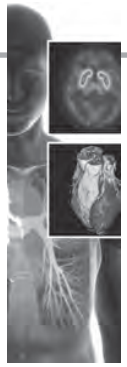

Catheters and guide wires for interventional MRI: are we there yet?

Clinical feasibility of interventional MRI has been shown for a number of procedures. However, MRI-guided endovascular interventions have not yet reached clinical routine due to the lack of suitable MR safe or MR conditional and MR visible devices. In this article, some of the MR tools currently under development are reviewed. Good handling and MR visibility properties both are critical factors for successful application of such novel devices. Finally, we argue that it is only when both MR catheters and guidewires are available on the market that real progress and impact will be made in the field of interventional MRI.

KEYWORDS: MRI; catheters; development; guidewires; interventional

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Introduction

Catheterization in humans started in 1929, when, Forssmann [1] introduced a ureteral catheter into one of his left forearm veins. Following his pioneering work, new tools and techniques were rapidly developed. However, it was only by the end of the 40s and beginning of the 50s that critical steps forward were made, in particular with the development of both thin-walled [2] and radiopaque [3] catheters (soon to be braided for improved mechanical properties [4]) as well as suitable guidewires. The availability of these novel instruments led to safe minimally invasive techniques, as we know it today, with millions of patients annually diagnosed and treated worldwide.

Interventional radiology and cardiology have proven to be successful. Yet, they present several drawbacks. Above all, the interventions are performed under 2D projection fluoroscopy/angiography guidance, which exposes both patient and medical staff to ionizing radiation. Today, we are witnessing yet another revolution in interventional radiology, based on the real-time magnetic resonance imaging. However, just like nearly 65 years ago, when new instruments were needed to take the first crucial steps forward in interventional radiology and cardiology, new MR suitable and visible catheters and guidewires are needed now to open the way for interventional MRI.

Magnetic resonance imaging (MRI), offers several advantages over conventional imaging modalities for both patients and interventionalists. MR imaging slices can be oriented in three dimensions [5, 6], no ionizing radiation is used, and, unlike X-ray images, MRI has an excellent soft-tissue contrast [5-11] with no known harmful effects [5]. Additionally, MRI provides morphologic as well as functional information. With these additional features, MRI may help to determine the result of an endovascular intervention [8-10, 12] and provide safety advantages over conventional X-ray-guidance, for example by revealing more rapidly vascular perforation or rupture [12,13].

In the last 10 years, the feasibility of MRI-guided vascular interventions has been demonstrated for a number of procedures in humans, such as angioplasty of femoral artery stenoses [14], iliac angioplasty and stenting [15], cardiac interventions [9,16,17], cardiopulmonary interventions [18], and others. Real-time MR sequences are now available [8] and most MR scanner manufacturers offer real-time MR sequences adequate to guide MRI catheterization [11]. Nevertheless, MRI-guided vascular interventions are not yet ready to be widely used in the clinical setting [19]. This is due to several issues linked to this imaging modality: increased operational complexity, reduced temporal and spatial resolution, restricted access to the patient and limited patient monitoring, and amount of noise during the scan [7-10,19,20].

For these reasons, critics argue that interventions performed under MRI-guidance represent a costly and cumbersome alternative to procedures that, otherwise, are conducted rapidly and efficiently under X-ray guidance and adjunctive ultrasound [12]. However, even if radiation exposure has been reduced over the years, X-ray guided procedures still pose significant health risks, particularly for children and young adults requiring multiple procedures,

and staff with chronic exposure [9,11,12,21-26]. Therefore, MRI-guided interventions might be justified. In order to reach clinical routine, the aforementioned mentioned issues need to be addressed and, most importantly, there is a need for suitable (MR safe or MR conditional) and visible MR instruments [5,7-10,12,19,20,27,28]. Such devices being under development are reviewed, together with their mechanical handling and MR visualization properties.

MR Instruments

■ Catheters and guide wires

Conventional devices designed for use under fluoroscopy-guidance cannot be used in MRI due to the frequent presence of ferromagnetic components (e.g., braiding in catheters) and/or of long conducting materials (e.g., guidewires) [9,27], which results in a risk of radiofrequency-induced heating [29,30]. Some commercially available catheters, stents, or balloons, though most not yet CE marked or FDA approved for MR-guidance, were used for MR-guided procedures, to a limited extent [9]. Indeed, MRI-guided interventions are still restricted by the lack of appropriate MRI instruments [28] with proper mechanical characteristics [5,31]. With conventional tools, proper pushability and torquability are achieved by the use of metallic cores (guidewires) and metallic braiding (catheters) [5], elements that have to be avoided, or limited in length, for the construction of MR instruments. As a result, MR instruments present usually lower bending and torsional stiffness and, therefore, reaching the target in the body may be difficult. As an example, non-braided angiographic catheters, used for cardiac catheterization under MRI-guidance, were described to have a low torque and poor steerability [9].

Consequently, nylon, aramid, and polyester (or other fibers), can be a solution for the construction of MR fiber-braided catheters with improved mechanical properties [32]. Examples of such tools can be found in the literature, e.g., with PEEK [33], nylon [34], or other [35] braids. The MR cardiac electrophysiology catheter developed on the basis of nylon braided tubing [34] was shown to have mechanical properties comparable to commercial MR incompatible catheters for cardiac catheterization. It seems that such fiber-reinforced catheters have the potential to become suitable catheters for MR interventions.

Nowadays, many MR catheter developments have been reported. Various groups or companies are getting interested in MR catheters for specific interventions such as cardiac electrophysiology (Imricor, Burnsville, USA; [16,33-35], biopsy catheters (ITP, Bochum, Germany), cardiac and renal ablation catheters (Imricor; [36]), cryoablation catheters [37], deflectable catheters (ITP, Bochum, Germany; [33,38]), as well as catheters for tracking [39-41], and many others. However, only a few of these catheters are suitable for use in the clinic and even less is available on the market. Also, to our knowledge, no MR visible catheters (and sheaths) suitable for MRI-guided endovascular navigation are CE marked or FDA, which makes the development of interventional MRI procedures more than challenging.

Till recently, the lack of MR guidewires has further limited the possibilities to perform MRI-guided interventions, although some centers perform studies on patients without the use of a guidewire [11,16,42]. However, without guidewire support, successful navigation can be difficult or even impossible [11,16], or catheter shaft kinking may occur [11]; both incidents possibly leading to interventional failure.

In the development of MR devices, most of the efforts have initially focused on catheters [43]. In fact, it was only in 2012 that the first MR conditional and MRI visible endovascular guidewire received CE Mark (EPflex GmbH, Dettingen, Germany). Originally, conventional nitinol guidewires were used [44,45] but were found to be unsafe [46]. Then homemade PEEK [43,47] or other polymer-based [46] guidewires have been developed. However, as for catheters, the polymer-based guidewires had low bending stiffness [43], and fiber-reinforced-polymer designs were introduced. For example, a 0.032" MR guidewire prototype was found to have improved mechanical properties compared to the polymer materials alone [20]. Another promising glass-fiber reinforced 0.035" guidewire [27] was developed and tested in several patients [17]. However, it was subsequently observed that with such glass-fiber reinforced tools, special precaution must be implemented in the design to prevent guidewire disruption during the intervention [48]. The possibility of guidewire disruption led to the development of a new composite version of the 0.035" MR guidewire [49] (MR conditional, MR visible, Fraunhofer Institute IPT, Aachen, Germany; Nano4imaging GmbH, Aachen,

Germany). The 0.035" MR guidewire from EPflex is also such a composite design: PEEK-based with fibers [50]. Finally, a MR safe fiber-reinforced MR guidewire portfolio (0.035" standard and stiff, 0.014", and soon 0.018"), comprising the first continuous visualization of the guidewire shaft in MRI over its entire length, is currently awaiting CE Mark (MaRVis Medical GmbH, Hannover, Germany). Alongside these promising MR guidewires with passive-negative markers, another MR conditional guidewire with active marker is under development [51].

MR visualization

In parallel to the development of catheters and guidewires for MRI-guided interventions with proper mechanical properties, special care has to be taken in order to ensure that the developed MR instruments are visible on the MR images. Even when the instruments are suitable to be used in MR environment, they may present visualization issues, i.e. too big artifacts that shade the anatomy or, quite the reverse, they may not be visible on the MR images. It is known that polymer-only tools are not visible unless modified [5], or they may only be indirectly visualized.

Some catheters, for example, can be perceived on MR images using various methods: placement of an MR visible guidewire [45] in its lumen, or by injecting MR contrast agent [52], or just relying on the (potentially weak) susceptibility artifact created by the plastic [38]. In the same way, some balloon catheters can also be visualized by filling the balloon with air or with contrast media [11], or with carbon dioxide [9,42]. These tricks remind us the ways by which the early catheters were visualized on X- ray images before they were made radiopaque, e.g., with a metal guidewire inserted in the catheter or by filling the catheter with contrast medium [3,53,54].

Alternatively, markers or equipment can be added on the catheter or device in order to make it MRI visible. However, if a device is modified in such a way, the instrument loses its approval for human application. Even if such an approach is a solution for *in-vitro* and *in-vivo* experiments, it is a problem to get approval for a clinical study on patients. Therefore, special care needs to be taken during instrument development in order to ensure they offer appropriate MRI visualization properties. The devices can either be visualized using passive, semi-active, or active MR markers [5]. In addition, there is an increasing desire by the interventionists to visualize the entire instrument shaft and the exact tip localization for safe endovascular navigation [55,56].

Discussion

Extensive developments in interventional radiology (and cardiology) only happened when both suitable guidewires and catheters were available. Currently, the development of interventional MRI is restricted by the limited availability of these crucial tools. While the field has been hampered for a long time by the lack of MR guidewires, the recent developments are hopefully going to provide clinics with suitable and visible MR guidewires (EPflex, Nano4imaging, or MaRVis). Now, that such guidewires are being developed and approved, tests should be performed to evaluate if these MR guidewires have suitable mechanical properties for endovascular navigation and catheter support. To our knowledge, no such tests have been published yet.

Moreover, even now that some specialized catheters are being developed and are currently waiting for regulatory approval (e.g., Imricor), there is still only a limited number of MR catheters on the market. Some solutions have been found for clinical applications, but these are not always suitable for application in human. Most importantly, so far no navigation/exchange catheters, or introducers or sheaths specifically for use in interventional MR have been developed. These simple instruments must be developed to be both safe under MRI-guidance and visible on the images. Of course, to make MRI intervention a reality, these instruments should come at reasonable cost, especially for single-use navigation catheters and guidewires, which excludes complex designs.

It has been frequently reported that the main obstacle for adopting MRI catheterization is the unavailability of visible and MR safe/conditional endovascular devices [5]. On one hand, the recently developed MR conditional and MR safe guidewires allow for a larger array of MR-guided procedures to be investigated. However, on the other hand, it is only when both MR guidewires and catheters, visible, reliable, and with suitable mechanical properties, are developed that real progress and impact will be achieved in the field of interventional MR.

Disclaimer

H.C.M. Clogenson is currently working for the start-up company MaRVis Medical (GmbH, Hannover, Germany), which is developing

MR-safe guide wires. The current manuscript was written as guest researcher at the Delft University of Technology, and it is based on H.C.M. Clogenson's PhD work [57].

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