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Why Low Field Imaging is Expected to Boost Interventional CMR Procedures

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Despite the numerous drawbacks to x-ray fluoroscopy for cardiac catheterization, including poor soft tissue visualization, need for repeated injections of iodinated contrast to depict the anatomy, inability to visualize the anatomy during interventions, harmful effects of radiation, and the need for lead protection that can induce orthopedic injuries, it continues to be the mainstay for catheterization imaging. The adverse effects of radiation are even worse in children, as tissue in growing children is particularly sensitive to the detrimental effects of radiation because of greater mitotic activity. In addition, congenital heart disease (CHD) patients need repeated cardiac catheterizations and radiation-based imaging throughout their lives, sometimes receiving accumulated lifetime doses that are associated with a detectable increased risk of cancer.[1,2] Children also have longer lifespans than adults, thereby having more time to develop radiation-induced cancer.

With its exceptional soft tissue imaging in multiplanar views in arbitrary directions and dynamic imaging of cardiac function, cardiac magnetic resonance (CMR) eliminates all the disadvantages of x-ray, but it comes with its own challenges for real-time interventional imaging. The field of interventional CMR (ICMR) has been slow to progress, due to radiofrequency-induced heating of catheterization equipment during scanning, inability to see standard catheters with MR, and large metallic artifacts from interventional wires that obstruct the imaging. The many faults of x-ray imaging, however, continue to be the impetus behind pursuing ways to overcome these limitations in the field of ICMR.

To date, the vast majority of the ICMR work has been performed in 1.5 Tesla scanners. Clinician investigators at the National Institutes of Health used real-time MR guidance to perform right heart catheterizations (RHC) in adults,[3] and Ratnayaka and colleagues were the first to move ICMR into the pediatric hospital on a large scale, reporting 50/50 successful RHC in children.[4] As the field progressed, specific MR equipment was developed for catheterization to make wires and catheters conspicuous. Nano4Imaging (Dusseldorf, Germany) has been a leader in this field and produced the first FDA-approved guidewire (EmeryGlide MRWire) for ICMR by placing passive markers on the distal tip of the wire, which is made of glass fibers and polymers and protected by a high-strength aramid fiber mantle covered with a Teflon sleeve. The markers create signal voids in MR, which provide their visibility, and they are also seen on x-ray, which allows for use in both settings. This technology helped to bring ICMR to CHD, allowing the successful completion of right or left heart catheterization (LHC) in 23/25 patients with CHD, to measure pressure gradients across stenoses with MR guidance,[5] and in 31/34 children and adults with CHD, including for Fontan fenestration test occlusion.[6]

While diagnostic catheterizations with MR guidance are being performed on a regular basis at some institutions, interventional procedures, such as angioplasty, stenting, and septal defect closures, are not part of clinical practice today, due to the lack of equipment that is both visible and safe in the MR environment, the absence of supporting software, and uncertainty about reimbursement. Early work is pointing to low-field (0.55T) MR scanners having great potential to overcome some of these long-standing problems, however. They may allow the use of commercially available catheterization equipment since radiofrequency-induced heating of interventional devices is reduced at low field strength (theoretical 7.5-fold difference in heating between 0.55T and 1.5T).[7] Campbell-Washburn and colleagues showed that two types of nitinol non-exchange length glidewires and two types of stainless-steel braided catheters were safe at 0.55 T (<1°C heating) during two minutes of continuous scanning.[7] They then performed low field MR-guided RHC successfully in 7/7 patients using a commercially available nitinol glidewire (180 cm 0.035" Micro J-tip Glidewire, Terumo, Tokyo, Japan) without complication or evidence of heating.[7] These studies were performed on an investigational, modified commercial MRI system (1.5T MAGNETOM Aera; Siemens Healthineers, Erlangen, Germany) that operated at 0.55 T but retained the gradient performance of the original 1.5T system (maximum gradient amplitude 45 mT/m, maximum slew rate 200 T/m/sec).

FIGURE 1 *CMR still frame from a real-time interactive scan showing CO2-filled wedge catheter balloon in IVC after 2 mg/kg ferumoxytol (red arrow).*

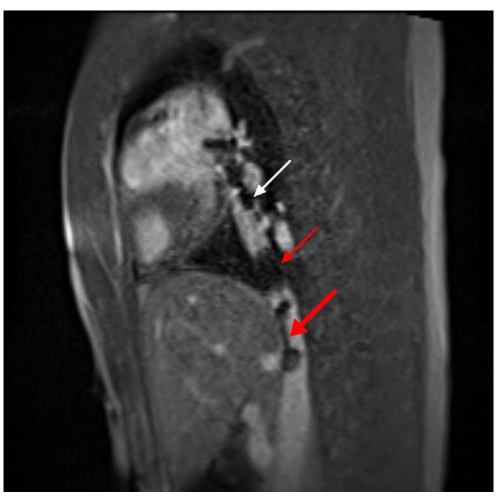

FIGURE 2 *CMR still frame showing platinum-iridium covered CP stent (red thin arrow) implanted in proximal IVC, causing significant artifact, and a 316L stainless steel 36 mm long Mega LD stent crimped on a 20 mm x 3 cm Z-Med balloon with 1 mm MagnaFy® MRI markers (stent edge cannot be distinguished from markers) (red thick arrow) over EmeryGlide® guidewire (white arrow shows EmeryGlide MR markers)*

Since these studies were performed, a low field scanner has become commercially available (0.55T MAGNETOM Free.Max MRI system, Siemens Healthineers, Erlangen, Germany), but it has limited gradient performance (maximum gradient amplitude 26 mT/m, maximum slew rate 45 mT/m/ms), which requires compromises in spatial resolution and frame rates. Stronger, faster gradient performance would come at a significantly higher cost due to the large 80 cm diameter bore of this system. The wide bore is ideal for patients with large body habitus and for adults and children who have claustrophobia and offers greater patient access for in-magnet procedures. The system is more affordable than high Tesla scanners, as it is less expensive to manufacture, transport, install, and operate. Susceptibility artifacts are reduced at lower field, and thus this system can provide improved imaging at the air-tissue boundaries like in the lungs and sinuses. Most importantly for interventionalists, it may be the breakthrough that is needed to allow MR-guided interventional procedures, because of the decreased RF-induced heating that can allow the use of standard equipment, improved access to the patient in the wider bore, and multiple simpler safety and maintenance features. With FDA approval of the MAGNETOM Free.Max and multiple installations around the world, there seems to be a renewed energy in ICMR by clinicians and industry alike, which was clearly visible during a live case at the Pediatric Interventional Cardiac Symposium (PICS) in Chicago in September 2022.[8] The current platform still needs considerable development, such as imaging techniques and pulse sequences required for cardiovascular imaging, but is expected to make the difference for interventional MRI in cardiology and interventional radiology.

Armstrong, Simonetti, and colleagues were the first to test the feasibility of performing R&LHC, inferior vena cava (IVC) angioplasty, and IVC stenting with real-time imaging in the 0.55T MAGNETOM Free.Max. While many types of standard catheterization equipment can be used safely at low field, they need to be made conspicuous, and this can be done by adding MR-visible markers to the standard equipment. Three different sizes of proprietary MagnaFy MR-visible markers (Nano4Imaging GmbH, Dusseldorf, Germany) were evaluated on Z-Med balloons (NuMED Inc., Hopkinton, NY) in nine juvenile Yorkshire pigs (62.4 ± 9.5 kg).[8]

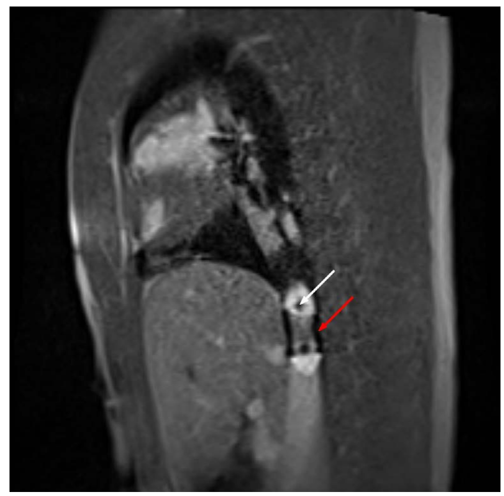

FIGURE 3 *CMR still frame showing 20 mm x 3 cm Z-Med balloon from Figure 2 inflated with 1% gadolinium provided with 1 mm MagnaFy® MRI markers (white arrow) well distinguished from implanted Mega LD stent (red arrow)*

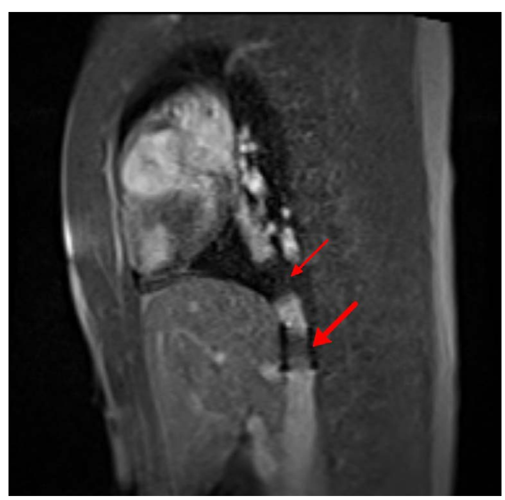

FIGURE 4 *CMR still frame showing implanted platinum-iridium stent with significant artifact (red thin arrow) and implanted 316L stainless steel Mega LD stent with good wall apposition demonstrated (red thick arrow)*

One of these cases was performed during a live case for PICS 2022. The pigs were under general anesthesia and had sheaths placed in the femoral vein and artery via cutdown. Arrow balloon wedge catheters (Teleflex, Wayne, PA) with CO2- or air-filled balloons were used for RHC, and Judkins Right catheters (Cook Medical, Bloomington, IN) were used for LHC. The 0.035" EmeryGlide® guidewires were used for both R&LHC. The first three pigs were imaged before and after infusing varying doses of ferumoxytol. Subsequent pigs were imaged after infusing 2 mg/kg ferumoxytol over 20 minutes to enhance blood pool signal and visualization of markers. Trade-offs between temporal and spatial resolution were investigated using the following spoiled gradient echo MRI sequences for real-time visualization of devices: high temporal resolution: 7 frames/sec, TE/TR = 2.8ms/6.0ms, Rate 3 GRAPPA, 3.5 x 3.5 x 10mm voxels; high spatial resolution: 2.2 frames/sec, TE/TR = 2.8ms/6.2ms, Rate 2 GRAPPA, 1.8 x 1.8 x 9.5mm voxels. In seven pigs, IVC angioplasty and/or stenting was performed using 20 mm x 3 cm Z-Med balloons with two MR markers of varying widths (0.25 mm, 0.5 mm, 1 mm) and 1% gadolinium in the balloon. Mega and Max LD 316L stainless steel stents (Medtronic, Dublin, Ireland) were deployed on Z-Med balloons, and a Covered Mounted CP stent (NuMED) was deployed in the IVC. In three of the stenting procedures, a custom-made 14French Flexor® sheath with proprietary markers on the tip of the dilator and sheath (Cook Medical) was used.

Yorkshire swine have known sensitivity to ferumoxytol; one pig expired during infusion, but catheterization was still performed. RHC was successful in all pigs with the balloon tip seen well in all MRI sequences **(Figure 1)**. LHC was attempted and successful in two pigs; the EmeryGlide guidewire entered the left ventricle retrograde easily. IVC angioplasty was attempted in four pigs and was successful in all. Implantation of seven stainless steel stents and one platinum-iridium stent was attempted and successful in all **(Figures 2 & 3)**. MagnaFy® MR markers were finetuned by different width and number of layers **(Figure 2 & 3)** on the Z-Med balloons. The 0.5 mm- and 1 mm-wide were more easily seen than 0.25 mm-wide markers. The platinum-iridium stent caused significant artifact, leading to inability to assess wall apposition **(Figure 4)**. The 316L stainless steel Mega and Max LD stents were seen well, however, before and after deployment, and wall apposition was assessed **(Figure 4).** Markers placed at the ends of the tapered tips of the balloons were more easily distinguished from the stent compared to the typical marker location on the shoulders of the balloons **(Figure 5)**. The markers on the Flexor® dilator and sheath were well seen in all cases and allowed proper placement of the sheath in relationship to the stent during implantation. Ferumoxytol 2 mg/kg led to superior imaging of all MR markers, balloons, and stents, compared to no contrast and to 1 mg/kg. Balancing spatial and temporal resolution for the anatomy and intervention was important. For IVC stenting, a higher resolution (144/192 matrix) lower frame rate (~5/2 fps) image yielded optimal visualization.

If low field MRI is going to be used for ICMR in the future, cardiovascular imaging needs optimization under the conditions of low signal-to-noise ratio and limited gradient performance. Fortunately, pre-clinical and clinical testing has demonstrated that a comprehensive CMR imaging protocol is feasible, including compressed-sensing 2D phase-contrast cine, dynamic contrast-enhanced imaging for myocardial perfusion, 3D MR angiography, and late gadolinium enhanced tissue characterization.[9]

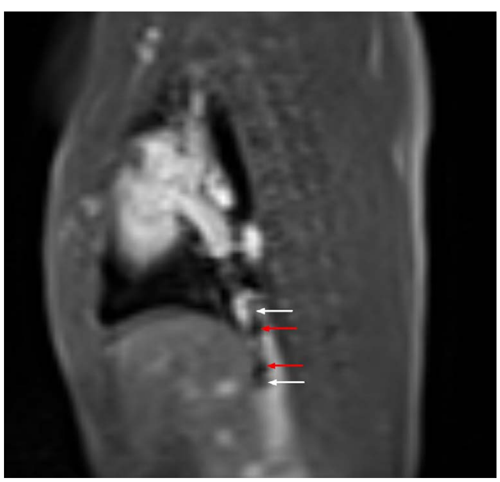

FIGURE 5 *CMR still frame showing 0.5 mm MagnaFy ®markers (white arrows) placed at the ends of the tapered tips of the 20 mm x 3 cm Z-Med balloon well distinguished from ends of crimped 26 mm long Mega LD stent (red arrows) compared to markers on the shoulders of the balloons, which are not well distinguished, seen in Figure 2*

The past 12 months have shown how a dedicated collaboration of clinical and industry partners is able to make big steps forward in bringing low-field MRI to the interventional space. The Ohio State University functioned as a field-lab to bring in devices and software from Siemens Healthineers, Nano4Imaging, Cook Medical, and NuMED to start performing the pre-clinical work necessary to bring interventional procedures with real-time MR-guidance to the bedside. Future studies will further optimize tools, software, and contrast to close the gap to routine clinical applications.

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