Universidade de Lisboa
Faculdade de Ciências
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Dissertação

Mestrado Integrado em Engenharia Biomédica e Biofísica

Engenharia Clínica e Instrumentação Médica

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Orientador externo: Professora Doutora Jenny Dankelman
Orientador Interno: Professor Doutor Nuno Matela

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Change may be for the better or may be for the worse but it is continuously occurring.

Robert W Tarr

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Resumo

Desde a realização da primeira angiografia cerebral por Egas Moniz em 1927, o tratamento de várias patologias da cabeça e pescoço foi revolucionado com a introdução dos procedimentos endovasculares. A possibilidade da visualização dos vasos sanguíneos em tempo real em conjunto com o desenvolvimento de novos instrumentos médicos permitiu o estabelecimento de procedimentos menos invasivos em Neurologia, nomeadamente, no tratamento de aneurismas, arteriosclerose, acidentes vasculares cerebrais, entre outros. A introdução de um cateter no sistema vascular através de uma pequena incisão na pele possibilita o acesso a zonas de patologia na neurovasculatura e a realização do respectivo tratamento através do envio de outros dispositivos médicos ou líquidos terapêuticos pelo lúmen do cateter. Com estes procedimentos minimamente invasivos o paciente beneficia de tempos de recuperação mais rápidos e eficazes, bem como de menor desconforto. No entanto, para o médico intervencionista existem várias desvantagens. O intervencionista perde o acesso à visualização directa do local de tratamento, sendo agora guiado através de imagens de fluoroscopia, o que pode conduzir a descoordenação motora-visual. Além disso, os instrumentos de cateterização têm graus de liberdade e *feedback* limitados. Os cateteres convencionais actualmente utilizados em procedimentos neuroendovasculares oferecem um controlo limitado da ponta do instrumento quando dentro do paciente. A ponta dos cateteres convencionais tem uma curvatura fixa e inalterável quando conduzido dentro do sistema vascular, tornando difícil a selecção de ramos na rede vascular de diferentes curvaturas. Isto exige muitas vezes a remoção e troca de cateter, aumentado o tempo do procedimento bem como a fadiga do intervencionista. O controlo destes cateteres é muito dependente das capacidades operacionais do intervencionista, requerendo um nível operacional muito elevado. Neste sentido, torna-se relevante a introdução de novos métodos de controlo mais intuitivos e efectivos. Cateteres direccionáveis cuja ponta pode ser deflectida dentro do paciente através da manipulação externa do instrumento pelo intervencionista oferecem um controlo mais preciso, solucionando a necessidade de troca de cateteres durante um procedimento. Diferentes tecnologias têm sido investigadas na literatura para realizar a deflexão da ponta do cateter. No entanto, para a sua implementação na prática clínica é importante avaliar a interacção homem-instrumento com os novos métodos de controlo introduzidos com estas tecnologias.

É neste contexto que se encontra a motivação para o presente projecto que consistiu na realização de uma experiência com o objectivo de avaliar diferentes métodos de controlo de cateteres direccionáveis, na tentativa de encontrar aquele que melhor contribuirá para a utilização destes instrumentos em procedimentos neuroendovasculares. Para isso, em primeiro foi realizada uma revisão de literatura sobre todos os cateteres, comercialmente disponíveis (usados já na prática ou não), em fase de protótipo e em fase de patente com possível aplicação a procedimentos neuroendovasculares. Desta pesquisa resultou a classificação das várias tecnologias encontradas que foram comparadas sobre aspectos relacionados com os requerimentos impostos em procedimentos neuroendovaculares: capacidade de miniaturização em

tamanhos inferiores a um milímetro para tratamentos que envolvam vasos muito pequenos do cérebro; estabilidade da ponta que se revela importante na entrega de outros aparelhos ou terapêuticas, havendo a necessidade de manter a posição da ponta constante; controlo preciso da ponta para o seu correcto posicionamento de acordo com a anatomia de cada paciente; fácil de ser utilizado pelo intervencionista, através de um método de controlo intuitivo e efectivo; e simples de produzir, para poder ser descartável. Na comparação destes parâmetros um tipo de cateteres direccionáveis sobressaiu-se, podendo constituir o tipo de cateter direccionável mais próximo de ser usado clinicamente. Este tipo de cateteres direccionáveis possui a sua estrutura assente num mecanismo composto por cabos ou outros componentes externos ao lúmen do cateter que ao serem manipulados permitem deflexão da ponta do cateter. Dois métodos de controlo que permitem a manipulação do utilizador para este tipo de cateteres foram encontrados. A manipulação pode ocorrer através da rotação ou deslizamento de um botão na interface do cateter. Ao realizar o deslizamento ou rotação do botão a ponta do cateter é deflectida, sendo assim controlada pelo intervencionista. A deflexão pode ser unidireccional, bidireccional e multidireccional. Para cada método de controlo, diferentes tipos de *design* da interface podem ser considerados.

Uma experiência foi concretizada no departamento de Engenharia Biomecânica da Faculdade de Engenharia de materiais, marítima e mecânica da Universidade Técnica de Delft, na secção de Cirurgia Minimamente Invasiva e Técnicas Intervencionais, para comparar os dois métodos de controlo descritos. Cada um dos métodos foi implementado em dois tipos alternativos de design para a interface com o utilizador. Deste modo, quatro interfaces foram consideradas e identificadas com as seguintes designações: *Rotator I*, *Rotator II*, *Slider I* e *Slider II*. As quatro interfaces foram utilizadas por dezasseis voluntários para a manipulação virtual da ponta de um cateter mostrado no ecrã de um computador. Um cenário simulador de um procedimento neuroendovascular foi montado: uma plataforma foi utilizada para simular o movimento do cateter dentro do paciente e um modelo visual foi construído para simular o sistema de imagem que monitoriza o procedimento. Na plataforma uma vara de metal utilizada como o corpo do cateter foi montada horizontalmente, conectada a um fio deslizante entre duas roldadas, podendo ser movida para trás e para a frente. Cada uma das interfaces de controlo podia ser conectada à vara. Dois sensores foram utilizados para a aquisição da manipulação do cateter. Um potenciómetro na interface mediu a manipulação do botão controlador e um encoder mediu a translação do cateter. O modelo visual foi construído usando linguagem de programação C# utilizando a aplicação *Windows forms* no *Microsoft Visual Studio*. Um modelo vascular foi construído com base em algumas referências geométricas das principais artérias que garantem o suprimento sanguíneo do cérebro. A representação de um vaso sanguíneo foi feita por meio de linhas delimitando um espaço que representava o interior do vaso. Quatro cenários diferentes foram construídos para definir quatro tarefas distintas. Cada cenário consistiu na representação da sequência de três artérias do cérebro, formando visualmente um “percurso vascular”. Apenas a ponta do cateter foi representada na imagem, representada por uma linha de cor distinta do modelo vascular. O movimento da ponta do cateter na imagem foi modelado através de uma relação matemática

dependente dos valores medidos pelos sensores fazendo a correspondência dos movimentos feitos pelo utilizador, medidos através dos sensores. O movimento foi modelado de forma a obrigar a que cada participante tivesse de realizar a deflexão constante da ponta para utilizar várias vezes o método de controlo ao longo de cada tarefa. A interacção do corpo do cateter com os tecidos não foi considerada.

A experiência consistiu em quatro sessões em cada qual o participante teve de completar dez tarefas com uma das interfaces. Na fase inicial de cada sessão duas tarefas foram realizadas apenas para praticar, seguidas de duas sequências iguais de quatro tarefas distintas. Cada tarefa consistiu na manipulação da ponta do cateter de um ponto inicial até ao fim do "percurso vascular" devidamente assinalado, tentando seguir o mais precisamente possível centro do percurso. O tempo para terminar a tarefa, a distância total percorrida, a distância média ao centro da linha e o número de erros efectuados foram medidos em cada tarefa. A comparação das interfaces em cada uma destas variáveis foi realizada na 1º sequência de tarefas contra a 2º sequências de tarefas para observar o efeito de aprendizagem. Assim para cada variável dependente foi considerada a soma das quatro tarefas correspondentes a cada sequência. No fim de cada sessão cada participante respondeu a um questionário que apresentava uma escala, criada pela NASA, que mede a carga de trabalho em termos de esforço mental, esforço físico, esforço temporal, performance, empenho e frustração. No fim da experiência cada participante respondeu a questões sobre a preferência pelas interfaces, a fadiga sentida durante a experiência, e a opinião sobre o estudo. As quatro interfaces foram comparadas estatisticamente por cada variável dependente. Para as variáveis contínuas aplicou-se o teste estatístico paramétrico ANOVA de um factor para medidas repetidas. Para as variáveis ordinais foi utilizado o teste de *Friedman*. Estes testes avaliam se existem diferenças estatisticamente significativas entre os quatro grupos.

Na análise da primeira sequência foram encontradas diferenças significativas para variável distância média ($F(3,45)= 3.949$, $p=0.014$) entre as quatro interfaces. Os testes *post hoc* usando a correcção de *Bonferroni* mostraram que as diferenças ocorreram entre as interfaces *Rotator I* e *Rotator II* ($p=0.018$), revelando que no início da experiência a trajectória da ponta do cateter da interface *Rotator I* (1.4425±0.2999mm) foi significativamente mais próxima da trajectória ideal comparativamente à realizada com a interface *Rotator II* (1.6303±0.3985 mm). No entanto, estas diferenças não foram significativas depois da segunda sequência de tarefas, sugerindo que o desempenho com as interfaces se iguala depois de um efeito de aprendizagem. De facto, depois da segunda sequência, as diferenças entre as quatro interfaces só são significativas relativamente ao número de erros cometidos ($\chi^2(3)=8.162$, $p=0.043$). Estas diferenças ocorreram entre *Slider II* e *Slider I* ($p=0.003$), *Slider II* e *Rotator I* ($p=0.021$), *Slider II* e *Rotator II* ($p=0.006$). A interface *Slider II* apresentou o rank de W*ilcoxon* médio da análise *post hoc* mais baixo, revelando que a manipulação com esta interface foi a mais precisa no que respeita ao menor número de erros realizados. Contudo, os dados subjectivos revelam que a preferência dos participantes foi maioritariamente pelas interfaces baseadas na rotação do botão da interface. Esta preferência foi justificada pelo facto de terem sentido mais facilidade em manipular este tipo de interfaces e o método de controlo ser mais intuitivo. A análise

dos resultados da avaliação da carga de trabalho mostra que diferenças significativas ocorreram na avaliação do esforço temporal com cada interface ($\chi^2(3)=10.008$, p= 0.019). As diferenças foram encontradas entre *Slider I* e *Rotator II* (p= 0.018) e entre *Rotator I* and *Slider II* (p=0.034), revelando pelos ranks médios de W*ilcoxon* que com as interfaces *Rotator II* e *Rotator I* o esforço temporal sentido foi menor quando comparadas com as interfaces *Slider I* e *Slider II*, respectivamente. Este resultado justifica a preferência subjectiva. Contudo, objectivamente, os dados do tempo médio para terminar cada sequência não comprovam que com estas interfaces as tarefas são executas mais rapidamente.

Posto isto, é difícil afirmar conclusivamente qual o método de controlo mais efectivo. Os dados sugerem que o método de rotação é mais intuitivo segundo a preferência subjectiva dos participantes, mas é com o método de deslizamento da interface *Slider II* que menos erros são cometidos. Como as diferenças não foram significativas para as outras variáveis na segunda sequência de tarefas, não se podem retirar conclusões definitivas. Melhoramentos no *design* da experiência podem ser realizados futuramente, bem como no *design* das interfaces, segundo alguns dos comentários e sentimentos descritos pelos participantes. Além disso, a continuação deste *design* e a sua expansão para uma simulação realista de procedimentos neuroendovasculares pode ser mais contributivo na avaliação das interfaces que nesse contexto deverão ser testadas por novos doutores a realizar especialização nesta área de intervenção.

Palavras-chave: Procedimentos Neuroendovasculares, Cateteres direccionáveis, métodos de controlo

Abstract

During the last twenty years vascular disease management in Neurology is changing dramatically with the introduction of neuroendovascular procedures. Through a small incision in the body accessing the vascular system, catheters can be navigated to reach the pathology site and realize treatment under a real-time imaging system. Currently, this type of minimally invasive surgery relies on catheters that have a fixed and unchangeable distal tip, offering a poor control method and requiring a high level of operation of the interventionist. Therefore, the introduction of intuitive and effective control methods in the neuroendovascular approach remains a challenge. Steerable catheters have been developed as an improvement of tip control inside the body, allowing direct manipulation of the tip bending through different control methods configured in different handles design. However is not yet clear how they perform and how is human-interaction with their handles designs. To evaluate which control method is most intuitive and effective, a study was conducted to assess performance of novices in steering a tip in a virtual scenario using different handles design. First a literature review was made about the different commercial available, prototypes and patents designs of catheters. The catheters were classified and compared. Two control methods clearly defined in the literature for manual control of bi-directional deflection of the tip were chosen to be compared. One method consists in the knob rotation and the other in sliding a knob of a handgrip.

Using four handles designs, two based on the rotation (Rotator I and Rotator II) and two based on the sliding (Slider I and Slider II), sixteen subjects performed virtual tasks over four sessions. At each session, two practice tasks were performed followed by two trials of four different tasks. Each task consisted of steering and moving a virtual tip on the screen. Each different task presented a different scenario, which consisted of a vessel path representation. The goal was to steer the tip via the center line of the path from a starting point to the end line. The performance was assessed by measuring task time, travel length of the tip, average distance to the center and the number of mistakes. Subjective evaluation was also measured using the NASA Task load index to assess the workload with each handle. One way ANOVA with repeated measures was used for the analysis of the four handles for each dependent continuous variable (task time, travel length, and average distance). For the ordinal dependent measures (number of errors, TLX-workload), the Friedman test was used. Statistically significant differences were observed in the second trial for the number of mistakes ($p=0.043$) between of the four handles. Specifically the differences occurred between Slider II and Rotator I ($p=0.021$), Slider II and Rotator II ($p=0.006$), Slider II and Slider I ($p=0.003$), showing that with Slider II fewer errors were made. However, Rotator I and Rotator II were strongly preferred by the participants, suggesting the rotating control method as more intuitive and easy to maneuver. As the best performing handles were not the preferred, further improvement of handles design is needed for more conclusive outcome.

Keywords: Neuroendovascular procedures, steerable catheters, control method

Contents

Acronyms

AVMs	Arterio-Venous Malformations
ACA	Anterior Cerebral Artery
CCA	Common Carotid Artery
CT	Computer Tomography
DOF	Degrees of Freedom
EAP	Electroactive polymer
ECA	External carotid artery
Fr	French. (Measure unit of catheter diameter)
ICA	internal carotid artery (ICA)
MCA	Middle Cerebral Artery
MRI	Magnetic Resonance Imaging
SMA	Shape-memory alloy
TLX	Task Load Index
US	Ultrasound

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1 Introduction

The introduction of cerebral angiography by António Egas Moniz in 1926 opened the possibility of using a less invasive approach to treat cerebrovascular diseases. Today, many of open surgical procedures to treat vascular diseases of the head and neck have been replaced by neuroendovascular procedures [1]. The patient benefits of less discomfort and lower recover time. Great advancements in instrument technology supported the establishment of the number of neuroendovascular procedures possible today. In many situations, however, the decision of using this minimally invasive technique over an open surgery is not easy. There are current technology limitations in control precision that in high risky situations, as in very small aneurysms, treatment option decision varies between medical institution [2]. Current control methods of catheter rely on the operator's skills offering poor control of the tip. Moreover, the distal tip is unchangeable, and only one configuration of it can be used when inside the vessel. This may lead to very time consuming procedures, requiring many catheter exchanges. Steerable catheters have been developed as an improvement of tip control, allowing direct manipulation of the tip through different control methods configured in different handles design, solving the need for catheter exchange.

A wide range of steerable catheters have been study [3]. To support neuroendovascular procedures there are requirements regarding size, flexibility, stability and maneuverability. A literature review on catheters for neuroendovascular procedures is given in chapter 2. Only manual controlled catheters were considered. The goal was to gain an overview of the catheter technologies already supporting the clinical practice of these procedures and the technologies in development, comparing them in regard of what can be an ideal catheter in the neuroendovascular context. In this overview, a classification of catheters is made that allows a clear description of all technologies, showing what are the limitations of current catheters and how close steerable catheters designs are to be applied to the neuroendovascular level. A project challenge is derived from the literature study in observing that there is lack of data about the use of the control methods. Assessing this data can be an important step in the design improvement of steerable catheters design for their approach to neuroendovascular procedures.

An experiment with four handles designs based on two manual control methods was conducted and it is presented here as the scope of this dissertation. The experiment goal is described in chapter 3 and the experiment design in chapter 4. Then the results are presented, in chapter 5, followed by a discussion in chapter 6 comparing the different handles. The report ends with some conclusions and description of future work, in chapter 7.

2 Literature Review on catheters for neuroendovascular procedures

This chapter presents the literature review. First the clinical setting of neuroendovascular procedures is presented (section 2.1). In section 2.2 the methods for conducting are described after the settlement of design requirements for catheters in neuroendovascular procedures. In section 2.3 a classification of catheters is presented and the discussion comparing the different groups takes part in section 2.4. The chapter ends with conclusions and project challenge.

2.1 Neuroendovascular Procedures

A neuroendovascular procedure is a minimal invasive method to treat vessel lesions of head and neck. A thin hollow tube called catheter is inserted into a small incision in the skin, typically in the groin area, and threaded up through the blood vessels until reach the site of pathology. The procedure is accomplished under x-ray fluoroscopy visualization.

Neuroendovascular procedures can be divided into three typical interventions to treat a wide range of lesions in the brain and neck: embolization, angioplasty and stenting. Embolization consists in closing abnormal vessels or abnormal parts of the vessels (such as aneurysms). Arterio-Venous Malformations (AVMs), which are abnormal communications between arteries and veins that can occur in the brain or in the spine, can be treated with this approach by injection of a non-reactive liquid adhesive material that blocks the AVM. Aneurysms can also be excluded from circulation by embolization technique. An aneurysm is a balloon-like dilatation in a blood vessel and can be treated by placing coils into the aneurysms, a procedure known as aneurysm coiling (Figure 1). Before coiling of aneurysms being possible, clipping the aneurysm was the only solution. Clipping aneurysms involve a craniotomy for accessing the target site and directly place a clip on the neck of the aneurysm in a very invasive way. Angioplasty is another endovascular technique that is used to open obstructed vessels with arteriosclerosis (accumulation of fatty material on arteries walls). A balloon catheter, which consists in a collapsed balloon on a catheter, is passed into the obstructed location and the balloon is inflated forcing the expansion of the inner clot plaque deposits and the surrounding muscular wall, opening the blood vessel and improving flow. Angioplasty is often combined with the placement of a small metal coil called a stent in the clogged vessel, which keeps the vessel open and prevents it from narrowing again. Carotid stenosis is commonly treated with angioplasty and stenting when traditional carotid surgery is not feasible or too risky.

Each neuroendovascular approach may differ in aspects of complexity and technical requirements, depending on the target vessel location. An overview about the clinical setting of neuroendovascular procedures is given in this chapter, starting with a description of how to perform a neuroendovascular procedure in subsection 2.1. Section 2.2 presents a better description of the actual image system used to conduit neuroendovascular procedures as well an overview of the current alternatives under

investigation. Finally, the chapter ends with risks and challenges raised by neuroendovascular procedures in general.

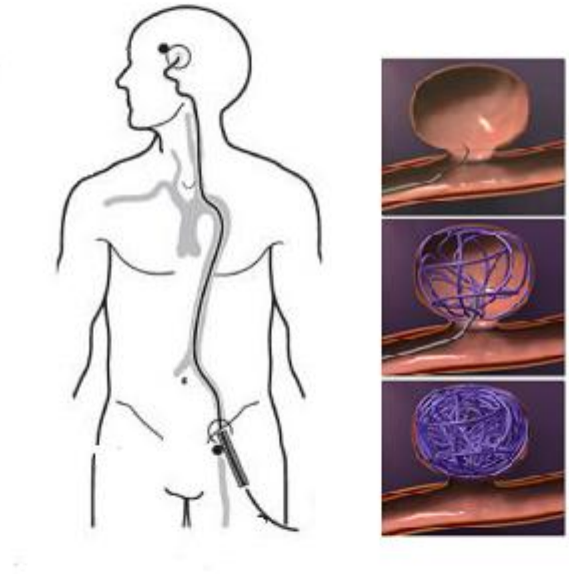


Figure 1. Aneurysm coiling procedure. Common route (left) and coil deployment inside the aneurysm (right). Adpated from [4] and [5].

2.1.1 The procedure itself

To describe how a neuroendovascular procedure is performed, first cerebral angiography is introduced as the first step before a neuroendovascular procedure; second the main steps common to all procedures are described.

2.1.2 Cerebral Angiography

Diagnostic cerebral angiography is, normally, considered the first step of a neuroendovascular procedure [6]. A catheter is placed through the femoral artery after numbing the groin. The catheter should be usually advanced over a hydrophilic guidewire inside from femoral artery into one of the carotid arteries (left and right) and/or the left subclavian artery, crossing the aortic arch. X-ray images help the interventionist to correct positioning. Once reached the site a contrast agent is delivered through the catheter and X-Ray images are taken - to see how it moves through the artery and blood vessels of the brain. These images allow to identify any blockages in blood flow and, thus, planning the neuroendovascular procedure. The radial artery can be used as an alternative access to fermoral artery the latter one is widely accepted as the easiest access.

2.1.3 Main steps of neuroendovascular procedures

The common steps to all neuroendovascular procedures can be summarized as follow:

1. Access into the artery – locate site, puncture it percutaneously using an entry needle.
2. Pass a guidewire through the entry needle.
3. Place a sheath over the guidewire. The sheath will keep the blood vessel open and allow the exchange and insertion of catheters and other guidewires.
4. Navigate of guidewire and catheter to the target location.
5. Visualize the progress of the catheter by fluoroscopy, injecting contrast agent when it is needed.
6. Perform the treatment: embolization, angioplasty or stenting.
7. Remove all the instruments used from the body.
8. Secure the puncture site.

2.1.4 Image System

Image visualization is a crucial aspect to perform neuroendovascular procedures. Angiograms are the images that allow the visualization of the blood vessels. Actually, in clinical practice, neuroendovascular procedures are conduct under X-Ray fluoroscopy guidance. X-ray has some advantages as an image system, for instance, a clean navigation in patent vessels, a high spatial and temporal resolution. Though patients are exposed to radiation, the medical benefits are assumed to outweigh the presumed risks [6]. Radiation exposure must be minimized both for patient and medical stuff during the procedure. A modern neurovascular suite is showed in Figure 2, consisting in a biplanar fluoroscopic system wherein vessels cans be seen in two planes at the same time.

Figure 2. Imaging equipment for endovascular procedures under fluoroscopy. From [7]

Despite the exposition to radiation, X-ray fluoroscopy imaging shows other drawbacks such as the lack of soft tissue visualization and the need of injection of contrast agent. Soft tissue visualization gives important information to access the function of an organ during the procedure. Regarding the disadvantages, other image

systems such as Angiographic Computer Tomography(CT), Ultrasound(US) and Magnetic Resonance (MRI) have been investigate as a possible alternative to improve neuroendovascular procedures in terms of safety and soft tissue visualization during the realization of a procedure.

Angiographic Computer Tomography is used to obtain pre-operative images. CT is a fast acquisition system and geometrically accurate. However, ergonomic problems with patient access and positioning make it unsuitable for guidance during a neuroendovascular procedure. Additionally, CT also involves the use of ionizing radiation. Ultrasound is also already used in neurovascular procedures but only to guide needles during vascular access. This image system is portable and low cost but it offers a limited penetration making it difficult to visualize catheters and guidewires. MRI provides the superior tissue contrast when comparing to the other systems described above. Nevertheless, MRI application to guide neuroendovascular procedures is limited to the costs involved and the compatibility of the actual instruments with the magnetic fields involved in this imaging systems. Table 1 summarizes the advantages and disadvantages of each image system, displaying a comparison among them.

	X-Ray Fluoroscopy	CT	US	MRI
Advantages				
High spatial and temporal resolution	++	++	+	+
Soft tissue visualization	-	-	+	++
Good quality image (instruments visualization)	+	+	-	+
Compatible with current instruments	+	+	+	-
Low cost	-	-	+	-
Disadvantages				
Radiation exposure	+	+	-	-
Difficult patient access and positioning	-	+	-	+

Table 1. Advantages and disadvantages comparison of the imaging systems; the scores are applied as follow: (-) the advantage or disadvantage is not present; (++) the advantage is present; (+) the advantage is present but less than others or the disadvantage is present.

MRI and US overcome the lack of soft tissue visualization and radiation exposure problems of CT and X-ray fluoroscopy. In practice, US is the only image modality capable of imaging soft tissue deformations quickly enough for interventional procedures. However the high level of expertise necessary to enhance a good quality is a disadvantage. Conversely, MRI detail tissue imaging have been of much interest of investigation [8]. Until now, some of the initial limitations of MRI have been overcome with the development of near real time MR imaging sequences [9] and with the advances in the magnet and system design that make access to the patient difficult [10].

2.1.5 Risks and Challenges

It is very challenging to perform neuroendovascular procedures: mortality risk is quantified in 1 to 2% in very experienced hands [11]. Risk rate increases with interventions above the skull base where thin-walled vessels are small and delicate.

Also, blood vessels location in the subarachnoid space complicates the procedures, once they float freely unsupported by bone or muscle. Procedure risks and performance challenges for the interventionist are listed as following.

Procedure Risks

Every medical procedure has risks that are not dependent on medical performance but raise from the procedure itself. For instance, any procedure where skin is penetrated carries risks of infection. Particularly when navigating the blood vessels of the body, risk of perforation and vessel dissection are always present. New medical devices have been developed along the past years to minimize procedure risks and, today, more medical conditions can be treated through the neuroendovascular approach. However, current medical devices still have limitations of operation. Many times multiple attempts with different catheters need to be made by the interventionist to reach difficult targets in neurovasculature. Thus, procedure time can be long and the risk of trauma increases.

Risks of complication and risk of side effects after a neuroendovascular procedure can occur. For example, during coil embolization of intracranial aneurysms the interventionist may unable to occlude wide-necked aneurysm and thromboembolic complications can happen. Interstices between coils allow thrombosis of significant volume of the aneurysm. During the procedure there is also a chance that embolic agent are lodge in the wrong place, depriving normal tissue to its oxygen. Moreover, there is in some cases the possibility of recurrence of aneurysm formation [7].

Radiation exposure is an essential part of neuroendovascular procedures due to the use of X-ray visualization and it can consider as a potential source of risks to the patient and interventionist as well. However, the measured effects have been considered as minor in deciding whether to undertake a neuroendovasculat procedure [12]. For each procedure there are specific procedural advices to minimize the exposure.

Challenges for the interventionist

The neuroendovascular procedure itself is a challenge for the interventionist, once his operability is limited to a more reduced area. Visualization of the anatomy is provided by radiographic images, so the interventionist no longer has a direct vision of the operation field and this may result in eye-hand discoordination.

Patient’s anatomy also raises other challenges:

1- Vessels size: in neuroendovascular procedures, navigating through the small vessels of the brain is a tuff task;

2- Tortuous neurovasculature: from patient to patient, doctors can face completely different anatomies; elder patients can have tortuous vasculature that makes navigation difficult;

Neuroendovascular procedures require precise control of the instrument tip inside the vessels. Therefore, a good dexterity of the necessary tools is needed. The interventionist must be well trained in doing such procedures. The training must give

the interventionist the ability to manipulate instruments as well as to coordinate that manipulation with image visualization.

However, manipulation of instruments can be very difficult and compromise interventionist's learning curve:

1- Poor haptic feedback: the force between the catheter and the blood vessel cannot be perceived by the interventionist;

2- Poor ergonomic control: the instrument itself can offer poor control in terms of intuitiveness, holding gesture (manipulation comfort) and dexterity.

Experience interventionist can achieve 2 mm precision which is not suitable for every procedure. Though, improving human-instrument interaction can play an important role in interventionist's learning curve, constituting a challenge for manufactures/researchers in instruments development.

2.2 Catheters for Neuroendovascular Procedures

Neuroendovascular procedures have become possible in current clinical practice due to the development of new tools and new techniques to safely navigate within vessels. Today we can find different type of instruments. Depending on the type of procedure, the interventionist may choose the most suitable tools. So, prior to any intervention a plan must be carried out.

The instruments used in these procedures can be summarized in three types accordingly to its function: introducers, catheters and guidewires. An introducer, or sheath, is a small tube that provides the access to the intravascular space by its insertion through the skin. Catheters are the devices insert into the body to reach the target vessel and perform the treatment. A flexible wire is used to guide the catheter, known as guidewires.

Typically a catheter comprises a proximal end, maneuvered by the interventionist outside the patient's body; a shaft, with variable length and a distal end (tip of the catheter), which has to be directed inside the vessel. Some catheters have a control handle connected its proximal end for manipulation. Figure 3 shows an example of one catheter embodiment with those portions signaled. Usually, the stiffness of the catheter decreases from the proximal to the distal end. The stiffer proximal end allows the interventionist to push the flexible tip into the patient's body without much trauma.

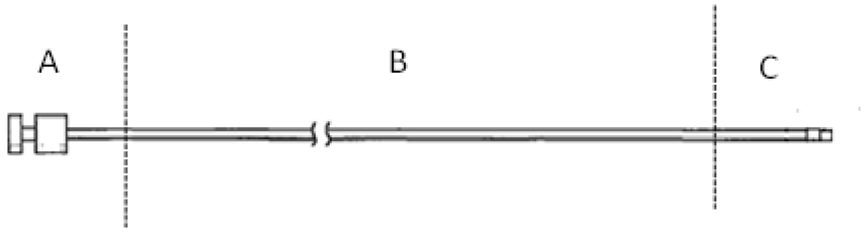


Figure 3. Example of one catheter embodiment. Typically consists in: A- proximal end: B- shaft and C- distal end. Adaptated from [13].

Today, interventionists have at their disposal a wide range of catheters. Catheters most commonly used in clinical practice present a fix shape at its tip. Manipulation requires twisting and push/pulling movements at the proximal end, which has poor precision. Different shapes are available to navigate different vessel bends in the neurovasculature. In a procedure many catheter exchanges may be needed to change tip configuration and this has been the major limitation of current catheters. Procedure time increase with the need of changing tip and this can increase risk of trauma and interventionist's fatigue. Therefore investigators started to research new type of catheters, known as 'steerable catheters', which are catheters whose tip can be deflected into different shapes eliminating the need of removal of the catheter. A wide range of approaches to steer the tip have been developed.

Besides eliminating the number of catheter removal, steerable catheters must achieve a better control of the tip (more precise). A good control of the tip requires a good manipulation of the instrument by the interventionist. To look deeper into these aspects a research about catheters for neuroendovascular procedures was conducted. The aim is to compare the different types of catheters and provide an insight about its limitations and challenges for future instrument development. To accomplish that, first, some design requirements for catheters for neuroendovascular procedures are settled, second the search criteria and engines used are explained and the chapter ends with the presentation of the search results. Commercial products, prototypes and patents were searched.

2.2.1 Design challenges

Size, flexibility and stability are very important characteristics in a catheter design. These three features are related to each other and vary according to the catheter purpose. A catheter used as a conduit to deliver other medical devices has to be stiff and large enough to serve as a conduit but flexible and small enough to navigate inside the vessel. Catheter stability is also important during the procedure. In aneurysm coiling, for example, when reaching the entrance of the aneurysm the tip position has to be maintained while placing the coils to prevent the rupture of the aneurysm. Stability is related to the capacity to hold position, thus, it is related with the capacity of the catheter to retain its tip shape. This capacity is related with the constituent materials of the tip and the deflection mechanism. Moreover, many neuroendovascular procedures require navigating through very small vessels and a proper catheter size is crucial to achieve successfulness. Small catheter can be very flexible though less stable during a procedure. So flexibility and size must be well balanced to achieve the most stable catheter to purpose of its use and location in the neurovasculature. Miniaturization of a catheter structure design should be possible to achieve several sizes from 6 to less than

3 French (Fr)[1]. Consequently, it must be simple to produce. Moreover, the cost involved should be low with respect to the single-used device principle.

Catheter's tip although its softness can be very harmful to the vessel when entering a new branch and change direction. A precise control on the tip is required for correct positioning. The way tip can be deflected and controlled can determine the precision of tip positioning. Moreover, the control method for the manipulation may influence the precision. In manual control, the interface interventionist-instrument must result in a control method that offers a precise control on the tip and that is easy to maneuver by the interventionist with accuracy.

Current available catheters have some limitations in some aspects considered in this section, not fulfilling all the requirements for an ideal catheter suitable for neuroendovascular procedures. According to the challenges described above, the design requirements for an ideal catheter can be summarized as follows:

- **Requirement 1:** is possible to miniaturize;
- **Requirement 2:** has a stable tip (capacity to hold shape);
- **Requirement 3:** offers a precise control mechanism for tip positioning;
- **Requirement 4:** is ease to maneuver (control method);
- **Requirement 5:** is simple to produce.

2.2.2 Search criteria and engines

Commercial products, patents and articles were searched. The search criteria was based in the following key words: Keywords as 'neurovascular catheters', 'microcatheters', 'steerable catheters', 'guide catheter', 'active catheter' and 'deflectable catheter'. As selection criteria the potential application of the design to neuroendovascular procedures was considered.

Google patents and *European Patent Office*, *Google Scholar, Google* and a book reference of neuroendovascular procedures [4] were used as engines. The last reference was a complement reference to select among commercial products, the ones commonly used in clinical practice. Additionally, only catheters with manual control were considered.

2.2.3 Search results

Only patents between years 2000 until the search date were considered. Table 2 and Table 3 show the results of patent search. Some scientific literature references were search in *google scholar* for the same period as patents. Additionally, some specific references cited in the review articles were searched, not considering the date of publication.

[1] Common unit of measurement of the size of a catheter. A catheter of 1Fr has a diameter of $^1/_3$ mm.

European Patent Office (www.espacenet.com)		
IP Class	**Description**	**Number of hits**
A61M 25/00	Catheters and hollow probes	
A61M25/001	Forming the tip of a catheter, e.g. bevelling process, join or taper	20
A61M25/0014	Connecting to a hub	37
A61M25/0021	Characterised by the form of the tubing	
A61M25/0041	Pre-formed, e.g. specially adapted to fit with the anatomy of body channels	72
A61M25/01	Introducing, guiding, advancing, emplacing or holding catheters	
A61M25/0125	Catheters carried by the bloodstream e.g. with parachutes; Balloon catheters specially designed for this purpose	11
A61M25/0133	Tip steering devices	---
A61M25/0136	Handles therefor (subdivision)	47

Table 2. Patent research through European Patent Office

Google Patents		
Keyword	**Number of hits**	**Reviewed**
'microcatheter'	12 200	20
'neurovascular catheter'	30 800	15
'flow directed catheter'	239 000	10
'deflectable neurovascular catheter'	3 740	30

Table 3. Patent research on Google Patents

2.3 Classification of Catheters for neuroendovascular procedures

From the reviewed products, prototypes and patents an observation was made: the catheter control relies on the capability of manipulate tip deflection to navigate specific bends in the neurovasculature. This manipulation differs with the tip properties making it possible to group the catheters with similar properties, as it is illustrated in Figure 4. According to its properties the tip can be shaped differently. The first level of classification divides the catheters in two major groups according to when the deflection (shaping) of the catheter occurs. The label 'Pre-procedure shaped' groups the catheters that are shaped (deflected) only outside the body, before the procedure. During the procedure the shape of this type of catheters cannot be changed. In the second large group, 'peri-procedure shaped', covers all the other catheters which tip can be deflected into different shapes during the procedure, inside the body.

Inside each of this large groups other subdivisions creating more levels of classification. In this way, the degree of similarity within each group increases and a comparison can be carried out among groups. The following sections of the chapter introduce each level of classification presented in Figure 4 and a description of the

common characteristics of each classification group is made according to the design requirements considered in the previous chapter. Additionally Table 4 is presented as reference for all the reviewed products, prototypes and patents grouped according to the classification.

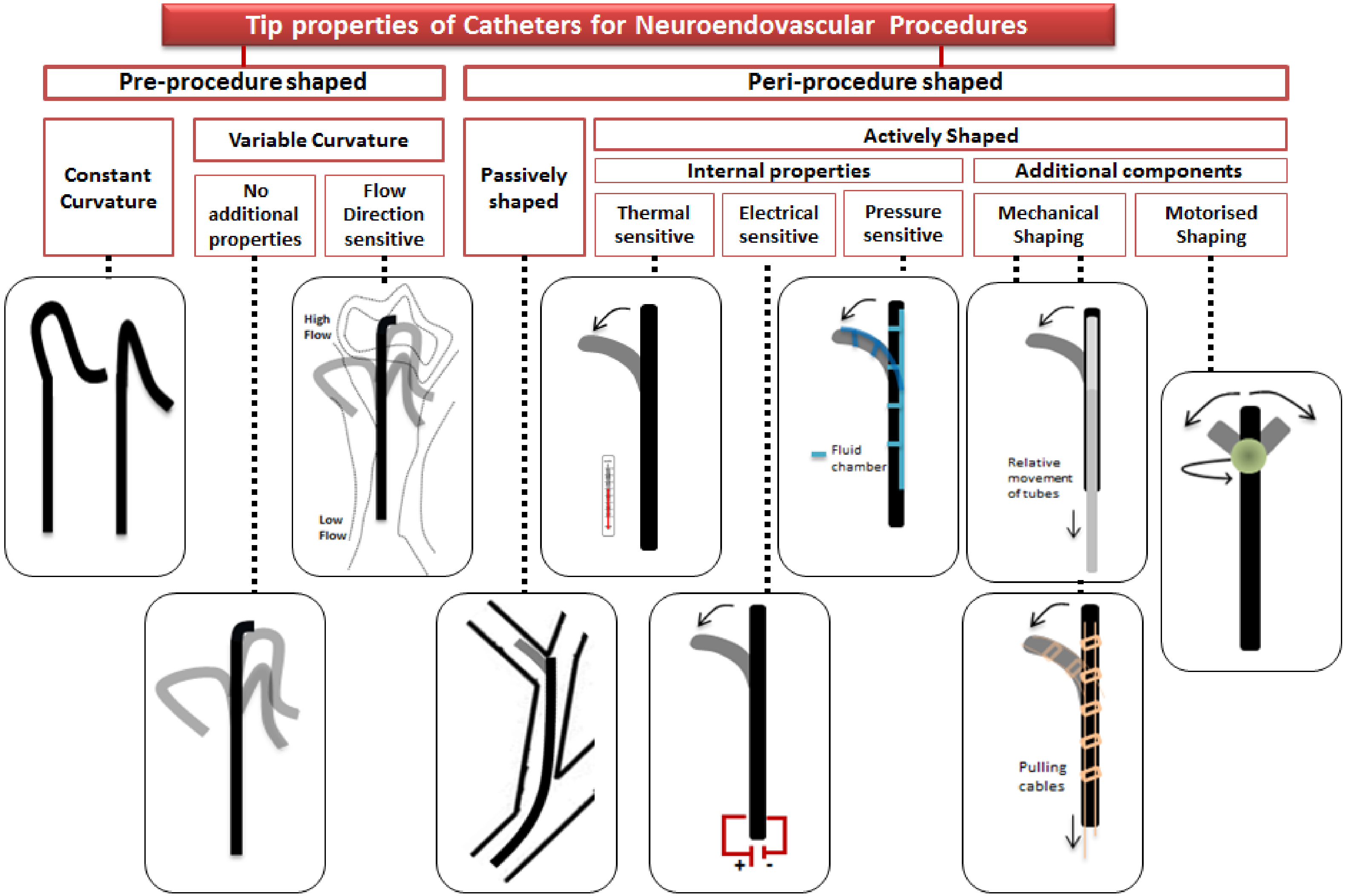


Figure 4. Catheters tip classification according to tip's properties.

Tip properties of catheters for Neuroendovascular Procedures								
Pre-procedure shaped			**Peri-procedure shaped**					
Constant curvature	**Variable curvature**		**Passively shaped**	**Actively shaped**				
	No additional properties	**Flow Direction Sensitive**		**Internal properties**			**External/additional components**	
				Thermal sensitive	**Electrical sensitive**	**Pressure sensitive**	**Mechanical shaping**	**Motorised shaping**
Commercial: Echelon, [14] Envoy, [15] DAC, [16] Neuron, [17] Simmons, [18] Vertebral (VERT), [18] Newton, [18] Headhunter, [18] Patents: EP2444116A1, [13]	Commercial: Headway [19] Rebar, [14] Renegade, [20] Prowler, [15] Excelsior, [20] Patents: US6245053B1 [21] US2011137282 A1 [22]	Commercial: Ultraflow, [14] Marathon, [14] Magic, [23] Sonic, [23] Patents: US6296631B2 [24] WO03047675A2 [25]		Patents: US6159187A, [26] US7037290, [27] Articles: Fukuda,[28] Mizuno, [29] Mineta, [30] Chang, [31] Fu, [32] Szewczyk,[33]	Patents: US2007100279A1 [34] US2009024086A1 [35] Articles: Fukuda, [36]	Patents: US2007/0100235A1 [37] Articles: Ikuta, [38] Haga, [39]	Commercial Courier Enzo. [40] Patents: US6074361,[41] US6976991 [42] US6126649 [43] US7918819 [44] WO2006012668 A1[45] US2010/0228152[46] US2008091169A1[47] EP2091603B1 [48] US 2008/0097293A1 [49] WO/2013/022727, [50] US20130012925A1 [51]	Articles: Yun, [52]

Table 4. List of the products found according to catheter classification.

2.3.1 Pre-procedure shaped catheters

Most catheters currently used in clinical practice are pre-procedure shaped, consisting in a flexible tube with a specific shape at its end that cannot be modified during the procedure when inside the vessel. However, properties of the catheters featured in this group still differ. The same catheter can be shaped in different curvatures by the interventionist outside the body or it can have a fix curvature that comes from manufacturing. Accordingly two subdivisions of this large group can be made: **constant curvature** and **variable curvature**.

2.3.1.1 Constant curvature

Pre-procedure shaped catheters with constant curvature have a specialized distal shape to navigate specific bends in the neurovasculature. Examples of different fixed curvatures available are in given in Figure 5. To adapt to different vessel anatomies companies have at disposal a wide range of selective shapes for their catheters.

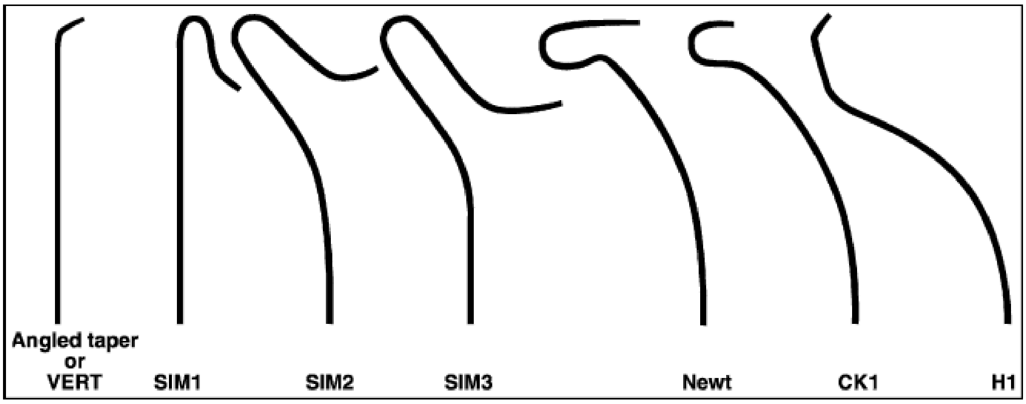


Figure 5. Example of some constant curvatures; these catheters are known as selective catheters: each curvature is specific designed for selection of specific vessel with a common shape. [6]

Size and motion ranges

Many commercial products currently used in clinical practice belong to this group. The sizes vary according to the function and the motion range of each catheter depends on its specific shape. Table 5 summarizes information about each commercial product relatively to the size, number of shapes available of the same catheter and the description of the common use of the catheter. It's possible to see in this way that a range of sizes - from 6Fr to less than 3Fr; and curvatures are covered with different commercial available catheters.

Catheter	Size(Diameter) Proximal/distal	Shapes available	Common use
Echelon	2.1/1.7 Fr, 2.4/1.9 Fr	3	Intracranial use, small vessels
Envoy	5Fr 6Fr	6	Guide catheter (conduit for placement of smaller catheters)
DAC	3.9 Fr 4.3Fr 5.2 Fr	---	Guide catheter (conduit for placement of smaller catheters)
Neuron	5Fr 6Fr	2	Guide catheter (conduit for placement of smaller catheters)
Simmons	4Fr 5Fr	3	Diagnostic cerebral angiography
Vertebral	4Fr 5Fr	1	Diagnostic cerebral angiography
Newton	4Fr 5Fr	5	Diagnostic cerebral angiography
Headhunter	5Fr	4	Diagnostic cerebral angiography

Table 5. Pre-procedure shaped catheters with constant curvature

Selection of the appropriate catheter or catheters necessary for an intervention depends on vessel size and tortuosity, considering the catheter stability during the procedure. For diagnostic purposes a 5 Fr or 4Fr catheter are use. Depending on vessel tortuosity different shapes can be suitable. For example, the *Vertebral* catheter can be used for all-purpose of diagnostic angiography but for patients with severe vessel tortuosity, the *Newton* catheter is more appropriate because of selective shapes available. To perform a procedure distally in the neurovasculature guide catheters are needed. They need to be stiff enough to allow small devices to pass within but also flexible enough to not cause vessel dissection. Normally, a 6Fr size is desirable to provide a good platform [4]. However, in some situations 5 Fr guide catheter may be employed because of vessel size. Among the reviewed commercial available guide catheters, Neuron guide catheter seems to be the prefer choice because it is extremely soft and flexible. However it is less stable than the others. Microcatheter's choice is based on the size needed for the procedure. Normally, the smaller the better choice, once small catheters are more likely to be soft and flexible. Nonetheless, smaller catheters can be less stable.

Control method

A high level of operation is demanded to maneuver selective catheters. The catheters featured in this section, normally, don't have a control handle at their proximal end. They consist in a tube from proximal to distal end, having a stiff proximal end that allows manipulation (Figure 6). The interventionist can hold, push and twist the catheter from its proximal end with his fingers, having 2 DOF movements possible: push/pull and rotation. Some catheters, additionally, can have a standard luer taper in the proximal end, which facilitates the attachment of accessories (Figure 7).

Figure 6. Catheter manipulation. Holding position. From this position the interventionist control the catheter by pushing and twisting. Adopted from [53]

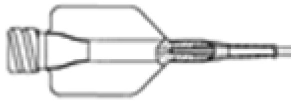


Figure 7. Standard luer tap - catheter proximal end [13].

Manipulation of the catheter is made over a guidewire, preventing the catheter tip from rubbing against the wall of the vessel. Figure 8 illustrates a technique to navigate an aortic arc with difficult anatomy using Simmons-2 catheter – the number 2 specifies the specific type of curvature of the catheter.

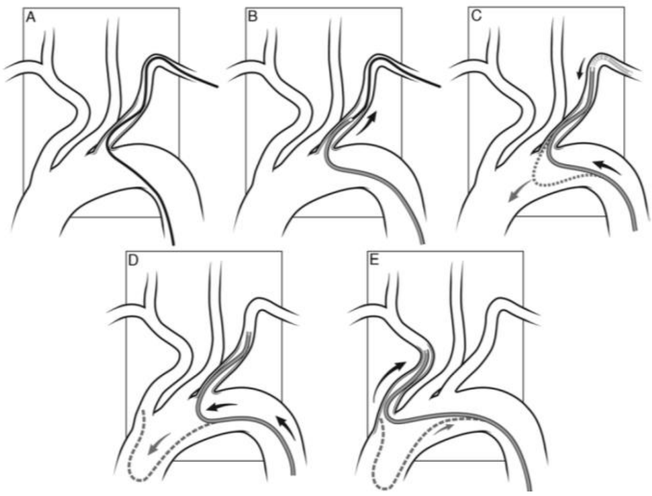


Figure 8. Illustration of the 8 Fr Simmons-2 catheter reconstitution in the left subclavian artery: A - a stiff guidewire is advance to gain distal access. B- Catheter is advanced over the wire. C- The wire is removed and the catheter is pulled back until the pre-shaped segment reaches the junction of the subclavian artery and aortic arch. At this point the catheter is pushed forward, bucking in pre-shaped segment and thus forming the Simmons-2 configuration. D- pushing forward the reconstituted catheter. E- Pushing forward until the catheter tip is proximal to the origin of the vessel of interest. Adopted from [54].

2.3.1.2 Variable curvature

While catheters with constant curvature can be used with only one specific tip configuration, catheters with variable curvature can be bent, by the interventionist, as different styles. The advantage of variable curvature catheters is that the interventionist

can shape it into the most useful curvature for the specific procedure. However, removal and reinsertion of catheter still is needed to change tip configuration.

The catheters in this category can be divided in a third classification of additional properties that are present in some of the products and patents grouped in this category. These additional properties are related to hemodynamic properties of tip. Two subdivisions are defined: 1) catheters with no additional properties and 2) flow direction sensitive catheters.

2.3.1.2.1 No additional properties

Some commercial catheters grouped in this subsection present two tip segments, such as the *Prowler* and *Excelsior* microcatheters. The distal segment fixed form while the proximal segment can be shaped in different configurations and for that they also fit in this section.

Size and motion ranges

Mainly catheters with sizes less or equal to 3Fr belong to this section, as presented in Table 6. Some differences in tip stability are found among these products. Tip's material construction influences the capacity to retain the shape. Fiber-braided catheters, as *Renegade* microcatheter, may retain their shape better than metal coil-braided (*Prowler* and *Echelon*) [6], having a more stable tip.

Catheter	Size Proximal/distal	Construction
Headway	2.4/1.7 Fr	Tapered PTFE Liner with Coil Reinforcement
Rebar	2.3/1.7 Fr	Stainless steel coil
Canata	2.5/2.5 Fr 2.8/2.8 Fr	Braided stainless steel, PTFE, PEBAX
Renegade	3.0/2.5 Fr	Fiber braid
Prowler	2.3 /1.7 Fr 2.3/1.9 Fr 3.0/2.3 Fr	Stainless steel braid, distal platinum coil
Excelsior	2.4/1.7 Fr 2.6/2.0 Fr	Stainless steel braid, distal coil

Table 6. Pre-procedure catheters with variable curvature and no additional properties.

Control method

Manipulation of these catheters is also realized over-the-wire by holding, pushing and twisting the catheter from its proximal end, as describe previously. These catheters don't have a control handle at its proximal end and a high level of operation is also demanded.

Shaping can be done by hand or steam. Catheter steam shaping technique involves a mandrel or stylette that is provided with the catheter. The malleable metal stylette is inserted into the tip of the catheter, and it is bent into a desired curvature. The

tip is held in its shape in steam for 30-90 seconds and then, it is cooled in sterile water. After cooling the stylette is removed [4].

2.3.1.2.2 Flow direction sensitive

Flow direction sensitive catheters present hemodynamic properties that confer flexibility to the tip in a way that it can be steered by blood flow. Typically they are used to reach target sites deep within the vasculature and indicated to treat arterio-venous malformations (AVMs), for liquid embolic delivery. AVMs high flow state permit rapid and accurate placement of the catheter to the desired position [6].

Size and motion ranges

Microcatheters presented in this section are ideal for vessels less than 2mm in diameter, once that due to their high flexibility and non-traumatic tip they can be advanced very distally in tortuous vessels. Tip stability of these catheters also varies between the types of construction of their tip. Non-braided catheters are more likely to retain their shape [6]. Additionally, each catheter can present different hemodynamic properties and there are ones that are considered more flow directed than others. *Magic* catheter is considered the best flow-directed system among the commercial available ones. It has an extremely flexible tip with a small bulbous structure.

Catheter	Diameter (Proximal/distal)	Construction
Ultraflow	3.0/1,5 Fr	Non-braided
Marathon	3.0/1.3 Fr	Nitinol braided
Magic	2.7/1.2Fr	Non-braided
Sonic	2.7/1.2 Fr	Braided with non-braided detachable tip

Table 7. Comercial flow direction sensitive pre-procedure catheters with variable curvature.

A changing flexibility and diameter shaft and an inflated balloon or other bulbous structure near the distal end allow the catheter tip to be carried along by blood flow, from low to high flow sites. This is present in the commercial products signed here and also in the '*Flow directed catheter*' patent [24], comprising a microcatheter catheter that can be steered without using of a guidewire, having an extremely flexible tip that allows flow guidance.

The '*Flow directed catheter guide with variable rigidity shaft*' patent presents a catheter that also has hemodynamic properties but without varying diameter [25]. It has on its distal end a deployable flow directed member that can direct the distal end of the catheter downstream following the blood flow in the vessel. Additionally it has a varying rigidity shaft, which can change from rigid mode to a more flexible, to function as guide catheter.

Control method

Flow direction sensitive catheters can also be steam shaped using a mandrel. At their proximal end they configure a luer taper. Manipulation of the catheter consists in the same movements as described.

2.3.2 Peri-procedure shaped catheters

Catheters which tip can be deflected into different curvatures, inside the body, are grouped as 'peri-procedure shaped' catheters. By manipulating the proximal end of the catheter from outside the body, the interventionist can control the tip deflection inside the blood vessel. Tip deflection control can occur either be passive or active. In the next subsections **passively shaped** and **actively shaped** catheters are described.

2.3.2.1 Passively shaped

A passively shaped catheter is a concept of a type of catheter which tip deflection occurs by interaction with patient's anatomy. Without a specific external control on the tip the catheter bends by itself when pushed against the vessel wall. It can be seen as a sort of 'intelligent-catheter' which by itself conforms naturally and smoothly the vessels curvature. In literature no product, prototype or patent of a catheter with these characteristics was found.

2.3.2.2 Actively shaped

Actively shaped catheters require external inputs to bend to a certain direction. The interventionist has active control over the tip deflection. Tip deflection may be a result of the external control of **internal properties** of the tip or a result of external control of **additional components** connected to the tip. These catheters are also designed to be manipulated over the wire, but with the possibility of in vivo deflection the same catheter can be used to fit several vessel bends.

2.3.2.2.1 Internal properties

According to the selected construction materials and structure, the tip is deflected by controlling its internal properties therefore it reacts to changes in physical properties, such as electric potential, temperature and pressure. Therefore, three subdivisions can be made to group catheters by their internal properties: **thermal sensitive**, **pressure sensitive** and **electrical sensitive**.

2.3.2.2.2 Thermal sensitive

Thermal sensitive catheters utilize materials that can be deformed when heated. Several prototypes and one patent were found describing the use shape-memory alloys (SMAs). These materials have temperature memory characteristics, being able to transform between a high temperature austenite phase and a low-temperature martensite phase. Austenite phase refers to the SMA structure when heated and a martensite phase refers to the crystalline structured acquired by the SMA after being rapidly cooled. SMAs actuation as part of the catheter is illustrated in Figure 9. When a SMA actuator is heated it shrinks and bends the catheter tip. Heat is generated through the application of a current *i*, by joule effect, which induces a phase transformation of the SMA actuator. More than one SMA actuator is usually integrated in the catheter tip to fully control its bending in 3-D space. Therefore, these catheters have a multi-link design to increase the bending angle and obtain complex shapes. The SMA actuator is naturally cooled when heating stops and the catheter can recover to its initial state. Figure 10 shows a flexible structure proposed by *Esashi et al* [55] that was widely adopted by most of these catheters.

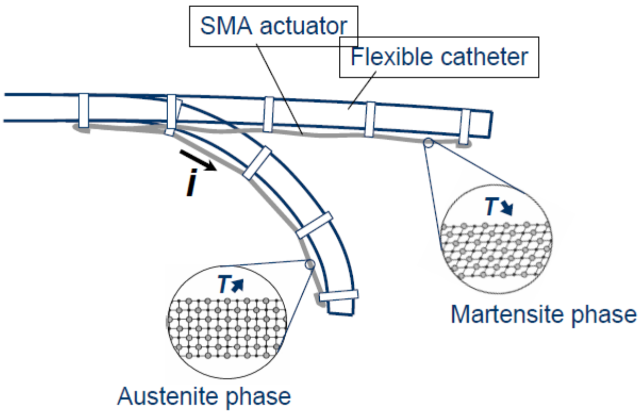


Figure 9. SMA actuated catheter – working princple. Adopted from [33].

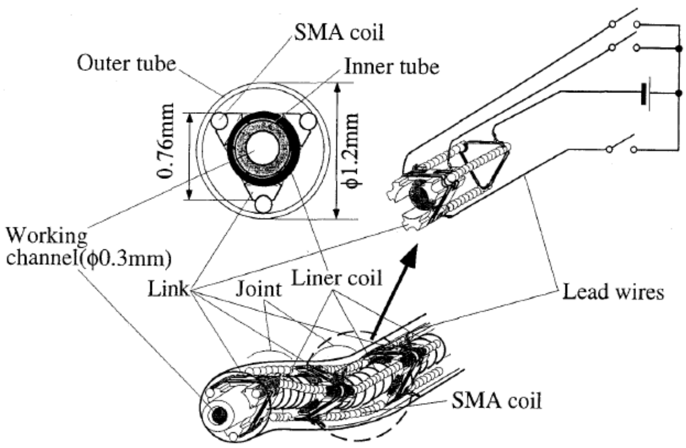


Figure 10. Structure of a SMA catheter. [55]

Articles and patents found with this steering mechanism present differences concerning the outer diameter and inner working channel, which is related to the type of

SMA actuator used [26-33]. The challenge is to reduce the outer diameter without reducing the inner working channel of the catheter, as required for neurovascular procedures.

Size and motion ranges

Different approaches to SMA-actuated catheters have been described and tested. Table 8 shows the main characteristics of the prototypes and designs featured in this section. These catheters differ in size, actuator shape type and maximum bending degree.

Catheter	External diameter (Fr)	Actuator Shape	Maximum Bending angle (deg)
Fukuda,[28]	4	Wire	32
Mineta, [30]	2,7	Flat Spring	35
Fu, [32]	3,9	Coil	90
Haga, [55]	4,8	Coil	45
Szewczyk,[33]	3,3	Wire	>70
Szewczyk,[33]	6	Wire	---
US6159187A, [26]	2-5	Coil	60
US7037290, [27]	6	Wire	---

Table 8. Characteristics of the different catheters actively shaped by thermal sensitive properties.

Wire shaped SMA actuators were first exploit by *Fukuda et al* [28]. With this design small bending degrees were achieved. Coil shaped actuators present a high strain capability and so they were also adopted in some catheters configurations. A multi-link structure (Figure 10) based in these actuator was first presented by *Haga* et al [55]. To produce smaller catheters SMA actuators with a shape of a flat spring were also approach. *Mineta* [30] presents the smallest catheter that uses this actuator. However, deflection of the catheter is limited to a smaller range.

Control method

Control mechanism by which the interventionist can manipulate the catheter has not been well presented out yet. However, *Kennet C. Gardeski* patent [27] describes a hub type that has an electrical connection to give electrical power to bend the catheter (Figure 11). The catheter keeps straight when no electrical current is applied. This patent describes a SMA based catheter with a specific design application to cardiology, for the placement of cardiac leads. This patent is referred here to give an idea of the one possible handle design for thermal sensitive catheters. Despite the handle design the control method for the interventionist relies on controlling the electrical power by turning it on and off and controlling its magnitude.

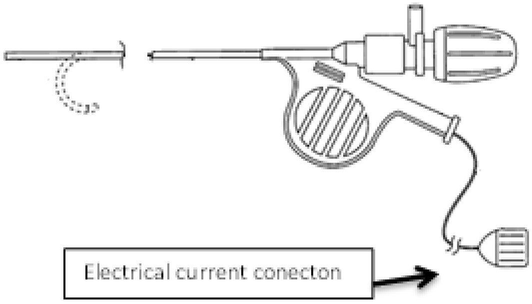


Figure 11. Universal hub for manipulation of a shape memory alloy steerable catheter presented at patent [27].

2.3.2.2.3 Electrical Sensitive

Electroactive polymers (EAPs) can also be used to steer catheter tips. These polymers can be stimulated by an electrical field and change their size or shape. They are use in actuators with application to catheters. *Guo et al* presented the first EAP actuator, employing ionic polymer- metal composite(IPMC), an ionic EAP, in an actuator for a catheter [36]. Figure 12 shows the mechanism of bending of this polymer. An electrical potential, around 1-2V, is applied across its thickness in an aqueous environment, triggering large bending deformation toward the anode.

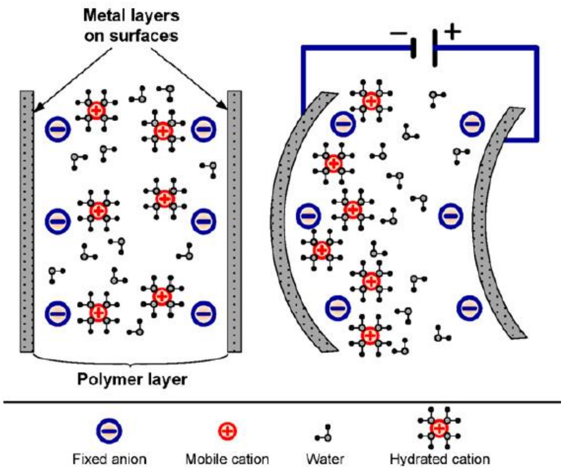


Figure 12. IPMC bending mechanism. From [56]

'*Micro-steerable catheter'* patent [35] also presents an EAP-based catheter based on different types of EAPs. Additionally, the invention presents a combination of an EAP with an SMA. In the absence of the applied electrical field, shapes resulting from bending actuation may be maintained by the memory effect of SMA.

Another approach of an electrical sensitive catheter is presented in patent [34]. This invention describes a balloon microcatheter made using nanotechnology. It incorporates carbon nanotubes arranged in layers within the wall of the distal portion, configured to electrical stimulation. In this manner, this catheter can also be steered by application of an electrical potential.

Size and motion Ranges

Fukuda et al described 3 prototype models of 3 Fr, 4 Fr and 6 Fr in outer diameter and they achieve a maximum bending degree of 42.3°. This is the only prototype featured in this section. The patents grouped in this category did not contain size and motion ranges information.

Control method

Manipulation of these catheters relies on the control of the applied electrical field. Only a few prototypes were found in this section, thus, the control method by which the interventionist can manipulate the catheter has not been well described yet. Additionally, EAPs actuators have not been widely investigated.

2.3.2.2.4 Pressure sensitive

Hydraulic control of catheters is obtained by pressurization of the tip structure. The flexible tip of the catheter can be bent in response to the fluid pressurization of a driving tube. Bending direction will be opposite to the location of the pressurized tube. These tubes are flexible and are connected to an electro-hydraulic valve that allows pressure control from outside the body. Two prototypes and one patent are featured in this section.

'*Steerable catheter devices and methods of articulating catheter devices'* patent [37] configures a pressure sentive catheter, with one control tube having a proximal opening and terminating in a chamber between a first and second end portions of the catheter. The distal end is elastically distensible under an internal fluid pressure. A change in the internal fluid pressure of the chamber will cause bending of the tip.

Another similar mechanism is proposed by *Haga et al* [39]. Their hydraulic-driven catheter consists in Ti-Ni super-elastic alloy tube hollowed out by femtosecond laser ablation covered with a thin silicone rubber tube. This catheter has one bending DOF as showed in Figure 13 . The tip bends in one by suction of the water filled inside the catheter.

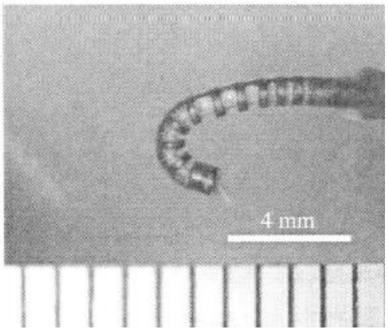


Figure 13. Bending motion of hydraulic driven catheter with one bending DOF. From [39].

According to this steering mechanism, the number of driven tubes had to be as much as bending segments added to the catheter for better flexibility. Therefore, a different strategy to allow bending more than one segment with only one control tube

was designed by *Ikuta et al* [38] based on a band-pass valve (BPV) - Figure 14. Each active segment has bellows-shaped bending actuator and a micro valve to control the opening and closing of the channel. Each micro valve has its range of pressures under which they open. All segments are connected to a single driven tube and each one of them as its own BVP. The BVP consists in a low-pass valve (LPV) and a high-pass valve (HPV) to respectively close and open in response to the applied pressure. There is no overlap between each segment range pressures, so each one is controlled independently.

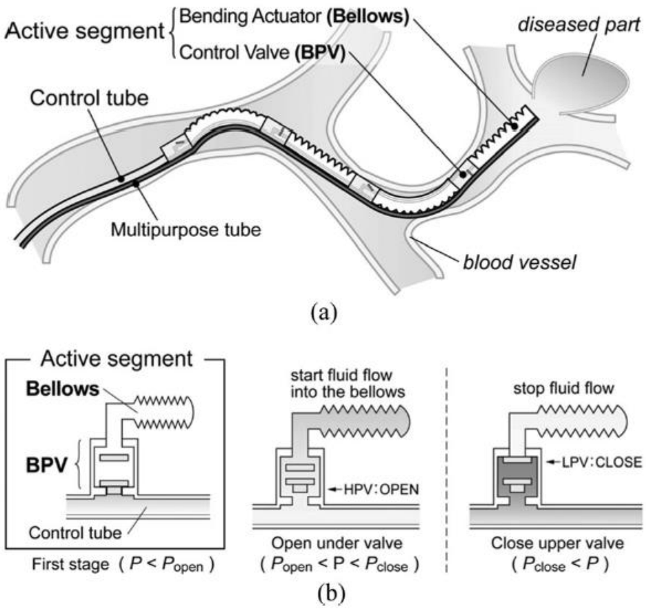


Figure 14. Basic concept of the hydraulic driven catheter (a). Drive principle of each bending segment. [38]

Size and motion ranges

Catheter	Size (outer diameter) (Fr)	Maximum bending angle (deg)
Haga, [39]	2.82	160
Ikuta, [38]	6	170

Table 9. Data of two hydraulic-driven catheters found in literature.

Haga's and *Ikuta*'s results showed sizes compatible to neuroendovascular procedures and a wide range of deflection (Table 9). Haga's prototype can feature a microcatheter and Ikuta's one can serve as a guide catheter.

Control method

Interventionist's manipulation of these type of catheters relies on controlling the pressurization of the control tube. *Haga* presents a control system that consists in a conventional inflator for balloon catheters connected to the proximal end of the catheter tube. These handle is showed in Figure 15 and allows pressure control. This handle functions has a syringe. The interventionist can manipulate it by push and pulling the plungner, controlling the pressure inside the control tube. The bending angle of the tip depend on the input pressure and input time.

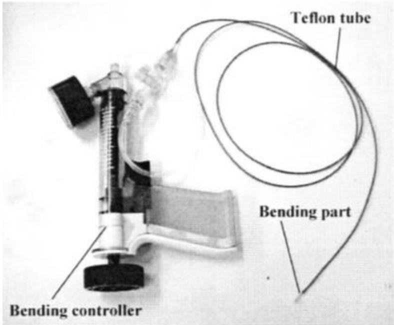


Figure 15. Bending controller of an hydraulic driven catheter developed by Ikuta et al [57].

2.3.2.3 External/additional components

Catheter tip steering with additional components can be realized mechanically or with a motor. This section is subdivided into **mechanical shaping** and **motorized shaping**.

2.3.2.3.1 Mechanical Shaping

Mechanical shaping of catheter's tip can be done in two different ways: a) using pulling cables or b) by the relative movement of tubes. In literature, mechanisms using pulling cables have been widely developed and researched and a lot of patents were found. The review patents configuring puller wire systems are referenced in [41-44] [46-50]. Additional one product with a puller wire system is also presented [40]. Steering by relative movement of tubes was also found in some patents [45, 51].

a) Pulling cables

One or more pulling cable can be used to steer the catheter. Typically, the cable is attached to the distal end of the catheter in one end, and to a mechanism in the handle at the other. By tensioning selectively the cable or one of the cables, tip bending will occur in a desired direction.

Three types of catheters can be considered, concerning the possible curvature directions: unidirectional, bi-directional or multidirectional. The number of pulling cables and the mechanism controlling them will determine the possible directions.

Unidirectional catheters can be pulled into a defined curve using one pulling cable [43, 44]. The patent referred in [43] is an example of a unidirectional catheter (Figure 16). This catheter has an external cable that when is pulled causes tip bending up to 90 degrees in one direction in the same plane. An additional feature of the catheter is the use of the pulling cable with a second function. When the cable is pushed it functions as an external guidewire, facilitating the forward movement of the catheter.

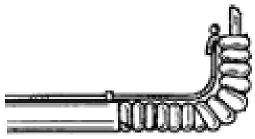


Figure 16. Unidirectional bending. From [43]

A tip can also be pulled in two directions using one or two pulling cables. '*Manipulatable delivery catheter for occlusive devices*' patent [42] presents a catheter with one pulling cable. In this design patent the cable is configured inside a tube structure, which when manipulated flexes the tip. Tip bends in one direction when pulling and in the other direction when pushing the cable tubing (Figure 17). The *Enzo Courier* microcatheter [40] is an example of a bi-directional catheter with two pulling cables. This is the only actively shaped catheter that is commercial available for neuroendovascular procedures. It configures two cables mechanically linked to the handle; each one bends the tip in one direction.

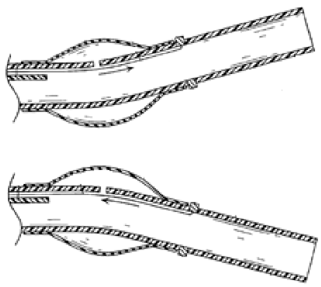


Figure 17. Bi-directional bending. From [42]

Adding more puller wires the catheter can be bent in multi-directions [49] [50]. The '*Steerable catheter with rapid exchange lumen*' patent projects a 4-way catheter, this is, a catheter that can be deflectable in four directions by utilizing four puller wires. This mechanism is already applied to some commercial products for cardiologic applications, also with robotic control [3]. However complexity increase with the adding of puller wires making miniaturization of this type of catheter not suitable to the neuroendovascular approach.

b) Relative movement of tubes

Some actively shaped catheters consist in an inner and an outer tube and deflection is done by moving the inner tube relatively to the outer tube. The '*Steerable Catheter*' patent [45] describes a catheter that is bent by longitudinal displacement of the inner tube relative to the outer tube. As showed in Figure 18, the inner tube presents a shim that came out from the outer tube, allowing pull the inner tube. When the inner tube is pulled the catheter bend right and vice versa. Another patent, the '*Steerable Delivery Catheter*' [51], also presents this type of mechanism but configuring an outer tubular sheath that once compressed will induced tip bending.

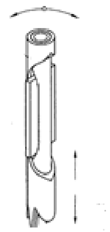


Figure 18. Relative movement of tubes. From [45]

Size and motion Ranges

In general, mechanical shaping catheter can be bent up to 90° in one or more directions. The only product found is available in two sizes: 3.0 Fr and 2.9 Fr. Others specific values of size weren't found in the patents.

Control method

Interventionist's handle movements match with tip deflection. For mechanical shaping catheters, two different control methods were found applied in different handles design (Table 10). The control methods are base in two types of movement: Sliding or push/pull movements and rotation movements. Sliding control method can executed by directly manipulation of the pulling cable of the catheter (which is accessible at the proximal end) or through a sliding motion of a knob mechanism (Figure 19). Rotation movements through a knob will indirectly push or pull the puller wires of the catheter. With one knob two puller wires can be controlled. *Enzo Courier* microcatheter control is done by interventionist's manipulation of a knob with the fingers. Thus by turning the knob one of the cables is pulled, causing the tip to bend in one direction or another.

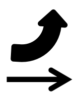
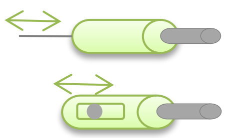
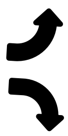
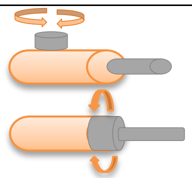
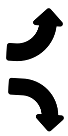
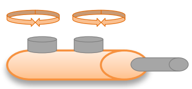
Control method	Handle (proximal end)	Tip bending (distal end)	Tip classification according to bending directions
Sliding (Push/pull)			Unidirectional
			Bidirectional
Rotation			Bidirectional
			Multidirectional

Table 10. Mechanical control methods: illustration of the handle designs and their maneuver outcome in the tip bending motion.

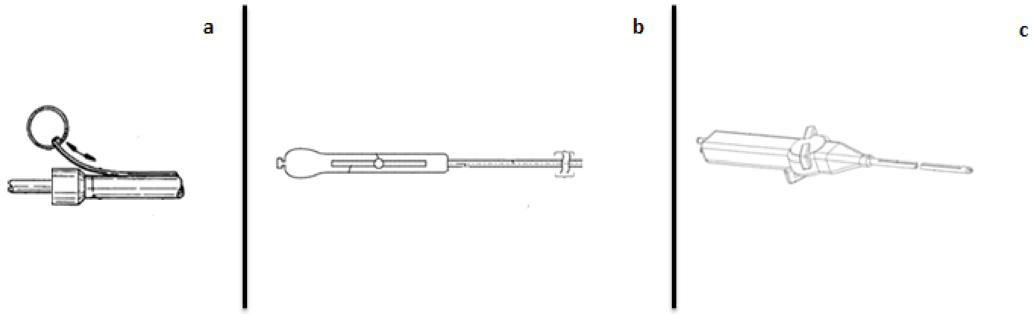


Figure 19. Example of different embodiments of the handle according to the control method: a. The handle consists of a cable that slides; b. The handle configures a sliding knob; c. handle configuring a rotation knob.

2.3.2.3.2 Motorised Shaping

Motors have also been approached as possible actuators to steer devices [52, 58]. *Yun et al* [52] presented an ultrasonic micromotor has a possible actuator for steering a catheter or guidewire during navigation. A cylindrical tip that can rotate and be bent in various directions can be achieved with this motor.

Yun's motor prototype (Figure 20) consists of a ball rotor, a cylinder stator and a PZT element (C–203 lead zirconate titanate, Fuji Ceramics, Ltd., Tokyo, Japan) and can be operated with three lead wires. The ball rotor allows tip rotation around three axes. The PZT and cylinder assembly forms a 'tilt' element that can be bent, changing the orientation of the tip motion. Two input electrodes are present in the PZT element. Application of a voltage potential on the electrodes causes this element to deform. The motion generated by the PZT's deformation causes bending and axial deformation in the cylinder mounted atop of it. Thus, cylinder tip motion orientation can be controlled by changing the phase between electrodes.

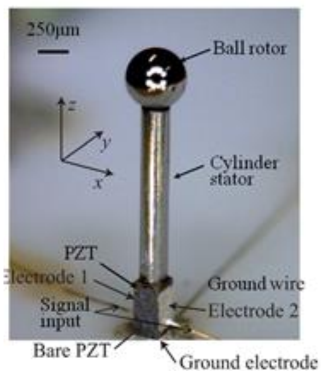


Figure 20. Multi-degree of freedom motor. From [52].

A motor as the one described may offer a great motion range to the catheter allowing control bending and rotation. However, there are some difficulties in the control-ability of the motor that still need more investigation and development.

2.4 Discussion

A detail description of each type of catheters was given according to the classification showed in Figure 4. Table 11 summarizes the comparison between catheters, which is based on the five design requirements listed in the “Design challenges” section of the chapter 2. The discussion will follow each topic of the comparison table and, additionally, safety related issues will be also approached.

Design characteristic (see section “design challenges” in chapter 2)				1 – possible to miniaturize	2 – Stable Tip	3 – Precise tip control	4 – Easy to maneuver(control method)	5 – Simple to produce
Pre-procedure shaped	Constant curvature			++	++	-	-	++
	Variable curvature	No additional properties		++	+	-	-	++
		Flow direction sensitive		++	+	-	-	++
Peri-procedure shaped	Passively shaped			?	?	?	?	?
	Actively shaped	Internal properties	Thermal sensitive	++	?	+	?	+
			Electrical sensitive	++	?	+	?	+
			Pressure Sensitive	++	?	+	?	+
		Additional components	Mechanical Shaping	+	?	++	?	+
			Motorized shaping	?	?	?	?	?

Table 11. Subjective evaluation of the Pre-procedure and Peri-procedure shaped catheters over the five design requirements of an ideal catheter for neuroendovascular procedure. The scores are applied as follows: (++) has the characteristic; (+) has the characteristic but less compared to others; (-) unlike to have the characteristic; (?) lack of data or not possible to judge.

2.4.1 Miniaturization

To navigate small vessels in neuroendovascular procedures, sizes less than 3 Frenches are required. Thus, when considering a catheter design for the possibility of miniaturization needs to be evaluated. Miniaturization of a catheter design depends on its internal structure and manufacturing processes.

Catheters classified as pre-procedure shaped, typically, consist of a simple flexible tube that can be easily constructed in different sizes, whereas the smaller catheters found are featured in this category. Over the peri-procedure shaped catheters, more complex structures are found. Complicated internal structures increase the difficulty in manufacturing and assembly. Catheters grouped in the ‘actively shaped catheters by internal properties’ can realize miniaturization; however, durability and reliability of the materials at small sizes must be taken into account. Catheters configuring a puller-wire system for mechanical shaping must be tick enough to provide adequate tensile strength for reliable cyclic operation, so that it cannot be too small. As for motorized catheters, micromotors under study still may fit requirements for miniaturization.

2.4.2 Stability

Stability of pre-procedure shaped catheters is evaluated in several articles. Typically, stability of a catheter is evaluated by its capacity of holding the tip shape. Typically, constant curvature catheters present the more stable tip when compared with catheters with variable curvature [59]. Catheters that can be shaped into several shapes by the interventionist retain less their shape, being less stable. Additionally, there are little differences in tip stability among the same type of catheters due to the tip construction as described in the previous chapter.

There is lack of information about peri-procedure shaped catheters, since most of them are in a patent or prototype phase. Only one commercial product featuring this section was found and one reference reporting its clinical use [60]. Michael E. Kely and David Fiorella described their successful attempt to coil a traumatic ophthalmic artery pseudoaneurysm with the Enzo microcatheter [40] after the failure of the procedure with the use of two pre-procedure shaped catheters. Using the mechanical shaping catheter, Enzo microcather, they reported that the tip remained very stable.

2.4.3 Control precision

Tip deflection mechanism can offer a precise control of the tip range deflection despite the method for its manipulation by the interventionist. Mechanical shaping catheters have a transmission mechanism that is easy to exploit, allowing a high precision control with fast response. In the same way, pressure sensitive catheters can realize fast and precise control but they still raise some difficulties in their driving mechanism. The driving tube is extremely thin and must be filled with liquid and sealed, which add some complication to the system. Catheters actuated by an electric circuit, as thermal and electrical sensitive catheters, have a multi-physical procedure to carry out control and its performance rest upon the capability of the materials. Thus, these catheters present difficulties to achieve good precision. SMA-based catheters have a low response time since their actuation is temperature-related, and in small devices is not possible to force cooling down. Comparatively, EAP-based catheters have a much faster response, but they don't generate larger forces. As for the motorized catheters, they can offer a higher precise control but still need further development regarding control-ability and safety.

Pre-procedure catheters cannot offer a precise control on the tip by their deflection mechanism itself. Inside the body these catheters have a fixed shape and the interventionist has no direct control on the tip. Thus, the precision of control relies on the expertise of the interventionist in manipulate these catheters.

2.4.4 Control method

Each type of catheter offers a different control method for interventionist's maneuverability of the instrument. Human performance with medical instruments have

been studied, however, there is lack of data about control methods for catheters manipulation that allows comparing the different types of catheter.

Doctors who specialized in neuroendovascular procedures require a high temporal demanding training. They have to be able to maneuver catheters and perform diagnostic using imaging. Pre-procedure shaped catheters require a high level of operation by the interventionist, demanding a high level of training. Since their tip cannot be dynamically deflected when inside the body, these catheters don't have a specific handle for maneuvering. The control method relies on direct manipulation of the catheter tube on its proximal end with twisting and push and pulling movements.

Peri-procedure shaped catheters can offer a control method that allows specific control on the tip instrument from outside the body during the procedure. This is an advantage over the pre-procedure shaped catheters, which allows the same instrument to conform several vessel curvatures inside the body without the need to retrieve the catheter. However, there are different control methods that can be applied to this type of catheter design. Thermal and electrical sensitive catheters control methods are not very clear yet in literature and they may also require a high level of operation once it relies on manipulation of physical properties. Pressure sensitive catheters may consist in the manipulation of a simple syringe interface. Relatively to mechanical shaping catheters, two control methods are described in the literature, which are summarized in Table 10, whereas different handles design adopted configuring each control method are illustrated. Each handle require simple manipulations with hand and fingers. Nevertheless, it is unknown how intuitive and accurate the control methods are and which handle design better applies the control method in terms of physical demand to the user.

2.4.5 Production

Manufacturing process becomes complex with the complex internal structures of the catheters. Comparing, pre-procedured shaped catheters are simpler to produce and less expensive. However, EAPs are inexpensive and suitable for disposable used when compared to the other types of peri-procedure catheters.

2.4.6 Safety

All of the presented catheters have a potential risk of perforation, since the operation of these catheters still depends upon interventionist's experience and decision and the contact force between the blood vessel and the catheter cannot be judged accurately. This risk, however, can be minimized by a better and more precise control of the tip. Other factors affecting safety may rely on the deflection mechanisms. Thermal and electrical sensitive catheters may interfere with the blood environment by heat transfer or electrical leakage that may cause danger.

2.5 Conclusion and research challenge

Pre-procedure shaped catheters are the currently used in clinical practice. However they have limitation over the precise control of the tip. Their limitation regarding the unchangeable tip inside the body during a procedure also raised further research and development to other types of catheters. Peri-procedure shaped catheters offer the possibility to select direction at the distal end, reducing complication of the current methodologies. Table 11 shows, however, that any of these catheters achieves all the requirements of an ideal catheter. Between them, mechanical shaping catheters stand out regarding the precise control of the tip. Currently, several commercial products based in these type of catheters are available for application in cardiology [61, 62]. For neuroendovascular procedures only one commercial product was found but there is few data of its use in clinical practice. Catheter size still is not suitable for every procedure. In terms of safety, mechanical shaping catheters and pressure sensitive catheters are superior to the other peri-shaped catheters.

Several deflecting mechanisms were described along the review, but little information was found about the control methods of such instruments. Only two control methods applied in mechanical shaping catheters design are clearly described in the literature through the description of different handles design, as listed in Table 4. However, it is unknown how they perform and how is human interaction with such control methods through each handle design.

In the design development of a new miniaturized mechanical shaping catheter, decision between control methods needs to be taken. In one hand, the control method applied to the catheter design may be the easiest and cheapest to develop and in the other hand it must fit the needs of the operator in terms of intuitiveness, mental demand and learning curve. Moreover, the handle design should give the interventionist the most comfortable and easiest maneuver for the precise use of the control method. Ergonomics of handles designs have been assessed in various studies that compare instruments in minimally invasive surgery. Pronounced ergonomic problems have been pointed out a variety of instruments with considered inefficient handle designs, that difficult the surgeon manipulation [63-65]. Poor handle designs can lead to pressure areas, nerve irritation and rapid fatigue, increasing the number of errors [66]. Specifically for neuroendovascular procedures no studies comparing different handles were found.

The importance of a supported decision in design development is to adapt the instrument to the interventionist hand, so that fatigue and muscular injuries can be avoided. The lack of data in literature reporting the use of the control methods for steerable catheters challenges a prior study before going further in a steerable catheter design, motivating the development of an experiment to compare different handles designs, accessing the use of rotation and sliding control methods.

3 Experiment goal – Research question

A clear motivation for developing a study on the use of control methods for steerable catheter was derived from the literature review. Catheters classified in the previous review as mechanical shaping catheters, can be very close to become the next generation of catheters for neuroendovascular procedures. However, its implementation on the clinical practice depends on how intuitively and accurately can be used by the interventionist.

The manual control of these catheters is based in two different control methods: rotation or sliding of o knob. Different handles designs can be achieved for implementing these control methods. Assessing the performance with the two control methods is important to support user oriented design decisions, contributing for development of more intuitive and effective control method.

The aim of this experiment is to answer the following question: which control method is more intuitive and effective for catheter manipulation in Neuroendovascular Procedures? The handle design that interfaces the control method applied to deflect the tip also influences the intuitive feeling of the control method. Thus, more than one handle design was considered for each control method, with a second objective of retrieving information about which handle design contributes for the easiest maneuver of the control methods.

4 Experiment Design

An experiment was designed to compare two control methods for catheter manipulation. The experiment was conducted at the department of Biomechanical Engineering of the Technical University of Delft, section of minimally invasive surgery and interventional techniques. A setup was built for measuring performance and a protocol was designed to realize the experiment.

4.1 Setup

The setup consists in three main components: - **Handle**, with which a user can maneuver the catheter, using different control methods; - **catheter platform**, which mimics the catheter inside of a blood vessel, allowing the forward and backward movements; - **visualization software,** which simulates an endovascular image on screen.

Figure 21 outlines the experimental setup design. At the proximal end, different handles can be connected to a rod that is mounted horizontally in a platform that allows it to be pushed and pulled, mimicking the catheter shaft. The visualization system consists in a vessel and catheter tip model displayed on the screen according to the catheter manipulation through handle maneuvering.

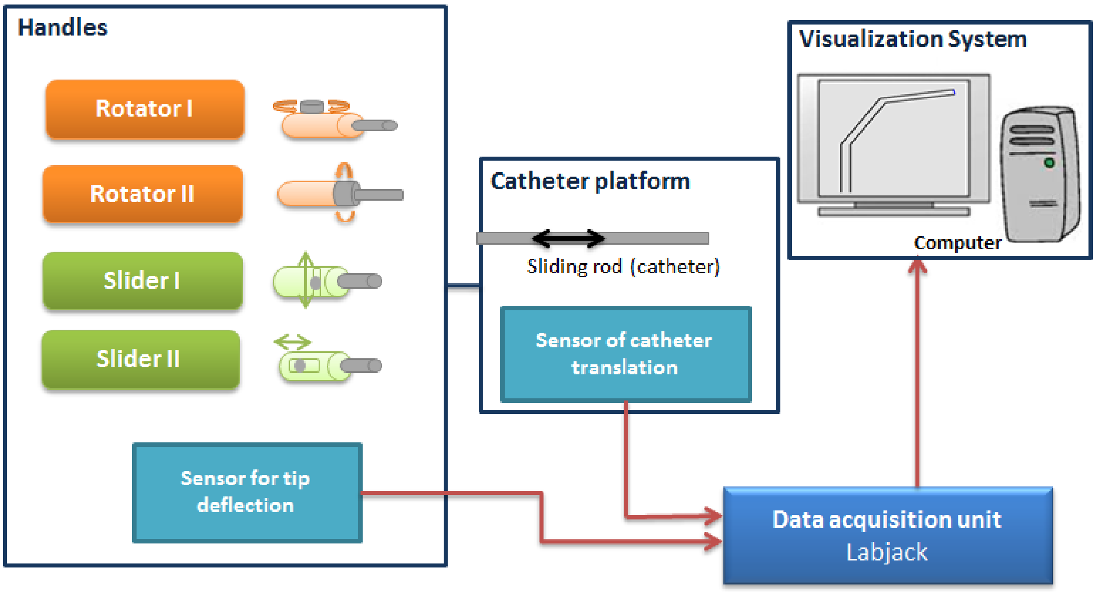


Figure 21.Experiment setup design.

4.1.1 Handles design

Four handles designs were built based on rotation and sliding control methods for a bi-directional steerable catheter. Each handle was named according to the control method applied, as showed in Table 12. Different position of the controller knob defines the

four designs. Rotator I, configures a rotary knob on the top of the handle and Rotator II configures a similar know in the front of the handle. The sliding knob in the handle Slider I is disposed to travel horizontally. Slider II present the sliding knob that travels vertically.

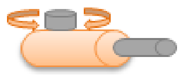
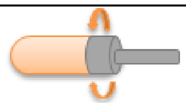
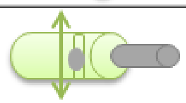
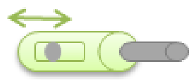
Control method	Handle design	Handle name
Sliding		Slider I
		Slider II
Rotation		Rotator I
		Rotator II

Table 12. Different handles designs for the two control methods and the respective name.

The final prototypes of the four handles are presents in Figure 22. Each constructed handle consists of a hard plastic tube (d=20 mm) that can be held by one hand, configuring one controller knob that can be manipulated with the fingers.

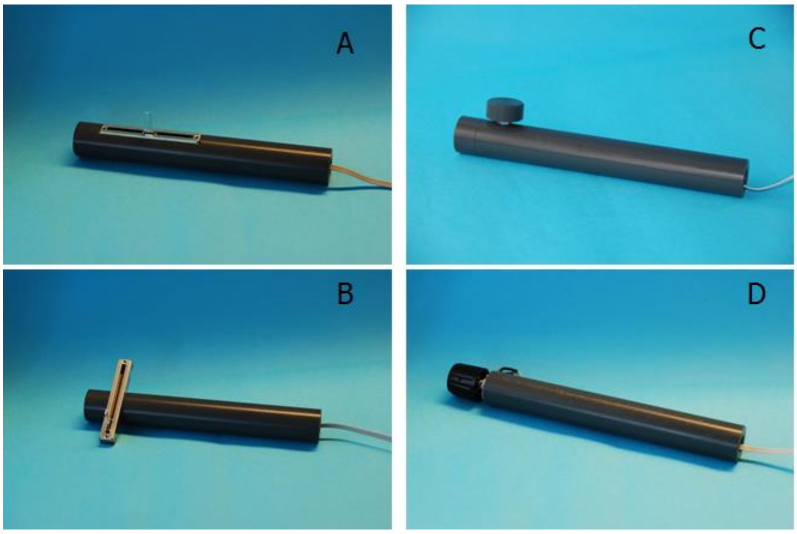


Figure 22. Handles final prototypes: A- Slider I; B - Slider II; C - Rotator I; D - Slider II

Manipulation of the controlling knob of each handle is accessed with a sensor connected to the knob. The knob of ‘Rotator I’ and ‘Rotator II’ is attached to a rotary potentiometer sensor, which measures the controller manipulation. The controller of the ‘Slider I’ and ‘Slider II’ handles consists of a slider potentiometer. A voltage signal between 0-5 Volt is read out from each sensor through the data acquisition unit and used to map the deflection movement of the catheter tip on the screen.

Sensors were chosen based on the following characteristics: track resistance between 5k to 10 k ohm and a linear electric characteristic. Additionally the added friction was taken into account to be similar for all sensors. The mechanical range of the rotary potentiometers is limited to one turn of 270° and the slider potentiometers have a travel length of 45mm. Tip deflection is bidirectional and the straight position corresponds to the middle of each controller.

4.1.2 Catheter platform

The catheter is mimicked with a rod, as showed in Figure 23. The handles can be connected to this rod at its proximal end. The distal end of the rod is attached to a connector fixed on a sliding wire mounted between two rollers in a metallic platform. The two rollers allow the forward and backward movement of the rod.

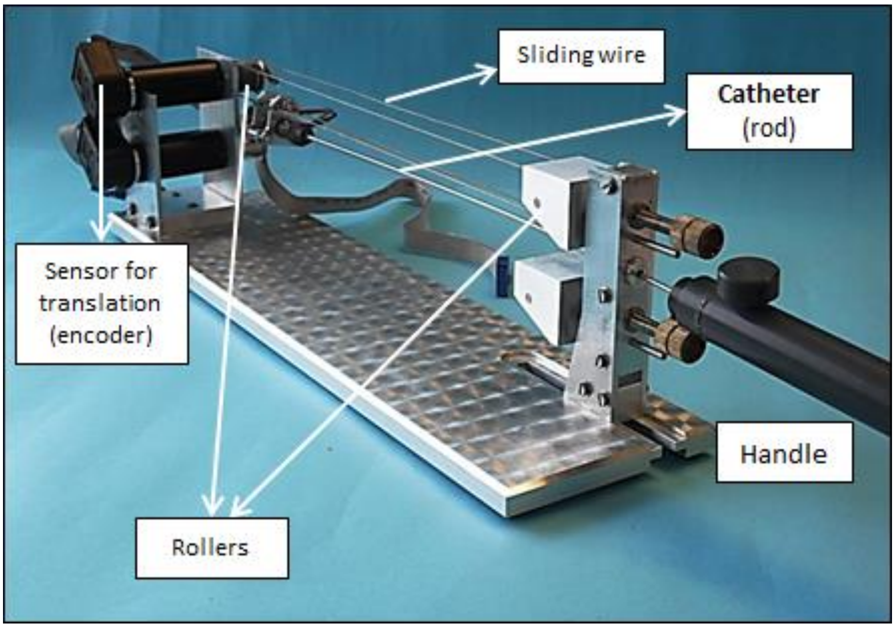


Figure 23. Catheter platform and its components with respective legend. The attachment with the handle is also shown.

One of the rollers is linked to an encoder that is read out to measure the position of the distal end of the rod. The total travel length of the catheter is 25 cm. The encoder sensor can precisely give information about how many centimeters the catheter moved backward or forward. When the catheter is pushed or pulled it makes the wire to slide and rotate the rollers. As the encoder is connected to one of the rollers, it also rotates and for each complete revolution 2000 counts are generated and read by the acquisition unit. These counts are then translated to the number of centimeters moved with the catheter.

The catheter platform was already available in the laboratory of Minimally Invasive Surgery and Interventional Techniques of the Department of Biomechanical Engineering of the Faculty of Materials, Maritime and Mechanical Engineering of the Technical University of Delft. The platform configures additional components that were

not used, as an additional level of rollers that can also configure an encoder, and a sliding wire. Additionally, each encoder is coupled to a motor, which was also not used.

4.1.3 Visualization System

The imaging system allows the interventionist to have visual access to the vessels and the instruments inside it. Currently, a 2D fluoroscopy image is used for instrument guidance inside the vessels. Typically, in the image a colored delineation of the vessels is visible by the contrast and the catheter tip is visible as a line.

For this experiment a visual model was built (Figure 24). The vessels to be navigated are represented as a set of lines that delineated the vessel lumen, within which the catheter is navigated. For the catheter only the tip is represented on the screen. This line positioning in the screen is a result of the catheter manipulation, modeled by a mathematical equation.

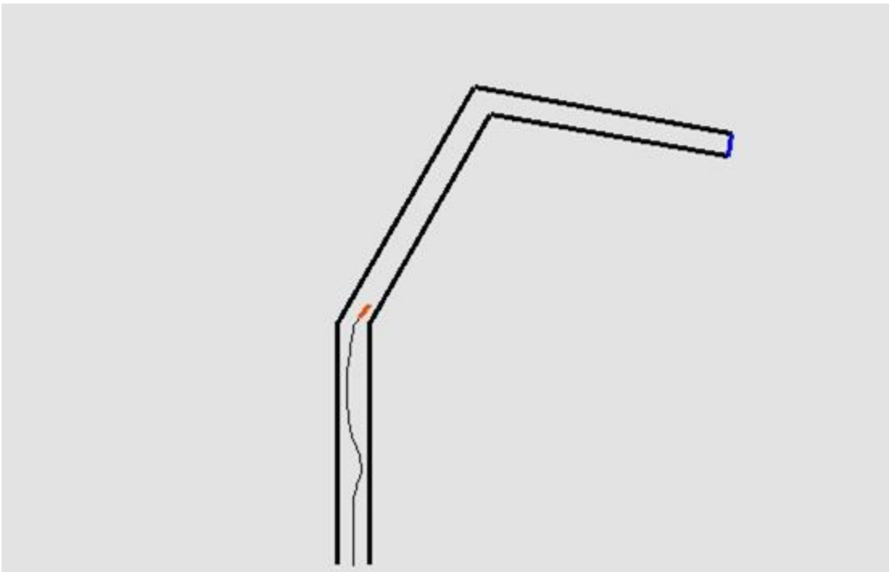


Figure 24. Visual model of vessel and catheter tip (in red) on the screen.

Image is displayed on the screen at a frame per second rate of 10. The model consists of lines that delimit the vessel path and marks the catheter tip. *Windows forms application* was used for displaying the interactive image and the model was programmed in *visual C#.*

4.1.3.1 Vessel model

The main suppliers of blood for the brain and neck are vessels derivate from the common carotid carotid artery (CCA). This artery bifurcates into an internal carotid artery (ICA) and an external carotid artery (ECA) at the level of the fourth cervical vertebra. The internal carotid takes a more internal path upward in the brain and the

external carotid gives rise to branches more closely to the surface, supplying the neck and face.

The vessel model was designed to represent the path of three consecutive vessels with different geometries. To approach the neuroendovascular procedures, the design was based on the path to reach the internal carotid and its branches, as they represent the main blood suppliers of the brain. The internal carotid artery ends with a bifurcation into the middle cerebral artery (MCA) and the anterior cerebral artery (ACA).

Two vessel sequences are represented at Figure 25, starting in the CCA artery and ending in one of the branches of the ICA bifurcation. From these two vessel sequences were used as reference to build two different vessel models, based on the geometric relation of these arteries. The inclination angle between branches and the respective width was searched in the literature, and the relations between each parent vessel and its branch is presented at Table 13. With these geometric relations the two models on Figure 26 were programmed and used in the experimental procedure as different tasks for the use of the control methods.

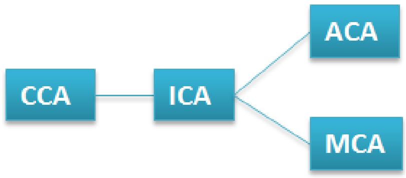


Figure 25. Representation of the blood brain vessels sequences used as reference. CCA – common carotid artery; ICA- internal carotid artery; ACA- anterior cerebral artery; MCA – middle cerebral artery;

Origin	Destination	Diameter relation to the parent vessel	Angle (°)	Reference
CCA	ICA	0.85	30	[67]
ICA	ACA	0.65	120	[68]
ICA	MCA	0.86	50	[68]

Table 13. Diameter relation between each pair of parent/daughter vessels.

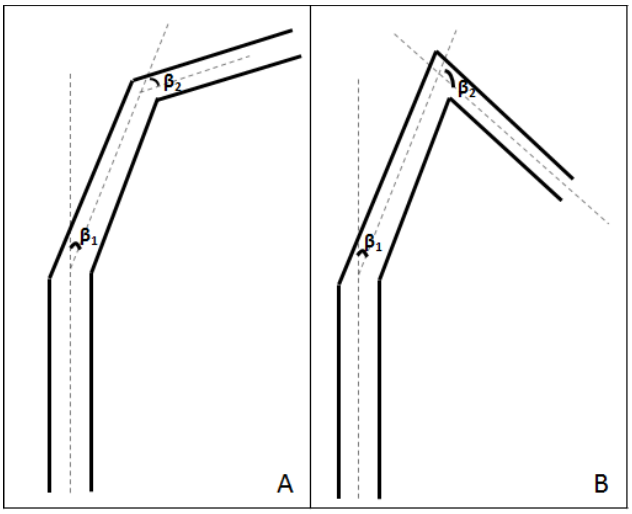


Figure 26. Vessel model designs; A- vessel model 1: CCA-ICA-MCA (β1=30°, β2=50°); B - vessel model 2: CCA-ICA-ACA (β1=30°, β2=120°).

4.1.3.2 Catheter model

The control methods are focused on the deflection of the tip. The aim of this experiment was to assess the main differences between the different handles and control methods. So the manipulation during the experiment had to be focused on steering the tip. Catheter behavior was not modeled approaching a real situation, where tissue deformation and the interaction of the catheter shaft with the vessel wall should also be taken into account. These interactions influence the movement of the catheter. Nevertheless, the aim was to provide a representative visual interaction for the user to maneuver each controller, in the same conditions.

Only the catheter tip was modeled to appear on the screen, according to the user input. Two movements were possible for the user: deflection of the tip by maneuvering the handle controller; move catheter forward or backward, by pushing and pulling the handle. These movements were the input for the catheter tip motion on the screen. To describe the tip motion on the screen a mathematical equation was defined and programmed for user input. The catheter tip bending can be precise controlled and when the catheter is pushed forward the tip deflection degree will determine the direction of the movement. As the forward movement occurs, there is change in the tip position and as its deflection angle remains constant the trajectory direction keeps changing, Figure 27. For controlling the direction it is necessary to correct tip orientation continuously. A curved trajectory is defined according to the tip bending angle. This type of motion can be seen as the motion of a wheel of a car.

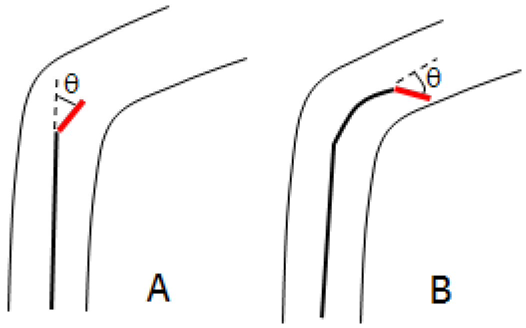


Figure 27. Representation of the catheter tip(in red) movement. A – Tip deflection of the catheter in a static position. The tip deflection determines the trajectory; B – While keeping the same tip bending the trajectory keeps changing. For no hit the vessel wall the tip needs to be re-directed.

Figure 28 shows the relation between the handle maneuver and the tip image displaying. Tip is modeled by the definition of two points in the 2D coordinate system. One point represents the origin of the tip, point O, and the second point represents the tip end, point T. Between these two points a line is drawn using the function *DrawLine* of the visual C#.

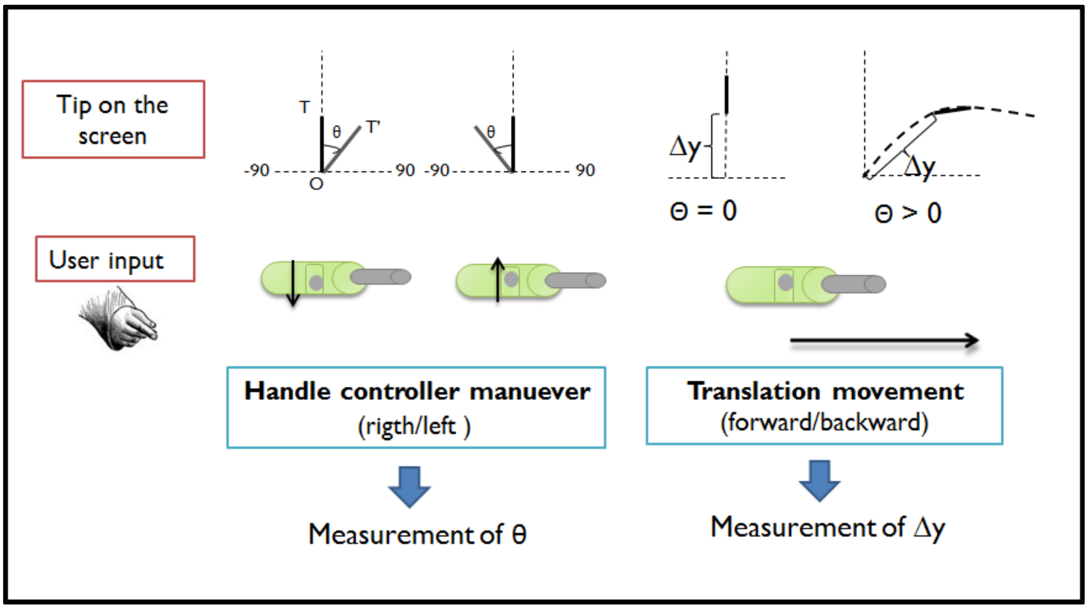


Figure 28. Relation of the tip movement on the screen to the user input, accordingly to catheter manipulation.

From the readings of the handle sensor and encoder two input measurements are taken: θ and Δy. The parameter θ represents the tip angle and Δy is the travel distance of the catheter between the previous and current position on the catheter platform measured by the encoder sensor. Position of the point O determines always the position of T, so that T coordinates are defined by the equations in the local coordinate system:

$$T(x, y) = \left(O_x + L \sin\theta\,, O_y + L\cos\theta\right) \quad (\chi_{local}) \tag{1}$$

where O_x and O_y represent the coordinates of the point O, θ is the tip bending angle read in the handle sensor and L the length of the tip, which is constant. Point O is the origin of the local coordinate system.

Tip motion is dependent on how point O is described in the world coordinate system, which is the user's reference. If point O follows the direction of T, it would follow a straight line in that direction. However, when pushing forward the catheter, the tip will be deviated according with its curvature, as showed in Figure 27. Point O is then defined by a directional angle dependent on θ and by the travel distance Δy. The parameter Δy defines the distance of the current point O to its previous point in the direction of a directional angle that will be named of transition angle (θ_{trans}).

Both points O and T are displayed in the windows forms application screen according to its world coordinates (Figure 29), which are calculated at each frame by the following equations:

$$O(x_i, y_i) = \left(O_{x_{i-1}} + \Delta y \sin\theta_{trans}\,, O_{y_{i-1}} - \Delta y \cos\theta_{trans}\right) \quad (\chi_{world}) \tag{2}$$

$$T(x_i, y_i) = \left(O_{x_i} + \Delta y \sin\theta + \theta_{trans}\,, O_{y_i} - \Delta y \cos\theta + \theta_{trans}\right) \quad (\chi_{world}) \tag{3}$$

where i represents the current position and $i-1$ the previous one.

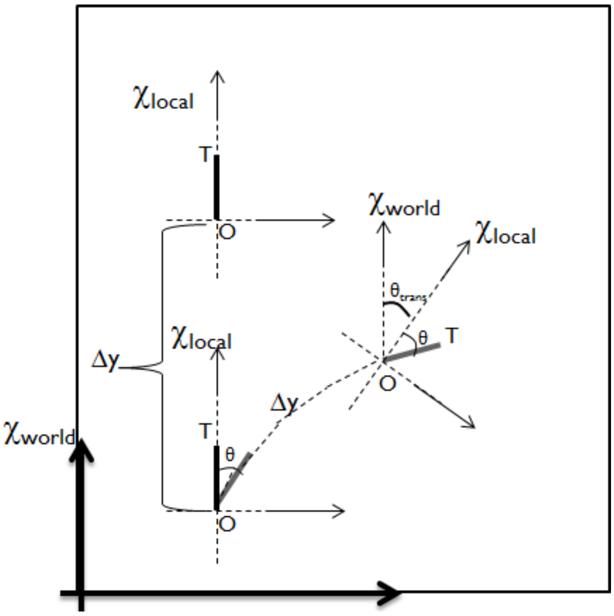


Figure 29. Illustration of the local coordinate's dynamics according to the catheter tip image display in the world coordinates system of the screen.

The parameter θ_{trans} was defined to achieve the smoother curve trajectory for the tip. It was defined to be equal to 0.4 times the deflection angle θ. In the beginning all variables are initialized, θ_{trans} is initialized as zero. At each frame, while $\Delta y \neq 0$, θ_{trans}= θ_{trans}+0.4*θ and the world coordinates of O and T are actualized according to the equations 2 and 3. If $\Delta y = 0$ then only the world coordinates of the point T are actualized since there is no forward or backward movements being made at this situation, but deflection can still occur with the change of parameter θ.

4.2 Procedure

4.2.1 Task

According to the vessel models presented, four distinct tasks were designed. Each of the two vessel models can be displayed in two orientations, one to the left and one to the right, defining four tasks, as showed in Figure 30.

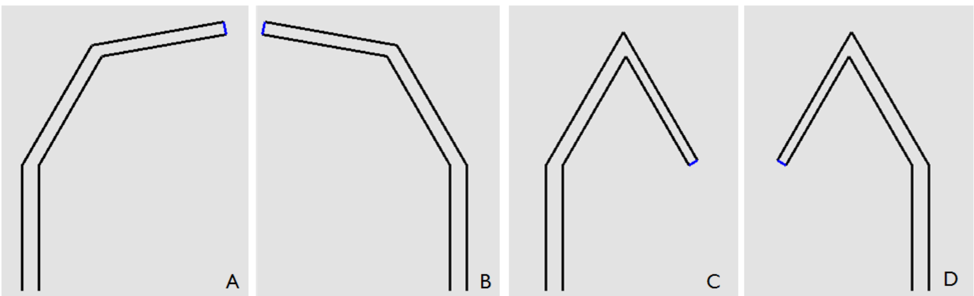


Figure 30. The four tasks: A - task 1; B - task 2; C – task 3; D- task 4.

Each task consists in maneuvering a catheter tip that it's presented as a red line on the screen within a vessel path which end is marked with a blue line (Figure 31). The

goal was to travel within the vessel trying to maintain the tip at the center line of the path. Besides the catheter tip, the tip origin point trajectory is also drawn to serve as reference for the user.

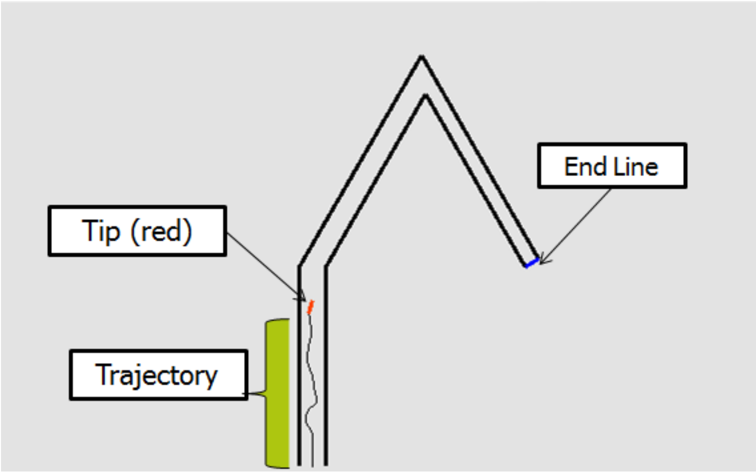


Figure 31. A task being performed with respective legends.

4.2.2 Protocol

The experiment consists in four sessions, in each a handle was used to perform 10 tasks. The first two tasks in each session corresponded to the practice phase of the session that is followed by the experimental phase. For the practice phase two different vessel models were used, as showed in Figure 32. The experimental phase of each session consisted in the two times performance of task 1, task 2, task 3 and task 4 (Figure 30). For reasons of reference along the text, the tasks performed for the first time will be named as follow: 1st task1, 1st task 2, 1st task 3 and 1st task 4. Equally, the tasks performed for the second time will be referred as: 2nd task 1, 2nd task 2, 2nd task 3 and 2nd task 4.

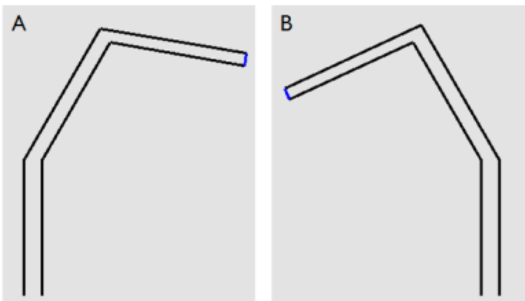


Figure 32. Practice tasks; A – Practice 1; B – Practice 2.

Figure 33 illustrates the entire experiment procedure. In the end of each session a questionnaire for measure the perceived workload with each handle was given to each participant. The NASA Task Load Index (TLX) was used to assess work load. Then a small break was given to the participant. When completed the four sessions, each participant answered four questions in the end of the questionnaire regarding:

1. Preferred handle and reason of choice

2. Feeling of fatigue during the test
3. Personal strategy to complete the test
4. Suggestions and commentaries about the experiment and control methods

During the experiment pictures were taken as a register of the holding gesture and how each participant executed the controller manipulation. Each subject was free to maneuver the handle in the most comfortable gesture, but it was required that only one hand was used for manipulation.

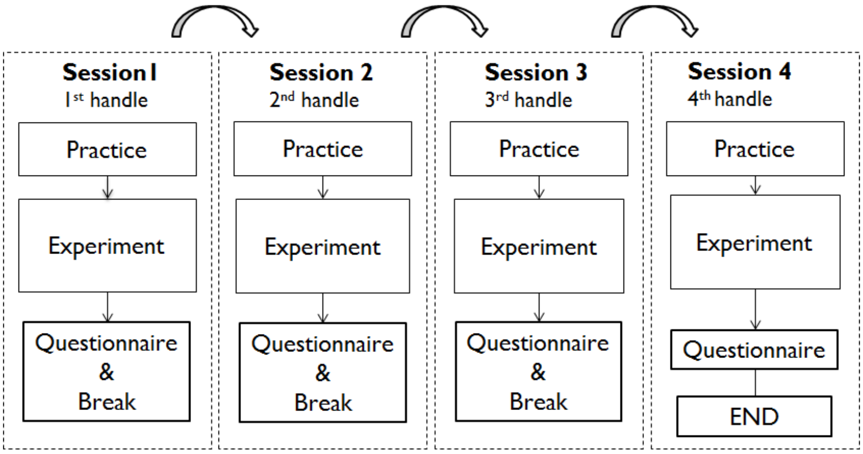


Figure 33. Experimental protocol

4.3 Participants

Sixteen subjects participate in the experiment. Each subject completed the 4 sessions using a different combination order for the use of the handles (Table 14). In a total each participant completed 40 tasks including the practice tasks.

Participant	Session 1	Session 2	Session 3	Session 4
1	H1	H2	H3	H4
2	H2	H3	H4	H1
3	H3	H4	H1	H2
4	H4	H1	H2	H3
5	H4	H3	H2	H1
6	H1	H4	H3	H2
7	H2	H1	H4	H3
8	H3	H2	H1	H4
9	H1	H3	H2	H4
10	H3	H1	H2	H4
11	H1	H3	H4	H2
12	H3	H1	H4	H2
13	H4	H2	H3	H1
14	H4	H2	H1	H3
15	H2	H4	H3	H1
16	H2	H4	H1	H3

Table 14. Control method used in each session by each participant. Different orders of the handles were used. H1 – Slider I; H2 – Rotator I; H3 – Slider II; H4 – Rotator II.

4.4 Data analysis

The results from each participant performance on the use of the different handles were measure as follows:

- Task completion time (in seconds): time that each participant used in one task
- Travel length of the tip (in centimeters): length of the trajectory travelled by the tip distal end in one task;
- Distance from the center line (in millimeters): average distance to the center line in one task. This measure indicates how closely the tip trajectory fits the center line of the path.
- Number of errors during the task: how many times the tip pass over the black line of that delineates the vessel path;
- Subjective data: TLX results, including mental load, physical load, temporal load, performance load, effort load and frustration load with the use of each handle.

A statistical analysis to the data was made to compare the four handles over the four sessions of the experiment at the 1st and 2nd trials, for the dependent measures. The 1st trial corresponds to the performance of 1st task 1, 1st task 2, 1st task 3 and 1st task 4 and the 2nd trial to 2nd task 1, 2nd task 2, 2nd task 3 and 2nd task 4. Task completion time, the travel length of the tip, average distance to the center and the number of errors parameters were evaluated as a sum of the four tasks of each trial.

The test for differences between of the four handles for the dependent continuous variables (task time, travel length and average distance) was made using one-way ANOVA with repeated measures. For the dependent ordinal variables (number of errors and workload scores) Friedman was used, as the non-parametric test alternative to the one-way ANOVA with repeated measures when the dependent variable is ordinal.

5 Results

5.1 Setup measurements

The average task time in the 1st trial for the Slider I, Rotator I, Slider II and Rotator II control methods was 275.01, 261.14, 258.06 and 258.37 seconds, respectively. There was no significance of the task time among the four groups ($F(3,45)=0.233$, $p=0.873$). In the 2nd trial the averages were 277.51, 261.41, 248.25 and 255.37 seconds, and also no significance ($F(3,15)=0.605$, $p=0.615$) was found between handles (Table 15, Figure 34).

	1st trial		2nd trial	
Control method	**Mean (SD)**	**p Value**	**Mean (SD)**	**p Value**
Slider I (SI)	275.01 (79.33)	0.873	277.51 (89.24)	0.615
Rotator I (RI)	261.14 (124.88)		261.41 (135.89)	
Slider II (SII)	258.06 (74.19)		248,25 (71.91)	
Rotator II (RII)	258.37 (92.89)		255.37 (88.26)	

Table 15. Mean task time of completion of the 1st and 2nd trials, in seconds. For each handle the mean and SD for task time is reported, followed by the p values for each linear contrast.

The average travel length in the 1st trial was 101.20, 103.57, 97.94 and 104.93 cm ($F(3,45)=2.194$, $p=0.102$). In the 2nd trial the average values were 101.72, 105.13, 98.53 and 103.61 ($F(3,45)=0.478$, $p=0.233$). No significance was found between handles at each trial (Table 16, Figure 34).

	1st trial		2nd trial	
Control method	**Mean (SD)**	**p Value**	**Mean (SD)**	**p Value**
Slider I (SI)	101.20 (9.18)	0.102	101.72 (9.88)	0.233
Rotator I (RI)	103.57 (18.68)		105.13 (20.70)	
Slider II (SII)	97.94 (7.56)		98.53 (10.16)	
Rotator II (RII)	104.93 (13.41)		103.61 (12.05)	

Table 16. Mean travel length for the 1st and 2nd trials, in centimeters. For each handle the mean and SD for the travel length is reported, followed by the p values for each linear contrast.

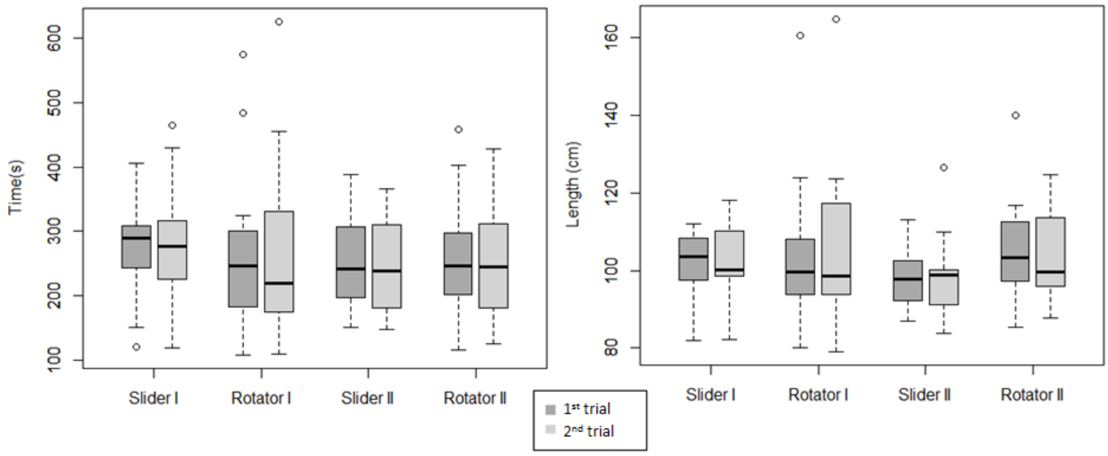


Figure 34. Task time and travel length results in the 1st and 2nd trials for the four handles. The results are presented as box plots, where every box has a line at the 25th quartile, median and 75th quartile.

The average of the average distance to the center over the 1st trial for the four control methods was 1.5250, 1.4425, 1.4349 and 1.6303 mm in the 1st trial. In the 2nd trial the averages were 1.5412, 1.5046, 1.4396 and 1.5866 mm. Over the first trial there are significant differences between control methods ($F(3,45)= 3.949$, $p=0.014$), but in the second trial the differences are no longer evident ($F(3,45)=1.996$,$p=0.128$) (Table 17, Figure 35). The post hoc analysis with the *Bonferroni* correction for the p values showed that the difference in the 1st trial occurs between Rotator I and Rotator II.

	1st trial		**2nd trial**	
Control method	**Mean (SD)**	**p Value**	**Mean (SD)**	**p Value**
Slider I (SI)	1.5290 (0.3277)	0.014	1.5412 (0.3449)	0.128
Rotator I (RI)	1.4425 (0.2999)		1.5046 (0.3247)	
Slider II (SII)	1.4349 (0.2872)		1.4396 (0.3769)	
Rotator II (RII)	1.6303 (0.3985)		1.5866 (0.3869)	

Table 17. Mean of the average distance to the center in the 1st and 2nd trials, in millimeters. For each handle the mean and SD are reported, followed by the p values for each linear contrast.

Distance (1st trial)	**Mean (SD)**	**SI vs RI**	**SI vs SII**	**SI vs RII**	**RI vs SII**	**RI vs RII**	**SII vs RII**
Slider I (SI)	1.5290 (0.3277)	0.856	0.648	1.000	1.000	0.018	0.094
Rotator I (RI)	1.4425 (0.2999)						
Slider II (SII)	1.4349 (0.2872)						
Rotator II (RII)	1.6303 (0.3985)						

Table 18. Mean of the average distance to the center during the 1st trial, in millimeters. The mean and SD are reported, followed by the p values resulted from the post hoc analysis.

The number of errors in the 2nd trial depending on the control method was statistically significant, $\chi^2(3)=8.162$, $p=0.043$ (Table 19, Figure 35). A *Wilcoxon* signed-rank test showed that the differences occur between Slider II and Slider I (z=-2.698, p=0.003), Slider II and Rotator I (z= -2.311, p=0.021) and between Slider II and Rotator II (z= -2.732, p=0.006) (Table 20). According to the mean ranks, fewer errors were made with Slider II when compared with the other control methods.

	1st trial		2nd trial	
Control method	**Mean Rank**	**p Value**	**Mean (SD)**	**p Value**
Slider I (SI)	2.69	0.419	2.81	0.043
Rotator I (RI)	2.44		2.75	
Slider II (SII)	2.09		1.72	
Rotator II (RII)	2.78		2.72	

Table 19. Number of errors in the 1st and 2nd trials: For each handle the mean ranks resulted of the Friedman test for the number of errors is reported, followed by the p values for each linear contrast.

Number of errors (2nd trial)	Mean Rank	SI vs RI	SI vs SII	SI vs RII	RI vs SII	RI vs RII	SII vs RII
Slider I (SI)	2.81	0.842	0.003	0.876	0.021	0.727	0.006
Rotator I (RI)	2.75						
Slider II (SII)	1.72						
Rotator II (RII)	2.72						

Table 20. Number of errors of the 2nd trial: the Friedman's mean ranks are reported, followed by the p values of the post hoc analysis, comparing each pair combination of control methods.

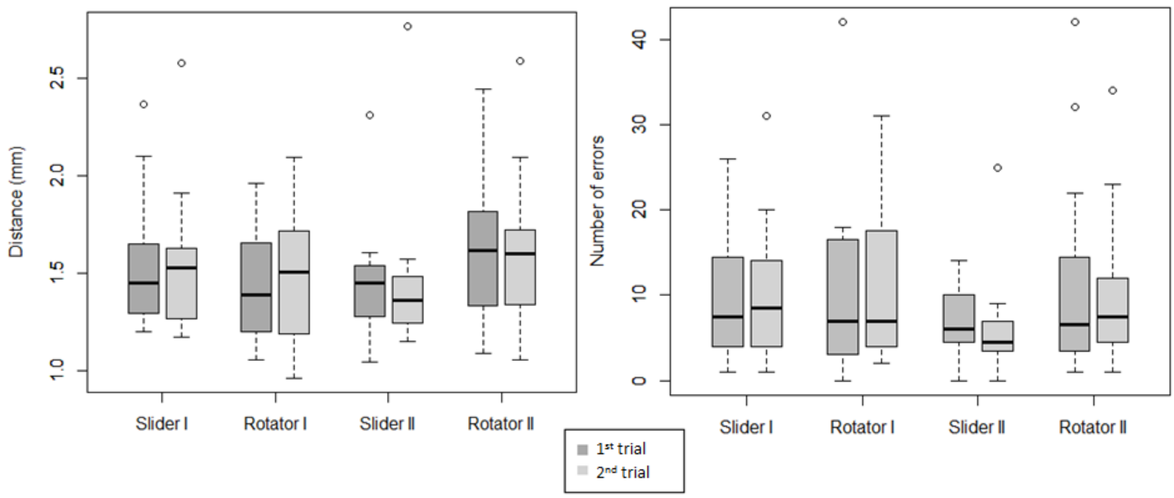


Figure 35. Distance to the center and number of errors results in the 1st and 2nd trials for the four handles. The results are presented as box plots, where every box has a line at the 25th quartile, median and 75th quartile.

5.2 Subjective evaluation

5.2.1 Workload

Statistical results of the Friedman test applied to the subjective workload scores over the four handles is presented in Table 21. There was statistically significant difference only in the temporal demand variable depending on the control method, $\chi^2(3) = 10.008$, $p = 0.019$.

	Slider I (SI)	Rotator I (RI)	Slider II (SII)	Rotator II (RII)	
Workload (TLX)	**Mean Rank**	**Mean Rank**	**Mean Rank**	**Mean Rank**	**p Value**
Mental demand	2.50	2.69	2.34	2.47	0.880
Physical demand	2.63	2.59	2.44	2.34	0.903
Temporal demand	2.84	1.88	3.03	2.25	0.019
Performance	2.19	2.69	2.41	2.72	0.547
Effort	3.06	1.97	2.50	2.47	0.090
Frustration	2.63	2.19	3.03	2.16	0.124

Table 21. Perceived workload. For each control method Friedman's mean rank for each dependent measure of the TLX is reported, followed by the p values for each linear contrast.

The differences of the subjective evaluation of temporal demanding were found between Slider I and Rotator II (Z= -2.371, p= 0.018) and between Rotator I and Slider II (Z=-2.125, p=0.034) (Table 22). Subjective evaluation indicates that Slider I temporal demand is higher than Rotator II. Rotator I was significantly different from Slider II, being the less temporal demanding according to the mean ranks (Table 22).

Temporal demand	Mean Rank	SI vs RI	SI vs SII	SI vs RII	RI vs SII	RI vs RII	SII vs RII
Slider I (SI)	2.84	0.058	0.888	0.018	0.034	0.781	0.090
Rotator I (RI)	1.88						
Slider II (SII)	3.03						
Rotator II (RII)	2.25						

Table 22. Temporal demand. The Friedman's mean ranks are reported, followed by the p values of the post hoc analysis, comparing each pair combination of control methods.

5.2.2 Personal preference, feelings and commentaries

From the open questions the control method preference and feeling of fatigue were accessed and they could be resumed in the bar graphics of Figure 36 and Figure 37, respectively. Rotators I and II were more frequently chosen as the favorite control method among subjects. Selection was based in the intuitiveness and simplicity to use

of the control method. In general, the rotators were reported to be more intuitive and easy to control than sliders. Nevertheless, for the four subjects that prefer sliders over rotators, rotator I and II were felt as more difficult to control.

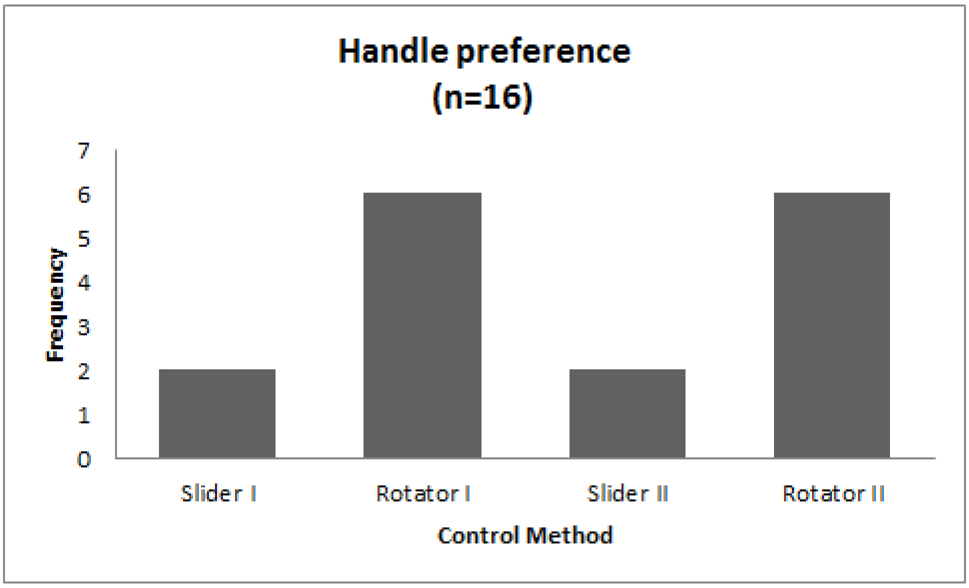


Figure 36. Subjective handle preference.

More or less 80% of the participants reported felling of fatigue during the experience (Figure 37). Fatigue in the arm was the most reported but also some subjects reported fatigue in the thumb, wrist and finger. Two other subjects reported fatigue in the form of tired eyes (Figure 38).

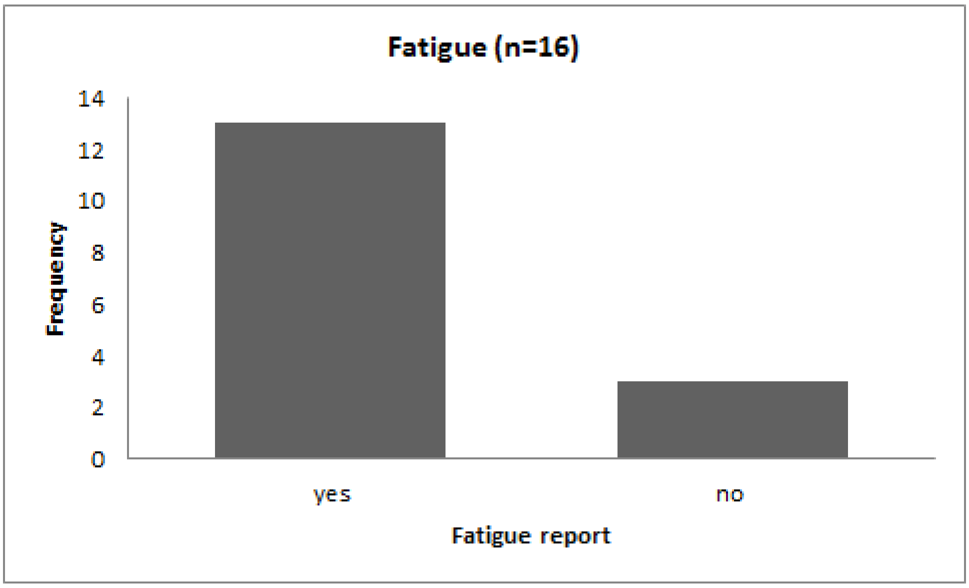


Figure 37. Subjective report about feeling of fatigue.

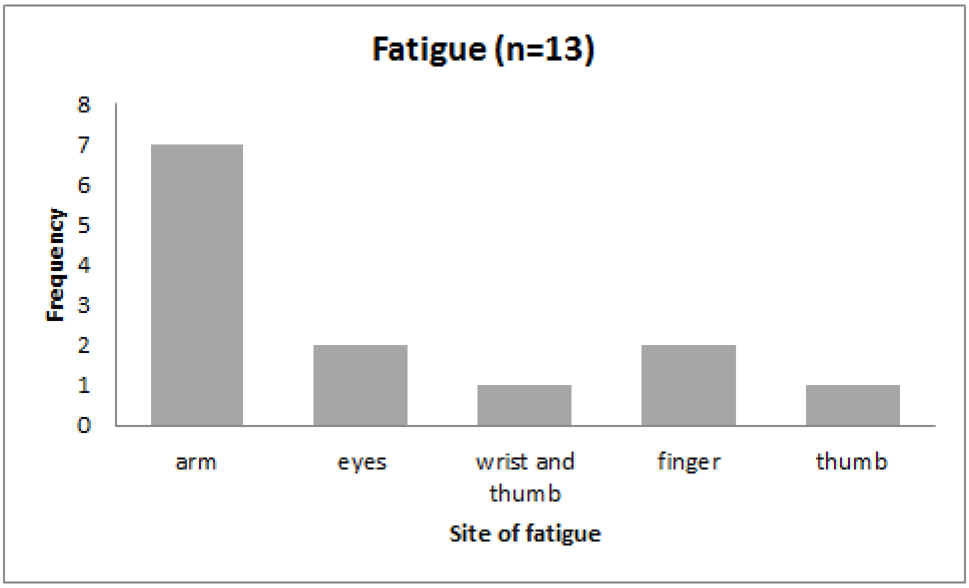


Figure 38. Reported body site where fatigue was felt.

5.3 Ergonomics

Figure 39 shows the most common holding gesture of the handles during the experiment. Typically, the maneuver of the knob of each handle was done with the thumb. In some cases, however, the index finger or both the thumb and index finger were used (Figure 40). For these cases the holding gesture slightly changed from the ones in Figure 39 In order to free the index finger.

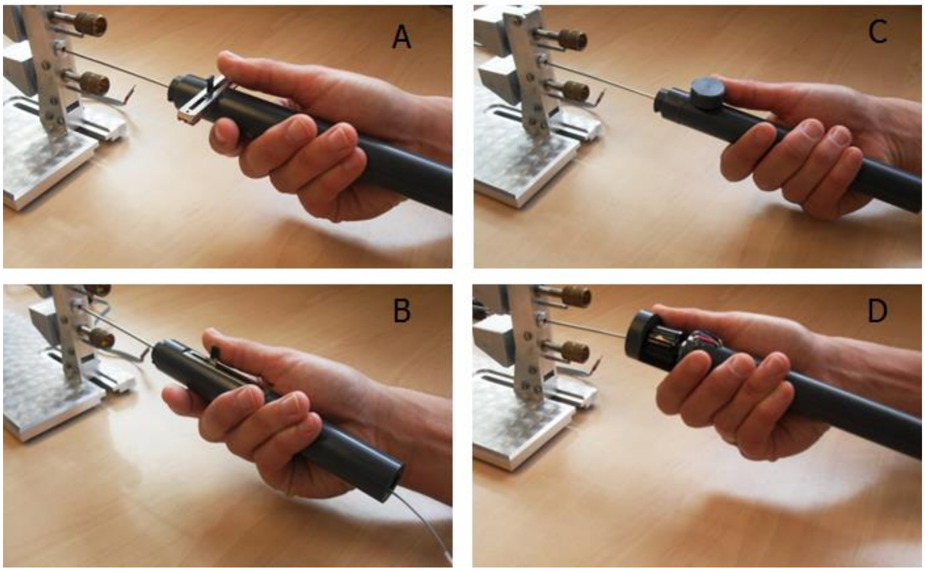


Figure 39. Common adopted holding gesture for each control method.

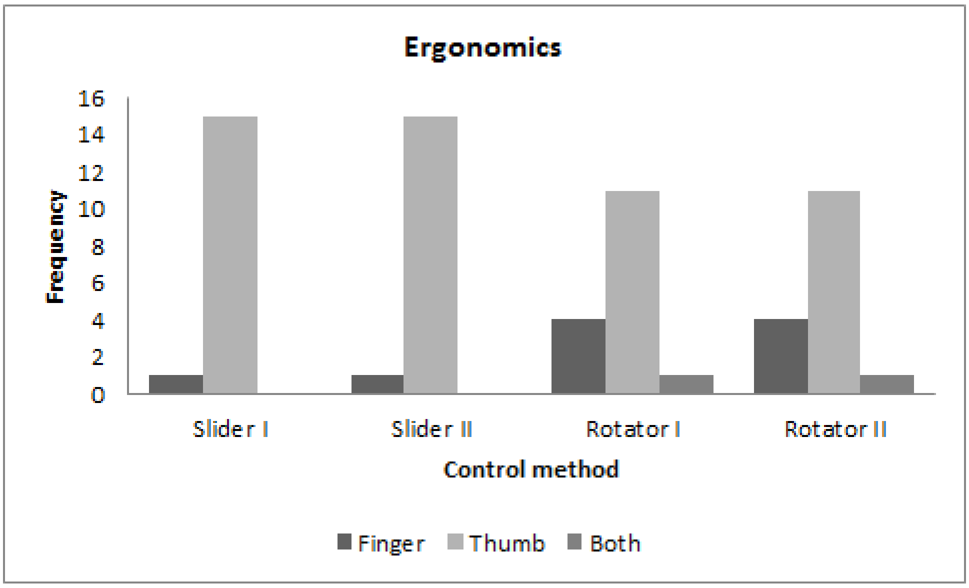


Figure 40. Statistical reference about how the manipulation of each control method occurred.

6 Discussion

6.1 Comparison of the four handles

Comparison of the four handles is based on experimental measurements and subjective evaluation of the subjects through the TLX workload. Figure 34 and Figure 35 show how the data of the four dependent measurements are distributed. In general, the distribution of data shows a wide range of variability at each group. Comparing the box plots of each handle group over the dependent measures, the variability for Slider II seems to be smaller and with lower median values, except for the time task variable that presents a similar variability range for all groups. The subjective preference indicated Rotator I and Rotator II were the preferred handles.

To analyze whether there are significant differences between handles, statistical tests were used. One way ANOVA with repeated measures results reported that there are no significant differences between handles for the continuous dependent measures task time and travel length, but was observed in terms of average distance and number of errors.

In the 1st trial, Rotator I and Rotator II showed significant differences for the mean of the average distance (p=0.018). Tip trajectories with Rotator I fitted better the center line of the path than with Rotator II. However, these differences don't remain significant after the 2nd trial. The learning effect in Rotator II seems to equal the two handles, whereas the opposite happens to Slider I, Slider II and Rotator I that present a higher average distance in the 2nd trial compared to the 1st trial. Despite that the significance only occurs between rotation based control methods in the 1st trial, Slider II presents the lowest mean values over the two trials.

The analysis of the number of the errors showed that significant differences occur in the 2nd trial ($\chi^2(3)=8.162$, $p=0.043$). The post hoc tests indicate that the differences occur between Slider II against the other three handles. By comparing the mean ranks of the Friedman test, the number of errors done by Slider II is significantly smaller that with the other handles, that present higher number of errors (Figure 35). After learning of the task occurs, it is easiest to control the catheter tip with Slider II with fewer errors.

From the perceived workload measurements, differences were found on the temporal demand measure ($\chi^2(3)=10.008$, $p= 0.019$). The post hoc tests showed differences between Rotator II and Slider I and between Rotator I and Slider II. Higher mean ranks of the Slider I and Slider II show that they were grade with higher scores than Rotator II and Rotator I, respectively. In general, participants felt more rush using the handles based on the sliding control method. This reveals agreement to the selected preference for the rotation control method. However, in task time comparison the four control handles don't have significant differences. Moreover, by the end of the 2nd trial there were no differences in the accuracy of following the center line, but the number of errors points Slider II as the best handle in doing fewer errors.

6.2 Handles design considerations

Despite the range of the sensors is similar, it was reported that rotation knobs required higher maneuver to achieve the same bending angle. This feeling may be related to the different mechanical perception. With rotation, the perception of the angular movement and its relation with the bending degree may differ from the perception with the sliding movement. This perception can be improved, however, in the knob design. The knob of the slider was reported to be too long, in such a way that during manipulation with the thumb, the thumb wasn't always kept on top of the knob but many times it was used the side of the knob for manipulation. This required more effort of changing the thumb position when steering to the left or right, whereas some participants reported that fatigue was felt mainly after manipulation of the handles based on sliding control method.

6.3 Experiment design considerations

Typically, each experiment took one hour and a half. Efforts were made to make the experiment the less time consuming. In long experiments, severe fatigue can compromise performance results.

Each participant completed four sessions. In the beginning of the experiment they start without any experience, but as they complete the sessions the learning effect of the task may influence their performance with the handles. To minimize that influence, the order of the handles used in each session was unique for each participant. Additionally, a practice phase in each session allowed erasing the very first impressions with the handle, giving the feeling of it to the participant before the experiment tasks.

In the task design it was decided that no visual warning was given to the subject when errors are made. Instead concrete instructions were given and when doing a mistake correction by pulling back the catheter could be made. The focus was to see how accurately was possible to follow the center line with each handle without any additional factors.

The catheter visual model was built in order to guarantee a continuously steering of the tip during the task. The motion of the catheter tip was defined to describe a curve trajectory that approximates the direction of the motion when pushing forward the catheter, making it necessary to steer the tip continuously as the catheter tip moves forward. The influence of the vessel wall in the catheter motion wasn't considered neither the catheter shaft was modeled.

Improvements to the experiment and handles design will be considered in the next chapter as possible future work.

7 Conclusion and Future Works

The best control method cannot be named yet. In this study, however, some considerations and suggestions can be made. Overall, without considering statistical significances Slider II seems to stand out as the more accurate handle. In fact, this can only be evaluated for the number of errors committed with each handle, where statistic test results shows that Slider II overcomes the other three handles. These results also suggest that the handles design influenced the sliding control method and possibly Slider II design is a best approach of this control method.

Accuracy to follow the center line is given by the average distance, representing how the trajectory fits the center line of the path. Slider II presents the lowest mean, but differences were found only in the beginning trial for Rotator I against Rotator II, whereas Rotator I overcomes Rotator II. The fact that that Slider II is not significantly different from Rotator II, makes it hard to judge its behavior at this dependent measure. Either is it similar with Rotator I or it is with Rotator II. The same happens for the judgment of Slider II. Nevertheless, after the learning of the tasks, the handles seem to equal to each other. Therefore, the accuracy of the control method cannot be well judged with the present data.

Subjective preference reveals that the rotation control method is easier and more intuitive, but, through the results this cannot be supported. However, it is clear that the some significant differences make Slider II and Rotator I designs more suggestive than the other handles. Even so, further studies need to be done to clear out specifically and conclusively which handle is better. Additionally, some handle design issues may have influence the data or the experiment design was insufficient to clear out the differences. Therefore, improvements to handles and experiment design are pointed out for future works in the next sections.

In this experiment only handles designs for bi-directional catheter were compared. Rotation and sliding control methods can be also applied to multi-directional bending of the tip. Future research on the differences between the two control methods should include handles designs for multi-directional steerable catheters.

7.1 Improvements to the handles design

Rotators were reported to be more difficult to feel the deflection, although they were easier to maneuver. Sliders were felt in general to offer more resistance, and so a better notion of the bending was felt. So a first improvement is to equal the deflection motion feelings when manipulating the knob of each control method. The sliding movement itself offers already some mechanic track resistance that maybe was higher than for rotation. To add resistance in the rotation motion the integration of a gear can be considered. Moreover the knob itself can be improved with rubber for higher haptic feedback. Sliders' knob was more difficult to maneuver. Maneuverability can be improved by lowering the knob. A more adequate height of the knob needs to be evaluated for a new design.

The handle size should also be improved. An adaptable size that accommodates different holding gestures for the higher resting of the hand would be ideal. However, simpler designs can also improve the comfort in holding the handle, making a ticker handle embodiment with more support for the palm and lower thumb joint.

7.2 Improvements to the experiment design

Support to the arm

The horizontal position of the platform forced the arm to be maintained sustained, so that the arm was not in rest during the task. A support to the arm would decrease fatigue that may have influence in performance.

Instructions

The instructions for doing the task may be not enough to force the subjects to make their maximum effort to follow the center line the more accurately possible. Some more interaction or warning to keep them in alert may be a good improvement of the task.

Vascular and catheter models

Improvements to the vascular and catheter models should approximate the realistic situation, using real fluoroscopic or MRI images and a catheter modeling that may include catheter-tissue interaction. The modeling of a catheter motion inside a vessel has been already approach in literature [69]. *Lawton et al* [69] proposed a realistic model for a catheter considering its motion over the guidewire and the influence of the vessel walls, mimicking the output of the push/pull and twist movements for manipulation of conventional catheters. Steerable catheters are still designed to be used over a guidewire when advancing it inside the vasculature and that interaction can be also modeled as a conventional catheter. However, the direct manipulation of the deflection of the tip may influence the procedure protocol in relation to the use of the guidewire, which has not been described yet in the literature, making it difficult to approach its real behavior. A further study of the motion behavior of steerable catheter, using a phantom, for example, may be useful to assess that information and support the considered improvements to the catheter model. Nevertheless, the presented model can be a good approach to the behavior of a more autonomous catheter that can be drive by its tip, without the need of using a guidewire.

Considering a realist model the experiment can be made by subjects with a medical background, specifically doctors specializing in neurointerventions.

Experiment Procedure

The results can be clearer for different procedure approaches. In this experiment differences in the number of errors and subjective preference occurred between the handles. Slider I and Slider II does not seem to be at the same level as it could be expected, as Slider II stand out from the number of errors results. This also happens between Rotator I and Rotator II comparing the average distance. A suggestion for a

future study is to divide the comparison into three experiments: 1) experiment comparing Slider I against Slider II; 2) experiment comparing Rotator I against Rotator II; 3) a third experiment would compare the best slider versus the best rotator that gain from experiment 1 and 2.

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