MAGNETICALLY-ASSISTED REMOTE CONTROL STEERING OF
ENDOVASCULAR CATHETERS IN INTERVENTIONAL MRI

by

Fabio Settecase, M.D.

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Institute of Medical Science
University of Toronto

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Abstract

Current applied to coils wound at the tip of an endovascular catheter can be used to remotely steer a catheter tip in a clinical magnetic resonance imaging (MRI) scanner. This study focuses on (1) derivation and experimental validation of an equation that characterizes the relationship between catheter tip deflection and a number of magnetic, mechanical, and physical factors, and (2) evaluation of resistive heating in a worst-case scenario due to application of current necessary for clinically significant deflections, and radiofrequency (RF) heating due to real-time MRI pulse sequences. The derived equation was found to accurately model the behavior of the specialized catheter tip. The equation also has implications for catheter design and device implementation, including minimization of resistive heating, which was physiologically significant (> 4°C) under certain worst-case scenario conditions. This catheter steering mechanism should improve navigational control and is a unique advantage offered by MRI-guidance of endovascular procedures.
Acknowledgements

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List of Abbreviations

AWG – American Wire Gauge
B – external magnetic field
B₀ – main scanner magnetic field
eiMRI – endovascular interventional magnetic resonance imaging
DICOM – Digital Image and Communications in Medicine
DC – direct current
DSA – Digital Subtraction Angiography
F – French
FIESTA – Fast Imaging Employing Steady State Acquisition
FISP – Fast Imaging with Steady State Precession
FOV – Field of view
FSPGR – fast spoiled gradient recalled echo in the steady state
Gd - gadolinium
GRE – gradient recalled echo
iMRI – interventional magnetic resonance imaging
M – magnetization
MARC – Magnetically-assisted remote control
MR – magnetic resonance
MRI – magnetic resonance imaging
PCTA – percutaneous transluminal angioplasty
RF – radiofrequency
SAR – specific absorption rate
SNR – Signal-to-noise ratio
ssFSE – single shot fast spin echo
T – Tesla
TE – echo time
TR – repetition time
Ta – Tantalum
V – Vanadium
1. General Introduction

The development of image-guided endovascular intervention

In the 20th century, the field of vascular interventional radiology developed as a result of several significant technological advances that made it possible to visualize blood vessels and perform interventions on them through small openings the skin. The genesis of the field begins with the birth of radiology as a medical sub-specialty in 1895 with Roentgen’s demonstration that X-ray radiation produced elegant shadows of bones of his wife’s hand. Seeking to improve the technique, Thomas Edison embarked on search for a chemical compound which fluoresced most brightly when exposed to X-rays. This search led to calcium tungstate, which has been replaced only recently by the use of rare-earth crystals. Since contrast in a radiographic image relies on differences in atomic densities of bone compared to soft tissues, the field was limited primarily to the study of bony structures in the body. In the 1920s it was shown that injections of potassium iodide could render the veins and arteries opaque to X-rays, leading to the development of injectable pharmaceuticals containing a radioopaque substance, known as contrast media. The development of relatively safe contrast media provided physicians and surgeons with the diagnostic opportunity to examine the anatomy and pathology of blood vessels using X-rays without gross dissection.

Unlike bone, however, blood could not be kept static. A way to capture sequential images was necessary in order to adequately visualize vessel anatomy using contrast media and X-rays. In 1929, after performing the first X-ray guided cardiac catheterization on himself, Dr. Werner Forsmann acquired the first X-ray cine strip of injected contrast cycling though a dog’s heart. In 1955, the x-ray image intensifier was developed and allowed the pick up and display of the x-ray movie using a television camera and monitor. Together with the cut-film changer, the image intensifier lighted the pathway for modern angiography, and allowed the routine imaging of blood vessels and the heart to be performed. Later, advances in computers and software led to improved visualization through digital subtraction angiography (DSA), a process by which a computer removes bones and soft tissue from the X-ray images of injected radioopaque vessels.
DSA provides sufficient temporal resolution to provide natural hand-eye coordination and a spatial resolution of the order of 0.1 mm, enough to resolve any vessel that can be catheterized.

Meanwhile, methods for vascular access improved. In 1953 Sven-Ivar Seldinger, introduced a technique that minimized complications when to gaining access to a blood vessel to inject contrast and perform vascular interventions\textsuperscript{8,9}. The Seldinger technique is widely used today and involves puncturing a desired vessel or cavity with a sharp hollow needle called a trocar. A round-tipped guidewire is then advanced through the lumen of the trocar, and the trocar is withdrawn. A "sheath" or blunt cannula is then passed over the guidewire into the cavity or vessel. Alternatively, drainage tubes can be passed over the guidewire (for example, chest drains or nephrostomies). After introduction of a sheath, the guidewire is withdrawn. If a sheath is used, it can be used to introduce catheters or other devices to perform endovascular (inside a vessel) procedures. Building on the Seldinger technique and combining it with the improvements in vascular visualization using X-rays, Charles Dotter developed percutaneous transluminal angioplasty (PCTA) and is credited as the father of the medical specialty of interventional radiology\textsuperscript{10}.

**Vascular Interventional Radiology**

During an endovascular intervention, instruments are inserted into the vascular system, positioned under guidance of DSA, and employed to perform a specific task. Navigation into target vessels can be achieved either by remote mechanical manipulation of the guidewire tip, along which the catheter may be advanced, or by the use of preformed catheter shapes (Figure 1.3). Current techniques using sheaths, guidewires and catheters of different geometries, sizes, and stiffness, allow catheterization of almost any vessel up to a few millimeters in diameter. A growing number of image-guided endovascular interventions are being performed each year as studies continue to demonstrate equivalent or greater efficacy and lower morbidity of minimally-invasive endovascular interventions when compared to traditional open surgical techniques\textsuperscript{11-15}. Image-guided endovascular techniques are now routinely used in the diagnosis and treatment of atherosclerotic disease\textsuperscript{14}, cancer\textsuperscript{16,17}, uterine fibroids\textsuperscript{12}, arterio-venous malformations\textsuperscript{16}, cerebral aneurysms\textsuperscript{11,16}, end-stage liver disease\textsuperscript{18}, the prevention of pulmonary artery
thromboembolization\textsuperscript{15}, embolization of bleeding vessels, and many other pathological states\textsuperscript{16}. The majority of endovascular interventions employ the Seldinger technique, requiring insertion of a guidewire, a small diameter metal wire with highly flexible tip and a hydrophilic coating. With the guidewire providing a stable rigid track, a flexible catheter is subsequently introduced “over the wire.”

Vessel stenoses may be treated by percutaneous transluminal angioplasty (PCTA), using a specialized catheter tip with an inflatable balloon at the tip. Vascular stents may be implanted to prevent recoil of the stenosis or complications of injury to the vessel wall after PCTA\textsuperscript{19,20}. In addition, a stent-graft, which is an artificial lumen (graft) supported at the ends or over the entire length by a stent, intended for placement within the lumen of a diseased vessel, can be used to treat arteriovenous fistulae, occlusive disease, and peripheral or aortic aneurysms\textsuperscript{19}.

Thrombosis may be treated by catheter infusion of a thrombolytic agent, or by a mechanical devices which macerate the clot by fragmentation and aspiration\textsuperscript{21,22}. Conversely, when vessel occlusion is desired, as in the case of hemorrhage, uterine fibroids, vascular malformations, or cerebral aneurysms, vessels are embolized by injection of particles, fluids, or deployment of small endovascular constructions to achieve permanent or temporary occlusion\textsuperscript{23}.

**Guidewires and Catheters**

A full discussion of the spectrum of endovascular techniques in vascular interventional radiology is beyond the scope of this thesis. The following brief overview of the tools of vascular interventional radiology, however, will provide an excellent background for later chapters.

Guidewires and catheters comprise the foundation of endovascular intervention, both technically and conceptually. Familiarity with the array of guidewires and catheters available as well as their technical mastery is essential for successful interventions. Guidewire-catheter skills are not necessarily intuitive and must be developed with experience.

Placement of a guide wire is usually the second step in an endovascular procedure, following puncture of the artery. An introducer sheath is then inserted over the guidewire, through which
the guidewire can be changed and catheters introduced. A typical multipurpose guide wire functions primarily to facilitate percutaneous introduction of a catheter and to guide a catheter to its target without causing vessel wall dissection. Guide wires also establish a pathway from the percutaneous access site to and across the target vascular segment. Using a guide wire for percutaneous catheter introduction allows the interventionalist more flexibility in the selection of the catheter. A guide wire can also facilitate the passage of a catheter through highly stenotic, occluded, tortuous, or very small diameter lumens. A wide range of guide wires are available. Guide wire selection criteria most often involve consideration of the following attributes:

*Length – must cover the cumulative distance from the access site to well beyond the lesion, so that access across the lesion will not be lost during the procedure.  
*Diameter – chosen in relation to the size of catheter used.  
*Stiffness - for axial force and rotational torque transmission, and to provide a stable track across a narrow lesion  
*Tip shape and flexibility - guidewires can be obtained with a straight, firm tip, or a steerable, angled tip.  
*Steerability – with torque device which imparts a high 1:1 torque transmission ratio between the shaft and the tip  
*Visibility - Guidewires are rendered visible on DSA by virtue of their metallic core.  
*Trackability – refers to the ability of a catheter follow the guidewire through tortuous vessels and around corners without pulling the wire out of its intended location  
*Coating – Teflon or silicone to increase slipperiness through a stenosis and minimize friction, antithrombotic surface

Multipurpose guidewires usually come in one of two designs. Traditional design involved a coil wire wrapped tightly around a rigid core wire, or mandrel (Figure 1.1). Single, multilayer composite wires (Figure 1.2), with straight or J tips, were introduced in 1989.
Guide wires can be generally grouped into 3 categories: starting guide wires, exchange guide wires, and selective guide wires. A starting guidewire (used to start the case) has a floppy tip and has no inner core which reduces the potential for endoluminal injury by buckling when it encounters resistance. Exchange guidewires are stiffer than other guidewires and have a firm inner core. Once a guidewire has been appropriately placed (e.g. into a side branch or across a lesion), control may be enhanced by exchanging the initial guidewire for an exchange guidewire. The increased strength of the guidewire makes it easier to pass devices over it and to maintain control across tortuous or distant passages. The steerable tip guide wire is useful for selective
cannulation of side branches or critical stenoses. Manipulation of the proximal end of the guide wire with a clamp adjusts the degree of curvature on the distal steerable tip.

**Catheters**

Many different types of catheters exist. The simplest catheter is a vascular dilator. This is a short, slightly firm catheter with a single hole in the end, most often used to secure vascular access or to enlarge a percutaneous arteriotomy. An exchange catheter is straight and long (at least 65 cm) and is used to change one type of guidewire for another. An exchange catheter may also be used for interval arteriography to assess the results of an endovascular procedure. A flush catheter is used for general arteriography. It is available in varying lengths (65 to 100 cm) and has an end hole and multiple side holes along its distal tip for administration of contrast. The shape of the catheter head promotes contrast administration in multiple directions to create a contrast blush. Finally, selective catheters come in a variety of distal tip shapes since they are used to direct a guidewire into a specific location. Some selective catheters are designed for catheterization of a specific artery (e.g., carotid, visceral, etc.).

Catheters differ with respect to their:

*Construction* - Angiographic catheters can be constructed from polyethylene, polyurethane, nylon, Teflon, or a combination of these materials. Each material provides specific advantages. Catheters made of polyethylene have a low coefficient of friction and they are pliable, have good shape memory, rotational torque, and are useful for selective catheterization. Polyurethane catheters are softer and more pliable and follow guidewires more easily, but they have a higher coefficient of friction. Nylon catheters, which are stiffer and tolerate higher flow rates, are typically used in balloon angioplasty, aortography, and general arteriography. Teflon, the stiffest material, is mainly used for dilators and sheaths.

*Diameter* - should be as small as possible to accomplish the task at hand. Most angiography is performed with 4 or 5 Fr catheters over 0.035-inch guidewires. Smaller catheters are required in the pediatric and neurovascular settings.
*Length - must cover the cumulative distance from target to the access site and still have enough length outside the patient for appropriate manipulations. Most catheters range from 65 to 100 cm in length.

*Trackability – refers to the ability of the catheter to follow the guide wire through tortuous vessels and around corners without pulling the wire out of its intended location.

*Pushability - The description of how a force applied by the operator at the proximal end of the catheter relates to the forward movement of the distal tip.

*Crossability - The facility with which a catheter follows the guidewire across a lesion or through a diseased arterial segment.

*Steerability - The steering responsiveness of the catheter tip to handling maneuvers performed at the proximal tip.

*Caliber - The scale used to size catheters is the French scale (1 Fr = 0.33 mm).

*Special features - Some special features of catheters include various coatings, radiopaque markers for visualization, and graduated measurement markers.

*Tip geometry - catheter head shape determines function.

Although hundreds are currently marketed, most endovascular practice is based on the consistent and well-developed use of just a few types. Each specialist develops favorites and the tendency is to use a select few that they are familiar with and they have used successfully. Flush and selective catheters have divergent purposes and substantially different appearances. The selective catheters may have either a simple curve or a complex curve. Some catheters commonly used in endovascular practice are listed in Table 1.1 and shown in Figure 1.3.

Table 1.1. Selective catheters for General Endovascular Practice
<table>
<thead>
<tr>
<th>Catheter Type</th>
<th>Function</th>
<th>Length (Fr)</th>
<th>Caliber</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective: simple curve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short bent tip</td>
<td>TegT</td>
<td>Direct guidewire through lesion or into branch (30°)</td>
<td>70, 100</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Kumpe</td>
<td>More angled than TegT (45°) directing a guidewire through a critical lesion or into a branch vessel</td>
<td>40, 65</td>
<td>5</td>
</tr>
<tr>
<td>Long bent tip</td>
<td>Multipurpose A</td>
<td>Direct guidewire, longer tip (45°)</td>
<td>65, 100</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Multipurpose B</td>
<td>More angled than MPA (70°)</td>
<td>100</td>
<td>5</td>
</tr>
<tr>
<td>Hook shape</td>
<td>RIM</td>
<td>turning an acute angle at a tight corner</td>
<td>65</td>
<td>5</td>
</tr>
<tr>
<td>Selective: complex curve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral</td>
<td>Simmons</td>
<td>Reshape to enter difficult arch branches, direct guide</td>
<td>100</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Vitek</td>
<td>Reshape to enter difficult arch branches</td>
<td>100, 125</td>
<td>5</td>
</tr>
<tr>
<td>Renal</td>
<td>C2 Cobra</td>
<td>Directs guidewire into side branch at 90° angle</td>
<td>65, 80</td>
<td>4, 5</td>
</tr>
<tr>
<td></td>
<td>Renal double curve</td>
<td>Directs guidewire laterally and inferiorly</td>
<td>80</td>
<td>5</td>
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Adapted from\textsuperscript{24}

**Figure 1.3** Some common selective catheter tip geometries\textsuperscript{24}.

A. Cobra catheter is used for renal artery catheterization. B. A Berenstein catheter is used for cannulation of the superficial femoral artery and aortic arch great vessels. C. A tightly curved hook-shaped catheter is used for catheterization of the visceral arteries. D. A headhunter catheter can be used to enter the branches of the aortic arch.
E. A Simmons catheter is used to cannulate the carotid and innominate arteries. F. A shepherd’s hook catheter is used to cross the aortic bifurcation.

Selective catheters have either a simple or complex curved head shape. A easy way to distinguish between the two is that a complex curve needs to be reshaped in the aorta before it can be used to selectively cannulate a side branch. The bent-tip Berenstein catheter (Boston Scientific Corp., Medi-Tech Division, Natick, Mass.) is a simple-curve selective catheter, but it can be used simultaneously for general applications. This catheter is useful for directing a guidewire through a critical lesion or into a branch vessel. The bend at the tip of the catheter confers directionality to the guidewire tip. Hook-shaped catheter heads are useful for turning an acute angle at a tight corner. Complex-curve catheter heads (e.g. Simmons, H3 Headhunter cerebral) have a curve in one direction, then back in the other direction. These are used primarily to select out aortic side branches for catheterization.

The location of a guide wire placed within the catheter may dramatically alter the shape of the catheter tip. Although this is true for all catheters that are not straight, catheters with a complex curve may assume the widest variety of configurations depending upon the location of the guide wire (Figure 1.4).
Figure 1.4 Catheter head shape depends on guidewire position.

The shape of the catheter head can be significantly modified by the position of the guidewire. This is especially true for flush catheters and complex-curve selective catheters. A. A guidewire is present within the shaft of a hook-shaped visceral catheter. B. The hook of the catheters head splays out as the guidewire enters the curve. C. As the floppy part of the guidewire tip exits the catheter, the head of the catheter splays further. D. The catheter straightens as the firm portion of the guidewire shaft occupies the curved portion of the catheter head. E. As the firm portion of the guidewire exits the catheter head, the catheter straightens out completely.

Guidewire-catheter pitfalls

Successful use of guide wires requires mastery of specific maneuvers. The speed and facility with which the interventionalist handles guide wires correlates with the outcome of the case.
Most guidewire-lesion interactions are predictable. The less predictable interactions usually occur because the fluoroscopy provides only a two-dimensional projection image of a three-dimensional process. These situations may require the use of a different guide wire or of selective catheters.

**Figure 1.5** Guidewire-lesion interactions.

Several possible outcomes may result from interaction between the tip of the guidewire and an occlusive lesion. **A**, A guidewire tip approaches a lesion. **B**, The guidewire traverses the lesion on its first pass. **C**, The guidewire’s leading edge catches on the proximal end of the stenosis. The floppy tip buckles allowing an elbow of guidewire to traverse the lesion. **D**, The floppy tip begins to buckle but catches on a ledge of plaque and is unable to cross the lesion. **E**, The guidewire tip hits plaque and is unable to find the eccentric lumen. **F**, The guidewire piles up proximal to the lesion. **G**, The guidewire finds a subintimal plane. **H**, The guidewire disrupts plaque, which results in embolization of atherosclerotic material.
Several problems may arise during a vascular intervention. Many of them are due to problems with the advancement or steering of a guide wire (Figure 1.5) or catheter, or both. Occasionally, for example, the catheter will not follow the guide wire. This can be due to a variety of causes. Kinking of the guide wire is one potential cause. Once a guidewire has a kink in it, it may be difficult to pass anything on it. If the guide wire pierces the vessel wall and becomes subintimal, a dissection may result. In addition, a narrowed lesion may be so critical that the guidewire itself has interrupted flow and there is not enough residual lumen to pass a catheter. Another common problem is negotiating tortuous arteries. Vessel geometry varies widely and arteries may exhibit tortuosity, kinks, and loops. Tortuous arteries place restrictions upon guidewires and catheters that may not be immediately obvious under the two-dimensional representation available with fluoroscopy. Despite a widely patent lumen, when several vessel turns have already been negotiated and manual purchase on the guidewire tip is limited, forces upon the guidewire-catheter combination may be such that they prevent the ensemble from advancing further into the vessel. Oblique views of the tortuous segments are useful to identify the true angles followed by the arteries. Catheter buckling is also an undesirable complication. This is usually because of distance or tortuosity. Catheter steering is also difficult when trying to enter an aneurysm whose neck is oriented 90 degrees to the parent vessel.

One or many of these factors may contribute to prolonging the procedure. Prolonged navigation can result in increased radiation dose to the patient and interventionalist, thrombus formation, as well as increased volume of contrast administered. In addition, the relative rigidity of the guidewires compared to the vessel walls can result in vessel wall dissection, perforation, and hemorrhage. Complication rates are low and vary across procedures and institutions, but are of clinical significance.

MRI

Nuclear magnetic resonance has its roots in the pioneering work of Bloch, Purcell, and others. It was not until the ground-breaking advances of Lauterber and Mansfield in the 1970s, however, that principles of magnetic resonance were first used to image tissue. Today, the use of MRI is widespread in the diagnosis of disease in almost all organ systems. In principle,
MRI is quite different from X-ray, CT, or ultrasound imaging. MR images rely not on differences in X-ray absorption between different tissues and fluids, but on slight differences in magnetic properties between them. The exquisite detail and information provided by MR images can be used to image almost any soft tissue in the body.

MR images are acquired by placing a patient on a bed in the bore of large superconducting solenoid wire or magnet. The high current running through the solenoid wire produces a very strong, linear and relatively homogenous magnetic field, called the main magnetic field. The characteristic effects on water protons of this constant main magnetic field, as well as other smaller varying magnetic fields (or gradients) applied in a specific spatial and temporal pattern (known as pulse sequences), produce signals that are interpreted mathematically by a computer and give rise to magnetic resonance images. A detailed treatment of the principles behind magnetic resonance imaging is beyond the scope of thesis. The focus here is on basic principles, especially those relating to later chapters.

**From proton to image: an MR physics mini-primer**

In the nucleus of every atom, individual protons and neutrons spin about an axis. This property, called spin angular momentum, can be considered to be the basis of nuclear magnetism. In an atomic nucleus, the combination of protons and neutrons gives rise to a total angular momentum, ℏI, also referred to as the nuclear spin. Rotating charges produce magnetic moments. Since atomic nuclei have charge, this spinning motion produces a magnetic moment along the spin axis. Therefore, as a result of the rotation of the proton’s positive charge, these nuclei have a magnetic moment, \( \mu \), (Figure 1.6A) with

\[
\mu = \gamma \hbar I, \quad (1.1)
\]

where \( \gamma \) is the gyromagnetic ratio for the specific nucleus.

In most nuclei, the particles are paired so that the net magnetic properties cancel. However, if the number of protons or neutrons is odd, complete cancellation is not possible. Nuclei with an unpaired proton or neutron such as hydrogen 1, carbon 13, and sodium 23, among others, exhibit
a net magnetic effect. The relative strength of this magnetic moment is a property of the type of nucleus and therefore determines the MR detection sensitivity. The hydrogen (1H) nucleus, which is highly abundant in biological systems, has the strongest magnetic moment. In the absence of an external magnetic field, at room temperature the proton spins and their resulting magnetic moments are at random orientations in 3-D space. In the presence of an external static magnetic field, B₀, the individual magnetic moments tend to align either parallel or antiparallel to the direction of the applied field, similar to the way a permanent bar magnet will align itself with the field or a compass needle aligns with the earth's magnetic field (Figure 1.6B). The quantization of the magnetic moment, however, results in a misalignment with the applied magnetic field. Due to this misalignment, the nucleus experiences a torque causing a precession around the applied magnetic field (Figure 1.6B). The angular frequency of this movement, ω_L, also known as the Larmor frequency, is given by

$$\omega_L = \gamma B_0$$  \hspace{1cm} (1.2)

where B₀ is the magnetic field strength. For water protons in a 1.5 T MR scanner the Larmor frequency is 64 MHz. In a given volume of tissue or fluid, all the magnetic moments add to give the net magnetization, M, (Figure 1.7), where

$$M = \sum_i \mu_i$$  \hspace{1cm} (1.3)

In the presence of a magnetic field, the quantization of the magnetic moments results in parallel and anti-parallel alignment of protons, with roughly the same number of protons in each state. There is a slight preference for the parallel alignment. The population difference Np − Nap (p for parallel, ap for anti-parallel), results in a net longitudinal magnetization along the axis of the magnetic field, M_Z (Figure 1.7B). The population ratio at equilibrium is given by the Boltzmann factor for the energy difference, γℏB:

$$\frac{N_{ap}}{N_a} = \exp\left( -\frac{\gamma \hbar B}{k_B T} \right)$$  \hspace{1cm} (1.4)
where $k_B$ is Boltzmann’s constant, and $T$ is the absolute temperature.

**Figure 1.6** Magnetic moment of a hydrogen nucleus

**A:** A nucleus has a property called spin. The spinning positive charge causes a magnetic moment $\mu$. **B:** In the presence of a magnetic field, $B_0$, the magnetic moment aligns with the magnetic field. Due to quantum spin states, the alignment is not perfect. The resulting torque on the magnetic moment makes it precess with an angular frequency, or Larmor frequency, $\omega_L$.

**Figure 1.7** Orientation of proton magnetic moments.
**A:** In the absence of an external magnetic field, at room temperature, no net magnetization from individual magnetic moments exists due to Brownian motion. **B:** In the presence of an external magnetic field, $B_0$, the magnetic moments align with the magnetic field. There is a slight preference for the parallel alignment.

In the plane perpendicular to the magnetic field $B_0$ (the transverse plane, or xy-plane), there is no net magnetization in the absence of a magnetic field (Figure 1.8A). If a magnetic field, $B_1$, varying at a radio frequency (RF pulse) matching the Larmor frequency, is applied, the magnetic field environment around the magnetic moments changes (Figure 1.8B). Some of the magnetic moments flip to antiparallel state, and less magnetic moments are in a parallel state. This leads to a decrease of the net longitudinal magnetization, $M_Z$. In addition, some of the magnetic moments will experience a torque from the $B_1$ field and will start to precess around the $B_1$ field in coherent phase, producing a net transverse magnetization, $M_{XY}$ (Figure 1.8B). The magnetic moments effectively experience two different magnetic fields and as a result precess about both fields, with the $\mu_z$ moments precessing about the $B_0$ at the Larmor frequency and the $\mu_{xy}$ moments precessing about the $B_1$ field at a frequency of $\gamma B_1$. If the $B_1$ field is applied for a specific time, $t$, such that the $M$ precesses about $B_1$ for $\frac{1}{4}$ cycle, or $\gamma B_1 * t$, the net magnetization, $M$, effectively flips 90 degrees onto the transverse plane. The process is simplified if observing the behaviour of $M$ while rotating in the xy-plane at the Larmor frequency. In this rotating frame of reference, $B_1$ appears motionless, $B_0$ effectively disappears, and during the RF pulse $M$ precesses about $B_1$ at a frequency $\gamma B_1$ (Figure 1.8C). An MR scanner receive coil is set to detect only the signal caused by the transverse magnetization, $M_{xy}$ and not $M_z$ (longitudinal magnetization).
Figure 1.8 Flipping of tissue magnetization

A: Initially, the main magnetic field of the MR scanner causes the tissue to obtain a net magnetization, $M_z$, aligned with the main magnetic field, $B_0$. This net magnetization is composed of the individual magnetic moments, $\mu_z$, of protons precessing about the main magnetic field axis, $B_0$. B: When a RF pulse, $B_1$, is applied at the Larmor frequency on the x-axis for a specific time, $t$, the individual magnetic moments and resultant net magnetization precess for a time, $t$, about both the $B_0$ field (hatched line) and the $B_1$ field (dotted line). The net effect is that the net magnetization spirals down onto the xy-plane after time, $t$, and continues to rotate around $B_0$ at the Larmor frequency. C: The rotating frame of reference. The process in (B) is simplified if observing the behaviour of $M$ while rotating in the xy-plane at the Larmor frequency. In this frame, $B_1$ appears motionless, $B_0$ effectively disappears, and during the RF pulse $M_z$ precesses about $B_1$ at a frequency $\gamma B_1$. After application of the RF pulse for a time, $t$, the $M_z$ has been flipped onto the XY-plane. This tranverse magnetization is the signal that is sampled by the MR scanner receiver to create MR images.

T1 and T2 relaxation time constants and MRI contrast

The $B_1$ field, however, is turned on briefly while the $B_0$ field is always on. The return of the magnetic moments to the favored parallel alignment state (with the main magnetic field, $B_0$) is a stochastic process. The energy difference between the favored parallel alignment state and the
anti-parallel state is dissipated as heat to the tissue or fluid. The waveform of this signal is an exponentially damped sine wave and is called the free induction decay (Figure 1.9). This return to thermal equilibrium leads to an increase of the longitudinal magnetization with a time constant T1 (Figure 1.10). Although the transverse and longitudinal magnetization are components of one magnetization, transverse magnetization decays more quickly and follows a time constant T2. T2 is always shorter than T1 because the rotating spins create their own “mini” magnetic fields which disturb the magnetic field of adjacent spins. This causes nuclei to precess around B0 at different rates, since $\omega = \gamma B$. This process is called spin dephasing. Dephasing, however, does not influence the state of the individual magnetic moments which determine the longitudinal magnetization, resulting in T1 being longer than T2.

Spins are also disturbed by slight variations in the static magnetic field. These disturbances cause the transverse magnetization to decay more rapidly, and the time constant used to describe this decay is the T2* constant. Methods used to eliminate T2* effects in MRI will be described later.

The contrast in an MR image is determined by differences in signal intensity between different tissues and fluids. Different tissues produce different signal because their T1 and T2 relaxation times differ. Thus the contrast in an MR image is determined by differences in the T1 and T2 constants of different tissues and fluids. Table 1.2 lists T1 and T2 values for a variety of tissues and fluids.

Table 1.2. T1 and T2 relaxation time constants of different tissues at 1.5 T.

<table>
<thead>
<tr>
<th></th>
<th>T1 (ms)</th>
<th>T2 (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain (Gray matter)</td>
<td>810</td>
<td>101</td>
</tr>
<tr>
<td>Brain (white matter)</td>
<td>680</td>
<td>92</td>
</tr>
<tr>
<td>CSF</td>
<td>1900</td>
<td>250</td>
</tr>
</tbody>
</table>
Figure 1.9 Free induction decay.

The voltage signal induced in the receiver coil versus time after an RF pulse is applied.

Figure 1.10 T1 and T2 relaxation constants.

T1 is determined by the rate at which excited protons return to equilibrium within the lattice after an excitation RF pulse. T1, also known as the longitudinal relaxation time, is a measure of the time taken for spinning protons to realign with the external magnetic field. The magnetization will grow after excitation from zero to a value of about 63% of its final value in a time of T1. T2 is a measure of the time taken for spinning protons to lose their phase
coherence among the nuclei spinning perpendicular to the main field due to interaction between spins, resulting in a reduction in the transverse magnetization. The transverse magnetization value will drop from maximum to a value of about 37% of its original value after a time equal to T2.

**Gradients**

To image a sub-volume or cross-section of tissue, the protons in different regions within that sub-volume or cross section must experience a unique magnetic field. This is accomplished by adding magnetic field gradients.

Slice selection gradient:
A RF pulse applied to the entire volume would result in transverse magnetization signal from the entire volume. MR scanners employ selective excitation to select a cross-section of volume to create an image. This is done by adding another magnetic field, called a gradient, that is stronger at one end and decreases gradually along an axis (Figure 1.11) perpendicular to the slice plane. At each location along the gradient, the gradient field either adds to the main field, $B_0$, or subtracts from it. Magnetic gradient causes the field strength to vary linearly with the distance from the center of the magnet. This gradient changes the frequency with which the protons precess around $B_0$. In other words, depending on the location of the proton along the gradient, the proton precesses at different frequency. For example, for a gradient along the z axis, the static magnetic field at any given point will be

$$B_0 + G_z \quad (1.5)$$

where $z$ is the location on the z axis and $G_z$ is the gradient magnetic field strength at that location. Therefore the frequency of precession of protons at location $z$ will be

$$\omega(z) = \gamma(B_0 + G_z(z)) \quad (1.6)$$

With the gradient on, a RF pulse applied at the Larmor frequency, $\omega_L$, will now “excite” only the protons precessing at that frequency. The protons precessing at the Larmor frequency are located at $z_L$, where $G_z = 0$. Therefore, the signal is produced by only the protons in the xy-plane at
location $z_L$ (Figure 1.11). For each image slice acquisition, a different $G_z$ gradient is used to select the appropriate cross-sectional volume.

**Figure 1.11 Slice selection.**

To create a cross-sectional MR image, signal must be isolated from tissue slice or volume. A magnetic field gradient, $G_z$, changes the frequency with which protons precess around $B_0$. As a result, while the gradient is turned on, protons precess at different frequencies depending on the location of the proton within the gradient. A RF pulse applied at the Larmor frequency, $\omega_L$, will “excite” only the protons precessing at that frequency, the protons at the center of the gradient, $G_z$, shown here. Therefore, the signal will be produced by only the protons in the xy-plane at location $z_L$. 

![Diagram of slice selection](image)
**Frequency-encoding and Phase-encoding Gradients**

To localize the voxels (single volume elements containing protons) within a slice of tissue, spatial information needs to be encoded into the MR signal. This is done using gradients. The frequency encoding gradient is similar to the slice selective gradient in that it is stronger at one end and decreases gradually along an axis but is applied perpendicular to the slice selective gradient. It causes protons within a different columns of tissue within a slice to precess at different frequencies (Figure 1.12). The frequency encoding gradient is applied during sampling of the signal (data acquisition). The phase encoding gradient is applied to the tissue volume perpendicular to the frequency encoding gradient. This causes protons within a column to precess faster (if they are closer to the stronger end of the gradient) or slower (if they are closer to the weaker end of the gradient). The protons within the same row, however, have the same phase. Thus, when the phase-encoding gradient is turned off, protons within columns are in different phases of their spin (Figure 1.12).

![Figure 1.12](image)

**Figure 1.12** Effect of frequency encoding and phase encoding gradients on a tissue slice.

**A.** Protons at the stronger end of the frequency encoding gradient (on the left) precess at a higher frequency than protons at the weaker end (on the right). This creates columns of protons precessing at a different frequencies. **B.** The phase encode gradient also increases the precession frequency of protons closer to its stronger end but along the perpendicular axis of the imaging plane. There is another difference between the frequency encoding gradient and the phase encode gradient. The phase encoding gradient is applied and for a specific period of time. The result is that
after a phase encoding gradient, protons are in different phase but still spinning at the Larmor frequency. Note, however, that protons within the same row have the same phase.

**K-space**

The MR signal for a given slice is the sum of all these individual proton signals, each with their own frequencies (encoding in the frequency-encoding direction) and phase shifts (encoding in the phase-encoding direction) as well as amplitudes. The raw data from the MR signal are digitized and stored into a data matrix called k-space. K-space data is equivalent to a Fourier plane and reconstructing the image from raw data requires a mathematical operation, the 2D inverse Fourier Transform. The Fourier transform is a mathematical procedure that decomposes a signal into a sum of sine waves of different frequencies, phases and amplitude. The inverse Fourier transform takes the frequency, phase, and amplitude information reconstructs it into an image.

K-space is best described as a 3D histogram. This histogram tabulates the frequency, phase, and amplitude of individual waves combining to form the MR signal. On one axis of k-space is the horizontal frequency domain (frequency encode direction). The other axis is the vertical frequency domain (phase encode direction). Each point along a frequency domain represents a wave of a specific frequency. Low frequency values are in the center of k-space and high frequencies towards the periphery. Image features that change in intensity over short image distances correspond to high spatial frequencies. Image features that change in intensity over large image distances correspond to low spatial frequencies. Each point in k-space also contains information about amplitude, with bright points corresponding to high amplitude, and phase, which is represented by color. An example of k-space is shown in Figure 1.13.
Figure 1.13 The k-space data for a brain MRI image.

**Pulse sequences**

The way k-space is filled depends on the specific RF pulses and gradient combinations. These nature and timing of these combinations are referred to as pulse sequences.

Spin-echo (SE) pulse sequence (Figure 1.14): In a classic spin-echo sequence, k-space is filled one line at a time. The first step is application of a slice selective gradient (SSG). With the SSG on, an RF pulse (which flips magnetization 90°) is applied to excite only the protons in the desired slice. The slice select gradient is turned off. The next step is to apply the phase encoding gradient. K-space is filled in horizontal lines (just as you would fill a page when writing) using the phase and frequency encode gradients. This requires many steps.

In a standard SE, the number of phase-encoding steps is equal to the number of horizontal lines of k-space. Each step is performed with an incremental change in the strength of the phase encoding gradient. For example, to acquire the first line of k-space, first, a strong negative phase-encoding gradient is applied which would place data in the bottom row of k-space. Second, a positive frequency-encoding gradient (the dephasing lobe) brings us to the lower right corner. To obtain T2 weighting of an image, a 180° RF pulse is applied with another SSG. The 180° RF pulse is responsible for canceling spin dephasing that has occurred since the initial 90° RF pulse due to static field inhomogeneities, so that the transverse magnetization decay is T2-dependent instead of T2*-dependent. The 180° RF pulse moves us to the opposite location, in the upper left corner of kspace. After a time, TE, called the echo time, since the initial 90° RF pulse, a positive
frequency-encoding gradient is applied during which the signal is sampled and data is acquired. This data acquired fills the top line of k-space. This sequence is repeated for each line with increasing phase-encoding gradient strength (negative to positive intensity). The amount of gradient phase change between adjacent lines is constant. This results in a sequential (line by line) filling of k-space from top to bottom. The time between two 90° RF pulses is called the repetition time, TR, and in conventional spin-echo it varies between 100 ms and 3 s. With a regular SE sequence, only one line of k-space is filled during a TR. The acquisition time for an image slice is therefore equal to the TR * number of lines. When TR is short, not all tissues will have undergone complete T1 relaxation and image contrast will become more dependent on the T1 relaxation process. When TR is long, the image will be more dependent on T2 processes.

Gradient echo (GRE) pulse sequence (Figure 1.15): The GRE pulse sequence differs from SE by its use of less than 90° RF pulses and by substitution of the 180° RF pulses with rephasing gradients. A lower flip decreases the amount of magnetization tipped into the transverse plane. The consequence of a low-flip angle excitation is a faster recovery of longitudinal magnetization that allows shorter TR/TE and decreases scan time. Since there is no rephasing, the contrast in GRE is due to T2* effects (pure T2 and static field inhomogeneity).

In the absence of the 180° RF pulse, a bipolar readout gradient (which is the same as the frequency-encoding gradient) is used to create an echo. The gradient echo formation results from applying a dephasing gradient before the frequency-encoding or readout gradient. The goal of this dephasing gradient is to obtain an echo when the readout gradient is applied and the data are acquired. The dephasing stage of the readout gradient is in the inverse sign of the readout gradient during data acquisition. Moreover, its dephasing effect is designed so that it corresponds to half of the dephasing effect of the readout gradient during data acquisition. Consequently, during data acquisition, the readout gradient will rephase the spins in the first half of the readout (by reversing the dephasing effect of the dephasing lobe), and the spins will dephase in the second half (due to the dephasing effect of the readout gradient). The time during which the peak signal is obtained is called Echo Time (TE). The resulting contrast in basic GE sequences is a variable mix of T1 and T2*. The higher the flip angle, the more T1-weighted the image. The shorter the TE, the less T2*-weighted the image. Lastly, the strongest MR signal is obtained at the optimal combination between the TR and the flip angle, called the Ernst angle. Ernst angles are tissue-specific.
Figure 1.14 Spin-echo pulse sequence.

SSG – slice selective gradient, PEG – phase encoding gradient, FEG – frequency encoding gradient, TE – echo time.
Figure 1.15 Gradient-echo pulse sequence.

SSG – slice selective gradient, PEG – phase encoding gradient, FEG – frequency encoding gradient, TE – echo time.

**Real-time MR pulse sequences**

To perform vascular interventions, high temporal resolution imaging is essential for guidance. MR-guidance of endovascular interventions is only possible because of the technical advances in MR hardware and software in the past decade. Several approaches to achieve faster MR imaging have been explored and are discussed below. In the case of pulse sequences, generic and proprietary names for pulse sequences are listed.
**Stronger and faster magnetic field gradients**

Traversing the same k space in a shorter time, also requires stronger gradients. Improvements in magnet coils capable of rapid switching and stronger magnetic field gradients, has permitted faster imaging. A TR of 3 ms, for example, will generate more than 300 distinct echoes per second. If TR is 1 ms, then 1000 echoes could be generated. Additional gains of gradient performance are expected but must be weighed against limitations in signal-to-noise ratio (SNR) and physiological consequences such as heating or peripheral nerve stimulation. Since magnetic resonance imaging is an art in optimization of imaging parameters, interventional imaging requires a compromise between temporal and spatial resolution that favors speed\(^{41}\) and real-time pulse sequences do not offer the high resolution of conventional sequences.

**Increased signal using balanced gradients (steady-state free precession [SSFP])**

<table>
<thead>
<tr>
<th>Pulse Sequence</th>
<th>Manufacturer</th>
</tr>
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<tbody>
<tr>
<td>TrueFISP (fast imaging with steady-state precession)</td>
<td>Siemens Medical Solutions</td>
</tr>
<tr>
<td>FIESTA (fast imaging employing steady-state acquisition)</td>
<td>GE Medical Systems</td>
</tr>
<tr>
<td>Balanced FFE (fast field echo)</td>
<td>Philips Medical Systems</td>
</tr>
<tr>
<td>BASG (balanced SARGE)</td>
<td>Hitachi</td>
</tr>
<tr>
<td>True-SSFP (steady-state free precession)</td>
<td>Toshiba</td>
</tr>
</tbody>
</table>

The most widely used pulse sequence for endovascular interventions is balanced gradient imaging technique because of its relatively high SNR in short TR sequences. Balanced SSFP sequences are sequences in which the net phase change caused by all three gradients (frequency, phase, and slice) is zero. This sequence has complex contrast characteristics, but the contrast between different tissues or between tissue and blood can be altered using intermittent magnetization preparation pulses or advanced excitation techniques\(^{42-48}\). Since SSFP images feature long T2 values, they are particularly valuable for tracking endovascular catheters and vascular anatomy\(^{49}\). Its limitations are the T2/T1 weighting, banding artifacts caused by imperfect shimming or susceptibility effects (minimized with use of a short TR). Balanced SSFP, however, does not show high sensitivity to T2* effects, as might a gradient-echo sequence.
Fast spin echo or RARE (Rapid Acquisition with Relaxation Enhancement)

<table>
<thead>
<tr>
<th>Turbo spin echo (TSE)</th>
<th>Siemens Medical Solutions, Philips Medical Systems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast spin echo (FSE)</td>
<td>Toshiba, GE Medical Systems, Hitachi</td>
</tr>
</tbody>
</table>

In a conventional spin echo sequence, only one line of k space is acquired after the single 180° refocusing pulse in each TR period. As a result, conventional spin-echo imaging is slow, particularly for T2-weighted sequences, in which TR values are long. Even "short" TRs are relatively long, to give longitudinal magnetization a chance to recover from the 90° flip. The RARE sequence is based on conventional spin echo but uses multiple refocusing pulses to acquire several lines of k space in a single TR period. It allows fast imaging while retaining the advantage of low sensitivity to susceptibility artifacts and magnet inhomogeneities seen with other spin-echo sequences. Its speed allows 3D T2-weighted imaging. RARE imaging, however, is prone to blurring, ghosting artifacts, and edge enhancement. Since many 180° pulses are transmitted in a single TR, RARE sequences can have a high specific absorption rate.

Ultrafast Gradient Echo

<table>
<thead>
<tr>
<th>TurboFLASH</th>
<th>Siemens Medical Systems</th>
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</thead>
<tbody>
<tr>
<td>TFE (turbo field echo)</td>
<td>Philips Medical Systems</td>
</tr>
<tr>
<td>Fast SPGR</td>
<td>GE Medical Systems</td>
</tr>
<tr>
<td>RSSG (RF spoiled SARGE [steady state acquisition with rewound gradient echo])</td>
<td>Hitachi</td>
</tr>
<tr>
<td>T1-FFE (fast field echo)</td>
<td>Toshiba</td>
</tr>
</tbody>
</table>

Gradient echo sequences that acquire an image in less than a second are considered ultrafast sequences. Achieving adequate signal and contrast in gradient-echo sequence with a very short TR and TE is a problem. For T1 weighting, a larger flip angle is needed, but the optimal flip angle for a good signal-to-noise ratio (SNR) (ie, the Ernst angle) at short TRs is small. Ultrafast sequences overcome this problem by incorporating a 180° RF pulse prior to the gradient-echo
host. The 180° flip introduces increased T1 weighting and all lines in k space are acquired after this single preparatory pulse.

**Echo planar imaging**

<table>
<thead>
<tr>
<th>EPI</th>
<th>Siemens Medical Solutions, GE Medical Systems, Philips Medical Systems, Toshiba, Hitachi</th>
</tr>
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</table>

Fast gradient-echo sequences generate a single echo with every RF excitation flip applied. In the EPI sequence, multiple echoes and k-space lines are acquired with a single RF pulse. In single-shot EPI, the entire k-space matrix is filled within a single TR. The result is an extremely fast T2* weighted sequence, often used to generate 2D images in a single subsecond shot.

Adaptations of the basic EPI sequence are used in diffusion imaging, perfusion imaging, and functional MR imaging. Its main limitation is that it is very artifact prone since it is sensitive to susceptibility effects and field non-uniformities that result in signal voids and image distortions. It is also susceptible to ghosting artifact in the phase-encoding direction.

**HASTE (Half-Fourier-Acquired Single-Shot Turbo Spin Echo)**

<table>
<thead>
<tr>
<th>HASTE</th>
<th>Siemens Medical Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS-FSE (single-shot fast spin echo)</td>
<td>GE Medical Systems, Philips Medical Systems</td>
</tr>
<tr>
<td>FSE-ADA (fast spin echo, asymmetric data allocation with half scan)</td>
<td>Hitachi</td>
</tr>
<tr>
<td>FASE (fast advanced spin echo)</td>
<td>Toshiba</td>
</tr>
</tbody>
</table>

HASTE is a modification of the RARE sequence that uses the redundancy of kspace for even faster imaging. Filling all of k space in a single shot with a RARE sequence is possible. However, considerable T2 decay takes place over the relatively long period of acquisition, and single-shot RARE is effectively restricted to imaging fluid (as in MR cholangiopancreatography examinations). The HASTE sequence is an adaptation of RARE that reduces total acquisition
time by acquiring only half of k space. Filling half of k space is sufficient to generate an image due to the symmetry of kspace. The HASTE sequence allows subsecond acquisitions of 2D slices. Also, due to its long echo train (all the echoes take place in a single TR), HASTE images will be T2-weighted.

**Alternative k-space trajectories**

Alternative k-space sampling trajectories require additional post-processing to normalize and re-grid the data but provide important advantages such as small field of view imaging or motion insensitivity. For example, frequency space can be sampled radially so that each echo intersects the center frequency. Spiral or more complex sampling of frequency space may also be used.

**Parallel imaging techniques**

Although impressive gains have been made and the acquisition times of many sequences have been reduced from minutes to seconds, some fundamental limitations have been reached due to technical and physiologic problems associated with faster and stronger, rapidly switching gradients. Recently, parallel imaging has emerged as a technique that can surmount many of these obstacles by using the inherent spatial sensitivity of phased-array coils to provide some of the spatial information in the image that would otherwise be obtained in the traditional manner of Fourier transform MR imaging.

Parallel imaging refers to the use of multiple receiver coils at different locations creating different sensitivity maps over the imaged area. In other words, multiple receiver coils receive signal from its neighborhood, the final sum being the combined signal coming from all protons modulated by their distances to the coil. This modulation or weighting constitutes the sensitivity profile of that coil. If one has the different combinatorial weighted sums of a signal population, one can compute the original signals via mathematical transformations. Parallel imaging techniques require multiple hardware receiver channel systems, special receiver coils, and increased computational power for image reconstruction. Parallel imaging allows a reduction in the number of phase-encoding steps (and consequently, the number of sampled k-space lines is reduced) but still produces images of reasonable quality and spatial resolution. Parallel imaging increases the acquisition speed by factors of 1.5 to 3 in most commercially available applications.
In theory, much higher gains are possible, but they are currently limited by reconstruction artifacts and decreased signal-to-noise ratio (SNR) due to short acquisition time and large FOV. New techniques include simultaneous acquisition of spatial harmonics (SMASH)\textsuperscript{53}, sensitivity encoding (SENSE)\textsuperscript{54}, and generalized autocalibrating partially parallel acquisitions (GRAPPA)\textsuperscript{55}.

**Hybrid schemes**

Multiple methods can also be combined. For example, the steady-state projection imaging with dynamic echo-train readout (SPIDER) sequence combines echo train readout (acquiring 3 echoes at each TR), partial echo readout at odd echoes (using k-space symmetry), and a radial k-space sampling\textsuperscript{56}. Variable and sliding window image reconstructions consisting of high temporal resolution echoes and high spatial resolution echoes can be alternated or used at the same time during continuous MRI. A slightly different approach can be used for multiple field of view imaging in Cartesian imaging\textsuperscript{57}.

The main pulse sequences used today for interventional MR imaging are T1/T2-weighted FISP and TrueFISP, T2-weighted turbo spin-echo, and T1-weighted FLASH. The specific clinical question, the underlying pathophysiology, and the procedure to be performed dictate which sequence is used. Each of these sequences has been written to acquire data in conventional rectilinear trajectories, radial k-space paths, or even spirals\textsuperscript{58}.

**MR-guided endovascular intervention**

X-ray fluoroscopy allows high spatial and temporal resolution, making it very useful for image-guidance of endovascular procedures. Recently, magnetic resonance imaging (MRI) has emerged as a potential alternative, offering distinct advantages and disadvantages compared to X-ray fluoroscopy (Table 1.2). Real-time MRI allows exquisite soft tissue visualization of anatomy not possible with projection X-ray images, at a comparable temporal resolution. In the vascular system, the excellent soft-tissue contrast permits evaluation of the anatomic context of vessels, and allows, in principle, imaging of the vessel wall and assessment of the composition of plaques\textsuperscript{59, 60}. For superficial vessels (eg carotid artery) sufficient signal-to-noise ratio in combination with sufficient spatial resolution can be obtained with surface coils\textsuperscript{61}, but for deeper vessels intravascular coils are necessary\textsuperscript{61-63}.
In addition, in contrast to X-ray fluoroscopy and DSA, which provide only projection images, MRI allows selection of any imaging volume. It offers multiplanar two-dimensional and three-dimensional imaging of the vascular anatomy and catheter position in any imaging plane. Changing the orientation of the imaging volume can be done without moving hardware or the patient. Appropriate selection of the imaging slice can prevent projection of other anatomy on the structure of interest. In the vascular system, the freedom in selecting imaging geometry and the 3D capabilities provided by MR are useful to prevent projection of vessels onto each other. The imaging plane or the view angle of a three-dimensional dataset can be optimized to show any bifurcation, clearly separating branch and parent vessel. Furthermore, asymmetric stenoses can be better resolved with MRI in cases where DSA projection images overestimate the size of their lumen.

Since MRI allows the visualization of both blood vessels and adjacent soft tissue pathology, planning of the interventional procedure and direct morphologic assessments of the therapeutic effects are facilitated. Of particular interest to vascular intervention is the ability to measure blood flow and volume flow rate using MRI, and the ability to perform MR angiography (MRA) both with and without the contrast media.

Another distinct advantage of MRI is the ability to perform functional measurements. Apart from images in which contrast is based on $T_1$ and $T_2$ and proton density, MR images can be qualitative and quantitative maps of many other parameters. These include temperature maps,$^{64-66}$ restricted diffusion,$^{67}$ and brain activation.$^{68}$ In addition, measurements of blood flow or perfusion of surrounding tissues, during and after an intervention, can be obtained$^{69-72}$. MR spectroscopy can also provide information about tissue composition,$^{73}$ and can be used to generate images that depict tissue elasticity or stiffness.$^{74,75}$ Maps based on these parameters offer new possibilities for treatment evaluation. Images acquired before, during, and after a vascular intervention can be used to assess functional improvement. Perfusion and flow quantification could be potentially useful, for example, in determining hemodynamic changes resulting from recanalization of a thrombosed vessel or embolization of an arteriovenous malformation. Combining anatomical and functional MR information would allow discrimination between an adequate or an inadequate therapeutic result.
In addition, there is no ionizing radiation exposure to the patient or the medical staff in the MRI environment. MR contrast agents also have the potential to provide functional information. MR contrast agents sensitive to a variety of physical parameters, such as pH, calcium concentration, and gene expression, have been designed.\textsuperscript{76-81} These contrast agents could yield information about physiology and metabolism, in combination with anatomy.

Table 1.2 Comparison of MRI and Xray fluoroscopy for endovascular intervention

<table>
<thead>
<tr>
<th></th>
<th>MRI</th>
<th>Fluoroscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High temporal resolution</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Soft-tissue imaging</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3D imaging capability</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Information on catheter position</td>
<td>Excellent</td>
<td>Fair</td>
</tr>
<tr>
<td>Functional Information (eg flow, perfusion, temperature)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ionizing Radiation</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Equipment Restrictions</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>eg ferromagnetic metals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient accessibility</td>
<td>Poor</td>
<td>Excellent</td>
</tr>
<tr>
<td>Cost</td>
<td>Higher</td>
<td>Lower</td>
</tr>
<tr>
<td>Imaging</td>
<td>Slice-selective</td>
<td>Projection</td>
</tr>
</tbody>
</table>

**Interventional MRI scanners**

One of the disadvantages of using MRI for guiding interventions is limited patient access due to the closed configuration of the magnet. Although MRI magnet bore lengths and inner diameters vary, a patient must be inside the bore during imaging, which severely restricts the space at the disposal of the interventionalist for performing tasks. In contrast, X-ray fluoroscopy C-arms are considerably smaller and their open configuration allows better patient access.
Diagnostic MR imaging is done today by placing a subject in the bore of a superconducting wire solenoid, called a magnet. The main magnetic field strength may range from 0.2 Tesla (T) and 3 T, although each individual MR scanner is engineered to produce only one constant main magnetic field strength. An MR scanner can be open or closed. A typical clinical MRI scanner is closed, that is, shaped like a large tube, open at both ends, in which the patient is placed lying on the scanner table. However, the inner circumference of a closed MRI is not large enough to accommodate obese individuals. This limitation, coupled with the claustrophobia some people experience in a closed MRI, prompted the development of the open MRI. Open MRI scanners, although more comfortable for patients, are limited by lower magnetic field strength, which leads to lower SNR and lower resolution, and, therefore, images clearly inferior to the closed MR scanners. Furthermore, MRA is possible only at high field strengths.

Initial attempts at performing interventional procedures under MR guidance have been on dedicated open MRI scanners\textsuperscript{82-94}, which facilitated instrumentation and ease patient access and handling. The limitation of open scanners, however, is their low field strengths (less than 0.5 T). Low field strength scanners can be useful for biopsies, which do not require high-resolution or real-time imaging. For vascular interventional procedures, however, the need for high spatial and temporal resolution for monitoring purposes renders low-field systems unsuitable\textsuperscript{95, 96}. This issue has been addressed by major MRI vendors through development of various types of 1.5 T and 3 T magnet configurations, including short-bore scanners with high-performance gradient coils, and combining X-ray and MRI systems (XMR) in a setup that enables quick patient transport between the two systems, using a floating tabletop.

**Catheter tracking and intravascular visualization**

Accurate and reliable visualization of interventional devices such as intravascular catheters or needles are indispensable requirements for safe and successful interventional procedures. In DSA, catheters, guidewires, stents, clips, and pacemaker leads are visible due to their high atomic number relative to blood. Different methods for device localization in MRI have been proposed and can be classified into two categories: passive and active. Passive techniques visualize the devices by changing their contrast properties in relation to blood. These methods are based on the use of susceptibility agents at the catheter tip creating a localized region of
signal attenuation or enhancement\textsuperscript{97-101}, contrast agents\textsuperscript{102-104}, or inductively coupled resonant circuits\textsuperscript{105, 106}. With passive techniques there is no connection from the device to the MRI system using elongated conductors or galvanic connections. Automatic visualization and correct imaging plane selection, however, is not possible with passive techniques since device coordinates are not registered. In addition, artifact size and thus visibility depend on various parameters, such as field strength, device orientation to the main magnetic field, and the image sequence. GRE sequences, for example, result in larger susceptibility artifacts and consequently poorer information on surrounding tissues, whereas spin-echo sequences produce smaller areas of signal cancellation\textsuperscript{107}.

Active tracking techniques employ a small RF coil in the catheter or guidewire, which can be connected to the MRI receiver system\textsuperscript{108-110}. The RF coil is a microcoil and loopless antenna similar to receive coils used for intravascular imaging\textsuperscript{43, 62, 101, 111-115}. In combination with fast projection measurements, actively tracked interventional devices can thus be localized in a few milliseconds\textsuperscript{108, 109, 116-120}. The RF coil is connected to the MR scanner via a coaxial cable and data processing unit. The coil position is determined by the sequential acquisition of one-dimensional signal profiles after three orthogonal gradients are applied in turn. Since the signal picked up by the RF coil comes from a very limited area, the one-dimensional signal shows a distinctive peak at the position of the coil. The location of the coil is displayed as a color-coded icon onto a separately acquired vascular roadmap image. This information can be used to change the imaging plane to that which contains microcoil. Superimposing the RF coil position marker on a set of images also makes bi- or triplanar tracking possible\textsuperscript{121}. 3D spatial coordinates can also be used to determine imaging planes that pass through the tracking point, allowing updates at the exact location of the coil in 2D imaging. Visualization of the full catheter curving and shape inside the vessel is necessary for vascular interventions. Elongation of the RF coil, for example, as electrically coupled, loopless antennas in the device produces a profile of the catheter or wire\textsuperscript{115, 118}. Use of such an antenna in this way is termed “MR profiling”\textsuperscript{119, 122, 123} and may provide enough signal for limited manipulation without an external roadmap. Since data for a full image must be collected for MR profiling, temporal resolution is limited more than in simple tracking.

With the development of these technologies, MR guided interventions have evolved into clinically viable options for a variety of minimally invasive surgical and therapeutic
MR guidance of vascular intervention would be extremely useful in the diagnosis and treatment of many disease processes, which might include, but not be limited to, stroke therapy, embolotherapy\textsuperscript{127}, angioplasty and stent deployment\textsuperscript{83, 84, 88}, cardiac catheterization\textsuperscript{103}, and endovascular delivery of drugs, genes\textsuperscript{128-130}, stem cells\textsuperscript{131-133}, and prosthetic valves\textsuperscript{134}, where information about the vessel wall, atherosclerotic plaques, and perivascular tissue in real-time is of great interest.

**MR safety and compatibility**

The MR imaging environment, with its strong magnetic field and RF fields, restricts the types of materials and devices that can be safely used in its vicinity. Ferromagnetic and highly paramagnetic materials experience strong magnetic forces in the presence of a magnetic field. Objects containing these materials may become dangerous projectiles when brought in the vicinity of the scanner. Medical devices made of ferromagnetic materials that must remain in fixed position, such as stents or aneurysm clips, may become dislodged in an MR scanner, with tragic consequences. The forces scale with the size of the object and with the volume susceptibility of the material\textsuperscript{96, 135}. A volume susceptibility > 10\textsuperscript{-2} should therefore only be used cautiously in the construction of interventional devices\textsuperscript{136}.

Nonferromagnetic conducting metals used in guidewire cores, braided catheters, and in coils for active catheter tracking of catheter tip position or intravascular imaging\textsuperscript{137, 138} can also pose a hazard to the patient. The development of any device for use in an MR setting precludes that patient safety is ensured against potential heating of tissues located in the vicinity of the metallic wire\textsuperscript{139-144}. Beyond the well-known case of metallic implants (even nonferromagnetic ones) that can cause heating hazards\textsuperscript{145}, several authors have investigated the specific case of metallic wires during interventional MRI\textsuperscript{135, 146-148}. Most studies have shown that the specific absorption rate (SAR) measured in the presence of a metallic wire can overcome the SAR limitation of 2 W/kg\textsuperscript{141, 143, 144}. This local SAR elevation induces an increase of temperature in the tissue near vicinity of the wire, and is potentially harmful to the patient. To avoid any potential damage to tissues or blood, the maximal temperature rise should not exceed 4°C\textsuperscript{149}. The Food and Drug administration recommends that the temperature rise be limited to a maximum of 1°C in the head and 2 °C in the torso\textsuperscript{150}. 

38
Heating of conductive wires in an MRI setting can arise from time-varying RF magnetic fields through a variety of mechanisms: 1) electromagnetic induction heating, 2) heating due to the antenna effect, and 3) heating in a resonant circuit. Tissue heating through these mechanisms is through resistive dissipation.

A change in the flux of the magnetic induction through a fixed circuit gives rise to an electromotive force (EMF), which lasts as long as the flux is changing. The magnitude of this induced EMF is proportional to the rate of change of flux with time\(^{151}\). These currents, referred to as Eddy currents, are induced by the changing magnetic field and result in joule heating of the conducting specimen\(^{152}\). In this case, the absorbed power is proportional to the area of the conducting loop. Therefore, inductive RF-heating by devices can be limited by excluding large conductive loops from the design.

A less predictable phenomenon is the coupling of the electric component of the RF fields to long conducting structures. When considering current induction in lengths of cable, the cable can be considered as a radiofrequency (RF) wire antenna. This type of antenna has a larger sensitivity for the electric component than for the magnetic component of the RF radiation. The additional electric field induced by the currents in this antenna has a maximum field line density at the antenna tip\(^{153}\).

Maximum electromagnetic induction heating can occur when the circuit is in a resonant condition, resulting in induction of a maximum current\(^{152}\). Peak current in a conducting coil exposed to time-varying magnetic fields occurs when the circuit is in a resonant condition,

\[
\omega = 1/(L/C)^{1/2} \quad (1.7)
\]

where \(L\) is inductance, \(C\) is the capacitance, and \(\omega\) is the frequency of the oscillating voltage.

The heating of tissue close to the wire follows the tissue bio-heat law established by Pennes in 1948\(^{154}\). According to this law, local heating can be expressed as the sum of the heat produced by: 1) the metabolic activity of the cells forming the surrounding tissues, 2) the energy evacuated
by the blood flow irrigating the tissues, and 3) the energy concentrated locally by the SAR. Without RF stimulation, the first two terms equilibrate to a steady level equal to the blood flow temperature. During MRI, the energy from RF fields is deposited and adds local heating. Indeed, since the metallic wire concentrates the RF electric field and may introduce an RF-induced current, the third term is emphasized in the close vicinity of the wire. In vitro temperature increases in the range of 18 to 48°C have been reported, using a standard conducting guidewire, coaxial cable, and miniature tracking coil\textsuperscript{141, 155}, levels that are incompatible with patient safety\textsuperscript{141, 143, 144}.

Studies on the temperature elevations caused by RF heating of conducting wires in MRI have demonstrated the following: 1) the heating occurs specifically at the wire tip, with no significant heating detected along the cable, 2) the temperature elevation ranges from moderate to extreme, 3) good reproducibility has rarely been observed, and 4) the wire geometry (diameter and length) determines the strength of the E-field concentration, 5) the primary heating mechanism is via coupling to the long wire between the intravascular coil and the scanner, 6) placing the wire near the isocenter produces less heating, 7) The smaller the radius of the wire, the higher the temperature increase, 8) the degree of heating at the RF coil is also directly proportional to the power of the RF pulses\textsuperscript{140, 141, 143-145, 156}. Wire length has also been found to be important. When the wire length increases, the heat deposition increases and, at a critical wire length, the heat deposition reaches its highest value and begins to decrease with further increases in the wire length. This critical length is sometimes called the resonance length and it is approximately half the wavelength of the transmitted RF pulse inside the object.

The above heating considerations are identical for both an isolated guide wire or a long wire connector for an intravascular coil. The conductivity of a wire and resulting potential heating in close proximity of the wire is a major hurdle preventing further progress and clinical applicability of MR-guided vascular interventions. Currently available state-of-the-art guide wires are made of a Nickel-Titanium alloy (nitinol) with a polyurethane coating and provide unsurpassed mechanical properties. Since nitinol is non-ferromagnetic, the magnetic susceptibility artifacts are small and confined to a submillimeter region around the material. Unfortunately, the wire is also a conductor which couples with the E-field of the RF pulse used in MR imaging. Using non-conducting materials such as plastic wires would circumvent this problem but their mechanical properties are inferior to nitinol. Guide wires with a stainless steel
core have an even greater conductivity, and being ferromagnetic they are sensitive to magnetic forces.

For small-area coils used in interventional intravascular imaging or tracking, the primary heating mechanism is via electric field coupling to the long cable between the coil and scanner and not due to magnetic field coupling to the coil. This was demonstrated by a number of experiments which showed that 1) heating did not depend on whether the coil was tuned or not tuned, 2) the heating was not dependent on the orientation of the coil within the $B_1$ field, 3) long cables without any RF coil showed significant heating, whereas RF coils without any cable attached showed no heating, 4) maximal heating was obtained when the cable was along the bore wall, whereas a cable near isocenter showed much less heating, indicating coupling to the $E_1$ field of the body coil. RF heating of long conducting structures in interventional MRI is a subject of intense ongoing investigation.

In addition, some materials, although safe in the MR environment, can still be MR incompatible if they interfere with the imaging process and result in image degradation. Components that do not possess a large magnetic susceptibility to experience magnetic forces still may have a susceptibility that is sufficiently different from that of tissues to noticeably disturb field homogeneity with associated signal loss and geometric distortions. This is typically the case for materials that have a magnetic susceptibility difference compared to tissue $> 10^{-5}$. Distortions of the RF field by conducting components result in artifacts that appear as abnormally bright and dark regions in the image. MR compatibility thus also supposes careful selection of materials to minimize image artifacts.

**Endovascular catheter steering using induced magnetic torque**

The magnetic field present in an MR scanner also provides a unique environment and a special opportunity for the development of novel endovascular catheter steering mechanism as well as passive visualization of the catheter tip. Using 1.5 F catheters in a 2 T scanner, Roberts et al. demonstrated that current applied to solenoid and modified Helmholtz-type coils wound at the tip of a catheter can be used to steer a catheter tip through simulated vessel branch points. This
was achieved using a current running through a wire solenoid which induces a magnetic moment, \( M \), within the solenoid, given by the equation,

\[
M = nIA,
\]

\( (1.8) \)

where \( n \), is the number of turns in the solenoid, \( I \), is the current applied in Amperes, and \( A \), is the cross-sectional area of the solenoid in meters squared. In a constant magnetic field, such as that of an MR scanner, the magnetic moment created in the solenoid experiences a torque, \( \tau_{\text{mag}} \), given by the equation,

\[
\tau_{\text{mag}} = M \times B,
\]

\( (1.9) \)

where \( M \) is the magnetic moment vector and \( B \) is the main magnetic field vector (Figure 1.16).

---

**Figure 1.16** Schematic for a single-axis (solenoidal) coil, perpendicular to the main field, B.

A positive current (arrowhead) in the coil wound around the catheter tip generates a magnetic moment, \( M \), (dashed arrow) which experiences a magnetic torque, \( \tau_{\text{mag}} \), and leads to a net upwards catheter tip deflection; conversely, a negative current leads to a downward catheter tip deflection.
By applying DC currents in the 100 mA range, using MR guidance with a real-time pulse sequence in a 2 T clinical MRI scanner, this catheter was successfully guided through a 3D vessel-mimicking phantom. Catheter steering using this mechanism may result in increased control of the catheter tip and improved navigation during endovascular intervention over traditional steerable guidewire or selective catheter-guidewire techniques. As a result, the incidence of complications due to dissection and perforation should decrease. By making navigation into branch vessels easier, procedure time should also decrease, resulting in decreased radiation dose as well as decreased risk of thrombus formation.

Further development of catheters incorporating MARC steering should begin with a fundamental understanding of the physical factors governing the behavior of the catheter tip. For the design of a control system, delivery of appropriate currents is critical for attaining desired deflections as well as minimizing unwanted heating. In addition, by maximizing deflection efficiency per mA of current applied, power usage (and resultant heating) can be minimized.

**Thesis contents**

**Chapter 2** of this thesis further investigates this novel catheter steering mechanism by derivation and experimental validation of an equation that characterizes the relationship between catheter deflection and physical factors affecting deflection. Based on these findings, implications for catheter design and implementation are discussed. In attempt to increase the magnetic moment for a given amount of current applied, and thus increase the resultant deflection, paramagnetic materials are inserted within the lumen of the catheter-solenoid tip and studied in **Chapter 3**. While studying these paramagnetic materials, the dependence of their magnetic susceptibility on temperature is proposed as a potential limitation. The change in magnetic susceptibility of a paramagnetic material around its Curie temperature (which is the temperature at which a paramagnetic material transitions from paramagnetic to ferromagnetic state) is studied in the **Appendix**. Since the change in magnetic susceptibility results in a change in the inhomogeneity artifact with changing temperature, the feasibility of employing this mechanism as a temperature reporter in MRI is investigated. The safety concerns regarding the heating of the coil and wires at the catheter tip are preliminarily studied using fiber-optic temperature probes in **Chapter 4**.
Finally, Chapter 5 concludes the thesis with a discussion of the implications of the work of this thesis in the context of interventional MRI.
2. Magnetically-assisted remote control (MARC) steering of endovascular catheters for interventional MRI: A model for deflection and design implications*

**Background and Objectives:** Current applied to wire coils wound at the tip of an endovascular catheter can be used to remotely steer a catheter under magnetic resonance imaging guidance. In this study, we derive and validate an equation that characterizes the relationship between deflection and a number of physical factors: \( \frac{\theta}{\sin(\gamma - \theta)} = \frac{nIABL}{EI_A} \), where \( \theta \) is the deflection angle, \( n \) is the number of solenoidal turns, \( I \) is the current, \( A \) is the cross-sectional area of the catheter tip, \( B \) is the MR scanner main magnetic field, \( L \) is the unconstrained catheter length, \( E \) is Young’s Modulus for the catheter material, and \( I_A \) is the area moment of inertia, and \( \gamma \) is the initial angle between the catheter tip and \( B \).

**Method and Materials:** Solenoids of 50, 100, or 150 turns were wound on 1.8 F and 5 F catheters. Varying currents were applied remotely using a DC power supply in the MRI control room. The distal catheter tip was suspended within a phantom at varying lengths. Images were obtained with a 1.5 T or a 3 T MR scanner using “real-time” MR pulse sequences. Deflection angles were measured on acquired images. Catheter bending stiffness was determined using a tensile testing apparatus and a stereomicroscope.

**Results:** Predicted relationships between deflection and various physical factors were observed (\( R^2 = 0.98-0.99 \)).

**Conclusion:** The derived equation provides a framework for modeling of the behavior of the specialized catheter tip. Each physical factor studied has implications for catheter design and device implementation.

Introduction

A growing number of image-guided endovascular interventions are being performed each year as studies continue to demonstrate equivalent or greater efficacy and lower morbidity when compared to traditional surgical techniques\textsuperscript{11-18}. Navigation into target vessels can be achieved either by remote mechanical manipulation of the guidewire tip, along which the catheter may be advanced, or by the use of preformed catheter shapes. Several problems can be encountered in endovascular navigation. Guidewires may kink, buckle, dissect, or perforate through a vessel wall. Navigation is also more difficult in tortuous vessels, especially after several turns have been negotiated, and into branch vessels oriented 90-180° to the parent vessel. Catheter steering difficulties lead to longer procedure times with resultant increased radiation dose and increased risk of thrombus formation.

Recently, magnetic resonance imaging (MRI) has emerged as an alternative to digital subtraction angiography (DSA) for image-guidance of endovascular procedures. Real-time MRI allows visualization of soft tissue anatomy not possible with projection X-ray images at comparable temporal resolution. The magnetic field present in an MR scanner also provides a unique environment and a special opportunity for the development of novel endovascular catheter steering mechanism as well as visualization of the catheter tip. Using 1.5 F catheters in a 2 T scanner, Roberts et al\textsuperscript{158} demonstrated that current applied to solenoid and Helmholtz-type coils wound at the tip of a catheter can be used to steer a catheter tip through simulated vessel branch points. The local field inhomogeneity created by the induced magnetic moment also allows passive visualization of the catheter tip.

The present study seeks to further investigate this novel mechanism by derivation and experimental validation of an equation that characterizes the relationship between catheter deflection and physical factors affecting deflection: the number of solenoid turns, applied current, catheter bending stiffness, and the magnetic field of the MR scanner, the initial angle between the catheter tip orientation and the main magnetic field direction and the unconstrained catheter length. Based on these findings, implications for catheter design are discussed.
Materials and Methods

Theory - Current running through a wire solenoid induces a magnetic moment, \( m \), within the solenoid, given by the equation,

\[
m = \mu n I A,
\]

(2.1)

where \( \mu \) is the magnetic permeability of water (or blood), \( n \), is the number of turns in the solenoid, \( I \), is the current applied in Amperes, and \( A \), is the cross-sectional area of the solenoid in meters squared. In a constant magnetic field, such as that of an MR scanner, the magnetic moment created in the solenoid experiences a torque, \( \tau_{\text{mag}} \), given by the equation,

\[
\tau_{\text{mag}} = m \times B,
\]

(2.2)

or,

\[
\tau_{\text{mag}} = mB\sin(\gamma - \theta),
\]

(2.3)

where \( m \) is the magnetic moment vector, \( B \) is the main magnetic field vector, \( \gamma \) is the initial angle between \( m \) and \( B \), and \( \theta \) is the angle through which the catheter tip is deflected (Figure 2.1). Note that \( \gamma - \theta \) is the final angle between \( m \) and \( B \). As a result, the magnetic torque pulls the distal catheter tip into alignment or anti-alignment (depending on the polarity of the current) with the main magnetic field (until \( \gamma = \theta \)). Since catheters are manufactured with materials with elastic or linear mechanical properties, the distal end of the catheter behaves like a cantilever beam free at one end and obeys Hooke’s Law. Therefore, the magnetic torque \( \tau_{\text{mag}} \) will cause the catheter to deflect until it is balanced by the mechanical restoring torque of the catheter, \( \tau_{\text{mech}} \), where

\[
\tau_{\text{mech}} = k\theta = (EI_A/L)\theta
\]

(2.4)

where \( k \) is Hooke’s constant, \( E \) is Young’s modulus for the catheter (in Pascals), \( I_A \) is the area moment of inertia (in m\(^4\)), \( L \) is the unconstrained length (in meters), and \( \theta \) is the deflection angle (in radians). Therefore, at equilibrium,
\[ \tau_{\text{mech}} = -\tau_{\text{mag}} \]

or,

\[ k\theta = mB\sin(\gamma - \theta) \quad (2.5) \]

Substituting for m and k, and rearranging to obtain a linear equation to simplify data fitting,

\[ \frac{\theta}{\sin(\gamma - \theta)} = \frac{\mu n I_{ABL}}{E_{IA}} \quad (2.6) \]

Device construction- 1.8 F Baltacci catheters (BALT, Montmorency, France) were obtained (1 F = 1/3 mm) and the most distal catheter tips containing heavy metal markers were cut to eliminate confounding magnetic forces and MR artifact. Solenoid coils of 50, 100, 150 turns of 44 AWG magnet wire (California Fine Wire, Grover Beach, CA) were wound on the tips of modified catheters to make three 1.8 F catheters with solenoids of 50, 100, and 150 turns, respectively (Figure 2.2). The final diameter of the wound tips was 2.25 F and the length of the solenoid coils were 3.2, 6.5 mm, and 10 mm, for the 50, 100, and 150 turn coil catheters, respectively. In addition, a 100 turn solenoid of the same wire was wound on the distal tip of a 5 F Pursuit angioplasty catheter (Cook Inc, Bloomington, IN). The 5 F catheters were also modified, by removing the angioplasty balloon tip (distal 5 cm). The final tip diameter was 5.6 F and the length of the coil was 3 cm. Loose wire ends were braided (to prevent local field inhomogeneity artifact from the wire) and wrapped around the catheter along its length.
Figure 2.1 Catheter position in the MR scanner magnetic field.

A. In the inset, the direction of the MR scanner main magnetic field, B, with respect to the bore and scanner bed is shown. The catheter tip is shown in initial position in MR scanner field, B, before current is applied. γ is the initial angle between the magnetic moment created by the solenoid, m, and B. Experiments in this study are conducted with the catheter tip in this initial position. B. After current is applied, the catheter tip is deflected (in a counterclockwise direction shown here) by a magnetic torque. The magnetic torque is the cross-product of the magnetic moment, m, and the magnetic field, B. By definition (right-hand rule), the direction of the torque is out of the page, perpendicular to M and B. When current polarity is reversed, the magnetic torque causes a clockwise deflection. The catheter comes to rest at a deflection angle, θ, when the magnetic torque, $\tau_{mag}$, is balanced by the mechanical restoring torque of the catheter $\tau_{mech}$. $F_{mag}$ is the magnetic force exerted at the catheter tip at a distance, L, the unconstrained catheter length. Similarly, $F_{mech}$ is the mechanical force exerted along the unconstrained catheter length, L.
Figure 2.2 1.8 F catheter with a 100 turn magnet wire solenoid wound at the tip.

Experimental setup - In device testing, the long axis of the solenoid on the distal catheter tips was suspended in the yz-plane (with B directed along the z-axis, x-axis parallel to floor, Figure 2.1) in glass phantom filled with water. The catheter tip/apparatus was then positioned in the center of the MR system, where the effect of torque from the 1.5 T static magnetic field is known to be the greatest, as previously described\textsuperscript{159-170}. The catheter-phantom setup was placed within an 8 channel head imaging coil. Currents in the ±300 mA range were applied remotely using a DC power supply in the MRI control room which was continuous with the solenoid wire.

Imaging - The yz-plane containing the catheter tip was identified by an initial 3-plane localizer pulse sequence. Images were obtained using pre-optimized “real-time” MR pulse sequences\textsuperscript{171} on a 1.5 T SIGNA Twinspeed Excite MR scanner (GE Healthcare, Wakesha, WI) using a Balanced Steady State Free Precession pulse sequence (FIESTA) with TR = 2.9 ms, TE = 1.0 ms, flip angle = 50º, 128 x 128 matrix, 5 mm slice thickness, FOV 23 cm x 23 cm, and an 8-channel head coil. For 3 T imaging, a Signa Excite HD 3T MR scanner (GE Healthcare, Wakesha, WI) was used with a Half-Fourier-Acquired Single-Shot Turbo Spin Echo (ssFSE) sequence, TR = 748.7, TE = 30.6, flip angle = 90º, 256 x 128 matrix, 10 mm slice thickness, FOV 23 cm x 23 cm, and an 8-channel head coil.
Measurements - Angles $\gamma$ and $\theta$ were measured on acquired DICOM images. For each experiment, the angle $\gamma$ was measured as the initial angle (before current was applied) between the long axis of the catheter tip and a vertical line drawn parallel to the z-axis (therefore, parallel to B). $\theta$ was measured as the difference between the catheter’s original position before current was applied, and its final equilibrium position after current application (Figure 2.1). Since the catheter deflection imparted a bending curvature to the distal catheter, deflection angle was measured using the long axis of the solenoid at the catheter tip (see Figure 2.3). By definition, at $\theta = 90$ degrees, the catheter tip was in parallel alignment with the MR scanner main magnetic field, B. Measurements were repeated 3 times and the mean and standard deviation are calculated and reported. Unconstrained catheter length was defined as the length from the catheter tip to the proximal point on the catheter held in fixed position (Figure 2.1).

Measurement of Bending Stiffness - The modulus of elasticity (or Young’s modulus), $E$, is the ratio of stress over strain for a slender rod undergoing tensile stress. The larger the value of $E$, the less elastic is the material. The area moment of inertia, $I_A$, measures the catheter’s ability to resist bending. The larger the value of $I_A$, the less the catheter bends when loaded. If $L$ is fixed, bending stiffness $= EI_A$. To measure $E$, axial tensile load-deformation testing was conducted on 5 cm long sections of 1.8 F Baltacci and 5 F Cook catheters clamped at least 1 cm away from the edge to minimize effects of any deformation caused by cutting. Testing was performed on a fully automated Instron 4301 (Instron, Canton, MA, USA) using a 1000 N load cell. The gauge length was set at 25.4 mm and a crosshead speed of 50 mm/min was used. Load and crosshead displacement were sampled at 24 Hz and recorded automatically using Labview 2.0 (National Instruments, TX, USA). In calculating the moduli of elasticity, a first-order polynomial was fitted to the data belonging to the initial linear portion of each of the stress-strain data plot for each catheter ($n = 3$). The slope of each of these lines represented the modulus of elasticity. The area moment of inertia, $I_A$, is a geometrical property that depends on an object’s cross-sectional shape. Assuming that the catheters have a uniform annular cross-section, $I_A$ is given by

$$I_A = \left(\frac{\pi}{64}\right)(d_o^4 - d_i^4) \quad (2.7)$$

where $d_o$ is the outer diameter of the catheter, and $d_i$ is the inner diameter. A section of each catheter was cut with a scalpel and measurements of $d_o$ and $d_i$ were made using a stereomicroscope (TM201, Mitutoyo MFG Co., LTD, Japan). No significant cross-sectional
shape deformation resulted from cutting. Measurements were repeated 3 times and a mean and standard deviation was calculated.

**Results**

To validate the derived equation (2.6), each independent variable was varied systematically while holding others constant. The first independent variable tested was the applied current, I. A 1.8 F catheter with 100 turns was placed in the 1.5 T main magnetic field and current was varied using a DC power supply. Unconstrained catheter tip length was constant at 7 cm. Images for a 1.8 F catheter with 100 turns (Figure 2.3) showed that the catheter deflection angle, θ and local field inhomogeneity artifact around the distal catheter tip increased with increasing current (Figure 2.4A, see Video). Without current, the catheter tip remained static. Significant catheter tip deflections of up to 90 degrees were obtained with applied currents of 300 mA. The increase in \( \frac{\theta}{\sin(\gamma-\theta)} \) was linear with increasing current (\( R^2 = 0.99 \)). Catheter deflection response time to applied current was within tenths of a second, with the catheter tip attaining the equilibrium deflection angle, \( \theta \), instantaneously. The catheter and solenoid device was able to tolerate currents as high as 1 A for over 1 minute without appreciable change in deflection angle. The linear relationship between \( \frac{\theta}{\sin(\gamma-\theta)} \) and current also held for reversed polarity, and for the 5 F catheter with 100 turns at 1.5 T (data not shown).

![Figure 2.3 MR images of catheter tip deflection with angle measurements.](image)

**A.** Without current, the catheter is shown in its initial position and the angle between the catheter tip (small arrow) and the main magnetic field, B (large arrow), is labeled here as \( \gamma \). Note: the initial angle is always less than 90° due
to the small bouyant force on the catheter which is suspended vertically in the water phantom. B. After 90 mA is applied, the catheter is deflected within tenths of a second to its final orientation. Note the movement of the catheter from its original position as well as the local magnetic inhomogeneity artifact induced by the solenoid at the catheter tip. The deflection angle, $\theta$, is measured as the change in the position of the catheter tip relative to its original position in A. Note: deflection is measured as a tangent to the tip of the catheter. Images were obtained in the yz plane of the MR scanner. 1.8 F catheter with $n = 100$, $B = 1.5$ T, $L = 7$ cm, using a FIESTA sequence.

A linear relationship between $\theta/\sin(\gamma-\theta)$, and the number of turns in the solenoid, $n$, was also observed (Figure 2.4B, $R^2 = 0.98$). For a 1.8 F catheters at 1.5 T with 60 mA applied and an unconstrained catheter length of 7 cm, the deflection angle, $\theta$, was $26 \pm 2$, $41 \pm 4$, and $42 \pm 4$ degrees for coils of 50, 100, and 150 turns, respectively.

The magnetic field strength was also systematically varied by carrying out experiments at 1.5 T and at 3 T. Doubling the field strength from 1.5 T to 3 T resulted in a doubling of $\theta/\sin(\gamma-\theta)$ over a wide range of current values (Figure 2.5) for a 1.8 F catheter with 50 turns and an unconstrained length of 7 cm.

The effect of unconstrained catheter tip length, $L$, on deflection was also determined. As $L$ increased, catheter tip deflection increased while keeping other variables constant (Figure 2.6). At a $L$ of 10 mm, $\theta/\sin(\gamma-\theta)$ was $0.06 \pm 0.02$ radians whereas increasing $L$ to 25 mm resulted in a deflection of $0.38 \pm 0.02$ radians. As expected (equation 2.6), $\theta/\sin(\gamma-\theta)$ increased linearly with $L$ ($R^2 = 0.99$).
Figure 2.4 Effect of current and number of solenoid turns on deflection

A. Plot of $\theta/\sin(\gamma-\theta)$ as a function of current. A linear relationship is observed as predicted by Equation 6, ($R^2 = 0.99$). Data obtained using a 1.8 F catheter, with $n = 100$, $B = 1.5$ T, $L = 7$ cm, $\gamma = 72 \pm 1$ degrees. B. Plot of $\theta/\sin(\gamma-\theta)$ as a function of number of solenoid turns. Once again, a linear relationship is observed as predicted by Equation 2.6 ($R^2 = 0.98$). Data obtained using a 1.8 F catheters, with $I = 60$ mA, $B = 1.5$ T, $L = 7$ cm, $\gamma = 72 \pm 3$ degrees.
Figure 2.5 Effect of magnetic field strength on deflection.

Plot of $\theta/\sin(\gamma-\theta)$ as a function of current at 1.5 T and 3 T. $\theta/\sin(\gamma-\theta)$ increased linearly with increasing current ($R^2 = 0.99$ at 1.5 T and $R^2 = 0.98$ at 3 T). The slope of the linear regression line of the 3 T data points is double that of 1.5 T linear regression line, as predicted by Equation 6. Data obtained using a 1.8 F catheter, with $n = 50$, $L = 7$ cm, $\gamma = 61 \pm 4$ degrees.

Figure 2.6 Effect of unconstrained catheter length, $L$, on deflection, $\theta/\sin(\gamma-\theta)$.

As $L$ increased, the catheter tip deflection increased linearly ($R^2 = 0.99$) for a 1.8 F catheter, $n = 100$, $I = 100$ mA, $B = 1.5$ T, and $\gamma = 88 \pm 3$ degrees.
The effect of initial angle between the catheter tip and the main magnetic field, $\gamma$, is shown in Figure 2.7. As the initial angle increased, the catheter tip deflection increased as a function of $\sin\gamma$, when other variables were held constant.

![Figure 2.7 Effect of initial angle between catheter tip and main magnetic field, $\gamma$, on deflection angle, $\theta$.](image)

As the initial angle increased, the catheter tip deflection increased for a 1.8 F catheter with $n = 100$, $I = 100$ mA, $B = 1.5$ T, and $L = 8.5$ cm. In accordance with Equation 2.6, the deflection resulting from the magnetic torque increases as a function of the sin of the initial angle between catheter tip and magnetic field.

To examine the effect of catheter bending stiffness, 1.8 F catheters were compared to 5 F catheters. Higher currents were necessary to achieve significant deflection of the 5 F catheter. For instance, after application of 200 mA to a solenoid of 100 turns at 1.5 T, $L = 4$ cm, starting at $\gamma = 87 \pm 3$ degrees, $\theta/\sin(\gamma-\theta)$ was $0.14 \pm 0.08$ rad for the 5 F catheter compared to $3.57 \pm 0.13$ rad for the 1.8 F catheter. This was correlated to the bending stiffness of the two catheters, as measured by the tensile test (Table 2.1).

Table 2.1. Measured Values and Calculated Parameters for Catheters

<table>
<thead>
<tr>
<th>Catheter Type</th>
<th>Outer Diameter, $d_o$ (mm)</th>
<th>Inner Diameter, $d_i$ (mm)</th>
<th>Moment of Inertia, $I_A$ (mm$^4$)</th>
<th>Elastic Modulus, $E$ (MPa)</th>
<th>Bending stiffness, $EI_A$ ($\times 10^6$ N*m$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8 F</td>
<td>0.720 ± 0.008</td>
<td>0.362 ± 0.014</td>
<td>0.21 ± 0.01</td>
<td>9.46 ± 0.19</td>
<td>1.86 ± 0.09</td>
</tr>
<tr>
<td>5 F</td>
<td>1.653 ± 0.003</td>
<td>1.302 ± 0.092</td>
<td>3.54 ± 0.57</td>
<td>246 ± 9</td>
<td>871 ± 144</td>
</tr>
</tbody>
</table>

Note: $n = 3$ for each catheter type
Discussion

The aim of the present study was to derive and validate an equation modeling catheter deflection for MARC steering of endovascular catheters. The relationship between deflection and a variety of physical factors was characterized. The results indicate that, as predicted by the derived equation (2.6), $\theta/\sin(\gamma-\theta)$ varies linearly with the number of solenoid turns, the applied current, the unconstrained catheter length, and the magnetic field strength, as well as inversely with catheter bending stiffness. Deflection has also been shown to be dependent on the initial angle between the magnetic moment and the main scanner magnetic field.

High $R^2$ values were calculated, indicating good fit of the model. High standard deviations for catheter deflections were also observed, however, since error in catheter deflection angle measurement increased as a function of current applied due to the dependence of the magnetic susceptibility artifact on current. Smaller standard deviations could be obtained in an experimental design that eliminates error in catheter deflection angle measurement. Using an optical camera taking photographs or video of catheter movement would eliminate magnetic susceptibility artifact, which occurs only in MRI.

Implementation of a catheter device based on this mechanism is dependent on fundamental understanding of the physical factors affecting tip deflection. The relationships predicted by the derived equation provide a framework for modeling the behavior of the specialized catheter tip under a variety of physical conditions and have important implications for catheter design.

From the data in this study it is apparent that the amount of current necessary to achieve a given deflection will depend on $\gamma$, the initial angle between the catheter tip (more specifically, the magnetic moment) and the main scanner magnetic field. At very low $\gamma$, for example, substantially more current may be necessary to obtain a few degrees of deflection, since deflection is proportional to $\sin\gamma$. Conversely, smaller currents will be sufficient when $\gamma$ is high (i.e. when the catheter tip is almost perpendicular to the main magnetic field). Therefore, during vessel navigation and current application, it will be necessary to track not only the location of the specialized catheter tip, but also the orientation of its coils with respect to the main magnetic field.
Deflection will also depend on magnetic field strength. The relationship between deflection and magnetic field strength was determined using 3 different field strengths, at 0 T, 1.5 T and 3 T. A fourth field strength would have provided further evidence of a linear relationship between $\theta/\sin(\gamma-\theta)$ and magnetic field strength. MRI scanners of field strengths other than the ones used, and with “real-time” pulse sequence capabilities, were unavailable at this institution. Nonetheless, the doubling of $\theta/\sin(\gamma-\theta)$ with the doubling of magnetic field strength, however, occurred consistently over a wide range of current values. It is evident that deflection is proportional to the magnetic field strength and, consequently, MARC steering may be more efficient, in terms of current use, at higher field strengths. This advantage, however, needs to be weighed carefully against the higher SAR associated with higher field scanners. Higher field strength may result in relatively more RF heating induced in the coils by time-varying magnetic fields, which has been proposed as a potential hazard of this mechanism\textsuperscript{17}.

The study also illustrates how the catheter tip material and geometry can affect deflection. Catheter bending stiffness was shown to be inversely related to tip deflection, with 5 F catheters demonstrating 16-64 times less deflection than the 1.8 F catheters when controlled for other variables. This was correlated to the results of tensile testing which showed that the 5 F catheters had a bending stiffness which was 468 times that of the 1.8 F catheter. The measured Young’s modulus values are in agreement with previous work on similar catheters using the same method\textsuperscript{172}. Although both tests support the conclusion that the 5 F catheter is stiffer than the 1.8 F catheter, there was a large discrepancy in the apparent bending stiffness between the deflection experiment and the tensile test. This was partly due to the effect of cross-sectional area, $A$ (see Equation 2.6), which was 5.3 times larger for the 5 F catheters, meaning the magnetic torque was also 5.3 times larger in the 5 F catheter deflection experiment. In addition, thermoplastic materials exhibit significant strain-rate sensitivity, making the estimation of Young’s modulus by tensile strength testing highly dependent on crosshead speed\textsuperscript{173}. Furthermore, a tensile test may not accurately reflect the stresses and strains encountered in the deflection experiment and in vivo setting\textsuperscript{174}. Regardless, optimal catheter tip design would involve use of material with a low bending stiffness. This can be achieved by use of a catheter tip material with a low Young’s modulus as well as a low area moment of inertia. Since moment of inertia is proportional the fourth power of diameter, an ideal catheter would have a small diameter and a thin wall. More proximal aspects, however, should have a larger Young’s modulus in order to maintain axial and torsional rigidity (which is important for the ability to transmit proximally exerted pushing forces.
and torques to the distal parts of catheter). Future work should also investigate the effect of temperature on Young’s modulus of the catheter material. Our tests were conducted at room temperature (22 ºC) and no change in deflection angle was seen after continuous application of current for periods of 15-30 seconds. Although Tsiu et al showed that small temperature differences (22 ºC vs 37 ºC) had no effect on catheter mechanical properties, the heat produced by the current in the coils may alter catheter stiffness (depending on the glass temperature of the catheter material). Furthermore, the heat produced will increase as the time continuous current is applied increases.

Catheter stiffness will also be affected by vessel geometry. For a given bending stiffness, an increase in the unconstrained catheter length resulted in larger deflection for the same applied current. Thus, a mechanical advantage is gained by increasing unconstrained catheter length. The unconstrained catheter length, however, determines the smallest vessel diameter that can be catheterized, since the distal catheter tip can only enter vessels with diameters of at least the same length. Therefore, the tip of a 1.8 F catheter with a 100 turn solenoid with a length of 7 mm used in this study cannot enter a vessel smaller than 7 mm. The unconstrained length of the catheter, therefore, should be limited the distal region of the catheter containing the solenoid and modified Helmholtz coils and a millimeter or two of low bending stiffness material to ensure the all bending forces concentrate within this small but flexible region. This would also ensure that the unconstrained length would remain consistently low, regardless of the number of vessel turns negotiated. The tip length could also be reduced by increasing the winding density. In fact, since the induced magnetic moment is proportional to n/l, where n is the number of turns and l is the length of the solenoid, a tightly wound solenoid would enter smaller vessels, require less current, and create less heat. In addition, tighter winding would increase the final outer diameter of the catheter by the diameter of the wire (only a tenth of a millimeter). Vessel shape would also affect bending stiffness. Although Young’s modulus is constant for linearly elastic catheter materials over a large range of stresses and strains, vessel geometry may affect the area moment of inertia. In this study, we have assumed that the catheter tip mimics the behavior of a cylindrical beam free at one end with a moment force applied at its tip. If the tip is located within a curved vessel, however, not only will L change, but the straight cylinder assumption would no longer holds. In such a setting, I_A changes with vessel geometry. As a result, complex vessel paths may require more current for desired deflections.
The relationships characterized in this study also have implications for image artifact. Visualization of the position and orientation of the catheter tip is essential for its proper guidance and prevention of complications. Heavy-metal markers at the catheter tip are typically used for tip visualization in X-ray fluoroscopy. In MRI, however, heavy-metal markers may either disrupt the image, or, due to their ferromagnetism, these markers can be unsafe. Therefore, alternative visualization methods such as passive and active catheter tip tracking are being developed\textsuperscript{117, 138, 176}. The specialized catheter studied here takes advantage of the magnetic moment induced in the solenoid at the catheter tip. In addition to experiencing a magnetic torque from the main MR scanner field, the magnetic moment causes local magnetic field inhomogeneity. As a result, in the area of the induced magnetic moment, signal from nearby water proton spins is therefore lost, resulting in a signal void on the MR image. This effect functions beneficially as a passive catheter tip tracking mechanism, since the catheter tip is located in the area of the signal void. If the effect is too large, however, the image can be severely distorted by the local magnetic inhomogeneity artifact. One approach used to mitigate this effect has been to use an MR pulse sequence that is relatively less sensitive to local magnetic inhomogeneities. The model provided here also provides a framework with which to optimize current delivery and, as a consequence, image artifact.

Subsequent to optimal visualization of the catheter tip, fine control of catheter tip deflection under a variety of conditions is essential for successful guidance and prevention of complications. In addition to the advantages of using MRI for guidance of endovascular procedures stated in the introduction, MARC steering may decrease complications related to the use of guidewires in DSA. More specifically, controlling deflection using current during MARC catheter steering may render a guidewire unnecessary for steering (although a stable “track” along which to advance the catheter using a guidewire, once a target vessel has been entered would still be required). This is significant since complications in endovascular interventions often arise from guidewire-induced vessel perforation, wall dissection, and hemorrhage. This mechanism may also provide better control over steering, for example, when trying to enter a vessel that is oriented 90 degrees to the parent vessel\textsuperscript{25, 26}, or when several vessel turns have already been negotiated and manual purchase on the guidewire tip is limited. In DSA, prolonged navigation can result in increased radiation dose to the patient and interventionalist, thrombus formation, as well as increased volume of contrast administered. The caveat, however, is that
current needs to be delivered slowly and incrementally to avoid large instantaneous deflection forces which may pose a risk to blood vessel wall integrity.

To achieve three-dimensional deflections, paired Helmholtz coils in addition to the solenoid coil are necessary. In a three dimensional setting, the physical principles are similar. Limiting this study to two-dimensions, facilitated experimental design and simplified understanding of the physical factors affecting deflection and subsequent catheter design.

Lastly, unwanted ohmic heating from power dissipation due to the applied current, and RF heating induced in the coils from time-varying magnetic fields, are issues that warrant further investigation (see Chapter 4). The model derived here provides a framework for minimizing the current applied and the resultant heat produced.

In summary, we have derived and validated an equation for magnetically-assisted remote control steering of endovascular catheters. The equation provides an excellent framework for modeling the behavior of the specialized catheter tip. Such understanding is pivotal to the application of this novel mechanism in MR-guided endovascular intervention and catheter design.
Introduction

Magnetic susceptibility refers to the degree of magnetization of a material in response to the presence of an external magnetic field \(^\text{177}\). When a substance is placed in a magnetic field, the magnetic field inside the substance will be the sum of the external magnetic field and the intrinsic magnetic field generated by the substance. This magnetic field generated in the substance is called the magnetic induction, \(H\), and is given by,

\[
H = \mu_0(B + m) \quad (3.1)
\]

where \(H\) is the magnetic induction, \(\mu_0\) is the permeability of free space, \(B\) is the external magnetic field (measured in amperes per meter), \(m\) is the magnetization (the magnetic dipole moment per unit mass, also measured in amperes per meter). For mathematical and experimental convenience, this equation if often written as

\[
\frac{H}{B} = \mu_0(1 + X_v) \quad (3.2)
\]

where

\[
X_v = \frac{m}{B} \quad (3.3)
\]

and \(X_v\) represents the volume magnetic susceptibility. This dimensionless unit is also represented in the literature by \(\kappa\) or \(K\). This definition is according to SI conventions, although many tables of magnetic susceptibility give cgs values that rely on a different definition of the
permeability of free space. The cgs value of susceptibility is multiplied by $4\pi$ to give the SI susceptibility value.

If $\chi$ is negative, then $(1+\chi) < 1$, and the substance is diamagnetic. As a result, the magnetic field is weakened in the presence of the substance. Alternatively, if $\chi$ is positive, then $(1+\chi) > 1$ and the substance is paramagnetic. In this case, the magnetic field is strengthened by the presence of the substance.

*Paramagnetic material and MARC endovascular catheter steering*

Experiments in this thesis have showed that substantial currents are needed to deflect larger stiffer 5 F catheters (Chapter 2), and that higher currents can lead to undesired heating effects (Chapter 4). Successful use of this mechanism of catheter steering for stiffer catheters will require larger deflections while minimizing applied current. An approach to this problem would be to insert a paramagnetic substance inside the solenoid core which effectively amplifies the magnetic moment produced at the catheter tip per unit of applied current, through magnetic induction. This process is evident for paramagnetic aneurysm clips and metallic implants which are associated with susceptibility artefact. These artefacts arise from differences in magnetic susceptibilities between the metal and substance surrounding the metal. The magnetization of a paramagnetic substance produced within an external magnetic field results in an increase in the local magnetic field around the substance and a resultant signal loss 136, 159, 162, 163, 170, 178-184. With a paramagnetic substance placed in the solenoid core, the magnetic permeability, $\mu$, is

$$\mu = \mu_0 (1 + \chi_v) \quad (3.4)$$

where $\mu_0$ is the magnetic permeability of free space, and $\chi_v$ is the volume magnetic susceptibility. Thus, the magnetic moment within the core should be,

$$M = \mu n I A \quad (3.5)$$

Therefore, with a paramagnetic solenoid core, the magnitude of the magnetic moment at the catheter tip should increase per unit of current applied. As a result, the magnetic torque per unit of current applied, and therefore deflection, should also increase. In this chapter, experiments
are preformed using a 5 F catheter and experimental setup used in Chapter 2, albeit with select paramagnetic substances, tantalum, vanadium, and gadolinium, inserted within the solenoid core to increase the magnetic torque and resultant catheter tip deflection per unit of current applied.

Materials and Methods

Device construction - A 100 turn solenoid of 44 AWG magnet wire (California Fine Wire, Grover Beach, CA) was wound on the distal tip of a 5 F Pursuit angioplasty catheter (Cook Inc, Bloomington, IN) (1 F = 1/3 mm). The 5 F catheters were modified by removing the angioplasty balloon tip (distal 5 cm) to eliminate confounding magnetic forces and MR artifact. The final tip diameter was 5.6 F and the length of the coil was 3 cm. Loose wire ends were braided (to prevent local field inhomogeneity artifact from the wire) and wrapped around the catheter along its length. 10 cm lengths of 1 mm diameter Gadolinium wire, Vanadium wire, or Tantulum wire, each of 99.9% purity (Goodfellow Corp., UK) were inserted into the solenoid core within the lumen of the catheter tip. The magnetic susceptibilities of the metals used are listed in Table 3.1. To minimize experimental safety hazards and for convenience, paramagnetic substances that are relatively stable at atmospheric pressure and temperature in air were used.

Table 3.1. Selected magnetic susceptibilities

<table>
<thead>
<tr>
<th>Substance</th>
<th>Magnetic susceptibility (x 10^-6 cm^3/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tantalum</td>
<td>+154</td>
</tr>
<tr>
<td>Vanadium</td>
<td>+285</td>
</tr>
<tr>
<td>Gadolinium (350 K)</td>
<td>+185 000</td>
</tr>
<tr>
<td>Water</td>
<td>-13</td>
</tr>
</tbody>
</table>

(Source: CRC Handbook of Chemistry and Physics\textsuperscript{185})

Experimental setup- In device testing, the long axis of the solenoid on the distal catheter tips was suspended in the yz-plane (with B directed along the z-axis, x-axis parallel to floor, as in Figure
2.1, in glass phantom filled with water. The catheter tip/apparatus was then positioned in the center of the MR system, where the effect of torque from the 1.5 T static magnetic field is known to be the greatest, as previously described\textsuperscript{159-170}. The catheter-phantom setup was placed within an 8 channel head imaging coil. Currents in the ±1 A range were applied remotely using a DC power supply in the MRI control room which was continuous with the solenoid wire.

**Imaging** - The yz-plane containing the catheter tip was identified by an initial 3-plane localizer pulse sequence. Images were obtained using pre-optimized “real-time” MR pulse sequences\textsuperscript{171} on a 1.5 T SIGNA Twinspeed Excite MR scanner (GE Healthcare, Wakesha, WI) using a Balanced Steady State Free Precession pulse sequence (FIESTA) with TR = 2.9 ms, TE = 1.0 ms, flip angle = 50º, 128 x 128 matrix, 5 mm slice thickness, FOV 23 cm x 23 cm, and an 8-channel head coil.

**Measurements** - Angles γ and θ were measured on acquired DICOM images. For each experiment, the angle γ was measured as the initial angle (before current was applied) between the long axis of the catheter tip and a vertical line drawn parallel to the z-axis (therefore, parallel to B). θ was measured as the difference between the catheter’s original position before current was applied, and its final equilibrium position after current application. By definition, at θ = 90 degrees, the catheter tip was in parallel alignment with the MR scanner main magnetic field, B. Measurements were repeated 3 times and the mean and standard deviation are calculated and reported. Unconstrained catheter length was defined as the length from the catheter tip to the proximal point on the catheter held in fixed position. Comparison was made with experiments done previously (Chapter 2) in the absence of a substance (other than air or water) in the solenoid core.

**Results**

After introducing a 99.9% pure tantalum wire 1 mm in diameter and 5 cm in length into the solenoid core, no increase in deflection angle per unit of applied current was observed (slope = 0.0198, \(R^2 = 0.99\)), when compared to an experiment with a hollow solenoid core (slope =
0.0256, $R^2 = 0.98$) (Figure 3.1A-B). An increase was also not observed when substituting a 99.9% pure vanadium wire solenoid core (slope = 0.0216, $R^2 = 0.97$) (Figure 3.1C). In fact, the presence of a tantalum or vanadium wire in the solenoid core slightly decreased the magnitude of tip deflection per unit of applied current (Figure 3.1).

Next, a catheter with a solenoid core of 99.9% gadolinium metal was studied. In this experiment, with no current applied, the catheter tip, initially aligned with a $\gamma = 80 \pm 3$ degrees to the magnetic field. Before the application of current to the system, the catheter tended to align itself with the magnetic field. This tendency was visible as a drifting of the long-axis of the catheter tip towards a more parallel position with the magnetic field (images not shown). Initial imaging, with no current, demonstrated a large signal void artifact on the image in the area of the catheter tip (Figure 3.2A). This signal void was not seen when imaging the catheter with either a tantalum, vanadium, or hollow solenoid core, when no current was applied (Figure 3.2B). When the current was introduced into the system, no amount of current (from 200 to 2000 mA) deflected the catheter and the catheter tip remained in its original position (Figure 3.2C). In addition, the signal voiding artifact remained unchanged after application of current, as in Figures 3.2A and C). Repetition of this experiment with 3 different gadolinium wires of the same geometry yielded the same result.
Figure 3.1 5 F PCTA Catheter tip deflection versus applied current graphs.

A: Empty solenoid core (slope = 0.0256, \( R^2 = 0.984 \)). B: Tantalum solenoid Core (slope = 0.0198 \( R^2 = 0.9971 \)) C: Vanadium solenoid core. (slope = 0.0216, \( R^2 = 0.9713 \)) No increase in catheter tip deflection per unit of applied current is observed for either the tantalum or the vanadium core.
Figure 3.2 Effect of gadolinium and tantalum cores on image

A: 5 F catheter with a gadolinium metal tip core without application of current. Note presence of artifact. B: 5 F catheter with a tantalum core without application of current. No large signal void is present. C: 5 F catheter with a gadolinium metal tip core with 200 mA current applied. There is no change in catheter position from A and the artifact size is unchanged.

Discussion

In an effort to achieve greater catheter tip deflection per unit of applied current for a stiffer catheter, pure tantalum, vanadium, and gadolinium metal wires were inserted into the solenoid core. None of these paramagnetic metals was useful for this purpose.

The small molar magnetic susceptibilities of Ta and V (+154 x 10^{-6} cm^3/mol and +285 x 10^{-6} cm^3/mol, respectively) likely provided an insignificant increase in the magnitude of the magnetic moment produced within the solenoid. Since

$$\mu = \mu_0(1 + X_v) \quad (3.2)$$

for Ta,

$$\mu = \mu_0(1 + 0.000 \ 154 \ \text{cm}^3/\text{mol})$$

represents a negligible (0.015%) increase in magnetic permeability. Furthermore, the tantalum and vanadium metal wires slightly decreased the magnitude of catheter tip deflection per unit of applied current likely due to the increase in weight that they imparted to the catheter tip. It is
unlikely that the metal cores increased the stiffness of the more proximal part of the catheter that bends with deflection.

With a molar magnetic susceptibility of +0.185 cm$^3$/mol, gadolinium should have provided 600-1200 times more magnetic moment/unit of current than tantalum or vanadium metal, and an 18.5% increase in magnetic induction. This should have translated to, approximately, an 18.5% increase in the magnitude of catheter tip deflection/unit of applied current. Instead, the insertion of gadolinium nulled the magnetic torque effect caused by the current-induced magnetic moment within the solenoid. Alignment of permanent dipoles in a paramagnetic or ferromagnetic substance occurs in a magnetic field. In our experimental setup, the magnitude and direction of the $B_0$ field may have been too strong (compared to the magnetic field generated by the solenoid) such that the majority of permanent dipoles within the paramagnetic substance line up with the $B_0$ field as opposed to the solenoid magnetic field. This alignment of dipoles was visible as the tendency of the gadolinium wire to align with $B_0$. Since, according to Equation 3.1 above, the magnetic induction, $H$, is given by

$$H = \mu_0(B + m)$$

the total magnetic field, $B$, that the metal experiences is that of the local magnetic moment created by the solenoid and that of the main magnetic field of the scanner.

Alternatively, as a potential ferromagnet, the gadolinium wire may have become permanently magnetized within the MR scanner after a prolonged period of time. The magnetic field the Gd wire may have generated as a ferromagnet may have disrupted the magnetic moment created by the current running through the solenoid. The magnetic behaviour of the gadolinium metal was not tested outside the MR scanner after placement in the 1.5 T field with other ferromagnetic objects, however. One approach to resolving this would involve experimental determination of whether the gadolinium core became saturated by adding a secondary winding to the catheter tip to measure DC voltage. If the voltage saturates at a level below the working input currents, then the material used in the core would not be suitable for the intended purpose.

The tendency of the gadolinium-packed catheter tip to orient itself parallel to the main scanner magnetic field is characteristic of a paramagnetic or ferromagnetic metal in a directional
In the MR setting, two types of magnet related forces can occur with a ferromagnetic or paramagnetic substance: (a) an attractive, translational force that is proportional to the strengths of the static magnetic and spatial gradient fields and the mass, shape, and magnetic susceptibility of the object; and (b) torque that attempts to align or rotate the material parallel to the magnetic field, which is proportional to the strength of the magnetic field and the dimensions and angulation of the object. The main scanner magnetic field is strongest in the center of the MR scanner bore and is oriented along its long axis. Therefore, in its initial orientation almost perpendicular to the MR scanner field, the gadolinium wire experienced both a translational force as it approached the edges of the MR scanner bore and a torque bringing the metal in parallel alignment with the main scanner magnetic field. Similar to our experiments in Chapter 2, the magnetic torque on the catheter tip must overcome the mechanical torque caused by the catheter stiffness. Since the catheter tip did not orient fully parallel to the field, the magnetic torque in this situation was insufficient to overcome the mechanical torque, leading to the incomplete alignment seen in Figure 3.2A.

These translational attractive and aligning forces between metallic objects and the static magnetic field have been the cause of most serious safety-related incidents in the MRI setting. This makes use of this substance particularly risky in a clinical setting.

In absence of current, the Gd wire within the catheter tip caused a signal void artifact. MR imaging artifacts associated with metallic objects are primarily dependent on the inhomogeneity of the magnetic field and the magnetic susceptibility of the specific materials used to make the object, as well as on the amount of metal, shape, orientation, and position of the object in relation to the main scanner magnetic field, the scan sequence used, the readout direction, the imaging bandwith per pixel, and the strength of the main scanner field. Eddy currents produced by RF fields during MR imaging also may contribute to the artifacts seen with metallic objects and are primarily dependent on the shape, orientation, and resistance of the metal(s) present. Additionally, MR imaging artifacts are dependent on the method used for image processing. Since experimentation was conducted at the centre of the bore, inhomogeneity of the scanner magnetic field is an unlikely cause of the artifact. The amount of metal, shape, and orientation of the metal, as well as imaging methods and parameters were also kept constant, leaving susceptibility as the culprit. Susceptibility artifacts occur as the result of microscopic gradients or variations in the magnetic field strength that occur near the interfaces of substances of different magnetic susceptibility. Large susceptibility artifacts are
commonly seen surrounding ferromagnetic objects inside of diamagnetic materials. These gradients cause dephasing of spins and frequency shifts of the surrounding tissue or substance. The net results are bright and dark areas with spatial distortion. Thus, the large magnetic susceptibility difference between gadolinium and water in this study likely caused the signal void artifact seen.

Although, tantalum and vanadium are also paramagnetic and also possess greater magnetic susceptibility than water, no signal void was seen. One possible explanation is that the FIESTA pulse sequence and parameters used was not sensitive enough to detect the much smaller difference in susceptibility between water and tantalum (or vanadium). Previous studies seem to support this conclusion. In a study on MRI artifacts caused by dental casings composed of differing paramagnetic and diamagnetic alloys, only an alloy that contained no traces of ferromagnetic metals, and was composed purely of weakly paramagnetic and diamagnetic material (Pd, In, and Sb) produced no artifact on both spin-echo and gradient-recalled sequences. In and Sb are diamagnetic, while Palladium is paramagnetic \( (X_m = +540 \times 10^{-6} \text{ cm}^3/\text{mol}) \), which is close to that of Ta and V, but several orders of magnitude smaller than that for Gd. In studies of MR artifacts produced by commercially available titanium aneurysm clips, aneurysm clips made of pure titanium \( (X_m = +151 \times 10^{-6} \text{ cm}^3/\text{mol}) \) produced little or no artifact on a variety of spin-echo and gradient-recalled pulse sequences. Another study reported that molar magnetic susceptibilities of > 2000 \( \times 10^{-6} \text{ cm}^3/\text{mol} \) were necessary to produce “clinically relevant” artifacts.

The gadolinium metal wire exhibited strong paramagnetism in the MR scanner. This conclusion is supported by both the sizable susceptibility artifact caused by the gadolinium metal wire, as well as the notable translational attraction and the rotational torque it experienced in the MR scanner in the absence of any applied current. In fact, the gadolinium metal may have transitioned to ferromagnetic state in the MR scanner room. Gadolinium is an unusual substance in that its Curie temperature is around room temperature. The Curie temperature is the temperature at which a ferromagnetic substance loses its ability to possess a net (spontaneous) magnetization in the absence of an external magnetic field (Figure 3.3). At temperatures below the Curie temperature, magnetic moments are partially aligned within magnetic domains, which is responsible for permanent magnetization. Above this critical temperature, which varies for different substances, the thermal motion of atoms is enough to disrupt the crystal structure.
and coupling interactions between magnetic dipoles and ferromagnetism disappears. The substance continues to retain permanent magnetic dipoles, however, and behaves paramagnetically and its magnetic susceptibility obeys the Curie-Weiss law\textsuperscript{192}. In this study, the Gd wire may have been in ferromagnetic state since the experiments were conducted at approximately the Curie temperature (Gadolinium has a Curie temperature of 20\textdegree C\textsuperscript{193}). The temperature in the MR scanner room during experimentation was between 18 and 21\textdegree C. In retrospect, therefore, gadolinium may have been a poor choice of paramagnetic substance. Other highly paramagnetic substances with higher Curie temperatures exist, such as Dysprosium ($X_m = 0.98$ cm$^3$/mol, $T_c = -188$\textdegree C)$\textsuperscript{185,194}$. Substances with high magnetic susceptibilities, however, are rare-earth lanthanides that are either severely toxic or hazardous, requiring special equipment and precautions not feasible in an MR scanner in a clinical medical imaging department, or they are extremely difficult to extract in pure form from the environment and to manufacture into a wire form. In addition, although metallic implants and stents made of weakly paramagnetic metals experienced no translational attractive force nor any torque caused by the main scanner magnetic field, implantable metallic devices containing ferromagnetic material have been shown to be unsafe for MR\textsuperscript{159-163, 166, 167, 170, 179, 190, 195-198}. Since there are no studies on metallic implants or devices composed of highly paramagnetic metals, the safety of using such material in an interventional MR setting remains a concern. An alternative approach could also involve creation of a gadolinium alloy with a material possessing a lower susceptibility, such as Ta, Va, or Cu). Nevertheless, the temperature dependence of the magnetic susceptibility of gadolinium carries potential as a novel MR thermometry method (Appendix 1).
Figure 3.3 Magnetic susceptibility versus temperature schematic curve for a ferromagnetic material.

The temperature at which a material in a ferromagnetic state transitions to paramagnetic state is known as the Curie temperature, Tc. The Curie temperature is an inherent property of ferromagnetic and ferrimagnetic substances. Above the Curie temperature for ferromagnetic substances, the magnetic susceptibility magnetic susceptibility is inversely proportional to temperature, according to the Curie-Weiss law.

In conclusion, the attempt to use paramagnetic metal to reduce the amount of current necessary to deflect a stiffer catheter failed for several reasons. In the case, of the tantalum and vanadium metals the magnetic susceptibility of the metals was likely too low to have any effect on the magnetic torque. Although the magnetic susceptibility of the gadolinium metal was visibly much higher, the magnetic state of the metal caused unwanted translational attractive force and torque on the catheter tip which could not be overcome by the application of current, posing undesired safety risks.
4. Evaluation of resistive and RF heating due to magnetically-assisted remote control steering coils for endovascular interventional MRI

Abstract— PURPOSE: To assess magnetic resonance imaging (MRI) resistive and radiofrequency (RF) related heating due to conductive wire coils used in magnetically assisted remote control (MARC) steering of endovascular catheters for interventional MRI. MATERIALS AND METHODS: To assess perfusionless worst-case scenarios, in vitro testing was performed using a 1.5 T/64 MHz MR system and a gel-filled agarose phantom designed to approximate a blood vessel with the same thermal properties of blood. MRI was conducted using the transmit/receive body radio frequency (RF) coil. RF heating was measured at various distances from the magnet isocenter and with varying flip angles (or varying RF pulse sequence powers). Resistive heating was measured before and after application of currents previously shown to cause clinically significant catheter tip deflections. A fluoroptic thermometry system was used to record temperatures at four locations at the catheter tip before and during scanning and application of current. RESULTS: The highest temperature changes were observed at higher distances from the magnet iso-center, with 0.35 °C increase at 10 cm from isocenter, and higher RF flip angles, with 0.25 °C increase observed using 80° flip angle. More significant temperature increases were seen after application of current, although clinically significant temperature increases were seen only with the use of currents above 200 mA (9 °C increase after 30 seconds of 300 mA applied to three coils simultaneously). CONCLUSION: The RF induced temperature increases were minimal and dependent on the distance from the magnet bore wall and the power of the pulse sequence. In contrast, significant resistive heating was observed using this prototype, especially at higher applied current levels. Improvements in catheter material, wire insulation, and coil tip design, however, should minimize resistive heating.
Introduction

The MARC catheter steering mechanism studied employs long conductive wires. In the setting of RF magnetic fields, these wires may cause unwanted RF heating of tissues according to the physical mechanisms described in Chapter 1. Perhaps more significantly, the applied direct currents necessary to achieve catheter tip deflections may result in large resistive dissipation and hazardous tissue heating. The focus of this chapter is a preliminary investigation of the heating changes associated with MARC steering of endovascular catheters in a tissue-mimicking agarose gel. RF induced heating of conductive wires due to the electric field coupling effects, and resistive heating caused by the application of current, will be quantified in the MR imaging using thermometric fiberoptic probes.

Theory

Direct current causes Joule heating (or resistive heating) of tissue, which is given by the equation,

\[ P = I^2 R \]  

(4.2)

where \( P \) is power measured in watts (one watt is equivalent to one joule/second), \( I \) is current (A), and \( R \) is the resistance (in Ohms). Joule heating is caused by interactions between the moving electrons that form the current and the atomic ions of the conductor. These charged particles give up some of their kinetic energy each time they collide with an ion. The increase in the kinetic or vibrational energy of the ions manifests itself as heat and a rise in the temperature of the conductor. Hence energy is transferred from the electrical power supply to the conductor and any materials with which it is in thermal contact.

According to the the first and second laws of thermodynamics, the amount of energy (heat) given up by one system which is interacting with another system is equal to the amount taken up by the other system, and heat flows from regions of higher temperature to regions of lower temperature. Three modes of heat transfer are commonly distinguished: conduction, radiation, and convection.
The primary mode of heat transfer in tissues, in the absence of blood flow, is conduction. When energy is deposited in tissue faster than it can be dissipated, the inevitable result is tissue heating, manifested as an elevation of temperature. As discussed above, prolonged periods of elevation may cause irreversible damage to tissue.

The rate of temperature rise for current carrying wire can be calculated from the following formula:

\[
\frac{dT}{dt} = \frac{I^2R}{C_vV} \quad (4.3)
\]

where \( I \) is the current, \( R \) is the resistance of the circuit, \( C_v \) is the volumetric specific heat, and \( V \) is the volume of the wires. A typical coil/cable length used in this thesis is made from 3 m of 44 AWG copper wire with a total volume of 0.0059 cc and resistance 25 ohms (the 10 m of speaker wire connecting this coil to the power supply is excluded from calculation given its negligible resistance). Therefore, after application of 300 mA, the expected temperature increase in blood (specific heat capacity similar to water, 4.1 J/°C), is

\[
\frac{dT}{dt} = \frac{(0.3)^2(25)}{(4.1)(0.0059)} = 93\, ^\circ \text{C/second}
\]

Several factors contribute to reducing the actual rate of temperature rise in the completed coil system within a blood vessel. Magnet wire such as the one used in these experiments is copper wire covered with an insulating material such as polyurethane (specific heat capacity 1700 J/kg•K). In addition to the coil, all of the materials at the distal end of the catheter are in intimate thermal contact. Each component contributes their thermal inertia to limiting the temperature increase. Thus, added to the heat capacity are the other two coils (each with the same volume of copper), the adhesive, and the catheter itself (also polyurethane). These catheter components alone reduce the temperature rise by a factor of 5 or 6. Thus, the adiabatic rate of temperature rise is less than about 19°C/sec. In vivo, blood flow would further reduce the heating effects by convective removal of warmed blood.
Materials and Methods

Device construction- a 1.8 F Baltacci catheters (BALT, Montmorency, France) was obtained and the most distal catheter tip containing heavy metal marker was cut to eliminate confounding magnetic forces and MR artifact. A three-axis coil using 44 AWG magnet wire (California Fine Wire, Grover Beach, CA) was wound on the tip of the modified catheter. The z–axis coil was solenoidal and consisted of 100 turns. The two orthogonal modified Helmholtz coils were wound along the catheter length, with each coil consisting of multiple coil-turns either side of the catheter lumen. They generate a magnetic moment perpendicular to the long axis of the catheter (in contradistinction to the solenoid). Approximately 40 turns were used in each of the orthogonal coils, but the effective area of the coils was approximately the same as that of the solenoidal coil. The final diameter of the catheter tip with wound coils was 4 mm. The length of the coil assembly was approximately 8 mm. Note that, given the cylindrical geometry of the catheter, the modified Helmholtz coils might be more readily described as paired “racetrack” windings, to recognize their elliptical form and the catheter-specific separation (whereas a true Helmholtz coil consists of a pair of coaxial circular windings of radius equal to separation). Loose wire ends were braided (to prevent local field inhomogeneity artifact from the wire) and wrapped around the catheter along its length.

Temperature measurements in the MR system

To assess possible RF heating of the solenoid and modified Helmholtz coils, temperature measurements were performed in the MR system. All temperature measurements were conducted with the catheter and associated coil wires embedded over a distance of 1 m in a tissue-mimicking gel (2% agar, 0.9% NaCl) that prevents thermal convection and has electrical properties similar to human blood (thermal conductivity = 0.6–1 S/m, relative permittivity = 73.6, specific heat = 4.2 kJ/kg.K). The gel and catheter were contained within a cylindrical plastic phantom of 5 cm in diameter. The phantom set up was aligned parallel to the long axis of the magnet bore. Temperature changes were measured using a fiberoptic temperature monitoring system (model 3204; Luxtron Corp., Northwestern Parkway, CA). Temperature values were recorded on a PC via a serial cable using an RS232 protocol and Microsoft HyperTerminal. Four
Luxtron temperature probes were fixed within the gel, adjacent to the catheter tip using as follows (Figure 4.1): Probe 1) at the distal tip of the solenoid coil, Probe 2) between two paired Helmholtz coils, Probe 3) At the more proximal end of solenoid, Probe 4) 2 cm away from coils/tip. During all experiments identical sensor positions are ensured by adhesive tape. The tip of the sensor was not masked by the tape, so that the temperature increase of the adjacent gel could be measured.
The catheter solidified in the center of the plastic tube phantom. The Luxtron thermometric probe tips were fixed in the various positions indicated during all experiments.

Experiments were carried out first without any applied current to isolate RF heating. Measurements were performed at off-center distances (x-position) between 0 cm (magnet center), 5 cm, 10 cm, and 15 cm (close to magnet bore). A true-FISP pulse sequence (TR= 4.2
ms, TE=1.6 ms, α =75°, slice thickness = 5 mm, matrix = 128 x 128, FOV = 20 cm) was used which provides a high specific absorption rate of SAR = 4.3 W/kg. At each off-center position the sequence was applied over a period of 15 min. The temperature increase, ΔT, was recorded during the 15 min periods. Temperature measurements were also performed over a period of 10 min for different flip angles between α=5° and 90°.

Separate experiments were carried out to quantify resistive heating due to applied DC current necessary to achieve clinically significant deflection in the MR system. Measurements were acquired as close to the bore wall as possible (in an off-center position) with the same true-FISP pulse sequence and fiberoptic probe configuration. Temperature increases were measured during application of DC current from 50-300 mA, in 50 mA increments. At each current increment, current was applied for 30 s. Time was allowed for cooling of the phantom/device between DC current increments. This protocol was carried out for DC current applied 1) to only the solenoid coil, 2) to both the solenoid and one pair of modified HelmHoltz coils, 3) to all 3 coils (1 solenoid and 2 paired modified Helmholtz coils) simultaneously.

**Results**

In the absence of applied direct current, experiments were carried out at various distances from the magnet bore wall to determine RF heating effects induced in the solenoid and helmholtz catheter coils due to RF pulse sequences during real-time MR imaging. At the isocenter of the magnet, no heating was detected by any of the probes after 15 minutes of imaging (Figure 4.2A). As the apparatus was moved 5 cm closer to the magnet bore wall, a slight increase in the temperature (0.2 ºC) recorded over the 15 min period was measured in probe 1 and probe 2 (0.14 ºC), close to the distal solenoid tip and helmholtz coils (Figure 4.2B). Furthermore, the change in temperature in probes 1 as well as probe 2 increased as distance to the magnet bore wall decreased (Figure 4.2B-D). Probes 3 and 4 showed no significant change in temperature distances from the bore (Figure 4.2A-D). At any distance from isocenter, however, the increase in temperature over the time 15 minute interval was not higher than 0.35 ºC.
Figure 4.2 Effect of distance from magnet isocenter on catheter tip temperature during real-time MR imaging.

A. At isocenter, no significant heating was observed in any of the probes. B. 5 cm from isocenter, a slight rise in temperature was seen close to the catheter tip in probes 1 (0.20 °C) and 2 (0.14 °C). No significant increase in temperature was detected away from the catheter tip in probes 3 and 4. C. 10 cm from isocenter, the rise in temperature was 0.35 °C in probe 1 and 0.33 °C in probe 2. Again, no significant increase in temperature was detected away from the catheter tip in probes 3 and 4. D. 15 cm from isocenter, the increase in temperature was
0.30 °C in probe 1 and 0.30 °C in probe 2. Again, no significant increase in temperature was detected away from the catheter tip in probes 3 and 4.

The power of RF pulses increases with increasing flip angles. Higher RF pulse flip angles resulted in increased RF heating of the catheter-coil (Figure 4.3). The increase in temperature observed was small, however. After 10 min of continuous MR imaging 15 cm from isocenter, 0.25 °C was the largest increase in temperature observed (80° flip angle).

![Figure 4.3 Effect of flip angle.](image)

RF heating was observed at higher flip angles. After 10 min of continuous MR imaging, the heating was minimal – the highest observed increase in temperature over baseline was 0.25 °C with an 80° flip angle.

Lastly, temperature increases were measured after the application of currents necessary to cause clinically significant catheter tip deflections. Since the application of current for 30 s represents the likely longest period of time needed to selectively catheterize a vessel during an attempt, temperature increases were monitored over 30 s time intervals. During continuous application of 50 mA to the solenoid coil, no significant increase in temperature is noted in the probes (Figure 4.4A). As the applied current increased, however, increases in temperature were observed as a result of ohmic (or resistive) heating. With 100 mA, probe 1 (closest to the solenoid coil) measured a 0.2 °C increase. No significant increase in temperature was noted in the probes 2 and 3 (Figure 4.4B). Probe 4, located 5 cm away from the catheter tip, served as a control and did not register a temperature change irrespective of the amount of current applied and to which coil it
was applied (Figures 4.4-4.7). With 200 mA applied to the solenoid, a 1.1 °C increase was measured by probe 1, and 0.1 °C increase was seen in probes 2 and 3 (Figure 4.4C). At 300 mA, heating continued to rise, with probe 1 measuring a 2.3 °C increase, and a 0.2 °C increase was seen probes 2 and 3. Similar increases in temperature were seen with current application to one of the Helmholtz coils alone (Figure 4.5).

To achieve three-dimensional catheter tip deflections, current must be applied to more than one coil at a time. Application of current to two coils (Figure 4.6) and all three coils (Figure 4.7), resulted in significant heating with higher currents. For example, with 300 mA applied to a solenoid and a helmholtz coil, probe 1 measured a 6.0 °C increase, a 2.7 °C increase was seen in probe 3 and probe 2 showed a 1.4 °C increase. 300 mA applied to all three coils for 30 seconds produced increases of 9.0 °C, 2.7 °C, and 5.5 °C in probes 1, 2, and 3, respectively (Figure 4.7). Lastly, a linear relationship between temperature increase and time period current was applied can be deduced from Figure 4.4-4.7.
Figure 4.4 30 second temperature monitoring during continuous application of current to the solenoid coil.

A. 50 mA current. No significant increase in temperature is noted in the probes. B. 100 mA. Probe 1 (closest to the solenoid coil) measured a 0.2 °C increase. No significant increase in temperature is noted in the probes 2 and 3. C. 200 mA. Probe 1 measured a 1.1 °C increase. A 0.1 °C increase was seen probes 2 and 3. D. 300 mA. Probe 1 measured a 2.3 °C increase. A 0.2 °C increase was seen probes 2 and 3. Probe 4 (5 cm away from the catheter tip) showed no temperature increase, independent of current.
Figure 4.5 30 second temperature monitoring during continuous application of current to one of the Helmholtz coils.

A. 50 mA current. Probes 1 and 2 measured a 0.2 °C increase. A 0.1 °C increase was seen probe 3. B. 100 mA. Probe 1 measured a 0.3 °C increase. A 0.1 °C increase was seen probes 2 and 3. C. 200 mA. Probe 1 measured a 1.5 °C increase. A 1.0 °C increase was seen in probe 3. A 0.5 °C increase was seen probe 2. D. 300 mA. Probe 1 measured a 3.5 °C increase. A 2.3 °C increase was seen in probe 3. Probe 2 showed a 1.2 °C increase. Probe 4 (5 cm away from the catheter tip) showed no temperature increase, independent of current.
Figure 4.6 30 second temperature monitoring during simultaneous application of continuous current to the solenoid coil and one of the Helmholtz coils.

A. 50 mA current. Probe 1 measured a 0.3 °C increase. A 0.1 °C increase was seen probes 2 and 3. B. 100 mA. Probe 1 measured a 0.7 °C increase. A 0.2 °C increase was seen probes 2 and 3. C. 200 mA. Probe 1 measured a 1.5 °C increase. A 1.0 °C increase was seen in probe 3. A 0.5 °C increase was seen probe 2. D. 300 mA. Probe 1 measured a 6.0 °C increase. A 2.7 °C increase was seen in probe 3. Probe 2 showed a 1.4 °C increase. Probe 4 (5 cm away from the catheter tip) showed no temperature increase, independent of current.
Figure 4.7 30 second temperature monitoring during simultaneous application of continuous current to the solenoid coil and both the Helmholtz coils.

A. 50 mA current. Probe 1 measured a 0.3 °C increase. A 0.1 °C increase was seen probes 2. No significant increase in temperature was seen in probe 2. B. 100 mA. Probe 1 measured a 0.7 °C increase. A 0.3 °C increase was seen probe 3, and a 0.2 °C increase in probe 2. C. 200 mA. Probe 1 measured a 2.5 °C increase. A 1.3 °C increase
was seen in probe 3. A 0.5 °C increase was seen probe 2. D. 300 mA. Probe 1 measured a 9.0 °C increase. A 5.5 °C increase was seen in probe 3. Probe 2 showed a 2.7 °C increase. Probe 4 (5 cm away from the catheter tip) showed no temperature increase, independent of current.

Discussion

Minimal RF-induced heating of MARC steering coils was observed during real-time MR imaging. The highest increase in temperature observed after 15 minutes of continuous imaging was 0.35 °C, which is below the 4°C increase that will cause irreversible tissue damage. Temperature increases around the coils were dependent on the proximity of the catheter-coil tip to the magnet bore wall as well as on the power of the MR pulse sequence (varied here by changing the RF flip angle), although heating observed using 80-90 degree flip angles was lower than expected. Since SAR increases as flip angle increases, the decreased heating at higher flip angles was likely due to automated scanner software programming which automatically limits SAR by changing TR and TE values once a threshold SAR level is reached for a given pulse sequence.

These findings show that RF heating previously observed in other types of conductive wires in MRI also occurs with MARC-steering of endovascular catheters. The mechanism by which this RF induced heating occurs is likely due to the same mechanism, the antenna effect, whereby the wire couples with the time-varying electric fields produced by the RF pulses. The amount of RF heating caused by conductive wires has been shown to be high in previous studies but results have been variable and inconsistent. In vitro temperature increases in the range of 18 to 48°C have been reported, in experiments involving a standard conducting guidewire, coaxial cable, and miniature tracking coil, levels that are incompatible with patient safety. A heating study involving intravascular imaging coils, however, which consisted of a loop with a length of 40 mm and a width of 6 mm, demonstrated much lower heating, probably due to the rounded end of the coil, which prevents a high concentration of E-fields.

Further experiments are necessary, however, to evaluate the effect of RF heating due to resonant lengths of wire. The experiments described in this chapter were done with a constant 1 m length of catheter/wire combination immersed in the tissue-mimicking gel phantom. RF heating depends on how much of the catheter is in the body since the wavelength of energy on the
wire is a function of the length of the catheter immersed within the body. A more thorough investigation of this effect would require a body volume phantom with electrical properties mimicking the human body, suited to catheter insertion of various lengths.

This study also shows that substantial resistive heating occurs under certain conditions, while others produce relatively minor, physiologically inconsequential temperature increases. Application of currents up to 300 mA to one coil or up to 200 mA to multiple coils did not result in physiologically hazardous temperature increases. Heating did reach hazardous levels, however, when using 300 mA currents in either 2 coils, or 3 coils, simultaneously. Theoretical calculations predicted a temperature increase of 93°C/s. As discussed above, however, several factors contribute to reducing the actual rate of temperature rise.

These experiments were performed in vitro and represent a worst-case scenario. The 30 second time interval used for application of current in this study represents the upper limit of the time necessary for selective catheterization of a vessel. Less heating would result from reduction of the time interval that continuous current is applied to the system. Applying current to all three coils simultaneously for 15 seconds instead of 30 seconds, for example, would approximately halve the increase in temperature (Figure 4.7). Furthermore, in vivo temperature increases, however, are likely to be lower than those observed in this study, since convective blood flow will remove heat produced.

Given the results of these experiments, MARC steering should and can be made safer for clinical applications. Resistive heating could be reduced by a number modifications to the catheter or coil. Increasing the efficiency of the catheter, i.e., increasing the amount of deflection obtained per unit of current, may involve the use of highly flexible materials (lower elastic modulus) for catheter construction. Since power dissipation is also proportional to the resistance, conducting wires of smaller with smaller resistance per unit length, such as thicker diameter wires, or gold wires, could also be used to reduce resistive heating. Catheter bending stiffness can also be decreased by reducing the diameter and wall thickness of the catheter, thus reducing the area moment of inertia (see Chapter 2). Since the induced magnetic moment is proportional to n/l, where n is the number of turns and l is the length of the coil, a tightly wound solenoid with higher number of turns would require less current and create less heat. Also, since the magnetic torque produced by this mechanism is the cross-product of the magnetic moment and the main
scanner magnetic field, doubling the magnet strength to 3 T, was shown to double the effective
catheter deflection (Chapter 2). This advantage, however, needs to be weighed carefully against
the higher SAR associated with higher field scanners since higher field strength may result in
relatively more RF heating. Other methods of minimizing RF heating include the use of coaxial
chokes\textsuperscript{142} and transmission lines\textsuperscript{200}. Heating can also be reduced by using catheter materials with
higher specific heat capacity. Such materials would absorb more heat and could be used to
further insulate the catheter coils. The prototypical catheter-coil design used in this thesis
involves winding of a magnet wire coil around the outside of the catheter. Catheter extrusion
with the coils built into the walls of the catheter would increase insulation. Lastly, infusion of
cooler normal saline within the lumen of the catheter during application of current could function
as a catheter cooling system.

The heating due to either RF or resistive factors may not only have an effect on the blood and
tissues, but also on catheter materials themselves. Although Tsiu \textit{et al} showed that small
temperature differences (22 °C vs 37 °C) had no effect on catheter mechanical properties\textsuperscript{175}, the
heat produced by the current in the coils may alter catheter stiffness (depending on the glass
temperature of the catheter material). Furthermore, heating may also release toxic catheter
material products into the bloodstream.

Although this study does not allow calibration of applied current-temperature increases, it
demonstrates that tissue heating that may result from use of this steering mechanism may only
reach clinically significant levels when using multiple coils with high currents. Furthermore, a
number of approaches to reducing the temperature increases exist, making further development
of this technology promising.
5. General Discussion

Endovascular interventional radiology procedures such as balloon angioplasty, stent placement, and coiling of aneurysms have become standard medical practice for the treatment of many patients with vascular disease. The ability of MRI to combine acquisition of high resolution anatomical images and functional information, including but not limited to flow velocities, perfusion, diffusion, and temperature, together with its multiplanar imaging capability and absence of radiation, have been proposed as advantages of the use of MRI for guidance of interventions. As a result, endovascular interventional MRI has emerged as a new and promising area within interventional radiology. Growing interest in iMRI has led to the development of faster imaging pulse sequences and several approaches to visualizing, tracking, and steering of endovascular instruments.

In this chapter, advances in interventional MRI that have been made during the past few years, and the role MARC steering may play in this context, in contributing to solving the problems presently limiting the use of MRI for guiding endovascular procedures are discussed.

Current status of iMRI

Although the feasibility of iMRI has been shown in many clinical settings, as discussed in chapter 1, currently none of these approaches has been widely adopted in medical practice. The major reasons for the slow clinical translation of this area of research include:

- High field MR scanners were developed for diagnostic and not interventional use. The bore configuration of these scanners makes patient access difficult. Once an introducer sheath is inserted into patient’s groin and the patient is advanced into the magnet bore, the entry point can be brought within reach using a sheath extender. This still leaves the physician in an awkward working position. In addition, with the patient partially out of sight, recognition of problems at the insertion site, such as bleeding, and communication with the patient, is hindered.
• Low-field open interventional scanners have been developed, but the temporal and spatial resolution necessary for guiding intervention is not achievable with such scanners.
• The temporal and spatial resolution, even at 1.5 T, is still lower than x-ray fluoroscopy.
• MRI is susceptible to many effects that can easily compromise image quality, such as magnetic field inhomogeneity, pulsatility or motion, and chemical shift.
• Few dedicated MR-safe instruments and equipment are widely available.
• Visualization of instruments that are MR safe requires the use of long conductive wires used in interventional instruments for active tracking which are susceptible to heating induced by RF fields.
• The advantages of using MRI for guidance of endovascular interventions have not been shown to be of enough added value to substitute for fluoroscopy and be incorporated into medical practice.

As a consequence of many unresolved problems, MR guided vascular interventions are still in experimental phase. The additional equipment constraints as well as material and component requirements needed to visualize devices in MRI has slowed progress.

Some MR scanner manufacturers have enthusiastically recognized the need for MR scanners that are more suited to interventions. Driven by the success of MR-guided interstitial interventions such as resections, ablations, and biopsies, a desire to improve access has led the development “double donut” high-field MR scanners and higher field open MR scanners, which allow easier patient access for MRI guided intervention. Planar gradient systems, RF coils, and magnet designs continue to be improved and 1 T open scanners are available. Rooms incorporating both C-arm x-ray fluoroscopy and an MR scanner (also called XMR suites) have also been installed at some institutions. Diagnostic scanners are now coming equipped with real-time imaging interfaces for interventional use. As interventional MRI grows in popularity, the demand for these types of MR scanners should result in further advancements.

Similarly, most currently available guidewires and catheters are not safe for use in the MRI setting. By avoiding ferromagnetic compounds, however, these instruments are quickly and easily made MR safe. Fiberglass guidewires and non-braided balloon angioplasty catheters (such as the one used in Chapter 1) are available, and have been tested successfully in phantom, animal, and human studies. It appears feasible to replace radio-opaque and high tensile strength
catheters and guidewires with MR safe devices that retain desirable mechanical properties such as torque, steerability, and flexibility (as the catheters used in this thesis), but the production of a new generation of MR safe instruments requires additional investment and clinical testing.

Unlike X-ray fluoroscopy, which allows increased temporal and spatial resolution simply by increasing the intensity of radiation, MRI demands a trade-off between scan time and spatial resolution. For a given scan, SNR is roughly proportional to voxel size and to the square root of image acquisition time. Faster acquisitions decrease SNR. They are also generally more sensitive to effects that compromise image quality. Recent improvements in pulse sequence acquisition times developed to fit cardiac imaging and abdominal and thoracic scans into comfortable breath holds, however, have resulted in significant increases in temporal resolution while maintaining SNR (see discussion of real-time pulse sequences in chapter 1).

Furthermore, advances in simultaneous catheter localization and scan plane orientation has made MR guided endovascular intervention much simpler. In room control of geometry and other scan parameters has been successfully demonstrated. Switching time between scans of differing functionality such as tracking and flow monitoring has been shortened. These technologies are essential to keeping the catheter tip visible at all times during the procedure. The magnetic inhomogeneity artifact produced by magnetic moments induced in MARC coils provides a passive catheter tip visualization mechanism. Furthermore, a MARC-steered catheter can also be combined with miniature coils for continuous active catheter tip localization and scan plane updates. MARC steered catheters can easily be integrated into any imaging system.

Active catheter tracking has gained popularity over passive tracking by virtue of its ability to simultaneously define catheter and scan plane orientation. Active tracking techniques are subject to RF heating challenges, however. Several remedies have been proposed. The problem of RF and resonant length wire heating may be resolved by using a wireless setup. Actively tuned and inductively coupled microcoils are being used without the need of any connection between the microcoil and the MR scanner obviating the need for longer conductive parts\textsuperscript{201}. The use of optical fibers instead of coaxial cables as connection line is another approach\textsuperscript{202}. Integration of chokes\textsuperscript{203} or transformers\textsuperscript{204} into the conductive parts can also be used for the development of safe transmission lines. The latter should allow for easy miniaturization and integration into a catheter wall.
A unique advantage of endovascular interventional MRI is the ability to steer endovascular catheters using the static magnetic field. As mentioned previously, the limitations of imprecise manual control of catheter tip orientation and steering of currently available guidewires and catheters can lead to kinking, buckling, dissection, perforation, as well as prolonged procedure time and resultant increased radiation dose and risk of thrombus formation, even in the hands of the most experienced interventionalists. In some procedures, such as RF ablation of cardiac arrhythmias poor catheter tip control can result in treatment failure. Each interventionalist relies on a distinct subset of guidewires and catheters that is in part determined by their experience and comfort level with the products. MARC steering would offer more precise automatic control and stability of the catheter or guidewire tip than is currently possible with manually directed products.

The use of an external magnetic field for catheter steering has been developed by Stereotaxis Inc., using computer-controlled, externally applied magnetic fields that precisely govern the motion of the an electromagnetic catheter tip on a specialized guidewire or catheter in an x-ray fluoroscopy suite. Such electromagnetic control allows the digitization of catheter steering and, as a result, should make endovascular catheter navigation easier and safer for the patient, by eliminating some steering problems in traditional fluoroscopic endovascular intervention. Initial feasibility studies using this technology have been promising, allowing more precise control, more complex maneuvers, and increased stability. Use of this technology is limited to X-ray fluoroscopy, however, as the hardware is not MR-compatible. In contrast, the MR-compatible MARC steering mechanism described in this thesis may allow the practitioner to combine the use of the magnetic field for both precision steering, soft-tissue imaging, intravascular imaging, and functional imaging. MR guidance and improved steering precision would be extremely useful in the diagnosis and treatment of many disease processes where information about the vessel wall, atherosclerotic plaques, and perivascular tissue anatomy and function in real-time is of great interest. In addition to improved control over the catheter tip using MARC steering, for example, visualization of the pulmonary vein walls in RF ablation for atrial fibrillation using MRI would further facilitate successful procedural outcome. Other procedures taking advantage of these characteristics might include, but not be limited to, endovascular delivery of cardiac stem cells to infarcted myocardium, delivery of drugs, genes, and prosthetic valves, stroke therapy, embolotherapy, angioplasty and stent deployment, cardiac
catheterization. Ultimately, the driving force for advancing the field of interventional MRI will be demonstration that MR guidance is of greater clinical utility for specific procedures than x-ray fluoroscopy, or new therapies that cannot be performed without MR guidance. MR guidance has already been used to guide procedures that would not succeed using x-ray fluoroscopy. Such procedures include targeted delivery of stem cell to areas of infarcted myocardium. MARC-steered catheters may pave the road to areas of vascular anatomy or pathology previously difficult or impossible to reach and treat.

Despite the progress made in the development and testing of MARC steering for interventional MRI, further investigation is required prior to its clinical use. Substantial support from industry is required for further improvements in coil and catheter design discussed in previous chapters with respect to maximizing current steering efficiency and minimizing resistive heating. A digital feedback control interface that allows simultaneous control of current applied to different catheter coils is also needed. Subsequently, feasibility testing of endovascular procedures should be performed in animals. Such work is planned in the near future at the University of California, San Francisco.

In conclusion, iMRI, and endovascular iMRI in particular, is still in its infancy. As with other modern medical technological developments, endovascular interventional MRI will need time to grow to maturity. Continued research in this field is important to demonstrate the clinical added value of endovascular interventional MRI over traditional x-ray fluoroscopy. It took more than 60 years from the discovery of x-rays by Wilhelm Roentgen in 1895, to the confluence of developments that make interventional radiology a thriving specialty today. Although MRI, in contrast, has been around only for 35 years as a diagnostic imaging modality, it is already being used for guiding interventions.
6. Appendix

A New Temperature-Sensitive Contrast Mechanism for MRI: Curie Temperature Transition-Based Imaging

Abstract A temperature-sensitive MRI contrast mechanism is proposed based on the physical property - the Curie temperature (Tc), at which a ferromagnetic material transitions to paramagnetic state and vice versa. To evaluate the feasibility of this new contrast mechanism, experiments were performed with solid gadolinium metal, which has a Tc of 200°C. In phantom and ex-vivo experiments, the magnetic susceptibility artifact area decreased with increasing temperature transitioning across Tc (p < 0.05). Similar results would be expected for a variety of ferromagnetic substances with substance-specific Tc values. Temperature-sensitive MRI contrast agents harnessing this mechanism may be used to 1) indicate regional attainment of specific temperatures in thermotherapy, 2) render an accumulated contrast agent more or less visible by the external application of appropriate heating or cooling, or 3) quantify tissue temperature based on MR image characteristics and magnetic susceptibility artifact caused by a ferromagnetic-paramagnetic transitioning substance.

Introduction

The ability to monitor changes in tissue temperature in vivo is of particular interest in interventional MRI procedures such as thermal ablation of tumors \(^{207-211}\), local hyperthermia for the treatment of cardiac arrhythmias \(^{212}\), and control of gene therapy using heat-sensitive promoters \(^{213}\). Precise monitoring of the magnitude and extent of heat or cold deposition and resulting damage is of extreme importance for the efficacy and safety of these procedures \(^{214}\). Conventional devices used for monitoring tissue temperature include thermocouples, thermistors, and fiberoptic probes \(^{215}\). Although these devices allow a high degree of accuracy (±0.1°C), they require insertion of the sensor into tissue. This is painful and hazardous, and allows temperature measurements in only a few localized regions. In addition, such instruments may interfere with the therapeutic instrument. To circumvent these problems, MR thermometry, in which relative changes in temperature are reflected by small changes in the proton resonant frequency (PRF) \(^{216}\), longitudinal relaxation time (T1) \(^{217}\), or apparent diffusion coefficient (ADC) \(^{218}\) of water, has been developed. This permits temperature imaging with high spatial and temporal resolution. These techniques, however, have relatively low temperature sensitivity, and are greatly influenced by local motion and magnetic susceptibility variations. For example, the temperature dependence of the \(^1\text{H}\) chemical shift of water is \(\leq 0.01\) ppm/°C, which corresponds to only \(\leq 0.7\) Hz at 1.5 T for a 1°C temperature change. The feasibility of MR thermometry based on the temperature dependence of the chemical shifts of lanthanide complexes has recently been explored \(^{219}\). These approaches, however, require very high field scanners (e.g. 9.4T) to resolve the small chemical shift differences. Others have studied liposome-encapsulated gadolinium chelates whose temperature response is linked to the phase-transition properties of the liposome carrier \(^{220}\). These techniques, however, are dependent on the design and chemical properties of the complex or liposome, in addition to the lanthanide ion.

Magnetic susceptibility differences between tissues and substances cause characteristic changes or artifacts in magnetic resonance imaging. Therefore, a substance whose magnetic susceptibility changes with temperature may yield useful information about tissue temperature in MRI. Certain derivatives of 6-fold coordinated iron(II) complexes, for example, have been shown to transition between diamagnetic state below a critical temperature and a paramagnetic state above this temperature \(^{221-223}\). Recently, Muller et al showed that the increase in magnetic susceptibility in the paramagnetic state, as temperature is raised above the critical temperature of these complexes, results in a magnetic susceptibility artifact on MR images \(^{224}\).

In this study, we present a new temperature-sensitive contrast mechanism that is based on another physical property, the Curie temperature (Tc). The Curie temperature is the temperature at which a
ferromagnetic substance loses its ability to possess a net (spontaneous) magnetization in the absence of an external magnetic field (Figure 3.3, Table 6.1). At temperatures below the Curie temperature, magnetic moments are partially aligned within magnetic domains, which is responsible for permanent magnetization. As the Curie point is approached, thermal fluctuations increasingly disrupt this alignment, until the net magnetization becomes zero at and above the Curie point. Above the Curie point, the material is purely paramagnetic and its magnetic susceptibility obeys the Curie-Weiss law. Table 6.1 lists the Curie temperatures of several substances. Due to the dependence of the magnetic susceptibility of a ferromagnetic material on temperature around its Curie temperature (Figure 3.3), and the sensitivity of T2*-weighted magnetic resonance imaging to local magnetic field variations, a contrast agent utilizing this property could serve multiple purposes: it could provide quantitative estimates of absolute tissue temperature in the absence of invasive probes or MR thermometric pulse sequences, report the attainment of a specific temperature in the tissue containing the contrast agent, or render an accumulated contrast agent more or less visible by the external application of appropriate heating or cooling. In addition, it may also provide a mechanism for a “switchable” MRI contrast agent which activates once a specific temperature has been reached.

Table 6.1. Curie temperatures (Tc) of selected substances

<table>
<thead>
<tr>
<th>Material</th>
<th>Curie temperature (K)</th>
<th>Material</th>
<th>Curie temperature (K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe</td>
<td>1043</td>
<td>Cu₂MnIn</td>
<td>500</td>
</tr>
<tr>
<td>Co</td>
<td>1388</td>
<td>EuO</td>
<td>77</td>
</tr>
<tr>
<td>Ni</td>
<td>627</td>
<td>EuS</td>
<td>16.5</td>
</tr>
<tr>
<td>Gd</td>
<td>293</td>
<td>MnAs</td>
<td>318</td>
</tr>
<tr>
<td>Dy</td>
<td>85</td>
<td>MnBi</td>
<td>670</td>
</tr>
<tr>
<td>CrBr₃</td>
<td>37</td>
<td>GdCl₃</td>
<td>2.2</td>
</tr>
<tr>
<td>Au₂MnAl</td>
<td>200</td>
<td>Fe₂B</td>
<td>1015</td>
</tr>
<tr>
<td>Cu₂MnAl</td>
<td>630</td>
<td>MnB</td>
<td>578</td>
</tr>
</tbody>
</table>

In this work, we explore the feasibility of exploiting the transition between ferromagnetism and paramagnetism across the Curie temperature as a method for generating temperature-sensitive contrast in MRI. For the purposes of these experiments, Gadolinium metal was used due to the fact that its Curie
temperature (20°C) is convenient for feasibility demonstration. In addition, gadolinium is stable in air and water in metal form, thus permitting the use of simple experiments and equipment.

**Materials and Methods**

Gadolinium (Gd) wire (99.9% purity) was obtained from Goodfellow Corporation (Devon, PA, USA). The wire used in the phantom experiment measured 25 mm in length and 0.5 mm in diameter. For the ex-vivo experiment, a 0.5 mm by 0.5 mm by 0.5 mm piece of gadolinium metal was used. Gadolinium metal was selected for this feasibility demonstration, since it has a Curie temperature of 20°C allowing convenient imaging both below and above this point.

In the phantom experiment, a 25 mm length of the gadolinium wire was suspended in water within a cylindrical glass phantom and the wire was aligned parallel to the main magnetic field. The initial temperature of the water bath was 60°C and was gradually cooled to 5°C. Cooling was accomplished by immersing the phantom into a larger ice water bath. Temperature was measured continuously using an MR compatible laboratory thermometer within the inner water bath.

*In the ex-vivo tissue experiment*, a gadolinium particle (approximatively 0.5 mm x 0.5 mm x 0.5 mm) was inserted into a 10 cm x 10 cm x 3 cm cut of boneless sirloin meat. The meat was suspended vertically into a glass phantom water bath. The temperature of the water bath was varied by addition of water of desired temperature (5°C and 36°C, corresponding to 15°C below and 16°C above the Tc, respectively). Temperature was measured using an MR compatible laboratory thermometer, allowing time for equilibration of water bath temperature and meat-gadolinium temperature.

Both phantom and ex-vivo experiment images were obtained on a 1.5 T SIGNA Excite MR scanner (General Electric, Milwaukee, WI, USA) with an 8-channel head coil. For the phantom experiments, a multi-slice 2-D Gradient-Recalled Echo pulse sequence was used: TR 171 ms, TE 2.6 ms, flip angle 30 degrees, 256 x 256 matrix, NEX 1, 2.5 mm slice thickness, and image acquisition time 43.8 s. For the ex-vivo experiments: TR 146 ms, TE 3 ms, flip angle 30 degrees, 256 x 256 matrix, NEX 1, 1.5 mm slice thickness, and image acquisition time 36.6 s.

Image analysis was carried out on eFilm version 1.9.3 (Merge, Milwaukee, WI, USA) and ImageJ (National Institutes of Health, Bethesda, MD, USA). At each temperature, the area of the magnetic
susceptibility artifact (signal void) created by the Gd wire was measured by drawing a region-of-interest (ROI) outlining the outermost border of the dark circular artifact (Figure 6.1 and 6.3, arrows) within the water bath or meat slice on the MR image. The ROI was made using a free-hand mouse tool provided by the software. The software calculated the area within the ROI automatically. This was repeated for each image at each temperature. Phantom and ex-vivo images were analyzed by three readers, blinded to the temperature of the tissue. Artifact area measurements were compared using a paired Student’s t-test.

**Results**

*Phantom experiment*

Axial images of the suspended Gadolinium wire inside the water bath at 10°C decrements (from 55°C to 5°C) are shown in Figure 6.1. At a temperature of 55°C, the MR image acquired demonstrated a large area of signal void (black area) within the water bath (Figure 6.1, arrows). This artifact was due to the large magnetic susceptibility difference between Gd wire (the long axis of which is oriented perpendicular to the plane of the images) and water. As temperature decreased, the cross sectional area of this signal void artifact became larger (Figure 6.1, arrows). Figure 6.2 plots the decrease in the artifact cross-sectional area with increasing temperature. This data indicates a decrease in magnetic susceptibility with temperature across the Curie temperature (20°C), continuing to lower values at higher temperatures, in accordance with the Curie-Weiss law.
Figure 6.1 Axial images obtained at 1.5 T for temperatures above and below the Curie temperature for gadolinium metal (20 °C).

The gadolinium wire is suspended in water within a cylindrical glass phantom. This glass phantom is placed within a larger cylindrical glass phantom water bath used for cooling or heating the inner water bath. The inner water bath temperature is indicated below each image. The larger magnetic susceptibility of gadolinium with respect to water caused a large circular artifact, or signal void (arrows), around the Gd wire (located at the center of the artifact but not visible on the MR image). This magnetic susceptibility artifact cross sectional area increased with decreasing water bath temperature. Ice cubes are the cause of the signal void artifacts in the outer water bath as temperature decreases.
The cross sectional artifact area was seen to decrease with increasing temperature. This indicates a decrease in magnetic susceptibility with temperature across the Curie temperature, in accordance with the Curie-Weiss law (see Figure 3.3).

**Ex-vivo experiment**

Figure 6.3 illustrates the results of the *ex-vivo* experiment with a fragment of Gd metal placed inside a piece of meat. As in the phantom experiment, the size of the magnetic susceptibility artifact caused by the piece of gadolinium metal decreased with increasing temperature. The artifact cross-sectional area was significantly smaller at a temperature 16 degrees above Tc, compared to 15 degrees below Tc (79 mm$^2$ vs. 119 mm$^2$) showing a 34% area reduction (p<0.05). This again indicates a decrease in magnetic susceptibility with temperature across the Curie temperature, clearly resolvable in a tissue setting.
Figure 6.3 Axial images obtained at 1.5 T for temperatures (A) below (5 °C) and (B) above (36 °C) the Curie temperature for pure gadolinium metal, 20 °C.

A 0.5 mm by 0.5 mm by 0.5 mm piece of gadolinium was inserted into a thick cut of boneless sirloin and imaged at temperatures indicated below each image. Similar to the phantom experiments, the size of the magnetic susceptibility artifact (arrowheads) caused by the piece of gadolinium metal varied with temperature. The artifact area was significantly smaller at 36 °C compared to 5 °C (79 mm$^2$ vs. 119 mm$^2$) showing a 34% area reduction ($p<0.05$). No effect on the meat signal outside of the artifact area is seen.

Discussion

Gadolinium is ferromagnetic below its Curie temperature (20 °C). Its high magnetic susceptibility below the Curie temperature leads to a large field disturbance and signal loss on gradient-recalled echo MRI. Above the Curie temperature, the same material becomes paramagnetic with commensurately less magnetic field disturbance, and thus less extensive magnetic susceptibility or signal voiding artifact on T2*-sensitive MRI. The decrease in magnetic susceptibility artifact with increasing temperature above Tc is in accordance with the Curie-Weiss law for paramagnetic substances (Figures 3.3 and 6.2). This
property of gadolinium and other ferromagnetic substances provides a novel mechanism for the design of temperature-sensitive MRI contrast agents and thermometric materials.

Calibration of the magnetic susceptibility artifact versus temperature curve would render the method suitable for detecting absolute temperature changes. While this study focused on pure gadolinium metal with a Curie temperature of 20°C, other elements or alloys will show similar characteristics at specific Curie temperatures. Varying the material or alloy composition would lead to a choice of critical transition temperatures (Table 6.1), such as the physiological 37°C, or 42°C for cell killing in thermotherapy. Other substances or alloys can also show a steeper magnetic susceptibility versus temperature curve, that is, a larger magnetic susceptibility change around its Curie temperature. The effect of the temperature change on the visibility (signal void area) would provide a mechanism for “activating” or “deactivating” a contrast agent or switching the appearance of a probe made of ferromagnetic material according to local environmental temperature, and changing its imaging characteristic based on a change of magnetic property.

Considerable research efforts have focused on the development of “intelligent” agents that can act as biochemical reporters. Examples have included agents responsive to specific enzymes, oligonucleotide sequences, specific RF pulses, or changes in calcium concentration, pH, and pO2. These methods mostly rely on a biological “switch” to activate the contrast agent. Recently, Muller et al. also used a physical “switch” from diamagnetic state to paramagnetic state to change the properties of a potential MR contrast agent. Similarly, our agent relies on a physical “switch” to change the potency of the contrast agent (namely temperature transition). In contrast, however, the mechanism described in the present report depends on a change in physical state from ferromagnetic to paramagnetic (or vice versa) in the material. Furthermore, the gradual change in magnetic susceptibility of a ferromagnetic substance such as gadolinium around its Tc allows for monitoring of a larger range of temperatures.

The method described here differs from other temperature-sensitive MRI contrast agents being developed by its reliance on a field disturbance effect of signal amplification (MRI visibility), obviating the need for water or tissue to come into direct contact with the contrast medium. Other temperature-sensitive contrast agents under development rely on chemical shift change. However, these require very high field scanners to achieve adequate temperature sensitivity. Since the Curie temperature is independent of the main magnetic field, the mechanism proposed in this study may be better suited for the field strengths of clinical scanners currently in use.

A limitation of this study, however, is that the use gadolinium wire of this geometry and dimensions in clinical MRI is both unsafe and impractical. Gadolinium and other lanthanides are toxic to living tissues.
Future work could therefore involve the development of methods for encapsulating gadolinium particles of much smaller dimensions, for instance, in liposomes or nanoparticle complexes, as well as exploring other metals and compounds with differing Curie temperatures and toxicity profiles. Lastly, this study relied on an indirect measure of magnetic susceptibility through T2* MR artifact area. Future investigation should also include direct measurement of the changes in magnetic susceptibility with temperature of the material or alloy and comparison of those measurements with the MR image artifact (using different imaging parameters, such as echo time) in order to accurately demonstrate the relationship between the ferromagnetic/paramagnetic transition and the size of T2* artifact.

Conclusions

The Curie temperature based transition phenomenon is a unique property of specific materials and holds exciting promise for developing temperature sensitive contrast agents. Due to the dependence of the material magnetic susceptibility on temperature around its Curie temperature, a contrast agent utilizing this property could provide quantitative estimates of tissue temperature in the absence of invasive probes or MR thermometric pulse sequences during hyperthermia or cryoablation treatment for tumors.
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