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Initial Experience of Superb Microvascular Imaging for Key Cardiac Views in Foetal Assessment before 15 Weeks Gestation

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Superb microvascular imaging · Foetal heart · Early echocardiography · First trimester · Congenital heart disease

Abstract
Background: In the first trimester, ultrasound confirmation of normal or abnormal cardiac anatomy is difficult. B-mode and colour flow Doppler (CFD) are used to assess the foetal heart. Superb microvascular imaging (SMI) can visualise blood flow within the heart and vessels in early gestation. ***Objective:*** We report an initial experience of SMI for visualisation of normal and abnormal cardiac anatomy in the first trimester. ***Methods:*** Transabdominal foetal echocardiography was performed between 11 + 6 and 14 + 3 weeks (Aplio 500 US system, Toshiba Medical Systems, Tokyo, Japan) from January 2017 to December 2017. All scans were performed at a tertiary foetal cardiology unit. To assess the potential utility of the technique for early gestation screening, normal scans were reviewed by foetal medicine trainees with respect to the B-mode, CFD and SMI. Three key views were selected to compare modalities: the 4-chamber view, outflow tracts and the 3-vessel and trachea view (VTV). Visualisation rates of key echocardiographic features of significant cardiac abnormalities by SMI were reviewed. ***Results:*** Fifty-five normal echocardiograms and 34 cardiac abnormalities were included. In the normal heart, when B-mode, CFD and SMI were assessed separately, SMI had the highest rate of visualisation of 4-chamber, outflow tracts and 3-VTV (93, 85 and 83%, respectively). Intra-observer reliability was moderate for SMI of the 3 standard views (kappa 1, 0.64 and 0.64); inter-observer for 4-chamber and outflow tract views was moderate (kappa 0.64 and 0.77). In 29/34 abnormal cases, SMI showed key features, enhancing greyscale visualisation. ***Conclusion:*** SMI has potential to become a useful, complementary modality for early foetal echocardiography. Further prospective studies are warranted to establish the place of the technique in assessment of the first trimester foetal heart.

Introduction

In clinical practice, ultrasound is the established standard for evaluation of the foetal heart, and previous studies have proved the reliability of ultrasonography in de-

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tecting an abnormal heart in the first trimester [1–5]. However, in the first trimester, the foetal heart is very small (cardiac length is approximately 8 mm at 13 weeks gestation) with a heart rate that challenges both spatial and temporal resolution. Advances in prenatal ultrasound technology have included enhanced greyscale, colour flow and power flow Doppler imaging.

A recent development in ultrasound technology known as superb microvascular imaging (SMI) allows visualisation of low-velocity blood flow. SMI suppresses tissue motion to extract flow signals from large to tiny vessels and depicts this information at high frame rates as a colour overlay image or as a greyscale map of flow (colour or monochrome SMI, respectively) [6]. Visualisation of flow within the heart chambers and vessels has the potential to highlight structures that are not clearly visualised on conventional greyscale imaging.

Until now, SMI has shown utility in general ultrasound in adults, particularly in investigation of tumours differentiating between malignant and benign thyroid nodules [7], breast lumps [8] and liver lesions [9]. In addition, its use has been reported as a diagnostic tool in carpal tunnel syndrome by displaying low blood flow in the median nerve [10] and in the detection of "endoleaks" after aneurysm repairs [11].

In this paper, we report an initial experience of SMI compared to greyscale ultrasound and colour flow Doppler (CFD) in the visualisation of key cardiac and vascular structures in the first trimester in the normal foetal heart. In addition, the potential of SMI to show vessels and structures, not visualised by greyscale imaging, is illustrated using side-by-side comparison of images in both normal and abnormal foetal hearts.

Methods

Between January and December 2017, 162 cases were evaluated by early foetal echocardiography (11–15 weeks) at our unit. All echocardiograms were performed or reviewed by the attending foetal cardiologist. In this period, SMI was being integrated into workflow as a complementary imaging modality to assist visualisation of key cardiac structures. SMI was used during scans according to the preference of the attending foetal cardiologist to achieve visualisation of key cardiac views including, most commonly, the 4-chamber view, cardiac outflow tracts and 3-vessel and trachea view (VTV). There was no protocol in place during this initial experience stipulating use of SMI in all cases. We elected to retrospectively review our experience of the technique and examine whether SMI might potentially assist in visualisation of key cardiac views early in gestation. These views included the 4-chamber view, outflow tracts and 3-VTV (Fig. 1.1–4). On review of the 162 consecutive cases, 55 foetuses, who had been reported to have normal cardiac findings, were identified in whom all normal key views had been stored using SMI. Thirty-four foetuses with congenital heart disease (CHD) had the 4-chamber view and outflow tracts examined using SMI. The gestational age ranged from 11 + 6 to 14 + 3 weeks. Referral indications included suspicion of abnormal heart anatomy, nuchal translucency above 99th percentile (NT >3.5 mm) or previous pregnancy affected with severe CHD. All cases were imaged transabdominally (as per our departmental preference) by means of conventional two-dimensional echocardiography greyscale, CFD and SMI. A high-frequency (10 MHz) curvilinear ultrasound probe on the first trimester echocardiography preset was used. All scans were performed using a Toshiba Aplio 500 ultrasound system (Toshiba Medical Systems, Tokyo, Japan).

For the purposes of this study, the images from the 55 normal foetuses in whom the necessary views were obtained conventionally and by SMI were reviewed by a trainee in foetal medicine (S.J.) and interobserver assessment was performed by a trainee (T.K.) in foetal medicine. The normal key views were binary scored using a visual analogue scale (Table 1). In practice, greyscale, colour flow and SMI were used in a complementary fashion to complete the clinical scan, but for the purposes of this retrospective comparison, the visualisation of key structures by greyscale, CFD and SMI was assessed separately. The features required to "pass" the "adequate visualisation test" are described specifically in Table 1. The choice of trainees rather than foetal cardiologists was deliberate to focus on potential assistance in visualisation of the foetal heart during early targeted sonography at the same examination as measurement of nuchal translucency. The use of SMI permits a twin-view display where the greyscale image or video is shown alongside that using SMI. The reproducibility and agreement in assessment of the foetal cardiac scans were established between the 2 observers (S.J., T.K.) in 20 randomly selected scans, and Kappa coefficient was calculated. In addition, the potential for SMI to illustrate key diagnostic features of significant cardiac abnormalities was assessed in 34 cases, and images of the key views alongside the simultaneous greyscale images are presented.

Results

In the normal first trimester foetal heart, the visualisation rate of the 3 key cardiac views using the 3 modalities is demonstrated in Table 1. SMI had the highest visualisation rate of the 4-chamber, outflow tracts and 3-vessel and tracheal view in 93, 85 and 83% of the normal cases, respectively (Fig. 2). Normal cardiac anatomy was confirmed at 20 weeks gestation, and normal outcome was ascertained after birth in all cases.

The intra-observer reproducibility was consistently higher than inter-observer reproducibility for all views visualised by all modalities, except the outflow tract visualisation by SMI. The intra-observer kappa coefficient showed strong levels of agreement for all modalities and sonographic views except outflow tract and 3-VTV by SMI where the agreement was moderate (kappa coefficient 0.64; Table 2).

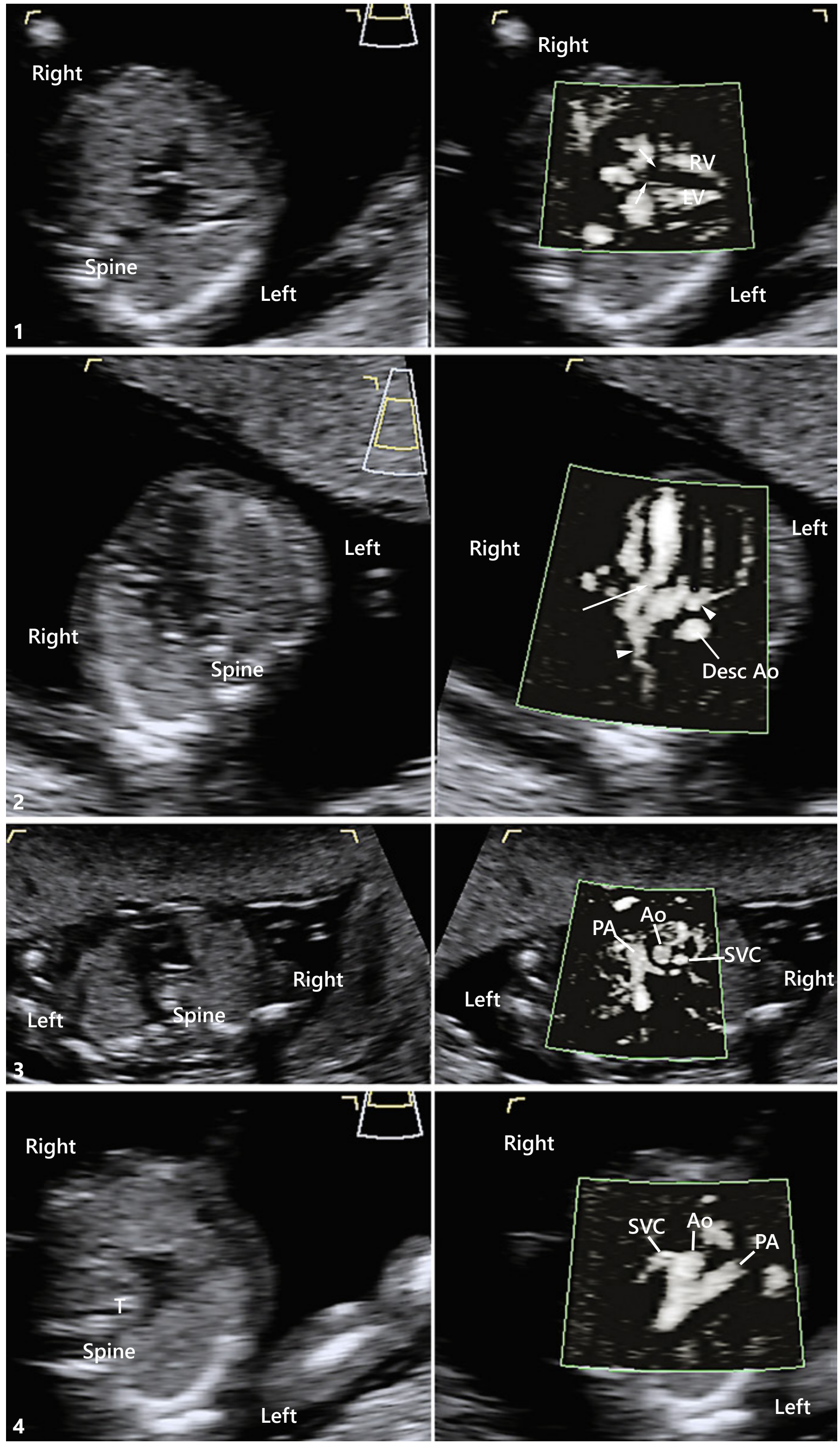

Fig. 1. 1 On the left-side panel, the 2D greyscale transverse section demonstrates the heart in a lateral 4-chamber view. This is a favourable orientation for examining the ventricular septum. On the right-side panel, the simultaneous image of the microvascular imaging emphasises the intact interventricular septum and differential insertion of the atrioventricular valves (white arrows) in this foetus at 13 weeks gestation. **2** On the left-side panel, this 2D greyscale transverse view demonstrates the left ventricular outflow tract with a great artery arising. On the right-side panel, the simultaneous image of the microvascular imaging delineates the interventricular septum and shows that the vessel arising from the left ventricle has no early branching and therefore is Ao (white arrow) in this foetus at 13 weeks gestation. In addition, 2 pulmonary veins (white arrowheads) are seen entering left atrium from each side. **3** On the left-side panel, the branch PA in continuity with the arterial duct and the right PA are seen in the transverse plane. This plane is obtained in slightly lower cut than in classic 3-vessel view in this foetus at 13 weeks gestation. On the right-side panel, the simultaneous image using SMI clearly confirms the anatomy of the PA showing both branch pulmonary arteries and the arterial duct. In addition, the Ao and SVC are seen in transverse section. **4** On the left-side panel, this 2D greyscale transverse view demonstrates a normal transverse aortic arch seen crossing the midline in front of T in the transverse plane in this foetus at 13 weeks gestation. On the right-side panel, a simultaneous image using SMI shows the transverse Ao and the PA meeting in a "V" shape anterior to the trachea confirming normal 3-VTV SVC. LV, left ventricle; RV, right ventricle; SVC, superior vena cava; PA, pulmonary artery; Ao, aortic; T, trachea.

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Table 1. The visual analogue scale used to assess 4-chamber, outflow tract and 3-vessel and trachea view by means of greyscale and superb microvascular imaging

Visual analogue scale	4 Chambers	Outflow tracts	3-Vessel and trachea view
Greyscale US and SMI			
All visualised	– Clear offsetting of the atrioventricular valves – Intact crux – Balanced ventricles	– Crossover of the great arteries – Equal size outflow tracts – Pulmonary artery branching	"V" sign clearly seen with balanced, aorta, pulmonary artery and duct
Not adequately visualised	Either 1, 2 or 3 not seen	Either 1, 2 or 3 not seen	One or more structures not seen
Colour Doppler			
All visualised	– Equal filling of ventricles – Flow across AV valves	– Crossover of the great arteries flow – Presence of flow (laminar antegrade) in both left and right outflow 3 Flows seen in pulmonary artery branches	Presence of flow (forward flow) seen in aorta, pulmonary artery and duct
Not adequately visualised	Either 1 or 2 not seen	Either 1, 2 or 3 not seen	Flow direction not seen in either of the vessels

SMI, superb microvascular imaging.

Table 2. Intra-observer and inter-observer reproducibility in the evaluation of the 3 key cardiac views using SMI

	Intra-observer (kappa coefficient)	Inter-observer (kappa coefficient)
4-Chamber 2D	0.9	0.107
4-Chamber colour	1	N/A
4-Chamber SMI	1	0.64
Outflow tracts 2D	1	N/A
Outflow tracts colour	1	N/A
Outflow tracts SMI	0.64	0.77
3-VTV 2D	0.9	0.05
3-VTV colour	1	0.68
3-VTV SMI	0.64	0.32

SMI, superb microvascular imaging; 2D, two-dimensional; VTV, vessel and trachea view; N/A, not applicable.

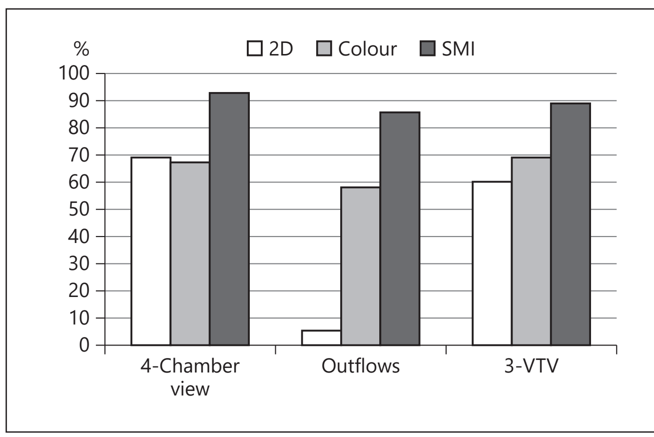


Fig. 2. Visualisation rate of normal foetal cardiac structures using 3 ultrasound modalities. 2D, two-dimensional; SMI, superb microvascular imaging; VTV, vessel and trachea view.

Comparison of greyscale and SMI images of the normal cardiac anatomy is illustrated in Figure 1.

SMI was used in assessment of 34 cardiac abnormalities that included coarctation of the aorta (Ao; $n = 6$), tetralogy of Fallot ($n = 6$), atrioventricular septal defect ($n = 8$), hypoplastic left heart ($n = 6$), right aortic arch and double aortic arch ($n = 4$), transposition of the great arteries ($n = 1$), Ebstein's anomaly of the tricuspid valve ($n = 1$), interrupted inferior vena cava ($n = 1$) and outpouching of the right ventricle ($n = 1$).

The key diagnostic features were visualised by SMI in 29/34 cases. The proportion of cases where the key diagnostic features were identified is shown in Table 3. A large aortic root overriding the ventricular septum in combination with a narrow pulmonary artery (PA) was seen in cases with tetralogy of Fallot (Fig. 3.1a, b). The loss of atrioventricular valve offsetting was well delineated on SMI in cases of atrioventricular septal defect (Fig. 3.2). A

Table 3. Diagnostic features of cardiac abnormalities seen on superb microvascular imaging

Diagnosis	Diagnostic features	Well seen/total (n = 34)
Atrioventricular septal defect	Loss of offsetting of the atrioventricular valves	6/8
Hypoplastic left heart	No flow across the left atrioventricular valve and no filling of the left ventricle	6/6
Coarctation of the aorta	Small aortic arch, head and neck arteries	6/6
Tetralogy of Fallot	Both: overriding aorta and small pulmonary artery with branches	4/6
Vascular rings (right aortic arch and double aortic arch)	Aortic arch on the right of trachea and left arterial duct	3/3
	Both: left aortic arch in front of trachea and right aortic arch on the right of trachea, left arterial duct	1/1
Interrupted inferior vena cava	Two vessels in front of spine	1/1
Transposition of the great arteries	Discordant ventriculoarterial connections	1/1
Outpunching of the right ventricle	Filling of the outpouching at the apex of the right ventricle	1/1
Epstein's anomaly of the tricuspid valve	Displaced tricuspid valve	0/1

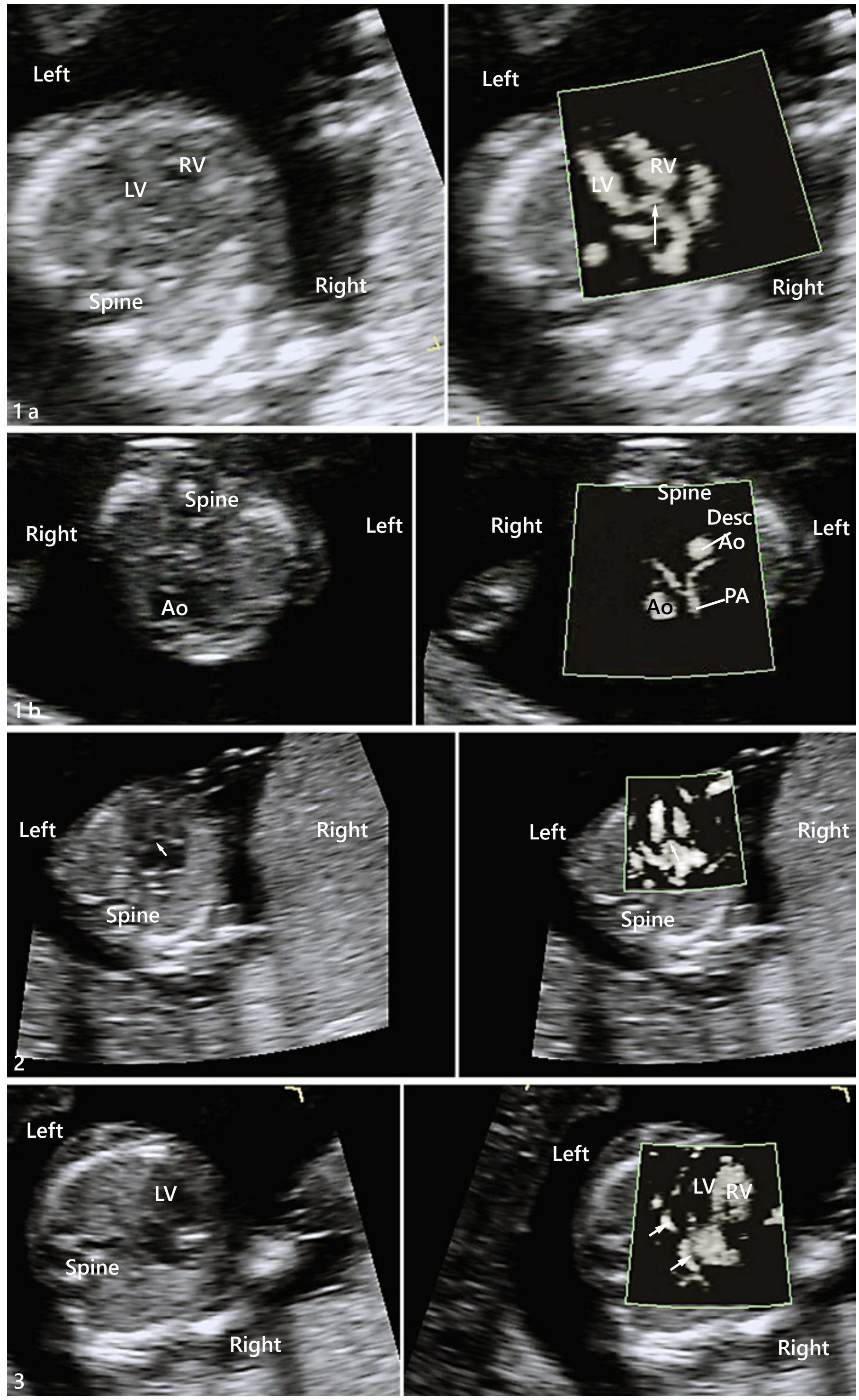
single ventricular inflow was present in the cases with hypoplastic left heart (Fig. 3.3). The sagittal view of the aortic arch demonstrated a hypoplastic aortic arch with a slender isthmus that was inserted into the arterial duct in cases with coarctation of the aorta (Fig. 3.4). Discordant ventriculo-arterial connections were evident by the presence of early bifurcation of the PA as it arose from the left ventricle in transposition of the great arteries (Fig. 3.5). SMI clearly showed the arrangement of the aortic arch, ductal arch and head/neck vessels in vascular ring anomalies (online suppl. Video 1, see www.karger.com/doi/10.1159/000450979) and interruption of the inferior vena cava in Figure 3.6a and b.

Discussion

This study describes the initial experience of SMI in the early assessment of the foetal heart. SMI was subjectively better in identifying the 4-chamber, outflow tracts and great arteries at the 3-VTV when compared to greyscale imaging or CFD alone. This means of analysis was undertaken to provide structured retrospective review of images obtained by foetal cardiologists and was applied to normal examinations. It is accepted that in real-life clinical practice, different ultrasound modalities are integrated rather than being used separately. Nonetheless, these results suggest that SMI has some value as a complementary technique in early foetal echocardiography. Previous studies describe the utility of greyscale imaging in combination with CFD to achieve diagnostic imaging in first trimester cardiac screening, but the use of SMI has not been reported [1–5, 12, 13].

Although the visualisation rates appear encouraging, the intra-observer and inter-observer agreement appeared poorer with SMI than with greyscale or CFD. We speculate that lack of user familiarity with the technique compared to the other modalities may have an impact on this. The results of outflow tract assessment using greyscale in isolation were less satisfactory in this study. This is likely due to high requirements set for the analysis, for example, visualisation of both branches of the PA and limited resolution of greyscale in the first trimester.

With advances in ultrasound technology, first trimester image quality has moved closer to that achievable in the second trimester but the resolution of standard ultrasound is still a limiting factor. The development of SMI shows particular advantage in the first trimester above that of conventional ultrasound, first by delineating the blood pool as a bright white structure. This facilitates visualisation of very small structures such as the aortic arch, branch pulmonary arteries, pulmonary veins, subclavian arteries and common carotid arteries (Fig. 1.3, 3.4, 5). Our presentation of side-by-side comparison with greyscale images illustrates that SMI may permit delineation of small or less distinct vessels or chambers that are not readily seen on greyscale imaging. Second, in contrast to colour flow mapping, SMI does not oversaturate the



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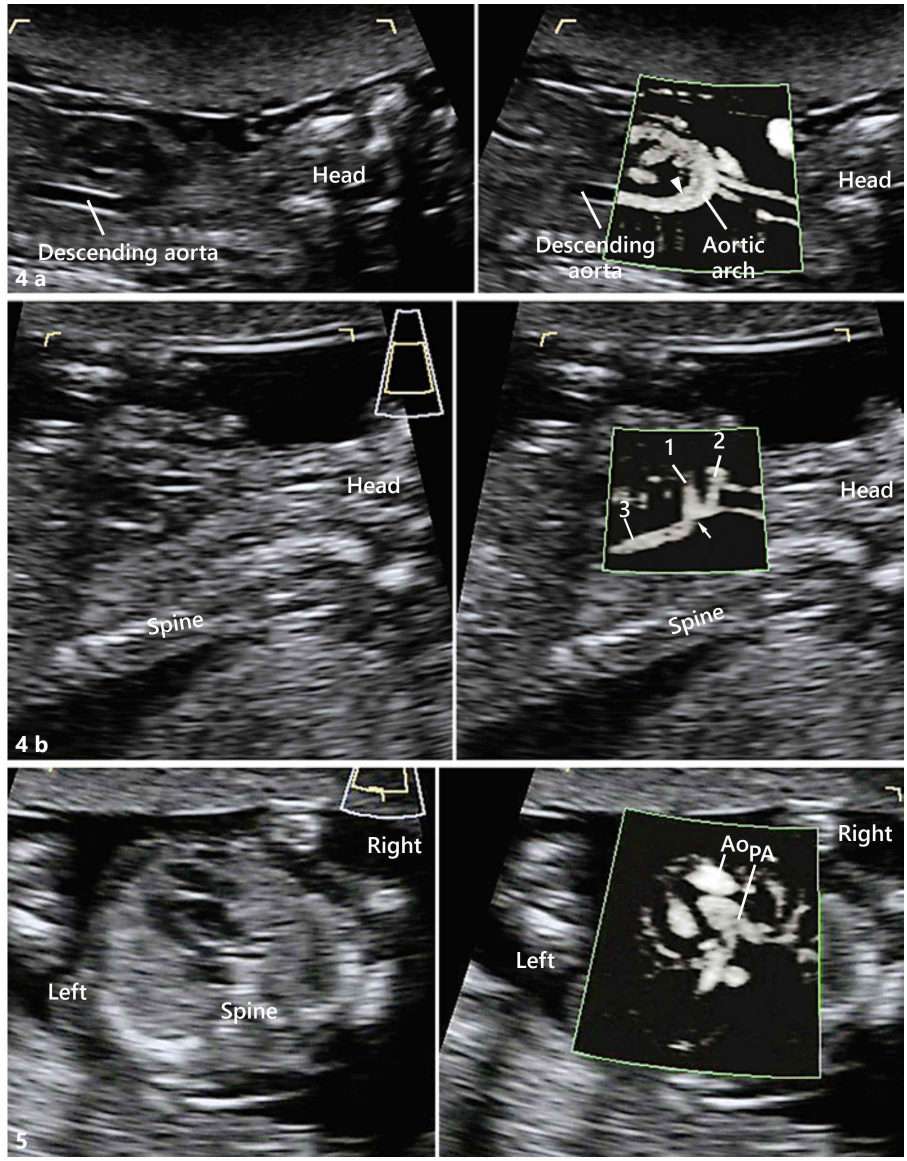
3 

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image causing "bleeding" of the colour, thus providing a clear delineation of cardiac structures. Third, the myocardium appears as a dark structure, thus enabling appreciation of offsetting of the atrioventricular valves and the interventricular septum.

This study represents an initial experience of a novel modality. There are significant limitations to our study. First, the retrospective design means that SMI was not used in all cases or for all views in the study period. Second, we cannot objectively assess the impact of factors such as foetal lie or maternal body mass index in relation to SMI. Third, it cannot be determined how modalities will compare when applied prospectively with the operator both acquiring and interpreting the relevant images. Studies, ideally prospective, using both expert and non-expert operators will both be required to establish the place of SMI in practice. Fourth, our examples of CHD show that in some cases the abnormality may be clearly delineated. However, the frequency of visualisation of abnormal structures in different forms of CHD merits further prospective study to answer important questions such as whether pathologically small vessels, for example, the pulmonary arteries in tetralogy of Fallot or the aortic arch in coarctation of the Ao, might be better seen with SMI in combination with conventional Doppler techniques. Furthermore, absence of flow into either ventri-

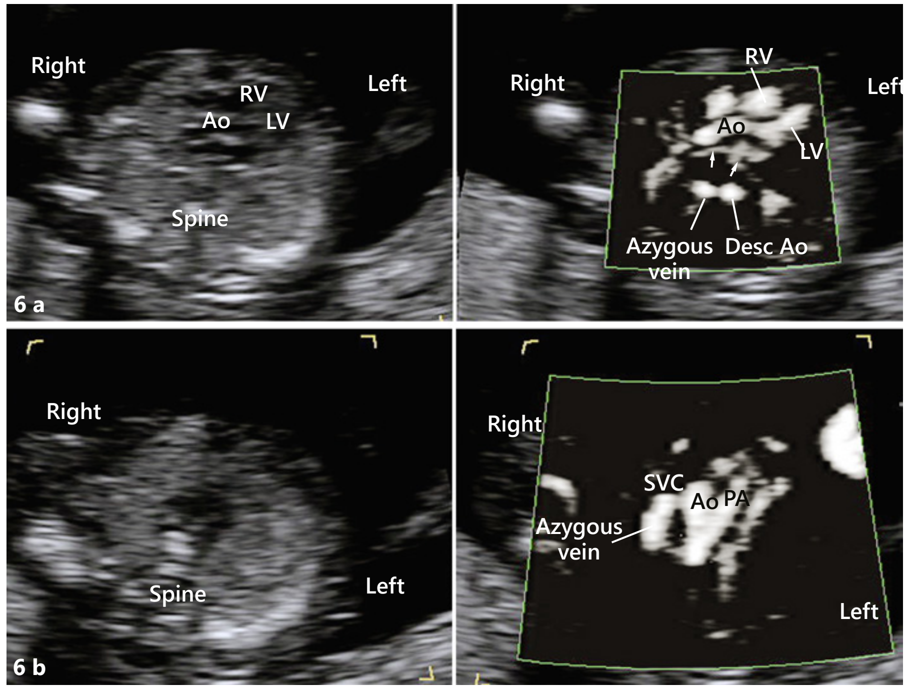

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Fig. 3. 1a On the left-side panel, the transverse section in 2D greyscale demonstrates the heart in a 4-chamber view in 13-week gestation foetus. On the right-side panel, a simultaneous image using SMI demonstrates 2 ventricles and 1 great artery (white arrow) with no early branching (Ao) arising from the middle of the heart and overriding ventricular septum. In this baby, tetralogy of Fallot was diagnosed on this first and subsequently confirmed on the second trimester scan. **1b** On the right-side panel, a slender PA with confluent branch pulmonary arteries and a large ascending Ao are seen in 3-vessel view. On the contrary, this cannot be appreciated in 2D greyscale on the left-side panel. **2** On the left -side panel, this 2D transverse view demonstrates an apical 4-chamber view. A common atrioventricular valve (white arrow) can be suspected on this image. On the right-side panel, a simultaneous image using SMI shows clear loss of offsetting (black arrow) of the atrioventricular valves indicative of a complete atrioventricular septal defect. The atrial septum extending to the atrioventricular junction is not seen in this 12-week foetus. **3** On the left-side panel, 2D greyscale transverse section demonstrates the 4-chamber view of the heart in this foetus at 13 weeks gestation. On the right-side panel, a simultaneous image using SMI demonstrates no filing in the LV and only a single inflow to the RV. In addition, 2 pulmonary veins (white arrows) are seen entering the left atrium from each side. This is an example of mitral atresia in setting of hypoplastic left heart syndrome. **4a** On the left-side panel, in the sagittal plane, the descending Ao is well seen in this foetus at 13 weeks gestation. On the contrary, on the right-side panel, a complete normal in size aortic arch with head and neck vessels as well as the ductal arch (arrowhead) using SMI are well seen. **4b** On the left-side panel, the sagittal plane demonstrates the aortic arch in this foetus at 13 weeks gestation. On the right-side panel, using SMI both ductal (1) and aortic arches (2) are seen. The aortic arch appears hypoplastic and inserts into the arterial duct (arrowhead) in this case of aortic coarctation. **5** On the left-side panel, 2D greyscale transverse section demonstrates 2 parallel great arteries arising from the heart at 13 weeks gestation. On the right-side panel, a simultaneous image using SMI demonstrates 2 parallel great arteries with PA as a posterior vessel with clear typical early branching pattern. Transposition of the great arteries was diagnosed in this foetus at first trimester and confirmed on later scans. **6a** On the left-side panel, this transverse view in 2D greyscale demonstrates the left ventricular outflow tract with a committed great artery. On the right-side panel, simultaneous SMI delineates the interventricular septum and shows that the vessel arising from the left ventricle has no early branching and therefore is the Ao. Two pulmonary veins (white arrows) are seen entering the left atrium from each side. The 2 vessels seen in transverse cut in front of spine are indicating a prominent azygous vein to the right of the descending Ao suggestive of an interruption of the inferior vena cava in this 12-week gestation foetus. **6b** On the left -side panel, the 2D greyscale transverse view demonstrates the 3-VTV in this foetus at 12 weeks gestation. On the right-side panel, a simultaneous image using SMI shows the transverse aortic arch (Ao) and the PA meeting in a "V" shape anterior to the trachea confirming normal 3-VTV. A generous azygous vein is draining into the SVC in this case of interrupted inferior vena cava. The intracardiac structures were reported as normal at first trimester and on later scans. The stomach was on the right, and thus, the concern of possible intestinal malrotation in setting of left isomerism was raised. There were no cardiac sequelae but the neonate required an operation for intestinal malrotation. LV, left ventricle; RV, right ventricle; Ao, aorta; PA, pulmonary artery; SVC, superior vena cava.

cle, for example, of hypoplastic left heart and lack of offsetting in cases of common atrioventricular valve may be observed by SMI.

There are, however, inherent limitations of the SMI technique: SMI allows visualisation of the blood pool in early gestation but does not achieve this beyond 16 weeks gestational age. Thus, studies later in gestation continue to depend on greyscale and CFD only. The lack of blood flow direction means that SMI does not provide the same type of information as CFD. However, the pulsed Doppler cursor can be placed on the SMI directly and both the direction of the blood flow Doppler waveform can be obtained. SMI is a proprietary technique and therefore currently limited to specific ultrasound systems used in prenatal scanning. As Quarello et al. [12] showed, a universal grading system to assess the completeness of an echocardiogram cannot be applied to abnormal cases, and therefore, further refinement in the use of SMI both for confirmation of normality and for detailed cardiac abnormalities merits prospective study.

Conclusion

Our preliminary data suggest that SMI might prove to be a useful adjunct for early foetal echocardiography to complement greyscale and CFD techniques to enhance imaging of the heart and great vessels in the first trimester to assist in early foetal echocardiography. It can also improve visualisation of selected abnormal cardiovascular features in the foetus with CHD.

Statement of Ethics

Ethics approval was not required for this study as it was a retrospective analysis of imaging performed for clinical reasons.

Disclosure Statement

The authors have no ethical conflicts to disclose. The authors declare no conflict of interest.

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