2009

FROM CONCEPT, TO DESIGN, EVALUATION AND FIRST IN VIVO DEMONSTRATION OF A TELE-OPERATED CATHETER NAVIGATION SYSTEM

Yogesh Thakur

FROM CONCEPT, TO DESIGN, EVALUATION AND FIRST IN VIVO DEMONSTRATION OF A TELE-OPERATED CATHETER NAVIGATION SYSTEM

(Spine title: Remote Catheter Navigation)

(Thesis format: Integrated-Article)

by

Yogesh Thakur

Graduate Program in Biomedical Engineering

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A thesis submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy

The School of Graduate and Postdoctoral Studies
The University of Western Ontario
London, Ontario, Canada

THE UNIVERSITY OF WESTERN ONTARIO
SCHOOL OF GRADUATE AND POSTDOCTORAL STUDIES

CERTIFICATE OF EXAMINATION

visor	Examiners
laria Drangova	Dr. Richard Frayne
rvisory Committee	Dr. Terence M. Peters
avid W. Holdsworth	Dr. Ting-Yim Lee
aron Fenster	Dr. David M. Pelz
aymond Yee	

The thesis by

Yogesh Thakur

entitled:

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Doctor of Philosophy

Date________________________

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Chair of the Thesis Examination Board

Abstract

Percutaneous transluminal catheter (PTC) intervention is a medical technique used to assess and treat vascular and cardiac diseases, including electrophysiological conditions. Interventional specialists use the vasculature as a passageway to guide the catheter to the site of interest, using fluoroscopic x-ray imaging for image-guidance. Common PTC procedures include: vascular angiography, inflating balloons and stents, depositing coils, and the treatment of cardiac arrhythmia via catheter ablation.

Catheter ablation has gained prevalence over the last two decades, as the treatment success rate for atrial fibrillation reaches 100%. The close proximity between the interventionalist and the radiation source combined with the increased number of procedures performed annually has lead to increased lifetime exposure; escalating the interventionalist probability of developing cancer, cataracts or passing genetic defects to offspring. Furthermore, the lead garments that protect the interventionalist can lead to musculoskeletal injury. Both these factors have lead to increased occupational risk. Catheter navigation systems are commercially available to reduce these risks. Lack of intuitive design is a common failing among these systems.

This thesis presents the design and validation of a remote catheter navigation system (RCNS) that utilizes dexterous skills of the interventionalist during remote navigation, by keeping the catheter in their hands of the interventionalist during remote navigation. For remote catheter manipulation, the interventionalist pushes, pulls, and twists an input catheter, which is placed inside an electromechanical sensor (CS). Position changes of the input catheter are transferred to a second electromechanical (CM) that replicates the sensed motion with a second, remote catheter.

Design of this system begins with understanding the dynamic forces applied to the catheter during intravascular navigation. These dynamics were quantified and then used as operating parameters in the mechanical design of the CM. In a laboratory setting, motion sensed and replicated by the RCNS was found to be 1 mm in the axial direction, 1° in the radial direction, with a latency of 180 ms. In a multi-operator, comparative study using a specially constructed multi-path vessel phantom, comparable navigation efficacy was demonstrated between the RCNS and conventional catheter manipulation, with the RCNS requiring only 9s longer to complete the same tasks.

Finally, remote navigation was performed *in vivo* to fully demonstrate the application of this system towards the diagnosis and treatment of cardiac arrhythmia.

Keywords: catheter navigation, RF ablation, fluoroscopy, image-guidance, tele-robotics, cardiac arrhythmia,

Co-Authorship

A version of Chapter 2 was published as "Characterization of Catheter Dynamics During Percutaneous Transluminal Catheter Procedures" by Yogesh Thakur, Dr. David W. Holdsworth and Dr. Maria Drangova in the IEEE Transactions in Biomedical Engineering, vol. 56(8), 2009. In this publication, I developed the mass-spring experiments under the guidance of Dr. David Holdsworth and recruited the experienced interventionalists and inexperienced operators for a study to determine the range of kinematics associated with catheter motion. In addition, I wrote custom software in python to record catheter motion and analyze the results.

A version of Chapter 3 was published as "Design and Performance Evaluation of a Remote Catheter Navigation System" by Yogesh Thakur, Jeffery S. Bax, Dr. David W. Holdsworth and Dr. Maria Drangova in the IEEE Transactions in Biomedical Engineering, vol. 56(7), 2009. In this publication, I designed the mechanical components of the Remote Catheter Navigation System and developed all the software. With guidance from Dr. David Holdsworth and Jeffrey Bax, I designed and executed experiments to independently validate each component of the Remote Catheter Navigation System, as well as the complete system.

A version of Chapter 4 was submitted as "Catheter Navigation Efficacy of a Tele-Operator Catheter Navigation System: Experimental Results in a Multi-Path Phantom" by Yogesh Thakur, Chris J. Norley, Dr. Irene B. Gulka, Dr. David W. Holdsworth, and Dr. Maria Drangova to Radiology (Submission #RAD-09-1965). This work compared the remote catheter navigation system with conventional catheter navigation, using a specially constructed multi-path phantom, and employing operators of different clinical experience levels. In this paper, I developed the experimental methodology and designed the navigation phantom used in the study. Chris Norley and Dr. Irene Gulka helped refine the experimental protocol. Chris Norley also assisted in data collection. Dr. Irene Gulka provided input into the multi-path phantom design and recruited the experienced interventionalists for the study. Dr. David Holdsworth provided guidance with respect to experimental methodology.

A version of Chapter 5 is in preparation for submission as "Tele-Robotic Catheter Navigation: First Remote Navigation In Vivo" by Yogesh Thakur, Dr. Doug L. Jones, Dr. Raymond Yee, Dr. Allen Skanes and Dr. Maria Drangova to the journal Circulation. In this publication I wrote the animal use protocol with the assistance of Dr. Doug Jones. I also developed the experimental methodology with input from Dr. Raymond Yee and Dr. Doug Jones and design equipment to adapt my tele-robotic catheter navigation systems for *in vivo* application. Dr. Allan Skanes executed the experiments with assistance from Dr. Doug Jones and Dr. Maria Drangova.

All the above work was performed under the guidance of my supervisor Dr. Maria Drangova.

This thesis is dedicated to the memory of my beloved grandmother, *mo-tdhee aa-ee*, who taught me to work hard to achieve my goals, and always enjoy life to its fullest.

Acknowledgement

First and foremost, I would like to thank my supervisor Dr. Maria Drangova for giving me the opportunity to do this project and providing me with direction and advice, Dr. David W. Holdsworth for his helpful insight towards experimental design and captivating discussions, and Dr. Aaron Fenster for his guidance and motivation. I would also like to thank Dr. Raymond Yee, Dr. Allan Skanes, Dr. Irene Gulka and Dr. Andrew Leung for their clinical input and advice.

I would also like to thank all my friends and colleagues in the Imaging Research Laboratories at Robarts Research Institute. Specifically, I would like to thank Hristo Nikolov, Chris Norley, Steve Pollman, Jacques Montrueil, Jeffrey Bax, Jeff Gardiner and Adam Guthrie, for your technical advice towards this project, and Maria Fontana, Jan Challis and Diana Timmerman for your administrative assistance.

Finally, I would like to thank my family: my parents, my sisters and my brother in-law. Your moral support and endless love have always motivated me to aim high and achieve higher.

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List of Abbreviations

AP	Accessory Pathway
AF	Atrial Fibrillation
AFL	Atrial Flutter
AV	Atrioventricular
AVNRT	AtrioVentricular Nodal Re-entrant Tachycardia
CCS	Catheter Controlled Sheath
CM	Catheter Manipulator
CS	Catheter Sensor
CoS	Coronary Sinus
CT	Computed Tomography
DAP	Dose Area Product
ECG	Electro-cardiogram
EP	Electrophysiological
FIESTA	Fast Imaging Employing Steady-State Acquisition
FGRE	Fast Gradient Recall Echo
FOV	Field of View
ICE	Intracardiac Echocardiography
ICRP	International Commission on Radiological Protection
MGS	Magnetic Guidance System
MRI	Magnetic Resonance Imaging
PCI	Percutaneous Coronary Intervention
PID	Proportional-Integral-Differential
RA	Right Atrium

RA-FW	Right Atrium Free Wall
RA-R	Right Atrium Roof
RCNS	Remote Catheter Navigation System
RF	Radio-Frequency
RV	Right ventricle
RV-A	Right Ventricle Apex
RV-FW	Right Ventricle Free Wall
RV-OT	Right Ventricle Outflow Tract
SNR	Signal-to-Noise Ratio
VF	Ventricular Fibrillation
VT	Ventricular Tachycardia
VR	Virtual Reality

Chapter 1 :

Introduction & Background

Catheterization is the process of inserting a catheter - a hollow or solid, flexible tube, into the body to perform a medical intervention. Employed to inject a contrast agent for anatomic visualization, place balloons and stents to open occluded arteries, to embolize blood vessels, to drain fluids from body cavities, to perform intra-cardiac electrocardiogram's, or to remove atherosclerotic plaque – catherization is common practice in present day medicine.

In 1929, Dr. Werner Forssmann (1904-1979) was the first to use radiography to confirm intra-cardiac placement of a catheter, after he manually pushed a urinary catheter from the brachial vein in his left forearm into the right atrium (RA) of his heart [1]. Over the past three decades, grown from Forssmann's intra-cardiac catheter demonstration, catheter-based x-ray guided intervention has become the gold standard in assessing and treating a variety of vascular and cardiac diseases and conditions.

The minimally invasive nature of catheter-based x-ray guided intervention provides many well-documented benefits, most notably – less trauma to the patient – resulting in:

shorter patient-hospitalization, accelerated return to the work force for the patient, and reduced economical burden on hospital resources [2, 3]. These benefits, combined with its high success rate have lead to a dramatic increase in the number of percutaneous catheterization procedures performed each year [4, 5]. Further increases in the number of annual procedures performed are expected to continue with demographic changes and the development and introduction of new technologies that exploit the advantages of the catheter-based approach in medical intervention.

During catheter-based, fluoroscopic x-ray image-guided intervention, the interventionalist is required to stand adjacent to the patient, while simultaneously manipulating the catheter inside the patient, and imaging the catheter inside the vasculature. Due to the close proximity between the radiation source and interventionalist during these procedures, the cumulative radiation exposure to the interventionalist who regularly performs these procedures has become a concern. Two categories classify radiation induced biological effects: 1) deterministic effects and 2) stochastic effects.

Deterministic effects occur when the radiation exposure exceeds a threshold and appear shortly after the procedure. Erythema - redness of the skin, is a common condition that occurs to patients that have undergone a catheter-based fluoroscopic x-ray guided procedure [6]; occurring when the entrance dose to the patient's skin exceeds a specific threshold (approximately 6 Gy; dose rate and patient physiology influence this value) [6]. An entrance dose above the threshold can result in more severe skin conditions and also affect other organs in the path of the x-ray beam. Deterministic effects to the interventionalist are rarely a concern, as the interventionalist is situated away from the primary x-ray beam.

On the other hand, stochastic effects do not occur after exceeding a dose threshold. Instead, the cumulative dose over many years will increase the probability of cellular degeneration, resulting in cancer or passing genetic defects to offspring. During x-ray fluoroscopy, radiation scatter from interactions between the x-ray beam and patient yield a low radiation dosage to the interventionalist. Due to the increase in the number of annually performed procedures, over the past two decades many studies have investigated radiation exposure to in-room personnel, and the occupational hazard associated with these procedures.

Results of these studies are mixed. McFadden *et al.* [7] measured monthly exposure to two interventional cardiologists over a six month period and concluded that exposure was safely below limits as set forth by the International Commission on Radiological Protection (ICRP) [8], but above that of other cardiology professions. Renaud *et al.* [9] looked at the exposure to all in-room personnel at three cardiac centres and found radiation exposure was below safety limits for every area of the body, except the lens of the eye. Other studies concluded with similar mixed results [10-13], generally stating that exposure levels that would result in a deterministic biological effect are below acceptable exposure levels for all areas of the body except the lens of the eye.

Due to many uncontrollable factors present during data collection, many authors acknowledge the difficulty in accurately measuring cumulative radiation exposure to in-room personnel, thus stating uncertainty in the reported data. These uncontrollable factors can include safety features of the imaging system, experience of the interventionalist, type of procedure performed, size of the patient, correct use of safety equipment (lead aprons, skirts, collars, and transparent lead screens), beam orientation during the procedure, and the sensitivity and proper use of the radiation detection badge. The presented list is not exhaustive, a more extensive list can be found in Rosenthal *et al.* [14], which looks at factors that help predict fluoroscopic time and also in a report outlining radiation safety by a British subcommittee gathered to investigate radiation hazards to cardiologists [15].

To reduce radiation exposure to the interventionalist, new safety equipment, and interventional methods constantly evolve. The dominant method uses pulsed fluoroscopic imaging instead of continuous fluoroscopy, which has been shown by Scanavacca *et al.* [16] to reduce fluoroscopic time by half during the radio-frequency (RF) ablation of various cardiac arrhythmias. In addition, lowering the x-ray imaging pulse rate from real-time imaging (30 pulses/second) to under 12 pulses/second can further reduce exposure without drastically affecting visualization of the catheter [15, 17]. Although radiation exposure can be reduced by these methods, stochastic biological effects still occur. Furthermore, it has been shown that lead vests, collars and skirts worn by the interventionalist to reduce exposure can in fact lead to the development of chronic neck and back pain [18]. As stated by Vano *et al.* [19], the simplest way to reduce exposure is to increase the distance between the radiation source and interventionalist during the procedure; an increase in distance of 40 cm can reduce scatter radiation exposure by over 25%. In 1993, Grant *et* al. [20] significantly reduced radiation exposure to the interventionalist by a factor of 2, using a mechanical pump to remotely inject contrast during coronary angiography. A further reduction in radiation exposure to the interventionalist can be attained by increasing the distance between the interventionalist and radiation source during the intravascular navigation and the final placement of the catheter.

The development and validation of a remote catheter navigation system for intravascular catheter navigation is the topic of this thesis.

1.1 Percutaneous Transluminal Catheter Intervention

The definition of catheterization, as stated in the opening sentence of this thesis, deals with the insertion of a tube into the body to perform a task. The specific task can be simple, like draining liquid from a cyst, or complex, such as monitoring intra-cardiac electrocardiogram's (ECG's). The latter intervention is part of a larger family of catheter interventions known as percutaneous transluminal catheterization or PTC. In PTC, the vascular anatomy acts as a channel to guide the catheter towards the area of interest. Upon placement of the catheter at this location, typically confirmed visually by fluoroscopic x-ray imaging, the catheter acts as a conduit for tools, chemicals, or other agents to diagnose and/or treat vascular and cardiac diseases, as well as electrophysiological conditions.

PTC interventions can be arranged into subgroups based on the targeted anatomy and the medical speciality performing the intervention. Interventional cardiology, including interventional cardiac electrophysiology, deals directly with the cardiac chambers and coronary vessels. The term "interventional radiology" refers to all other vascular interventions, including peripheral vascular intervention, with the exception of cerebral interventions, which is specially termed as "interventional neuroradiology."

Despite varied background and experience of the intervening physicians, intravascular catheter navigation is similar across each medical speciality. First, using the Seldinger technique [21, 22] the catheter is inserted into the vasculature through an introducing sheath. The Seldinger method for catheter insertion is depicted in Fig. 1-1. Depending on the anatomical target, either a vein or an artery can be chosen. Common insertion points include the femoral or brachial vein and artery, or the jugular vein. Once the catheter is in the vasculature, the interventionalist manipulates the catheter to the point of interest by pushing, pulling and twisting the shaft of the catheter. To facilitate intravascular

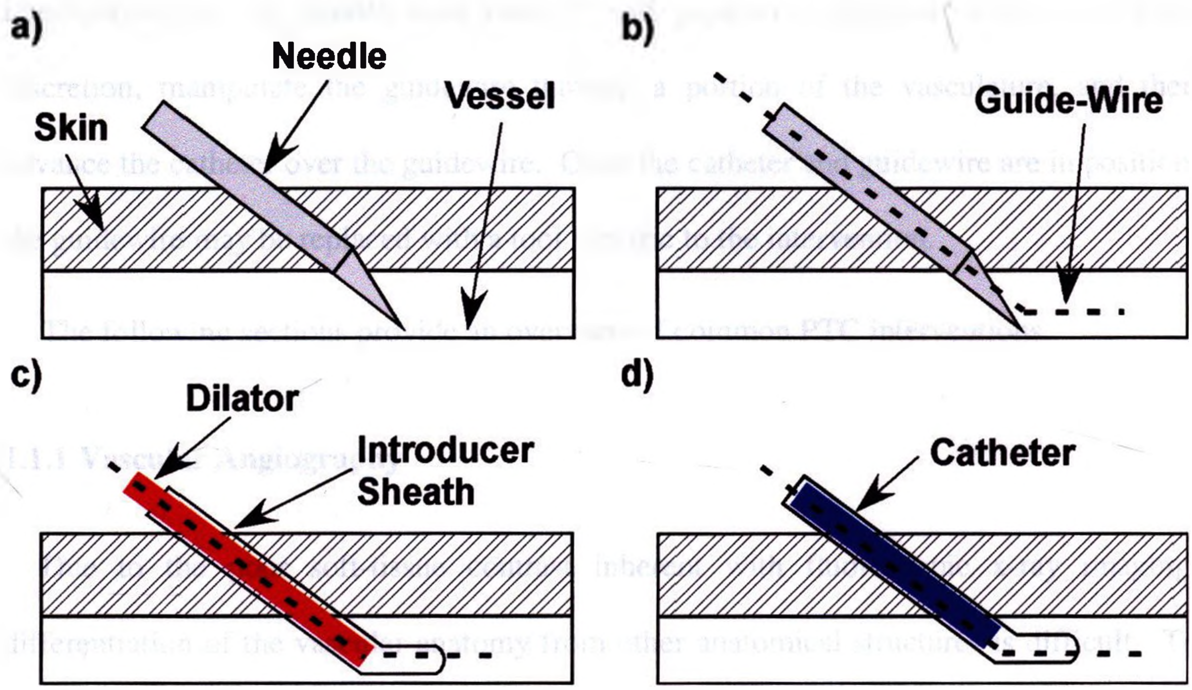

Fig. 1-1: The Seldinger technique for percutaneous catheter insertion consists of four steps. First, the interventionalist inserts a needle through the skin into the vasculature (a). A guide-wire is then inserted through the needle (b). The needle is withdrawn, and an introducer sheath containing a vessel dilator is slid over the guide-wire (c) into the introducer sheath and blood vessel. Finally, the vessel dilator is replaced with the catheter (d).

navigation, the interventionalist uses fluoroscopic x-ray imaging to localize the catheter in the vascular anatomy.

Many PTC interventions may use a catheter-guidewire combination during intra-vascular navigation. A guidewire is a fine, small diameter wire, with a limber tip, that inserts through the catheter's lumen, providing the interventionalist with increased dexterity during catheter manipulation through small and tortuous vessels. Manipulation of the catheter-guidewire towards the site of interest is an iterative process. The interventionalist can handle both catheter and guidewire simultaneously, or at their discretion, manipulate the guidewire through a portion of the vasculature, and then advance the catheter over the guidewire. Once the catheter and guidewire are in position, the guidewire may be replaced with a tool specific to the intervention.

The following sections provide an overview of common PTC interventions.

1.1.1 Vascular Angiography

Due to the poor soft-tissue contrast inherent with fluoroscopic x-ray imaging, differentiation of the vascular anatomy from other anatomical structures is difficult. To enhance blood vessel visualization a contrast agent (commonly iodine-based) is injected into the body. The contrast agent mixes with blood, increasing photon attenuation, thus darkening the vasculature in the radiograph. By subtracting a non-enhanced radiograph (a mask image) from the vascular enhanced radiograph, the vascular anatomy is highlighted and can then be used as a "roadmap" for catheter navigation. The use of contrast agent to enhance vascular anatomy is referred to as vascular angiography, and in addition to providing a roadmap for intravascular navigation, vascular angiography is a fundamental procedure to visually diagnose vessel stenosis and dilation (aneurysm).

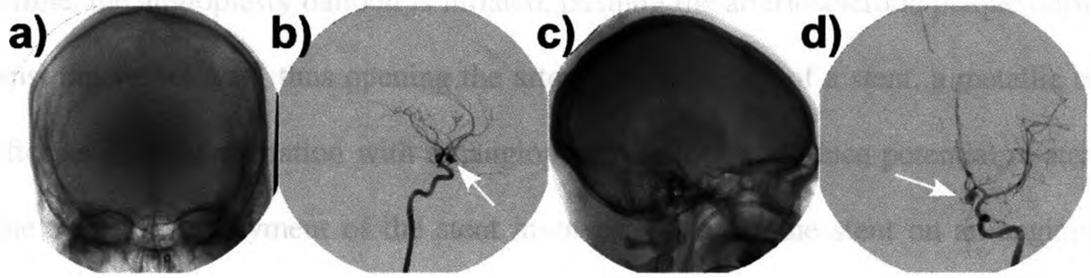

Fig. 1-2: A cerebral vascular angiography, with contrast injected from the left internal carotid artery. Images (a) and (c) are mask images of anterior-posterior, and left lateral, images, respectively. Images (b) and (d) illustrate contrast-enhanced images of (a), and (c), respectively. Arrows (b and d) mark the vessel dilation (aneurysm) from the anterior communicating artery. Images courtesy of Dr. Irene Gulka, University Hospital, London Health Science Centre.

1.1.2 Vessel Stenosis & Dilation

A vascular angiogram provides a visual depiction of blood flow through vessels. Vessel stenosis, a narrowing of the blood vessel, and vessel dilation (an aneurysm), an expansion of the blood vessel, are two medical conditions that can be visually diagnosed with vascular angiography. An example, shown in Fig 1-2, depicts the cerebral angiogram of a patient suffering from an aneurysm extending off the anterior communicating artery.

The majority of catheter-based treatment for arterial stenosis is performed in the coronary arteries by interventional cardiologists. In these procedures, a guidewire is carefully pushed across the atherosclerotic plaque, and then an angioplasty balloon catheter is slide over the guidewire until the angioplasty balloon covers the plaque. At this time, the angioplasty balloon is inflated, pushing the arteriosclerotic plaque outwards against the vessel wall, thus opening the artery. Application of a stent, a metallic mesh, is often used in combination with an angioplasty balloon to reduce potential re-stenosis of the vessel. Deployment of the stent involves mounting the stent on an angioplasty balloon, and then positioning the angioplasty balloon and stent across the atherosclerotic plaque. As the angioplasty balloon is inflated, the stent expands. Once the stent has been expanded fully, the balloon is deflated, and the catheter withdrawn, leaving the expanded stent in place to act as a support structure for the diseased artery.

The carotid bifurcation is another vascular location that suffers atherosclerotic plaque build up. Due to the risk of a cerebral infarct caused by atherosclerotic plaque rupture during catheter-based treatment, surgical angioplasty is still the preferred treatment method. Advances in stent technology, catheter and guidewire construction, and interventional technique, have enable catheter-based intervention in patients deemed too risky for surgical intervention [23, 24].

Treatment of an aneurysm is typically performed by interventional radiologists, and commonly employs coil "depositing" to form thrombi, as first demonstrated by Guglielmi *et al.* [25, 26]. These procedures consist of carefully placing the catheter at the base of the aneurysm, then depositing small coils through the catheter into the aneurysm. The body responds to the presence of the coils by forming a blood clot around the coils, thus blocking blood flow through the aneurysm.

The stated treatments of vessel stenosis and dilation are briefly described here, but the general interventional concept remains the same – manipulating the catheter towards the site of interest by pushing, pulling and twisting the catheter under fluoroscopic x-ray guidance, and then performing the medical treatment.

1.1.3 Cardiac Arrhythmia

Diagnosis and treatment of cardiac arrhythmia is a PTC procedure that has gained prevalence over the past three decades. A cardiac arrhythmia occurs when abnormal electrical signals in the heart cause the mechanical pumping of each heart chamber to lose synchrony. An arrhythmia can lead to nausea, dizziness, stroke and sudden cardiac arrest. Atrial fibrillation (AF) is the most common form of cardiac arrhythmia, affecting 1% of the general population, and 4% of people over the age of 65 [27]. The underlying AF mechanism is beyond the scope of this thesis, readers interested in this topic are encourage to read Clifford Garratt's book "Mechanisms and Management of Cardiac Arrhythmias" [27]. Many other cardiac arrhythmia's exist and are classified by the location where the abnormal signals originate and how the abnormal signal propagates through the heart (i.e. sinus tachycardia, atrial tachycardia, atrial flutter, junctional tachycardia and ventricular tachycardia) [28-30].

Treatment of cardiac arrhythmia includes; drug therapy, surgery, and most commonly catheter-based RF ablation. Traditionally, drug therapy is prescribed to reduce arrhythmic occurrence by controlling the heart rate of the patient. The results of drug therapy are generally poor, requiring the cardiologist to constantly adjust pharmaceutical dose levels [31, 32]. The minimally invasive nature of catheter ablation, combined with the high success rate of treatment, has lead to catheter-based ablation as the preferred method of treatment for the vast majority of cardiac arrhythmia [33, 34].

Successful treatment of AF using RF ablation ranges from 80-100% [32, 35-41]. These rates are highly dependent on the ability of the interventionalist to reach the arrhythmic site, and then control the catheter while creating a lesion in the tissue to cut-off the arrhythmic circuit. The process of confirming the arrhythmic location and then applying RF energy to create a lesion is iterative in nature, leading to long procedure times, and thus increased radiation exposure to the interventionalist, patient and staff.

The long procedure times associated with the RF ablation of cardiac arrhythmia, combined with increased prevalence of these procedures makes remote catheter navigation for these procedures an ideal choice. Thus, the majority of remote navigation systems presented in the subsequent sections deal with remote catheter navigation to diagnose and treat cardiac arrhythmia.

1.2 Literature Review: Remote Catheter Navigation Systems

A number of remote catheter navigation systems (RCNS) have recently become available commercially or developed independently in an academic setting. The general operational approach of each system is similar; the interventionalist uses a specialized peripheral input device connected to a control console, located in a radiation safe area, to control the remote catheter placed inside the patient. The interventionalist uses conventional fluoroscopic x-ray imaging during the procedure to visualize the intravascular catheter. This approach, commonly termed a master-slave system, requires two specialized components: the master device; generally referred to in this thesis as a peripheral input device, and a slave device, required to manipulate the remote catheter. This section provides a literature review of current RCNS, starting with the two most popular navigation systems: Magnetic Guidance System (MGS, Stereotaxis Inc, St. Louis, MO, USA), and the Sensei Catheter Controlled Sheath (CCS, Hansen Medical Inc., Mountain View, CA, USA), followed by other navigation systems described in the literature. Articles published by Schmidt *et al.* and Chun et al. [42, 43] describe the operation and evolution of both the MGS and CCS systems, from first in vivo testing in animal models, to recent clinical trials, as well as the strengths and weaknesses of both systems. Both these articles provide a foundation for a review of the MGS system, and the CCS system, described in the following sections.

1.2.1 Magnetic Catheter Navigation

The concept of magnetic catheter navigation has been around for over half a century, a review on the historical development of magnetic navigation was published by Mitchell Faddis and Bruce Lindsay [44]. Magnetic catheter navigation was first described in 1951, by H. Tillander [45]. In this method of remote navigation, a catheter with a steel articulated tip was navigated through the vasculature using an external magnet. In 1956, H. Tillander improved this navigation technique by incorporating a lumen within the catheter for contrast injection [46]. Montgomery *et al.* from the National Magnet Laboratory [47, 48] further improved this remote navigation method by implementing an array of compact yet powerful superconducting magnets, which via superposition, could direct the magnetic field onto the catheter, increasing the magnetic force on the catheter, to allow for tip orientation through tortuous vessels. The first in-human demonstration of remote catheter navigation was conducted by Ram and Meyer in 1991, using a simple permanent magnet system proposed by Tillander [49]. Howard *et al.* [50, 51] built and patented the first multi-coil electromagnetic system incorporating six orthogonal magnets, a user interface for the operator, and the ability to register real-time fluoroscopic images to a preoperative Magnetic Resonance Imaging (MRI) image of the brain, and demonstrated the application of this system in cerebral catheter navigation.

Magnetic catheter guidance in coronary arteries using the commercially available MGS, depicted in Fig. 1-3, has been successfully demonstrated in humans, leading to the use of magnetic guidance in percutaneous coronary intervention (PCI) [52-55], and navigation of the cerebral and peripheral vasculatures [56, 57]. Faddis *et al.* [58] performed the first *in vivo* RF ablation of common arrhythmic sites in canine and porcine models.

Magnetic catheter guidance has been predominately used in the treatment of cardiac arrhythmia. Application of this technology towards cardiac arrhythmia treatment is not coincidental, as RF ablation is becoming the preferred method to treat cardiac arrhythmia, but suffers from both, long procedure times and long fluoroscopic times. These factors, combined with increases in the number of annual procedures performed have increased the occupational risk to interventional electrophysiologists. Various types of cardiac arrhythmia have been treated using magnetic guidance, such as AtrioVentricular Nodal Re-entrant Tachycardia (AVNRT) [59], right side anterolateral Accessory Pathway (AP) [60], left side AP using the retrograde approach [61, 62], and left side Ventricular Tachycardia (VT) [63-65].

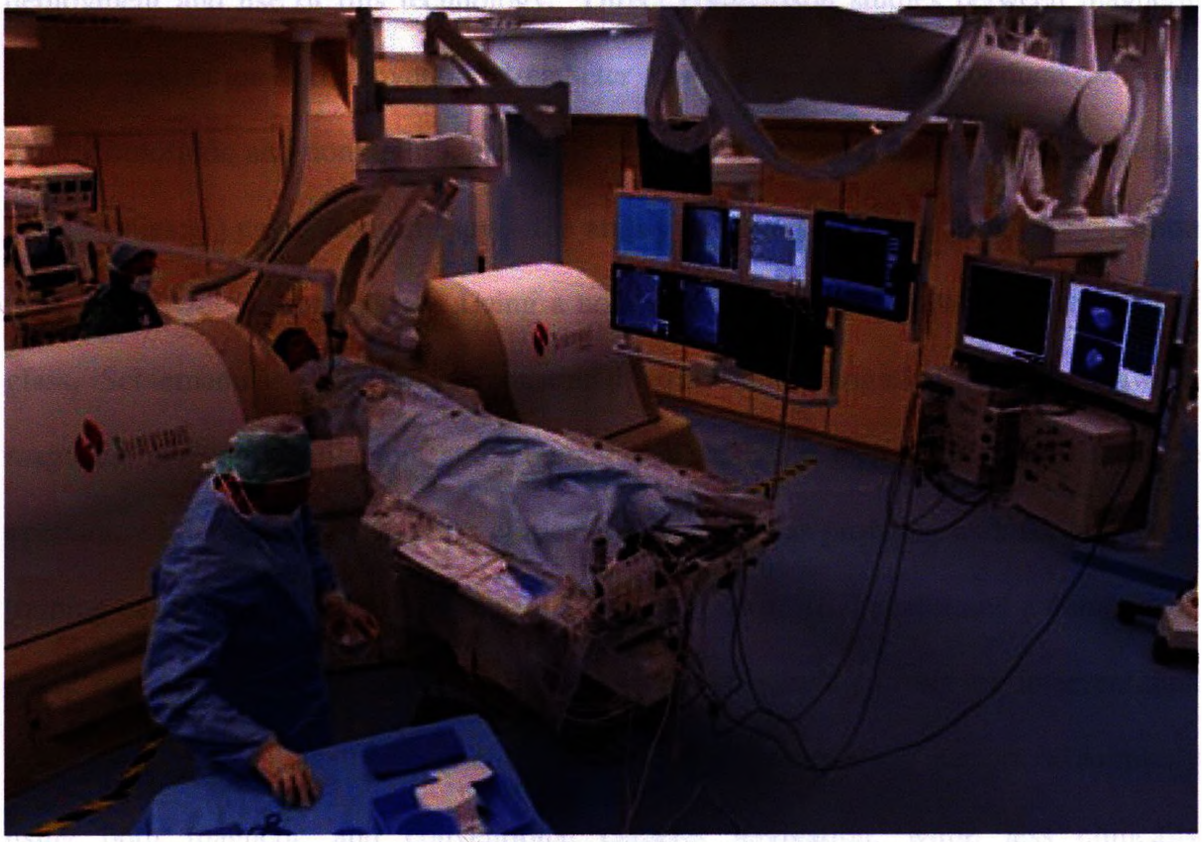

Fig. 1-3: The MGS system by Stereotaxis Inc. Two large magnets, mounted on mechanical arms, create a magnetic field inside the patient. Changes in the orientation of these large magnets, causes a change in the magnetic field. To achieve remote manipulation, a small magnet is placed at the tip of the catheter, and the catheter is placed in the magnetic field. The operator inputs a 3D vector in the control console, which then changes the magnetic field gradient in the patient's chest. The small magnet in the catheters tip aligns to the changed magnetic field, causing the catheters tip to deflect. (Reprinted from Patterson *et al.* 2006, permission in Appendix B)

The question of "how well" magnetic catheter navigation compares with conventional catheter navigation is a logical question that must be asked to justify widespread deployment and use of this technology. Direct comparison studies between magnetic catheter navigation and conventional catheter navigation have been conducted in both anthropomorphic and non-anthropomorphic models. Three metrics are typically used in these studies: 1) navigation efficacy – the ability to traverse a given path, 2) navigation time, and 3) fluoroscopic dose. Using a non-anthropomorphic phantom constructed of glass, Schiemann *et al.* [66] demonstrated equivalent navigation efficacy between magnetic catheter navigation and conventional catheter navigation, after a single operator, with more than five years clinical experience, was provided with six months of training using magnetic catheter guidance. Krings' *et al.* [67] performed a comparison study using three phantoms, and four operators of varying levels of interventional experience. The clinically experienced operators in Krings study performed similarly using both magnetic and conventional catheter navigation, while less clinically experienced operators performed better with the magnetic catheter navigation system. Krings study demonstrates that prior clinical experience is the dominant factor affecting navigation speed. Other comparative studies conclude with similar results (Ramcharitar *et al.* [68] and Garcia-Garcia *et al.* [69]), demonstrating equivalent navigation efficacy between magnetic catheter guidance and conventional catheter navigation and comparable navigation time, but only after significant training and experience using the magnetic catheter navigation system.

In vivo comparative studies have been conducted using magnetic catheter navigation to ablate arrhythmic sites in humans [60, 62, 70, 71]. Kim *et al.* [72] retrospectively analyzed 721 arrhythmia cases treated with RF ablation that used either magnetic navigation or conventional catheter navigation. Their results showed no significant difference in the mean fluoroscopic time required to navigate and treat arrhythmia, between navigation methods. However, magnetic catheter navigation required a mean increase of 89 minutes in overall procedure time, compared with conventional catheter navigation.

The increased procedure time required for magnetic catheter navigation may be attributed to the new skills required by the interventionalist to effectively operate the navigation system. During magnetic catheter navigation, the operator super-imposes a 3D vector, corresponding to the catheter's tip, onto a pre-operative Computed Tomography (CT), MRI, or an angiographic image, which is preloaded into the navigation software. After the interventionalist inputs the desired movement, changes in the catheter's tip take between 1-3 seconds to occur [58], increasing procedure time.

Lack of bi-plane and oblique imaging may influence the increased procedure time using magnetic catheter guidance. Due to the position of the large permanent magnets, adjacent to the patient bed, bi-plane imaging of the patient is not possible during intravascular navigation. The large size of the magnets places a mechanical constraint on oblique anterior-posterior images, limiting rotation of the x-ray gantry to ±30°. This limitation, along with removing the catheter from the hands of the interventionalist changes the workflow of the intervention, and thus requires the interventionalist and other staff to modify the intervention to include the use of this technology.

Magnetic catheters are softer than conventional EP catheters, to allow for magnetic deflection, and are not available with non-irrigated tips. The malleability of these catheters can cause entanglement on the papillary musculature, causing prolapse on the catheter-tip, shown during retrograde access and ablation of left-side AP [62]; a procedure that was successfully completed after reversion to conventional catheter navigation. The inability to irrigate the catheter during intervention can cause charring at the catheter-tip. These catheter-specific limitations may be addressed in the next generation of magnetic-tipped catheters.

Other limitations of this technology, elegantly described by Schmidt *et al.* [42], include: exclusion of patients with metallic implants (i.e. pacemaker), system cost, and restricted to integration with CARTO (BioSense Webster Inc., Diamond Bar, CA, USA), an electro-anatomical mapping system. Furthermore, the magnetic component of this system may require special shielding in the procedure room, an additional capital cost.

A reduction in overall procedure time to levels comparable with conventional catheter navigation is achievable, as the operator gains experienced using the magnetic guidance system [70, 72-74]. For ablation treatment of arrhythmia, even after training on the magnetic guidance system, resulting in comparable navigation times, no improved benefit to patient outcome has been reported. In fact, Di Biase *et al.* [71] state the present magnetic technology shows feasibility for arrhythmia treatment, but effective lesions are difficult to create, affecting the cure rate of AF patients.

1.2.2 Robotic Controlled Catheterization

Currently, the second most popular remote catheter navigation system described in the literature is the Sensei Robotic Catheter Navigation System by Hansen Medical Inc. (Mountain View, CA, USA). This catheter navigation system is relatively new, receiving FDA approval for clinical use in 2007. Thus, the majority of literature describing experience with this system is limited to animal models, and pilot studies.

Operation of the Sensei has been detailed previously [75]. Sensei is an electromechanical system composed of two steerable sheath catheters, the ablation catheter, an articulated robotic arm, and a workstation. An outer steerable sheath (14F) and inner steerable sheath (10.5F) each contain a pull-wire mechanism that allows both sheaths, in combination, to control the tip of a standard ablation catheter. The robotic arm controls the pull-wire mechanism, based on motions of the stylus, via the workstation. This system is commonly referred in the literature as a Computer Controlled Sheath (CCS) and is depicted in Fig. 1-4.

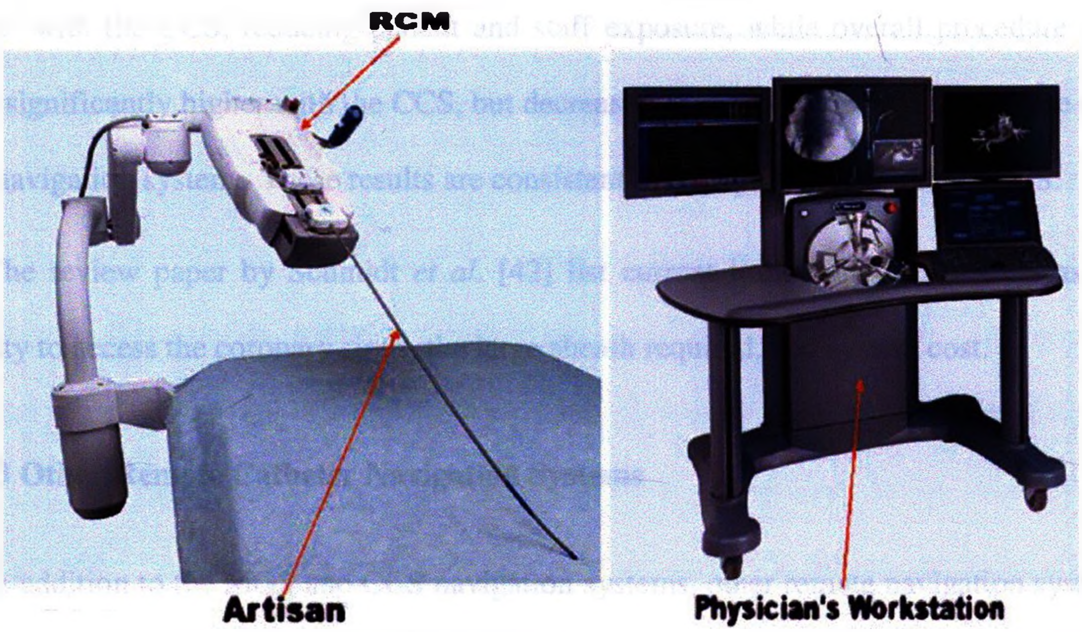

Fig. 1-4: The Sensei Remote Catheter Navigation by Hansen Medical Inc. The physician manipulates a stylus, placed on a remote console (right). Motion of the stylus is transferred to a robotic arm, which then manipulates the Artisan, steerable sheaths (left). (Reprinted from Kanagaratnam *et al.* 2008, permission in Appendix B)

Saliba *et al.* [76] used the CCS system, in conjunction with intracardiac echocardiography (ICE) and CARTO to successfully map the 3D electro-anatomical activity of five predefined targets in each of the four heart chambers of canine models. In addition, the authors demonstrated the first remote trans-septal puncture. Clinically, arrhythmia treatment using the CCS has been successful in the treatment of AP, Atrial Flutter (AFL), and AF [77, 78].

To date, only one published study compares remote ablation using the CCS with conventional catheter navigation, in 50 randomized patients suffering from AFL (25 patients per group) [79]. Fluoroscopic time, X-ray dose, and RF ablation duration were lower with the CCS, reducing patient and staff exposure, while overall procedure time was significantly higher with the CCS, but decreased as operators gained experience with the navigation system. These results are consistent with experiences with the MGS.

The review paper by Schmidt *et al.* [42] list current limitations of the CCS as: no ability to access the coronary sinus, the large sheath required, and system cost.

1.2.3 Other Remote Catheter Navigation Systems

In addition to the MGS and CCS navigation systems, other remote navigation systems have been described recently. The infancy of this field has yielded limited publications describing system operation, and both *in vitro*, and *in vivo* validation. This section provides an overview of these systems.

Corindus Inc. (Natick, MA, USA) has developed a remote navigation system, called CorPath, which utilizes a joystick, touchscreen, workstation, and mechanical transmission module [80-82]. The operator uses a touch screen in conjunction with a simple joystick, to control advance, retract, and rotation of a remotely placed catheter. Pilot studies have demonstrated the ability to navigate balloon/stent catheters in a sheep model [82] using generic catheters and guidewires. Clinical trials have shown successful remote deployment of stents in the coronary arteries in 15 out of 17 cases, with the two failed cases completed manually [81]. At present, no further information regarding this navigation system is available.

Three other navigation systems have been also been described. Negoro *et al.* [83] described a simple navigation system comprising of a force-feedback joystick, workstation, and mechanical transmission module. Contained in the mechanical transmission module are strain gauges to measure force exerted on the catheter, which are then used to provide tactile sensation to the operator. Fukasaku *et al.* [84] proposed the use of two PHANToM (SensAble Technologies, Woburn, MA, USA), Virtual Reality (VR) stylus devices, containing tactile sensors, connected in a master-slave configuration. A catheter or guidewire, fixed to the slave VR device, replicates motion exerted by the operator on the master VR device. Force exerted by the vasculature on the catheter is measured by the slave VR device, and transferred to the operator, via the master VR device. Cercenlli *et al.* [85] described the operation of a tele-robotic system, where the operator uses a robotic hand to control an EP catheter. Initial experiments *in vivo* demonstrate the ability to navigate an EP catheter to the high RA, tricuspid annulus, lateral-wall of the RA, and RA septum.

1.3 Design Approach: Remote Catheter Navigation System

At present, both the MGS system and CCS system have not shown a benefit towards patient outcome, in catheter-based treatment of arrhythmia. This is expected, as many of these procedures occur with a high success rate using the conventional navigation approach. Instead, these navigation systems demonstrate comparable navigation efficacy with conventional, bedside catheter manipulation, but only after sufficient training on the systems use.

The primary benefit of remote navigation, then, is the ability to reduce cumulative radiation exposure to the interventionalist, by increasing the distance between them and patient during intravascular navigation of the catheter. Furthermore, remote navigation should also reduce musculoskeletal injury, by reducing time required to stand next to the patient bed, while wearing heavy lead garments.

This thesis covers the design, implementation, and validation of a tele-operated catheter navigation system, which aims to achieve the same benefits as other navigation systems, namely reduced cumulative radiation exposure to interventional specialists, and reduced musculoskeletal injury, but with minimal operator training. In addition, the RCNS should easily integrate with existing fluoroscopic X-ray suites, and take advantage of generic catheters, thereby minimizing the interruption to conventional workflow.

The RCNS proposed aims to utilize the dexterous skills and eye-hand coordination of an experienced interventionalist during remote catheter navigation, by keeping the catheter in the hands of the interventional specialist. To achieve this, the RCNS has been developed as a conventional master-slave system, with a specialized peripheral input device (master) that accepts a local catheter, instead of a joystick, touch screen, or any other non-intuitive peripheral device, to control a remotely placed, patient catheter. Manoeuvres applied by an interventionalist during conventional bedside navigation, are

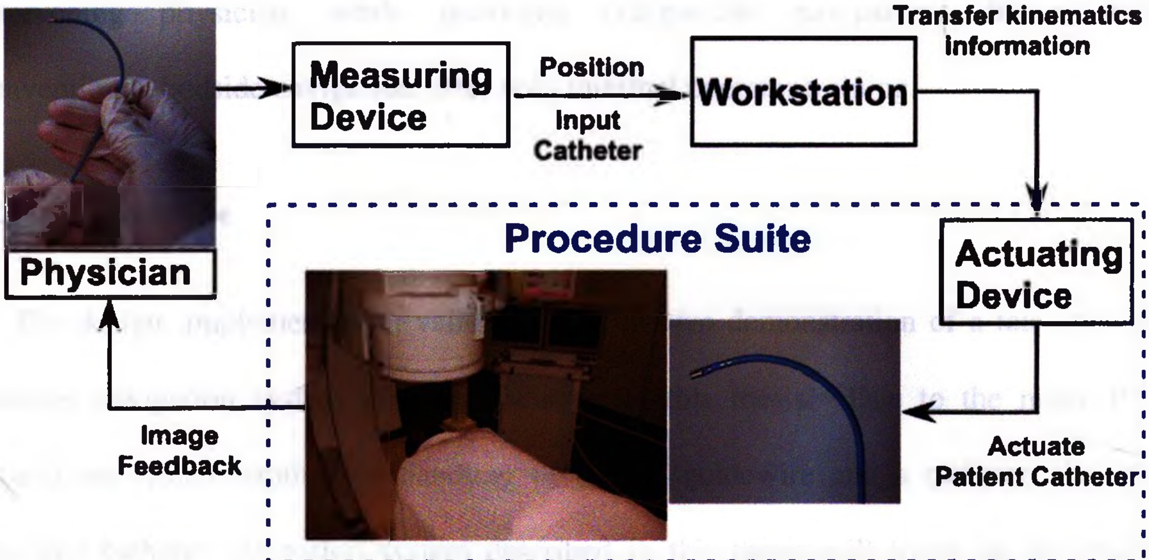

Fig. 1-5: The RCNS concept of operation. The interventional physician stands outside the procedure room, applying the same push, pull, and twist motions to the input catheter. A special peripheral input device measures these motions, and then via a workstation, replicates the motion with a patient catheter, using a second specialized catheter-actuating device. Standard fluoroscopic x-ray images provide image guidance.

instead applied to the local catheter. The kinematics applied to the input catheter, measured by the peripheral input device are transferred, via a workstation, to a manipulating device that replicates the same motion on the patient catheter. The proposed method of remote navigation is depicted in Fig. 1-5. Throughout this thesis, the peripheral input device (master device) is referred to as the Catheter Sensor (CS), and the actuating device is referred to as the Catheter Manipulator (CM).

By utilizing the same manoeuvres applied during conventional, bedside navigation, remote catheter navigation with this system will reduce the occupational risk to intervening physician, while providing comparable navigation efficacy with conventional, bedside navigation, after only minimal operator training.

1.3.1 Thesis Scope

The design, implementation, validation and *in vivo* demonstration of a tele-operated catheter navigation system will be discussed in this thesis. Due to the many PTC procedures which require the handling of both a guidewire and a catheter, the tele-operated catheter navigation system described in this thesis will focus on the remote manipulation of RF ablation catheters for the diagnosis and treatment of cardiac arrhythmia. These procedures do not require a guidewire during manipulation, thus implementation of the RCNS is simplified to manipulation of a single catheter. Furthermore, for clinical use the device must be sterilized after each intervention. This requirement will not be addressed in this thesis. Instead, this thesis will describe the development and validation of a prototype remote navigation system for "proof of concept" purposes.

1.4 Thesis Outline

This thesis is divided into six chapters. This chapter introduces the reader to the risks associated with PTC procedures, the different types PTC interventions, and the state of the art in remote catheter navigation systems.

The mode of remote navigation proposed, namely – remote catheter navigation via sensing and replicating the motion of a local catheter – requires an understanding of the range of forces, torques, velocities and accelerations an operator can apply to the catheter. Chapter 2 presents a series of bench-top experiments to quantify the range of external dynamics applied by an operator to a catheter. This chapter has been published in a paper entitled: "Characterization of Catheter Dynamics During Percutaneous Transluminal Procedures," IEEE Transactions in Biomedical Engineering, vol. 56(8), pg's 2140-2143, August 2009.

Chapter 3 of this thesis utilizes the results from Chapter 2 to design and construct the RCNS. In addition to describing the RCNS, Chapter 3 also describes a series of bench-top experiments to evaluate the performance of the RCNS. This chapter has been published in a paper entitled: "Design and Performance Evaluation of a Remote Catheter Navigation System," IEEE Transactions in Biomedical Engineering, vol. 56(7), pg's 1901-1908, July 2009.

Chapter 4 of this thesis evaluates how well catheter navigation with the RCNS compares with conventional bedside navigation, in a multi-operator trial, utilizing a custom fabricated 2D multi-path phantom. A manuscript of this chapter entitled: "Catheter Navigation Efficacy of a Tele-Operator Catheter Navigation System: Experimental Results in a Multi-Path Phantom," has been submitted to the journal, Radiology, (Submission #RAD-09-1965).

Chapter 5 of this thesis evaluates the safety and feasibility of *in vivo* application of the RCNS, by emulating treatment of cardiac arrhythmia in porcine models. In addition, this chapter examines the impact of the RCNS on workflow and compares *in vivo* navigation of the RCNS with conventional guidance. Based on this chapter, a manuscript is in preparation for the journal Circulation.

Finally, Chapter 6 summarizes the contributions and limitations of this thesis. Future work, based on the results and experience gained during the development of this RCNS are considered.

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Chapter 2 :

Characterization of Catheter Dynamics During Percutaneous Transluminal Catheter Procedures[1]

2.1 Introduction

Percutaneous transluminal catheter (PTC) procedures represent a minimally invasive approach to diagnose and treat vascular and cardiac diseases, including electrophysiological (EP) conditions. During these procedures, the interventionalist manipulates a catheter by applying a series of pushes, pulls and rotations to the catheter's shaft using fluoroscopic x-rays for image feedback. To reduce radiation exposure to the interventionalist and staff, numerous approaches and guidelines have been developed, including reducing the image frame-rate, employment of specific beam orientations, as well as the requirement that safety equipment, such as lead aprons and neck collars, be

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worn by all staff [1]. Although safety equipment reduces exposure risk, long-term use can lead to development of chronic neck and back pain [2]. As the number of annual PTC procedures continues to increase [3, 4], the long-term associated risk to the interventionalist is greatly enhanced.

To reduce occupational risk, catheter navigation systems have been developed to enable PTC intervention from a location remote to the patient [5-7]. The common design of these systems is a master-slave control configuration in which the interventionalist sits at a console outside the procedure room and uses a peripheral input device (master) to manipulate the catheter with a specialized catheter manipulator (slave). The master device can range from a simple joystick [5], touch screen [5], or stylus [6, 8, 9] to more complex 3D vector inputs [7, 10-12]. For the slave device, mechanical transmission modules [5], a specialized mechanical catheter-sheath [6, 8, 9] or large magnets [7, 10-12] are used to drive the catheter through the vasculature. These remote catheter navigation systems have been successfully used to treat cardiac arrhythmia [6-9, 11, 12] and to place stents to open occluded coronary arteries [5].

Despite the recent development of remote catheter navigation systems, development has occurred with little fundamental knowledge of the catheter dynamics observed during intervention. Skilled operators must apply a range of forces to overcome friction between the catheter and an introducer sheath, which is required to introduce the catheter into the vasculature [13], and between the catheter and the vasculature. A series of axial motions (pushing and pulling of the catheter) and shaft rotations are performed to navigate the catheter through vascular branch points. Knowledge of the range of forces, torques, velocities and accelerations applied during interventional procedures, would enable catheter manipulators to be designed with performance characteristics similar to current bedside practice.

To address the need to quantify the kinematics range of catheter motion, a novel in-line motion sensor that measures the catheters radial and axial position has been developed. This device has been used to characterize the range of axial and rotational kinematics applied by an interventionalist during catheter manipulation. Preliminary work characterizing this was previously shown in [14]. In addition to catheter kinematics, the range of force and torque applied to the catheter by an interventionalist is important, as the applied force allows them to overcome friction during the procedure. The maximum applied force and torque have also been characterized using a series of simple but appropriate bench-top experiments. This paper reports results on the range of kinematics undergone by the catheter during an interventional procedure, the minimum force and torque required to move the catheter and the maximum force and torque a user can apply to a catheter. Knowledge of these parameters promises to be useful in the design and optimization of remote catheter manipulation devices.

2.2 Methods

2.2.1 Kinematics Range

A study was performed to determine the range of velocity and acceleration of a catheter during an interventional procedure. To measure the axial and radial positions of a catheter, a device consisting of two independent optical encoders (US Digital, Vancouver, WA), each connected to an electronic counter (AD4®, US Digital, Vancouver, WA) capable of measuring up to 400 kHz count frequency, was constructed (Fig. 2- 1). Measurement of radial motion was achieved by passing the catheter through three bearings coupled to one of the optical encoders, thereby providing a direct measurement of radial position (Fig. 2-1a). Measurement of axial motion was achieved by transducing the axial motion to a passive roller, which in turn rotated the second optical encoder (Fig. 2-1b).

Ten operators, five experienced interventionalists and five inexperienced users, each moved a 6 F EP catheter through the measurement device into a straight-tube phantom. The experienced interventionalists manipulated the catheter in both the axial and radial directions based on their professional training, while the inexperienced operators controlled the catheter without specific instruction. The axial and radial positions of the catheter were each sampled at 20-ms intervals and logged during the entire experiment. Each operator repeated the experiment five times; each trial lasted less than 1 minute. A

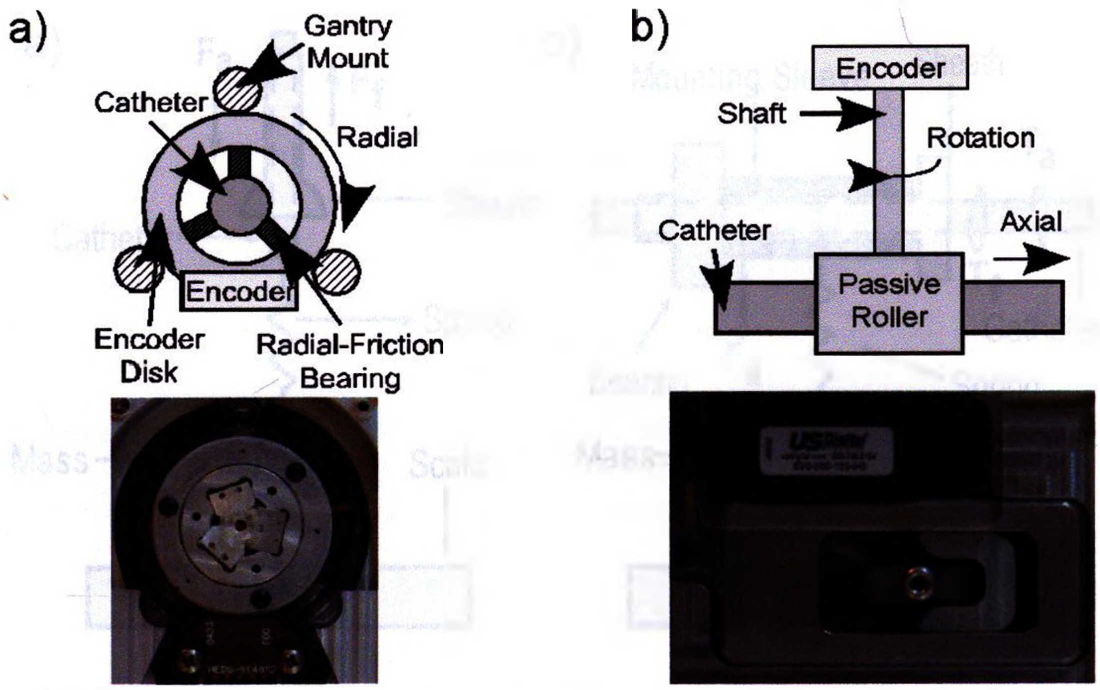

Fig. 2-1: Motion sensing device: a) catheter rotation is measured by rotating the optical encoder disk via 3 radial-friction bearings, and b) axial motion is measured as the catheter moves against a passive roller, which rotates the disk of a second optical encoder. Below each schematic is a photograph of the corresponding manufactured sensor.

three-sample moving boxcar average was applied to each motion profile prior to calculating maximum velocity and acceleration.

2.2.2 Minimum Required Force and Torque

As the catheter is navigated through the vasculature, an introducer sheath, used to insert the catheter into the vasculature [13], adds friction to the procedure, impeding

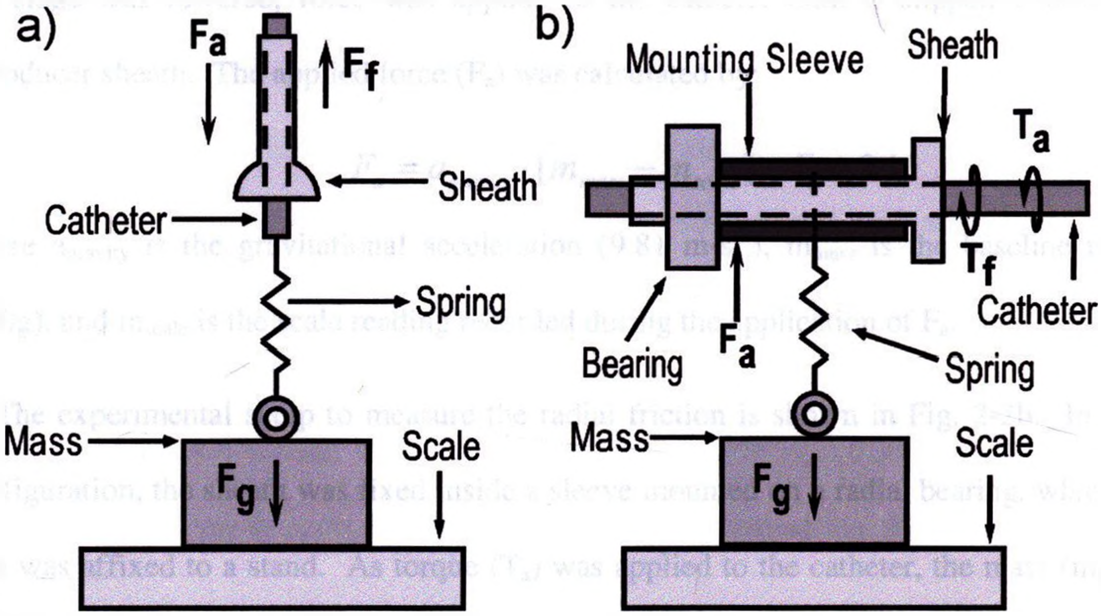

Fig. 2-2: Experimental setup to measure resistive force caused by introducer sheath in a) axial direction (vertical stand not shown), and b) radial direction.

motion. This friction represents the minimum force required to move the catheter during an interventional procedure.

To measure the axial and the radial friction exerted by the sheath on the catheter, the experimental apparatus shown in Fig. 2-2 was assembled. For the measurement of axial friction in (Fig. 2-2a), a mass was placed on a scale (PE3600, Mettler-Toledo, Columbus, OH) and attached, via a spring, to a 15-cm segment of a generic 6F angiographic catheter. The catheter segment was then inserted into an introducer sheath, which was fixed to a vertical stand. The scale was placed on a vertical stage (not shown), which enabled the mass to be lowered; at rest the scale measured the weight of the mass and as the stage was lowered, force was applied to the catheter until it slipped within the introducer sheath. The applied force (F_a) was calculated by:

$$F_a = a_{gravity} \cdot [m_{mass} - m_{scale}], \quad \text{Eqn. 2-1}$$

where $a_{gravity}$ is the gravitational acceleration (9.81 $m \cdot s^{-2}$), m_{mass} is the baseline mass (500g), and m_{scale} is the scale reading recorded during the application of F_a.

The experimental setup to measure the radial friction is shown in Fig. 2-2b. In this configuration, the sheath was fixed inside a sleeve mounted on a radial bearing, which in turn was affixed to a stand. As torque (T_a) was applied to the catheter, the mass (m_{mass}) was lifted and Ta was calculated from the scale reading (m_{scale}) as follows:

$$T_a = r \cdot a_{gravity}[m_{mass} - m_{scale}]. \quad \text{Eqn. 2-2}$$

In Eqn. 2-2, r is the radius of the mounting sleeve (4.76 mm). The maximum applied force was the force measured when the catheter slipped within the introducer sheath.

The maximum applied axial force and radial torque were measured five times; the sheath and catheter were replaced following each measurement.

2.2.3 Maximum Applied Force and Torque

The ability of the interventionalist to manipulate the catheter corresponds directly to their capability to apply force and torque to the catheter. To measure the maximum user-applied axial force, we fixed one end of a 15-cm catheter segment to a force scale. Each user gripped the catheter's free end between their index finger and thumb, and then pulled the segment until the catheter slipped between their fingers. To measure the maximum user-applied torque, a setup similar to that described in Fig. 2-2b was used, but the catheter was attached directly to the mounting sleeve, without going through the introducer sheath. The user applied torque on the catheter until the catheter slipped in their fingers and their maximum applied torque was recorded. Both experiments were performed using 5 F and 6 F polyurethane catheters and a 6 F polyethylene catheter, which are commonly used in PTC interventions. Eight operators carried out each experiment. All participants wore surgical gloves to emulate the friction between the interventionalist's hands and the catheter during an actual clinical procedure.

2.2.4 Data Analysis

For all measurements, the mean and standard deviation were calculated. To determine if the catheter size or material affected the maximum applied radial torque and axial force, a paired t-test (two-tailed) was performed. An unpaired two-tailed t-test was used to compare the maximum kinematics of experienced and inexperienced users. All statistical analysis was performed using Prism™ 4 (GraphPad Software Inc., San Diego, CA).

2.3 Results

2.3.1 Kinematics Range

The calculated values for maximum velocity and acceleration measured in the experienced and inexperienced operator groups are listed in Table 2-1. Statistical analysis found that inexperienced users reached higher radial velocities and accelerations ($P < 0.05$), when compared to the experienced interventionalists.

2.3.2 Minimum Required Force and Torque

To overcome the friction of the introducer sheath, an applied force of 0.29±0.06 N and an applied torque of 1.15±0.3 mN·m were required in the axial direction the radial direction, respectively.

Table 2-1: Motion Profiling Results

	Axial		Radial	
	Velocity ($mm \cdot s^{-1}$)	Acceleration ($mm \cdot s^{-2}$)	Velocity ($rad \cdot s^{-1}$)	Acceleration ($rad \cdot s^{-2}$)
Experienced	300 ± 80	16,000 ± 7,000	$11 \pm 9^{*}$	$500 \pm 365^{**}$
Inexperienced	360 ± 180	22,000 ± 14,000	$19 \pm 7^{*}$	$900 \pm 510^{**}$

Maximum kinematics observed by experienced interventionalists and inexperienced operators. Statistical analysis showed significant difference ($P<0.05$) between groups for the radial velocity (*) and acceleration (**).

2.3.3 Maximum Applied Force and Torque

The average measured torque applied by the eight users on the three different catheters was 8.4±1.0 mN·m, 12.3±1.3 mN·m, and 7.6±1.0 mN·m for the 5 F and 6 F polyurethane catheters and the 6 F polyethylene catheter, respectively. The maximum torque applied was 14.2 mN·m, which was achieved using the 6 F polyurethane catheter. Statistical analysis indicated that catheter material and catheter size significantly affect the maximum achievable torque applied to the catheter ($P < 0.05$).

In all cases, the maximum axial-force that a user could apply on a catheter exceeded 40 N; in some cases the catheter broke before the maximum force could be reached.

2.4 Discussion

In this study, we have determined the range of axial and radial velocities and accelerations that a catheter undergoes while being manipulated through the vasculature during traditional bedside PTC interventional procedures. An in-line motion sensor, which did not interfere with catheter motion, was constructed to make the measurements. Both experienced and inexperienced operators participated in the study in order to provide limits on the velocities/accelerations that would need to be replicated by remote catheter manipulators. The inexperienced users applied higher velocities and accelerations on the catheter, when compared to the experienced interventionalists, although statistical significance was observed only for the radial acceleration and velocity.

The measured kinematics parameters set stringent limits on the design of remote catheter manipulator devices. The electrical and mechanical components of catheter manipulators must be selected based on their ability to deliver the required range of velocities and accelerations (Table 2-1). For example, using a mechanical transmission module, of a sufficiently compact size for clinical use, to produce the high velocities and accelerations encountered clinically will require careful motor selection and mechanical design. Motor selection, and by extension the mechanical design, is not trivial, as it is well known that motor velocity is inversely proportional to acceleration.

The forces and torques required to grip and manipulate a catheter through an introducer sheath were also characterized. These forces and torques place stringent requirements on the mechanical components used in the design of a catheter manipulator, specifically the components needed to grip and advance the catheter through the vasculature (e.g. rollers). Torques as high as 15 mN·m must be replicated in order to mimic the grip an interventionalist exerts while rotating a small-diameter catheter, well above the minimum torque required to overcome the friction required to rotate the catheter through an introducer sheath. The maximum axial force that a user could apply while gripping a catheter was above 40 N – a value that is not relevant to clinical application. The minimum force required to grip and axially advance the catheter should be greater than the force required to advance the catheter through the introducer sheath at maximum acceleration, i.e. a minimum force of 2.5 N for a 100g catheter.

The present study was performed using a limited subset of catheter types, in terms of size, material, and construction. The maximum kinematics observed is not expected to vary with catheter size, but the ability to apply force/torque will likely be reduced using smaller-diameter catheters. Another potential study limitation is the use of a straight-tube rigid phantom during the kinematics study. Measurements in vivo or the use of an anthropomorphic phantom are not expected to affect the maximum kinematics, parameters which place the most stringent requirements on catheter manipulator design.

Knowledge of catheter dynamics, as presented, will enable the design of catheter manipulators that more closely replicate the interventionalist during remote PTC procedures. Other applications that will benefit from this knowledge include the design of training simulators, which have been developed [15, 16], but have relied on assumptions regarding the forces and kinematics applied to the catheter.

Acknowledgments

The authors would like to thank our clinical collaborators: Dr. Raymond Yee, Dr. Allan Skanes, Dr. Rodney Allen, and Dr. Irene Gulka from the University Hospital in the London Health Sciences Centre for their expertise in this work. We also thank Hristo Nikolov and Jason Cakiroglu for their technical contributions towards this project.

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Chapter 3 :

Design and Performance Evaluation of a Remote Catheter Navigation System[2]

3.1 Introduction

Percutaneous transluminal catheter-based interventional procedures have become the common practice for diagnosis and treatment of cardiac and vascular diseases, including electrophysiological conditions. These procedures typically use fluoroscopic x-ray images to visually assist the interventionalist during intravascular navigation and the final placement of the catheter. The high success rate of catheter-based interventions, combined with their minimal invasiveness, has lead to a significant increase in the number of procedures performed annually [1, 2]. As the number of procedures increases, radiation exposure to the medical staff has become a concern, as the effects of radiation exposure are well documented. Increased radiation training, proper utilization of safety

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equipment and improved imaging technology have helped reduce exposure levels [3-5]. However, these reductions may be offset by procedure complexity and other factors (such as interventionalist skill), which can increase exposure to the patient and medical staff [6]. In addition, the lead aprons and neck collars used to protect physicians and staff from radiation has been linked to the development of chronic back and neck pain [7, 8]. Reductions in radiation exposure and chronic pain would be achieved if percutaneous procedures could be performed from a location remote to the patient [9] and remote catheter navigation systems are being pursued to achieve this [10-13].

Catheter navigation systems developed by Negoro [12], Corindus Inc. [10], Hansen Medical Inc. [13-15] and Stereotaxis Inc. [11, 16-21] all employ a master-slave control architecture that uses a peripheral input device to control the remote catheter. The CorPath™ (Corindus Inc., Auburndale, MA, USA) and the Negoro system each employ a specialized mechanical transmission module to advance the catheter using the push, pull and rotate technique; in Negoro's implementation [12], the interventionalist uses a joystick to control the remote catheter, whereas the CorPath™ system [10] allows the interventionalist to perform continuous motion with a joystick and discrete movements through a touch screen. The system offered by Hansen Medical Inc. [13-15] (MountainView, CA, USA) uses input from a stylus to manipulate a remote catheter by a specialized, controllable catheter sheath and guidewire system. The Stereotaxis system (Niobe™, St. Louis, MO, USA) [11, 16-22] uses large permanent magnets mounted on mechanical arms that enable them to move and drive a small magnet placed at the tip of a guidewire through the vasculature. The path of this small magnet (corresponding to the catheter tip) is defined during the procedure by the interventionalist, who draws the intended 3D path of the tip while sitting at a remote workstation.

Unlike the conventional bed-side technique, which requires interventionalists to manipulate a catheter manually, employment of these remote navigation systems removes the catheter from the interventionalist's hands, thus removing his/her dexterous and intuitive skills from the procedure. Furthermore, the technological complexities of these systems may require long training times to ensure the interventionalists are skilled in their use. For example, a study conducted by Schiemann et al. [23] demonstrated that equivalent navigation efficacy was achieved when comparing conventional navigation to remote navigation using the Niobe™ system in a glass phantom, after six months of interventionalist training on the system. Therefore, it should be beneficial if a remote catheter navigation system incorporated the dexterous skill set of an experienced interventionalist during the procedure.

Our group has addressed this need by developing a novel remote catheter navigation system to manipulate percutaneous transluminal catheters from a location remote to the patient, while allowing the interventionalist to apply conventional push, pull and twist of a catheter's shaft during the remote procedure. To remotely navigate the catheter using this method, the interventionalist applies axial (push and pull) and radial (twist) forces to a catheter's shaft held inside a motion-sensing device, the sensed motion is transferred, via a computer console, to a second device, which replicates the motion along a second catheter's shaft. This method of catheter navigation via remote motion replication, promises to provide a platform that incorporates the pre-existing skills of an experienced interventionalist, while maintaining the objective of reducing the occupational hazards associated with conventional bedside therapy.

In this chapter we describe this new remote catheter navigation system (RCNS). The custom mechanical design of the master device – the Catheter Sensor (CS), the slave device – the Catheter Manipulator (CM), and the software used to interface them are described in detail. The results of experiments performed to evaluate the accuracy and precision of sensed and replicated motion, as well as the latency in replicated motion are presented.

3.2 System Description

The RCNS, shown in Fig. 3-1, was designed to consist of a CS (to be placed at a remote location) capable of measuring the axial and radial motions of an input catheter, a CM (to be placed at the patient bed side) capable of replicating the motions measured by the sensor, and a computer console that relays information between the sensor and

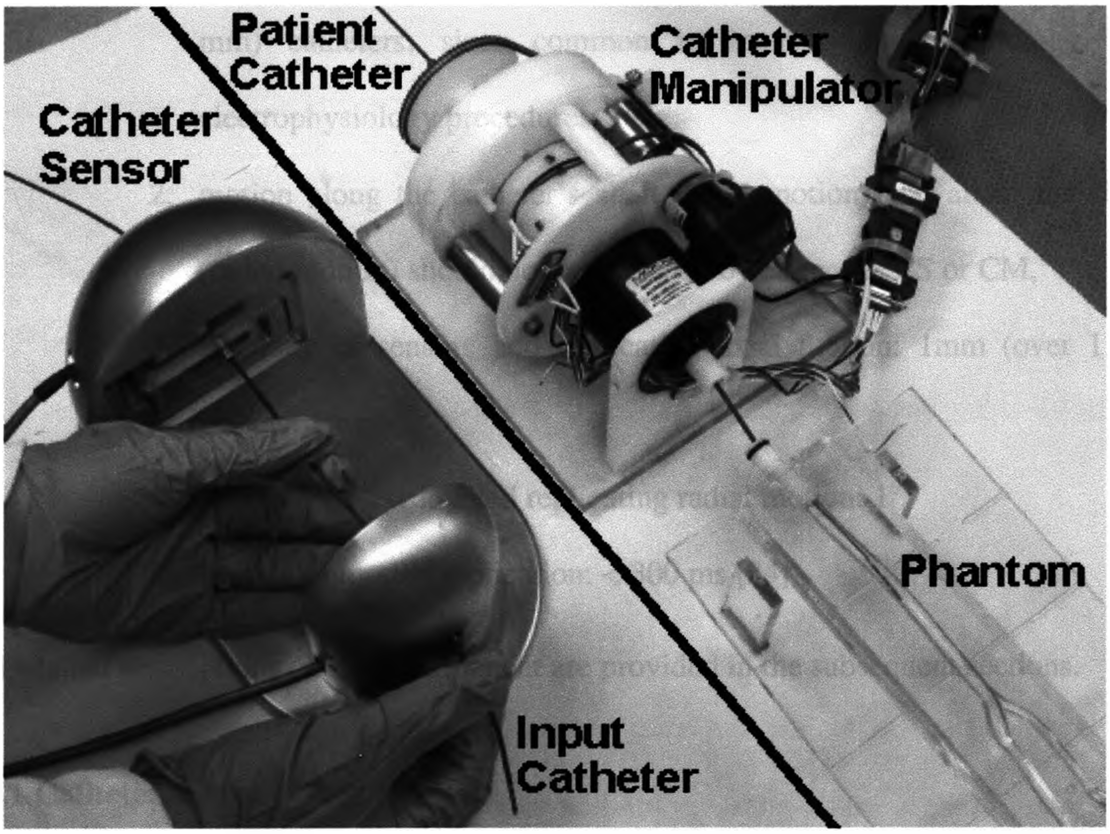

Fig. 3-1: The remote catheter navigation system: The interventionalist can pull, push or twist the input catheter inside the catheter sensor. Motion measured by the catheter sensor is then replicated with the patient catheter using the remotely placed catheter manipulator. Image feedback is provided by a standard fluoroscopic x-ray system (not shown).

manipulator. To ensure navigation with this system is compatible with conventional bedside navigation, the following criteria were used in the design process:

1. the system should be compatible with generic 6-7 F (diameter: 2-2.3 mm) catheters, sizes common in interventional cardiology and electrophysiology procedures,
2. motion along the catheter's shaft (axial motion) and about the shaft (radial motion) should not be impeded by either the CS or CM,
3. accuracy of sensing and replicating axial motion: 1mm (over 1.5m catheter length),
4. accuracy of sensing and replicating radial motion: 1°,
5. latency of motion replication: < 300 ms [24].

Detailed descriptions of each component are provided in the subsequent sections.

3.2.1 Catheter Sensor

The prototype CS, previously described in [25, 26], and schematically shown in Fig. 3-2, is an electromechanical device that measures the axial and radial motion of the input catheter's shaft using two mechanically independent passive sensors. Each sensor contains a 2000 count-per-revolution quadrature encoder, mechanically coupled to the shaft of the catheter. The axial position of the catheter shaft is measured using a mechanical transducer that converts the axial motion of the catheter to a rotation of the shaft of an optical encoder (E5S, US Digital, WA, USA) using two rollers that mechanically couple to the catheter (Fig. 3-2a). The primary roller is directly coupled to the encoder, while the second idler roller passively ensures continuous contact between the primary roller and catheter. The position of the second roller is adjustable to allow variable contact friction between the catheter and the primary roller. The rollers were manufactured from Delrin™ to ensure dimensional stability and low inertia. The axial position of the input catheter's shaft is determined as the product of roller circumference (40 mm) and digital encoder counts divided by the total number encoder counts (2000). In the current implementation, detection of a single counter increment yields a motion sensitivity of 0.02 $mm \cdot count^{-1}$ in the axial direction.

To measure radial motion, the input catheter is used as the shaft to the radial encoder (Fig. 3- 2b). A cylindrical assembly is constructed to house the sensor components; three miniature bearings and the optical encoder. The three miniature bearings (diameter 4.8-mm) grip the catheter in the radial direction and hold it at the centre of the encoder disk, while allowing it to move freely in the axial direction; one of the miniature bearings is spring-loaded to ensure continuous contact between the bearings and catheter. On the outer edge of the cylindrical housing assembly is a guide track, which in conjunction with three support bearings (diameter 9.52-mm) enables the catheter to freely rotate the optical disk through the optical sensor. The radial position of the catheter's shaft is measured directly by the encoder. In the current implementation, detection of a single counter increment yields a motion sensitivity of 0.18° $mm \cdot count^{-1}$ in the radial direction.

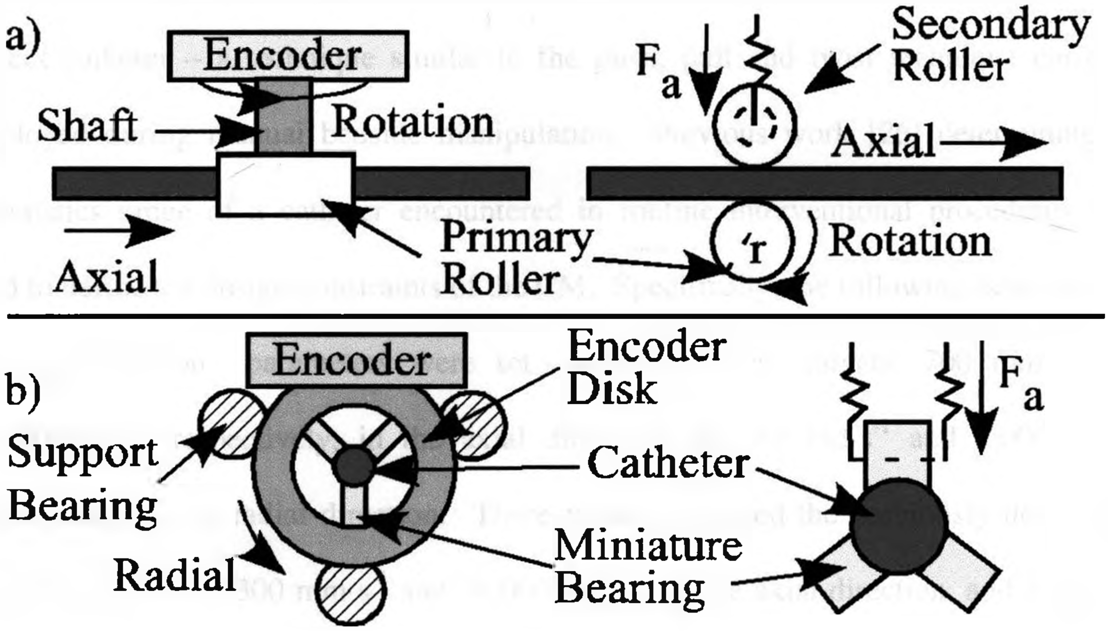

Fig. 3-2: Motion is measured by the catheter sensor in: a) the axial direction by mechanically transducing the axial motion of the catheter to a rotation of the encoder disks shaft via friction between the catheter and primary roller; adjustment of a second passive roller ensures continuous contact between the catheter and primary roller, and b) in the radial direction by rotating the radial optical disk through the sensor via three miniature bearings encased a housing which floats on three support bearings. Contained in each electromechanical sensor are springs that apply a force (F_a) to ensure the catheter does not slip in the apparatus. A picture of the constructed sensor has been previously shown in Fig. 2-1.

3.2.2 Catheter Manipulator

The CM was designed to actuate the patient catheter using motion sensed along the shaft of the input catheter by the CS, and then applying that motion along the shaft of the patient catheter – a technique similar to the push, pull and twist technique currently employed during manual bedside manipulation. Previous work [26] determining the kinematics range of a catheter encountered in routine interventional procedures were used to define the design constraints of the CM. Specifically, the following peak velocity and acceleration parameters were set as the design targets: 700 $mm \cdot s^{-1}$ and 30,000 $mm \cdot s^{-2}$ respectively, in the axial direction; and 43 $rad \cdot s^{-1}$ and 1,000 $rad \cdot s^{-2}$ respectively, in the radial direction. These values exceeded the previously determined peak kinematics of: 300 $mm \cdot s^{-1}$ and 16,000 $mm \cdot s^{-2}$ in the axial direction, and 11 $rad \cdot s^{-1}$ and 500 $rad \cdot s^{-2}$ in the radial direction [26].

The prototype CM, illustrated schematically in Fig. 3-3, consists of an axial driver mechanism mounted within a slip-ring gantry. The axial-driver mechanism consists of a servomotor (Coreless-DC 2342, MicroMo, FL, USA) coupled to the catheter via a high-friction wheel (urethane 70A, 1.27-cm diameter) through a 1:1 bevel gear; a secondary spring-loaded urethane idler roller mounted opposite the drive wheel acts to hold the catheter with sufficient frictional force. Contained in the gantry are two additional pairs of passively rotating spring-loaded urethane rollers that guide the catheter through the device. To ensure the catheter does not slip in the mechanism when actuated, springs were integrated into the design to provide an axial gripping force of 4 N and a radial gripping torque of 18 mN·m; these values were chosen to exceed the maximum axial force (2.5 N) and radial torque (14 mN·m) applied by interventionalists on a catheter in a previous study [26]. The entire slip-ring mounted gantry is rotated, via a sprocket-chain drive, by a second servomotor (Coreless-DC 3863, MicroMo, FL, USA), thereby rotating the catheter. Single-axis motion controllers (MVP®, MicroMo, Clearwater, FL, USA), which communicate with the computer console, drive the two servomotors.

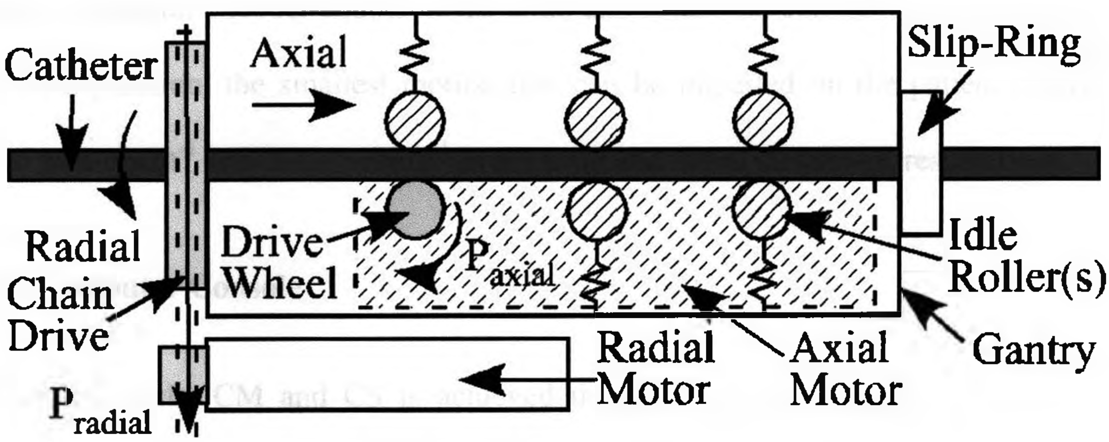

Fig. 3-3: The patient catheter is placed inside the catheter manipulator. Radial motion (Eqn. 3-1: θ_{CM}) is achieved by rotating the slip-ring gantry by a servomotor via a sprocket gear and chain. Mounted on the slip-ring gantry is a second motor, which is used to actuate the catheter in the axial direction (Eqn. 3-1: a_{CM}) via a bevel gear and the drive wheel. A series of spring-loaded urethane coated rollers are placed inside the roller housing to grip the catheter. Each motor is controlled by a single axis motion-controller (not shown).

The position of the patient catheter's shaft is determined by the gear ratios of the bevel and sprocket gears used, the internal gear ratios of the servomotors, and the radius of the urethane rollers, and are described by:

$$P_{patient}[a_{CM}, \theta_{CM}] = \left[\frac{2\pi \cdot counts_{CM-axial} \cdot r_{CM}}{k_{axial} \cdot cpr_{CM}} \quad , \quad \frac{2\pi \cdot counts_{CM-radial}}{k_{radial} \cdot cpr_{CM}} \right]. \qquad \text{Eqn. 3-1}$$

In the prototype CM, the calculated values of the constants k_{axial} and k_{radial} were 3.3 and 16.5, respectively. The drive roller radius (r_{CM}) was 6.35 mm, the number of encoder counts per revolution (cpr_{CM}) was 2000; $counts_{CM-axial}$ and $counts_{CM-radial}$ are the respective number of digital encoder counts of the axial and rotational components. Based on this CM configuration, the smallest motion that can be imparted on the patient catheter is 0.006 mm$\cdot$count^{-1} and 0.011°$\cdot$count^{-1} in the axial and radial directions, respectively.

3.2.3 Computer Console

Control of the CM and CS is achieved through a computer console (1 GHz dual Athlon®, Linux kernel 2.16.15) via RS-232 serial communication. Control software was implemented using C++; to enable simultaneous motion control in the axial and radial directions, device control was multithreaded. The axial and radial motions measured by the CS are substituted for $P_{Patient}[a_{CM}, \theta_{CM}]$ (defined above: Eqn. 3-1) and solved to determine the corresponding position of the CM in motor space (Eqn. 3-1: $counts_{CM-axial}$,

$counts_{CM\text{-}radial}$). The position of each CS component is sampled at 20 ms intervals; the corresponding velocity and acceleration values are determined and commands then issued to the CM controllers at 60 ms intervals. This sampling strategy was used to optimize update time, while minimizing motion jitter. The motion controllers are provided with position, velocity and acceleration by the console and then use a trapezoidal motion profile [27], in conjunction with a PID control loop, to drive the patient catheter [28].

3.3 Methods

3.3.1 Evaluation of Catheter Sensor

The axial accuracy of the CS in measuring axial motion was evaluated by advancing a 6 F catheter (Viking™, BardEP, MA, USA), containing four 2-mm long electrodes, inside a 2.4-mm (3/32 inch) diameter straight acrylic tube, while monitoring the catheter position using a calibrated fluoroscopic x-ray system (MultiStar®, Siemens, DE). The catheter was advanced, and then retracted, in the CS in 25-mm increments (approximate) over a 300-mm range. At each catheter position, five digital radiographic images (FOV/FOVeff: 40/36-cm, image matrix: 880x880, technique: 73 kVp and 47 mA) were obtained. Following correction for pincushion distortion [29], the five digital radiographs were averaged and the catheter's axial position was determined by calculating the weighted centroids of three catheter-shaft electrodes [30]. These values were compared with the corresponding position reported by the CS and trueness was calculated as the average difference between CS-measurement and the radiographically derived position. These measurements were first performed to determine any deviation in the primary roller radius from the nominal value, thereby generating a calibration constant to linearly scale axial measurements; experiments were then repeated to determine the trueness of the CS.

To evaluate axial-measurement precision, an acrylic rod with a flat end was placed inside the 2.4-mm (3/32 inch) diameter acrylic tube; the end of the rod was used to mark the position to which the catheter would be advanced. The catheter was advanced through the CS into the guide tube until it made contact with the acrylic rod; the position reported by the CS was then recorded. The procedure was executed over a 60 mm range, repositioning the rod at 10 mm steps, at each position five independent CS measurements were made. Measurement precision of the CS was calculated as the standard deviation of the error in the measured position.

The accuracy of radial position measurements were evaluated using a 2-mm diameter carbon-fibre rod in place of the 6 F catheter. This substitution was made to avoid measurement errors introduced due to the elastic properties of the catheter. Placed on the rod's end was a 12.7-mm (0.5 inch) diameter cylindrical sleeve with a flat edge precision machined into the cylindrical surface. To evaluate accuracy, the rod was rotated until the flat edge aligned with a gauge block (type 516-423-26, Mitutoyo Inc., JP) and a reading was acquired by the CS. Trueness was evaluated by obtaining measurements at 180° increments over 1080°, then calculating the mean error in the measurement. Radial-measurement precision was evaluated by rotating the rod by 360° ten times, recording the CS measurement, and then calculating the standard deviation.

3.3.2 Evaluation of Catheter Manipulator

The accuracy of the CM was evaluated using the calibrated CS. Consistent with the CS experiments, a 6 F catheter was used for all axial experiments and a carbon-fibre rod was used for all radial experiments. Prior to evaluating the accuracy of the CM, a series of experiments were performed to characterize the mechanical backlash of the CM. In the axial direction, mechanical backlash was measured by moving the catheter from 0 mm to 100 mm then back to 0 mm, ten times in succession. The difference between the start position and final position, as reported by the CS, was divided by the total number of iterations to determine error per direction-change. The backlash error was then software corrected. This process was repeated iteratively until the final error was under 1-mm. In the radial direction, the methodology to calculate the mechanical backlash was similar; rotating the carbon-fibre rod from 0-360°, ten times, and then adjusting the backlash constant until it was under 1°.

To evaluate the trueness of axial motion, the catheter was advanced by the CM through the CS in 25-mm increments over a range of 400 mm at a speed of 10 mm·s^{-1}; readings of the catheter position were made at each increment. To evaluate axial-precision, the catheter was advanced to the 40 mm position, ten times, and the standard deviation of the error in the position was calculated. These measurements were first performed to determine any deviation in the drive roller radius (r_{CM}), thereby generating a calibration constant to linearly scale a_{CM} in Eqn. 3-1, then repeated to determine the CS accuracy.

Radial position trueness was evaluated by rotating the carbon-fibre rod at a rate of $1°\cdot s^{-1}$ over a range of 720°, with measurements taken using the CS at 45° increments. To evaluate precision the catheter was rotated 360° ten times, recording the radial position using the CS at each trial.

3.3.3 Evaluation of Lag in Replicated Motion

Two studies were performed to evaluate the lag time between the sensed and replicated motion. In the first study, the CS was replaced with a data file containing prescribed motion profiles (step, square, ramp and triangle) in order to remove human factors from the experiments. For the step and square motion profiles, the manipulator was instructed to move the catheter from rest to a prescribed position (up to 350 mm in the axial and 350° in the radial directions) then return back to the original position (square response only, after a 9-s rest at the prescribed position). For the ramp and triangle motion profiles, the manipulator was instructed to move the catheter at a prescribed constant velocity; velocities up to 350 $mm\cdot s^{-1}$ or $350°\cdot s^{-1}$ in the axial and radial directions, respectively.

In the second study, eight operators with no interventional experience, or experience using this catheter navigation system, were provided with 10 minutes of training on the system. They then proceeded to navigate a 6 F catheter through an acrylic model of a normal carotid artery [31]; the operators were instructed to navigate the catheter from the common carotid to the internal branch, retract the catheter into the common carotid, then direct it into the external carotid. Inexperienced operators were chosen for this study due the results of a previous study that demonstrated they manipulated catheters with peak radial velocities and accelerations [26]. Each operator repeated the procedure 12 times in succession, under direct visual feedback. Fluoroscopic imaging was not used in this case because the type of feedback mechanism was not expected to affect the measured lag of the RCNS. In both studies, the catheter navigation system logged the motion profiles of both the input catheter and the patient catheter.

To determine the lag in replicated motion, the input and replicated motion profiles were re-sampled at 20 ms intervals, and then filtered (10^{th} order rectangular low-pass filter $F_{cut\text{-}off}$=2.5 Hz) to remove frequencies in the replicated profile that are the result of "on-the-fly" motion profile generation, which occurs at 16.7 Hz. The cross-correlation between motion profiles was then calculated using the *xcorr* function in Matlab® (R2007b, MathWorks Inc., MA, USA), and the lag measured as the maximum correlation value. To determine if the lag in replicated motion was operator-dependent, lag-time results were compared using one-way ANOVA, performed using Prism™ V4 (GraphPad Software Inc., CA, USA).

Table 3-1: Results – Accuracy of the Catheter Sensor and Catheter Manipulator

	Catheter Sensor		Catheter Manipulator	
	Axial (mm)	Radial (°)	Axial (mm)	Radial (°)
Trueness	0.04	0.10	0.07	-0.18
Precision	±0.14	±0.15	±0.11	±0.33

3.4 Results

3.4.1 Evaluation of Catheter Sensor

The measured calibration constant for axial motion was $1.0062\text{-mm}\cdot\text{mm}^{-1}$. Listed in Table 3-1 is the measured accuracy for the CS.

3.4.2 Evaluation of Catheter Manipulator

The measured mechanical backlash was 0.17-mm in the axial direction. Mechanical backlash was not observed in the radial direction. An axial calibration constant of $0.95\text{-mm}\cdot\text{mm}^{-1}$ was observed for the axial drive mechanism. The accuracy of the CM, measured after backlash correction and calibration, is listed in Table 3-1.

3.4.3 Evaluation of Lag in Replicated Motion

The lag in motion replication using prescribed motion profiles, shown in Fig. 3-4, demonstrates a dependency on the amplitude of the requested motion, as well as the requested velocity and acceleration. A minimum system lag of 0.18s was observed in all cases. As expected, the lag was greater when the prescribed motion profile included larger accelerations (Fig. 3- 4: step and square profiles vs. ramp and triangle).

In the second study, all operators were successful in navigating the catheter into both the internal and external carotid arteries. The replicated-motion lag is plotted in Fig. 3-5, for the radial (a) and axial (b) directions. Average lag times in the radial and axial directions were 0.28±0.04s (range: 0.2-0.36s) and 0.23±0.01s (range: 0.2-0.26s), respectively. Statistically significant differences in the measured lag times were observed between operators ($P<0.0001$) in both the axial and radial directions.

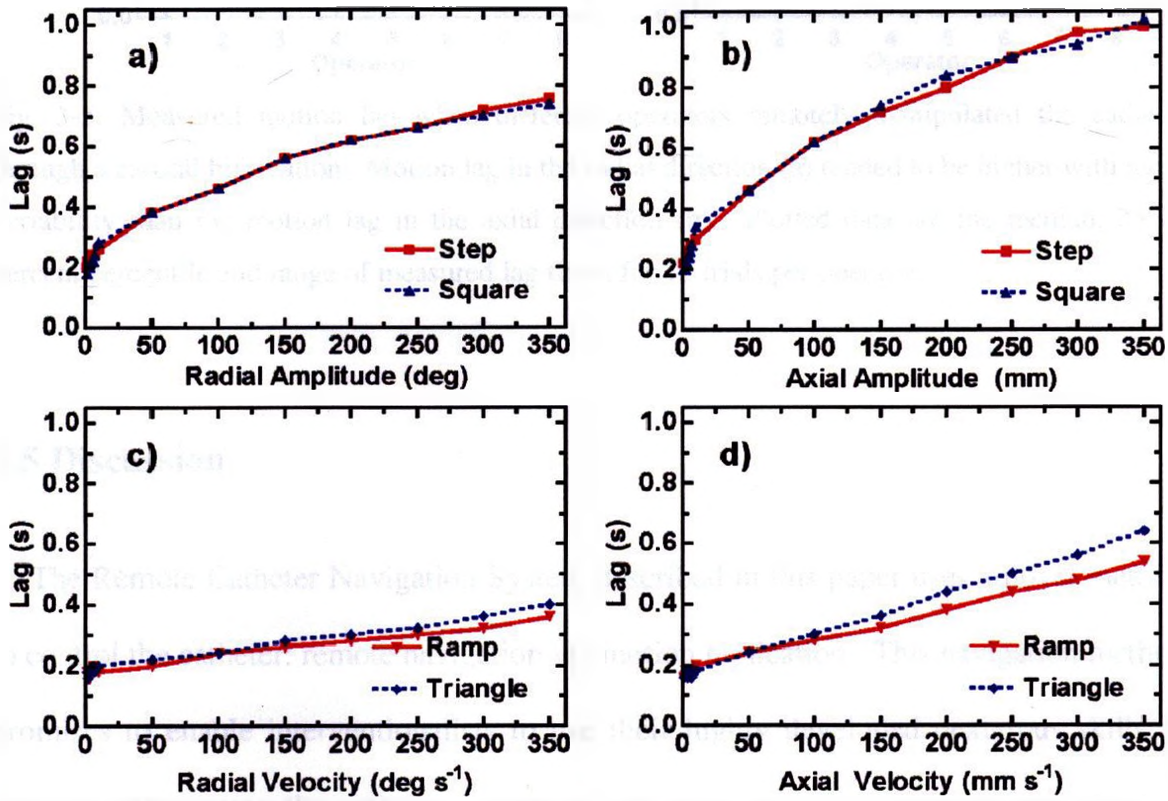

Fig. 3-4: Measured replicated motion lag time using known motion profiles: a) step/square response in the radial direction, b) step/square response in the axial direction, c) ramp/triangle response in the radial direction, and d) ramp/triangle response in the axial direction.

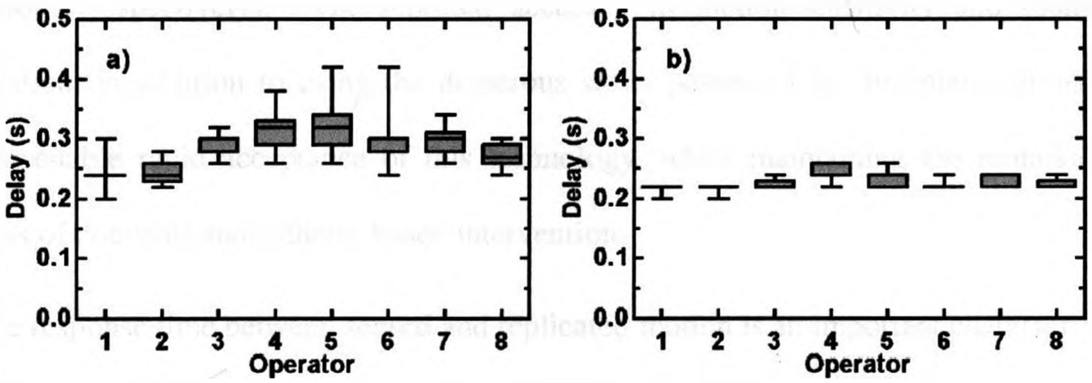

Fig. 3-5: Measured motion lag when different operators remotely manipulated the catheter through a carotid bifurcation. Motion lag in the radial direction (a) tended to be higher with more variability than the motion lag in the axial direction (b). Plotted data are the median, 25-75 percent percentile and range of measured lag times for 12 trials per operator.

3.5 Discussion

The Remote Catheter Navigation System described in this paper uses a novel method to control the catheter: remote navigation via motion replication. This navigation method promises to enable interventionalists to use their highly developed dexterous skills to remotely manoeuvre the catheter, potentially reducing radiation exposure and physical stress during long procedures. The current implementation of the RCNS was designed for use with 6-7 F catheters, commonly used in electrophysiological procedures, but is easily adaptable for catheters of different sizes. The performance evaluation of the RCNS demonstrated the system's ability to sense and replicate catheter motion within the intended specifications (accuracy better than 1 mm and 1° in the axial and radial directions, respectively). The reported accuracy in motion-sensitivity and motion-replication, in addition to using the dexterous skills possessed by the interventionalist should enable rapid acceptance of this technology, while maintaining the remarkable success of conventional catheter-based intervention.

The response time between sensed and replicated motion is an important characteristic of any tele-operated system. The minimum achievable lag with the current implementation of the system was 180 ms, attributable to the inherent communication lag between the CS and the CM. However, longer lag times were observed when motion profiles (requiring increased velocities and accelerations) were executed by the CM, as shown in Fig. 3-4 and Fig. 3-5. Specifically, the observer study demonstrated that the lag times measured for some operators were significantly longer, and in the radial direction lag times of as much as 360 ms were measured. In comparison, motion lag in the axial direction varied only by 60 ms between all operators. There are two related factors that explain this operator-dependent increase in the radial direction lag time. First, inspection of the motion profiles in the radial direction demonstrated that operators who navigated the remote catheter with longer and more variable lag times (Fig.3-5), tended to apply higher peak velocities (Fig. 3-6) than operators with lower and less variable lag times (e.g. operator 5 vs. operator 2). Second, the ability to visualize changes in catheter orientation and position also influence the motion profile and thereby the measured lag time: in the axial direction, changes in the position are easily perceived, while changes in the radial orientation of the catheter are obscured both by the catheter's radial symmetry and its deformability. This inability to visualize the radial orientation of the catheter seemed to result in a move-wait-visualize-repeat mode of navigation in the radial direction, instead of moving and visualizing the catheter simultaneously, which occurs in the axial direction. Inspection of the recorded axial and radial velocities of the operator's motion profiles supports this hypothesis; an example motion profile shown in Fig. 3-7 illustrates smoothly varying motion in the axial direction (Fig. 3-7b and d) and intermittent motion in the radial direction (Fig. 3-7a and c). The lack of perception of the radial motion of the remote catheter observed in these studies is consistent with catheter navigation and visualization in clinical practice, where motion applied to the proximal end of the catheter is not fully transferred to the distal end, and rotation about the catheter's axis is poorly perceived in the fluoroscopic images. Overall, these results suggest that lower lag times are achievable when the operator navigates the catheter using smoother motion. Furthermore, our earlier study (Chapter 2), comparing catheter kinematics while operated by novices and experienced interventionalists, demonstrated that experienced interventionalists navigate catheters with lower peak velocities and peak accelerations than inexperienced users, suggesting that in a clinical setting the lag times will be dominated by the inherent communication delay, which in future implementations can be decreased using a more sophisticated communication strategy, such as USB or TCP IP protocols. Nonetheless, even the lag times observed with inexperienced users are still within the previously defined limit of 300 ms, established by Fabrizio et al. [24] as

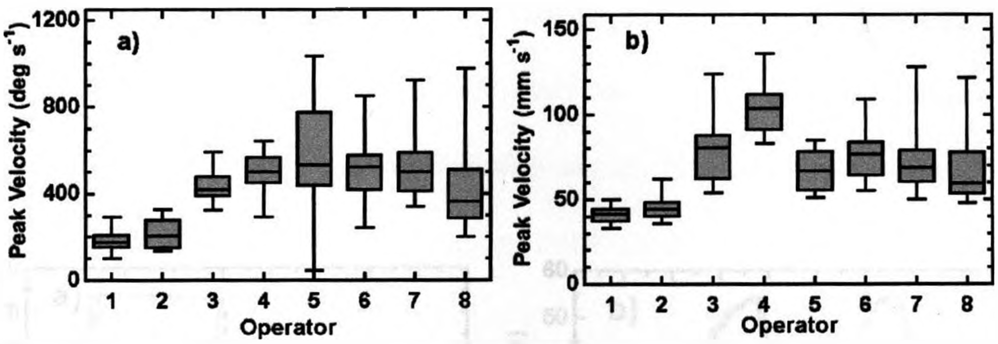

Fig. 3-6: Peak velocity in the (a) radial and (b) axial directions. Plotted data are the median, lower median, upper median, and range of calculated peak velocity for the 12 trials per operator.

the maximum acceptable image-display latency needed to ensure safe remote surgical manipulation.

The simplicity of the experiments performed to evaluate mechanical backlash and the phantom used to determine lag in replicated motion represent limitations of this study. Correcting mechanical backlash was iteratively performed until ten changes in direction resulted in an observed error of less than 1 mm and 1° in the axial and radial directions, respectively. Increasing the number of directional changes may result in a larger discrepancy between the starting position and final recorded position, as quantization effects of the backlash correction factor become more apparent. Although this may occur, the iterative error per direction change is very small and may not be perceived by the operator, who in practice will use fluoroscopic x-ray imaging as position feedback of the patient catheter

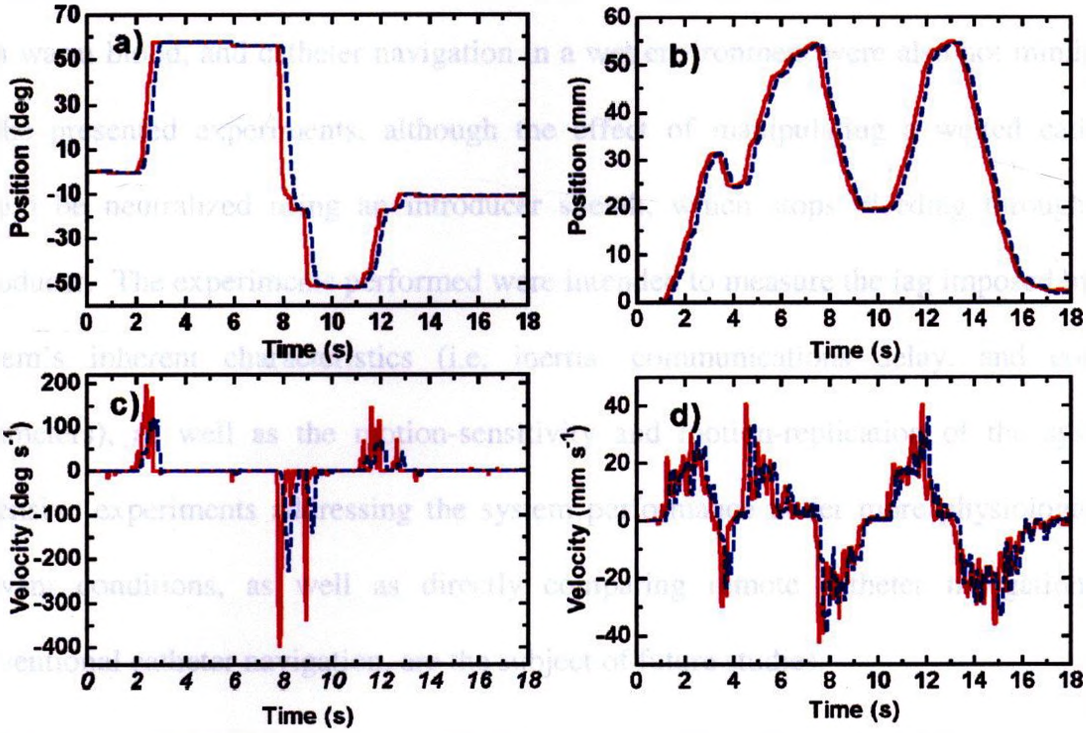

Fig. 3-7: a) Radial motion profile, (b) axial motion profile, (c) radial velocity, (d) and axial velocity observed during remote catheter navigation through the normal carotid model (Operator 6, trial 10). The red solid line represents motion of the input catheter, while the blue dotted line is the motion of the patient catheter. In the axial direction, replicated velocity is fluid with the input velocity (c), in contrary to replicated velocity in the radial direction (d), which is visually intermittent.

Furthermore, the phantom used in the motion lag study presented a simpler path trajectory than those commonly encountered in clinical practice, which require manoeuvring of the catheter through tortuous vessels and tight curvatures (e.g. vessel selection through the aortic arch). Softening of the catheter, which occurs due to contact with warm blood, and catheter navigation in a wet environment were also not mimicked in the presented experiments, although the effect of manipulating a wetted catheter should be neutralized using an introducer sheath, which stops bleeding through the introducer. The experiments performed were intended to measure the lag imposed by the system's inherent characteristics (i.e. inertia, communications delay, and control parameters), as well as the motion-sensitivity and motion-replication of the system. Extensive experiments addressing the system performance under more physiologically relevant conditions, as well as directly comparing remote catheter navigation vs. conventional catheter navigation, are the subject of future studies.

The prototype RCNS was designed for compatibility with generic 6-7 F catheters; catheter sizes used commonly during interventional electrophysiology procedures, but in its current implementation it does not contain the mechanics required to manipulate deflectable-tips found on some EP catheters. The mechanical mechanisms used to deflect these catheters are not standardized, and thus would require a specialized mechanical device for compatibility with each different deflectable catheter type. In addition, the compatible catheter sizes (6-7 F) are larger than catheter sizes found in routine interventional cardiology and interventional neuroradiology procedures, which are typically 4-5 F. Utilizing this system with smaller catheters will require modifying the mechanism that grips and actuates the catheter in the CM, as well as the electromechanical sensors in the CS. The CM is predominantly composed of Delrin®, an easily machinable low-cost plastic, which provided a cost effective method to demonstrate the proposed method of remote catheter navigation. However, Delrin® cannot be placed in an autoclave, thus limiting the ability to easily sterilize and reuse the CM. Future versions of the RCNS will address these concerns.

The RCNS presented has many potential advantages over commercially available systems. Unlike magnetic catheter navigation [11], where large permanent magnets are used to orient the catheter, thereby removing bi-plane imaging capabilities, limiting oblique projection views to ±30°, requiring magnetic shielding in the procedure room, and requiring specialized catheters, the RCNS presented can be easily integrated into existing fluoroscopic suites. The current system also uses generic catheters, with performance characteristics known to the interventionalist, during remote navigation. Most other commercially available remote navigation systems utilize joystick-type input devices to navigate the remote catheter, and all but the device described by Negoro et al. [12], manipulate the remote catheter without providing tactile sensation to the interventionalist. Because of the flexible nature of catheters, external forces applied to the catheter during catheter guidance occur when the tip of the catheter pushes directly into tissue or when twisting the catheter pushes its body against the vascular wall. In both situations, the external forces applied to the catheter are not fully transferred to the interventionalist, but instead result in catheter deformation. The operator uses these visual cues (sometimes termed "image haptics") during catheter guidance and we expect that the ability to exploit prior dexterous skills during remote catheter navigation, as provided by our RCNS, may provide added benefit over navigation systems employing joysticks or other non-intuitive master devices [10,13-15].

The system description and performance evaluation provided here demonstrate the ability of the RCNS to accurately sense and replicate catheter motion within acceptable lag. Performance validation of this system in vivo is required. The diagnosis and treatment of cardiac arrhythmia is an ideal choice, as these procedures use 6-7 F catheters, and these procedures can be long, enhancing radiation exposure and fatigue to the interventionalist. Application of this system during other interventions such as vascular angiography or placing balloon/stents to open stenosed arteries is possible, but for each application, the logistics of this technology must be examined to ensure patient safety and positive clinical outcome. Further investigation and developments are underway to address these issues.

3.6 Conclusion

The RCNS presented is a unique platform that provides the interventionalist with the ability to use their dexterous skills while performing catheter-based interventions from a location remote to the patient. The present study has demonstrated the system's ability to accurately sense and replicate catheter motion with acceptable lag. Combining accurate motion replication with the system's ability to easily integrate within existing facilities promises to make this RCNS a cost-effective approach to reducing interventionalist's radiation exposure and physical discomfort. In the future, utilizing this system to perform a range of catheter-based interventions in vivo is required to establish the limitations of this technology in clinical practice.

Acknowledgements

The authors are grateful to Dr. Raymond Yee, Dr. Allan Skanes, Dr. Rodney Allan, and Dr. Irene Gulka for their clinical input towards this project. We would also like to thank Jason Cakiroglu, Steve Pollman, Hristo Nikolov and Jacques Montreuil for their technical contributions.

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Chapter 4 :

Catheter Navigation Efficacy of a Tele-Operator Catheter Navigation System: Experimental Results in a Multi-Path Phantom[3]

4.1 Introduction

Percutaneous transluminal catheterization, a minimally invasive medical procedure, is the gold standard technique used in the diagnosis and treatment of vascular and cardiac diseases. After insertion of the catheter, the interventionalist stands adjacent to the patient, and manipulates a catheter through the vasculature towards the site of interest, using fluoroscopic x-ray imaging to localize the catheter with respect to the patient's anatomy. The close proximity to the ionizing-beam exposes the interventionalist to

[3] A version of this chapter has been submitted as a manuscript to *Radiology*, entitled: "Catheter Navigation Efficacy of a Tele-Operator Catheter Navigation System: Experimental Results in a Multi-Path Phantom," Thakur, Y., Norley, C.J., Gulka, I.B., Holdsworth, D.W., and Drangova, M. (Submission #RAD-09-1965)

harmful radiation, increasing their cumulative radiation exposure, and thus, their long-term risk of developing a malignancy, cataracts, or passing genetic defects to offspring. Remote catheter navigation systems have been developed to address interventionalist safety, by allowing the intravascular navigation of a catheter by the interventionalist from a radiation safe location [1-4].

Three commercial remote catheter navigation systems have recently become available. The Magnetic Guidance System (MGS, Stereotaxis Inc., St. Louis, MO, USA) [4] uses large permanent magnets, mounted on mechanical arms, to drive a small permanent magnet embedded in the distal tip of a specialized remote catheter. The operator sits at a console and draws a 3D vector, corresponding to the intended path of the catheter, on the console screen. The mechanical arms of the navigation system change position and orientation, aligning the catheter-tip with the intended path. The two other systems – CorPath™ (Corindus Inc., Auburndale, MA, USA) and the Sensei Robotic Catheter System™ (Hansen Medical Inc., Mountain View, CA, USA) – utilize a joystick [1, 2], stylus [3] or touch screen [2] to drive the remote catheter using either a mechanical transmission module [1, 2], or a specialized catheter sheath [3]. These remote catheter navigation systems have been successfully used to remotely deploy stents, or perform RF ablation therapy for the treatment of cardiac arrhythmia. Although they have been introduced into the clinic, the non-intuitive interface of these navigation systems may impact procedural workflow. With respect to magnetic navigation, the large permanent magnets placed adjacent to the patient bed remove's biplane imaging capabilities, limit oblique anterior-posterior views to ±30°, and require specialized catheters with embedded magnets for intravascular navigation. By using specialized catheters, with characteristics unfamiliar to an experienced interventionalist, and removing the catheter from the interventionalist's hands, thus removing the experienced interventionalist's eye-hand co-ordination from the intervention, long training times may be required for proficient use of these systems. In some instances, the lack of an intuitive catheter navigation method has resulted in the interventionalist reverting to conventional catheter manipulation to complete a procedure [5].

Our group has recently described a remote catheter navigation system that utilizes the intuitive and dexterous skills of an experienced interventionalist by keeping a catheter in the hands of the interventionalist, while they navigate a second intravascular catheter from a location remote to the patient (Chapter 3). The navigation method is intuitive – using current bedside technique, the interventionalist pushes, pulls, and twists a local *input catheter*, placed inside an electromechanical sensor. Changes in position of the input catheter are sensed, and then transferred via a work console and a remotely placed mechanical transmission module, to a remote *patient catheter*.

This paper compares the navigation efficacy of this remote catheter navigation system vs. conventional catheter navigation, in a custom-built multi-path navigation phantom using multiple operators of varying interventional experience. Based on the mode of remote catheter navigation – remote catheter manipulation via the motion sensing and replication of a local catheter in the hands of the interventionalist, catheter navigation using this system is expected to be comparable with conventional catheter navigation, with respect to navigation efficacy (the ability to traverse a given path) and catheter navigation time, after minimal operator training.

4.2 Methods

4.2.1 System Description

The remote catheter navigation system (RCNS) depicted in Fig. 4-1 and previously in Chapter 3, is a tele-operator controlled catheter navigation system. The operator manipulates the shaft of an input catheter, placed inside an electromechanical sensor; using exactly the same motions (push, pull and twist) and technique that are used in conventional bedside navigation. The sensor measures axial and radial changes in the input catheter's position, then transmits this information to a mechanical catheter driving mechanism via a work console, which then replicates the sensed motion using a second catheter placed inside the vasculature using the traditional Seldinger technique.

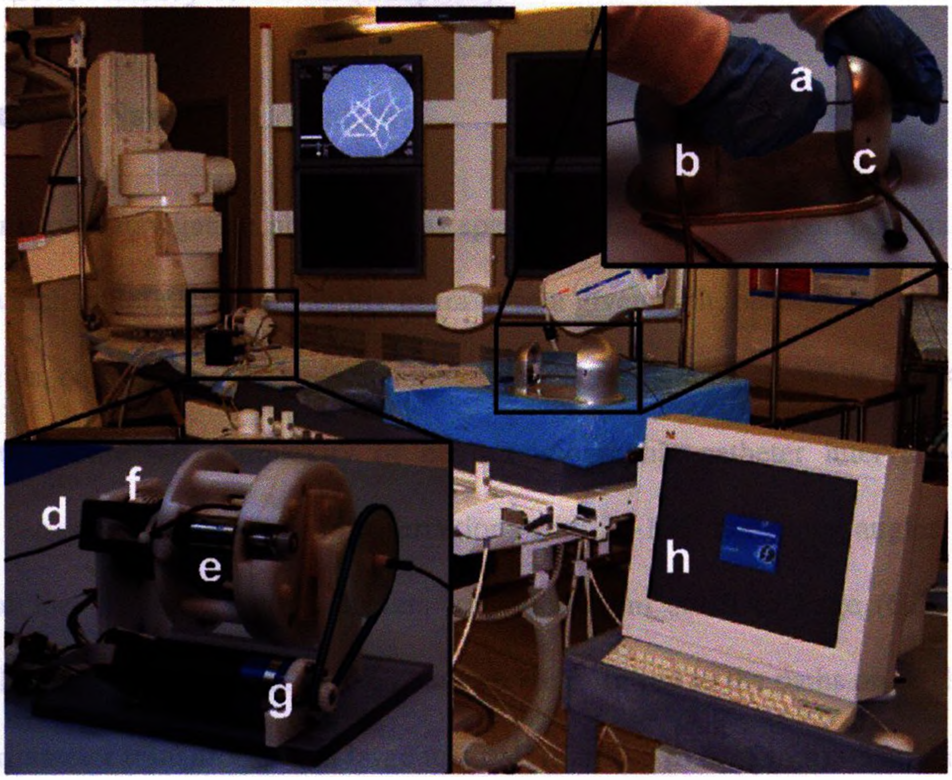

Fig. 4-1: Position of the patient catheter (a) is measured by two independent sensors (axial – (b), radial – (c)) inside the Catheter Sensor. Axial and radial motion of the input catheter is replicated using a second patient catheter (d), placed inside the Catheter Manipulator. The Catheter Manipulator contains two servo motors; one for axial motion (e), mounted on a slip-ring gantry (f), and a second for radial motion (g). A work console (h) relays information from the Catheter Sensor to the Catheter Manipulator.

The system has been previously shown to sense and replicate motion to within 1 mm in the axial direction (push and pull), and 1° in the radial direction (twist), with a replicated motion latency of 180 ms (Chapter3).

4.2.2 Multi-Path Navigation Phantom

The multi-path navigation phantom was specially constructed to compare navigation efficacy, which is defined as the ability to traverse a given path, between remote catheter navigation vs. conventional bedside manipulation. The phantom, shown in Fig. 4-2, was designed to mimic the complexity of neuro-angiographic catheter intervention, and contains a series of bifurcations and trifurcations with 30-135° branching angles. On the left side of the phantom, path diameters transition from small to large (6.35 to 8 to 9.5 mm). Paths on the right side of the phantom are mirrored to the paths on the left side, with path diameter transitions from large to small (9.5 to 8 to 6.35 mm). The multi-path navigation phantom has an overall size of 30.5x30.5x2.54 cm and is constructed of transparent acrylic.

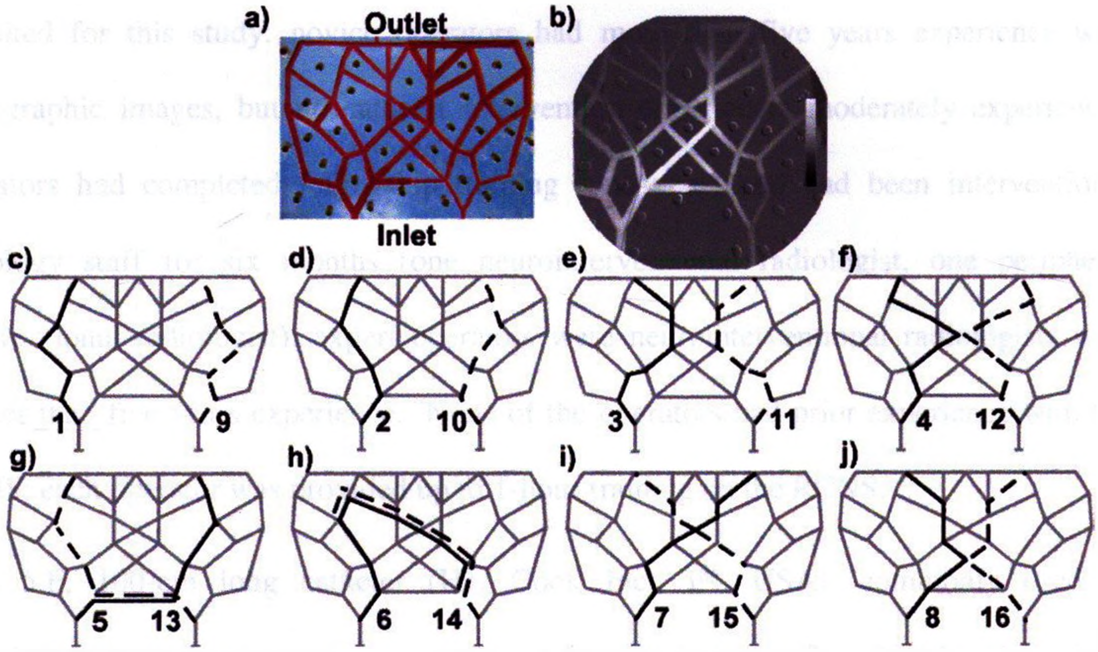

Fig. 4-2: The multi-path navigation phantom injected with a dye for contrast (a). On the left side of the phantom, vessel diameter transitions, moving from the phantom's inlet to outlet, go from large to small (9.5-8-6.35 mm). On the right side of the phantom, vessel diameter transition, moving from inlet to outlet, go from small to large (6.35-8-9.5 mm). A radiograph of the multi-path phantom, shown in (b), is used to guide navigation through paths starting on the left side of the phantom. Images c-j illustrate the 16 predefined paths navigated by the operators; solid lines represent paths originating on the left-side of the phantom, while dashed lines represent paths originating on the right side of the phantom.

4.2.3 Study Parameters

Six operators, categorized into three groups based on clinical experience, were recruited for this study: novice operators had more than five years experience with radiographic images, but no catheter intervention experience; moderately experienced operators had completed fellowship training (one year) and had been interventional radiology staff for six months (one neurointerventional radiologist, one peripheral interventional radiologist); expert operators were neurointerventional radiologists with greater than five years experience. None of the operators had prior experience with the RCNS; each operator was provided up to 1-hour training on the RCNS.

A 5 F, 100-cm long catheter (H1, Cook Inc., IN, USA), commonly used in neurointerventional procedures, containing a fixed guidewire (TSF-38-145, Cook Inc., IN, USA) was inserted through a 7 F introducer sheath into the multi-path, navigation phantom. Each operator manipulated the catheter through sixteen, preselected paths in the phantom (shown in Fig. 4-2): eight paths traversed the right side of the model and eight paths traversed the left side. Each path contained 4 to 8 turns, for a total of 88 turns. Manipulation through the sixteen paths within the phantom was first completed using conventional bedside navigation and then, after a minimum period of one week, repeated using the remote navigation system. The minimum of one week between experiments reduced *apriori* knowledge of the navigation technique required to traverse each predefined path.

An x-ray imaging system (Axiom Artis™, Siemens Inc., DE) provided fluoroscopic image feedback to the operator during all trials, using common neurointerventional technique: 58 keV, 18 mA, 7.5 frame/s, 7.5 pulse/s, 33/30 cm FOV/FOV_{eff}. Successful path and turn manipulation, total navigation time and fluoroscopic dose to the phantom were recorded for each path. Fluoroscopic dose to the phantom was measured directly by the imaging system in the form of dose-are-product (DAP), which is product of the skin dose with the cross sectional area of the radiation beam. For either navigation method, failure was defined by a navigation time exceeding 120 seconds. To standardize timing, the catheter was positioned at the entrance of the first bifurcation at the beginning of each trial. Timing concluded when the tip of the catheter fully entered the final vessel branch. This study protocol is similar to the method implemented by Schiemann *et al.* [6] to compare the navigation efficacy of the Magnetic Guidance System (Stereotaxis Inc, St. Louis, MO, USA) vs. conventional navigation in a glass phantom.

During the study, water heated to 37°C was continuously pumped through phantom model. Prior to each study, Omnipaque (300 $mg \cdot I \cdot ml^{-1}$, 20 ml) was manually injected into the phantom to obtain a radiographic roadmap for navigation.

4.2.4 Data Analysis

For each path, the number of successfully completed turns was expressed as a percentage of the total number of turns comprising the path. The percentage of completed turns, navigation time, and fluoroscopic dose were first compared for all operators, regardless of experience level, between remote and conventional navigation methods using a paired t-test (one-tail). To examine the effect of clinical expertise, the differences observed between remote and conventional catheter navigation for: percentage of completed turns, navigation time, and fluoroscopic dose, were grouped based on operator experience and analyzed with a repeated measures ANOVA.

All statistical analysis was performed using Prism™ V4 (GraphPad Software Inc., CA, USA); $P < 0.05$ was considered significant.

4.3 Results

Using the RCNS, all operators successfully navigated 91 out of 96 paths (94.8%) and 512 out of 528 turns (97.0%) within the 120 second time limit. Using the conventional technique, all paths and turns were successfully completed (100%) within the 120 second time limit. Ensemble operator performance for the remote and conventional methods were small (<4%) but significantly different ($P = 0.037$) for normalized turn success rate. Only the novice and moderate operators failed at navigating paths remotely within the allotted time period, while expert operators were successful in navigating all paths and turns (100% success). Moderate operators were successful in remotely navigating 29 out of 32 paths (90.6%) and 169 out of 176 turns (96.0%). Novice operators were successful in remotely navigating 30 out of 32 paths (93.8%) and 167 out of 176 turns (94.9%).

Comparing operator experience, analysis of variance found no statistical difference between the difference in successfully completed turns (P=0.45). Successfully completed path and turn data for all operators is shown in Table 4-1.

While comparable navigation efficacy was observed with minimal training on the RCNS, navigation time using the RCNS was slightly longer than conventional catheter navigation, requiring an ensemble average increase of 13.4 seconds per path in navigation time, for all operators (P<0.001). Based on operator experience, analysis of variance found no statistical difference between the difference in navigation time (P=0.98). Average navigation time per operator is listed in Table 4-2.

For both navigation methods, ensemble average navigation times through each path are illustrated in Fig. 4-3. Navigation times through eight out of sixteen paths had mean differences of 10 seconds or less. On average, two paths (paths 4 and 10), required less navigation time using the RCNS, than with the conventional catheter navigation technique, while navigation time through three paths (paths: 5, 6 and 15) required much longer navigation time (over 33 seconds) using the RCNS, than with conventional catheter navigation. All operators, except novice operator 2, were able to successfully navigate at least 1 path within less time using the RCNS than using conventional catheter navigation.

The mean difference in navigation time through paths with vessel diameter transitions from small to large (paths 9 through 16) was 10.2 seconds, while the mean in navigation time through paths with vessel diameter transitions from large to small was 16.9s (paths 1 through 8).

Measured dose area product was highly correlated with procedure length. Results for all operators, using both methods, are listed in Fig. 4-3. Overall, a mean-increase of 0.6 $\mu Gy \cdot m^2$ was observed when using the RCNS system, and was proportional to the increased navigation time. Since the exposure between methods was large, the difference in exposure between methods was compared to test whether this difference was attributed to operator experience. Statistical analysis found no difference exposure dose based on operator experience (P=0.14).

Table 4-1: Operator Performance: Successfully Navigated Paths and Turns Using Remote (R) and Conventional (C) Navigation Techniques

Group	Operator	R- Paths (16)	C- Paths (32)	R- Turns (88)	C- Turns (88)
Novice	1	16/16	16/16	87/88	88/88
	2	14/16	16/16	80/88	88/88
	Group	30/32	32/32	167/176	176/176
Moderate	3+	14/16	16/16	82/88	88/88
	4++	15/16	16/16	87/88	88/88
	Group	29/32	32/32	169/176	176/176
Expert	5	16/16	16/16	88/88	88/88
	6	16/16	16/16	88/88	88/88
	Group	32/32	32/32	176/176	176/176
All	-	91/96	96/96	512/528	528/528

+ - 1st year neurointerventional radiologist, ++ - 1st year peripheral interventional radiologist. Note all statistical tests performed using successful turn data.

Table 4-2: Observed Operator Navigation Times Using Remote (R) and Conventional (C) Navigation Techniques

Group	Operator	Remote Time: $\mu \pm \sigma$ (s)	Conventional Time: $\mu \pm \sigma$ (s)	Mean Time Difference (s)
Novice	1	42±24	24±9	18.2
	2	39±15	31±13	7.9
	Group	41±20	27±20	13.4
Moderate	3⁺	35±16	28±13	6.5
	4⁺⁺	49±33	29±30	19.9
	Group	42±27	29±17	13.2
Expert	5	34±20	24±11	10.0
	6	43±22	26±13	17.0
	Group	38±21	25±12	13.5
All	-	40±23	27±14	13.4

$^{+}$ - 1st year neurointerventional radiologist, $^{++}$ - 1st year peripheral interventional radiologist. Data shown: μ - mean, σ – standard deviation. Mean time difference equals remote navigation time minus conventional navigation time. Times attributed to path failures omitted from data.

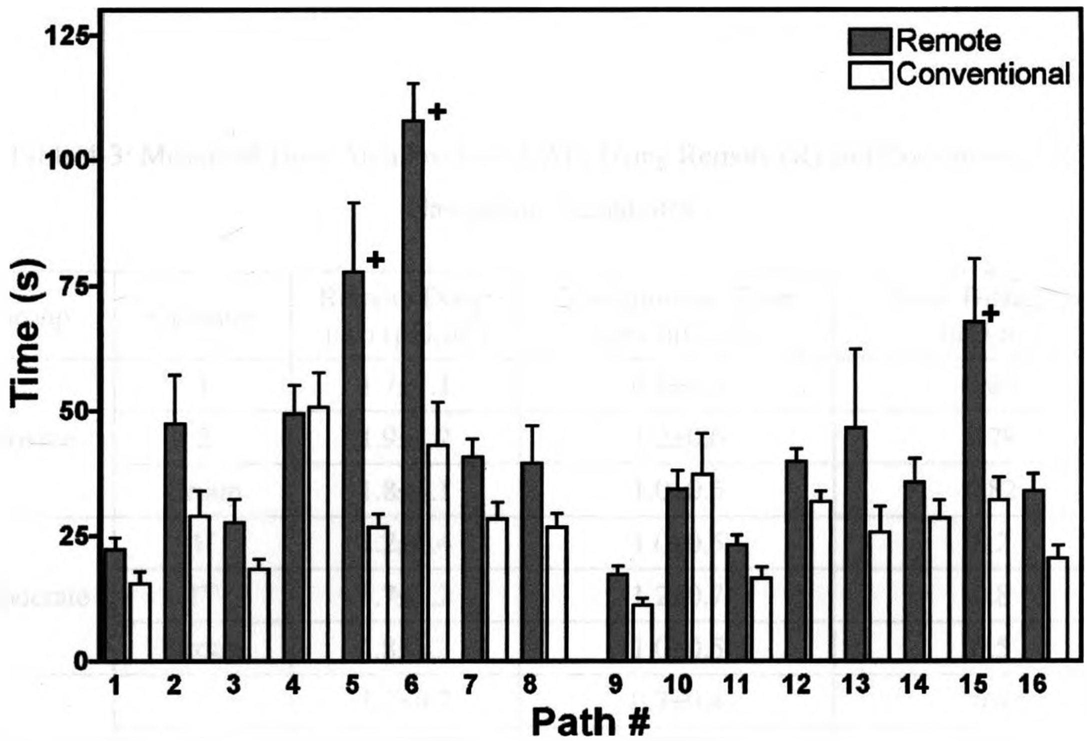

Fig. 4-3: Catheter navigation times recorded for each path using both remote catheter navigation and conventional catheter navigation techniques (each bar represents mean+sem.). Navigation using the RCNS took an ensemble average of 13 seconds longer than conventional catheter navigation. Remote navigation through paths with large to small vessel diameter transitions (paths: 1-8), required on average 22 seconds longer, while paths with small to large vessel diameter transitions (paths: 9-16), required on average 12 seconds longer with the RCNS. Three paths, labelled '+' (paths: 5, 6 and 15), took 33 seconds longer with the RCNS. Omitting these paths, the ensemble average increase in navigation time using the RCNS was only 9 seconds for all other paths.

Table 4-3: Measured Dose Area Product (DAP) Using Remote (R) and Conventional (C) Navigation Techniques

Group	Operator	Remote Dose: $\mu\pm\sigma$ ($\mu G_y m^2$)	Conventional Dose: $\mu\pm\sigma$ ($\mu G_y m^2$)	Dose Difference ($\mu G_y m^2$)
Novice	1	1.7±1.1	0.8±0.3	0.85
	2	1.9±1.2	1.2±0.6	0.79
	Group	1.8±1.1	1.0±0.5	0.82
Moderate	1^+	1.2±0.4	1.0±0.5	0.2
	2^{++}	1.7±1.2	1.2±0.7	0.8
	Group	1.8±1.3	1.0±0.5	0.5
Expert	1	1.2±0.7	0.7±0.4	0.4
	2	1.5±0.8	0.9±0.4	0.6
	Group	1.3±0.7	0.8±0.4	0.5
All	-	1.6±1.1	1.0±0.5	0.6

$^+$ - 1st year neurointerventional radiologist, $^{++}$ - 1st year peripheral interventional radiologist. Data shown: μ - mean, σ – standard deviation. Mean dose difference equals dose during remote navigation minus dose during conventional manipulation. Dose attributed to path failures is omitted from data.

4.4 Discussion

For remote catheter navigation systems to become clinically successful, the ability to remotely manipulate the catheter must, at a minimum, maintain the navigation efficacy of conventional bedside catheter manipulation. In this study, two expert operators, two moderately experienced operators and two novice operators, each used conventional navigation and the RCNS to traverse 16 predefined paths in a custom-built phantom. All operators were successful in navigating all 16 paths, within the prescribed time of 120 seconds, using the conventional navigation technique. Using the remote navigation system, expert operators were successful in navigation all paths, and turns, results which were better than both moderate and novice operators. This suggests catheter navigation using the RCNS has navigation efficacy comparable to conventional bedside manipulation, after minimal training on the system.

The difference between remote and conventional navigation time was compared to determine whether operator experience effected overall navigation time. The results show no significant difference between operator experience groups. However, novice and moderate operators were unable to successfully traverse 5 paths using the RCNS. Navigation times for these paths were omitted from statistical calculation, as the time value (120 seconds) is capped and does not represent the true navigation time required by these operators to successfully traverse these paths. Expert operators, on the other hand, were successfully able to traverse these paths within the allotted time, requiring only 13.4 seconds of increased navigation time.

Total catheter navigation time using the RCNS was slightly longer than the navigation time observed during conventional catheter manipulation. A small increase in catheter navigation time was expected, based on the remote navigation method employed. The RCNS utilizes the same catheter motions applied by the interventionalists during conventional, bedside manipulation, but occurs with a 180 ms systemic delay in replicated motion (Chapter 3). Because of this delay, comparable navigation efficacy was expected, but with a slightly longer navigation time. In future implementations of the RCNS, a reduction in replicated motion time can be achieved by enhancing the communication strategy communication protocol to reduce motion latency. This should reduce the time difference observed between remote and conventional navigation methods. Further operator experience with the RCNS may also reduce the time difference to allow the operator to adjust to the latency in replicated motion, as demonstrated by Rayman *et al.* [7].

In three paths, a large difference in navigation time was observed between navigation methods (paths: 5, 6 and 15). It was speculated that the multi-path phantom, which is constructed of rigid acrylic, required operators to apply excessive axial force on the catheter to navigate through these paths. This assertion was anecdotally confirmed by the moderate and expert experienced operators, who stated that during conventional catheter navigation, the forces applied to the catheter to overcome "axial and torsional" tension in the catheter, caused by path friction, were substantially higher than axial and torsional tension encountered clinically. This would explain why, during remote navigation, the operators required longer navigation time through these three paths. The catheter manipulator in the RCNS is force limited, providing a maximum axial force of 4 N, a value determined previously to provide enough axial force to replicate motion, while minimizing the chance of vessel perforation (Chapter 2). Attempting to apply more than 4 N axially will result in motion cessation of the patient catheter, a result observed during the navigation of these paths.

Of the commercially available remote catheter navigation systems only the Magnetic Guidance System (MGS, Stereotaxis Inc., St. Louis, MO, USA) has been compared directly with conventional navigation. This remote navigation system has been successfully used *in vivo* to remotely guide catheters into the cerebral [8], peripheral [9], and percutaneous coronary vasculature [10, 11]. Comparing remote-navigation efficacy with conventional navigation has been predominantly done in phantom models, both anthropomorphic and non-anthropomorphic. Schiemann *et al.* demonstrated equivalent navigation efficacy between magnetic navigation and conventional navigation in a glass phantom after a single operator with five years clinical experience was provided with six months of training on the MGS system [6]. Krings *et al.* performed a comparison study using three phantoms, and four operators of varying levels of interventional experience [12]. Krings' results showed experience with conventional navigation was the dominant factor affecting navigation speed. The experienced operators performed similarly using both magnetic and conventional catheter navigation, while less experienced operators performed better with the magnetic system. Ramcharitar *et al.* also conducted an operator study using five paths in a custom phantom, with three operator-groups categorized by experience with the MGS system [13]. Their results showed navigation efficacy and navigation time was better using magnetic navigation, but highly dependent on the operator's prior experience with the MGS system. Garcia-Garcia *et al.* found in another comparison study using a coronary phantom, with two operators of similar experience (both conventional and MGS), that magnetic navigation took significantly longer than conventional navigation [14]. Overall, these studies demonstrate comparable navigation efficacy of magnetic navigation when the navigation system is operated by experienced interventionalists who have had extensive training/experience using the magnetic navigation system. Unlike the magnetic navigation system, our results demonstrate that only minimal training on the RCNS is required to achieve comparable efficacy between remote and conventional catheter navigation, when operated by a clinically experienced operator.

The use of a non-anthropomorphic phantom in this study is consistent with other comparison studies. [6, 12-14], but does present some limitations. The custom made multi-path phantom is 2D, where all navigation paths lie in a common plane, unlike human anatomy. The phantom is constructed of rigid acrylic and does not mimic vessel compliance. Although these limitations exist, the custom design of the phantom allowed for many different navigation paths, some more tortuous than common percutaneous routes encountered clinically. For example, in path 6 the operators were asked to traverse two 90° turns and five trifurcations; in contrast, the human vasculature has only one trifurcation. The wide range of turn angles, bifurcations and trifurcations was required to ensure the paths were not too easy for the operators to traverse. Due to these attributes, our clinical collaborators have expressed keen interest in the phantom as an interventional training tool.

A benefit specific to this study provided by the non-anthropomorphic nature of the phantom was that it contained paths unknown to clinically experienced operators; by removing *apriori* knowledge of vascular anatomy from the study, only their expertise in manipulating a catheter under fluoroscopic image guidance remained as an operator-dependent variable. The minimum period of one week between remote and conventional trials ensured that operators did not remember the catheter manipulation sequence used to traverse a given path.

In addition to utilizing the manual dexterous skills of experienced interventionalists, and the ability to use generic catheters, the RCNS can also be adapted for use in any fluoroscopic imaging suite, allowing easy integration into most catheter laboratories, without additional capital expenditures. The use of pre-existing dexterous skills, and pre-existing experience with the fluoroscopic x-ray imaging system, is expected to facilitate the use of this RCNS following minimal training time. Further investigation *in vivo* is warranted based on these results.

4.5 Conclusion

A study was conducted to compare the navigation efficacy of a novel remote catheter navigation system, which utilizes the manual dexterous skills of bedside navigation, with conventional bedside catheter navigation. Using a custom built, 2D multi-path phantom and six operators with three different interventional experience levels, we found the navigation efficacy of the remote navigation system to be comparable to the navigation efficacy of conventional bedside navigation, when operated by experienced interventionalists.

Acknowledgments

The authors would like to thank all the participants of this study, Hristo Nikolov for the construction of the 2D multi-path navigation phantom, Syed Haider for his assistance during experimental setup and data collection, and the Medical Imaging Department, University Hospital in London Health Science Centre, for use of their fluoroscopic x-ray imaging system. This work would not be possible without the generous funding from the Canadian Institutes of Health Research (grant #: MOP49536), Ontario Research Fund, and The University of Western Ontario.

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Chapter 5 :

Tele-Robotic Catheter Navigation: First Remote Navigation In Vivo[4]

5.1 Introduction

Catheter-based ablation procedures are the treatment of choice for many supraventricular arrhythmias, and are evolving into the first line therapeutic choice for treatment of atrial fibrillation (AF) and ventricular tachycardia [1-8]. Successful ablation treatment of AF is currently between 80-100%, continually improving with better interventional techniques. However, long procedure times associated with catheter based intervention has led to a growing concern regarding the cumulative exposure to the interventionalist. An active magnetic navigation system and a robotic navigation system are now commercially available to alleviate this risk, as well as improve control of the catheter inside the cardiac chambers. [9-12]. Comparison of these technologies with conventional, bedside catheter manipulation has been performed using physical models

[4] This chapter by: Thakur Y., Jones D.L., Skanes A., Yee R., and Drangova M., is a manuscript in preparation for submission to the journal *Circulation*.

[13-15], animal trials [10, 16], and in the clinical arena [17, 18]. Although comparable navigation efficacy has been shown between remote and conventional techniques; deficiencies including: increased procedure time, steep learning curve, specialized procedure rooms and cost, exist in both systems [19]. Since the use of these technologies has yet to provide a clear patient benefit, the cost (capital and training) of these technologies may not be warranted.

A simpler remote catheter navigation system has been developed to utilize the conventional navigation skills of an experienced interventionalist, but from a location remote to the patient [20]. This navigation system has also been designed to easily integrate into existing procedures without affecting clinical workflow or requiring large capital expenditures.

The primary objective of this study is to evaluate the safety and feasibility of the RCNS, *in vivo*. The ability to navigate a catheter to seven anatomical locations in the two right chambers of the heart was tested with the RCNS and conventional catheter manipulation. Navigation time, exposure, and exposure time were compared between navigation methods. Lesions were placed at the seven anatomical locations and overall procedure time was recorded for each remote navigation procedure. In addition, the time required to integrate the RCNS into the procedure room was measured to assess impact to workflow.

5.2 Methods

5.2.1 Animal Preparation

All animal studies were performed in accordance with institutional and national guidelines and approved by the University of Western Ontario Council on Animal Care (Protocol #2008-046-05). Eight male pigs, weighing 25 to 35 kg, were used in this study.

Each pig was injected with atropine (0.04 mg/kg, IM) and pre-medicated with Telazol reconstituted with Xylazine (5 ml of 100 mg/ml) and administered at a dose of 0.5 to 1.0 ml per 23-45 kg), then intubated and maintained under general anaesthesia (1-2% isoflurane in O_2 and NO mixture). To access the vasculature, a 9 F introducer sheath (Fast-Cath, St. Jude Medical, St. Paul, MN) was inserted into the right femoral vein using the Seldinger technique.

5.2.2 RCNS and Experimental Setup

The RCNS, previously described in Chapter 3, consists of two electromechanical devices, connected in a master-slave configuration. The master device is an electromechanical sensor (the Catheter Sensor: CS) that accepts a generic catheter, termed the *input catheter*, while the slave device is an electromechanical actuator (the Catheter Manipulator: CM) that accepts a second generic catheter, termed the *patient catheter*. During remote catheter manipulation, the interventionalist can push, pull, or twist the input catheter - applied motions similar to conventional, bedside navigation.

Position changes of the input catheter are measured by the CS and then transferred, via a workstation, to motion-controllers connected to the CM. The motion applied to the input catheter is then replicated using the second patient catheter, with a motion latency of 180 ms.

For all experiments, the RCNS was used in conjunction with a portable, clinical grade X-ray system (9900 Elite, GE HealthCare, Waukesha, WI), in digital fluoroscopy mode (technique: 88 kVp, 8 P/S. 15 F/s). To integrate the two systems, the CS, CM, and workstation were placed on a portable cart inside the imaging suite. The CM was mounted on an articulated arm and attached to the patient bed. Movement of the articulated arm allowed the position of the CM to adapt for the physiological size differences of each pig, which can result in different positions of the introducing sheath. The experimental setup is depicted in Fig. 5-1.

Unless otherwise stated, all experiments were performed using a 7 F deflectable catheter (non-irrigated, 4 mm electrode, 7 F, F-type curvature, BioSense Webster Inc., Diamond Bar, CA).

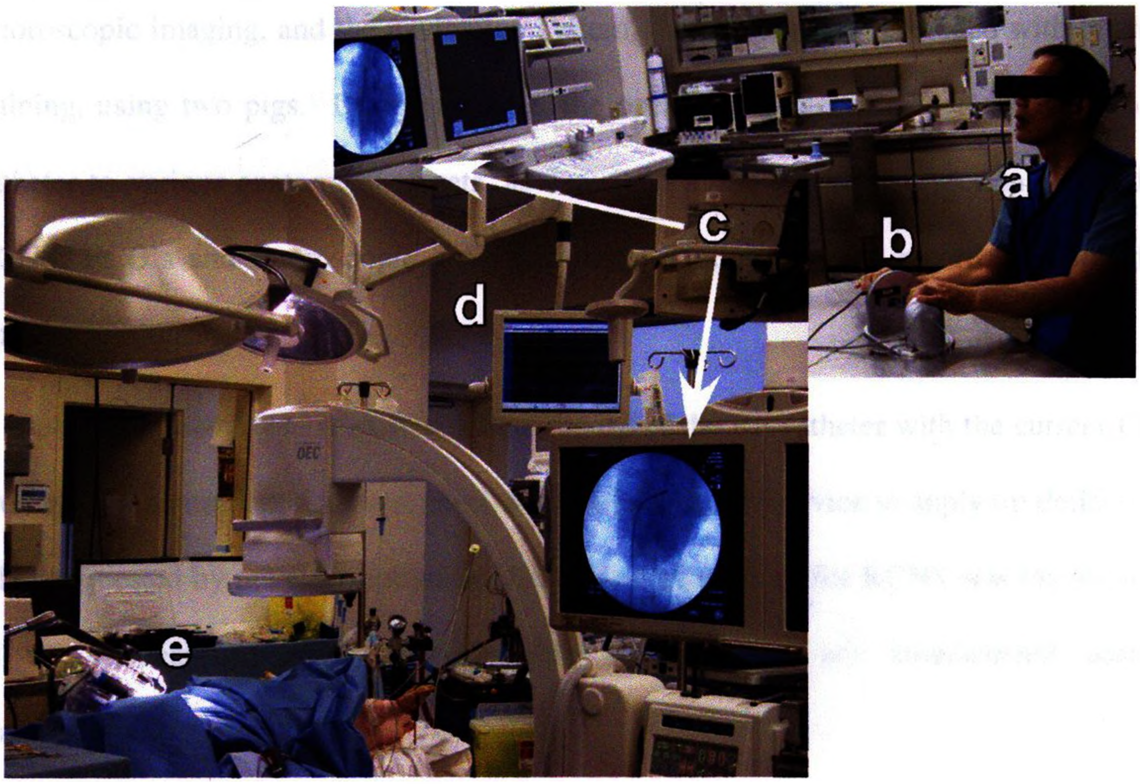

Fig. 5-1: The RCNS integrated into an experimental procedure suite. The operator (a), situated approximately 3 meters from the patient bed, manipulates the input catheter inside the CS (b) while viewing the 2D fluoroscopic images (c), and the ECG (d). Mounted on an articulated arm, the CM (e) replicates the motion of the input catheter, inside the pig. The workstation of the RCNS is placed beside the operator (not shown).

5.2.3 Operator Selection and Training

One electrophysiologist with more than ten years of clinical experience participated in this study. To ensure familiarity with porcine electrophysiology and anatomy under fluoroscopic imaging, and the navigation system, the operator was provided with *in vivo* training, using two pigs. During training, the operator remotely navigated the ablation catheter to various anatomical targets, as described in the subsequent section, using the RCNS, ECG's and fluoroscopic x-ray imaging. Timing was not recorded during the training sessions.

Due to the inability to remotely deflect the tip of the RF catheter with the current CM prototype, a second operator was positioned beside the CM device to apply tip deflection when requested by the electrophysiologist. This limitation of the RCNS was intentional, as the mechanisms used in deflectable catheters are not standardized across manufactures.

5.2.4 Procedure and Data Collection

5.2.4.1 Initial Setup

Prior to evaluating the feasibility of remote navigation, the impact of integrating the RCNS into workflow was evaluated by measuring the time required to setup the RCNS inside the procedure suite. Since the majority of initial setup occurred in parallel with animal preparation, timing commenced once the veterinary technologist completed animal preparation, consisting of the time required to: mount the CM on the articulated arm, load the CM with the patient catheter, position the articulated CM, and finally advance the patient catheter to the apex of heart, just above the diaphragm in a fluoroscopic image.

5.2.4.2 Navigation to Anatomical Locations

Navigation to seven anatomical locations in the right chambers of the heart was performed with the RCNS (six pigs, 33.2±3.2 kg) and conventional catheter navigation (four pigs, 32.2±3.5 kg), using a combination of posterior-anterior (P-A) fluoroscopic imaging, and electrogram analysis. To standardize navigation timing, the catheter was positioned in the fluoroscopic image, just above the diaphragm, prior to all trials. Navigation time concluded when the electrophysiologist confirmed the catheter was at the correct anatomical location, using conventional electrophysiology criteria. Total navigation time, exposure and exposure time were recorded for all remote and conventional trials. The following seven anatomical locations were targeted in sequential order, using both navigation techniques: Right Ventricle Free Wall (RV-FW), Right Ventricular Outflow Tract (RV-OT), Coronary Sinus (CoS), Right Atrial Free Wall (RA-FW), Right Atrial Roof (RA-R), Right Ventricle Apex (RV-A), and finally, the HIS bundle

Once the catheter was positioned remotely with the RCNS at the intended anatomical location, a RF lesion was placed (RF power: 30 s at 25 W). The ECG was monitored throughout the delivery of RF power and post ablation. Confirmation of a successful RF lesion was assessed by the electrophysiologist using the post-ablation ECG. Ablation was not performed during conventional catheter navigation.

Total procedure time to remotely navigate the catheter from the diaphragm to the intended site and perform one RF ablation was recorded for all remote navigation trials. Upon placement of all RF lesions the pig was euthanized and the heart excised for visual confirmation of RF lesions.

5.2.5 Statistical Analysis

For the initial setup and integration the mean and standard deviation were calculated. Navigation time, exposure, and exposure time were compared between navigation method and anatomical target using a two-way ANOVA (unmatched).

Repeated measures ANOVA with a post test for linear trend was applied to overall procedure time and remote navigation time, to test whether a learning effect occurred.

All statistical analysis was performed using Prism™ 4 (GraphPad Software Inc., San Diego, CA); $P < 0.05$ was considered statistically significant.

5.3 Results

Seven anatomical targets were successfully reached using the RCNS in all but one animal. Using conventional navigation in four animals all anatomical targets were successfully reached with the exception of the CoS in one pig. One operational failure of the RCNS occurred due to an incorrect calibration of the CM. All data points for this animal were omitted from calculations, thus all remote experiments report five completed animals (N=5, 33.1±1.7 kg). A poor connection between the workstation and CM occurred once during setup of the CM, and was repaired onsite. On three different occasions a software reboot was required after the operator failed to properly engage the RCNS, upon reboot the experiments were carried out successfully.

5.3.1 Initial Setup

Setup of the RCNS within the procedure room required 5 minutes to complete, on average (mean ± std: 300 ± 77s,). In trial 3, the CM of the RCNS would not correctly manipulate the remote catheter due to a poor connection between the motion-controllers and the workstation; timing was recorded while this malfunction was corrected. This malfunction did not adversely affect the overall initial setup time.

5.3.2 Anatomical Target Navigation

Using the RCNS, remote catheter placement at all anatomical sites was successfully completed. One navigation failure was reported during conventional catheter manipulation when the operator was unable to place the catheter in the coronary sinus of one animal. The operator switched from an F-type curvature to a D-type curvature and then successfully completed the procedure. For this data point (conventional pig 2, CoS), the combined navigation time, exposure and exposure time for both catheters are reported.

Due to the high susceptibility to ventricular fibrillation (VF) in pigs, ablation at ventricular sites always induced VF. In each instance of VF, the pig was successfully defibrillated, and resumed sinus rhythm. For these sites, ablation was terminated as soon as the VF was initiated, and the procedure was considered complete (*i.e.* defibrillation was not included in the measures of procedure time).

5.3.3 Procedure Time

Procedure time for all anatomical targets per animal reached using the RCNS were analyzed using a repeated measures ANOVA. Statistically significant differences were found between animals ($P<0.01$) and demonstrated a decreasing linear trend over sequential trials (Fig. 5-2a). Repeated measures ANOVA was also used to compare remote navigation time (a component of procedure time) but no significant differences were found between animals ($P=0.4$) and no linear trend over sequential animals was observed (Fig. 5-2b).

These results indicate that the decrease in overall procedure time was not due to the use of the RCNS, and mostly likely due to improvements in experimental workflow (including increased experience with the imaging system, ECG system, and ablation unit)

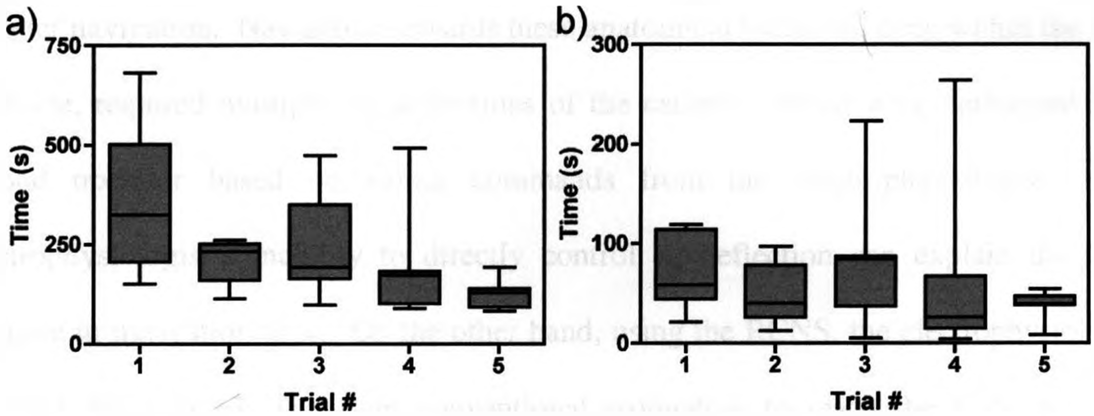

Fig. 5-2: Total procedure time (a) and navigation time (b) over sequential trials. A statistically significant downward trend is clearly visible over sequential trials for total procedure time but not remote navigation time. Data shown: median, 25th and 75th percentile, and range.

5.3.4 Navigation Time, Exposure and Exposure Time

Two-way ANOVA applied to navigation time, exposure, and exposure time using both navigation methods (remote and conventional), showed that the anatomical target had a large effect on navigation time ($P<0.001$), exposure ($P<0.0001$) and exposure time ($P<0.001$), while the navigation method had no statistically significant effect. Overall, this suggests navigation with the RCNS is comparable to conventional catheter manipulation.

Although navigation times did not differ significantly with navigation method, large differences in navigation time, between methods, were measured at four anatomical targets (Fig. 5-3). Using the RCNS, the electrophysiologist required an average of 29s longer to reach the RV-FW and 64s longer to reach the RV-A than with conventional catheter navigation. Navigation towards these anatomical locations, deep within the right ventricle, required multiple tip deflections of the catheter, which were performed by a second operator based on verbal commands from the electrophysiologist. The electrophysiologist's inability to directly control tip-deflection can explain the large increase in navigation time. On the other hand, using the RCNS, the electrophysiologist required 46s and 63s less than conventional navigation to reach the CoS and HIS, respectively. The faster navigation times with the RCNS may be the result of prior anatomical knowledge of the animal, as conventional catheter navigation was performed on three animals prior to the RCNS. Although experiments were performed in the same three animals with both remote and conventional navigation methods, a matched two-way ANOVA applied to navigation times from the three animals showed anatomical target had a large effect on navigation time, and that matching was not effective ($P=0.13$).

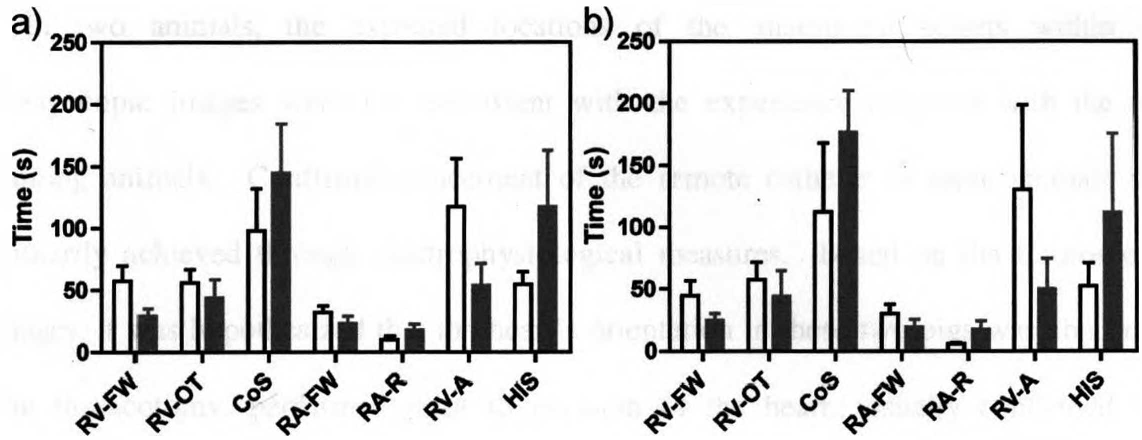

Fig. 5-3: a) Navigation time to all targets, in all animals, using the RCNS (white), and conventional catheter manipulation (grey). Navigation towards two anatomical targets (CoS and HIS) took much longer with conventional catheter navigation (CoS: 144s vs. 98s, HIS: 117 vs. 54s), while remote navigation took much longer than conventional navigation to reach the RV-FW and RV-A (RV-FW: 58s vs 29s, RV-A: 117s vs. 53s). b) Navigation time to all targets, in 3 matched animals, using the RCNS (white), and conventional catheter manipulation (grey). Matching was not statistically significant. Data shown: mean±sem.

5.3.5 RF Lesion Placement and Physiological Variability

RF lesions were successfully delivered to all anatomical sites in all animals using remote navigation of the catheter. Large lesions were visible directly after excising and inspecting the heart in 30 out of 35 ablated targets, with examples shown in Fig. 5-4. Lesions placed at the CoS were seen in only 2 of 5 animals directly after the procedure, but were confirmed following formalin fixation of the heart. Smaller lesions (visualized only post fixation) were also observed in the first pig at the RV-OT and RA-R.

In two animals, the expected locations of the anatomical targets within the fluoroscopic images were not consistent with the experience obtained with the two training animals. Confirmed placement of the remote catheter in these animals was primarily achieved through electrophysiological measures. Based on the fluoroscopic images, it was hypothesized that the heart's orientation in these two pigs was abnormal. The thoracotomy, performed prior to excision of the heart, visually confirmed this assumption, as the heart's orientation inside the thorax was visually twisted about its long axis. This physiological variability can be appreciated in the fluoroscopic images of the catheter placed at the RV-OT and HIS locations in a pig with an abnormal heart orientation (Fig. 5-5a and Fig. 5-5c) and one with expected orientation (Fig. 5-5b and Fig. 5-5d). A consequence of physiological variability is increased navigation time, as the electrophysiologist may primarily rely on electrograms instead of imaging, further supporting the observation that anatomical target, and not navigation method, is the primary contributor to navigation time.

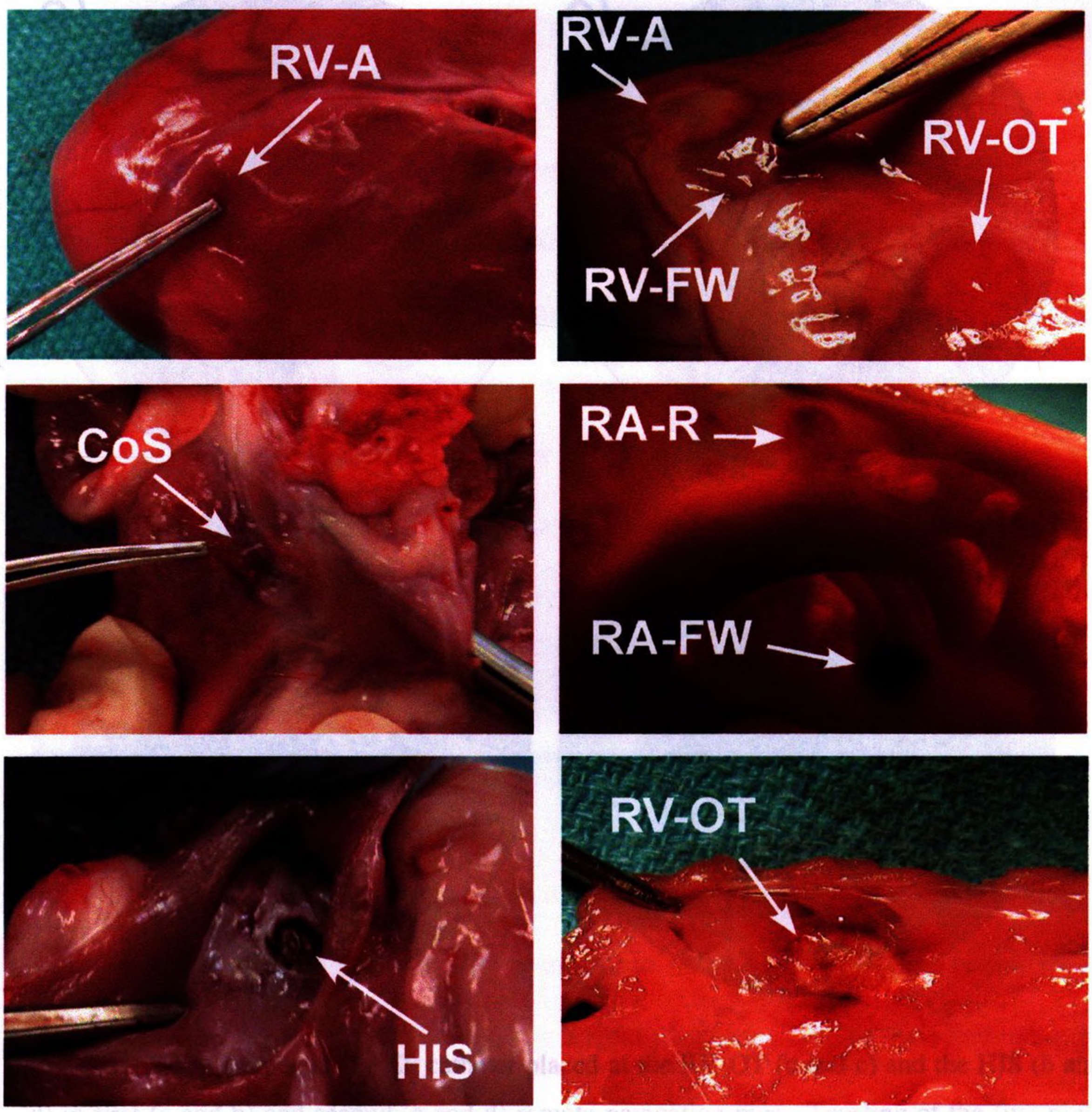

Fig. 5-4: Visual confirmation of the created RF lesions. Lesions placed at the RV-A, RV-FW, RV-OT, and CoS can be seen on the epicardium (top row and middle-left). Lesions placed at the RA-R, RA-FW, HIS, RV-OT, can be clearly seen on the endocardium (middle-right, bottom row).

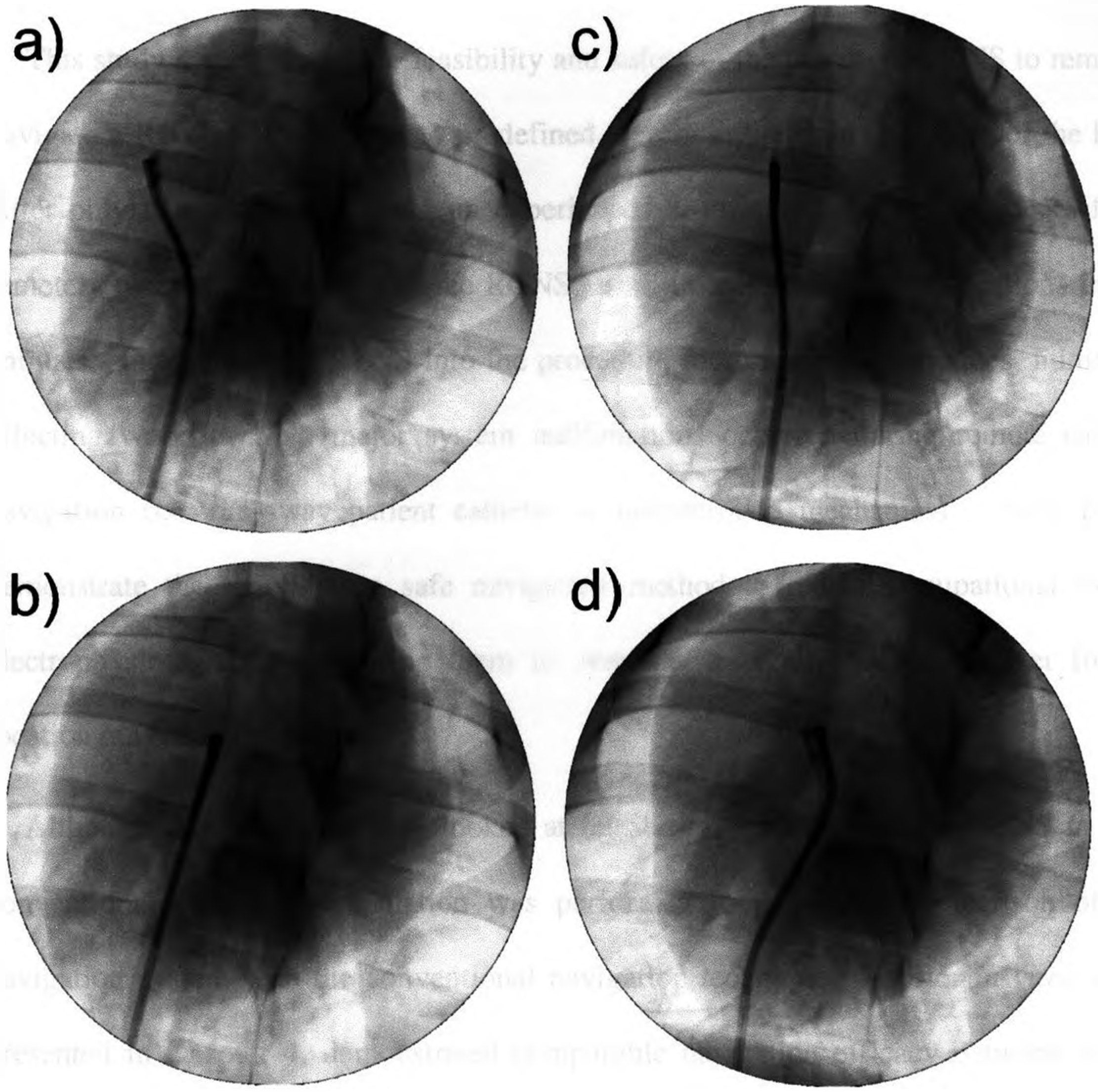

Fig. 5-5: X-ray images of the EP catheter placed at the RV-OT (a and c) and the HIS (b and d) in first (a and b) and second (c and d) remote navigation pigs. Twisting of the first pig's heart changed the expected anatomical target locations, clearly visible with the change in the heart's silhouette. This can be seen by comparing the catheters position at the RV-OT in pig 1 (a) and pig 2 (c), or the catheter's position at the HIS in pig 1 (b) and pig 2 (d).

5.4 Discussion

This study demonstrated the feasibility and safety of the prototype RCNS to remotely navigate a RF ablation catheter to predefined targets in the right chambers of the heart. After only two training sessions, an experienced electrophysiologist was successful in remotely placing a catheter with the RCNS, at all intended anatomical locations in five animals. Integrating the RCNS into the procedure room required 5 minutes, minimally affecting workflow. No major system malfunctions occurred during remote catheter navigation (i.e. run-away patient catheter or uncontrolled mechanics). These results demonstrate the RCNS as a safe navigation method to reduce occupational risk to electrophysiologists by allowing them to remotely navigate the RF catheter from a location remote to the patient.

Although this study primarily looked at feasibility and safety of the RCNS *in vivo*, conventional catheter manipulation was performed to provide a comparison of this navigation system with the conventional navigation technique. A prior *in vitro* study, presented in Chapter 4, demonstrated comparable navigation efficacy between remote and conventional navigation methods using a rigid phantom. The rigid phantom required operators in that study to perform the same navigation tasks without variability, which resulted in a slight increase in remote navigation time (9s) due to the latency in replicated motion. Based on the Chapter 4 study, remote navigation time was expected to be longer than conventional catheter navigation. The results obtained in the present study are contrary to this, which demonstrated that navigation time was not affected by the navigation method, but strongly affected by the anatomical target. Overall, this result indicates the 180 ms latency in replicated motion in the prototype RCNS is sufficiently small for tele-operated catheter navigation.

A natural extension of navigation time is the impact of remote catheter navigation on procedure time. If remote catheter navigation considerably increases procedure time, the interventionalist will benefit from reduced occupational risk, while the patient may suffer from longer duration of anaesthesia and immobility during the procedure. In addition to this "trade-off," increased procedure time would unnecessarily occupy procedure rooms. A study by Kim *et al.* [22] showed magnetic catheter navigation required 89 minutes longer than conventional navigation to map and ablate various cardiac arrhythmias in a clinical setting. Similarly, Ray *et al.* [23] compared magnetic navigation with conventional navigation in a swine model, concluding that procedure time was 35 minutes longer when using the magnetic navigation system. In contrast, the RCNS required 5 minutes to integrate into an existing procedure room, and no difference was found between navigation methods.

It should be noted that the studies presented by Ray *et al.* and Kim *et al.* were full arrhythmia treatment, where the procedure incorporated: catheter navigation, electro-anatomical mapping, arrhythmia localization, ablation and post-ablation monitoring. Since these are complete studies, lesion placement occurred with high fidelity to minimize placement of unnecessary lesions in the heart, thus direct comparison of these procedure times with the present study is not valid. Nevertheless, procedure times using magnetic navigation were much higher than conventional navigation. In a clinical setting, since the RCNS incorporates the conventional catheter manipulation technique, navigation times between conventional manipulation and the RCNS are not expected to differ.

In the current implementation, the prototype RCNS has one major limitation - the inability to remotely deflect the catheter tip. To overcome this limitation, an operator was positioned bedside to change the tip curvature based on verbal commands from the electrophysiologist, potentially increasing the overall remote navigation time. A simple method to overcome this limitation in future version would be to implement a motorized assembly, placed on the handle of the catheter, to remotely change tip curvature. However, this solution would make the RCNS catheter specific, as the mechanism used to deflect catheter tips is not standardized across manufacturers. RF ablation catheters containing a motorized assembly within the handle, supplied by the manufacturer would be an ideal long-term solution.

In the presented study, remote catheter manipulation was not used to localize arrhythmic circuits prior to ablation. The iterative process of localizing the arrhythmic circuit and applying curative lesions, remotely, is a crucial step towards validating this navigation system. Utilizing the RCNS to remotely localize and apply RF ablation in animals with induced arrhythmia will be the subject of future work.

5.5 Conclusion

This *in vivo* study demonstrates the RCNS as a safe, effective technology to reduce the occupational risk to electrophysiologists. Only five minutes was required to integrate the RCNS into the procedure room, minimally affecting workflow. Remote catheter navigation with the RCNS and conventional catheter navigation were successful in reaching all seven anatomical locations. No statistical differences between remote and conventional catheter manipulation were observed. Utilizing the RCNS to perform a full arrhythmia procedure, from arrhythmic localization to curative ablation will be the topic of future work.

Acknowledgments

The authors would like to thank our registered veterinary technologists Sheri VanLingen and Karen Siroen for the preparation of all animals, Syed Haider and Preet Desai for their assistance in data collection, Joy Dunmore-Buyze for assistance during experimentation and Dr. Gerard Guiraudon for excising the hearts and confirming lesion placement. This work would not be possible without the generous funding from the Canadian Institutes of Health Research (CIHR), Ontario Research Fund (ORF), and The University of Western Ontario.

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Chapter 6 :

Contributions, Limitations and Future Direction

6.1 Contributions

The goal of this thesis was to alleviate the occupational risk to physicians who frequently perform catheter-based interventions, by increasing the distance between the interventionalist and the radiation source during intravascular catheter manipulation. This thesis describes the design and validation of a prototype remote catheter navigation system for this purpose.

In addition to the development and validation of a prototype remote catheter navigation system, this thesis has also contributed: 1) the quantification of the range of catheter dynamics during interventional procedures (Chapter 2), and 2) the design and fabrication of a multi-path phantom (Chapter 4 and Appendix D).

6.1.1 The Remote Catheter Navigation System

Each chapter of this thesis concerns itself with the design, development and validation of a remote catheter navigation system. During the design phase, criteria were set forth to develop a remote catheter navigation system that could: utilize generic catheters, integrate easily into existing x-ray imaging suites, and was easy to use. The last criterion, “easy to use”, is fundamental towards the remote navigation concept – utilizing the dexterous skills of an experienced interventionalist – during catheter manipulation from a remote location with respect to the patient.

To utilize the dexterous skills of an experienced interventionalist, keeping the catheter in the hands of the interventionalist, during remote catheter manipulation, was a logical choice. From an engineering design prospective, keeping the catheter in the hands of the interventionalist during remote manipulation would require two complementary devices: one to sense the motion of the catheter held by the interventionalist, and a second to replicate the sensed motion.

Design of these devices required knowledge of catheter dynamics during interventional procedures, a topic that is scarce in the literature. Thus, Chapter 2 investigated this topic using very simple, yet elegant, bench-top experiments. Results from Chapter 2 provided the technical parameters required to develop the motion actuating device (the catheter manipulator: CM).

Chapter 3 began with a conceptual description of the design and operation of the remote catheter navigation system (RCNS). Using the technical parameters measured in Chapter 2, the design of the CM was conceived and implemented. Validation of the RCNS, *in vitro*, demonstrated the RCNS could sense and replicate motion within the intended design parameters: < 1 mm in the axial direction, < 1° in the radial direction, and replicate motion within 300 ms.

Maintaining the navigation efficacy of manual catheter manipulation during remote navigation is fundamental towards acceptance of this technology. Chapter 4 of this thesis described a study comparing remote and conventional navigation techniques, by employing operators with varied clinical experience and the specially constructed multi-path vessel phantom. The results demonstrate comparable navigation efficacy was achieved by the expert operator group, after only 1 hr training with the RCNS.

Finally, Chapter 5 of this thesis demonstrated *in vivo* application of the RCNS. The RCNS was safely utilized to remotely navigate and perform RF ablation at seven anatomical targets in five porcine models. No difference in the navigation time required to reach the anatomical targets was observed between remote navigation with the RCNS and conventional catheter manipulation. In addition, only 5 minutes was required to integrate the RCNS into an existing operating room. These results demonstrate the RCNS as feasible technology to reduce the occupational risk to electrophysiologists, by allowing them to perform procedures from a location remote to the patient.

6.1.2 Catheter Dynamics

In addition to providing technical parameters towards the development of the CM, the results from Chapter 2 are applicable elsewhere. A likely application is the development of computer simulators to train interventionalists. Typically, simulator developers rely on assumptions regarding external forces and torques applied to the catheter as well as the range of kinematics. Simulators developed by Alderliesten *et al.* [1] and Lawton *et al.* [2] set the velocity and acceleration parameters to zero when calculating the change in the simulated catheters position. Alderliesten justified this by stating that human motion is moderate, and that propagation of the catheter can be done piece-by-piece in a controlled manner. Lawton bases this assumption on the principle that the mass, velocity, and acceleration of the catheter is so small that inertial forces are instantaneously dampened with respect to catheter movement. The results in Chapter 2 provide a range of velocities and accelerations subjected to the catheter during navigation. Simulator design engineers can utilize these results to validate their assumptions and improve simulator performance.

6.1.3 The Multi-Path Vessel Phantom

In Chapter 4 of this thesis, a multi-path vessel phantom was specially constructed to provide catheter navigation tasks to compare remote verse conventional catheter navigation. One expert operator who participated in the study presented in Chapter 4 has requested the use of this phantom to examine whether the phantom can be used to develop core catheter manipulation skills in residents and fellows. The parameters of this study are described in future work (section 6.3.3). A manuscript describing the design considerations and construction of this phantom is available in Appendix D.

6.1.4 Conclusion

A tele-operated, remote catheter navigation system, which is easy to use and minimally affects workflow, has been constructed and validated in both *in vitro* and *in vivo*, for use in fluoroscopic x-ray image guided percutaneous transluminal catheter interventions. The range of catheter motion and dynamics applied by interventionalist was quantified (Chapter 2) and used to design and construct an electromechanical device that can replicate catheter motion with the same dynamic range as interventionalists. Custom software was implemented on a Linux workstation to provide real-time sensing of an input catheter, and real-time replication of a second patient catheter. *In vitro* results demonstrate the system can sense and replicate catheter motion to within 1mm in the axial direction, 1° in the radial direction, with a motion latency of 180 ms. Furthermore, comparison of this navigation system, with the gold standard, conventional catheter manipulation, showed that after only 1 hour of training on the system, an experienced interventionalist can navigate a catheter with the comparable navigation efficacy as conventional catheter navigation.

Finally, the feasibility of this system was evaluated *in vivo* by remotely navigating a RF ablation catheter to seven anatomical targets in five porcine animals. No differences were observed between remote catheter navigation and conventional catheter navigation.

Overall, the *in vivo* results validate the design assumptions and methodologies described throughout this thesis, demonstrating the RCNS as a safe, easy to use, remote catheter navigation system.

6.2 Limitations

6.2.1 Clinical Limitations

For clinical application, all devices and instruments that make contact with the patient must be sterile. In the RCNS, the CM manipulates the patient catheter inside the patient's vasculature, thus contaminating the CM. After each procedure, the CM is dismantled and manually cleaned, a task that is time consuming and leads to unnecessary wear on the CM components. This cleaning method does not include sterilization, as some components cannot withstand the temperature and pressure of an autoclave. Future implementations of the CM will require a sterilization method. This may be achieved by constructing the CM with a material that can be placed in an autoclave (*i.e.* PEEK), or designing a set of replaceable parts that are easily exchanged in the CM after each procedure. These are challenges that must be overcome prior to clinical use.

6.2.2 Technical Limitation

Motion replication delay, as evaluated in Chapter 3, demonstrates a system induced replicated motion delay of 180 ms. Although this delay was better than the target delay of 300 ms, and was found to be acceptable by experienced practitioners (Chapter 4 and Chapter 5). A reduction of this delay would improve the motion sensitivity of the system, further reducing the training time required to efficiently use the RCNS, as well reducing the difference in navigation time between the RCNS and conventional navigation, as determined in Chapter 4. In addition, a reduction in the difference in navigation time should also lead to reduced radiation exposure to the patient during remote navigation.

As described in Appendix C, the delay time is affected predominately by the RS232 serial communication strategy implemented with the CM. A minimum communication time of 140 ms is required to update the single-axis motion controllers with new position, velocity and acceleration parameters. Utilizing either a USB or CAN-based communication protocol will provide faster communication, resulting in shorter communication time, which will lead to improved motion sensitivity in the RCNS.

The use of deflectable tip catheters in the CM is also limited. In arrhythmia studies, deflectable tip catheters allow the interventionalist to change the curvature of the catheter's tip, while the catheter is inside the heart. The method of tip deflection is not standardized, and was intentionally omitted from the prototype RCNS. Future versions of the RCNS should incorporate a mechanism to handle common deflectable tip catheters.

In the current implementation, the RCNS does not provide tactile feedback. Lack of tactile sensation is adequate for catheter-based treatment of cardiac arrhythmia, where tactile forces at the catheter-tip are not required for successful catheterization. In some PTC interventions, in which the interventionalist needs to traverse a vessel containing atherosclerotic plaque or calcification, tactile sensation of the guidewire through vessel maybe essential for safe passage. Potential methods to sense tactile sensation will be explored in Section 6.3.1.3.

6.3 Future Direction

Based on the work presented in this thesis, future directions of work include: 1) design enhancements of the CM, 2) current development of an improved MRI compatible CM, 3) assessment of the multi-path vessel phantom as a training tool for residents and fellows, and 4) direction towards clinical application. These future directions are subsequently described.

6.3.1 Technical Development

6.3.1.1 Design Improvements

Although the prototype RCNS operated within specification and was successfully demonstrated *in vivo*, the technical knowledge and experience gained throughout this thesis will lead to an improved second generation RCNS, specifically the CM.

In the mechanical design implementation, described in Chapter 3, inserting the patient catheter into the device was difficult due to the stiff resistance from the single, spring-loaded, axial drive roller. Replacing the axial drive mechanism with a spring-less, dual roller system, will facilitate insertion and extraction of the patient catheter in the CM.

Detection of micro-slips is a feature that can be implemented in a future CM. Micro-slips occur when loss of 1:1 movement between the patient catheter and remote catheter occurs. Although calibration of the CM rectifies this, calibration occurs *in vitro*, while micro-slipping has been seen *in vivo*. Fortunately, the occurrence of micro-slips is rarely noticed by operators, as the operator is unable to see micro motions of the catheter under fluoroscopic x-ray imaging. The ability to detect and correct for micro-slips will enable the RCNS with the ability to precisely playback a recorded navigation. This feature will allow for accurate repositioning of the remote catheter, a tool that will be useful arrhythmia studies, where the catheter can be accurately repositioned to a prior ablation site to reapply a healed lesion [3]. Adding passive encoders coupled to the patient in the CM should provide the RCNS with this capability.

6.3.1.2 MRI Compatible Manipulator

Application of MRI towards the diagnosis and treatment of vascular and cardiac disease is well documented. No ionizing radiation, enhanced soft tissue contrast, and 3D imaging, are just a few of the benefits of MRI over fluoroscopic imaging. Catheter visualization and tracking have been explored to exploit the benefits of MRI as a single imaging modality to provide both diagnosis and treatment of vascular and cardiac diseases [4-6]. Access to the patient inside the MRI bore and the sound impediment caused by gradient switching during the imaging sequence are two challenges that can be overcome with a MRI compatible catheter manipulator.

Advances in MRI compatible mechatronics and real-time imaging have enabled the development of MRI compatible robots [7-10]. Typically, MRI compatible robots use pneumatic or hydraulic motors placed outside the MRI bore to control the end effecter inside the MRI bore. Recently, MRI compatible piezoelectric motors have been developed and shown to operate safely inside the MRI bore [11].

Until recently, the velocity and torque produced by piezoelectric motors were unable to satisfy the design specifications for tele-operated catheter navigation, as outlined in Chapter 2. Advances in piezoelectric motor technology have improved, enabling the ability to translate our current design, with design improvements (section 6.3.1.1) into an MRI-compatible manipulator. This new MRI compatible manipulator is depicted in Fig. 6-1.

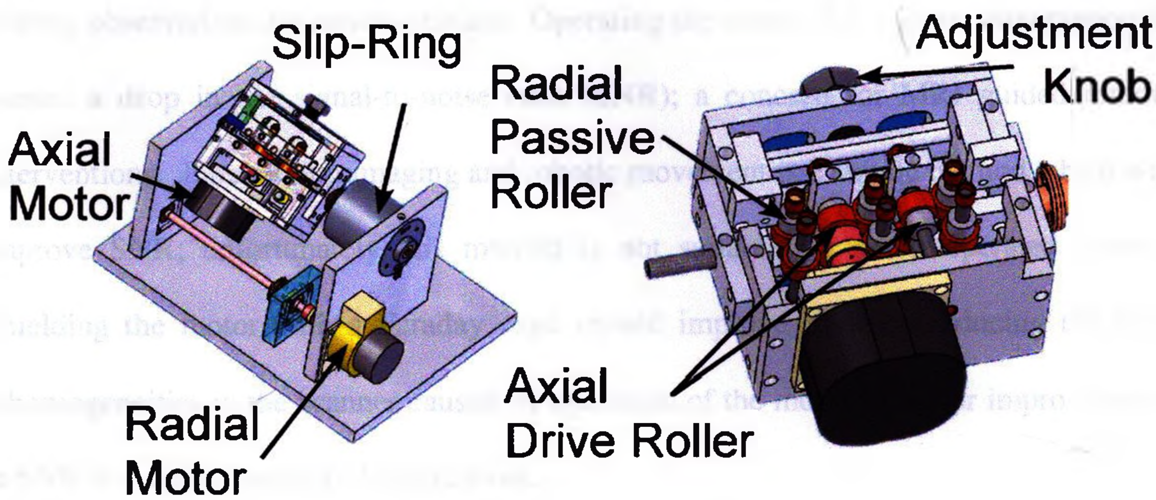

Fig. 6-1: Depiction of the MRI compatible catheter manipulator. Design and operation of this catheter manipulator is analogous to the CM presented in Chapter 3. Assembly and disassembly of the gantry is simplified, facilitating easy cleaning of gantry components, after use.

Preliminary experiments have been performed to assess the safety of operating piezoelectric motors while simultaneously imaging a quality assurance phantom at 3T (3T-MR750, GE Healthcare Inc., Waukesha, WI). The quality assurance phantom was imaged with FGRE and FIESTA imaging sequences (FGRE: fast gradient recall echo, FIESTA: fast imaging employing stead-state acquisition), while an unshielded piezoelectric motor was placed at the periphery of the scanner bore, 75 cm from the isocenter of the scanner. The motor was operated in four modes, idle, low rpm, high rpm, and changing rpm.

Preliminary results demonstrate safe, simultaneous operation of the MRI system and the piezoelectric motor. The motor was not pulled into the scanner, nor was excessive heating observed on the motors surface. Operating the motor and scanner simultaneously caused a drop in the signal-to-noise ratio (SNR); a concern for MRI guided remote interventions. Interleaving imaging and robotic movement is a simple method which will improve SNR; unfortunately this method is not suitable for a tele-operated system. Shielding the motor with a Faraday cage should improve SNR by reducing the field inhomogeneities in the scanner caused by operation of the motor. Further improvements in SNR will be the subject of future work.

6.3.1.3 Tactile Sensors

As described in section 6.2.2, some PTC interventions require the interventionalist to safely traverse vessels containing atherosclerotic plaque or calcium deposits. Traversing these vessels may require tactile sensation between the guidewire and vessel wall. The simplest method to measure tactile sensation is to mount a sensor directly onto the guidewire-tip, with the sensor leads embedded inside the guidewire or acting as the guidewire. The maximum size of this device would be limited to 1-mm (0.038-inch) in diameter, so that the guidewire and sensor can pass through the lumen of a 5 F catheter. Unfortunately current micro sized pressure transducers and force sensors have a minimum size between 2-4 mm, making them too large to for this application. Advances in micro sensory design and fabrication may enable this ability in the future.

Exploring the torque-current relationship of servo-motors may also provide a measure of the tactile force reflected through the catheter onto the manipulator. In this method, the exact tactile force would not be directly measured. Instead, measurement of the current through each motor can provide a measure of torque used by the manipulator to actuate the patient catheter. As friction between the catheter and vessel change, torque provided by the motors will also change, thus changing the current through the servomotor. Correlating the current changes through the motor with the changes in force at the catheter-tip will be first step towards evaluating this methodology.

6.3.2 Core Interventional Skill Development

As described in section 6.1.3, after being exposed to the vast vessel trajectories and simple construction of the multi-path vessel phantom, Dr. Andrew Leung has initiated a study to determine whether interventional trainees can develop core, catheter manipulation skills with this phantom; a direct benefit of this thesis work. These core skills include: the dexterity required to manipulate the catheter, operate the fluoroscopic system and effectively inject contrast, all in a safe manner. It is hypothesized that after a few hours of training with the phantom, novice operators will substantially develop these core interventional skills. These core skills will then translate into more effective clinical training, as trainee can focus on developing therapeutic skills.

6.3.3 Clinical Application

6.3.3.1 Cardiac Arrhythmia

Chapter 5 of this thesis demonstrated *in vivo* application of the RCNS. In clinical treatment, the origin of arrhythmogenesis is carefully determined prior to ablative therapy. To determine the origin of arrhythmogenesis, the interventionalist sweeps the catheter around the heart until the signal is localized, a process not performed in the Chapter 5 study. Utilizing the RCNS during this process is required prior to clinical use.

Either of two future studies can validate the RCNS during the arrhythmia localization process. In the first study, the acute study presented in Chapter 5 could be extended into a chronic study by inducing a ventricular arrhythmia [12], performing arrhythmia localization, delivery ablative treatment, and then assess treatment effectiveness over time. This chronic study would emulate clinical practice, but in a laboratory setting.

In the second study, the RCNS can be used in conjunction with humans that suffer from cardiac arrhythmia. In this study, the RCNS would simply replace the interventionalist beside the patient, inside the procedure room. All other clinical protocols for diagnosis and treatment should remain the same.

6.3.3.2 Other Interventional Applications

In addition to cardiac arrhythmia, the introduction of this thesis described three commonly performed catheter-based, medical interventions: vascular angiography, vessel stenosis and vessel dilation. Utilizing the RCNS in these procedures would benefit interventional specialists who perform these procedures.

Utilizing the RCNS during vascular angiography is an obvious first step, as vascular angiography is the simplest of the three interventions. To date, a single remote vascular angiography of the left carotid artery has been attempted in a porcine model using a 6 F catheter (H1, 100 cm, Cook Inc., IN, USA). This experience has provided valuable insight towards understanding two challenges facing remote angiography: handling the guidewire and the limited catheter length.

Handling the guidewire is related to the logistics of integrating the RCNS into the procedure. In the single experiment performed, the guidewire was fixed inside the catheter and remotely navigated to the left carotid artery. Once the catheter was in position the guidewire was manually retracted for contrast injection. When the guidewire was fully removed from the catheter, blood leaked from the proximal end of the catheter into the CM, reducing the device's ability to manipulate the catheter. In the conventional approach, the interventionalist places their finger over the proximal end of the catheter to stop bleeding. Including a hemostat at the proximal end of the catheter, as shown in Fig. 6-2, should remove bleeding in future remote angiography attempts.

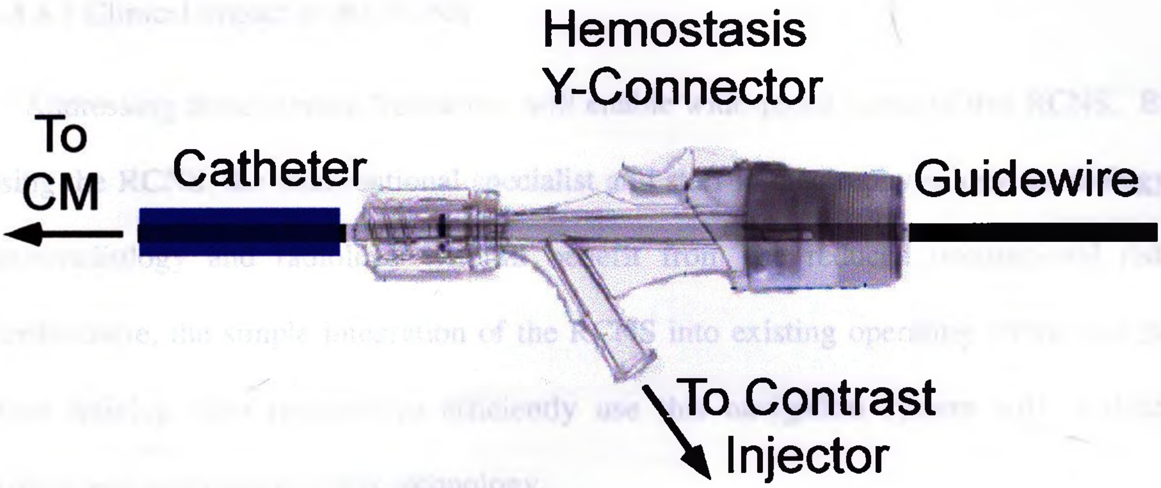

Fig. 6-2: A hemostasis connector placed at the proximal end of a catheter during remote vascular angiography. Once the guidewire is withdrawn, an o-ring (not shown) placed inside the connector stops bleeding through the catheter. A mechanical contrast injector can be connected to the open connector for remote contrast injection.

The second challenge refers to the length of the inserted catheter. In the single experiment performed, the catheter was too short to reach the internal carotid artery of the animal via access through the femoral artery. Although a 100 cm catheter was used, a length consistent with cerebral intervention in adults, 22 cm of the catheter is lost inside the CM. Reducing the length of a new CM device or using a longer catheter should remove this challenge in future remote angiography procedure.

Addressing these two challenges with the adaptations provided here should allow for successful remote angiography in animal models; an important step towards remote treatment of vessel stenosis and dilation.

6.3.3.3 Clinical impact of the RCNS

Addressing these clinical limitations will enable widespread usage of this RCNS. By using the RCNS, the interventional specialist and staff in electrophysiology, cardiology, neuroradiology and radiology will all benefit from the reduced occupational risk. Furthermore, the simple integration of the RCNS into existing operating rooms and the short training time required to efficiently use this navigation system will facilitate widespread acceptance of this technology.

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2) Thakur* , Y., Bax, J. S., Holdsworth, D. W., and Drangova , M. "Design and Performance Evaluation of a Remote Catheter Navigation System," IEEE TBME, vol. 56(7) pg. 1901-1908, 2009.

These two articles will be included as separate chapters of my PhD thesis, entitled: From Concept To Design, Evaluation and First In Vivo Demonstration of a Tele-Operated Remote Catheter Navigation System (a working title), in Biomedical Engineering, from The University of Western Ontario, London, Canada. As listed, I am the first author on both publications.

Please let me know if this request is permissible, if so, please attach a letter granting permission. This letter will be included as an Appendix in the final published thesis.

Thank You in advance,

Yogesh

Appendix B :

Animal Ethics Approval

Western

May 5, 2008

This is the Original Approval for this protocol
A Full Protocol submission will be required in 2012

Dear Dr. Drangova:

Your Animal Use Protocol form entitled:
Catheter Navigation Using a Remote Navigation System to Ablate Arrhythmic Sites in a Pig Model - Pilot
Funding Agency CIHR - Grant #MOP49536

has been approved by the University Council on Animal Care. This approval is valid from **May 5, 2008 to May 31, 2009.** The protocol number for this project is **2008-046-08**

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2. Animals for other projects may not be ordered under this number.
3. If no number appears please contact this office when grant approval is received.
   If the application for funding is not successful and you wish to proceed with the project, request that an internal scientific peer review be performed by the Animal Use Subcommittee office.
4. Purchases of animals other than through this system must be cleared through the ACVS office. Health certificates will be required.

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Species	Strain	Other Detail	Pain Level	Animal # Total for 1 Year
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320 Euthanasia
322 Criteria for Early Euthanasia/Mammals/Non-rode

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1. Please review Addendum 3 - Hazardous &/or Biological Agent Use of the attached protocol as additional requirements have been included by the Safety Officer.

c.c. Approved Protocol - M. Drangova, W. Lagerwerf
Approval Letter - W. Lagerwerf

Appendix C :

System Implementation & Software Design

C.1 System Layout

Chapter 3, Section 3.2, provided a brief description of the RCNS layout and software implementation. This appendix provides a detailed description of the system layout, depicted in Fig. C-1 and the software interaction, depicted in Fig. C-2. As described previously in Section 3.2, the main components of the RCNS are: the workstation, the CS, and the CM. In addition to these components, there are two encoder-to-RS232 interface boxes (AD4B, USDigital, WA, USA), and two single axis motion controllers (MVP, MicroMo Inc., Clearwater, FL, USA). Each interface box connects a single axis sensor, in the CS, with a RS232 serial port on the workstation. Each single axis motion-controller connects to an independent motion axis in the CM, and is controlled through independent RS232 serial ports on the workstation. All software used in the workstation (1 GHz dual Athlon®, Linux kernel 2.16.15) used to communicate with the interface boxes and motion-controllers were custom written in C++.

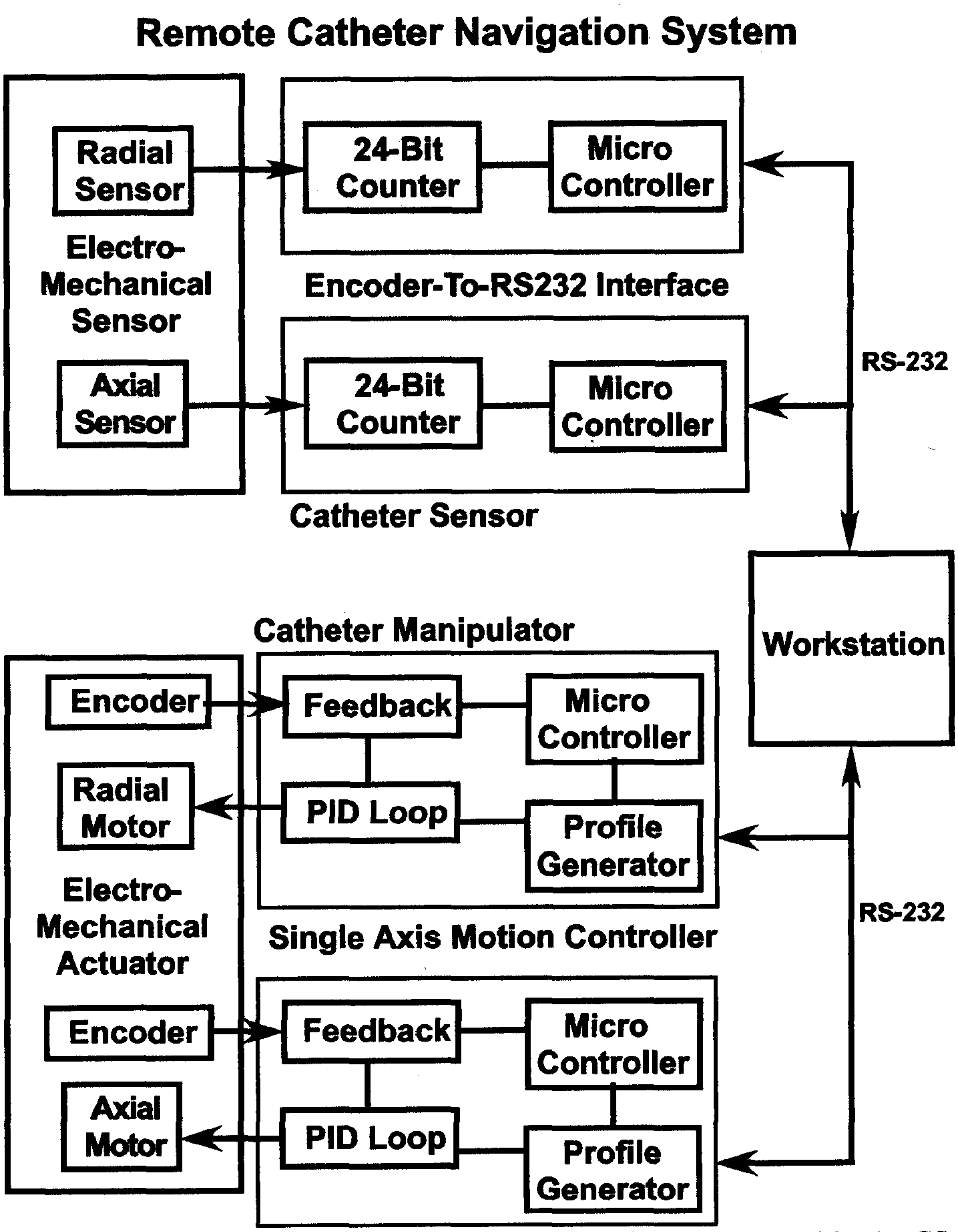

Fig. C-1: The system layout of the RCNS. Electromechanical sensors placed in the CS transmit encoder counts to an encoder-to-RS-232 interface. A microcontroller, contained in the encoder-to-RS232 interface, handles communication with a digital counter and remote communication with the workstation, via RS-232. Single-axis motion-controllers actuate the each servo-motors contained in the CM. These motion-controllers utilize a standard industrial control system, consisting of: a motion profile generator, PID loop and encoder feedback.

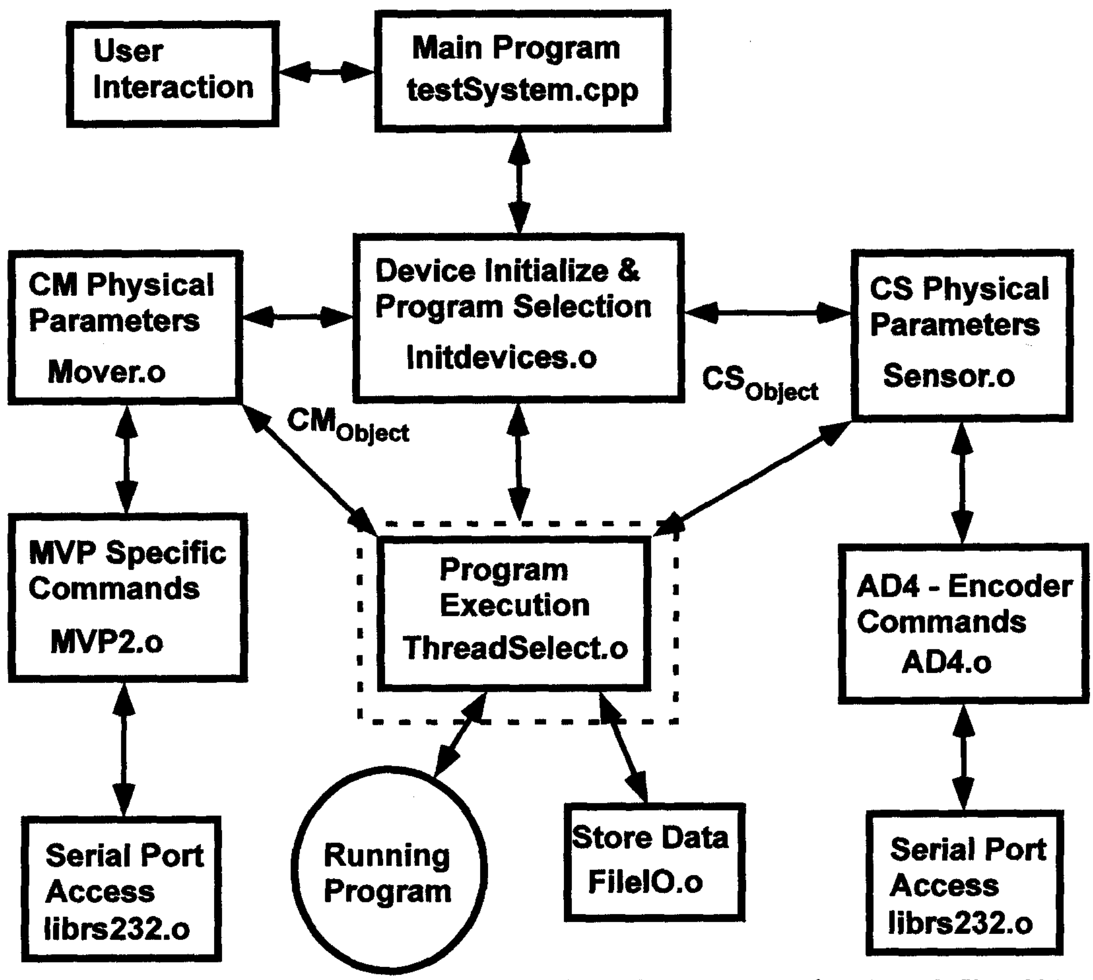

Fig. C-2: Software interaction of the custom written C++ program for the RCNS. Objects CS_{Object} and CM_{Object} are initialized by the object *Initdevices.o*. Using the *pthread* Linux library, the *ThreadSelect.o* accepts references of the CS_{Object} and CM_{Object} objects (gray arrows), and then creates two separate threads – one for each referenced object, arranged in a producer-consumer model, where the CS_{Object} is the producer and the CM_{Object} is the consumer. *FileIO.o* writes two separate files during remote catheter navigation, one for each axis of motion (axial and radial).

C.2 Software Layout

In general, the method of remote navigation is to map position measurements of the CS to the corresponding motion axis of the CM. Since both axis sensors in the CS, and both motion axis of the CM, are connected to the workstation using RS232 serial port communication, this method is essentially linking the RS232 serial ports connected to the CS, with the RS232 serial ports connected to the CM. A major software building block of the RCNS is a custom written serial port driver: *librs232.o*, which provides communication with the interface boxes and motion-controllers using RS232. This object specifically handles port: initialization, reading, writing, and flow control, and is the primary building block in which all subsequent software modules interact.

Communication with the interface boxes connected to the CS is achieved using two other custom C++ objects: *AD4.o* and *Sensor.o*. *The AD4.*o object is the driver for the AD4 encoder-to-RS232 interface box, containing all commands required to interact with the microcontroller inside the interface box. The *Sensor.o* object handles all information pertinent to either: the axial sensor or radial sensor. This includes geometric details of each sensor, calculation of sensor position, and application of all calibration factors required for the CS.

Software interaction with the CM is similar to the CS. *MVP2.o* is the driver for with the single axis motion controllers, containing all pertinent motion-control commands. Parameters specific to the motion axis of the CM (either the axial axis or the radial axis) are contained in the *Mover.o* object. Similar to the *Sensor.o* object, the *Mover.o* object includes details of each servomotor, the geometric detail of each motion axis, calculation of motor position and velocity, and application of all calibration factors required for the CM.

Operation of the main program occurs in three main steps. First, upon boot-up, all devices are initialized by the *Initdevices.o* object. This object creates four local objects; one for each peripheral device, which for simplicity can be labelled: $CS_{Object\text{-}Axial}$, $CS_{Object\text{-}Radial}$, $CM_{Object\text{-}Axial}$, and $CM_{Object\text{-}Radial}$. Second, the operator selects an operation from the main program (*testSystem.cpp*). Based on the operation selected, *Initdevices.o* object passes the peripheral objects by reference to *ThreadSelect.o*, which then manipulates the objects as required.

To enable simultaneous, real-time, motion sensing and replication for both axes of the input catheter, and both axes of the patient catheter, a multi-threaded software approach was implemented. Four threads are created using the *pthread* library, one for each sensed and replicated motion axis by the *ThreaSelect.o* object. Corresponding motion axes are mapped together in a producer-consumer model (i.e. $CS_{Object\text{-}Axial} \rightarrow CM_{Object}$), as depicted in Fig. C-3.

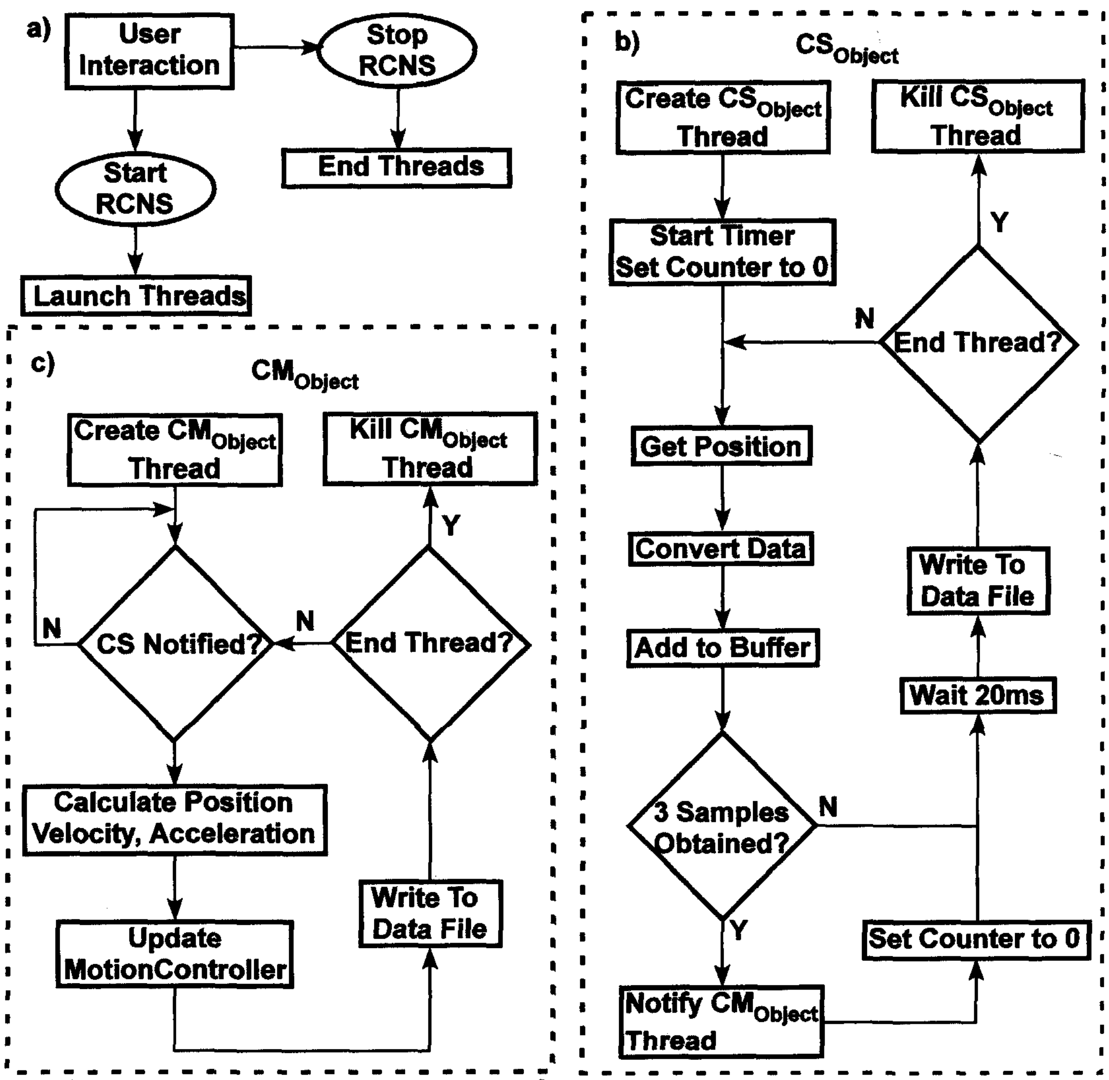

Fig. C-3: Interaction of software threads for an independent motion axis. The operator enables tele-operated catheter navigation (a), creating four software threads, one for each peripheral device axis, which run independent of the main program. A thread corresponding the CS axis, samples the CS at 20 ms intervals, after three samples the thread notifies the corresponding CM thread.

C.3 Sampling Strategy

To update position, velocity and acceleration of the motion-controller, requires 80 ms to complete using the current RS232 protocol (19,200 bps, 1 stop bit, and 1 stop bit). To calculate velocity and acceleration, a minimum of three samples, taken at 20 ms intervals, are required. This leads to a delay of 60 ms before updating the CM with new position information. The 80 ms communication delay, plus the 3 sample delay cause a minimum motion replication delay of 140 ms. A depiction of the ideal CM response is shown in Fig. C-4.

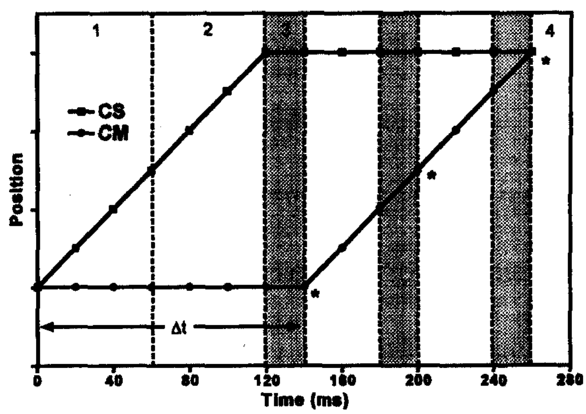

Fig. C-4: Replicated motion by the CM occurs in 4 stages. In the first stage (1), motion applied to the CS is sampled 3 times by the workstation. During the second stage (2), kinematics of the input motion from stage 1 are transferred to the CM from the workstation, which takes 80 ms. After receiving new kinematics, motion is executed by the CM, marked by *. During new updates, the CM utilizes 'on the fly' motion generation, to concurrently receive new data, while executing past motion commands. Concurrent times are highlighted by shaded boxes. Stages 2 and 3 are repeated until the CM reaches a steady-state position with the CS (stage 4). Overall, a 140 ms delay is forced into the system (Δt).

Appendix D :

Design and Construction of a Multi-Path Vessel Phantom for Interventional Training[5]

D.1 Introduction

X-ray fluoroscopic guided percutaneous transluminal catheterization plays an important role in the diagnosis of vascular and cardiac disease. Improvements in balloon, stent, coil, guidewire, and catheter technology have transformed catheter-based procedures from a solely diagnostic intervention to routine therapeutic intervention. Currently, training residents and fellows on safe and efficient catheter manipulation is achieved under the guidance of an experienced interventional physician in the clinic. This apprenticeship training method is expensive and time consuming for the trainer, and

[5] A version of this chapter has been submitted as a manuscript to the *British Journal of Radiology*, entitled: "Design and Construction of a Multi-Path Vessel Phantom for Interventional Training," Thakur, Y., Nikolov H.N., Gulka, I.B., Holdsworth, D.W., and Drangova, M. (Submission #BJR-D-09-00878)

may not guarantee sufficient development of core interventional skills: the dexterity required to manipulate the catheter and inject contrast, while simultaneously operating the x-ray imaging system and viewing images.

While software simulators have been developed to assist with training [1-3], these simulators usually focus on micro interactions of the catheter inside the vasculature, *i.e.* friction. Although understanding micro interactions is important, the skill of manipulating the catheter/guidewire while simultaneously operating the imaging system is overlooked.

In a parallel effort, vascular models have been described in the literature [4]. However, the application of these vascular models has typically been to optimize image reconstruction algorithms, perform hemodynamic studies and calibrate imaging systems. Vessel models can provide anatomically realistic vasculature, but for training purposes lack physiological variability. To emulate physiological variability during training, multiple phantoms with different geometrical considerations would be required, a time consuming and costly approach. Instead, the use of non-anthropomorphic phantoms, containing multiple vessel trajectories can be used to assist training efforts. Recently, such phantoms have been used in catheter navigation studies, comparing conventional vs. remote catheter manipulation [5-7].

A simple, cost effective, non-anthropomorphic phantom has the potential to accelerate interventional training by providing a platform to learn the core skills required in the clinic. In addition, as an perpetual platform, a non-anthropomorphic phantom may provide specific catheter manipulation tasks to assess new catheter technologies, monitor the progression of core skill development in trainees and also provide a standardized platform for assessing the developed core skills of graduating trainees.

This technical innovation describes the design and fabrication steps of a simple, non-anthropomorphic phantom, termed the multi-path vessel phantom, which is intended to complement current interventional training methods.

D.2 Materials and Method

D.2.1 Design Considerations

To provide a variety of vessel trajectories, a 2D non-anthropomorphic phantom was designed. Considerations during the design of the phantom were as follows:

1. Radio-translucency,
2. Provision for a range vessel complexity,
3. Inclusion of different vessel diameter transitions (vein – small to large, artery large to small),
4. Simplicity in construction,
5. Physiologically relevant physical size,
6. Compatibility with flow.

To provide a range of vessel complexity, a 2D pattern, shown in Fig. D-1, containing vessel trajectories of varying angulations was conceived. Vessel angulations vary between 30-135° in order to simulate commonly encountered branch vessels within the neuro-vasculature. In addition to vessel angulations, on the left side of the phantom, the pattern incorporates a transition from large to small diameter vessels (9.5-8-6.35 mm). On the right side of the phantom, the pattern is identical to that of the left side of the phantom, except vessel diameters transition from small to large (6.35-8-9.35 mm). Manipulating the catheter through the left side of the phantom provides training similar to arterial intervention (i.e. large to small vessel diameters), while manipulation of the catheter through the right side of the phantom provides training similar to venous intervention (small to large). Furthermore, a catheter can pass from the left to the right side (or *vice versa*), providing increased training paths. The vessel diameters selected are similar to the size of carotid arteries [8].

The size of the phantom is constrained to 30x30 cm, thereby ensuring the phantom is visible within the field of view of most clinical x-ray systems.

To enable contrast injection, the phantom must also be flow-compatible. This consideration is examined in the next section.

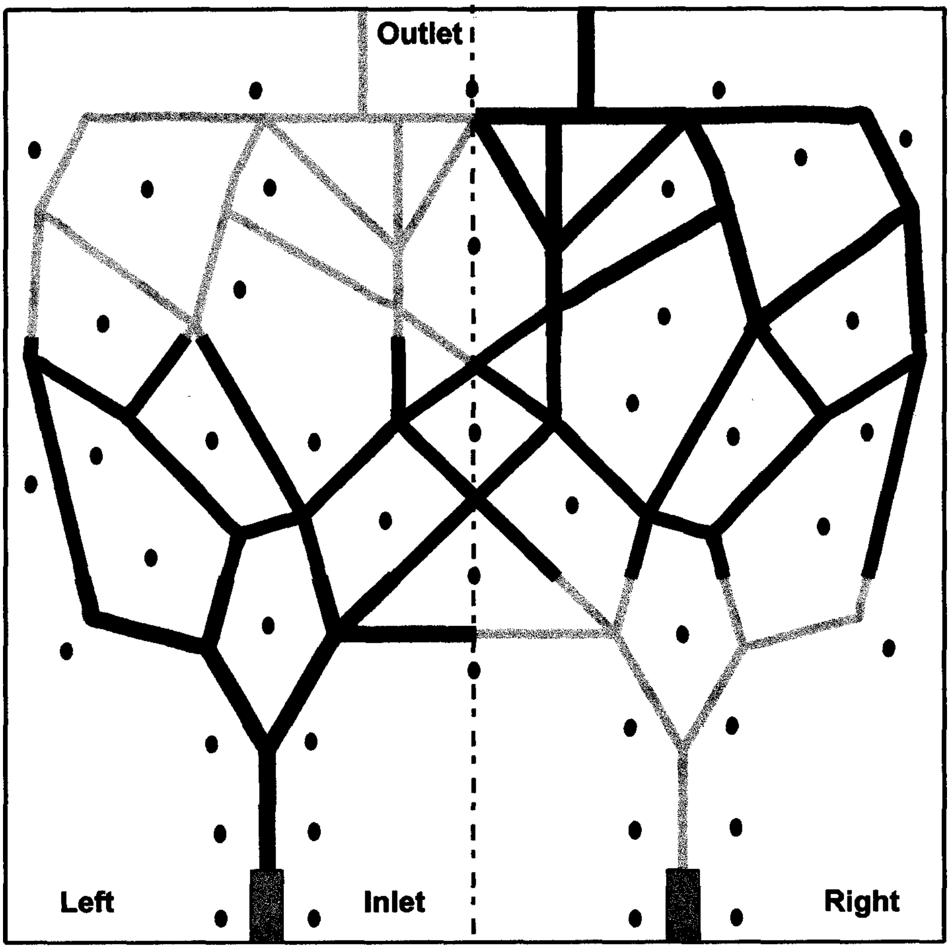

Fig. D-1: Pattern of the non-anthropomorphic multi-path training phantom (top view). The catheter is inserted into the phantom through either the bottom left or bottom right inlets. Inside the phantom, the catheter can be manipulated within vessels of three diameter sizes (dark gray: 9.5 mm, light gray: 6.35 mm, and black: 8 mm). To provide cross-training for interventional trainees, catheter manipulation through the phantom's left side provide vessel-diameter transitions from large-to-small (9.5-8-6.35 mm), while the phantom's right side provides vessel-diameter transitions from small-to-large (6.35-8-9.5 mm). Branching angles inside the phantom – ranging from 30 to 135° – provide the trainee with paths of varying difficulty. Black circles indicate fasteners, which hold the two machined acrylic plates together.

D.2.2 Phantom Construction

For simple construction, the multi-path phantom is comprised of two acrylic sheets, each measuring 30x30x1.27 cm, for an overall size of 30x30x2.54 cm. The pattern, shown in Fig. D-1, was milled into each sheet using an automated 3-axis numerically controlled milling machine with standard hemi-spherical mill bits (6.35 mm, 8 mm and 9.5 mm diameter).

Quick-disconnect fluid connectors (APC series, Cole Parmer Canada, Inc., Montreal, QC) are placed at the inlet and outlet of the multi-path vessel phantom. A Y-connector is connected to an inlet, providing an access point for the catheter/guidewire and connection to a pump.

Finally, the edges of the phantom were sealed with silicone sealant to prevent fluid leakage.

The completed phantom is shown in Fig. D-2.

D.2.3 The Multi-Path Vessel Phantom

Radiographic images of the phantom are shown in Fig. D-3. To highlight the various navigation paths, water was pumped through the phantom, while iodinated contrast was manually injected into the left inlet (Fig. D-3a) or the right inlet (Fig. D- 3b).

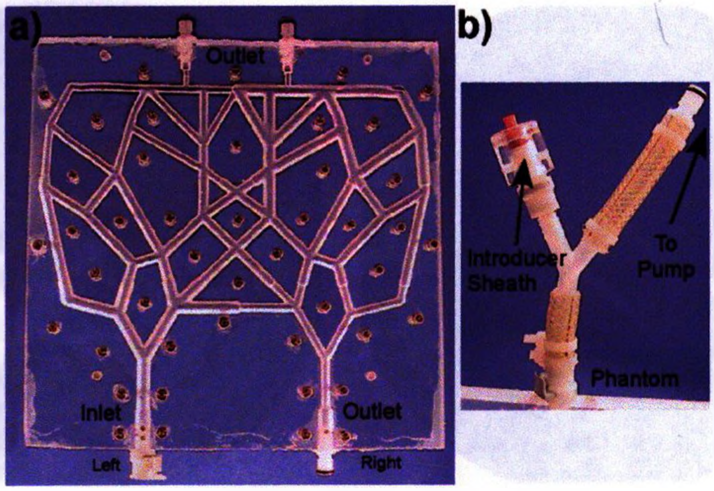

Fig. D-2: a) The constructed multi-path vessel phantom with Y-connector, labelled for catheter manipulation through the phantoms left-side. The Y-connector contains an introducer sheath, allowing the catheter and guidewire to enter the phantom and a second connector that connects to a standard pump. For catheter manipulation starting in the left-side of the phantom, the setup is configured with the Y-connector (b) attached to the left inlet of the multi-path vessel phantom. All other connectors on the phantom act as outlets. For catheter manipulation from the phantom's right side, the Y-connector is attached to the right inlet, and the left inlet becomes an outlet.

Flow through the phantom is highlighted by the diffusion of contrast. In areas of high flow and volume, more contrast is present, thus a brighter image of the vessel is obtained. In the smaller diameter vessels, there is lower flow and volume, thus a lower concentration of contrast agent results in reduced image contrast between the vessel lumen and the rest of the phantom. As shown in Fig. D-3, the diffusion of contrast throughout the phantom is not uniform. The varied contrast throughout the phantom will

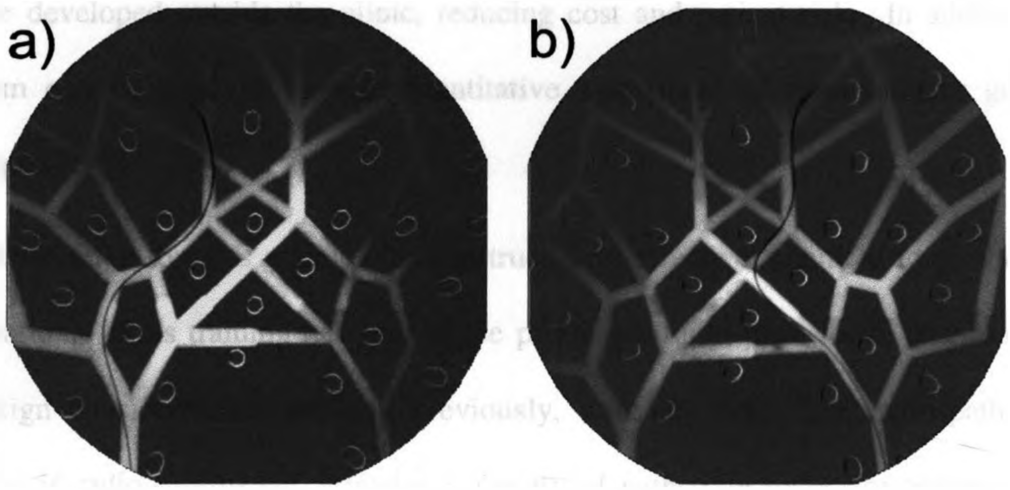

Fig. D-3: Radiographs of the multi-path training phantom injected with contrast via the left inlet (a), and right inlet (b). The catheter is clearly visible in both images.

allow trainees to practice catheter manipulation in a variety of visualization scenarios, similar to clinical intervention where some vessels, are difficult to visualize after contrast injection.

D.3 Discussion

Core, catheter-based interventional skills are required in common medical interventions, including: angiography, balloon and stent placement, coil deposition, and intra-cardiac electrophysiology studies. Trainees currently develop core skills and therapeutic skills, simultaneously, in the clinic, under the guidance of experience interventionalists; a costly method. Using a simple, cost-effective phantom, core skills may be developed outside the clinic, reducing cost and patient risk. In addition, this phantom can be used to provide quantitative assessment of new catheter guidance techniques [5-7].

Consideration towards a simple to construct, cost-effective, phantom to provide core interventional skills training has lead to the presented, multi-path vessel phantom. The six design considerations, outlined previously, were all met. The multi-path vessel phantom is radio-translucent, contains a variety of path trajectories for training and is compatible with fluid for contrast injection. In addition, the phantom is easily constructed using two acrylic sheets and common machining tools. The simplistic construction will allow most centres to independently construct and validate this phantom. Furthermore, the CAD files can be easily modified to accommodate advanced tasks.

As with any phantom, limitations exist. Vascular elasticity, 3D geometry and friction are not mimicked by the multi-path vessel phantom. These factors were intended omissions, as the phantom's purpose is to provide a cost-effective platform for core-skill development. Softer materials, such as silicon, have previously been used to create realistic 3D geometry; these phantoms are not suitable for catheter manipulation, as the soft materials cause the catheter to stick to them during manipulation, and can be perforated by a catheter or guidewire. The use of a rigid material completely removes the trainee's ability to perforate the phantom.

It should be noted, this multi-path vessel phantom is not intended to replace current training methods, but instead complement current methods by allowing core skills to be developed outside the clinic. Clinical training would still be required to learn specific therapeutic skills, such as inflating balloon/stents. Using the training phantom should allow training programs to focus therapeutic skill development, instead of core skill development, a methodology used similarly in sport, where athletes use cross-training to develop strength, agility and endurance. A study is currently underway to assess the validity of this phantom for skills training. The results of this study will be the topic of future work.

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