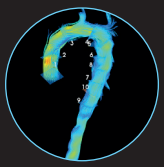
ISSUE #1

JANUARY 2024

NORTHH MEDICAL

BEATING HEARTS

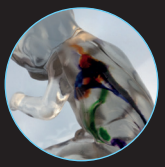
THE WORLD OF FETAL CARDIAC MRI



STATE OF THE ART

EXPERT INTERVIEWS

CLINICAL APPLICATION



FUTURE HIGHLIGHTS

WELCOME

Dear Friend of Fetal Cardiac MRI,

Welcome to our first edition of “Beating Hearts”, a pioneering magazine dedicated to the rapidly evolving field of fetal cardiac MRI (CMR). At Northh Medical, we believe in the power of innovation. With the development of *smart-sync*, we have dedicated our work to the prenatal diagnosis of congenital heart disease (CHD) using the MRI to enable the best possible decision making for further treatment. We are excited to launch this magazine as a platform to share, learn, and grow together with the global medical community.

In just two years, our journey with *smart-sync* has been nothing short of extraordinary. From a research concept to a diagnostic tool, our product has reached over 60 healthcare providers worldwide and starts to impact fetal care. This magazine aims to extend this impact by fostering a space for sharing knowledge, experiences, and the latest advancements in the field.

In this issue, you will find a rich tapestry of articles ranging from a summary of the first fetal CMR workshop and the newest developments. We delve into best practise approaches and bring you voices from the front lines – clinicians and researchers who are not only using *smart-sync* but also contributing to its evolution. Their stories are a testament to the collaborative spirit that drives progress in medical science.

As we look to the future, we are mindful of the rapid pace of technological advancement and its implications for medical practice and education. In the section “Future Application” we talk about new and developing approaches to further advance this field.

This magazine is not just about sharing information; it’s about building a community. We encourage you to engage with us, share your thoughts, and contribute to future editions. Your insights and experiences are invaluable in shaping the conversation around fetal cardiac MRI.

In closing, we want to express our gratitude to everyone who has been a part of this journey. Your trust in *smart-sync* and your commitment to innovation inspire us every day. Together, let’s continue to push the boundaries of what’s possible in fetal cardiac care.

Warm regards,
Your Northh Medical Team

CONTENT

STATUS OF FETAL CMR TODAY

Latest advancements open a new era in prenatal diagnosis.

Fetal CMR has emerged as a new tool in prenatal diagnostics, helping in understanding of fetal heart development and CHD.

The journey of fetal heart imaging began with conventional methods like ultrasound, which, despite their utility, has limitations especially in the third trimester. The advent of fetal MRI can help to overcome such limitations as the strength of fetal MRI is dominant at the third trimester due to less fetal motion and larger size of cardiac structures. Initially used for neurological assessments, MRI's application in cardiac imaging was a leap forward, driven by technological advances such as the introduction of *smart-sync* and post-processing methods that allowed detailed imaging of the complex fetal heart structure.

To measure the impact and development of fetal CMR can mainly be done by evaluating the current scientific literature. As Northh Medical we could see the development also by the increase of users, especially in the USA and Europe. The use of *smart-sync* increased within only two years to about 60 hospitals, the worldwide distribution is shown in *Figure 1*. We have also asked the users frequently if they perform fetal CMR for research, clinical application or both; the result is illustrated in *Figure 2*. It is very interesting to observe the increase in clinical use as it underlines the fast development of fetal CMR. Maybe one can say that the introduction of fetal CMR filled a critical gap in prenatal diagnostics, particularly for conditions challenging to diagnose through ultrasound and that this development is at its early stage.

The current capability of fetal CMR is showcased by recent publications in 2023[1-9]. These advancements emphasize that fetal CMR can have an impact on diagnosis and management of CHDs. Desmond et al. highlighted the integration of prenatal CMR in managing CHD, showing how it complements echocardiography, influences postnatal care strategies and how it can be integrated in the clinical pathway *(Figure 3)*[7]. Vollbrecht et al.'s study on Doppler US-gated fetal cardiac cine MRI further underscores the technology's diagnostic accuracy, comparing favorably with traditional echocardiography[8]. Minocha et al. provided valuable reference values for fetal cardiac dimensions, volumes, and function[9]. This work is an important advance, as establishing a range of normal structural and functional values allows more for effective diagnosis. It is particularly interesting as their results found a difference in volume compared to echocardiography by up to 48%. More studies are needed to understand these differences, but the results emphasize the potential impact of the MRI for quantitative measurements that can impact diagnosis. Moreover, a recent study by Dargahpour et al explored the utility of myocardial strain assessment for CHD[10]. They found a significant difference in strain parameters between fetuses with CHD and normal controls that indicates a new diagnostic approach to eval-

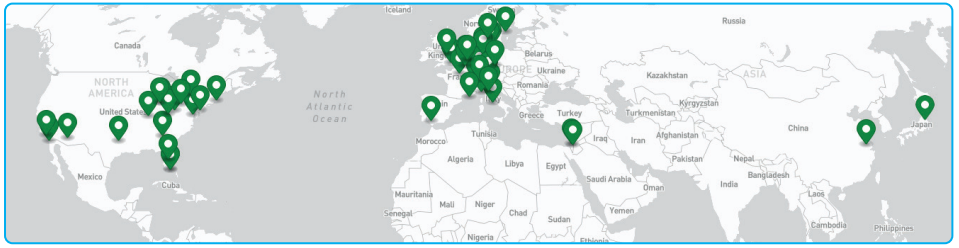


Figure 1: Worldwide distribution of hospitals performing fetal CMR with *smart-sync*.

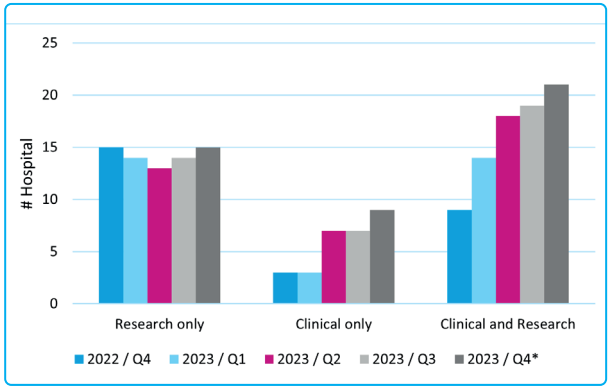


Figure 2: Overview of the temporal development of the clinical and/or research applicationof fetal CMR with *smart-sync*.
*The information of 8 hospitals is missing.

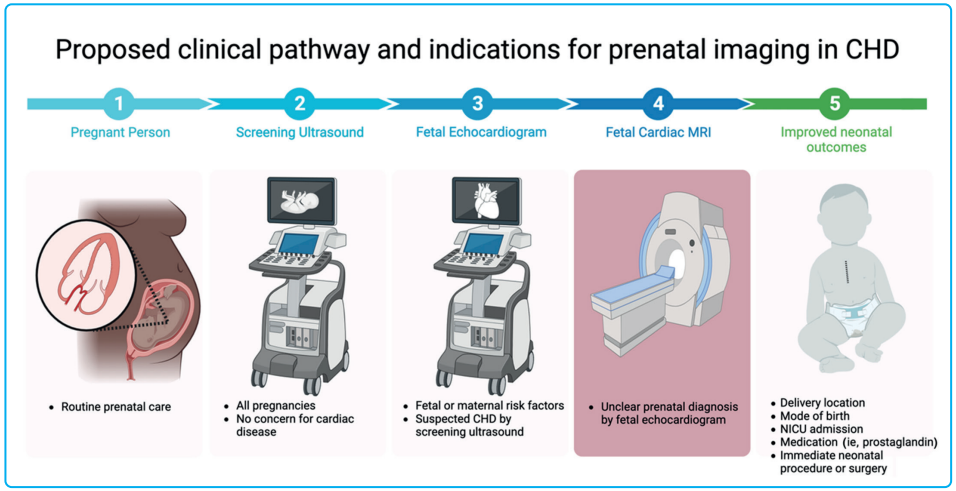
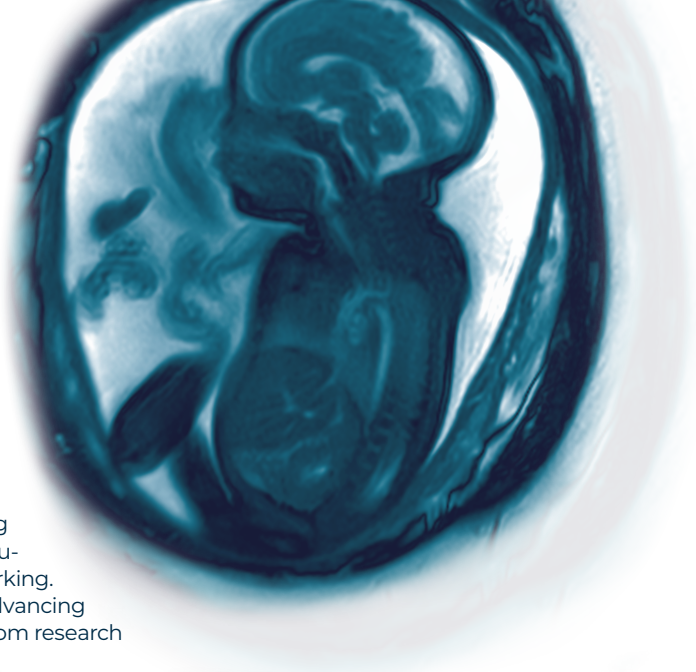


Figure 3: Proposed clinical pathway and indications for prenatal imaging in congenital heart disease. CHD indicates congenital heart disease; MRI, magnetic resonance imaging; and NICU, neonatal intensive care unit. Image from Desmond et al. [7]



uate fetal cardiac function. Based on the strength of the MRI for quantitative imaging one future direction of fetal CMR will be complementing fetal echocardiography with functional cardiac information that supports in decision making. However, more studies are needed, and it is essential to foster a common platform for exchange, develop standardized MRI protocols, enhance post-processing techniques, and provide mutual support and networking. These efforts are key to advancing the transition of fetal CMR from research to clinical application.

Despite its advancements, fetal CMR is not without challenges and further developments are urgently needed. The primary hurdle remains fetal movement and small structures that prevents fetal CMR to be adopted as a standard clinical tool. To overcome this limitation, it is essential to be able to correct fetal motion in post-processing steps and to acquire a reliable gating signal even in cases of large movements. It will be one of the key goals of Northh Medical to support this development and to ensure seamless image acquisition of exceptional quality, making the process of imaging the fetal heart with MRI straightforward and efficient for the technician responsible for data capture.

Do you want to stay up to date with the recent literature in the field of fetal CMR?
Then simply scan this code and check out the list of recent literature on the Northh Medical Homepage:

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BEST PRACTICE FOR FETAL CARDIAC MR IMAGING

Fetal CMR is a relatively new and challenging field without established guidelines on how to obtain high quality imaging. To bridge this gap, Northh Medical has developed an application guide. With this guide we aim to offer guidance from the use of *smart-sync* to the attainment of high-quality fetal CMR images. As input for the guide, we have summarized the feedback from over 60 customer sites worldwide.

The guide is divided into three parts, as indicated in *Figure 4*. While it provides tips and tricks for implementing *smart-sync*, the primary focus is on aiding with sequence planning and adaptation. Therefore, we also included MR vendor dependent acquisition information. You can view and download the guide directly here:

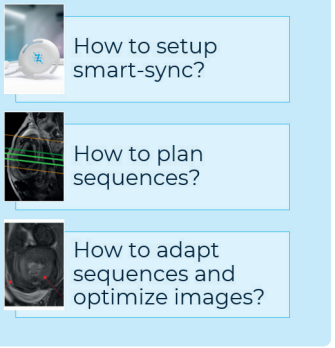


Figure 4: Structure of fetal CMR application guide.

- Visit **www.northh.de**
- Click on the **register icon** in the top right-hand corner
- Your registration **will be confirmed** by Northh Medical
- **Log in** and navigate to **"Customer support"**

2ND WEBINAR SERIES 2024

FETAL CARDIAC IMAGING USING MRI

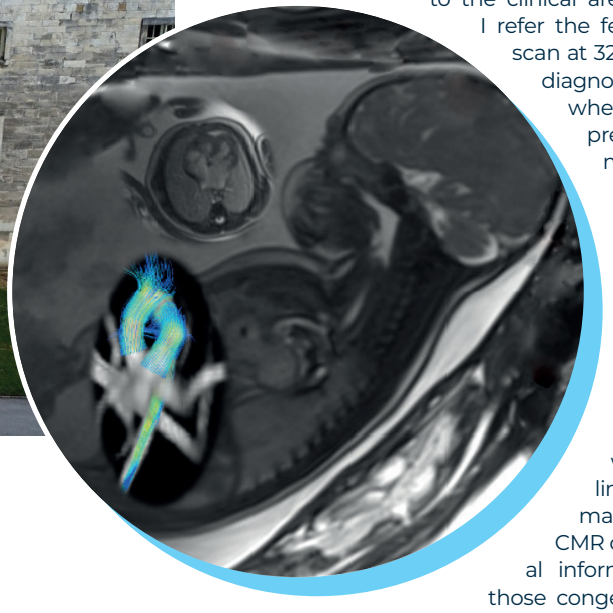
Due to the ongoing development in the world of fetal CMR and the growing community **Northh Medical is hosting the 2nd free educational webinar series** in which practical content for fetal CMR will be presented by experts in the field. Save the dates below and make sure you register right now.

1/10 | 3/20 | 6/12 | 9/18 | 12/11

A FREE one hour educational webinar

SCAN ME TO JOIN

https://www.northh.de/webinar-registration



1ST FETAL WORKSHOP IN HAZLEWOOD

A summary of the first face to face fetal CMR workshop written by Dr. Malenka M. Bissell

In July 2023, the Northh Medical team joined us at our 1st fetal workshop in York at Hazlewood castle, a quintessentially English affair with a themed pride and prejudice dinner. While the participants mingled to find out who the author lady Whistlewind was (the author didn't even suspect it himself), much discussion also focussed on the challenges in fetal CMR, and there are plenty.

Some are a specific wish list for Northh Medical, and overall, most requests were quite realistic (and some are already in progress). A larger transducer, ideally flexible with a large enough area to cover a moving fetus (in early gestation) was the most frequent request, closely followed by having a wireless option. Though we all agreed, our ultimate wish is to have the transducer built into the coil itself (but that would require us to agree what the ideal fetal coil is, which is a separate discussion entirely). Other wishes are already around the corner such has having unlimited injected triggers, identifying which triggers are true and which are artificial triggers, real time monitoring and exporting of the data. A higher depth sensor is important to those countries with growing obesity rates.

We all agreed that additional motion correction is often still necessary even with the DUS device, and having packaged sequences and post-processing tools would make application in purely clinical centres much easier (and Northh Medical have listened and are already working on simplifying the black blood motion correction pipeline).

Apart from the most obvious challenge – the moving fetus – clinicians face a number of other challenges when moving fetal CMR to the clinical arena. "So, why would I refer the fetus for a fetal CMR scan at 32-36 weeks when the diagnosis and decision on whether to continue the pregnancy was already made weeks ago?" is the most commonly asked question, and the answer is not straight forward. Fetal CMR is not a primary diagnostic tool but an adjunct to fetal echocardiography. In late gestation when views are more limited especially in maternal obesity, fetal CMR can provide additional information especially in those congenital heart diseases that can show progression throughout the pregnancy. This includes borderline left ventricles, Coarctation of the aorta and the assessment for restricted septum in transposition of the great arteries. The room was divided whether fetal CMR's strengths lie in the intra-cardiac or extra-cardiac structures, but all agreed that it was superior to fetal ultrasound when assessing lung volumes and pathologies such as nutmeg lung pattern in hypoplastic left heart syndrome.

Though, is the lung still within the remit of the fetal CMR scan or does this fall within the expertise of the fetal radiologist? This highlights the next big challenge: buy in from a number of crucial stake holders. In most centres fetal CMRs are read by either a fetal cardiologist with fetal CMR experience or a paediatric cardiologist with CMR expertise. Therefore, dual reporting with a fetal

Figure 5: The participants of the 1st fetal cardiac MRI workshop in York at Hazlewood Castle.

radiologist who assesses all other organs which more or less deliberately get imaged during fetal CMR scanning (especially when doing fetal volumetric assessments), is paramount. This is also the go to person with incidental findings. In addition to radiology, fetal cardiology or fetomaternal medicine as the referring team also need to be on board (and refer the patients). Building confidence in a new diagnostic tool takes time, and one of the earliest tangible benefits for the referring team is often the additional images available for parental counselling around delivery planning. And so – hopefully – over time a clinical demand establishes.

This is met with additional challenges:

- Finding time on the MRI scanner when – at least initially – reimbursement is not available and upfront costs for equipment are high. Some centres overcome this with research grants and/or charitable funding.
- Training staff – initial throughput will be slow, so having a small, dedicated team is advisable, but ultimately this team needs to grow to a size that can support the continuous running of a clinical service (and absorb annual leave and other absences).
- Necessary validation and CE /FDA clearance for sequences and post-processing can provide additional unique challenges.

So how did other centres successfully manage the step into clinical practice?

Patience and persistence are key. Detailed feedback to the referrer helps to involve stakeholders. Furthermore, a two-way conversation is key: "What is it that the referrer is really interested in?" is the most important question. Not all colleagues will be early adopters, often only one or two key "champions" within the team will become these early adopters and help drive the clinical implementation.

And getting good at fetal scanning takes time. Many centres have started by adding a few fetal cardiac sequences to their fetal brain MRIs. Other centres trained and optimised sequences with healthy volunteer participants. Fetal lung imaging is an easier way to get started, as non-gated sequences can be used. Analysis pipelines should ideally be automated and the analysis software user-friendly.

And once all of this is set up and running smoothly, the last top tip is making sure there is a centralised coordinated booking service in place so that fetal echo and CMR can be booked on the same day.

You might wonder: Is it really worth all this effort?

And the answer is yes, because once you found the perfect soundtrack to calm the dancing fetus, you will have unboxed the power of postnatal CMR in fetal life and add a little more certainty to one of the most important questions in late gestation fetal cardiology: "Will this baby be in trouble in the delivery room?".

UNITED STATES UNIQUE CPT CODE FOR FETAL CARDIAC MRI

As fetal CMR becomes more widely used and accessible, the billing structure will need to keep pace. In the US, this would involve creation of a unique CPT code for fetal CMR. This code would recognize fetal CMR as a distinct procedure which utilizes unique acquisition methods (DUS gating) and unique expertise (fetal cardiology). US Groups wishing to assist with this effort can contact Dr Schuchardt at ***ESchuchardt@health.ucsd.edu***

WHAT DO THE EXPERTS SAY?

We have talked to four outstanding experts, those who perform fetal CMR already for a long period of time.

What is your motivation to perform fetal CMR today?

Malenka: Cardiac MRI is a valuable tool for the diagnosis and management of patients with CHD throughout their lifespan, but its application in fetal life has so far been limited. Fetal CMR has the potential to provide crucial and complementary information in some cases of fetal CHD. Pregnancies complicated by fetal CHD are challenging for parents due to the persistent uncertainty about the prognosis and treatment options. Fetal CMR can assist in reducing this uncertainty and in predicting the postnatal outcomes and need for surgical interventions for the affected fetuses, thus offering significant benefits for parents and our future patients.

David: Our primary motivation has always been to understand the value that fetal CMR can bring to patients with fetal CHD. I see this value not just in terms of improving clinical diagnosis, but also in furthering our understanding of the effects (and even causes) of CHD in the context of the fetal circulation. Our service and approach have continually evolved to meet these needs, and I'm very proud of how much we have achieved so far. I'm sure there will also be much more to learn in the future!

Alex: Our ultimate motivation for researching fetal CMR is to enhance the care of our fetal patients with suspected CHD. While our focus is on improving patient care, we are also keenly interested in developing and exploring the technology's potential to extend beyond fetal applications.

How does fetal CMR fit into your clinical workflow?

Malenka: Our fetal cardiologist usually refer for fetal CMR after the 28 week check up. For the final monitoring visit at around 32-34 weeks, we streamline the process for our patients, many of whom travel long distances, by scheduling a joint fetal clinic and fetal CMR appointment. This helps ensure efficient care.

Following the fetal CMR, we promptly send a clinical report back to the referring clinician.

While most of the time, fetal CMR results align closely with echo results, if there are significant different findings, our fetal cardiology team arranges an additional appointment to discuss it with the patient. We have a clear protocol in place to address such cases.

"The most rewarding thing about doing fetal CMR is to have the privilege to show our parents to be - who often really have a tough pregnancy - their baby on the screen and sending them a 3D reconstruction of their unborn baby. It brings some happiness and bonding and reminds parents that they are about to bring new life into the world. It's not just a heart problem, there's a real baby behind it."

What is your procedure in terms of referrals?

David: As a result of our early experiences with fetal CMR, particularly the engagement and support from our clinical colleagues in fetal cardiology, we were able to start a clinical fetal CMR service in 2019. This means our patients can now effectively be referred for fetal CMR as they would for any other imaging investigation. We are fortunate to have experienced clinical (Evelina London Children's Hospital) and research (King's College London) teams co-located on the same site St Thomas' Hospital, and in practice

Malenka Bissell, M.D.,
Pediatric Cardiologist
at Leeds teaching hospitals and clinical lecturer at University of Leeds

Use of *smart-sync* since summer 2021

a lot of the administration of the scans is still split between both. The vast majority of our clinical patients consent for research at the time of their MRI which really supports the ongoing development of the programme. Of course, running the programme as a clinical service means we also need robust processes for data management, reporting, managing incidental findings etc. This has taken a lot of time and effort to put in place, but works pretty seamlessly now.

Alex: In the early days it was crucial to build trust and closely involve our maternal-fetal care team in our development process. My colleague Dr. Lorna Browne, a pediatric radiologist, took the initiative to personally discuss each case with the maternal-fetal care team, particularly the fetal cardiologists, surgeons and obstetricians. This involved extra effort when we were starting up to share and educate the team on what the capabilities of the technology were. As a result, there has been an increase in referrals for both research exams (to

explore diagnostic capability under IRB approval) and to integrate the cardiac examination into clinically-indicated standard fetal MRIs for diagnostic insight. We've reached a point where we are no longer actively seeking referrals; instead, colleagues are referring patients to us.

How did the cooperation between the teams (gyn, card, rad) change since you apply fetal CMR?

Eleanor: There is a strong collaboration between the teams, with perinatologists and cardiologists conducting monthly case reviews together. The determination of specific objectives for each scan is a collective discussion, but the final decisions are ultimately made by me.

Malenka: I now collaborate much more closely with my radiology colleagues compared to before, primarily because our fetal CMR also generate a fetal body report. This has led to significantly increased communication and collaboration with the radiology department compared to the past.

David: Since the beginning of our programme we have consistently maintained a strong partnership with our clinical colleagues in fetal cardiology. This means working together to establish what needs they have in terms of cardiac imaging, and developing sequences and post-processing methods to complement those needs. In practice this often means engaging proactively with the referring clinicians, for example via one-on-one discussions where we can present and discuss imaging results directly, participating in multi-disciplinary meetings, and engaging with other specialities involved with patient care.

It's important to remember that just because we are imaging the fetal heart we still have to consider broader health needs of the patient and their unborn baby. In my view, it's essential when embarking on a clinical fetal CMR program to establish strong connections with professionals involved in maternal care – for example fetal medicine, obstetrics, radiology – who can assist in interpreting imaging data related from the mother as well as the fetal cardiac brain, body, and lungs.

From the reporting perspective, our fetal CMR team generate a cardiac report while radiology colleagues formally assess and report the fetal brain and body. We have robust local protocols both for dissementing these reports and for handling maternal or fetal incidental findings, all of which have been agreed with the relevant specialists locally.

Alex: The process involved building trust, learning how to collaborate effectively and fostering relationships for easy communication. We made sure to advertise our capabilities, even though there's no formal structure currently in place.

Dr. Browne and Dr. Richard Friesen were and are integral members of our family meetings, where the care implications of a suspected or confirmed diagnosis are discussed with the family members. This is also where the care team has seen the capabilities of this new technology.

> *"smart-sync has proven to be a really valuable tool acquiring gated sequences, such as phase-contrast flows."*

For other sites or hospitals looking to start a similar initiative, the key is to take the plunge and start the process. It will be a lengthy journey to identify key stakeholders in multiple departments who believe in the approach. Having invested experts within those departments is crucial; it's not just about doing the imaging, but also a commitment to demonstrating value of the approach to the care team.

Did fetal CMR change your diagnostic impact? And how?

David F. A. Lloyd, MBChB MRCPCH PhD,

Paediatric and Fetal Cardiology at Evelina London Children's Hospital and Senior Research Fellow at King's College London

David has been doing research on fetal CMR since 2015. He has gained lots of experience with the motion correction technology and has already integrated that tool into clinical practice at St Thomas' Hospital in London. In this interview he told us about his experience with fetal CMR and some the advantages brought by using *smart-sync*.

Between 3-4 scans/week

Malenka: In cases involving Transposition of the Great Arteries (TGAs), fetal CMR can help to confirm or strengthen the suspicion of a restrictive atrial septum. There was for example a specific case where the atrial septal flow looked sufficient on echocardiography, but fetal CMR indicated a high suspicion of restriction, and indeed, saturations post-delivery were critically low and the baby required emergency septostomy. In other, especially complex cases, fetal CMR can serve as a valuable piece in the diagnosis puzzle, offering additional certainty and contributing to the diagnostic process.

David: Yes, absolutely! Congenital heart disease represents a wide range of conditions, so naturally fetal CMR will also have a range of impacts depending on the underlying diagnosis. But yes we have certainly seen many cases where fetal CMR has unequivocally identified associated features in a fetus – cardiac or extra-cardiac – that have had an important impact on counseling and the overall management of the patient. We have also had cases where we have detected less severe (but still important) incidental findings, or simply served to confirm the accuracy of initial impressions from fetal echocardiography. I think fetal CMR can serves an important role in all of these scenarios.

Alex: When prioritizing congenital heart disease indications, we particularly focus on Coarctation of the Aorta (CoA) as it has significant implications for delivery planning and postnatal care.

By combining structural information with 4D flow CMR analysis, we feel we have built up enough (soon to be published) evidence to improve the rate of true positives and false positives in cases of suspected CoA. This has had an impact on the diagnostic confidence among the care team for these patients. Of course, this is all saidwith the caveat that it is still very early days and all cases

Eleanor Lehnert Schuchardt, M. D.,
Cardiologist
at Rady Children's Hospital,
San Diego, USA

require a holistic approach in which fetal CMR is only one part of the puzzle.

Beyond our efforts with CoA, a particularly memorable case was a large pericardial teratoma that contributed to 5% of the baby's overall weight. Using dynamic fetal CMR images, we were better able to delineate how much of the tumor was compressing the heart. This is important because it helped inform whether to perform something called the Ex-utero intrapartum (EXIT) procedure. This is a very invasive procedure in which the baby is partially delivered to operate on it, all while maintaining a connection to the placenta. After review of the fetal CMR results it was decided that the tumor did not severely compress the heart and that information, combined with echo, directly impacted the care of the patient, where it was decided to delay the procedure because the tumor was not severely limiting the function of the heart.

Have the therapy options changed since the application of fetal CMR?

"I love taking care of fetal patients and using all available tools to guide expectations through the perinatal period."

Alex: Yes, but it's crucial to reemphasize that our approach is holistic, which means that we don't rely solely on one piece of information to guide patient care. Instead, all available data is taken into consideration, including CMR, ultrasound, echo, and more, to make well-informed decisions. This comprehensive approach informs surgical planning, enhancing our confidence in deciding whether to perform invasive procedures, plan postnatal care, or simply monitor with 'watchful waiting'.

How did you manage to get the examinations reimbursed (in case you get it at all)?

Eleanor: We currently need prior authorization for cases, but our team has not encountered denials so far. After completing the exam and ensuring it meets billable quality standards, we use fetal MRI CPT codes (74712 for singleton pregnancies). Looking ahead, I have plans to seek the creation of a new CPT Code within the U.S. medical system specifically for billing clinical fetal CMRs. This new code would enable cardiologists to receive separate payment for fetal CMRs, distinguishing them from fetal CMRs of the brain and body, similar to the distinction between hest MRI and traditional CMR procedures.

Alex: We don't receive reimbursement for fetal CMR; we conduct it primarily for research purposes. Sometimes, we're asked to include cases for research studies which have potential to impact care; we have IRB approval to investigate the potential diagnostic potential of this technology, thus we include these cases for research and are approved to share our imaging findings with the care team.

In terms of potential reimbursement, we believe our current approach indirectly benefits us during the research translation process. Doctors may choose to refer a pregnant mother for an MRI primarily to gather brain or lung-related information. But the potential for an added fetal CMR may play a role in some of the referral decisions where insurance will reimburse a non-cardiac MRI. This may contribute to MRI referral volumes, but also allows us to incorporate research into the care of these patients in the form of IRB-approved add-on exams.

What do you believe will be the future application of fetal CMR?

Malenka: Fetal CMR becomes particularly valuable in the later stages of gestation, especially in complex cases where 3D reconstruction is beneficial. It proves especially useful in cases where hemodynamic measurements are of use, such as coarctation and TGA, or severe AV valve regurgitation. Additionally, it offers insights into lung volumes and lung pathologies, evaluating the lung-cardiac interface.

David: Big question! In the short term, we still lack a clear consensus on how fetal CMR will be deployed clinically, as existing methods mature and more people globally gain access to it. We have scanned over 700 patients in our service, and so are confident that fetal CMR can be effective, add to clinician confidence and improve patient care – but it is critical that this can also be demonstrated more widely. I think it's crucial to observe what other centers are doing and collaborate with each other to understand how fetal CMR functions in different settings. Building a consensus on its usage, identifying scenarios where it can be beneficial, and understanding its potential impact across different fetal medicine and cardiology centres should be the next steps.

In the longer term, I see huge potential for fetal CMR in reshaping our understanding of the maternal-fetal-placental circulation. There is still so much we don't understand about the development of CHD – particularly difficult lesions such as coarctation of the aorta - and how CHD interacts with other organ systems such as the placenta and the developing fetal brain. I think fetal CMR could also have applications in other settings, such as placental insufficiency, twin pregnancies – the list is endless. It's a really exciting field to be involved in!

Alex: We're actively working on improving 4D flow CMR techniques, although we currently face limitations related to spatial-temporal resolution. Collaborating with Drs. Pim van Ooij, PhD and Eric Schrauben, PhD in Amsterdam, we're exploring motion-corrected strategies to enhance the quantitative hemodynamic information we can obtain.

While we've made significant progress in obtaining high-quality structural images, we recognize the immense value of functional information, especially given MRI's ability to provide multiple contrast mechanisms. If we can overcome motion-related challenges and speed up our imaging processes, we anticipate exciting possibilities in functional assessments, including areas like oxygenation and 2D/4D flow analysis. Additionally, I am excited to apply these advancements to our complex pediatric cases where gating has been challenging in the past.

Eleanor: It is my hope that fetal CMR will become a robust tool to help resolve uncertainty in individual cases, for both the expectant family and for medical providers who care for some of the most critically ill infants. I believe the modality could be useful beyond structural CHD – to study hydrops, fetal growth restriction, TTTS, CDH, and more.

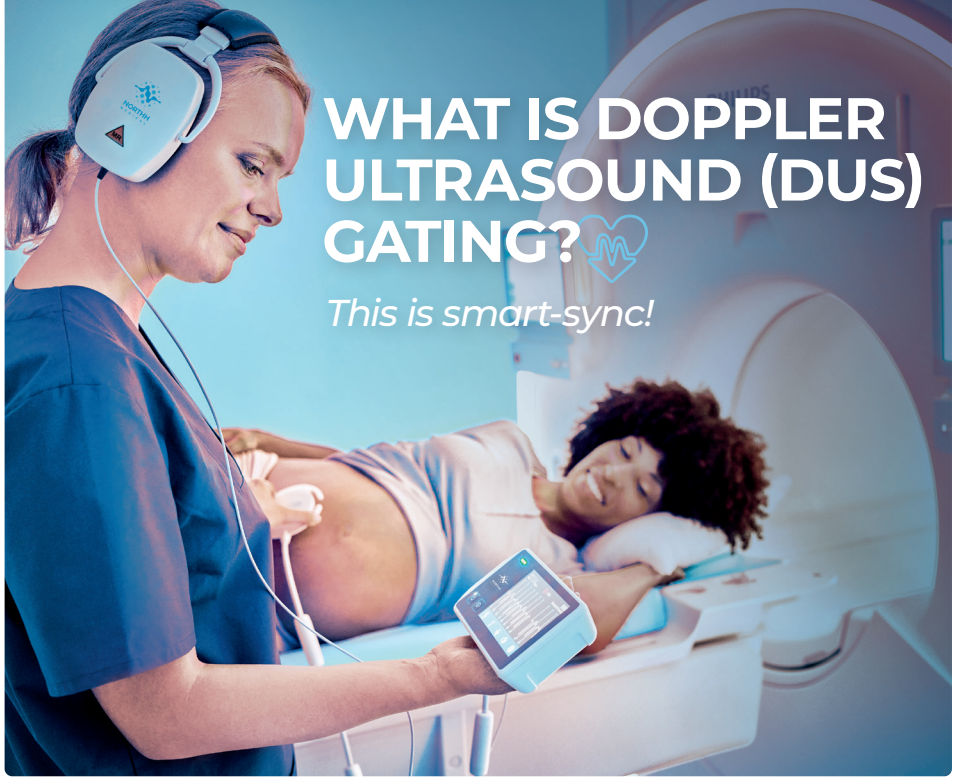
What has changed when using smart-sync in comparison to use metric optimized gating (MOG)?

David: *smart-sync* has proven to be a really valuable tool acquiring gated sequences, such as phase-contrast flows. The fact that we can have a real-time gating signal at the time of the scan allows us much more flexibility to use "off-the-shelf" sequences, and removes the need for extensive post-processing associated with retrospective gating methods. Having gated sequences allows us to make a better assessment of image quality "on-scanner", as we no longer have gating artefacts which could be interpreted as fetal motion. We are also exploring the option combining the *smart-sync* with motion correction to generate time-resolved 3D sequences, which is another direction we are really excited about.

Alexander Barker, PhD,
Associate Professor Radiology at University of Colorado

Alex started using the *smart-sync* prototype as early as 2018. Today he and his team perform about 1-2 scans/week.

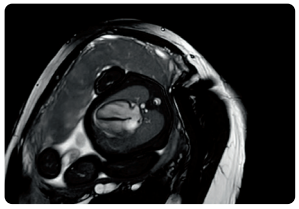
"Our collaboration started rather fortuitously in 2018 at the ISMRM in Paris when Fabian mentioned he is commercializing the device and "[We] should use the device". I happened to have some surplus funding to support the effort and that is how the journey has started. Back in the hospital everybody was asking why? "Echo is good enough", It was really considered some off the wall stuff until Dr. Browne started showing the maternal fetal medicine team our results."



Integrates easily in your clinical workflow

smart-sync detects cardiac motion and synchronizes the fetal cardiac cycle with the MR image acquisition. In that way, fetal CMR becomes possible and can be used for anatomical and functional imaging. The quick setup in less than three minutes requires no special training. *smart-sync* utilizes standard cardiac MR sequences, being a plug and play solution that can be easily incorporated in your daily workflow. Its clinical utility is proven: *smart-sync* helps with delivery planning, organization of early postnatal care and provides valuable information for parental counseling.

Assisting on all levels



Physicians gain greater diagnostic confidence through crisp images, enabling effective counseling and thorough delivery planning.

Parents are reassured with a better grasp of the diagnosis thanks to more understandable imaging.

Working with one of a kind MR technology allowing you to stand out as a pioneer in prenatal diagnostic.

UPCOMING HIGHLIGHTS AND NEW APPLICATIONS

An insight into the new and developing approaches to further advance the field of fetal CMR.

In the coming year, we're expecting some exciting developments in fetal CMR. There are of course several topics that need to be addressed when thinking about the future. This includes improvements of *smart-sync*, important clinical findings how fetal CMR can impact treatment and care and of course new applications that are needed to bring fetal CMR to the next level. We as Northh Medical are continuously working on every front of this topic and are eager to contribute to the further development of fetal CMR.

Thinking about further improvement of *smart-sync* for the next year, we will release a new software update in 2024 that will improve the reliability of the gating signal especially in cases of an anterior placenta, high BMI patients and in cases where the fetal heart is very close to the transducer.

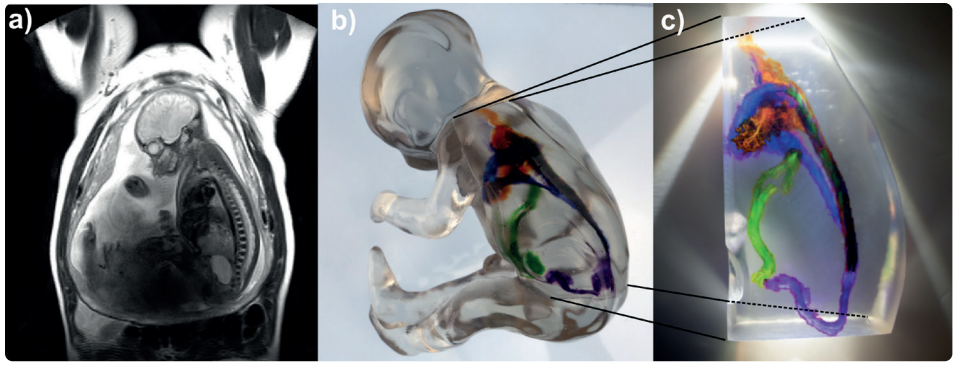


Figure 6: a) T2 weighted single shot fast spin echo localizers were used to obtain the fetal volume and b) 4D flow MRI was fused with the 3D volume. A 3D printed insert c) was created to minimize the optical distortion of the 4D flow MRI data.

In cooperation with the Childrens Hospital Colorado and Alexander Barker we are also working on increasing the acoustic window of the ultrasound transducer. This will enable a gating signal even in cases of larger fetal movement.

Until today, an amazing increase and presence of fetal CMR on conferences and publications has been observed. We anticipate this trend to continue in 2024 and we are more than curious on the results. With the increasing application of fetal CMR by the best specialists in the world we also anticipate advancements not solely in the realm of anatomical imaging, but also in the burgeoning area of fetal cardiac functional assessment. The refinement of imaging sequences, specifically tailored to meet the precise needs of paediatric radiologists and cardiologists, is expected. Moreover, enhancements in data acquisition acceleration and the improvements of techniques for motion artifact correction are anticipated. Additionally, advancements in flow imaging will facilitate a deeper understanding of specific complex CHD cases and possible outcome. This comprehensive understanding is an important objective in the context of ongoing progress in fetal cardiac diagnostics and therapeutic interventions.

One of the most important developments that is needed to establish fetal CMR in clinical care is to overcome fetal motion and to provide additional value to the already powerful fetal echocardiography. In this issue we are focusing on the development of 4D Flow and 3D postprocessing.

To provide an insight into the current state of fetal 4D flow imaging, a patient specific 3D print of a 33-week gestational age fetus combined with 4D flow MRI is shown in *Figure 6*. The greater vessels illustrate unique features of the fetal cardiovascular system and mixing patterns. For example, left heart flow is shown in orange (left atrium, left ventricle, aorta), right heart flow is shown in purple (right atrium, right ventricle, pulmonary artery, ductus arteriosus), and umbilical vein flow is shown in green. The data was acquired at the Children's Hospital Colorado and the University of Colorado Denver, Anshutz Medical Campus (postprocessing and 3D printing by Takashi Fujiwara, Conor Brady, and Nick Jacobson) where the group around Alex Barker is using 4D flow to calculate flow ratios between vessels in order to predict i.e. cases of aortic coarctation.

Building on this methodology, Dr. Pim van Ooij and his 4D Flow group at UMC Amsterdam have started their *FetalFlow* project end of 2023 in cooperation with

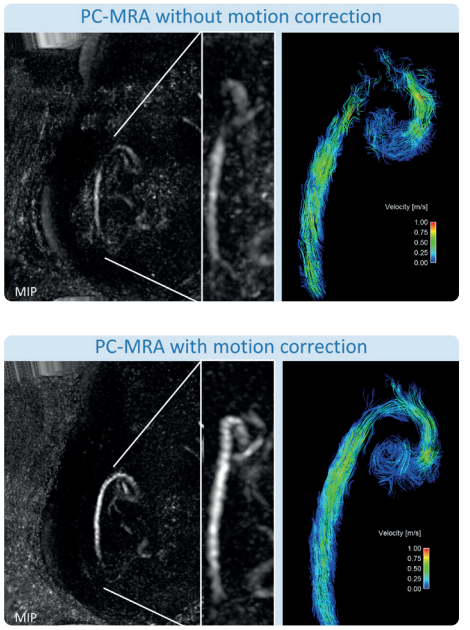


Figure 7: Fetal blood flow from the left heart to the descending aorta, shown in maximum intensity projections in the sagittal direction (left) and magnified inserts in the coronal direction (middle) of phase contrast magnetic resonance angiography (PC-MRA) images generated through 4D flow acquisition, with corresponding streamline visualizations (right). Motion compensated images have been corrected for maternal respiration and fetal bulk motion.

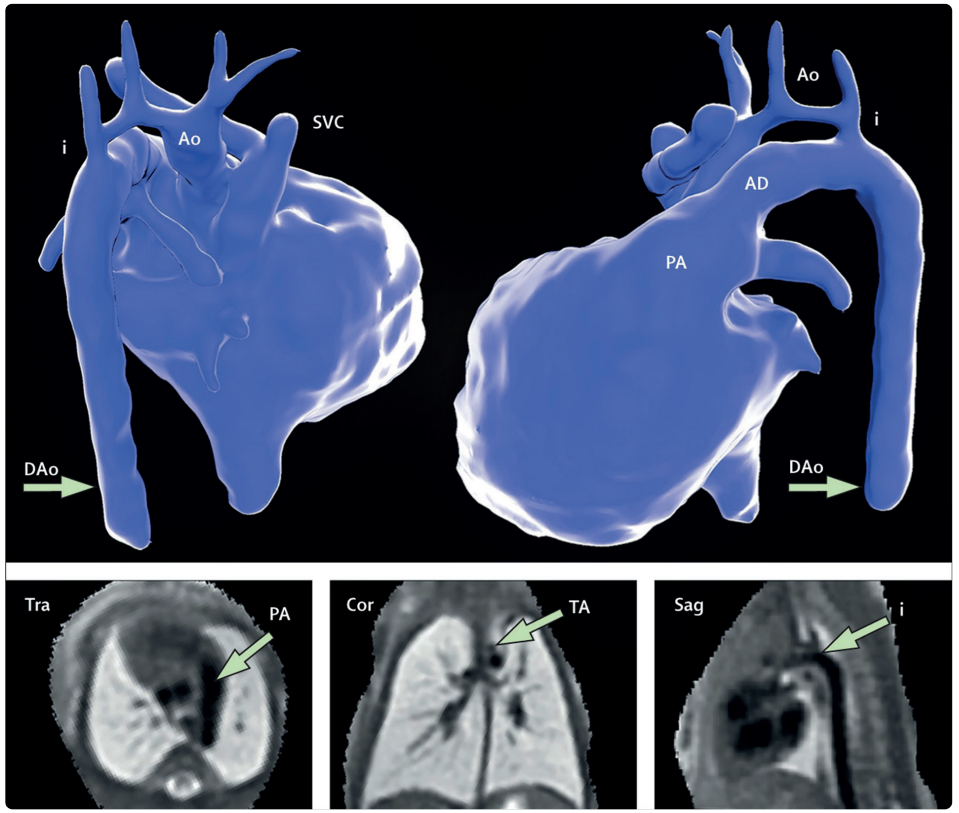


Figure 8: Segmentation of motion-corrected MRI data of a fetus with suspected coarctation of the aorta at 33 weeks' gestation. Posterior projection (top left) and left lateral projection (top right) are shown. The aorta (Ao), arterial duct (AD),descending aorta (DAo), aortic isthmus (i), and superior vena cava (SVC) are labelled. Coarctation was confirmed after birth and treated surgically. The bottom panel shows planes from the reconstructed 3D dataset in a transverse (Tra), coronal (Cor), and sagittal (Sag) orientation. See video 2 for more detail. TA=transverse arch. PA=pulmonary artery. Figure from Lloyd et al.[11]

Northh Medical. Their main objective is to employ advanced techniques such as 4D-Flow phase contrast, 3D Cine, and black blood imaging, enabling a detailed view of fetal cardiac flow dynamics and anatomy. Novel imaging technology will be developed to overcome motion artifacts caused by maternal respiration and fetal movements, compare *Figure 7*. Utilizing the *smart-sync* device to assess fetal cardiac motion, they aim to synchronize imaging sequences for precise motion compensation. To help with that, Northh Medical has developed a data logging function that allows the acquisition of fetal movement in real time. *FetalFlow* aims to redefine fetal health assessments through cutting-edge imaging innovations.

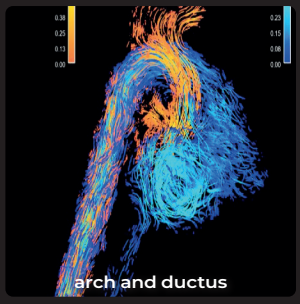
The use of *smart-sync* allows acquisition of intracardiac information and cardiac function, but it does not allow motion compensation or a 3D visualisation of the extracardiac vessels. However, extracardiac vessels are often necessary to visualize, especially in 3D, for a full understanding of the pathology. As the best possible prenatal diagnosis is the driver for the work of Northh Medical, we have decided to develop a post-processing tool based on the method developed at Kings College London and published by David Lyod et al. in the Lancet[11]. This method is based on a "slice to volume" reconstruction were several 2D single shot black blood images are used together with a motion compensation algorithm to calculate an isotropic high resolution 3D data set of the fetal heart. This data set can then be used to visualize the extracardiac vessels in 3D. One example is shown in *Figure 8* that illustrates the use of this post-processing tool.

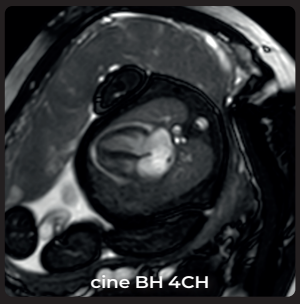
We are happy to share the news that we already have developed a first beta version of this software and are currently testing it. We have simplified the workflow whereas the software only uses DICOM images as input. After a processing time of 10-20min the user will get an email notification that the motion compensated 3D dataset is ready to be downloaded. If you are interested to use this tool, please reach out to Dr. Fabian Kording at ***fk@northh.de.***

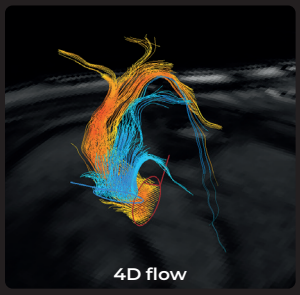
REFERENCE

11. Lloyd et al., „Three-Dimensional Visualisation of the Fetal Heart Using Prenatal MRI with Motion-Corrected Slice-Volume Registration".

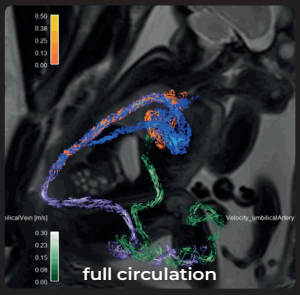

T2 loc sag


arch and ductus

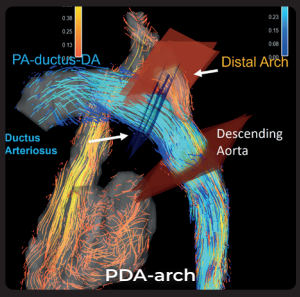

cine BH 4CH


4D flow


T2 loc ax


full circulation


maternal cor localizer



PDA-arch


fetus sag


maternal sag localizer


arch-ductus posterior 3D


smart-sync positioning

Northh Medical GmbH
Röntgenstraße 24
22335 Hamburg
www.northh.de / info@northh.de