## Fetal CMR Today and in the Future

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### Benefits of fetal CMR1 today

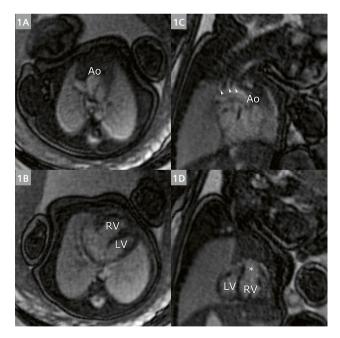
Approximately 1% of neonates are affected by congenital heart defects [1]. Even though prenatal diagnosis has improved, it needs to be further perfected in order to reduce morbidity and mortality [2]. Fetal echocardiography is widely available and plays the main role in enhanced prenatal diagnosis. Ultrasound image quality nowadays is exceptional compared to a decade ago. However, diagnosis based on ultrasound is still limited as it is highly operator-dependent and may be particularly challenging in late pregnancy or in maternal obesity [3, 4].

Fetal magnetic resonance imaging has been used for almost 40 years, mainly for diagnosing fetal thoracic, abdominal, and brain malformations. This is mostly achieved using static anatomical images. Dedicated fetal cardiovascular magnetic resonance (CMR) was performed at only a few centers worldwide 5–10 years ago. Nowadays, approximately 30 centers are running or setting up fetal CMR as part of their clinical service and research. Static balanced steady-state free precession (bSSFP) images (Fig. 1) are more than sufficient to depict anatomy. Early real-time acquisitions depicted fetal cardiac systolic function, but the spatial resolution was too low to clearly portray detailed fetal cardiac anatomy or regional function (Fig. 2A).

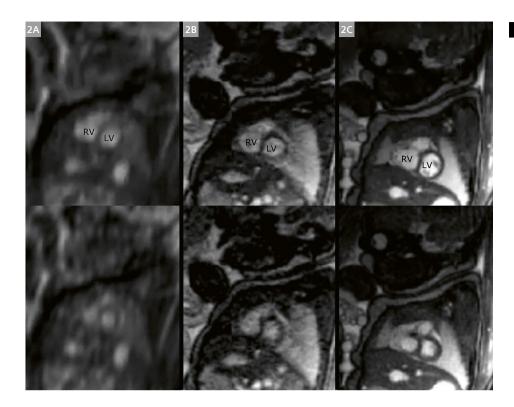
Dynamic fetal CMR took off with the introduction of the metric optimized gating (MOG) postprocessing method for phase-contrast CMR flow measurements [5], which was also applied for fetal cardiac cine imaging (Fig. 2B) [6]. This method introduced sufficient temporal and spatial resolution to study the fetal heart in detail using CMR, and overcame the lack of fetal cardiac gating.

Self-gated postprocessing methods, such as 2D iGRASP (Fig. 2C) [7–9], have since been introduced and used to assess fetal cardiac malformations, along with methods with shorter acquisition times and greater tolerance to fetal motion [10–12]. These methods rely on computationally demanding postprocessing, and currently images are not immediately visualized on the scanner, which

limits the information available directly after the fetal CMR examination. Image reconstruction time depends on local setup and engineering expertise. It is therefore crucial to have local pipelines or faster postprocessing methods in place so that images can be reconstructed soon after data acquisition is complete. On a positive note, imaging sequences and postprocessing methods are quite openly shared and there is a growing community that supports making fetal CMR available for routine patient scans.



1 Static balanced steady-state free precession images of a fetal heart at gestational week 33 with transposition of the great arteries (TGA). Transversal images (1A, B) show the left (LV) and right ventricles (RV) with the aorta (Ao) coming from the right ventricle. Sagittal images (1C, D) correspondingly show the left and right ventricles with the aortic outflow tract (\*) from the right ventricle, aortic arch, and normal aortic arch vessels (white arrowheads).



A short-axis basal slice in diastole (top row) and systole (bottom row) showing images acquired using a real-time sequence (2A), metric optimized gating (MOG, 2B) [6], and original 2D iGRASP (2C) [7]. Note the higher spatial resolution with MOG and iGRASP compared to the real-time images. A movie showing the three methods side-by-side was published as supplemental material to Haris et al. [7].

The next leap in improving dedicated fetal CMR was the introduction of an MR-compatible cardiac gating device that uses Doppler ultrasound for gating the MR data acquisition to the fetal heartbeat (smart-sync, northh medical GmbH, Hamburg, Germany) [13, 14]. This made it possible to use standard bSSFP cine sequences for fetal CMR. Standard sequence parameters need to be adjusted to the high fetal heart rate of approximately 140 bpm, for the small structures with a total heart diameter of approximately 4 cm (toward term) with myocardium just a few millimeters thick, for vessel diameters of approximately 5–10 mm, and for taking into account SAR and noise levels (Figs. 3, 4).

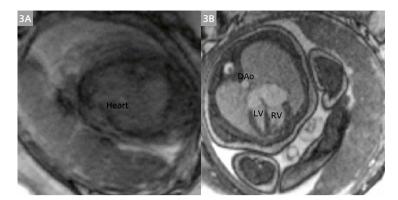
For assessing vascular anatomy, the aforementioned methods also work for producing static and cine white-blood images. An alternative is to use a 2D oversampling method for creating a 3D volume using black-blood images [15]. This is an image-based approach and could be implemented on various MR systems.

# Beyond anatomy and cardiac function: Physiology by blood flow and oxygenation

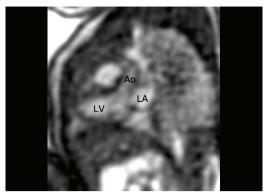
Although anatomy and cardiac function by fetal CMR improve diagnosis and impact clinical decision-making [16], fetal cardiovascular physiology can be assessed more extensively in the same session. This includes blood flow

and oxygenation measurements as well as 3D imaging for fetal weight for normalizing blood flow volumes and for calculating oxygen delivery and consumption [17, 18]. Whereas blood flow is central in pediatric and adult CMR, a clear clinical purpose for blood flow quantification in the individual fetus remains to be seen. However, several studies indicate potential uses, ranging from analysis of blood streaming in cardiac malformations to changes during maternal hyperoxygenation. More recent studies on fetal blood flow show higher accuracy and less variability than in the original studies [19, 20]. Standardization is needed for a wider clinical application, particularly with respect to phase-contrast background phase correction in the moving fetus.

Whereas non-invasive quantification of fetal blood oxygenation has been validated both in vitro [21] and in vivo [22], the concept is still challenging because results are dependent on the specific pulse sequence, and other centers have proposed methods that yield saturation measurements outside the fetal physiological range. One such implementation is available via a C2P exchange from The Hospital for Sick Children (SickKids), Toronto, Canada, and its availability may move the field forward toward standardization. However, in vivo validation is still needed in a multicenter setting and to show that data are of low variability and comparable between centers. Known errors between centers are related to using different T2 fitting



3 An example of a fetal CMR cine image corrupted by fetal motion and lack of gating (3A). No cardiac structures can be clearly seen. Corresponding image (3B) acquired using Doppler-ultrasound gated cine bSSFP optimized for fetal heart size and heart rate. Left (LV) and right (RV) ventricles, atria, mitral and tricuspid valves, and descending aorta (DAo) are clearly depicted. Cf. Online Movie 1 available at https://www.magnetomworld.siemens-healthineers.com/clinical-corner/case-studies/fetal-cmr-today-and-in-the-future



4 An example in which ultrasound was challenging: no fully diagnostic images, but suspicion of ventricular asymmetry with narrow aorta. Fetal CMR in gestational week 35 shows normal systolic function, and in the 3-chamber view a normal-sized aortic annulus and ascending aorta (Ao). LV = left ventricle. LA = left atrium. Cf. Online Movie 2 available at https://www.magnetomworld.siemens-healthineers.com/clinical-corner/case-studies/fetal-cmr-today-and-in-the-future

algorithms and different shimming methods. One also needs to consider that data are sensitive to blood flow, with fetal data commonly acquired over both systole and diastole [23, 24]. Acquisition of oxygenation data using the aforementioned MR-compatible ultrasound device for gating is not yet possible because the acquisition is too long for the short fetal RR interval. Sequence development is needed before taking this approach, which would otherwise be interesting for decreasing the impact of different flow profiles.

#### Conclusion

Fetal CMR is increasingly used and offers benefits for patients and clinical decision-makers. Although echocardiography is and should remain the first-line examination and screening tool, fetal CMR will likely strengthen its position as an important tool for further improving the prenatal diagnosis of cardiovascular malformations and reducing morbidity and mortality. For this to happen, standardization of both pulse sequences and analysis methods is crucial, in conjunction with simpler methods for acquisition, motion correction, and online image reconstruction.

MR scanning has not been established as safe for imaging fetuses and infants less than two years of age. The responsible physician must evaluate the benefits of the MR examination compared to those of other imaging procedures. Note: This disclaimer does not represent the opinion of the authors.

#### References

- 1 van der Linde D, Konings EEM, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJM, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. J Am Coll Cardiol. 2011;58(21):2241–7.
- 2 Bensemlali M, Stirnemann J, Le Bidois J, Lévy M, Raimondi F, Hery E, et al. Discordances Between Pre-Natal and Post-Natal Diagnoses of Congenital Heart Diseases and Impact on Care Strategies. J Am Coll Cardiol. 2016;68(9):921–30.
- 3 Tegnander E, Eik-Nes SH. The examiner's ultrasound experience has a significant impact on the detection rate of congenital heart defects at the second-trimester fetal examination. Ultrasound Obstet Gynecol. 2006;28(1):8–14.
- 4 Thornburg LL, Miles K, Ho M, Pressman EK. Fetal anatomic evaluation in the overweight and obese gravida. Ultrasound Obstet Gynecol. 2009;33(6):670–5.
- 5 Jansz MS, Seed M, van Amerom JFP, Wong D, Grosse-Wortmann L, Yoo S-J, et al. Metric optimized gating for fetal cardiac MRI. Magn Reson Med. 2010;64(5):1304–14.
- 6 Roy CW, Seed M, van Amerom JFP, Nafisi Al B, Grosse-Wortmann L, Yoo S-J, et al. Dynamic imaging of the fetal heart using metric optimized gating. Magn Reson Med. 2013;70(6):1598–607.
- 7 Haris K, Hedström E, Bidhult S, Testud F, Maglaveras N, Heiberg E, et al. Self-gated fetal cardiac MRI with tiny golden angle iGRASP: A feasibility study. J Magn Reson Imaging. 2017;46(1):207–217.
- 8 Bhat M, Haris K, Bidhult S, Liuba P, Aletras AH, Hedström E. Fetal iGRASP cine CMR assisting in prenatal diagnosis of complicated cardiac malformation with impact on delivery planning. Clin Physiol Funct Imaging. 2019;39(4):231–235.
- 9 Haris K, Hedström E, Kording F, Bidhult S, Steding-Ehrenborg K, Ruprecht C, et al. Free-breathing fetal cardiac MRI with doppler ultrasound gating, compressed sensing, and motion compensation. J Magn Reson Imaging. 2020;51(1):260–272.
- 10 Roy CW, Seed M, Macgowan CK. Accelerated MRI of the fetal heart using compressed sensing and metric optimized gating. Magn Reson Med. 2017;77(6):2125–2135.

<sup>&</sup>lt;sup>1</sup> Siemens Healthineers Disclaimer:

- 11 van Amerom JFP, Lloyd DFA, Price AN, Kuklisova Murgasova M, Aljabar P, Malik SJ, et al. Fetal cardiac cine imaging using highly accelerated dynamic MRI with retrospective motion correction and outlier rejection. Magn Reson Med. 2018;79(1):327–338.
- 12 Berggren K, Ryd D, Heiberg E, Aletras AH, Hedström E. Super-Resolution Cine Image Enhancement for Fetal Cardiac Magnetic Resonance Imaging. J Magn Reson Imaging. 2021 Oct 15. Online ahead of print.
- 13 Kording F, Yamamura J, Much C, Adam G, Schoennagel B, Wedegärtner U, et al. Evaluation of an Mr Compatible Doppler-Ultrasound Device as a New Trigger Method in Cardiac Mri: A Quantitative Comparison to ECG. Biomed Tech (Berl). Epub 2013 Sep 7.
- 14 Kording F, Yamamura J, de Sousa MT, Ruprecht C, Hedström E, Aletras AH, et al. Dynamic fetal cardiovascular magnetic resonance imaging using Doppler ultrasound gating. J Cardiovasc Magn Reson. 2018;20(1):17.
- 15 Lloyd DFA, Pushparajah K, Simpson JM, van Amerom JFP, van Poppel MPM, Schulz A, et al. Three-dimensional visualisation of the fetal heart using prenatal MRI with motion-corrected slice-volume registration: a prospective, single-centre cohort study. Lancet. 2019;393(10181):1619–1627.
- 16 Salehi D, Fricke K, Bhat M, Arheden H, Liuba P, Hedström E. Utility of Fetal Cardiovascular Magnetic Resonance for Prenatal Diagnosis of Complex Congenital Heart Defects. JAMA Netw Open. 2021;4(3):e213538.
- 17 Seed M, van Amerom JFP, Yoo S-J, Nafisi Al B, Grosse-Wortmann L, Jaeggi E, et al. Feasibility of quantification of the distribution of blood flow in the normal human fetal circulation using CMR: a cross-sectional study. J Cardiovasc Magn Reson. 2012;14(1):79.
- 18 Sun L, Macgowan CK, Sled JG, Yoo S-J, Manlhiot C, Porayette P, et al. Reduced fetal cerebral oxygen consumption is associated with smaller brain size in fetuses with congenital heart disease. Circulation. 2015;131(15):1313–23.

- 19 Salehi D, Sun L, Steding-Ehrenborg K, Bidhult S, Kording F, Ruprecht C, et al. Quantification of blood flow in the fetus with cardiovascular magnetic resonance imaging using Doppler ultrasound gating: validation against metric optimized gating. J Cardiovasc Magn Reson. 2019;21(1):74.
- 20 Goolaub DS, Xu J, Schrauben E, Sun L, Roy CW, Marini D, et al. Fetal Flow Quantification in Great Vessels Using Motion-Corrected Radial Phase Contrast MRI: Comparison With Cartesian.

  J Magn Reson Imaging. 2021;53(2):540–551.
- 21 Portnoy S, Seed M, Sled JG, Macgowan CK. Non-invasive evaluation of blood oxygen saturation and hematocrit from T1 and T2 relaxation times: In-vitro validation in fetal blood. Magn Reson Med. 2017;78(6):2352–2359.
- 22 Saini BS, Darby JRT, Portnoy S, Sun L, Amerom J, Lock MC, et al. Normal human and sheep fetal vessel oxygen saturations by T2 magnetic resonance imaging. J Physiol. 2020;598(15):3259–3281.
- 23 Johansson SL, Testud F, Hedström E, Aletras AH. T2 measurements in blood with T2-prepared SSFP: Effects of shimming and trigger delay at high flow velocity. SCMR 2021.
- 24 Johansson SL, Testud F, Hedström E, Aletras AH. T2 measurements in blood with T2-prepared SSFP: Effects of varying imaging parameters and flow. SCMR 2021.



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**Further Reading** 

### Small Structures Big Challenges: Fetal Cardiac Magnetic Resonance Imaging

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