Criterion

According to Figure 5.11(a), it has been noticed that increasing (n) is not always associated with an increase in FoM. In addition, a substantial increase in FoM mainly occur when increasing n from 1 to 2 for all tested open durations. In most cases when $n = 1$, the highest FoM was associated with the schedule of open duration equals 30 minutes. On the other hand, the highest for n greater than 1 was associated with open duration 15 and 20 minutes. It can noticed from

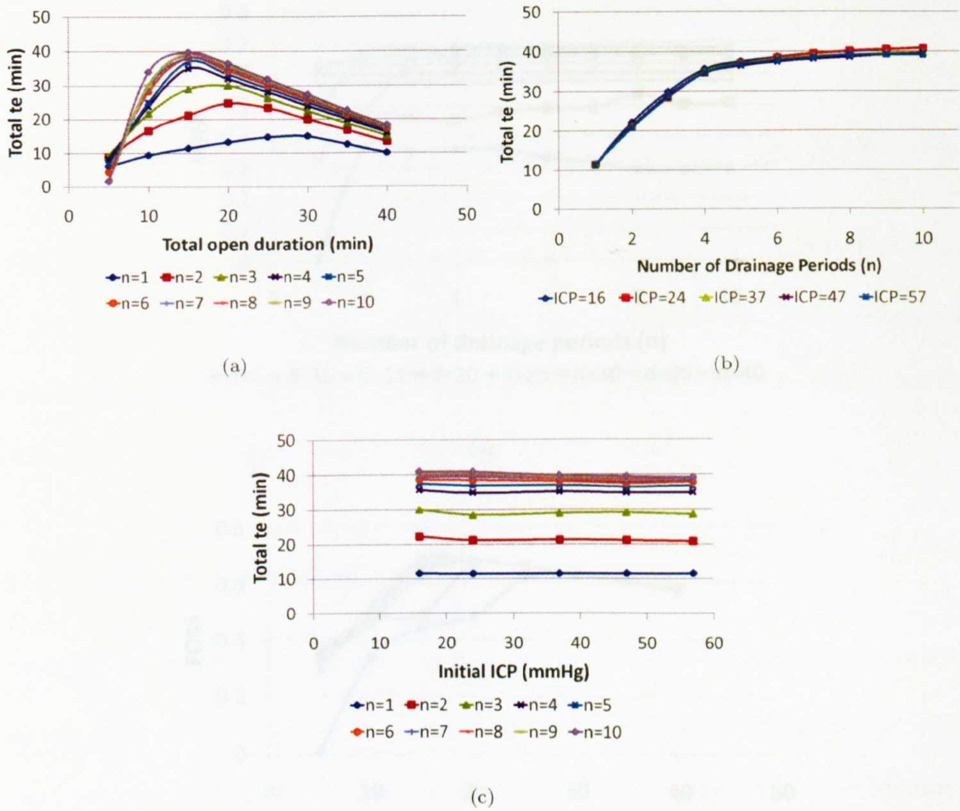
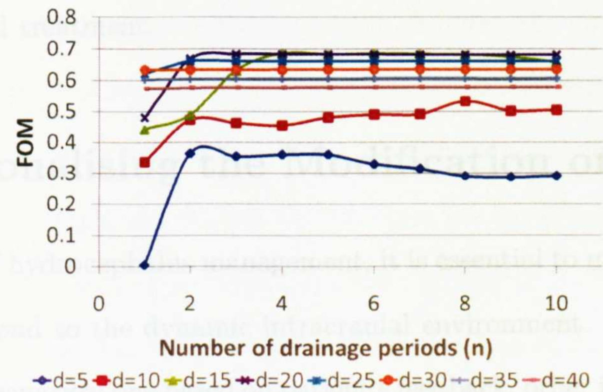


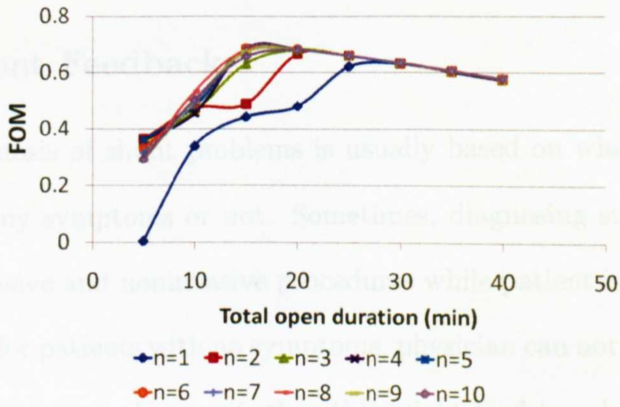
FIGURE 5.10: The effect of schedule parameters on total effective open duration: (a) Total t_e versus open duration, (b) Total t_e versus number of drainage periods, and (c) Total t_e versus initial pressure.

Figure 5.11(b) that FoM has parabolic relation with open duration. Thus there should be an optimum FoM for each d_{tot} and n combination. One can conclude that open duration equals either 15 or 20 minutes can be considered as an initial open duration in the initial valve schedule.

To conclude, based on the FoM criterion, selected n should be more than 2 to eliminate the effect of initial ICP and at the same time optimise FoM, schedule should be d_{tot} = 15min and n = 4,5,7. These empirical models can help in selecting subschedule's parameters that achieve the maximum FoM easily and quickly, especially when the shunting system need to be responsive to the dynamic needs



(a)



(b)

FIGURE 5.11: The effect of schedule parameters on FoM: (a) FoM versus total open duration, (b) FoM versus number of drainage periods.

of the patient in real time situations. Best schedule that satisfied all the criteria was for d_{tot} =15min and n =4.

The resultant schedule based on the above criteria can be used as golden rule for the initial valve schedule and respective relations with ICP, t_e, FoM can be used for modifying the schedule online. The above investigation has proved that using FoM, t_e and ICP as evaluation parameters for the performance of the intelligent shunt is effective whether it is used offline or online, since they can give sensitive relative indication of the management success. On the other hand, these parameters will not be less effective when used in designing the schedule for hydrocephalus management and treatment.

5.4 Personalising the Modification on Schedule

In later stages of hydrocephalus management, it is essential to modify the schedule in order to respond to the dynamic intracranial environment. Such modification will have three scenarios; one based on patient's feedback, other is based on medical intervention and the last based on patient's ICP data.

5.4.1 Patient Feedback

Nowadays, diagnosis of shunt problems is usually based on whether patients are suffering from any symptoms or not. Sometimes, diagnosing such symptoms requires some invasive and noninvasive procedures while patient is hospitalised. On the other hand, for patients with no symptoms, physician can not tell whether their shunts are working properly or not, thus this might lead to a lost opportunity of detecting shunt independence (*i.e.* shunt removal).

Patients suffering from symptoms while having a mechatronic shunt, will be able to reflect the symptoms by giving their feedback to their shunts through the patient device. This feedback will play a vital role in tuning both the management and treatment of hydrocephalus. Thus patient will receive a timely diagnosis and management modification to release the symptoms in almost no time. Thus avoid the uncomfortable experience of waiting for medical consultation, hospitalisation and diagnosis procedures.

In this type of schedule modification, when the patient logs his/her feeling of having some sort of symptom, the shunting system will autonomously request measuring ICP. These readings will be analysed and a decision will be made whether the cause of the symptom is an abnormality in intracranial hydrodynamics. Based on this decision, shunting system would either modify the schedule according to the new situation and inform the patient the problem has been solved or just inform the patient that the cause of the symptom was not due to ICP abnormality. The flow chart in Figure 5.12 illustrates this modification based on patient feedback.

5.4.2 Medical Intervention

Mechatronic shunting system will have the option of enabling the physician to intervene the management at any time. This intervention could involve any update on the schedule, or on the parameters affecting the decision making process *e.g.* normality limits of ICP, symptoms interpretation, or the intelligent software, *e.g.* by adding more parameters to be involved in the modification process. In addition physician with the help of the shunting system will withdraw a decision regarding the progressive shunt removal procedures.

5.4.3 ICP Data

Schedule can be modified based on either the average ICP per hour or reference values calculated for different patient parameters.

5.4.3.1 Modify Schedule Based on Average ICP

In this method, the schedule is modified by following the same algorithm described in Section 5.3.3, where schedule parameters are calculated based on the real-time

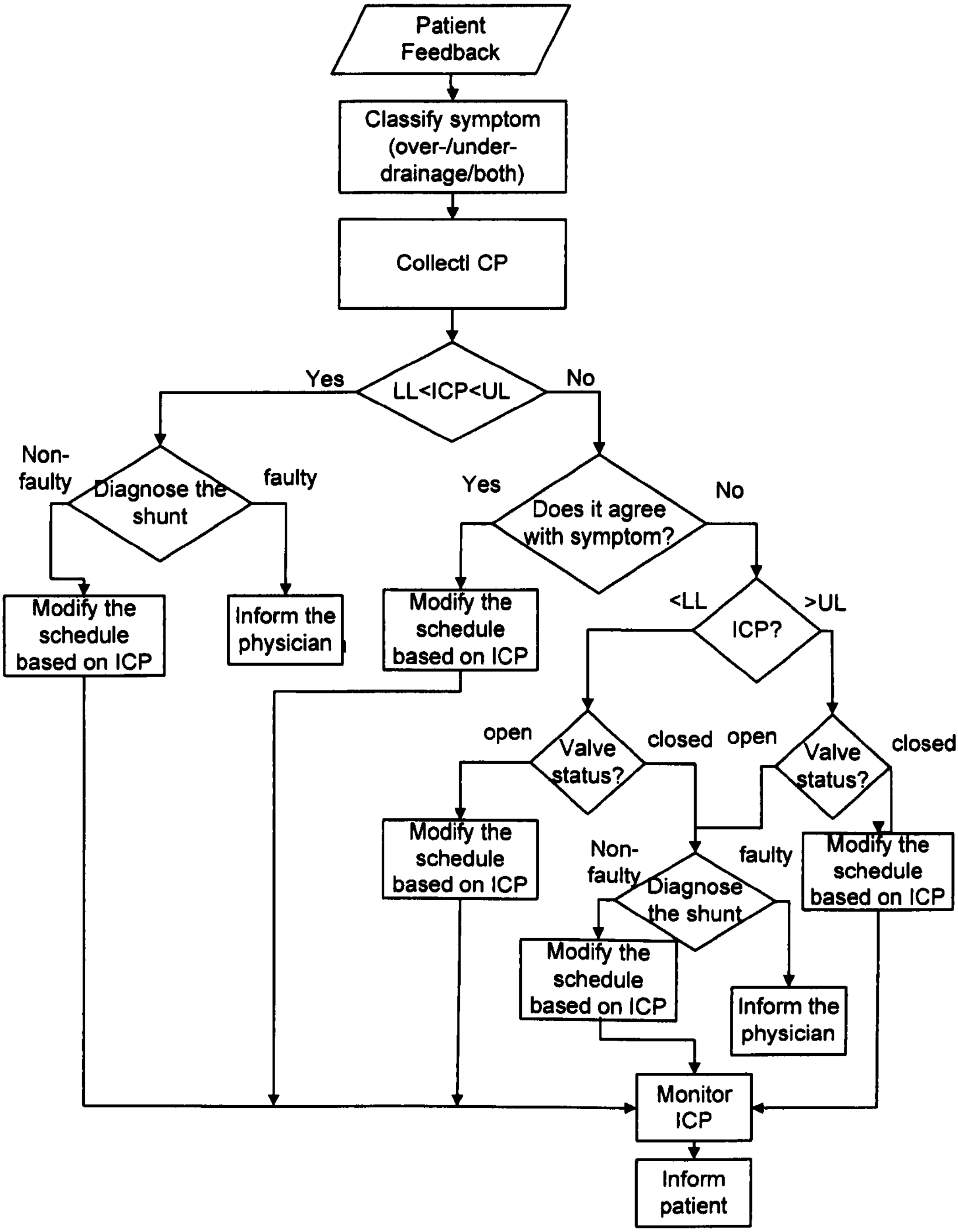


FIGURE 5.12: Schedule modification based on patient feedback.

average ICP per hour. Thus responding to the dynamic changes in real-time and personalising the management.

5.4.3.2 Modify Schedule Based on Reference Values

In this section different parameters that characterise the mechatronic valve behavior were identified and investigated to help in understanding the effect of using this type of valves on the intracranial hydrodynamics. As a result, these parameters would facilitate the process of selecting a personalised schedule that respond to the patients' needs.

To maximise the gain of such investigation, the relations among management parameters (*e.g.* effective open duration, FoM), schedule parameters and initial ICP values were modelled. Such models would be valuable assets and considered as rules of thumb for an implanted shunting system that would autonomously modify the valve schedule based on these rules.

In this work, the following parameters were investigated,

- Average ICP (ICP_{avg}): is the average ICP per hour after applying a sub-schedule. Studying the relation of this parameter with d_{tot} and n, would help in selecting and modifying processes of the valve schedule. In other words, this relation could give an indication of the effect of using specific values of d_{tot} and n on the value of the average ICP.

- Rate of ICP change ($\frac{\delta ICP}{\delta t}$): This rate is calculated while the valve is open. Estimating such parameter helps in the process of diagnosing the shunt for the occurrence of faults. In real-time the shunt would calculate this parameter from the measured ICP values and compare it with an estimated one. This parameter also can be used to predict the behaviour of ICP when valve is open thus help in selecting an appropriate valve schedule. In addition, the direction of change in $\frac{\delta ICP}{\delta t}$ is a good indication of occurence of any risk especially when applying treatments. Three types of $\frac{\delta ICP}{\delta t}$ were investigated,

1. Rate of ICP change of the first opening period (for each hour) (as shown in Figure 5.13(a),

$$\left(\frac{\delta ICP}{\delta t}\right)_{first} = \frac{ICPs_{S_{first}} - ICP_{E_{first}}}{d_{ON}} \tag{5.7}$$

where $ICP_{S_{first}}$ and $ICP_{E_{first}}$ are the average ICP at the start and end of the opening period, respectively. d_{ON} is the open duration.

2. Rate of ICP change between the start of the first opening period and the end of last opening period for each hour (as shown in Figure 5.13(b)),

$$\left(\frac{\delta ICP}{\delta t}\right)_{first-last} = \frac{ICP_{S_{last}} - ICP_{E_{first}}}{d_{tot}} \tag{5.8}$$

where $ICP_{S_{first}}$ and $ICP_{E_{last}}$ are the average ICP at the start of the first open period and the end of the last opening period for specific hour, respectively. d_{tot} is the total open duration for that specific hour.

3. Rate of average ICP change per hour,

$$\frac{\delta \overline{ICP}}{\delta t} = \frac{\overline{ICP}_{before} - \overline{ICP}_{after}}{60min} \tag{5.9}$$

where $\overline{ICP}_{before}$ and $\overline{ICP}_{after}$ are the average ICP for specific hour before and after modification, respectively.

- Effective opening duration (t_e): It is the subsequent interval following the opening period (while valve is closed) during which ICP maintained within normal range as a result of the previous opening period. t_e is illustrated in Figure 4.3. The estimated t_e will help in selecting and modifying the valve schedule according to the following formula,

$$(d_{ON} + d_{OFF}) \geq (d_{ON} + t_e) \tag{5.10}$$

This inequality should apply on the schedule parameter in order to avoid the overlapping between consecutive open duration and effective time (*i.e.* open the valve while ICP is already normal). And for the schedule to be efficient, t_e should equal d_{OFF} to avoid any abnormality while valve is closed.

Knowing that,

$$\frac{T}{n} = d_{ON} + d_{OFF} \tag{5.11}$$

where T is duration covered by this subschedule, in this work it was considered one hour (60 min).

and that,

$$d_{ON} = \frac{d_{tot}}{n} \tag{5.12}$$

then Equation (5.10) would be,

$$\frac{T}{n} \geq (\frac{d_{tot}}{n} + t_e) \tag{5.13}$$

or,

$$T \geq (d_{tot} + n \cdot t_e) \tag{5.14}$$

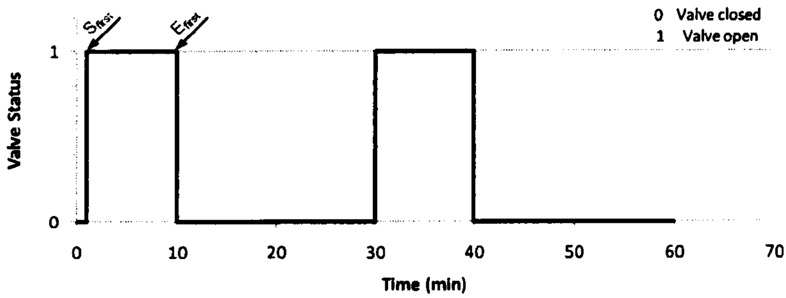
So if an estimated value for t_e is known then d_{tot} and n can be calculated that satisfy the inequality in the previous equation.

- FoM: It is a measure for the performance of the schedule. The objectives of studying this parameter are to measure the improvement in the delivered management and determine the corresponding d_{tot} and n that correspond to the optimum FoM. Thus the possibility of delivering better management is increased.

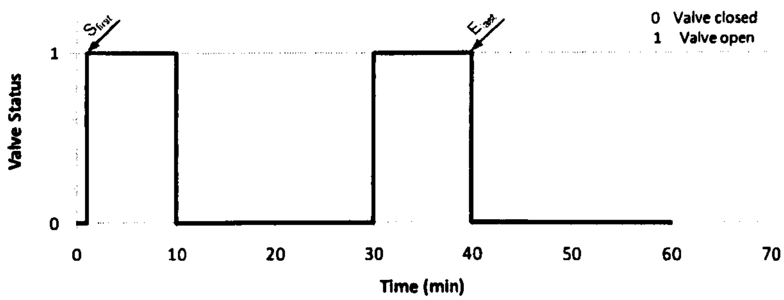
5.4.3.3 Simulations

Numerical simulations were carried out to find out the effect of opening duration and number of drainage periods per hour on different patient's and valve's parameters, *e.g.* average ICP, rate of ICP change, effective opening time and figure of merit. This is an intermediate step to attempt generating rules of thumb for the mechatronic shunt behavior which can help in personalising the schedule and on the long run helping in revising the schedule dynamically to interact with the environment.

For different intracranial pressure levels, opening duration per hour (d_{ON}) and number of drainage periods per hour (n) were varied and the corresponding simulated intracranial hydrodynamics was studied. Furthermore average ICP (ICP_{avg}), rate of ICP change ($\frac{\delta ICP}{\delta t}$), effective opening duration (t_e) and figure of merit (FoM) were calculated and compared.



(a)



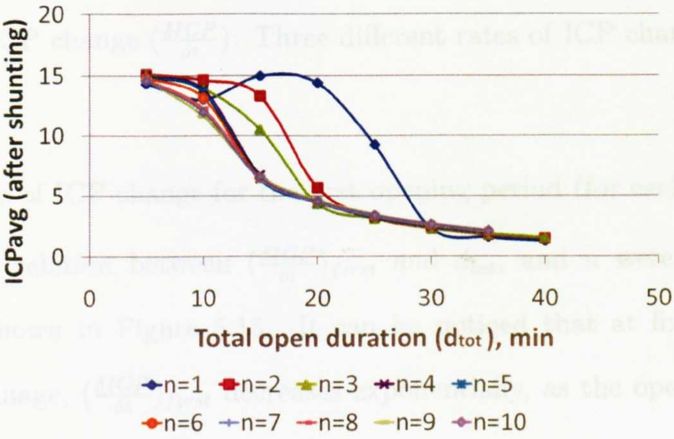
(b)

FIGURE 5.13: Locations at which ICP was measured. (a) at the beginning and end of the first open period per hour, (b) at beginning and end of the hour.

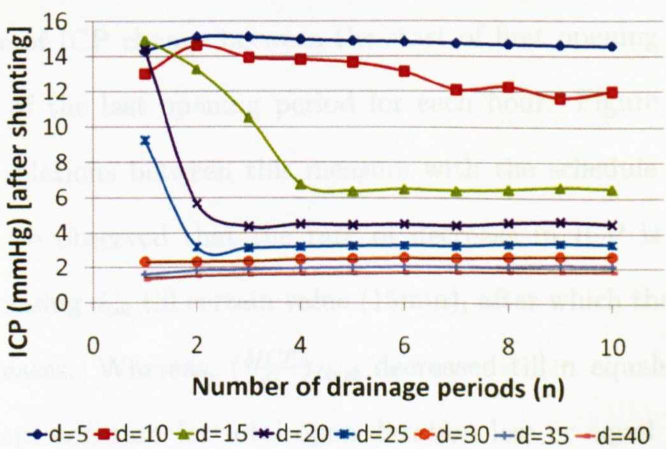
5.4.3.4 Results and Data Analysis

The outcome of the numerical simulations for the effect of ICP, d_{ON} and n on the different parameters has been analysed and the relations among them were modelled using the minimum square error fitting in an attempt to derive some rules of thumb that might help in personalising the valve schedule. Thus knowing ICP, d_{ON} and n, can be used to predict the response of ICP, which can be utilised a reference point for the implanted intelligent system to use it to modify the schedule and detect any fault (*i.e.* ICP and shunt monitoring).

- Average ICP (ICP_{avg}): The effect of different schedules on the average ICP after shunting was observed. Figures 5.17(a) and 5.17(b) illustrate such effect. The following notes were concluded about these relations:



(a)



(b)

FIGURE 5.14: The effect of schedule parameters on average ICP: (a) average ICP vesus open duration, and (b) average ICP vesus number of drainage periods.

It was noticed that there is no significant effect of the initial pressure (before modifying) on the average pressure after applying the modification. Thus it was not taken into consideration when modelling average ICP with the total open duration as follows,

$$ICP_{avg} = A \times d_{tot}^2 + B \times d_{tot} + C \tag{5.15}$$

where the values of A, B and C are dependent on the number of drainage periods.

- Rate of ICP change ($\frac{\delta ICP}{\delta t}$): Three different rates of ICP change were modelled,

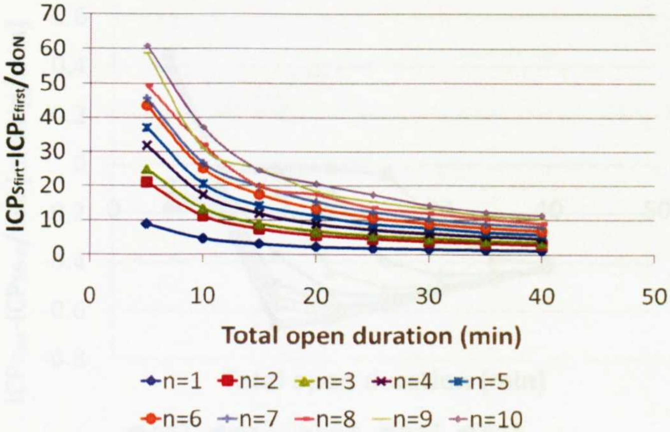
  1. Rate of ICP change for the first opening period (for each hour):

     The relation between $(\frac{\delta ICP}{\delta t})_{first}$ and d_{tot}, and n were modelled. It is shown in Figure 5.15. It can be noticed that at fixed number of drainage, $(\frac{\delta ICP}{\delta t})_{first}$ decreases exponentially, as the open duration increased. On the other hand, the relation between the rate of ICP change varies proportionally with the number of drainage periods.

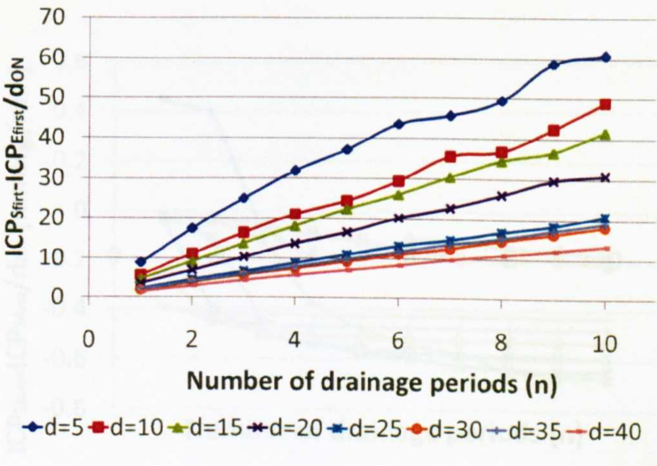
  2. Rate of ICP change between the start of first opening period and the end of the last opening period for each hour: Figure 5.16 illustrates the relations between this measure with the schedule parameters. It can be observed that the rate of decrease in ICP is increased with increasing d_{tot} till certain value (15min), after which the $(\frac{\delta ICP}{\delta t})_{first-last}$ increases. Whereas, $(\frac{\delta ICP}{\delta t})_{first}$ decreased till n equals 3, after which it kept constant for total open duration less or equal 30 min. Above these values of open duration, n did not have effect on $(\frac{\delta ICP}{\delta t})_{first}$. It has been noticed that the effect of n on $(\frac{\delta ICP}{\delta t})_{first-last}$ is very small especially when n greater than 1 for d grater than 5min.

  3. Rate of average ICP change ($\frac{\delta \overline{ICP}}{\delta t}$):

     It has been observed from Figure 5.17 that n had almost negligible effect on $\frac{\delta \overline{ICP}}{\delta t}$ for all d_{tot} values. And as expected $\frac{\delta \overline{ICP}}{\delta t}$ increased with increasing total open duration.



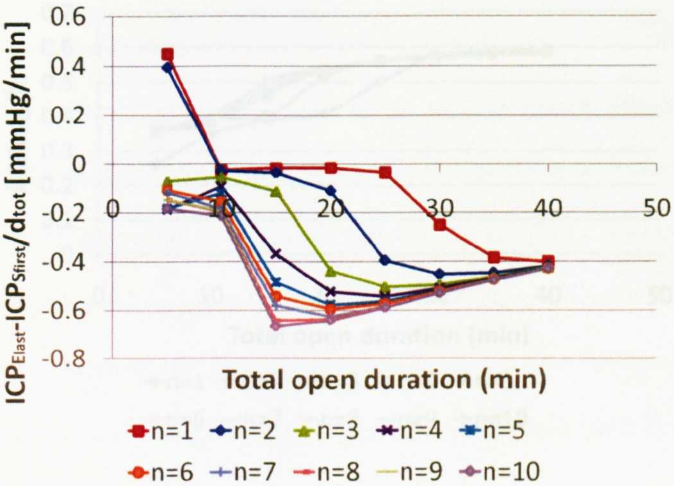
(a)



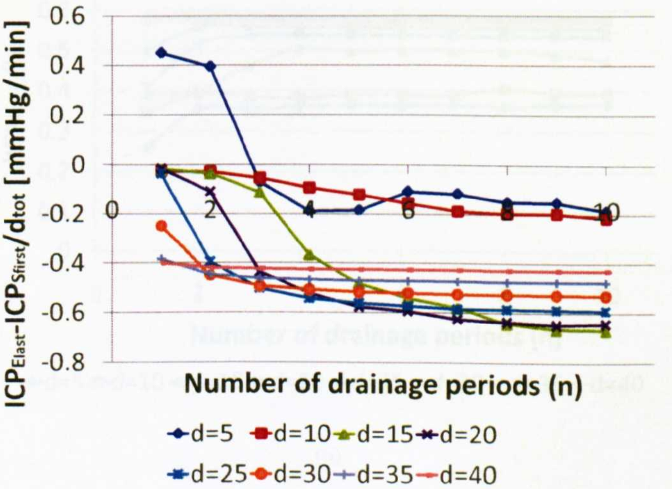
(b)

FIGURE 5.15: The effect of schedule parameters on average ICP: (a) $(\frac{\delta ICP}{\delta t})_{first}$ vesus open duration, and (b) $(\frac{\delta ICP}{\delta t})_{first}$ vesus number of drainage periods.

- Effective opening duration (t_e): A formula has been statistically derived to estimate t_e. The effect of ICP, n, and d_{tot} on t_e is investigated. As a result of numerical simulation, it was found that t_e dependant only of d_{tot} and n. The effect of ICP on t_e is negligible as shown in Figure 5.18(a). Figures 5.18(b) and 5.18(c) illustrate the relation of t_e with d_{tot} and n, respectively. As the number of drainage increases, effective open duration decreased per



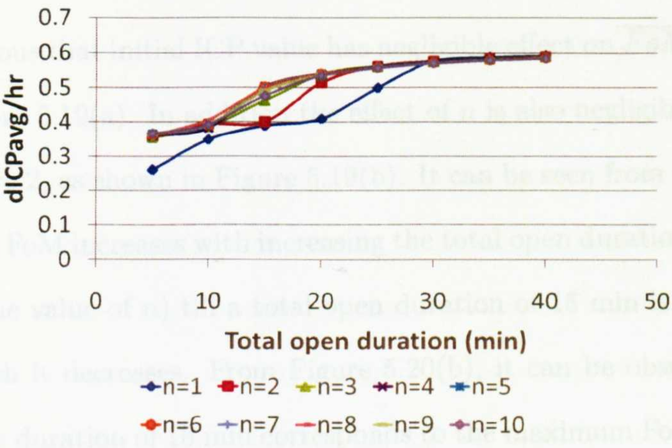
(a)



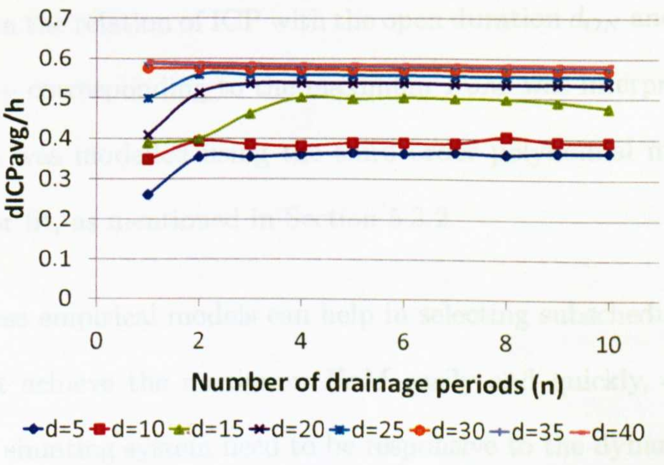
(b)

FIGURE 5.16: The effect of schedule parameters on average ICP: (a) $(\frac{\delta ICP}{\delta t})_{first-last}$ vesus open duration, and (b) $(\frac{\delta ICP}{\delta t})_{first-last}$ vesus number of drainage periods.

an open period but the overall effective duration per hour increases as shown in Figure 5.10(b). Thus helping in maintaining ICP normal for longer time. As for the relation between t_e with d_{tot}, t_e is increased with the increase in d_{tot} till it has reached a maximum value, after which it has decreased. The



(a)



(b)

FIGURE 5.17: The effect of schedule parameters on average ICP: (a) $\frac{\delta \overline{ICP}}{\delta t}$ vesus open duration, and (b) $\frac{\delta \overline{ICP}}{\delta t}$ vesus number of drainage periods.

decrease in t_e is due to the fact that open duration is too long thus it overlaps with the effective open duration, *i.e.* there is redundancy in open duration. Knowing the value of total open duration that maximises the effective open duration would help in optimising the open duration. At this turning point, t_e and its corresponding open duration increase with the increase in n.

- Figure of merit ($\overline{FoM}$) FoM was investigated in two aspects.

    1. First the relations between $\overline{FoM}$ and ICP, d and n were explored. It is obvious that initial ICP value has negligible effect on $\overline{FoM}$, as shown in Figure 5.19(a). In addition the effect of n is also negligible for n values above 2, as shown in Figure 5.19(b). It can be seen from Figure 5.20(a) that FoM increases with increasing the total open duration (irrespective of the value of n) till a total open duration of 15 min is reached, after which it decreases. From Figure 5.20(b), it can be observed that the open duration of 15 min corresponds to the maximum FoM for n equals to 3.

    2. Then the relation of ICP with the open duration d_{ON} and close duration d_{OFF} corresponding to the maximum FoM was interpreted. The relation was modelled using the third order polynomial minimum square error fit, as mentioned in Section 5.3.2.

    These empirical models can help in selecting subschedule's parameters that achieve the maximum FoM easily and quickly, especially when the shunting system need to be responsive to the dynamic needs of the patient in real time situations.

All relations were modelled using minimum square error fit and are enclosed in Appendix E. Utilising these models in estimating a reference values for the above measures at specific schedule parameters can help in developing and modifying a personalised schedule with an intelligent shunting system.

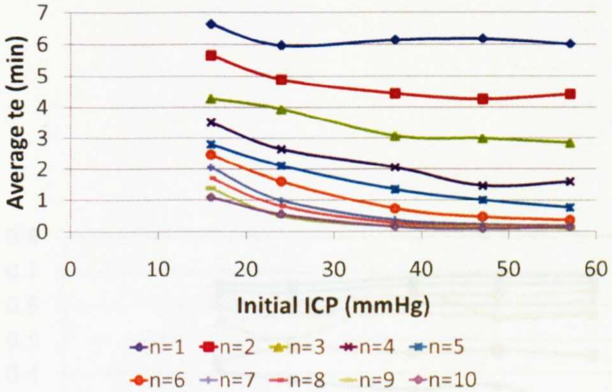
5.5 Conclusions

Algorithms were proposed that would help in developing a personalised schedule for mechatronic valve that dynamically change based on the patients own data (*e.g.* ICP and feedback), a novel figure of merit and other performance measures, thus providing the physician with an easy tool that facilitate the use of such valve. The numerical simulations have illustrated the effectiveness of the algorithm in providing a personalised schedule that maintain ICP within the normal limits.

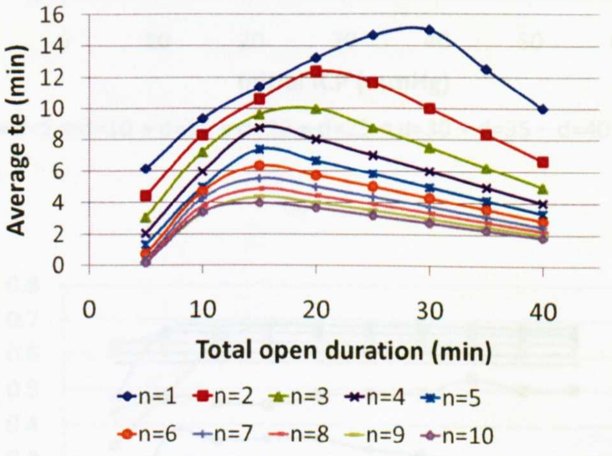
Personalising the management of hydrocephalus in the proposed intelligent shunting system is not an easy task. Thus integrating any additional inputs, *e.g.* reference values for the performance measures, would help in tuning and enhancing the personalised schedule.

Reaching a stage at which the mechatronic shunt autonomously could personalise the management of hydrocephalus would dramatically reduce the number of patient's complaints about their shunts. Such management is especially vital for patients suffering of unresolved problems with their conventional shunts.

Treating hydrocephalus by training the natural drainage system to either accommodate moderate intracranial pressures or to be (re)activated is the objective of the next chapter. By resolving such issue, the desire of hydrocephalus patients of being shunt-free, become a step closer to realisation.



(a)



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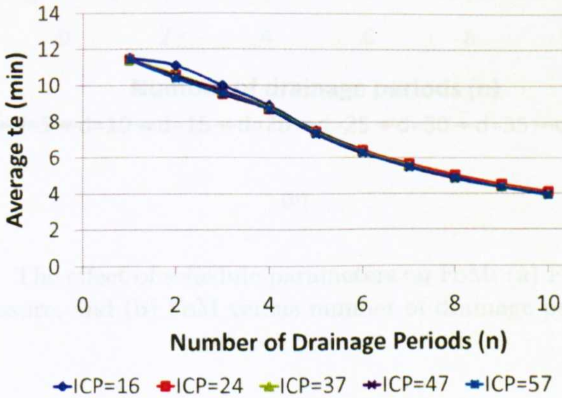
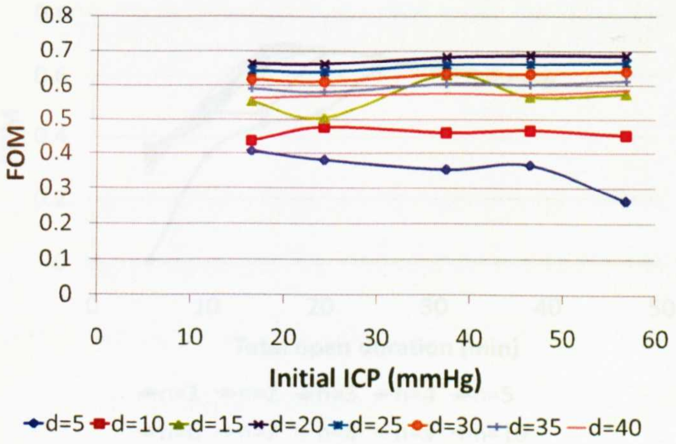
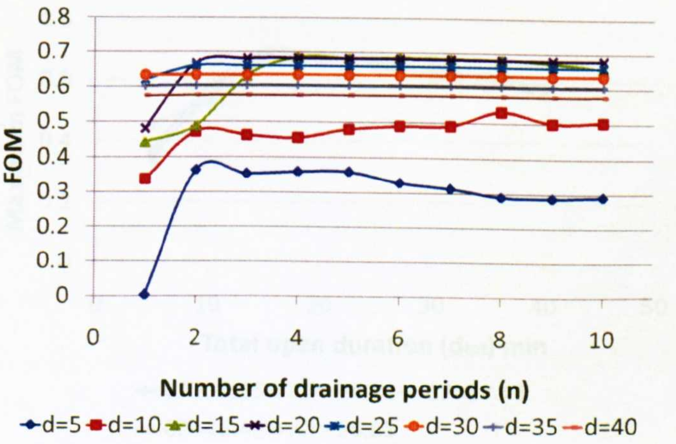


(c)

FIGURE 5.18: The effect of schedule parameters on effective open duration: (a) te versus initial pressure, (b) te versus open duration, and (c) te versus number of drainage periods.

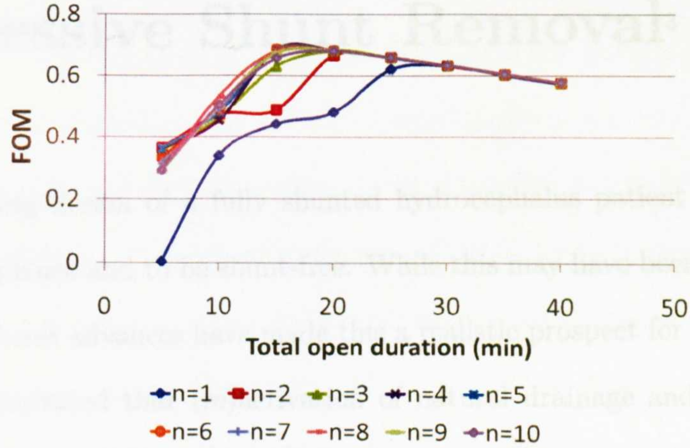


(a)

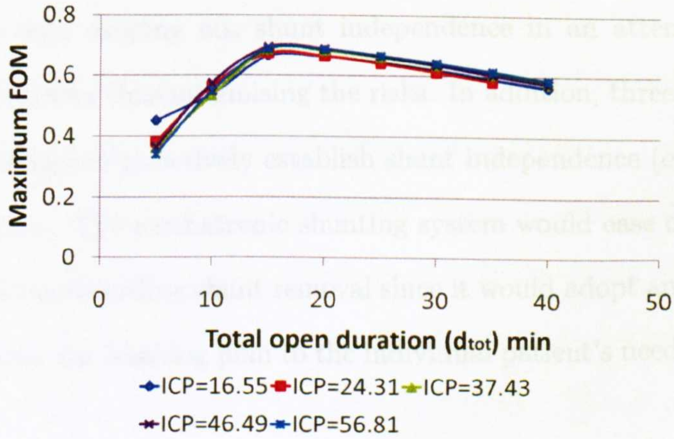


(b)

FIGURE 5.19: The effect of schedule parameters on FoM: (a) FoM versus initial pressure, and (b) FoM versus number of drainage periods.



(a)



(b)

FIGURE 5.20: The effect of schedule parameters on FoM: (a) FoM versus total open duration, and (b) Maximum FoM versus total open duration.

Chapter 6

Progressive Shunt Removal[3]

The ever-lasting dream of a fully shunted hydrocephalus patient is to (re)gain shunt independence and to be shunt-free. While this may have been only a dream in the past, recent advances have made this a realistic prospect for some. Clinical trials have illustrated that (re)activation of natural drainage and adapting the patient to abnormal ICP levels is achievable.

In this chapter, a new technique is introduced to determine the actual shunt dependence and then singling out shunt independence in an attempt of progressively shunt removing thus minimising the risks. In addition, three novel enhancements are investigated to actively establish shunt independence (controlled arrest of hydrocephalus). The mechatronic shunting system would ease clinician and researchers concerns regarding shunt removal since it would adopt an algorithm that would personalise the weaning plan to the individual patient's needs and response.

6.1 Introduction

Shunt designers modified shunt goals to have the option of re-establishing shunt independence step by step. Especially that most patient seems to be only partially

[3]Part of this chapter has been published under the title "Reduction of Mechatronic Shunt Dependency for Hydrocephalus Patients" , 4th Annual Symposium of the Benelux Chapter of the IEEE Eng Med Biol Soc. (EMBS), November 9-10, 2009, University of Twente, The Netherlands.

shunt dependent which even allows the eventual removal of the shunt. This means that the statement of Hemmer "once a shunt, always a shunt" may no longer be true, as the next generation of shunts should be able to achieve a controlled arrest of hydrocephalus in the long run.

The possibility of shunt removal for hydrocephalus patients has been controversial. In the 80s and 90s, shunt removal in hydrocephalus patients has been intensively argued and investigated in literature. Nowadays this interest has faded even though the valve technology has developed significantly since then.

So-called "weaning" has been considered in the literature in two different aspects. First one was passive, in which all trials were directed towards singling out shunt independence that has been naturally and spontaneously developed by the patient for different reasons (*e.g.* premature babies' natural drainage developing with time). Thus the patient no longer needs a shunt. In this case, the researchers' and clinicians' focus was on developing methods to identify such shunt independence to help in making a decision regarding shunt removal. In general, methods used were based simply on detecting the non-functionality of the valve that might have occurred for various reasons such as blockage, disconnection or mechanical faults. As patients in these cases do not tend suffer from any symptoms, they do not complain, making the identification of such cases difficult. In the other aspect, only few researchers [107] handled shunt removal and shunt dependence actively, *i.e.* the controlled arrest of hydrocephalus (shunt weaning). This is defined as shunt removal after subsequent steps of gradual brain adaptation to high intracranial pressure (ICP) that will not only normalise the ventricular size but also activates the regular circulation of cerebrospinal fluid (CSF).

6.1.1 Current Methodologies for Shunt Removal

Nowadays, some issues are considered before removal of the shunt such as hydrocephalus type (*e.g.* communicating and non-communicating) and status (*e.g.* not present anymore, arrested, compensated, uncompensated), shunt status (*e.g.* functional, non-functional) and the risks and benefits of shunt removal [119]. Current methodologies for shunt removal can grouped into singling out shunt independence and shunt weaning.

6.1.1.1 Singling Out Shunt Independence

Special tests have been used to measure CSF flow in an attempt to detect valve functionality through measuring shunt dependent flow. For example, thermometric measurements, *i.e.* heating/cooling of the flowing CSF [93] or valvography (*i.e.* injection of radiopaque dye into shunt) [44]. These methods are considered unreliable and impractical in the clinical settings. Others [43] have used implantable devices to measure CSF flow, but it is difficult to draw conclusion when the test shows no flow whether flow is so low that it can not be detected or there is no flow at all due to non functionality/idleness of the valve. In addition, some methods (*e.g.* [65]) for singling out shunt dependence are based on determining outflow resistance of the natural drainage system. These tests were extremely invasive and involved temporal occlusion of the valve, placement of an ICP monitor and infusion of fluid into the subarachnoid or ventricular space under general endotracheal anesthesia.

6.1.1.2 Shunt Weaning

Controlled arrest of hydrocephalus is performed by shunt removal after subsequent steps of gradual brain adaptation to high intravenous pressure that is expected not only normalise the ventricular size but also activate the regular circulation of CSF [10]. Takahashi [107] attempted to increase the pressures of adjustable valves stepwise, and managed to remove 59% of shunts out of 114 shunted patients within 2 years. Unfortunately, this study lacks longer observations and sufficient data, although these trials demonstrate that there is an unexhausted potential for a controlled arrest of hydrocephalus [119]. His work illustrated that the success rate of shunt removal becomes significantly higher when programable valves are used restoring normal CSF circulation by gradually increasing the pressure. He also concluded that it is possible to remove the shunt systems in 50% or more of pediatric hydrocephalus cases in which programmable valves was used [107]. According to Takahashi's methodology, if the patient did not develop symptoms of intracranial hypertension and there was no significant ventricular enlargement, the valve pressure was quickly increased over months to 14.7 mmHg (200 mm H_2O) and then removed. Patients who developed intermittent symptoms were weaned more slowly, and if "clear" symptoms did not develop, the shunt was removed. Takahashi's interesting investigation, and some basis for his approach may come from earlier studies in cats suggesting that increasing ICP may open or activate existing CSF absorptive pathways [34]. However, Whitehead [119] has raised a question whether shunt removal ever worth the risk. And he concluded that it is difficult to draw firm conclusions from Takahashi's work because follow-up is short and ill defined, and objective neuropsychiatric evaluations were not performed [119].

6.1.2 Risks and Benefits

Generally clinicians believe that there are limited clinical situations that would warrant a trial of shunt removal because of the significant risks involved. In addition, considerable literature sources agree that regardless of circumstances, removing a shunt from a patient who needs it can lead to subtle intellectual and developmental decline, intracranial pressure increase with irreversible injury to neural tissue and even sudden death [119]. These concerns are mainly due to the lack of non-invasive means to determine shunt dependence and to monitor intracranial hydrodynamics thus making shunt removal a highly risky proposition that could potentially endanger patient's life.

Removal of the shunt can have psychological benefits for the patient and family. In addition, the patient is no longer threatened by the complications of infection or overdrainage. The risk in shunt removal that there is no absolute indication to put a patient through a trial of shunt removal [119].

6.2 Progressive Shunt Removal

Invention of mechatronic valve [74] has inspired the introduction of mechatronic shunting system that autonomously monitors both ICP and shunt itself and responds to patient needs. The mechatronic shunt will decide when to start weaning process based on patient's intracranial hydrodynamics after consulting this decision with a physician.

The mechatronic valve is easily opened at any required pressure. The wean threshold (*i.e.* opening pressure) will be increased in smoother steps thus providing safer shunt weaning process with much less risk than programmable valves, since the patient and the shunt are continuously monitored. In addition, the proposed system will be able to identify any possibility of sudden increase in ICP thus eliminating the risks associated with current wean methodologies.

The proposed system will be similar to Logatti and Carteri implantable system [64], except that it is implementing an implantable pressure sensor and mechatronic valve. At the same time the system will be following the basics of Takahashi's methodology in achieving controlled arrest of hydrocephalus.
The proposed system will have two main tasks; capture the actual shunt dependence and gradually reduce it.

6.2.1 Capturing the Actual Shunt Dependence

Capturing actual shunt dependence is an important issue in determining whether the patient (still) requires a shunt or not. Especially that in most of the cases, the patient is only partially shunt dependent, varying from 1% to 100%. Unfortunately, current shunts do not distinguish the patients in this aspect, thus most probable, on the long run, patients are turned to be fully shunt dependent. A scheduled closed loop will be implemented to capture the actual shunt dependence. A schedule will determine the periods of time at which the valve is either closed or operating in closed loop mode. This schedule that has been personalised in Chapter 5 and it satisfies this specific-patient for a reasonable period of time. While the valve is in a closed loop mode, it will only open if the ICP readings are above certain threshold, *i.e.* the upper normal limit, Th_n (10 mmHg). For each hour the percentage of time per drainage at which the valve was open is calculated. Then this value is used in addition to the percentage of time ICP is maintained within normal limits per hour and the rate of change of ICP during closed valve periods, to update the schedule of the closed loop for that hour. Open duration will be decreased till it reaches a point at which the increase in ICP can not be handled.

$$\%\text{Open duration per hour (OD)} = \frac{\text{Actual open duration}}{\text{Duration of closed loop mode}} \times 100\%$$

$$\%\text{Duration of ICP normal} = \frac{\text{Duration ICP is normal}}{\text{One hour}} \times 100\%$$

$$\text{Rate of ICP change (at closed valve)} = \frac{\Delta ICP}{\text{One hour}}$$

The resultant percentage of open duration will represent the actual shunt dependence. In the long run, if the open duration is around zero and ICP is still maintained normal, this indicates a possibility of shunt removal. The decision is empowered if the rate of change of ICP at close periods is around zero.

6.2.2 Reducing the Shunt Dependence

After the actual dependence is captured, an algorithm will reduce the dependence to a level that is accommodated by patient in an attempt of achieving shunt independence. Utilising a mechatronic valve with an implanted pressure sensor will enable fine tuning of the opening valve pressure thus performing the weaning process more smoothly. In contrast to the documented trials, when shunt independence is reached, the mechatronic shunt will not be removed but kept in sleeping mode. The shunt would be only activated as a closed loop system in case of any arising emergency thus avoiding any risk on patient's life. At this stage, the system would non-invasively monitor the activity of the shunt thus warranting the success of prospective shunt removal on the long run. Having such system should give a relatively absolute indication whether to put a patient through a trial of shunt removal.

Three methodologies for controlled arrest of shunting system were investigated and compared. These methodologies are closed-loop timed threshold, schedule with shrinking slots and scheduled closed-loop. Each of these methodologies will gradually attempt in its way to personalise the reduction of shunt dependence while considering patient response based on evaluation measures such as rate of ICP increase, the figure of merit, average ICP and mean absolute deviation. Implementing such methodologies would avoid subjecting the patient to any shunt removal disappointments and avoid endangering his/her life.

6.2.3 Characteristics of Proposed Shunt

The proposed system will reduce the risks associated with current shunt removal, due to its ability to give relatively absolute indication whether to remove the shunt or not. In addition, it will be able to monitor the ICP and the shunt itself for the patient before, during and after weaning process. Thus most issues (aspects) that usually arise when removing a shunt would either answered or does not apply. As a result of this, long fellow-up periods will be provided. Especially that the shunt will not be removed, it will be just monitoring ICP and valve is kept in sleeping mode for a reasonable period of time to be activated in case of emergency. It also could have the option of performing psychiatric test for the patient that is embedded in the patient device. Mechatronic shunt, in contrast to current weaning methodologies will aim to single out the functionality and idleness of the valve instead of just its functionality. Finally, the valve does not need to be changed while increasing the open pressure threshold during weaning process, as it is the case in the programmable valves, since mechatronic valve can be opened at any pressure.

6.3 Patient Types

Previous shunt removal studies (*e.g.* [107], [64]) revealed that intracranial hydrodynamics respond to temporarily occluded valves in different ways. These can be grouped into four types, as shown in Figure 6.1.

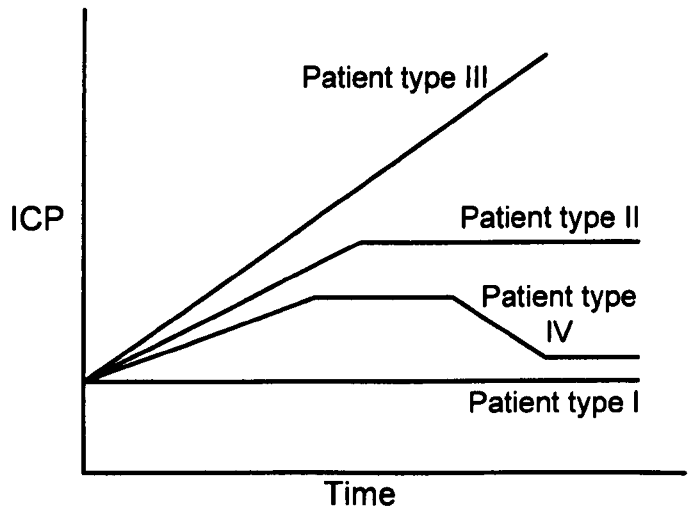


FIGURE 6.1: ICP response upon valve occlusion for the different patient types.

- Patient type I: ICP is within the normal range even though valve is occluded. From this it can be interfered that this type of patient is no longer needs the shunt. In other words, his/her natural drainage has been activated spontaneously. According to Takahashi's trial [107], such type can be weaned step by step without being accompanied by any adverse symptoms. Developing such type of patients is the objective of any weaning process.

- Patient type II: Intracranial hydrodynamics proportionally increase with time then stabilise at certain ICP level which is above the upper limit of the normal ICP range. Such type is usually accompanied with intermittent symptoms and ventricle size increases to certain level at which it stabilises. It can be inferred that such patient is partially shunt dependant and according to Takahashi [107] there is an opportunity to wean such patient but it takes longer time and higher valve opening pressures, *i.e.* greater risk.

- Patient type III: In this type, ICP keeps increasing when valve is occluded and might reach high levels at different rates, thus endangering patient's life. The ability to identify such patient is the objective of any shunt weaning or removal process, in order to avoid any risk on the patient and try intelligently maneuver the ICP to convert such patient into type II.

- Patient type IV: This represents Takahashi's patient that adapt and respond to the weaning treatment by reactivating the natural drainage system, thus maintaining ICP within acceptable normal limits after being abnormal.

Ability to identify patients of type III, maneuver and adapt their hydrodynamics to be of type II is an objective of weaning process in order to avoid any risk. These types were simulated using Simulink, and used as a testing environment for the proposed weaning techniques.

6.4 Modelling the Change in Intracranial Hydrodynamics Parameters

Modelling the effect of weaning process on the intracranial hydrodynamics (*i.e.* the natural drainage system) parameters is essential in improving the weaning methodologies. An empirical formula was derived to relate the change in natural absorption resistance with the accumulated CSF volume through the natural drainage system which has a direct relation with intracranial pressure.

Assuming that the natural absorption resistance (R) varies exponentially with the weaning duration, as shown in Figure 6.2(a). At starting time of weaning (*i.e.* t=0), the natural absorption resistance has the value of R_H which is R in hydrocephalus case. On the other hand, t_r is the expected period (in months) for a weaning process to be accomplished, at which R has the value of R_N (*i.e.* R in normal case). Thus this relation can be presented as follows,

$$\begin{aligned} R &= a \cdot \exp(-bt) \qquad (6.4.6.1) \\ a &= R_H \\ b &= -\frac{1}{t_r} \times ln\frac{R_N}{R_H} \end{aligned}$$

The values of R_H, R_N, and t_r were estimated based on the outcomes of Takahashi's trial.

Then the relation between the natural absorption flow (F) with weaning period was drawn (as shown in Figure 6.2(b)) based on the following equation,

$$F = \frac{ICP}{R} \qquad (6.2)$$

The integration of this equation gives the natural absorption volume (V)that is accumulated with the weaning time, as shown in Figure 6.2(c).

From Equations 6.4.6.1 and 6.2, the relation between R and V can be projected as shown in Figure 6.2(d). These equations were modelled using *Simulink*^{TM}. As a result of the numerical simulations and by using the minimum square error, a

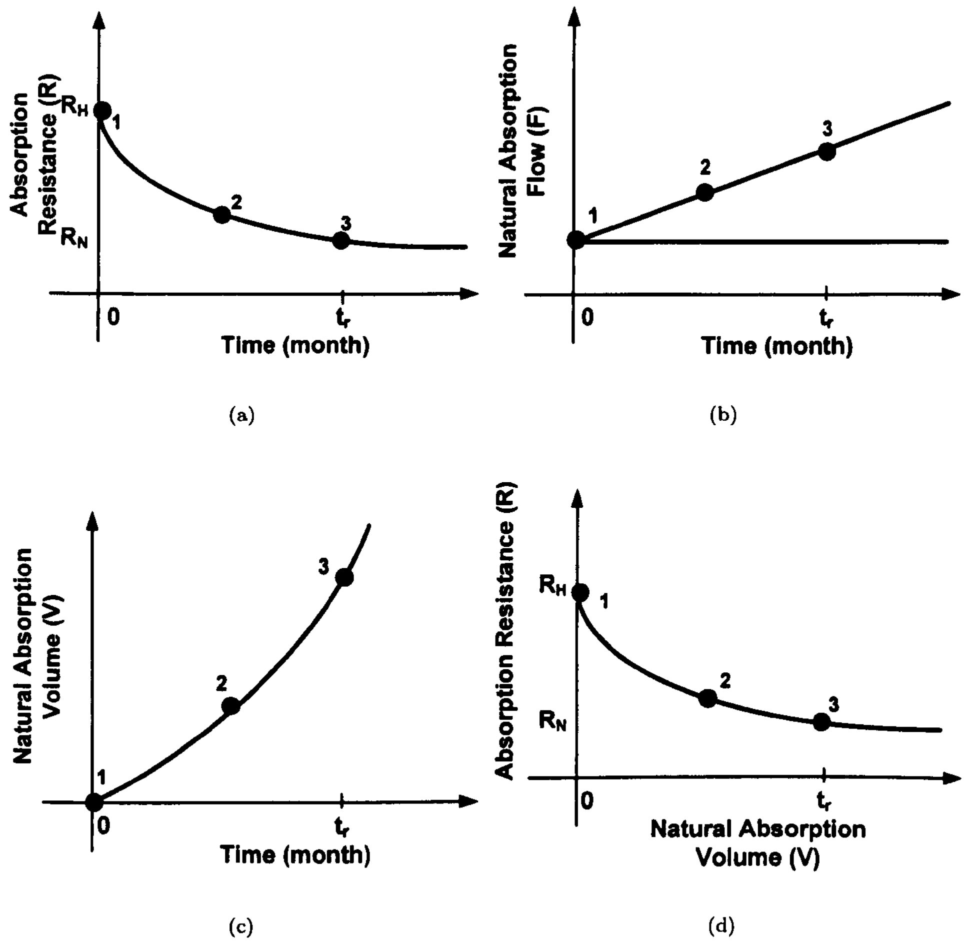


FIGURE 6.2: Modelling the Change in the natural drainage parameters. (a) Natural absorption resistance versus wean duration, (b) Natural drainage flow versus wean duration, (c) Natural drainage volume versus wean duration, and (d) Natural absorption resistance versus Natural drainage volume.

best fit model is roughly estimated as follows,

$$R = 3000 \cdot \exp(-5 \times 10^{-6} V) \tag{6.3}$$

This model is simulated using *Simulink*^{TM} thus the effect of different shunting methodologies on such type of patient can investigated and improved.

6.5 Proposed Methodologies

In this section the terms normal (Th_n) and weaning thresholds (Th_w) will be used to represent the upper normal ICP limit (10 mmHg) and a variable ICP value at which valve should open (0, 10 ... 40 mmHg), respectively. The following three methodologies were investigated:

- Closed loop timed threshold: This methodology is implemented in realtime. A block diagram of this methodology is shown in Figure 6.3. Here a timer is used where it is turned on when ICP crosses the normal threshold. On the other hand it is turned off when ICP falls within normal limits. The wean threshold is increased with time (0, 10, 20, ... , 40 mmHg). According to this methodology the valve will open either if ICP crosses the wean threshold (Th_w), or the timer duration elapsed. And the valve will close when ICP is below the normal threshold (Th_n).

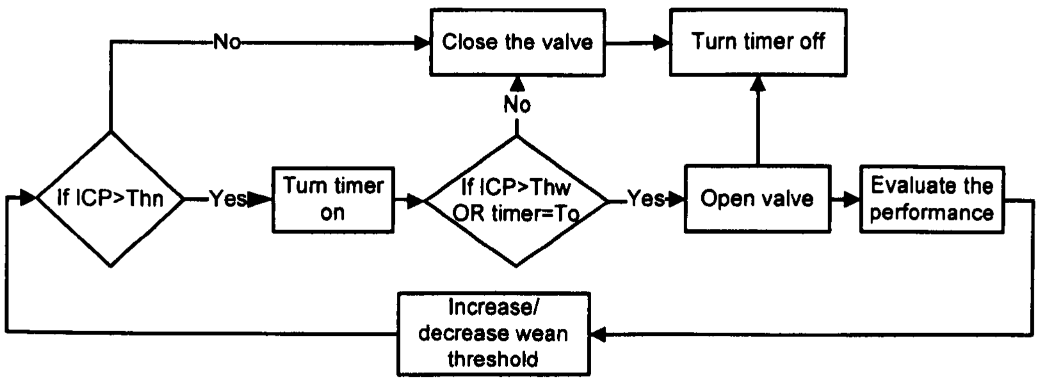


FIGURE 6.3: An illustration of closed loop timed threshold technique.

- Scheduled closed loop: In this methodology, a schedule will be used to determine whether to close the valve or open it in closed loop mode. The weaning threshold (Th_w) will be active only when the closed loop mode is turned on. This threshold will vary with time according to the influence of the treatment on the patient. Figure 6.4 illustrates this methodology.

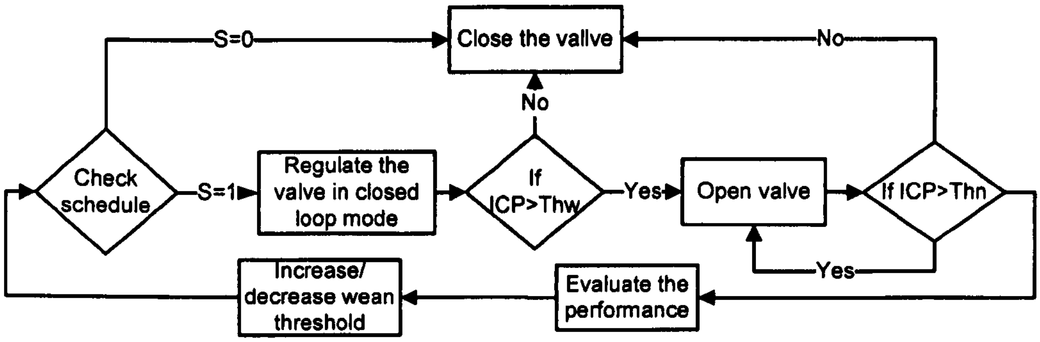


FIGURE 6.4: An illustration of scheduled closed loop technique.

- Schedule with shrinking slots: This methodology will be implemented off-line, *i.e.* the changes will implemented over days not instantaneous. In this methodology the open duration will be reduced for each hour subset individually. The hour subset will be chosen based on the minimum average ICP per hour. This methodology is illustrated in Figure 6.5. This step is repeated, i.e open duration is reduced, till either reaching a zero open duration or there is a negative dramatic influence on the intracranial hydrodynamics.

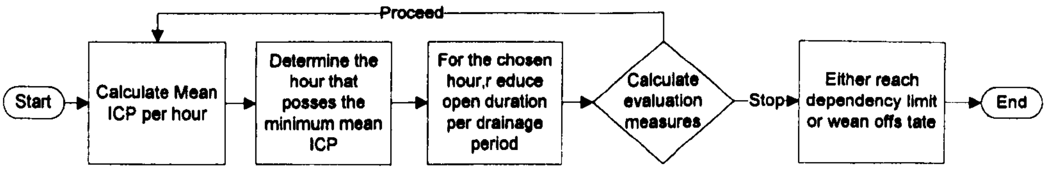


FIGURE 6.5: An illustration of schedule with shrinking slots technique.

6.6 Performance Measures

Three performance measures were used to hourly evaluate the effect of each weaning step,

- Rate of ICP change in closed-valve periods

$$\frac{dICP}{dt} = \frac{\overline{ICP}_{End} - \overline{ICP}_{Start}}{\text{one hour (min)}}$$

- Rate of change in mean absolute deviation (MAD)

$$\frac{dMAD}{dt} = \frac{\overline{MAD}_{End} - \overline{MAD}_{Start}}{\text{one hour (min)}}$$

- A multi-dimensional FoM

6.6.1 Decision Criterion

Table 6.1 presents the interpretation of the values of the performance measures. Based on this, a decision is made regarding the next step and early diagnosis is established for any possible problem. The interpretation of the cases is as follows,

Case A: Patient is cooping well and the reactivating the natural drainage or removing the shunt is possible; (a) if ICP $\leq Th_n$, this indicate shunt dependence is minimal, and (b) if ICP $\geq Th_n$ and ICP $\leq Th_n$, this indicate partial shunt dependence. Next step would be increasing the wean threshold.

Case B: Shunt dependency is high. Next step to decrease wean threshold or maintain it at same level.

Case C: Patient is shunt dependent, but the natural drainage is partially active. Nevertheless, not enough to keep ICP constant, *i.e.* ICP increase at low rate. Next step, in would be monitoring the situation in the next hour and maintain wean threshold at the same level.

Case D: This is critical situation, wean step should be re-evaluated.

Case E and F: ICP increases at high rate, thus endangering the patient life. Wean threshold should be reduced.

TABLE 6.1: Decision criterion based on performance measures.

$\frac{dICP}{dt}$ per hour		Average ICP per hour: $\leq Th_w$	Average ICP per hour: $\geq Th_w$
Zero	$\frac{dICP}{dt}$ t	A MAD	B MAD
Constant (low)	$\frac{dICP}{dt}$ t	C MAD	D MAD
Constant (high)	$\frac{dICP}{dt}$ t	E MAD	F MAD
Two constants	$\frac{dICP}{dt}$ t	G MAD	H MAD
Constant & zero	$\frac{dICP}{dt}$ t	I MAD	J MAD

Case G and H: Natural drainage is working at its maximum power, but this is not enough to handle the excess of CSF. Thus ICP is increasing at new rate. Wean step should be re-evaluated.

Case I: ICP was increasing, then kept at constant low level. Wean step has succeeded in reducing shunt dependence by reactivating natural drainage.

Case J: ICP was increasing, then kept at constant high level. Wean step has succeeded partially in reducing shunt dependence by reactivating natural drainage. But further steps needed to reduce ICP to be within normal range.

6.7 Results and Discussion

A mathematical model was utilised to simulate the intracranial hydrodynamics in three types of a hydrocephalus patient that are shunted with a mechatronic shunt. Each of the above methodologies was implemented on every patient type and the corresponding intracranial hydrodynamics were analysed. Performance measures would be used to interpret the best methodology that suits each patient case. Figure 6.6 show a sample report that is generated after each weaning step. This report contains a summary of the evaluation parameters.

Weaning Performance Measures
Results

Patient Type: II
Weaning Technique: Closed Loop Timed Threshold
Timer Duration = 5 min
Normal Threshold = 10 mmHg
Closing Threshold = 10 mmHg
Weaning Threshold = 15 mmHg

	Hours		
Hourly parameters	1	2	3
ICPavg (mmHg)	8.01	8.02	8.01
ICPavg at start(mmHg)	8.01	8.02	8.02
ICPavg at start(mmHg)	8.01	8.02	8.01
Rate of ICP change (mmHg/min)	0.0001	0.0000	-0.0000
MADavg at start(mmHg)	1.41	1.41	1.42
MADavg at end(mmHg)	1.41	1.41	1.41
MADavg (mmHg)	1.41	1.41	1.41
Rate of MAD change (mmHg/min)	0.0000	-0.0000	-0.0000
No. of drainage periods	60.00	62.00	64.00
Summation of drainage periods (min)	10.00	10.33	10.67
FoM1	1.2122	1.2120	1.2122
FoM2	1.0000	1.0000	1.0000
FoM3	1.0000	1.0000	1.0000
FoM4	0.8333	0.8278	0.8222
FoM5	-0.0000	-0.0000	-0.0000
FoM6	0.8333	0.8278	0.8222
FoMavg	0.8131	0.8113	0.8094
Effective open duration (min)	0.8333	0.8011	0.7708
False open	1.0000	1.0000	1.0000
False close	0.0000	0.0000	0.0000

FIGURE 6.6: Sample report consisting summary of evaluation parameter for closed loop technique.

Evaluation parameters were calculated after every weaning step. They were able to give a good indication whether the patient is shunt dependent or not, *i.e.* Patient Type I, thus helping to decide whether patient needs shunt for that specific hour/day. And in case of deciding shunt removal on the long run, it helps in providing answers to the aspects commonly considered at the time of removal. In addition, these parameters were able to identify patient type III thus avoiding any unexpected consequences that might result due to weaning. Figure 6.7 shows a sample of the calculated evaluation measures for different modelled patients and weaning methodologies. Figure 6.8 presents a sample of ICP responses for patient type II before and after implementing closed loop timed threshold, scheduled closed loop and schedule with shrinking slots, respectively. The rest of the results are enclosed in Appendix G.

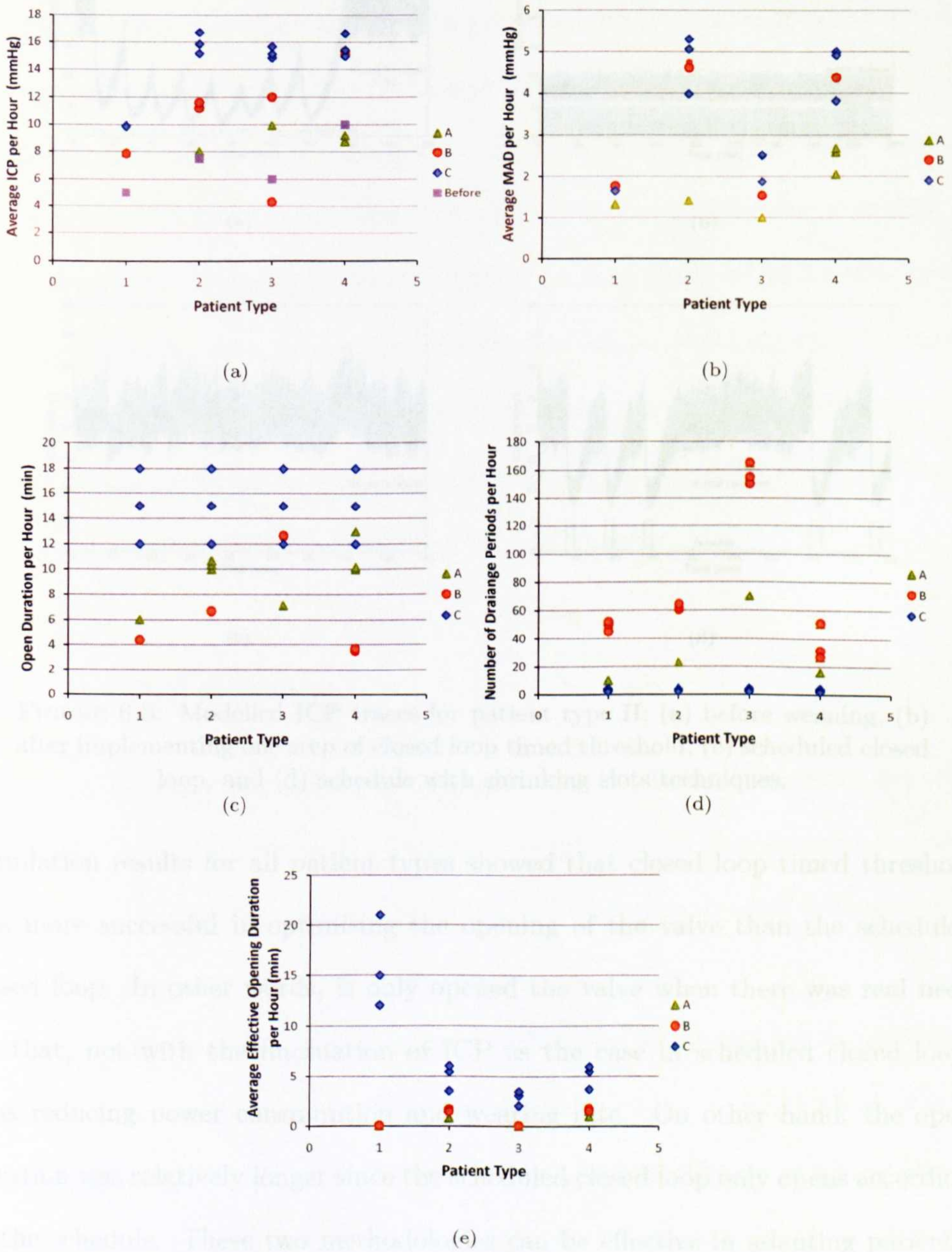


FIGURE 6.7: Sample of the calculated evaluation measures per hour for different modelled patients and weaning methodologies; (a) Mean ICP, (b) Mean MAD, (c) Open duration, (d) No. of drainage periods, and (e) Effective open duration.

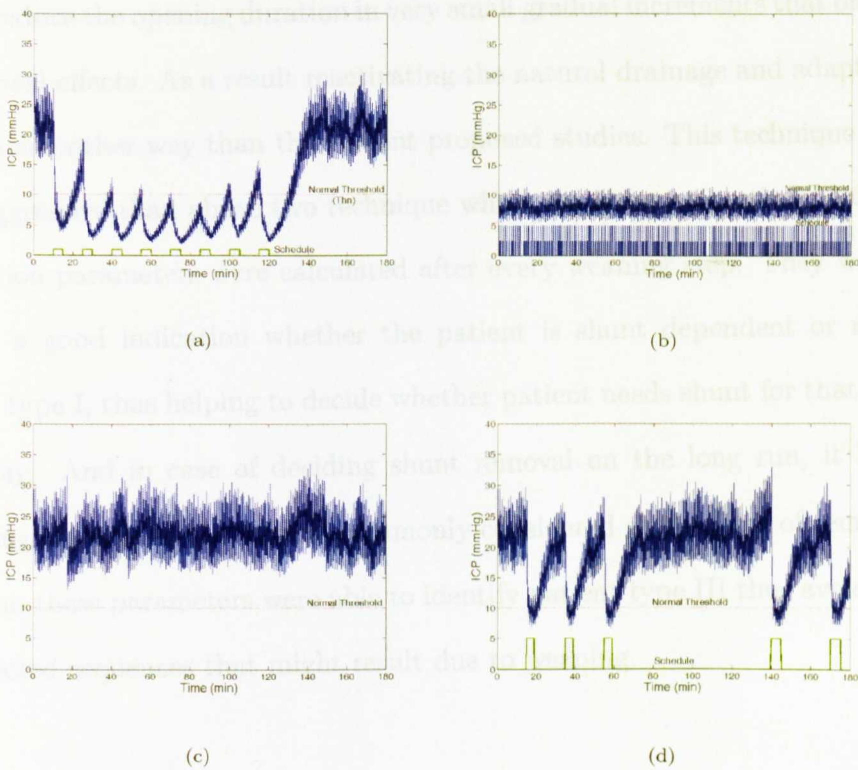


FIGURE 6.8: Modelled ICP traces for patient type II; (a) before weaning, (b) after implementing one step of closed loop timed threshold, (c) scheduled closed loop, and (d) schedule with shrinking slots techniques.

Simulation results for all patient types showed that closed loop timed threshold was more successful in optimising the opening of the valve than the scheduled closed loop. In other words, it only opened the valve when there was real need for that, not with the fluctuation of ICP as the case in scheduled closed loop, thus reducing power consumption and wearing rate. On other hand, the open duration was relatively longer since the scheduled closed loop only opens according to the schedule. These two methodologies can be effective in adapting patient's brain gradually to moderate pressure as intermediate step before reducing opening duration (if it was applicable). To gain the advantages of both techniques, they can be merged to have scheduled closed loop timed threshold. Thus the valve will only operate in closed loop mode based on a schedule. During which the valve opens based a timer and threshold.

As for the third technique, schedule with shrinking slots, has proved to be a good way to reduce the opening duration in very small gradual increments that only have minor local effects. As a result reactivating the natural drainage and adapting the brain in smoother way than the current proposed studies. This technique is little more aggressive than above two technique which are more patient's ICP driven.

Evaluation parameters were calculated after every weaning step. They were able to give a good indication whether the patient is shunt dependent or not, *i.e.* patient type I, thus helping to decide whether patient needs shunt for that specific hour/day. And in case of deciding shunt removal on the long run, it helps in providing answers to the aspects commonly considered at the time of removal. In addition, these parameters were able to identify patient type III thus avoiding any unexpected sequences that might result due to weaning.

6.8 Conclusions

Shunted hydrocephalus patients are susceptible to becoming fully shunt dependent in the long run. As a proactive step to preventing such dependence, the actual shunt dependence is here determined thus providing the natural drainage system with only the required amount of assistance.

A scheduled closed loop timed threshold technique has proved (in simulations) to be an effective way in attaining minimum shunt dependence. After which, schedule with shrinking slots can be used to smoothly and gradually attempt to wean the patient. Based on simulation results, these two techniques seems to be suitable for any type of patients.

Utilising the proposed evaluation parameters could help in identifying patient type. As a result, they give an indication whether it is safe to remove the shunt as is the case for Patient Type I or it is of high risk as the case for Patient Type III. The outcome of this study could play important role in reducing patient suffer and at the same time reducing if not eliminating the risk of achieving controlled arrest of the shunt using conventional means. Implementing AI methods to arrive at a decision concerning shunt withdrawal/removal when to proceed to the next weaning step and determine its parameters would enhance and automate the weaning methods.

Chapter 7

Multi-Agent Approach[4]

This chapter describes the design of a multi-agent system for an intelligent and personalised CSF management system. As mentioned before, patient feedback and intracranial pressure readings will play important roles in the process of CSF regulation and weaning, introduces an element of personalisation to the treatment. The new shunting system would deliver both reactive solutions for hydrocephalus management and goal-driven solutions for the treatment, at the same time the intelligent part of the system will be monitoring how well the shunt is performing. These tasks can be achieved by implementing an agent approach in designing this system. Such a system would help us to understand more about the dynamics of hydrocephalus.

In this chapter, the motivation for using the agent based approach is explained. Also a brief literature about agents are reviewed. Prometheus methodology is introduced and its implementation on the case of intelligent shunting is illustrated. In addition, the design of the intelligent shunting system based on two different architectures, *i.e.*, Belief, Desire, Intention (BDI) and Blackboard, are described.

[4]Part of this chapter has been published under the title "Design of an Intelligent and Personalised Shunting System for Hydrocephalus", in Conf Proc IEEE Eng Med Biol Soc., Vancouver, Canada, pp 779-782, 2008.

7.1 Introduction

One of the reasons that cause faults in the current shunts is the dynamic behaviour of intracranial hydrodynamics which not only differs within different patients, but also varies with age, health, lifestyle and other factors for the same patient. In the previous chapter, it was shown that the problem can be avoided by using a closed loop shunt, consisting of mechatronic valve and pressure sensor, that respond dynamically to the changes in intracranial pressure. Such a shunting system would be theoretically successful, but its practical feasibility would be limited by the current technology. For example, current implantable pressure sensors are inaccurate on long-term and implanatatable batteries have short life due to size limitations.

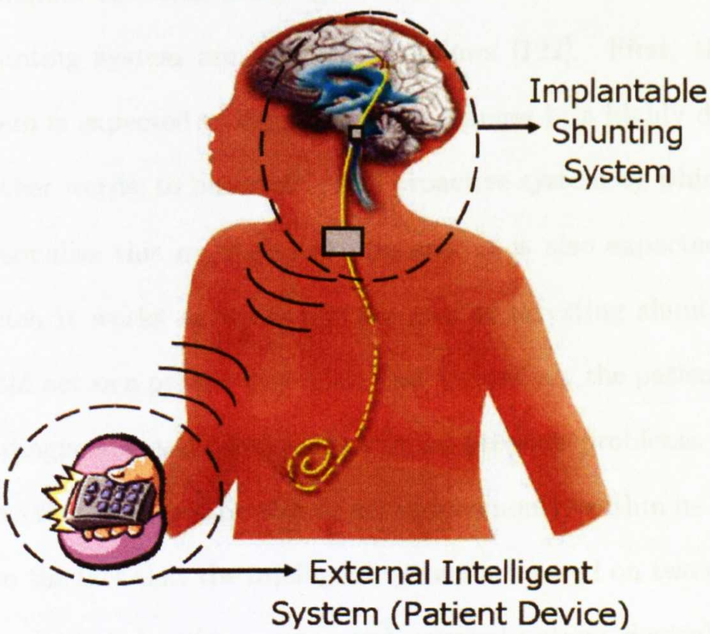


FIGURE 7.1: Patient-specific intelligent shunting system.

This prompted the consideration of an intelligent system that would regulate the mechatronic valve according to certain valve schedule and update it according to the intracranial pressure that is measured when needed. And the best paradigm that can be used to develop such system is a multi-agent paradigm. Multi-agent systems are well-suited to operating in such dynamic environments, where agent systems integrate knowledge and experience, and adapt rapidly to the change in the environment [110].

The proposed system, shown in Figure 7.1, would manage and treat hydrocephalus in real-time. This system would provide personalised, reactive, goal-driven treatment: treatment that aims to cure, *i.e.* arrest shunt dependance.

Intelligent agent software [15, 110] is a new paradigm of computer software that aims to bring human-like capabilities to software – such as learning, proactivity, inference, heuristic problem solving, goal-based action and communication. It is a profound change from today's software, which mostly acts like a passive tool, performing fixed data-manipulation functions only on demand.

The reasons behind selecting multi-agent approach to build the software of the intelligent shunting system are outlined as follows [122]. First, the intelligent shunting system is expected to respond to the changes in a highly dynamic environment, in other words, to be reactive and proactive system by which it manages CSF and personalise this management. Second, it is also expected to be goal-driven by which it works on achieving the goal of arresting shunt dependence. Third, it should act as a private physician that accompany the patient all the time and work on diagnosing and solving intracranial pressure problems. For the software to achieve this, it should be able to act autonomously within its environment. Fourth, due to the fact that the intelligent system is located on two different platforms (*i.e.* implanted shunting system and external patient device), its software should have the ability to communicate over the two platform. Fifth, it should be able to adapt and learn from its experience in order to reach the optimum valve schedule.

Many researchers reported that multi-agent systems have an increasingly important role to play in health care domains in that they significantly enhance the ability to model, design and build complex, distributed health care software systems. Agents were used in many different medical applications such as data-mediated knowledge discovery, especially from multiple heterogeneous data resources, a diagnosis aid expert system, data sharing and communication, hospital patient scheduling and treatment.

Multi-agent system can not only integrate the medical knowledge and clinical experience and make decision support, but also adapt the system rapidly to the change in environment [110].

7.2 Multi-Agent Approach

One way of defining artificial intelligence (AI) is by saying that it is the subfield of computer science which aims to construct agents that exhibit aspects of intelligent behaviour. Agents are now widely discussed by researchers in mainstream computer science, as well as those working in data communications and concurrent systems research, robotics, and user interface design. A British national daily paper recently predicted that: "Agent-based computing (ABC) is likely to be the next significant breakthrough in software development".

Multi-agent system approach has been widely used in the development of large complex systems. Agents have the autonomy and social ability, and multi-agent system is inherently multi-threaded for control [109].

A multi-agent system is a system that consists of a number of agents, which interact with each other, typically by exchanging messages through some computer network infrastructure. An agent is a computer system that is capable of independent action on behalf of user or owner. A multi-agent system is also a dynamic society made up of a great number of "intelligent agents", so it is an intelligent society.

7.2.1 Agent Definitions

Although the term is widely used, by many people working in closely related areas, it defies attempts to produce a single universally accepted definition. This need not necessarily be a problem: after all, if many people are successfully developing interesting and useful applications, then it hardly matters that they do not agree on potentially trivial terminological details. However, there is also the danger that unless the issue is discussed, agent might become a noise term, subject to both abuse and misuse, to the potential confusion of the research community. Here is a number of definitions that are used by different researchers [122].

An agent is a computer system that is situated in some environment, and that is capable of autonomous action in this environment in order to meet its design objectives. In most domains of reasonable complexity, an agent will not have complete control over its environment. It will have at best partial control, in that it can influence it. Thus agents in all but the most trivial environments must be prepared for the possibility of failure. Examples of agents are any control system can be viewed as an agent. A simple example of such a system is a thermostat. Other example is most software daemons, (such as background processes in the UNIX operating system), which monitor a software environment and perform actions to modify it, can be viewed as agents [122].

Ferber [36] had defined an agent as a physical or virtual entity (a)which is capable of acting in an environment, (b) which can communicate directly with other agents, (c) which is driven by a set of tendencies, (d) which possesses resources of its own, (f) which has only a partial representation of this environment, (g) which possesses skills and can offer services, (h) which may be able to reproduce itself, (i) whose behaviour tends towards satisfying its objectives, taking account of the resources and skills available to it and depending on its perception, its representations and the communications it receives. A physical entity is something that acts in the real world: a robot, an aircraft or a car are examples of physical entities. A software component and a computing module are virtual entities, since they have no physical existence.

Wooldridge *et al.* have distinguished two general usages of the term 'agent': the first is weak, and relatively uncontentious; the second is stronger, and potentially more contentious. A weak notion of agency is to denote a hardware or (more usually) software-based computer system that enjoys the following properties [121]:

1. autonomy: agents operate without the direct intervention of humans or others, and have some kind of control over their actions and internal state;

2. social ability: agents interact with other agents (and possibly humans) via some kind of agent-communication language;

3. reactivity: agents perceive their environment, (which may be the physical world, a user via a graphical user interface, a collection of other agents, the INTERNET, or perhaps all of these combined), and respond in a timely fashion to changes that occur in it;

4. pro-activeness: agents do not simply act in response to their environment, they are able to exhibit goal-directed behaviour by taking the initiative.

A simple way of conceptualising an agent is thus as a kind of UNIX-like software process, that exhibits the properties listed above.

A stronger notion of agency adopted by some researchers, is that an agent to be a computer system that, in addition to having the properties identified above, is either conceptualised or implemented using concepts that are more usually applied to humans. For example, it is quite common in AI to characterise an agent using mentalistic notions, such as knowledge, belief, intention, and obligation. Some AI researchers have gone further, and considered emotional agents. Another way of giving agents human-like attributes is to represent them visually, perhaps by using a cartoon-like graphical icon or an animated face. Such agents are of particular importance to those interested in human-computer interfaces. There are other attributes of agency, such as, mobility which is the ability of an agent to move around an electronic network; veracity is the assumption that an agent will not knowingly communicate false information; benevolence which is the assumption that agents do not have conflicting goals, and that every agent will therefore always try to do what is asked of it; and rationality is the assumption that an agent will act in order to achieve its goals, and will not act in such a way as to prevent its goals being achieved at least insofar as its beliefs permit [121].

Agents differ from expert systems, where an expert system is one that is capable of solving problems or giving advice in some knowledge rich domain. The most important distinction is that expert systems are inherently disembodied. This means that they do not interact directly, with any environment. As for objects, they are computational entities that encapsulate some state, are able to perform actions, or methods on this state, and communicate by message passing. The agents differ from objects in three main distinctions. First distinction is that agents have higher degree of autonomy than objects. Second one is that agents are capable of flexible behaviour, whereas standard object model has nothing to say about such types of behaviour. The third one is that a multiagent system is inherently multi-threaded, so each agent is assumed to have at least one thread of control [122].

7.2.2 Levels of Organisation

Three levels of organisation can be distinguished in multi-agent systems [36].

- The micro-social level, where it is essentially interested in the interactions between agents and in the various forms of link which exist between two agents or between a small number of agents. It is at this level that most studies into distributed artificial intelligence have been undertaken.
- The level of groups, where it is interested in the intermediary structures which intervene in the composition of a more complete organisation. At this level we study the differentiations of the roles and activities of the agent, the emergence of organisational structures between agents, and the general problem of the aggregation of agents during the constitution of organisations.
- The level of global societies where interest is mainly concentrated on the dynamics of a large number of agents, together with the general structure of the system and its evolution.

7.2.3 Agent Architectures

Agent architecture represents the movement from specification to implementation. For intelligent agents, architectures can be divided to five classes:

- Logic Based architectures: in which decision making is realised through logical deduction. An agent's decision making strategy (program) is encoded as a logical theory and the process of selecting an action reduces to a problem of proof. Logic based approaches are elegant and have a clean semantics. Decision making in such agents is predicated on the assumption of calculative rationality.

- Reactive architectures: in which decision making is implemented in some form of direct mapping from situation to action. There are obvious advantages to reactive approaches such as simplicity, economy, computational tractability, robustness against failure, and elegance. All make such architectures appealing, but there are some fundamental, unsolved problems [122]. This necessarily makes it very hard to engineer agents to fulfill specific tasks and one must use a laborious process of experimentation, trial, and error to engineer an agent.

- Blackboard architectures: Blackboard systems are a class of systems which can include all different representational and reasoning paradigms. They are composed of three functional components, namely, knowledge sources component, blackboard component, and control information component. Knowledge sources component represents separate and independent set of coded knowledge, each of which is a specialist in some limited area needed to solve a given subset of problems. The blackboard component, a globally accessible data structure, contains the current problem state and information needed by the knowledge sources (input data, partial solutions, control data, alternatives, final solutions). The knowledge sources make changes to the blackboard that incrementally lead to a solution. The control information component may be contained within the knowledge sources, on the blackboard, or possibly in a separate module. The control knowledge monitors the changes to the blackboard and determines what the immediate focus of attention should be in solving the problem [52].

- Belief-Desire-Intention architectures (BDI): in which decision making depends upon the manipulation of data structures representing the beliefs, desires, and intentions of the agent. The BDI model is attractive for several reasons. First, it is well recognised that the processes of deciding what to do and then how to do it, and have an informal understanding of the notions of belief, desire, and interior. Second, it gives a clear functional decomposition, which indicates what sorts of subsystems might be required to build an agent. But the main difficulty, as ever, is knowing how to efficiently implement these functions. The basic components of a BDI architecture, data structures representing the beliefs, desires, and intentions of the agent and functions that represent its deliberation (deciding what intentions to have) and means-ends reasoning (deciding how to do it). Intentions play a central role in the BDI model, they provide stability for decision making, and act to focus the agent's practical reasoning. A major issue in BDI architectures is the problem of achieving a balance between being committed to and over-committed to one's intentions: the deliberation process must be finely tuned to its environment, ensuring that in more dynamic, highly unpredictable domains it reconsiders its intentions relatively frequently [122].

- Layered architectures: in which decision making is realised via various software layers, each of which is explicitly reasoning about the environment at different levels of abstraction. Wooldridge identified two types of control flow within layered architectures [122]:

  - Horizontal layering: In horizontally layered architectures, the software layers are each directly connected to the sensory input and action output. In effect, each layer itself acts like an agent, producing suggestions as to what action to perform. The great advantage of horizontally layered architectures is their conceptual simplicity: if there is a need for an agent to exhibit (n) different types of behaviour, then should be implemented (n) different layers. In order to ensure that horizontally layered architectures are consistent, they generally include a mediator function, which makes decisions about which layer has "control" of the agent at any given time. The need for such central control is problematic: it means that the designer must potentially consider all possible interactions between layers and it also introduces a bottleneck into the agent's decision making.

- Vertical layering: In vertically layered architectures, sensory input and action output are each dealt with by at most one layer each. This simplicity comes at the cost of some flexibility: in order for a vertically layered architecture to make a decision, control must pass between each different layer. This is not fault tolerant: failures at any one layer are likely to have serious consequences for agent performance.

7.2.4 Agent Languages

Designers of multi-agent systems make use of a large number of languages and formalisations in order to encompass all aspects of these systems. They can be grouped into four main categories, depending on whether one is interested in the implementation or formalisation of MASs, in representing the knowledge of agents, in defining their behaviour, or in their communications [36].

- Type Ll: Implementation languages

  These are used for programming the multi-agent system. This covers the computing structures used for agents and for the environment (if it is simulated), the computing mechanisms making possible inter-agent and intra-agent parallelism, the efficient implementation of behaviours, the activities of transmitting and receiving messages, the perception of objects, and all the tools required for finalising an MAS. The classic programming languages such as Lisp, C/C++, Prolog, Java or Smalltalk, which already carry parallel execution mechanisms such as actors' languages.

- Type L2: Communication languages

  These are used for providing interactions between agents (communicators) by means of data transmissions and reciprocal requests for information and services. Knowledge Query and Manipulation Language (KQML) is a good example of such a language.

- Type L3: Languages for describing behaviours and the laws of environment

  Describing behaviours and the laws of the universe for the environment in implementation languages adds a certain number of details which are necessary for comprehending the system, and which mask essential principles. Languages can be used which are based production rules.

- Type L4: Languages for representing knowledge

  Languages for representing knowledge are used by cognitive agents to describe internal models of the world in which they move and to allow them to reason and to make predictions about the future on the basis of the data available to them. In this family, it was essentially found AI languages, such as rules-based or blackboard based languages, and languages for the structured representation of knowledge such as semantic nets or frames.

- Type L5: Formalisation and specification languages

  On the most abstract level are the languages used on the one hand to formalise what is understood by multi-agent systems, by the notion of interaction, by the concept of intention and so on; and on the other hand to specify the conditions that have to be respected in modelling and implementation of such systems.

7.2.5 Applications

Some examples of multi-agent paradigm applied in medical applications are summerised below.

Guillou *et al.* [40] have developed a study which is interested in the upper digestive endoscopy and its imagery with the aim of conceiving a diagnosis aid expert system. Their study had been articulated around two bases, one of case images and another of endoscopic knowledge, in order to perform a Case-Based Reasoning (CBR), well adapted to elucidate a case, *i.e.* to find the similar ones. They integrated all this information in a blackboard typed multiagent architecture. In addition, Case Based Reasoning merged with blackboard architecture to conceive a modular and evolutive diagnosis aid system in upper digestive endoscopy.

Riano *et al.* [92] have applied a distributed computer system for telemedicine to the Palliative Care Unit (PCU) at the Hospital de la Santa Creu y Sant Pau and have performed the first tests. The system permits the data sharing and communication of patients and doctors with the PCU by means of internet and mobile phone services. So, patients can have remote access to their case histories, and doctors can prepare their visits, introduce evolution parameters or clinical data, and change the patient medication or treatment wherever the doctor is attending the patient (patient home, hospital pavilion or consulting room).

Distributed artificial intelligence and multi-agent systems play a very important role in hospital patient scheduling and treatment. Aknine *et al.* [2] had described the design of an artificial agent system for cooperative work aided applications in general, and for hospital patient medical assistance and organising medical staff in particular. The key aspect of their software agent model is that it encapsulates several agents in the same structure. The agent model that was proposed is a generic agent model. It is composed of various primitive agents (agents of decision, an agent of execution, an agent of perception/communication and a working memory). This multi-agent architecture presents several advantages: parallelisation of agent tasks, reuse of agent components and partial mobility and cloning of the agent code.

Data-mediated knowledge discovery, especially from multiple heterogeneous data resources, is a tedious process and imposes significant operational constraints on end-users. Zaidi *et al.* [66] demonstrated that the autonomous, reactive and proactive intelligent agents provide an opportunity to generate end-user oriented, packaged, value-added decision support/strategic planning services for healthcare professionals and managers. They proposed the use of intelligent agents to implement a distributed Agent based Data Mining Infostructure that provides a suite of healthcare-oriented decision-support/strategic planning services.

Liu *et al.* [63] have presented a Mobile Multi-Agent Image Retrieval System with application in mammography. The image retrieval strategy suggested uses the inherent strengths of mobile agents to return the best possible matches from a distributed set of images in Digital Medical Image Libraries available on the Internet. The approach proposed is to perform a simulation of the Digital Library and to study the dynamics of the system from the perspective of parallel processing, intelligent pre-processing and communication. Their study examined three levels of sophistication in the Mobile Agent based image Retrieval System: (1) Simply the power of paralleling the search, (2) Pre- processing images to provide some means of predicting the results of detailed processing, and (3) sharing information across a swarm of agents so that a global optimum can be achieved.

It should be stressed that the classical emphasis in Distributed Artificial Intelligence (DAI) has been on macro phenomena (the social level), rather than the micro phenomena (the agent level). DAI thus looks at such issues as how a group of agents can be made to cooperate in order to efficiently solve problems, and how the activities of such a group can be efficiently coordinated. DAI researchers have applied agent technology in a variety of areas. Example applications include power systems management, air-traffic control, particle accelerator control, intelligent document retrieval, patient care, telecommunications network management, spacecraft control, computer integrated manufacturing, concurrent engineering, transportation management, job shop scheduling, and steel coil processing control [121].

Interface agents can be defined as computer programs that employ artificial intelligence techniques in order to provide assistance to a user dealing with a particular application. The metaphor is that of a personal assistant who is collaborating with the user in the same work environment. There are many interface agent prototype applications: for example, the NEWT system is an USENET news filter. A NEWT agent is trained by giving it a series of examples, illustrating articles that the user would and would not choose to read. The agent then begins to make suggestions to the user, and is given feedback on its suggestions. NEWT agents are not intended to remove human choice, but to represent an extension of the humans wishes. Another example is McGregor, who imagines prescient agents intelligent administrative assistants, that predict our actions, and carry out routine or repetitive administrative procedures on our behalf [121].

An information agent is an agent that has access to at least one, and potentially many information sources, and is able to collate and manipulate information obtained from these sources in order to answer queries posed by users and other information agents (the network of inter-operating information sources are often referred to as intelligent and cooperative information systems. An example of such system is a prototype system called IRA (information retrieval agent) that is able to search for loosely specified articles from a range of document repositories. Another important system in this area is called Carnot, which allows pre-existing and heterogeneous database systems to work together to answer queries that are outside the scope of any of the individual databases [121].

Believable agents are agents that provide the illusion of life, thus permitting the audiences suspension of disbelief. A key component of such agents is emotion: agents should not be represented in a computer game or animated film as the flat, featureless characters that appear in current computer games. They need to show emotions; to act and react in a way that resonates in tune with our empathy and understanding of human behaviour. The Oz group have investigated various architectures for emotion [121].

7.3 Prometheus Methodology

The Prometheus methodology [80] defines a detailed process for specifying, designing, implementing and testing/debugging agent-oriented software system. This methodology consists of three phases; the system specification phase, the architectural design phase and the detailed design phase.

In this work the Prometheus methodology was used in determining the specifications of the intelligent system for the personalised management and treatment of Hydrocephalus, as shown in Appendix H. And since this methodology is an iterative process, only the final findings were mentioned in Appendix H. In the system specification phase, the goals of the intelligent system were identified, case scenarios were developed, the basic functionalities of the system were identified, and the interface between the system and its environment in terms of actions and percepts were specified. Furthermore, the types of agents were decided on. This was achieved by grouping the functionalities into agents and considering all alternatives, reviewing coupling by using agent acquaintance diagrams and deciding on the best grouping. After this , the dynamic aspects of the system were captured by developing interaction diagrams and protocols. System overview diagram was developed to finalise the architectural phase. In the detailed design phase, capabilities needed for every agent were identified. Also the agent overview diagrams and process specifications were realised.

7.4 Shunting System Requirements

The new generation of shunting systems are expected to overcome the drawbacks and limitations of the current shunting systems. Accordingly the suggested requirements and functionalities of the next generation of shunting systems that would upgrade the current mechanical shunt systems' level to a "smart" level are as follows,

- Autonomously manage the CSF flow, by regulating CSF flow through the mechatronic valve in order to maintain ICP within the normal range,
- Personalise the management of CSF flow through involving real-time intracranial pressure readings and patient's feedback, and responding to them,
- Autonomously manage and personalise the treatment of hydrocephalus, which gradually reduce shunt dependence and eventually establish a controlled arrest of the shunt,
- Being able to monitor performance of its components, thus minimising the shunt revisions, and

- Establish distant treatment database (*e.g.* computer-based patient record) and exchange treatment information, by regularly reporting the patient's record to the physician.

In this chapter, a design for such system is proposed that would autonomously manage and treat hydrocephalus, control the CSF flow and enable the patient to play a vital role in the treatment process. This objective would be achieved by implementing multi-agent approach to develop a system that would provide personalised, reactive, pro-active,goal-driven and distributed treatment for hydrocephalus. The short term goal of the intelligent system would be to maintain ICP within acceptable limits and eliminate patient's symptoms. Whereas, the long term goal is to reduce shunt dependence if not eliminating it.

7.5 Shunting System Components

The intelligent personalised hydrocephalus management system would consist of both hard and soft components. The overall system is shown in Figure 7.1, where it can be seen that it comprises two subsystems (platforms), namely the implanted shunting system and external intelligent system.

The implanted shunting system lies inside the patient's body where its hardware components would consist of a microcontroller, a mechatronic valve, a pressure sensor, a wireless transceiver and drainage catheters. The hardware of the external intelligent system (called the external patient device) is built up of a smartphone, a wireless transceiver and a microcontroller, along with suitable interfacing circuitry.

7.6 Intelligent Shunt Based on BDI Architecture

Two different architectures were used to design the multi-agent system to find the best architecture that suits the application. BDI and Blackboard architecture were implemented.

The multi-agent system for this intelligent shunting system is first designed using the Belief, Desire and Intention (BDI) architecture. In this architecture, decision making depends upon the manipulation of data structures representing the beliefs, desires, and intentions of the agent.

In this section, the sensory inputs are identified. Different types of agents were proposed. This is followed by a description of the modes of operation.

7.6.1 Sensory Inputs

The sensory inputs will have an essential effect in tunning the management and treatment of hydrocephalus. The sensory inputs comprise of:

- Patient Feedback

  The patient would participate directly in his/her treatment by giving direct feedback to the intelligent system. He/She would give such feedback to show his/her dissatisfaction when he/she is not feeling well at that particular moment, *i.e.* experience symptoms of an increase/decrease in ICP beyond the normal limit.

  This feedback would trigger the intelligent system to investigate whether the cause of this dissatisfaction is due to abnormality in ICP or due to other cause.

- ICP and Valve Flow Readings

  The real-time ICP readings and valve flow are collected, by implanted sensors, regularly or upon request. These readings would be sent wirelessly to the external patient device where it will be analysed, summarised and saved. Subsequently, it will be transferred via mobile communication to the patient's personal record in the medical centre. The ICP and flow are analysed for different reasons; verifying the patient feedback, monitoring the performance of the shunt and learning more about patient-specific intracranial hydrodynamics and hydrocephalus.

- Clinician Intervention

  The clinician would be able to intervene the management and treatment process when there is a need for it *e.g.* in case of emergency or in case of updates on the software and valve schedule.

  Decision of schedule modification is made based on integration of all sensory inputs, but in case of conflicts between the inputs, priority will be first for the medical intervention, second the measured ICP, and then the patient feedback.

7.6.2 Real-time Databases

The external device would contain three real-time databases; patient feedback, ICP readings and valve schedule. The aim of these databases is to keep a record of the above that would be used for monitoring, analysis, adaptation and learning.

7.6.3 Agents

The Prometheus methodology [80] was used to develop the multi-agent system of the intelligent shunting system. As a result of this detailed process, seven agents were developed; four of them located on the external patient device; Decision Maker, Adjustment Handler, Weaning Manager, External Communicator agents, and the other three agents located on the implanted shunting system; Valve Manager, Sensor Manager and Internal Communicator. These agents were selected according an iterative process where data coupling diagrams and agent acquaintance diagrams were used. The agents within the same platform would communicate through messages. While the agents at different platforms (the external patient device and implanted shunting system) would communicate through the Communication agents wirelessly using an RF data link at 402-405 MHz.

Figure 7.2 presents the agents' interaction diagram for the intelligent shunting system. The agents and their roles are as follows.

The decision maker agent intelligently analyses the sensory inputs for the following purposes, (i) reach a decision regarding optimising the valve schedule, (ii) monitor the performance of the shunt, (iii) assess the quality of the continuous ICP readings, and (iv) monitor and assess the weaning process. This agent would trigger Adjustment handler agent to deal with any updates needed for the valve schedule. The Weaning manager agent is also initiated on the long run by the decision manager. Its responsibility would be to handle the weaning schemes to force the body to gradually adapt to high pressure and it may activate the body's natural drainage.

The External and Internal communicator agents are responsible of communication among the implanted shunting system, the external intelligent system and the medical centre.

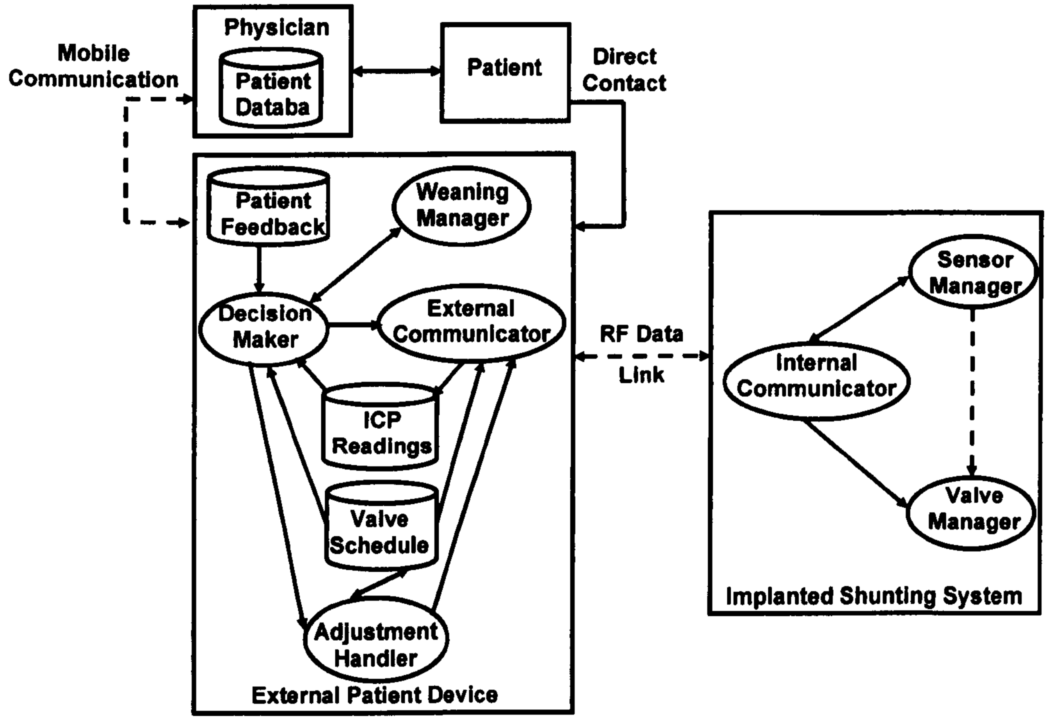


FIGURE 7.2: The layout of the proposed system.

The Valve manager agent manages the real-time opening and closing of the valve according to the latest valve schedule. The Sensor manager agent manages the collection process of the ICP and flow readings from the implanted sensors.

7.6.4 Modes of Operation

The proposed system is designed to operate in three modes; routine monitoring, manual intervention and weaning.

- Routine Monitoring

  In routine valve handling, the implanted software tool (*i.e.* Valve Manager agent) would continuously regulate the opening of the mechatronic valve according to the current valve schedule.

  Collection of ICP readings is done on routine basis at the absence of patient feedback, where they are used for monitoring purposes. The ICP would be intelligently analysed to monitor the performance of the overall shunting system; mainly the valve and the sensors. This would help in detecting and correcting the inaccuracies in the pressure/flow sensor and faults in the valve in early stages, thus reducing the risks and the need for invasive shunt revisions. ICP analysis are also used to update the valve schedule. If the analysis revealed that the ICP is above the normal limit or is very low at a specific period of time within the day, and this incident is repeated for a couple of days, then an action would be taken to change the schedule according to the valve status at that period of time.

- Manual Intervention

  Responding to patient feedback is accomplished when a manual patient feedback is received through external patient device, then the external software system would request for ICP readings to be collected by the implanted pressure/flow sensors. Upon receiving those readings, the external intelligent software would analyse, archive and decide whether the patient feedback is due to ICP abnormality or shunt fault and accordingly whether to adjust the valve schedule or not. In both cases, a message would be shown on the smartphone display to assure the patient either that the problem has been solved or that the cause of symptoms is not due to ICP/shunt abnormality.

- Weaning

  Shunt weaning is achieved by applying a personalised scheme to gradually reduce a patient's shunt-dependence with a long-term goal to achieve zero dependance. This means a shunt would no longer be needed for some patients. Sensory inputs, *i.e.* patient feedback and ICP, would provide a real-time feedback for the applied weaning scheme, whereby the gradual implementation enables the patient's brain to adapt to it current circumstances.

7.7 Intelligent Shunt Based on Blackboard Architecture

Hybrid Blackboard architecture was the second architecture that was used to design the Multi-Agent system, in which different types of agents are used, *i.e.* Data gathering agent, Data processing agent, control agent. The architecture was hybrid blackboard architecture, *i.e.* a mix of reactive to the changes in the environment and deliberative to initiate the proper weaning process. The system would consist of two blackboards, *i.e.* external and internal. Most of the agents would have access to internal blackboard on which all patient's real time records are saved and retrieved by agents. Whereas, the external blackboard, which can be accessed by the communication agent, is informed of the real time records on regular basis.

In this section, the requirements of the system were determined. And the architecture were designed to consist of three major parts; blackboards, agents and control entity. Then the roles and responsibilities of agents were identified and the belief structure was determined. The resulted system consisted of two blackboards, *i.e.* external and internal. Most of the agents would have access to internal blackboard on which all patient's real time records are saved and retrieved by agents. Whereas, the external blackboard, which can be accessed by the communication agent, is informed of the real time records on regular basis.

7.7.1 Requirement Analysis

The Intelligent system must provide the following services for the hydrocephalus patient on a daily basis:

- Monitoring the patients in real time and processing the monitored data immediately.
- Responding to the sensory inputs by adjusting treatment.
- Controlling the flow of CSF through the electronic valve of the shunting system.
- Logging and sharing patient's response to the adjustment.
- Attempting to wean off the treatment (shunting system).
- Learning from experience of other patients.
- Interacting with other systems, *e.g.* medical centre, patient.

7.7.2 Blackboard Architecture

This architecture would consist of three major parts, *i.e.* Blackboards, Agents and Control entity. A blackboard is an information sharing zone in which the agents' outcomes would be saved, updated and shared. An agent, which is usually called knowledge source in blackboard models, is going to perceive, decide and act depending on its own knowledge. A control entity would cooperate between agents and allow them to communicate either directly by messages or through the blackboard [40].

A. The blackboards

Two blackboards are incorporated in this system; Internal blackboard and External blackboard. The internal blackboard , can be also called the local blackboard,would be implanted within patient body and contain data for short period that can be shared by the agents of this particular system. Whereas the external one, that would be global, would be located at the medical centre, would contain data for longer periods (as long the data is useful) and the data is shared among other patients and medical centres.

Each blackboard is distinguished into three levels, *i.e.* Low, Intermediate and High. In the low level, patient's primary information is stored, *e.g.* biological information and history. Whereas,the intermediate level would contain patient's response, *e.g.* current status, sleep patens, emergency signals. On the other hand, high level would deal with flow gating functions and weaning regimes.

B. The Knowledge Sources

The knowledge sources or agents would attacked in details in the following sections.

C. The Control Entity

It aims to manage the system in away that would achieve the short- and long-term goals, which often conflicts. Therefore, the control entity is divided into two directions.

- Task control: It manages agents to perform their tasks in order to maintain ICP within acceptable boundaries.
- Strategy control: It manages the whole system to bring about a controlled hydrocephalus arrest, *i.e.* an eventual termination of agents status.

7.7.3 Identification of the Roles and Responsibilities of Agents

In the intelligent system for hydrocephalus, the medical services would include monitoring the patient in real time, responding to patient feedback, adjusting treatment, transmitting the information to physician, sharing patient's response with other patient and learning from other databases, then providing the patient with weaning treatment. These services are implemented by data gathering agent, statistical analysis agent, clustering agent, data processing agent, flow regulating agent, communication agent, decision making agent, control agent, and weaning agent. The responsibilities of agents are summarised as follows.

Data gathering agent receives the sensory data from the communication agent or internal blackboard (through Database wrapper agent) and classifies them according to their types.

Statistical analysis agent performs different statistical analysis to find out whether the changes in the inputs are random or systematic. Besides that it measures the stability of the system.

Clustering agent differentiates the patient cluster by integrating various knowledge.

Data processing agent produces derived data from the collected data in the form of flow gating function *i.e.* distribution of valve status over time domain.

Flow regulating agent regulates the opening/closing of the electronic valve, according to the flow gating function.

Communication agent sends any update, *e.g.* of the patient response or flow gating function, to the external systems and databases (External Blackboard). It also receives the sensory inputs *i.e.* it keeps the link with patients and other systems.

Decision making agent integrate various knowledge and provide the data processing agent with effective decision whether to update the current flow gating function or not by taking into consideration the outcomes from the statistical analysis and clustering agents. It also provide the control agent with a decision whether to start the weaning process or not.

Database wrapper agent controls the access to a database (Internal Blackboard) that contains patients records and updates.

Control agent implements the control of the whole implanted system. It assigns the work and mediates the conflicts between agents.

Weaning agent provide a regime for the controlled arrest of hydrocephalus.

7.7.4 Identification of the Goal and Plan to Implement

The intelligent system must not only provide the hydrocephalus patient with immediate medical services through monitoring the patients in real time and processing the monitored data, regulating the CSF flow through the electronic valve and providing weaning therapy, but also it should interact with other systems, *e.g.* medical centre, patient for the functions of sharing, learning and database.

The multi-agent system would consist of three groups, *i.e.* communication, implementation and control groups. The proposed architecture are shown in Figure 7.3. In the implement group, there are many agents that work individually and orderly to carry out their responsibilities.

7.7.5 Determination of the Belief Structure

This is to determine the information requirement for each plan and goal in the interactions between agents [122]. In the multi-agent system, the external interactions focus on the integration with other systems and its environment, while the internal interactions focus on the cooperation between agents to realise the goals

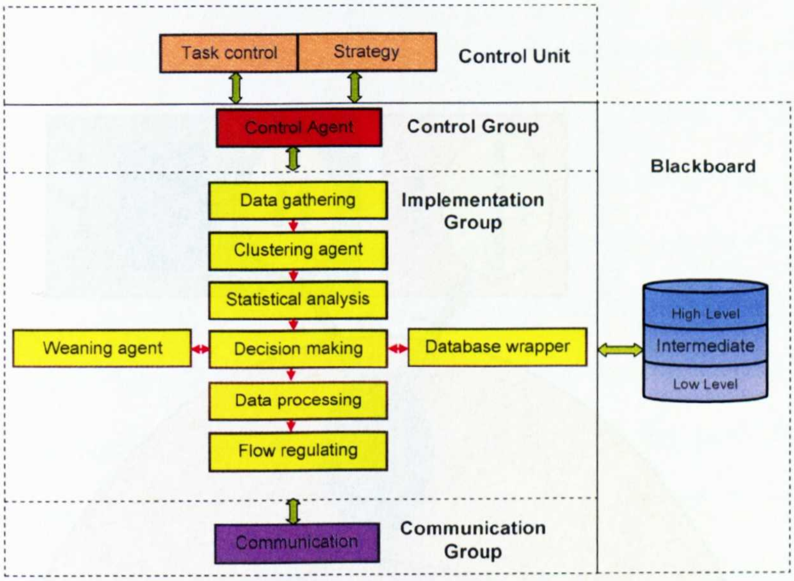


FIGURE 7.3: The architecture of the proposed multi-agent system.

of the system, as shown in Figure 7.4, where the bi-directional arrow represents the interactions [110].

In Figure , the bigger continuous ellipse represents the range of the implantable multi-agent system while the smaller dashed ellipse represents the range of the implementation group of the system. So arrow 1 and 2 indicate that the multi-agent system interacts with its environment; patient and medical centre, respectively. And arrow 3 and 4 indicate that the implementation group interacts with the control group and communication group , respectively. In the implementation group, decision making agent plays an important role. Moreover, database wrapper agent directly interacts with the internal blackboard, as shown by arrow 5. Whereas, arrows 6 and 7 show the interaction between weaning agent with the data gathering agent and decision making agent, respectively.And flow regulating agent implement the flow gating function obtained from data processing agent as shown by arrow 8. Arrow 9-19 represent the internal interactions between agents in implementation group of the system, which can be described by a matrix, as

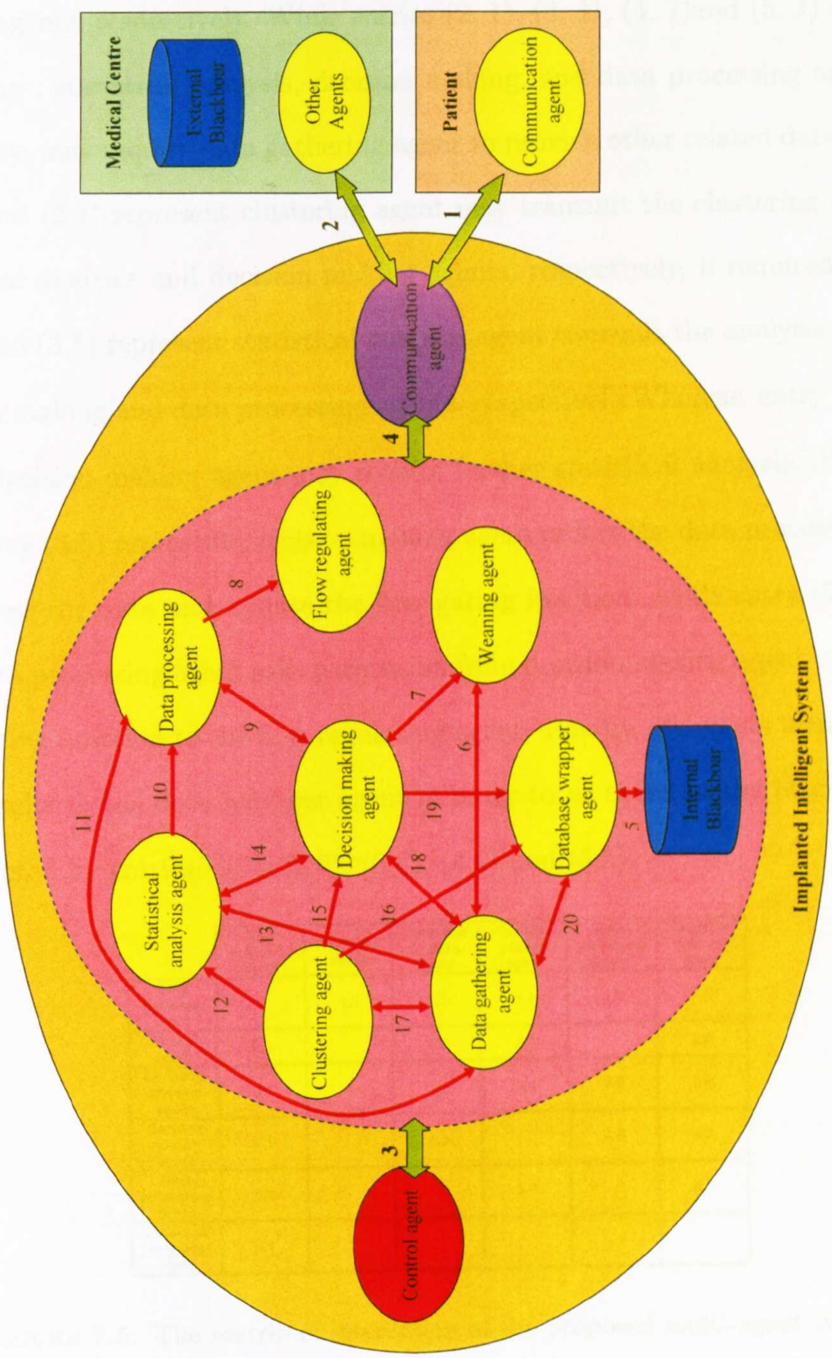


FIGURE 7.4: The interactions between agents in the proposed multi-agent system.

shown in Figure 7.5.The interactions in the matrix are explained as follows. Entries (1, 2),(1, 3),(1, 4) and (1, 5) represent data gathering agent transmits the collected data to clustering, statistical analysis, decision making, and data processing agents, respectively. While entries (2, 1), (3, 1), (4, 1)and (5, 1) represent clustering , statistical analysis, decision making, and data processing agents, respectively, may require data gathering agent to provide other related data. Entries (2, 3) and (2,4) represent clustering agent may transmit the clustering results to statistical analysis and decision making agents, respectively, if required. Entries (3, 4) and (3,5) represent statistical analysis agent transmit the analysis results to decision making and data processing agents, respectively.Whereas, entry (4,3) represent decision making agent may require further statistical analysis, if required. And entry (4,5) represents decision making agent orders the data processing agent to process the data and update the flow gating function. while entry (5,4) represent data processing agent asks permission from decision making agent to transmit flow gating function to the flow regulating agent. Finally, all agents transmit their own results to the data wrapper agent in order to be saved in the blackboard, as represented by entries (1,6), (2,6), (3,6), (4,6) and (5,6).

	Data gathering agent	Clustering agent	Statistical analysis agent	Decision making agent	Data processing agent	Database wrapper agent
Data gathering agent		1,2	1,3	1,4	1,5	1,6
Clustering agent	2,1		2,3	2,4		2,6
Statistical analysis agent	3,1			3,4	3,5	3,6
Decision making agent	4,1		4,3		4,5	4,6
Data processing agent	5,1			5,4		5,6
Database wrapper agent	6,1					

FIGURE 7.5: The matrix of interaction of the proposed multi-agent system.

7.8 Implementation

The intelligent software of the system is implemented using a Java-based interpreter for an extended version of AgentSpeak called Jason [12]. Currently a prototype version of the intelligent personalised CSF management system is under development. In order for such software to be implemented, a mechanical valve is insufficient; rather a mechatronic valve is needed, that can be regulated electronically by microcontroller.

7.9 Conclusions

The proposed system differs from the available and proposed shunting systems in the following aspects. First, the application of Multi-agent approach, where the agent system is located within the patient environment (his/her body and his/her external device) and it acts as a private physician that accompanies the patient all the time. Second, ICP monitoring and archiving, where the agent system would monitor how well the shunt is performing through analysing the real-time ICP. This would help in understanding more about the dynamics of hydrocephalus. Third, personalisation, where it addresses an element of personalisation to the CSF management and treatment through utilising ICP readings and patient feedback. Fourth, weaning, where it strives to achieve controlled arrest of the shunt in which real-time ICP and patient feedback are collected after each weaning step thus verifying the treatment in real-time.

Chapter 8

Conclusions

This work proposes an intelligent system that would upgrade the current mechanical shunt systems to an intelligent level, autonomously managing and treating hydrocephalus, and personalising the management and treatment by incorporating the patient feedback and ICP readings in the therapy. A model of the intracranial hydrodynamics is developed to investigate the influence of varying the shunting system parameters on the intracranial hydrodynamics. Furthermore, three different valve types are modelled and their performances are compared based on a novel multi-dimensional FoM, specially developed to evaluate the management and treatment of hydrocephalus.

An algorithm was proposed to help in developing a schedule for a mechatronic valve that dynamically changes based on each patient's intracranial pressure data and the derived figure of merit, thus providing the physician with an easy tool that facilitates the use of the mechatronic valve. Different valve parameters that characterise the mechatronic valve behaviour were identified and investigated. Furthermore, to optimise the gain of such an investigation, the relations among valve parameters, schedule parameters and initial ICP values were modelled. As an outcome of this investigation, vital parameters were identified and used as inputs for the schedule selection, modification and weaning processes.

A new technique was introduced to determine the actual degree of shunt dependence. In addition, three novel enhancements were investigated to actively establish shunt independence (controlled arrest of hydrocephalus). The change in the intracranial hydrodynamics as a result of weaning process was mathematically modelled and simulated to provide an interactive environment for testing the above enhancements.

Different architectures were used to design the multi-agent system to find the best architecture that suits the application. In which different types of agents were used. Belief, Desire, and Intention (BDI) and Blackboard architectures were implemented. A systematic process (Prometheus methodology) was used to design the agent system. The intelligent software of the system was implemented using a Java-based interpreter for an extended version of AgentSpeak called Jason.

A brief discussion of the conclusions and future prospects follows.

8.1 Conclusions

The realisation of truly autonomous shunting systems for personalised hydrocephalus treatment is closer than ever. This requires the use of implanted mechatronic valve, pressure sensor, smart hand held device, improved algorithms to analyse the inputs (*e.g.* ICP readings and patient feedback) and extract relevant information from raw data, and rule-based decisions controlled by the local intelligence. The Management of intracranial hydrodynamics, shunt self-diagnosis, and treatment of hydrocephalus can be continuously and autonomously monitored and parameters changed as necessary by the intelligent software in the handheld device via wireless communication and data will be sent on demand to the clinician for further evaluation. Such a shunting system would give hydrocephalus patients the freedom to go anywhere they like while receiving medical services and health care in a timely fashion. Visits of patients to hospitals or the doctor will be reduced to a necessary minimum, while increasing the quality of care that is provided.

In order to develop an intelligent agent based shunting system, some obstacles were faced. Lack of ICP data and good understanding of intracranial hydrodynamics, *e.g.* the effect of shunting and weaning on the intracranial hydrodynamics, are considered two of the main obstacles for this research. These obstacles directed the path of this work. In an effort to overcome such obstacles, a dynamic environment is developed that mimic the intracranial hydrodynamics of hydrocephalus patient. Such environment would work as test bed for intelligent shunt in order to optimise it.

From the investigation of different paradigms that could regulate CSF flow, a conclusion can be drawn that despite of the tremendous achievement of current valves in managing hydrocephalus, in order to overcome some of the most frustrating problems it is proposed that future management and treatment approaches shift from passive mechanical to active mechatronic valves.

Exploring the options for controlling the mechatronic valve revealed the need for further investigation to develop a shunting system that would deliver an intelligent and personalised treatment for hydrocephalus patients. In addition, the results showed that the closed loop system and a fixed schedule of moderate opening frequency have scored the highest FoM. Nevertheless, the later alternative lacks flexibility and ignores the intracranial dynamic behaviour while the first is impractical. As a result, integrating the schedule and the closed loop shunting systems and incorporate some sort of intelligence that would give more effective solution at the same time overcomes their shortages. In addition, the inclusion of sensory feedback from the patient could improve and inform the adaptation of this scheduled valve by adjusting the on and off times to best suit the patient's individual circumstances.

For a scheduled shunt to be efficient, it should be carefully selected. The proposed scheduling algorithm would help in developing such a schedule that dynamically change based on the patients own intracranial pressure data and a novel figure of merit, thus providing the physician with an easy tool that facilitate the use of the mechatronic valve. The resulting schedules along with the resulting intracranial pressure data have illustrated the effectiveness of the algorithm in providing schedule that maintain ICP within the normal limits. An initial valve schedule and respective relations with ICP, t_e, FoM along with patient feedback and physician intervention can be used for modifying the schedule online. It has been shown that using FoM, t_e and ICP as evaluation parameters for the performance of the intelligent shunt is effective whether it is used offline or online, since they can give sensitive relative indication of the treatment success. On the other hand, these parameters will not be less effective when used in designing the schedule for hydrocephalus management and treatment. Reaching a stage at which the mechatronic shunt autonomously personalise the management of hydrocephalus would dramatically reduce the number of patient's complaints about their shunts. Such management is especially vital for patients suffering of unresolved problems with their conventional shunts.

The mechatronic shunting system would ease clinician and researchers concerns regarding shunt removal since it would adopt an algorithm that would personalise the weaning plan to the individual patients needs and response. Based on simulation results, scheduled timed threshold and schedule with shrinking slots are proposed to be used in establishing an auto shunt weaning process.

The proposed system differs from the available and proposed shunting systems in the following aspects. First, the application of Multi-agent approach, where the agent system is located within the patient environment (his/her body and his/her external device) and it acts as a private physician that accompanies the patient all the time. Second, ICP monitoring and archiving, where the agent system would monitor how well the shunt is performing through analysing the real-time ICP. This would help in understanding more about the dynamics of hydrocephalus. Third, personalisation, where it addresses an element of personalisation to the CSF management and treatment through utilising ICP readings and patient feedback. Fourth, weaning, where it can capture the actual shunt dependence and achieve progressive shunt removal in which real-time ICP and patient feedback are collected after each weaning step thus verifying the treatment in real-time. And at the same time, it would provide long and safe fellow up periods after weaning is established.

8.2 Future Prospects

Future enhancements should incorporate more parameters in developing and modifying the valve schedule. For example, patient daily activities (sleeping and working times, type of work (sitting, standing)) and other parameters derived from ICP traces would enhance the performance of the valve schedule if taken into consideration when deriving or modifying a schedule. Therefore, incorporating more sensory inputs, such as posture sensor, would provide such parameters that help fine tuning the management and treatment.

Implementing a CSF management system that delivers an intelligent personalised treatment that has self auditing ability would be a big step towards reducing the drawbacks of the current systems and improving the quality of treatment that not only manages the disease but try to cure it. In such shunt, faults are detected and fixed in their early stages thus avoid the patient from any inconveniences that usually associated with a faulty shunt.

The work done in this thesis can be modified to suit all types of hydrocephalus (*i.e.* not only high pressure hydrocephalus). In addition, the significance of such intelligent personalised shunting system can be extended by incorporating it into a distributed network of intelligent shunts, where data mining and knowledge acquisition techniques are deployed to analysis and interpret hydrocephalus patients' data for case enquiring, treatment plan advising, and ICP classification and patient clustering. In addition it would let patients exchange and share the treatment and management process.

Appendix A

Commercial Valves

TABLE A.1: Some Commercial Valves for Hydrocephalus.

Type	Company	Characteristics
PS Medical Delta valve	Medtronic [69]	(1) has anti-siphon device (2) does not need to perceive atmospheric pressure to work
Strata valve	Medtronics [69]	a programmable valve with variable pressure settings which can be coupled with their Delta valve anti-siphoning system
Horizontal-vertical valve	Integra [47]	(1) closes when a person in standing and opens when they are lying down (2) used in shunts running from the lower spinal canal into the abdominal cavity in individuals with communicating hydrocephalus
NMTs Orbis valve	Integra [47]	(1) offers a variable resistance to flow as a function of variations in pressure within the ventricles (2) avoids over drainage due to transient, normal rises in pressure within the head such as happen when an individual coughs or sneezes
Orbis-Sigma Valve II Smart Valve	Integra [47]	(1) manages hydrocephalus through flow-regulation rather than conventional differential-pressure regulation (2) A 3-stage, variable resistance mechanism that regulates at a rate close to that of CSF secretion (min. under or overdrainage)
Hakim Anti-Siphon Devices	Integra [47]	(1)responsive to atmospheric pressure (2) Gravity Compensating Accessory
Hakim Valve System	Integra [47]	Differential pressure valve
Low Flow valve	Integra [47]	automatic, self-adjusting choice for NPH
Hakim programmable	Codman [20]	(1) a pressure differential valve (2) its resistance can be altered using a magnet field transmitted through the skin (3) used in the treatment of normal pressure hydrocephalus (NPH) (4) could lead to overdrainage
Hakim Programmable Valve with a Siphon-Guard Valve	Codman [20]	This system has both a programmable pressure differential valve and an anti-siphon valve distal to it

Appendix B

Simulink Models for the Simulated Shunting Systems

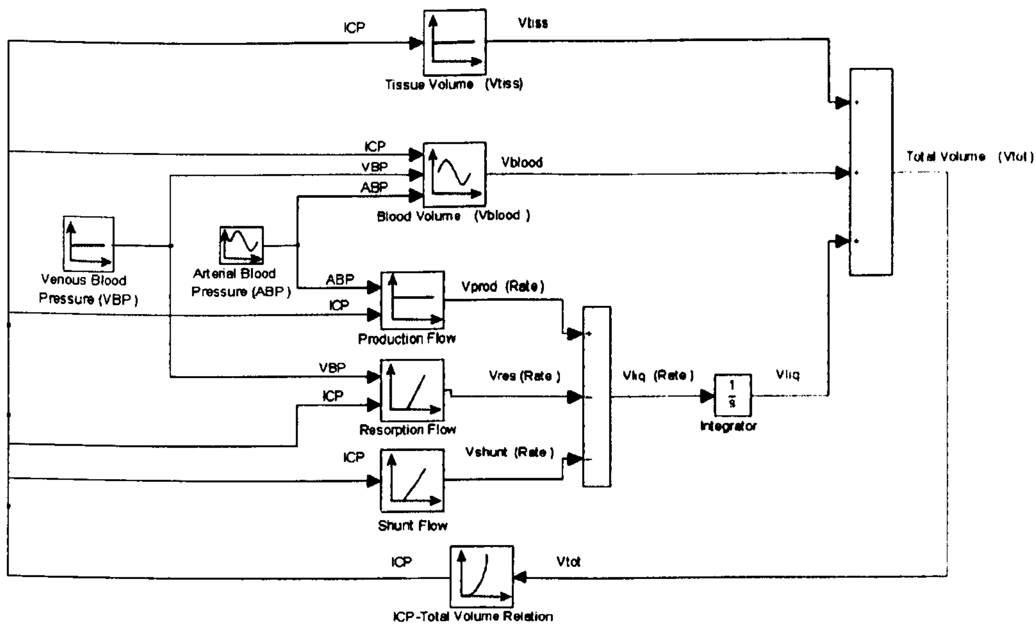


FIGURE B.1: The overall model of the hydrodynamics of the intracranial system.

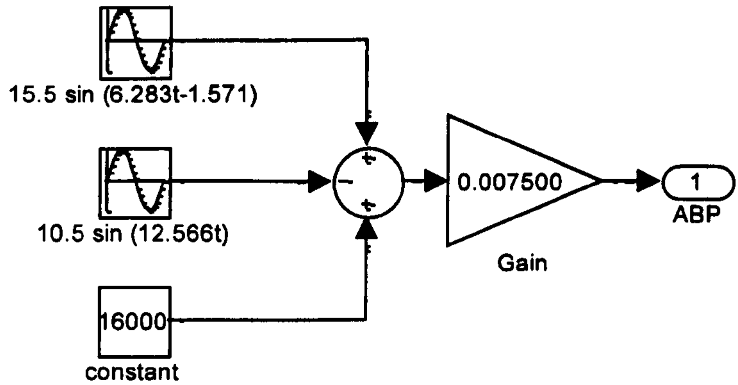


FIGURE B.2: The model of the arterial blood pressure.

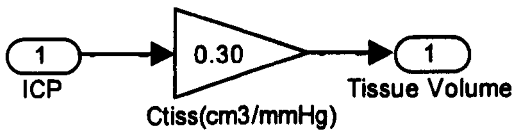


FIGURE B.3: The model of the brain tissue volume.

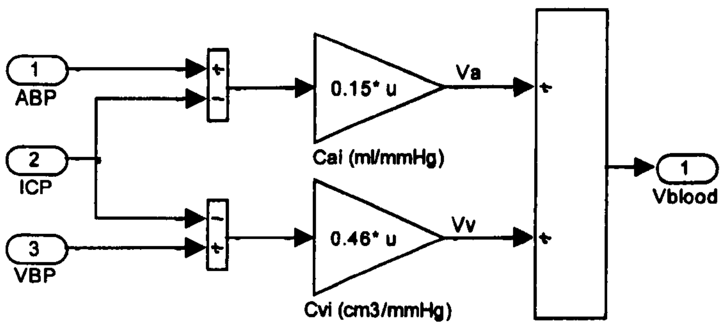


FIGURE B.4: The model of the blood volume.

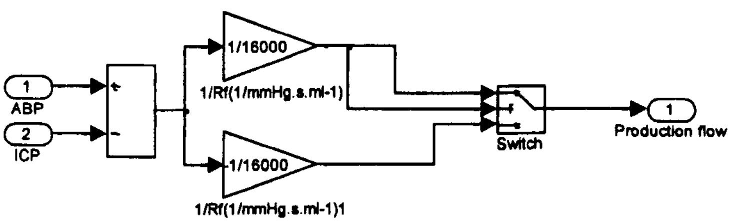


FIGURE B.5: The model of the blood volume.

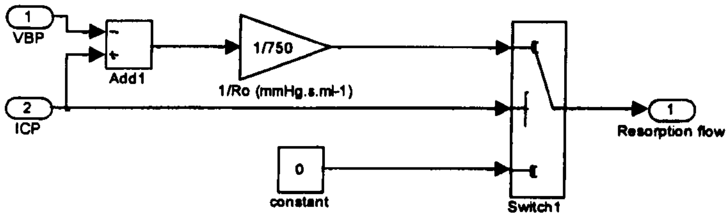


FIGURE B.6: The model of the blood volume.

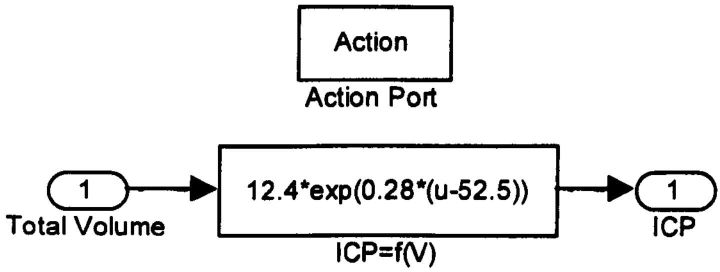


FIGURE B.7: The model of relation between ICP and the total volume.

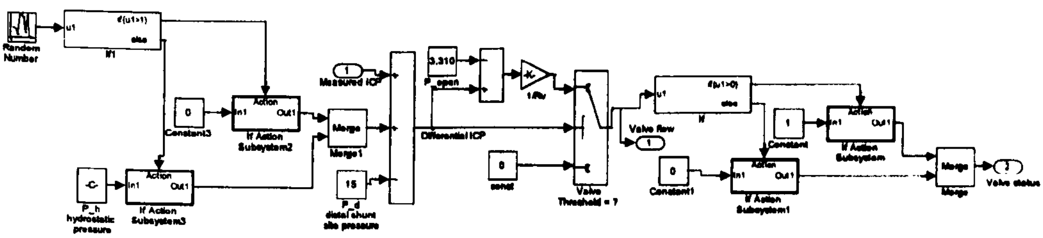


FIGURE B.8: The model of the standard valve.

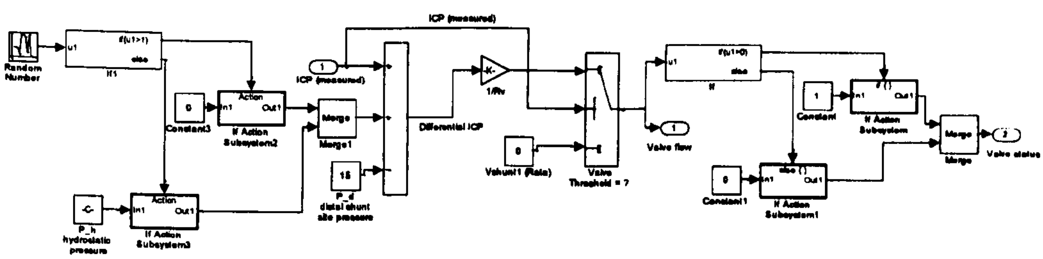


FIGURE B.9: The model of the closed loop shunt.

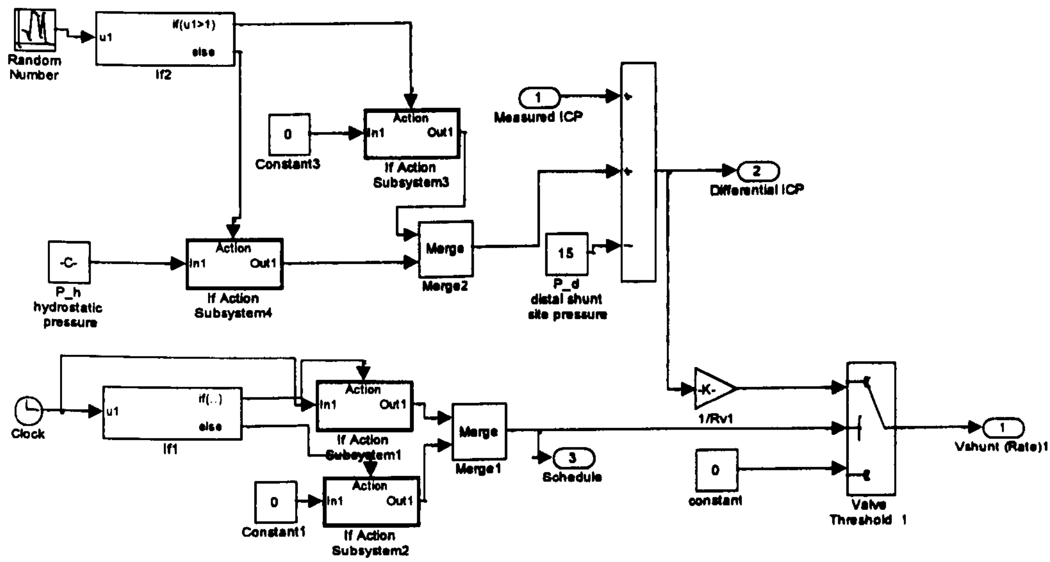


FIGURE B.10: The model of the scheduled valve.

Appendix C

Simulation Parameters

TABLE C.1: Parameters of the simulated valves.

Standard Shunt [30]	
P_{open}	3.31 mmHg
R	264.78 mmHg.s/ml
Closed Loop Shunt	
P_{open}	10 mmHg
R	264.78 mmHg/ml/sec

Appendix D

Results for Simulating Different Shunting Systems

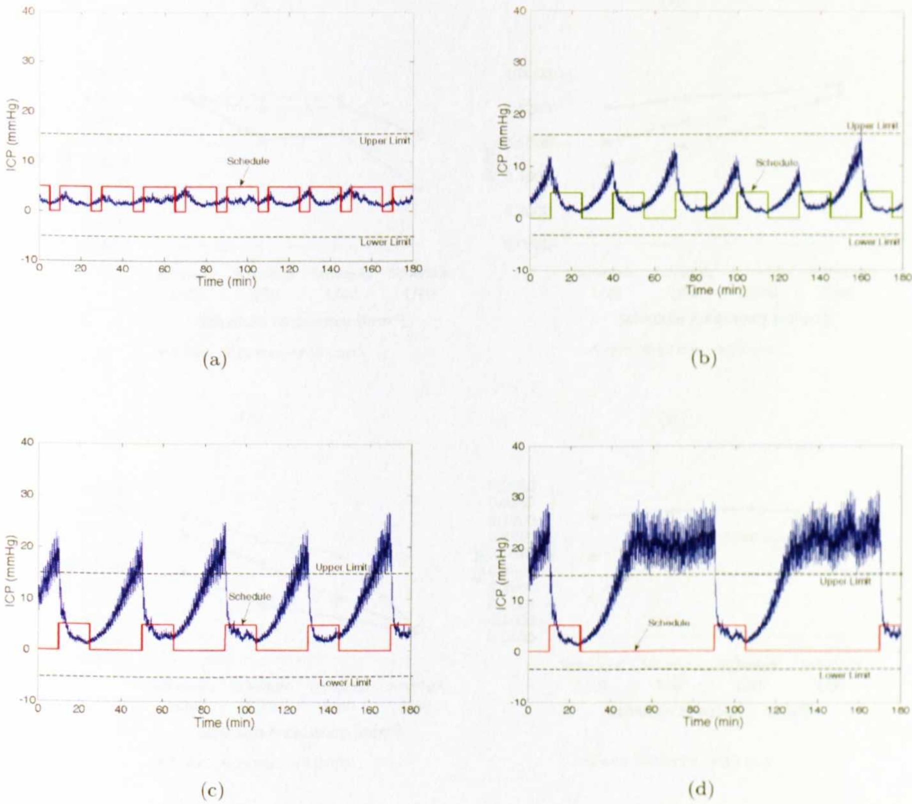


FIGURE D.1: Resulting ICP waveforms for scheduled shunts that alternate between states for 15 minutes every (a) 20min, (b) 30min, (c) 40min, and (d) 80min.

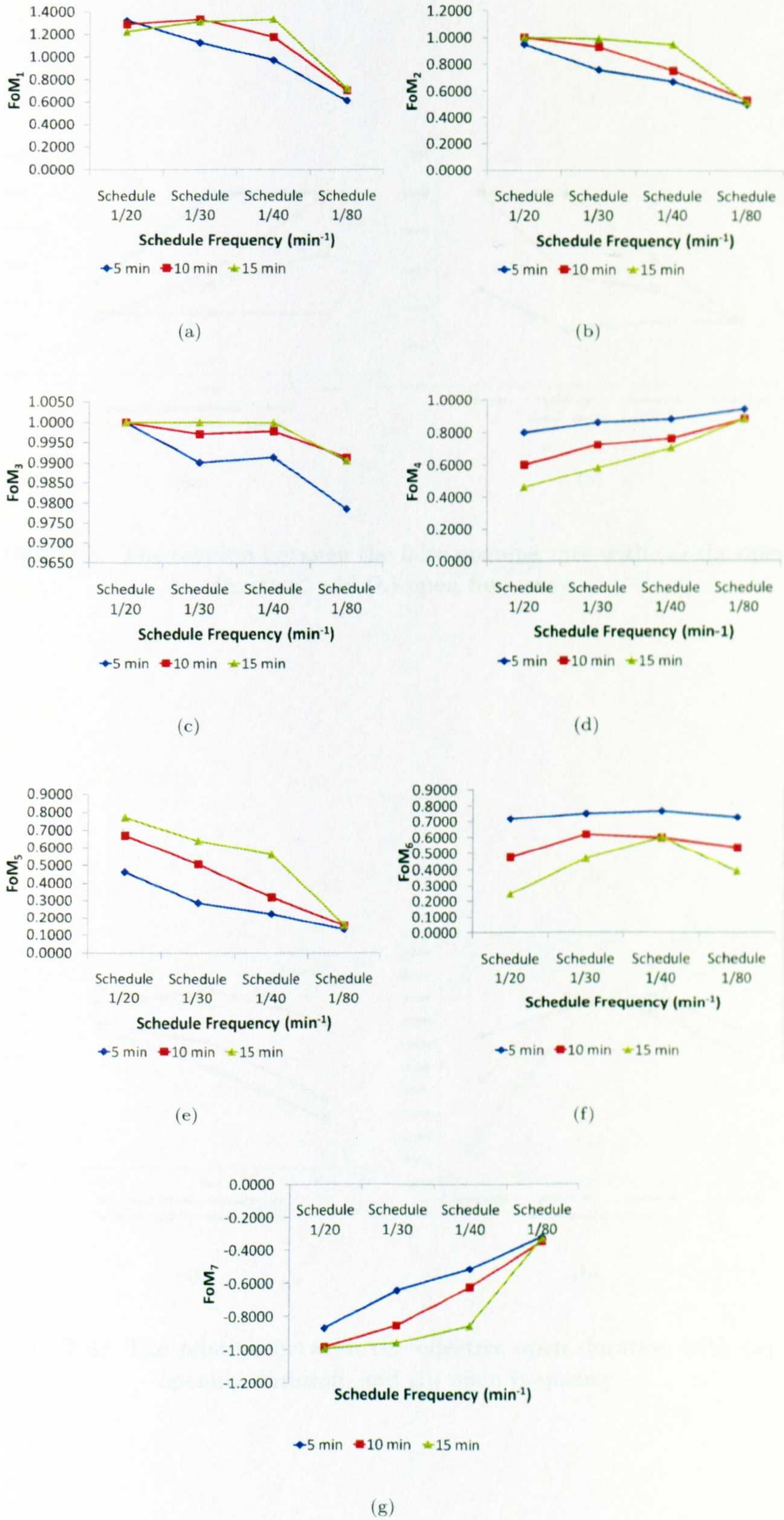
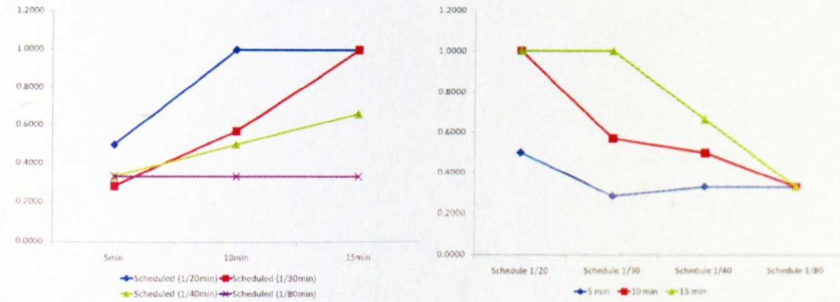
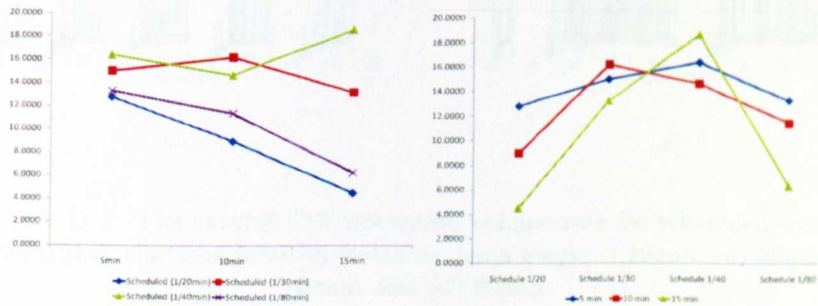


FIGURE D.2: The figure of merits versus the opening frequency; (a) FOM_1, (b) FOM_2, (c) FOM_3, (d) FOM_4, (e) FOM_5 (f) FOM_6, and (g) FOM_7.



(a) (b)

FIGURE D.3: The relation between the false opening rate with (a) the opening duration, and (b) open frequency.



(a) (b)

FIGURE D.4: The relation between the effective open duration with (a) the opening duration, and (b) open frequency.

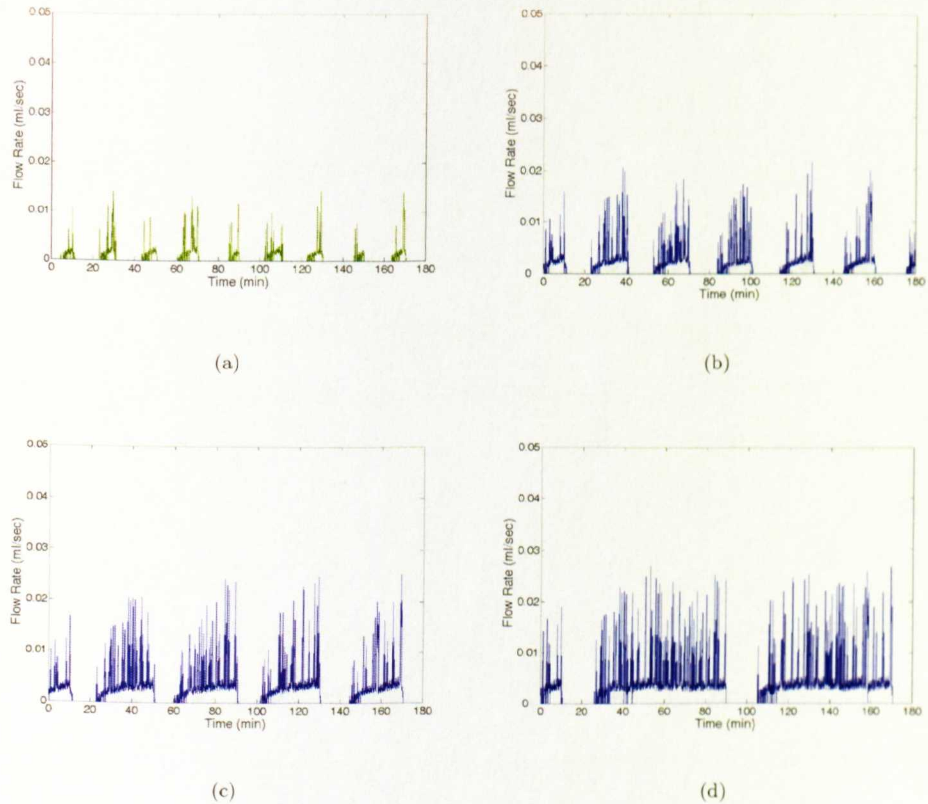


FIGURE D.5: The natural CSF resorption volume rate for scheduled shunting systems that alternate between states for 5min every(a) 20min, (b) 30min, (c) 40min, and (d) 80min.

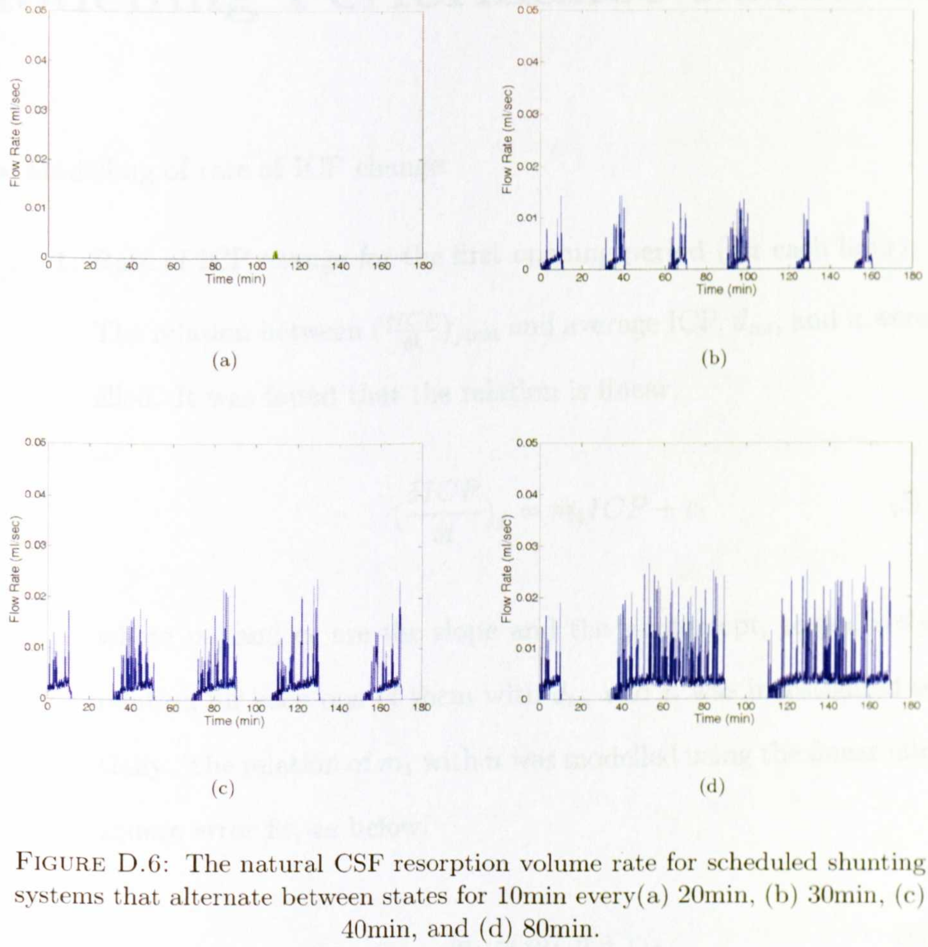


FIGURE D.6: The natural CSF resorption volume rate for scheduled shunting systems that alternate between states for 10min every(a) 20min, (b) 30min, (c) 40min, and (d) 80min.

Appendix E

Modelling Performance Measures

- Modelling of rate of ICP change:

  1. Rate of ICP change for the first opening period (for each hour):

     The relation between $(\frac{\delta ICP}{\delta t})_{first}$ and average ICP, d_{tot}, and n were modelled. It was found that the relation is linear,

     $$(\frac{\delta ICP}{\delta t})_f = m_1 ICP + c_1 \qquad \text{(E.0.E.1)}$$

     where m_1 and c_1 are the slope and the y-intercept, respectively. The relation for each one of them with d_{tot} and n was investigated sequentially. The relation of m_1 with n was modelled using the linear minimum square error fit, as below:

     $$m_1 = m_{1a} n + c_{1a} \qquad \text{(E.0.E.2)}$$

where m_{1a} and c_{1a} are the slope and intercept of this relation. The effect of d_{tot} on them is represented through the following relations,

$$m_{1a} = 0.9976 d_{tot}^{-0.94}, R^2 = 0.9859 \quad \text{(E.0.E.3)}$$

$$c_{1a} = 8 \times 10^{-7} d_{tot}^4 - 9 \times 10^{-5} d_{tot}^3 + 3.3 \times 10^{-3} d_{tot}^2 - 0.051 d_{tot} + 0.2657, R^2 = 0.8526 \quad \text{(E.0.E.4)}$$

As for the relation of c_1 with d_{tot} and n is derived as below,

$$c_1 = m_{1c} n + c_{1c} \quad \text{(E.0.E.5)}$$

where m_{1c} and c_{1c} are the slope and intercept of this relation. The effect of d_{tot} on them is represented through the following relations,

$$m_{1c} = -2.7 \times 10^{-3} d_{tot}^2 + 0.1651 d_{tot} - 2.4932, R^2 = 0.8960 \quad \text{(E.0.E.6)}$$

$$c_{1c} = 40.878 d_{tot}^{-1.513}, R^2 = 0.9424 \quad \text{(E.0.E.7)}$$

2. Rate of ICP change between the start of first opening period and the end of the last opening period for each hour,

$$\left(\frac{\delta ICP}{\delta t}\right)_{first-end} = m\overline{P} + c \quad \text{(E.0.E.8)}$$

$$m = m_1 n + c_1 \tag{E.0.E.9}$$

$$m_1 = 5 \times 10^{-5} d_{tot} - 0.0015, R^2 = 0.3726 \tag{E.0.E.10}$$

$$c_1 = 1.2805 d_{tot}^{-1.008}, R^2 = 0.9998 \tag{E.0.E.11}$$

$$c = m_2 n + c_2 \tag{E.0.E.12}$$

$$m_2 = -8 \times 10^{-5} d_{tot}^2 + 0.0053 d_{tot} - 0.088, R^2 = 0.9310 \tag{E.0.E.13}$$

$$m_2 = 0.015 d_{tot} - 0.4597, R^2 = 0.3818 \tag{E.0.E.14}$$

It has been noticed that the effect of n on $(\frac{\delta ICP}{\delta t})_o$ is very small epceciallly when n greater than 1 for d grater than 5min.

3. Rate of average ICP change $(\frac{\delta \overline{ICP}}{\delta t})$. The relation between $\frac{\delta \overline{ICP}}{\delta t}$ and average ICP $(\overline{ICP})$ was modelled using minimum square error fit at fixed total open duration d_{tot}, as below:

$$\frac{\delta \overline{ICP}}{\delta t} = m\overline{P} + c \tag{E.0.E.15}$$

It was noticed that slopes of the lines for different d_{tot} were parallel. The relation between the slope (m) and y-intercept of the previous model with n was investigated. It was clear that n has negligible effect on m,

$$m = 1 \times 10^{-18} n + 0.0162 \qquad \text{(E.0.E.16)}$$

Whereas n has the following relation with c,

$$c = m_1 n + c_1 \qquad \text{(E.0.E.17)}$$

The effect of d_{tot} on m_1 and c_1 was also found to be,

$$m_1 = -8 \times 10^{-8} d_{tot}^4 + 9 \times 10^{-6} d_{tot}^3 - 0.003 d_{tot}^2 + 0.0047 d_{tot} - 0.0181, R^2 = 0.6535 \qquad \text{(E.0.E.18)}$$

$$c_1 = 2 \times 10^{-6} d_{tot}^4 - 0.0001 d_{tot}^3 + 0.0045 d_{tot}^2 - 0.0417 d_{tot} + 0.1176, R^2 = 0.9928 \qquad \text{(E.0.E.19)}$$

It has been observed that n had negligible effect on $\frac{\delta TCP}{\delta t}$ when d_{tot} was less than 15min and greater than 25min. Also when d_{tot} was between 15 and 25 mins at n was greater than 2.

- Effective opening duration (t_e) A best fit curve was taken for the data, which end up to be exponential,

$$t_e = Ae^{Bn} \qquad \text{(E.0.E.20)}$$

where n is the number of drainage times per hour, A and B are the exponential constants.

A model of A and B with respect d_{tot} was derived using minimum square error fitting,

$$A = A_1 d_{tot}^5 + A_2 d_{tot}^4 + A_3 d_{tot}^3 + A_4 d_{tot}^2 + A_5 d_{tot} + A_6 \quad \text{(E.0.E.21)}$$

$$B = B_1 d_{tot}^6 + B_2 d_{tot}^5 + B_3 d_{tot}^4 + B_4 d_{tot}^3 + B_5 d_{tot}^2 + B_6 d_{tot} + B_7 \quad \text{(E.0.E.22)}$$

A_i's and B_i's are dependant on average ICP. It has been noticed that the effect of average ICP was negligible, so these values were assumed constant as follows,

$$A = -5 \times 10^{-6} t_{tot}^5 + 6 \times 10^{-4} t_{tot}^4 - 3 \times 10^{-2} t_{tot}^3 + 0.6453 t_{tot}^2 - 5.5905 t_{tot} + 25.512, R^2 = 0.9 \quad \text{(E.0.E.23)}$$

$$B = -2 \times 10^{-8} d_{tot}^6 + 2 \times 10^{-6} d_{tot}^5 - 1 \times 10^{-4} d_{tot}^4 + 4.6 \times 10^{-3} d_{tot}^3 - 7.97 \times 10^{-2} d_{tot}^2 + 0.695 \quad \text{(E.0.E.24)}$$

Appendix F

Simulink Models for Different Weaning Methodologies

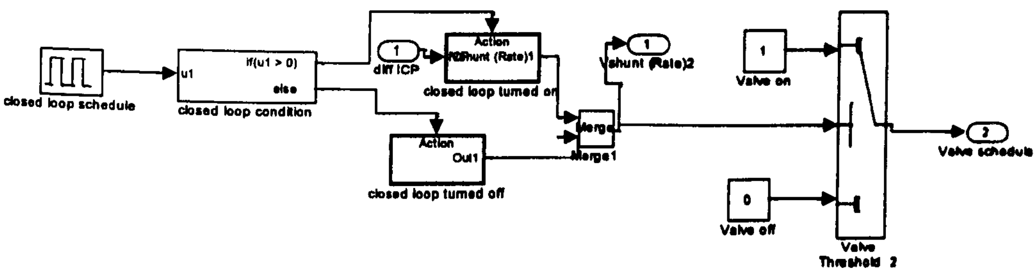


FIGURE F.1: Simulink model for scheduled closed loop technique.

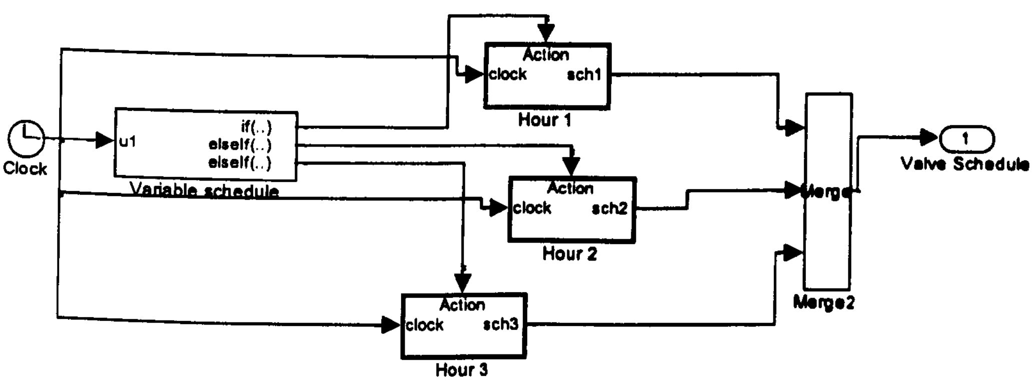


FIGURE F.2: Simulink model for shrinking slot technique.

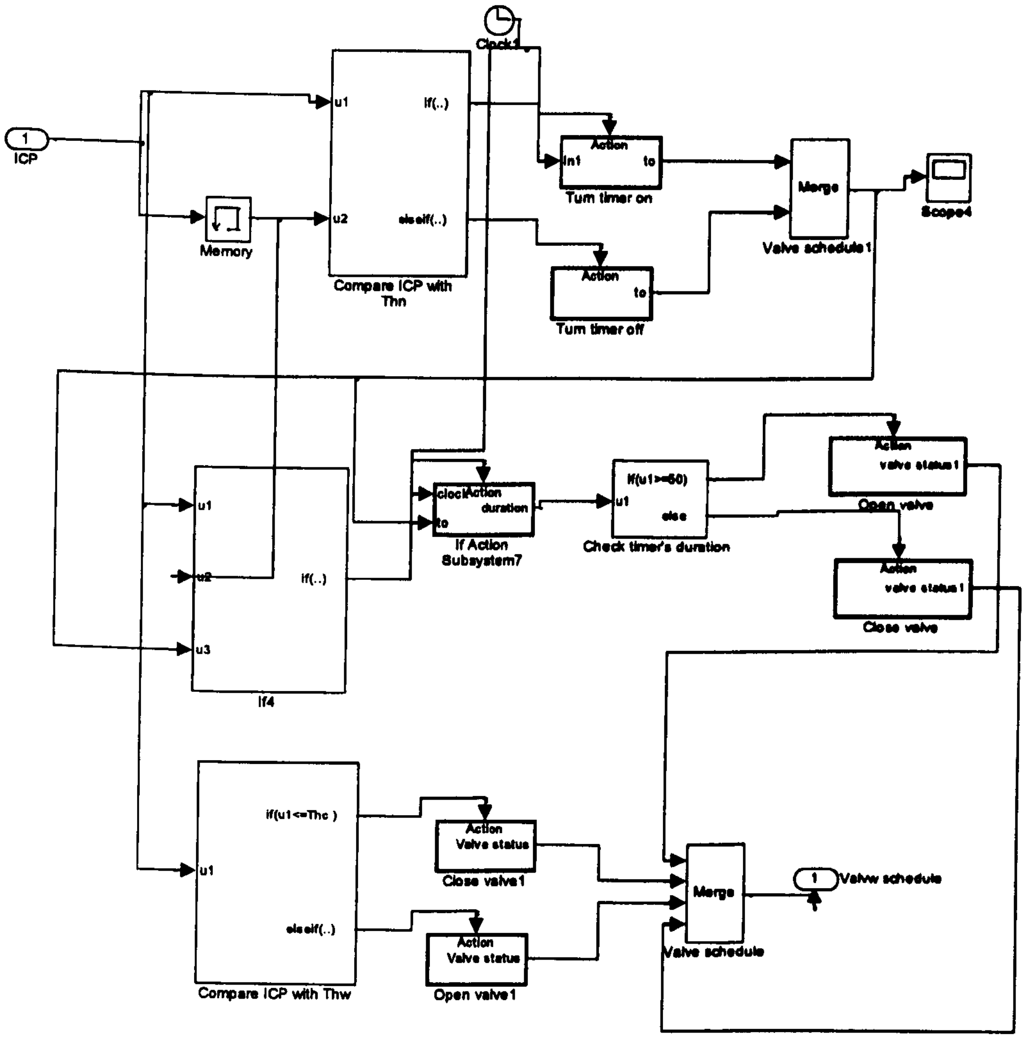


FIGURE F.3: Simulink model for closed loop timed threshold technique.

Appendix G

Results for Different Weaning Methodologies

Figure G.1 show a sample report that is generated after each weaning step. This report contains a summary of the evaluation parameters.

The ICP's traces for the simulated patient types before and after valve occlusion are shown in Figure G.2.

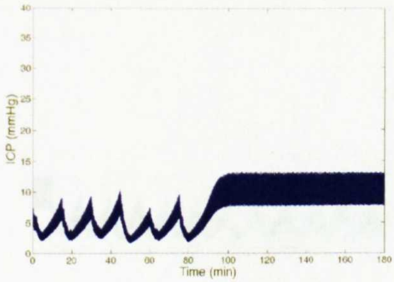
ICP for all patient after weaning off one drainage slot

Weaning Performance Measures
Results

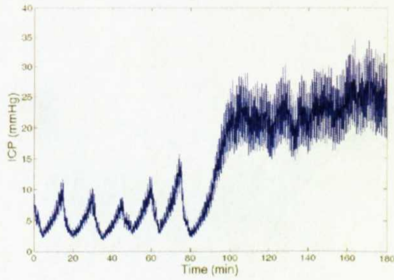
Patient Type: II
Weaning Technique: Closed Loop Timed Threshold
Timer Duration = 5 min
Normal Threshold = 10 mmHg
Closing Threshold = 10 mmHg
Weaning Threshold = 15 mmHg

	Hours		
Hourly parameters	1	2	3
ICPavg (mmHg)	8.01	8.02	8.01
ICPavg at start(mmHg)	8.01	8.02	8.02
ICPavg at start(mmHg)	8.01	8.02	8.01
Rate of ICP change (mmHg/min)	0.0001	0.0000	-0.0000
MADavg at start(mmHg)	1.41	1.41	1.42
MADavg at end(mmHg)	1.41	1.41	1.41
MADavg (mmHg)	1.41	1.41	1.41
Rate of MAD change (mmHg/min)	0.0000	-0.0000	-0.0000
No. of drainage periods	60.00	62.00	64.00
Summation of drainage periods (min)	10.00	10.33	10.67
FoM1	1.2122	1.2120	1.2122
FoM2	1.0000	1.0000	1.0000
FoM3	1.0000	1.0000	1.0000
FoM4	0.8333	0.8278	0.8222
FoM5	-0.0000	-0.0000	-0.0000
FoM6	0.8333	0.8278	0.8222
FoMavg	0.8131	0.8113	0.8094
Effective open duration (min)	0.8333	0.8011	0.7708
False open	1.0000	1.0000	1.0000
False close	0.0000	0.0000	0.0000

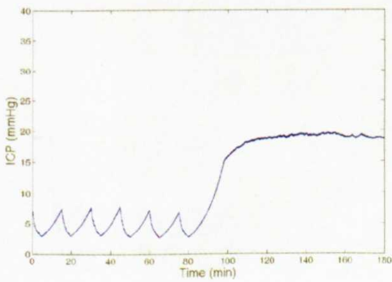
FIGURE G.1: Sample report consisting summary of evaluation parameter for closed loop technique.



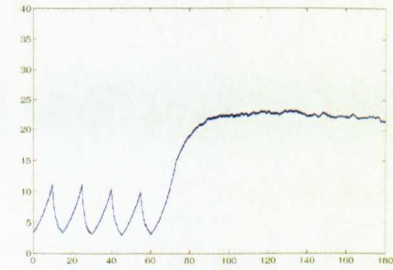
(a)



(b)



(c)



(d)

FIGURE G.2: Different patient types based on ICP traces (a) patient type I, (b) patient type II, (c) patient type III and (d) patient type IV.

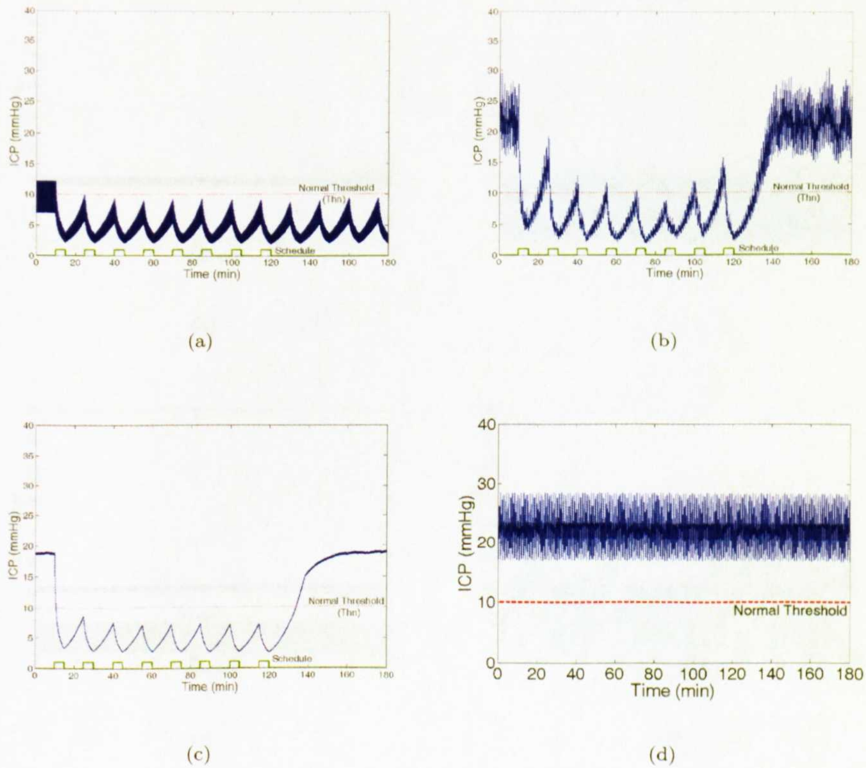


FIGURE G.3: Patient's ICP traces before performing weaning techniques (a) patient type I, (b) patient type II, (c) patient type III and (d) patient type IV.

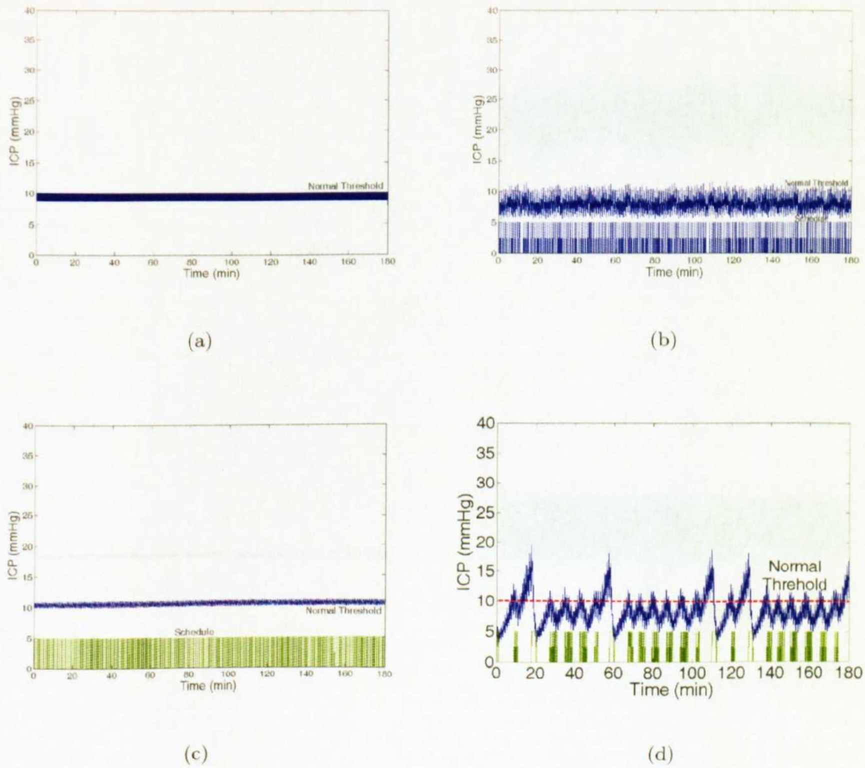


FIGURE G.4: Patient's ICP traces after implementing closed loop timed threshold technique (a) patient type I, (b) patient type II, (c) patient type III and (d) patient type IV.

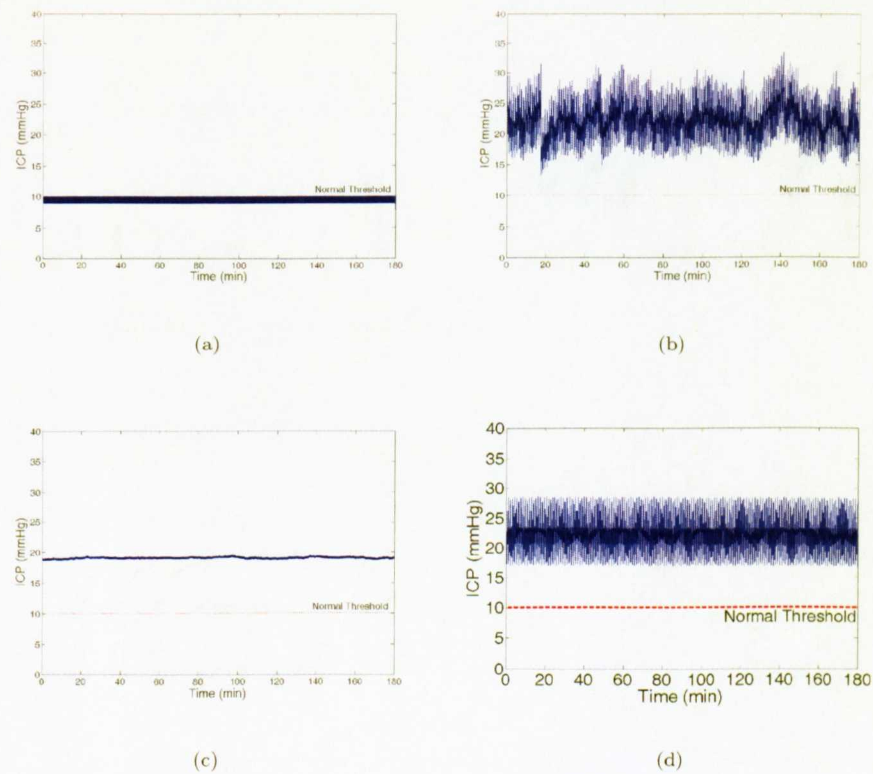


FIGURE G.5: Patient's ICP traces after implementing scheduled closed loop technique (a) patient type I, (b) patient type II, (c) patient type III and (d) patient type IV.

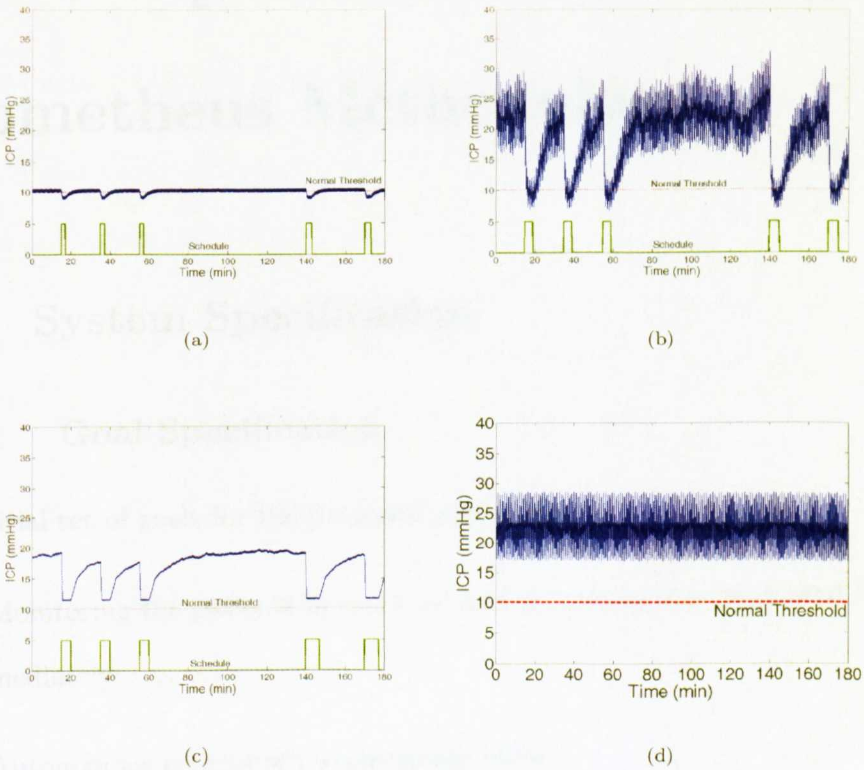


FIGURE G.6: Patient's ICP traces after implementing schedule with shrinking slots technique (a) patient type I, (b) patient type II, (c) patient type III and (d) patient type IV.

Appendix H

System Specification by Using Prometheus Methodology

H.1 System Specification

H.1.1 Goal Specification

The initial set of goals for the proposed system were:

- Monitoring the patients in real time and processing the monitored data immediately.
- Autonomous control of the electronic valve.
- Responding to the sensory inputs.
- Adjusting treatment.
- Logging and sharing response to adjustment.
- Attempting to wean off treatment.
- Learning from the experience of other agents.

- Autonomously adapt to the needs of the patient.
- Intelligent and personalised treatment.
- Satisfy the patient.
- Maintain ICP level.
- Learn about hydrocephalus.
- Distributed learning system.
- Interacting with other systems.

The set of goals of the intelligent system that were developed after identifying the initial goals, refining and adding goals as needed:

- Adjusting time-based program
  - send/receive messages to/from the outer system
  - save the adjustments (keep a record of the changes)
- Shunt wean off
  - Follow weaning regime
  - Change duration / timing of opening
- Intelligent And Personalised Treatment
  - statistical analysis
  - follow the program
- Managing sensory inputs
  - log and share

  - respond to feedback
  - feedback diagnosis
- Satisfy the patient (abstract goal: motivator for more concrete goals)
- Maintain ICP level (abstract goal)
- Learn about hydrocephalus (abstract goal)

H.1.2 Functionalities

Functionalities of the intelligent system, which is chunk of behavior, are described below through their descriptor.

- ***Valve Management Functionality***

  Description This functionality regulates the opening/closing of the electronic valve according to the pre-set program, emergency call or weaning regime.

  Goals follow the program, respond to emergency call, follow weaning regime.

  Actions send an order to open valve, send an order to close valve, save valve status.

  Triggers pre-set program, patient feedback, physician update, sensors inputs (ICP sensor).

  Information used pre-set program, emergency feedback, weaning regime, valve status.

  Information produced valve status.

- ***Adjustment Handling Functionality***

Description This functionality monitors the updates on the gating program, amend the program and save them. It keeps the outer station updated with any changes in the program and at the same time allows the outer system (patient feedback or physician update) to upgrade/change the program.

Goals keep a record of changes, inform the outer station of the changes, implement the changes.

Actions save the adjustments, amend the program.

Triggers approved changes in the program.

Information used outcome of the statistical analysis results, updates on the program.

Information produced updated program

- ***Weaning Management Functionality***

Description This functionality manage weaning regime. It gradually apply the weaning in order to reduce shunt dependence in later stages. Regime implementation differs according to patient response.

Goals follow weaning regime, satisfy the patient.

Actions change duration of opening, change timing of opening.

Triggers stability in statistical analysis (stability in patient response).

Information used regimes, statistical results of feedback.

Information produced updated gating program, request feedback, weaning next step.

- ***Data Management Functionality***

    Description This functionality manages the sensory data. This is achieved by receiving data from outer station* and classify them according to their types i.e. feedback, program update.

    Goals gather the sensory data.

    Actions classify data, send feedback for statistical analysis, save data, request feedback.

    Triggers arrival of sensory data, need for sensory data.

    Information used sensory data.

    Information produced a request for feedback.

    * Outer station is either patient or physician.

- ***Statistical Analysis functionality***

    Description This functionality performs different statistical analysis to find out whether the changes in the inputs are random or systematic. Besides that it measures the stability of the system.

    Goals feedback diagnosis.

    Actions statistical analysis of feedback.

    Triggers arrival of feedback.

    Information used patient feedback (satisfaction), ICP readings.

    Information produced statistical analysis results.

- *Communication functionality*

  Description This functionality receives the sensory inputs and sends any updates to the outer station. It is considered the link between the internal system with the external one.

  Goals log and share

  Actions receive sensory input, send updates, request feedback.

  Triggers arrival of sensory inputs, request for updates/feedback, need for information.

  Information used request for updates/feedback, sensory input.

  Information produced - - -

- *Decision Making functionality*

  Description This functionality integrate various knowledge and statistical results to provide an effective decision whether to update the current gating program or not. It also provide the decision whether to start the weaning process or not.

  Goals autonomously updating the program, shunt wean off.

  Actions decide to update the program, decide to start weaning.

  Triggers arrival of statistical results, request for statistical analysis.

  Information used statistical results, agent library.

  Information produced request to update the program, request to start weaning.

TABLE H.1: Routine Scenario.

	Step Type	Step	Functionality	Data used and produced
1	Goal	Follow the program	VM	PP, EFB, WR —
2	Action	Send an order to Open/close valve	VM	PP, EFB, WR —
3	Action	Save valve status	VM	PP, EFB, WR —
4	Action	request for a feedback	DM	— request for feedback
5	Other	Waiting for response		
6	Percept	Arrival of feedback		
7	Action	Save feedback	DM	Feedback Feedback
8	Goal	Autonomously update the program	DEM	
9	Goal	Feedback diagnosis	SA	Statis. results Approved adjust.
10	Action	Statistical analysis	SA	Feedback over period of time Statis. results
11	Action	Decide to update/wean	DEM	Statis. results
12	Action	Amend the program	AH	Approved adjust. updated program

H.1.3 Scenario Development

Scenarios show the sequences of steps that take place within the system.They are used primarily to illustrate the normal running of the system and it also can be useful when used to indicate what is expected to happen when something goes wrong [80].

Fully developed steps for the scenarios that are expected to happen in our intelligent system are shown below. Table H.5 is the key for functionalities and data abbreviation.

1. Routine Scenario is illustrated in Table H.1.

2. Weaning Scenario is illustrated in Table H.2.

3. Program Adjusting scenario is illustrated in Table H.3.

TABLE H.2: Weaning Scenario.

	Step Type	Step	Functionality	Data used and produced
1	Percept	Int/ext signal to start up weaning	DEM/-	
2	Goal	Follow weaning regime	VM	
3	Action	send order to open/close valve	VM	
4	Goal	change duration/timing of opening	WM	Regime program
5	Action	Request for feedback	DM	
6	other	Wait for a feedback or fixed time pass by		
7	Percept	Arrival of feedback	DM	— Feedback
8	Action	Statistical analysis	SA	Feedback Statistical results
9	Goal	Check patient satisfaction	DEM	Statistical results Approving the change

TABLE H.3: Program Adjusting Scenario.

	Step Type	Step	Functionality	Data used and produced
1	Percept	Arrival of approved update		
2	Percept	Receive message from outer station		
3	Goal	Keep record of changes	AH	
4	Action	Amend the program	AH	Approved adjust. Updated program
5	Action	Save the adjustments	AH	Updated program Updated program
6	Action	Send message to outer station	AH	— Updated program

4. Emergency Scenario is illustrated in Table H.4.

H.1.4 Interface Description

H.1.4.1 Percepts and Actions

Typically, an application has some number of obvious percepts and actions that are the initial definition of how the system will interact with the environment [80]. In the proposed intelligent system, some of the initial percepts and action were identified below.

TABLE H.4: Emergency Scenario.

	Step Type	Step	Functionality	Data used and produced
1	Percept	Arrival of emergency feedback		
2	Goal	respond to feedback	VM	EFB Open/Close valve
3	Action	Send an order to open/close valve	VM	Open signal —
4	Action	Save valve status	VM	Valve status
5	Action	Save the feedback	DM	Feedback
6	other	Wait for back-to-normal signal or passing a period of time without E signal		
7	Percept	Arrival of feedback	VM	Updated program Updated program
8a 8b	Action Action	Send an order to close valve Send message to outer station in case of non-stopping Emergency FB for a certain period of time AH EFB Emergency call	VM	Close signal

TABLE H.5: Key for functionalities and data abbreviation.

Functionalities	Abbrev.
Valve Management	VM
Data Management	DM
Statistical Analysis	SA
Adjustment Handling	AH
Weaning Management	WM
Emergency feedback	EFB
Approved adjustment	Approved adjust.
Statistical results	Statis. results
Statistical Analysis	Statis. Analysis
Pre-set program	PP
Weaning regime	WR
Decision making	DEM

Precepts

- Arrival of emergency feedback
- Arrival of feedback
- Arrival of satisfactory feedback
- Arrival of an update on the program

- Internal/external signal to start up weaning
- Receive a message from outer station

Actions

- Amend the program
- Request a feedback
- Save the adjustments
- Save the feedback (and its timing)
- Save valve status
- Send an order to close valve
- Send an order to open valve
- Send internal message to inform statistical results (internal)
- Send message to outer station (in case of non-stopping EFB for a certain period of time)
- Send updates
- Statistical analysis
- change duration/timing of opening
- Classify data
- Send feedback to statistical analysis
- Request feedback

- Decide to update
- Decide to wean

H.1.4.2 Data

There are two types of data in this phase; used data and produced data. At the system specification phase, the external data to the agent system should be especially noted [80]. In the proposed system there are two External Databases; Patient device DB and Physician Device DB. And the information can be grouped to the following clusters.

Patient DB- contains information about patient, their medical history , visits to hospital or physician

Patient feedback DB- contains records of recent feedback (satisfied, unsatisfied or emergency) that have been sent (saved) and their timing action taken to respond to them.

Libraries DB- a comprehensive libraries that contain heuristic guideline for opening/closing the valve and weaning regimes.

Valve status- open or close

Program updates- contains the recent updates on the program

Statistical analysis- contains the results and decision taken regarding the opening/close of the valve depending the recent feedback.

H.1.5 Checking for completeness and Consistency

One of the advantages of doing design in structured way is that it becomes possible to specify a range of checks for consistency and completeness [80]. The following checks were done to ensure consistency and completeness,

- Names should be consistent.
- All goals are covered by the scenarios and functionalities.
- There are scenarios and functionalities for every action and percept.

Next step will be architectural design through specifying the agents types,specifying the interactions and finalizing the architectural design. This will be covered in the next report.

H.2 Architectural Design: Specifying the Agents Types by Using Prometheus Methodology

Architectural design of a system consist of three aspects;deciding on the agent types, describing the interactions between agents and designing the overall system structure.

This report will cover the first aspect. And this was achieved by following three steps. First step is grouping the functionalities into agents and considering all alternatives. Second step is reviewing coupling by using agent acquaintance diagrams and deciding on the best grouping [80].

H.3 Grouping Functionalities

The functionalities of the system were grouped into agents. The grouping into one agent was done if the functionalities seems related or they require a lot of same information. On the other hand, the reason for not grouping some of the functionalities was due that functionalities exist on different hardware platforms or different number of functionalities are required at run time [80].

Data coupling diagram was developed to systematically examine the properties that lead to coupling and cohesion. Figure ??show the initial and final data coupling diagram for our system, respectively. And Figure H.3 shows the agent-functionality grouping diagram.

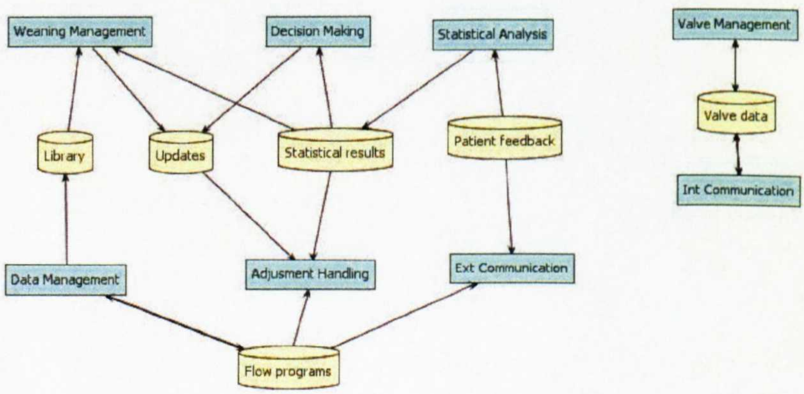


FIGURE H.1: The initial data coupling diagram.

H.4 Review Coupling

In order to evaluate a potential grouping for coupling, an agent acquaintance diagram was used. In this diagram, each agent is represented and linked to the agent it interacts with. The interactions are extracted from the functionality descriptors [80]. Figure H.4 show the resulted agent acquaintance diagram. The resulting diagram was analysed through analysing the the density of links. Where

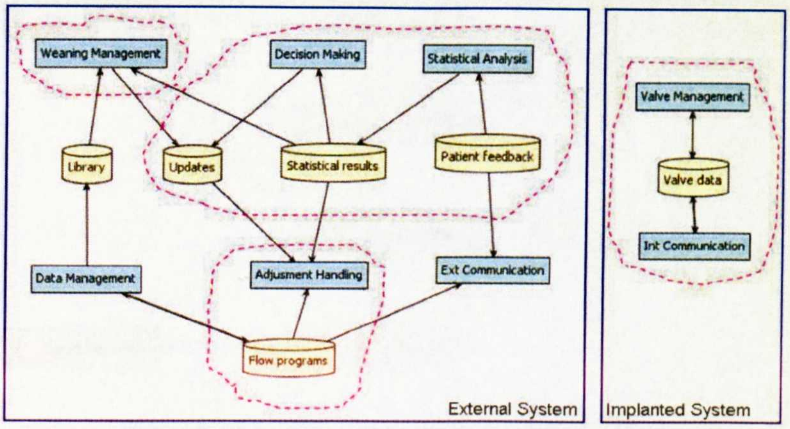


FIGURE H.2: The Final data coupling diagram.

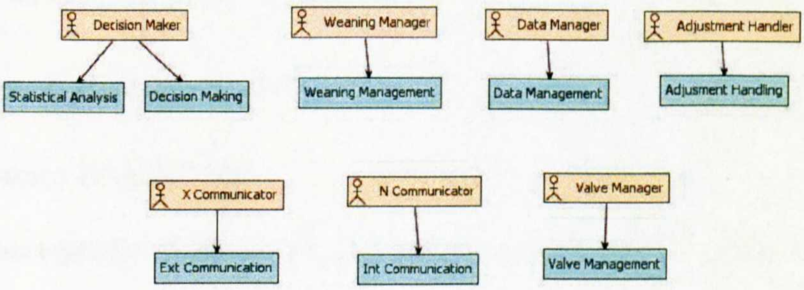


FIGURE H.3: The final agent-functionality grouping diagram.

a lower link density is less highly coupled and therefore more preferable. Also issues like bottlenecks, cohesion and agent size were taken into consideration. For the agent acquaintance diagram shown in Figure H.4, the maximum potential links between the seven agents is (7 multiplied by (7-1) and divided by 2) 21. Then the link density would be the actual number of links between agents divided by the maximum potential links, which is for this case is (8 divided by 21) 0.38. This value is low enough to consider the system has low coupling among its agents.

H.5 Develop Agent Descriptors

Each agent will be entitled with a descriptor which consist of agent name, description and other relevant information. The following is the list of agent descriptor

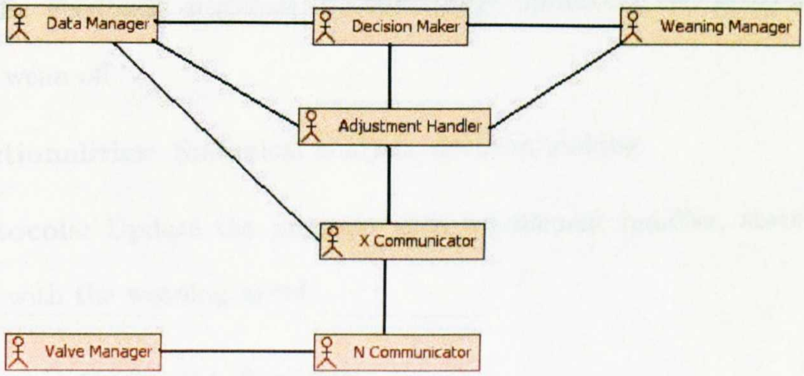


FIGURE H.4: The agent-acquaintance diagram.

for each agent in the proposed system.

- ***Agent Decision Maker***

  Name: Decision Maker

  Description: Deals statistically with the sensory inputs (patient feedback, ICP readings) and conclude a decision regarding updating the flow program or not. It also decides if is the proper time to start weaning.

  Cardinality: minimum: 0, maximum: 1.

  Lifetime: ongoing

  Initialization: Data from library.

  Demise: —

  Percepts: Arrival of feedback, arrival of physician update.

  Actions: Analyse statically the feedback, decide to update the program, decide start weaning.

  Uses data Patient feedback, library data.

  Produces data: Program update decision, program update, weaning decision.

Internal data: Statistical results.

Goals: Feedback diagnosis, autonomously updatting the program, shunt wean off.

functionalities: Statistical analysis, decision making.

Protocols: Update the program with adjustment handler, start weaning with the weaning agent.

- ***Agent Adjustment Handler***

Name: Adjustment Handler

Description: Deals with all changes on the program. It amend program, save adjustment and ensure the implanted unit is informed.

Cardinality: Minimum: 0, maximum: 1.

Lifetime: While there is adjustment to be made or weaning to be implemented.

Initialization: Previous program restored.

Demise: Save updated program, ensure updated program reaches communication agent.

Percepts: arrival of program update decision, arrival of program update, arrival of weaning update.

Actions: Save the program, amend the program.

Uses data: program updates

Produces data: updated program

Internal data: —

Goals: keep record of changes, follow weaning regime

functionalities: Adjustment handling, weaning management.

Protocols: Ensure adjustment informed through communication agent.

- ***Agent Adjustment Handler***

Name: Adjustment Handler

Description: Deals with all changes on the program. It amend program, save adjustment and ensure the implanted unit is informed.

Cardinality: Minimum: 0, maximum: 1.

Lifetime: While there is adjustment to be made or weaning to be implemented.

Initialization: Previous program restored.

Demise: Save updated program, ensure updated program reaches communication agent.

Percepts: arrival of program update decision, arrival of program update, arrival of weaning update.

Actions: Save the program, amend the program.

Uses data: program updates

Produces data: updated program

Internal data: —

Goals: keep record of changes, follow weaning regime

functionalities: Adjustment handling, weaning management.

Protocols: Ensure adjustment informed through communication agent.

- ***Agent Valve Manager***

Name: Valve Manager

Description: Manage the opening and closing of the valve according to the approved flow program.

Cardinality: Minimum:1, Maximum:1.

Lifetime: Ongoing

Initialization: Following the flow program is ongoing.

Demise: N/A Keep record valve status is ongoing.

Percepts: Program update, emergency feedback

Actions: Send an order to open/close, save valve status.

Uses data: Valve updates.

Produces data: Valve status.

Internal data: —

Goals: Follow program.

functionalities: Valve management.

Protocols: Updated through internal communication agent.

- ***Agent External Communicator***

Name: External Communicator

Description: Deals with sending the ICP data and schedule updates to implant/physician and receiving updates and sensory inputs.

Cardinality: Minimum:0, Maximum:1.

Lifetime: While there are income/outcomes to be informed.

Initialization: —

Demise: Ensure communication lines is closed, ensure information is sent to the inner/outer station.

Percepts: —

Actions: Recieve/send sensory inputs

Uses data: —

Produces data: —

Internal data: —

Goals: Keep physician/implanted shunt up to date

functionalities: Communication, data management

Protocols: —

- ***Agent Internal Communicator***

Name: Internal Communicator

Description: Deals with sending the ICP data and schedule updates to patient device and receiving updates.

Cardinality: Minimum:0, Maximum:1.

Lifetime: While there are income/outcomes to be informed.

Initialization: —

Demise: Ensure communication lines is closed, ensure information is sent to the inner/outer station.

Percepts: —

Actions: Recieve/send sensory inputs

Uses data: —

Produces data: —

Internal data: —

Goals: Keep physician/patient up to date

functionalities Communication, data management

Protocols: —

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