Super-resolution Reconstruction MRI Application in Fetal Neck Masses and Congenital High Airway Obstruction Syndrome

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Abstract

Objective. Reliable airway patency diagnosis in fetal tracheolaryngeal obstruction is crucial to select and plan ex utero intrapartum treatment (EXIT) surgery. We compared the clinical utility of magnetic resonance imaging (MRI) super-resolution reconstruction (SRR) of the trachea, which can mitigate unpredictable fetal motion effects, with standard 2-dimensional (2D) MRI for airway patency diagnosis and assessment of fetal neck mass anatomy.

Study Design. A single-center case series of 7 consecutive singleton pregnancies with complex upper airway obstruction (2013-2019).

Setting. A tertiary fetal medicine unit performing EXIT surgery.

Methods. MRI SRR of the trachea was performed involving rigid motion correction of acquired 2D MRI slices combined with robust outlier detection to reconstruct an isotropic high-resolution volume. SRR, 2D MRI, and paired data were blindly assessed by 3 radiologists in 3 experimental rounds.

Results. Airway patency was correctly diagnosed in 4 of 7 cases (57%) with 2D MRI as compared with 2 of 7 cases (29%) with SRR alone or paired 2D MRI and SRR. Radiologists were more confident \((P = .026)\) in airway patency diagnosis when using 2D MRI than SRR. Anatomic clarity was higher with SRR \((P = .027)\) or paired data \((P = .041)\) in comparison with 2D MRI alone. Radiologists detected further anatomic details by using paired images versus 2D MRI alone \((P < .001)\). Cognitive load, as assessed by the NASA Task Load Index, was increased with paired or SRR data in comparison with 2D MRI.

Conclusion. The addition of SRR to 2D MRI does not increase fetal airway patency diagnostic accuracy but does provide improved anatomic information, which may benefit surgical planning of EXIT procedures.

Keywords

fetal neck mass, CHAOS, magnetic resonance imaging, super-resolution reconstruction, trachea, EXIT

Received September 20, 2021; accepted October 6, 2021.

Fetal tracheolaryngeal obstruction is a life-threatening condition associated with substantial mortality of 80% to 100% if unrecognized before delivery. Fetal airway

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compromise can occur due to extrinsic causes, such as complex neck masses, and intrinsic factors, such as congenital high airway obstruction (CHAOS). A patent airway is necessary to complete the transition from fetal to neonatal life, but ex utero intrapartum treatment (EXIT) can be performed to treat or bypass the structural defect at birth. This modification of a caesarean section temporarily delivers only the fetal head through the maternal uterine incision while maintaining fetal oxygenation via placental circulation. This provides a crucial time window allowing the fetal airway to be secured by endotracheal intubation or tracheostomy. EXIT procedures have a significant rate of maternal complications, which includes hemorrhage due to deep maternal anesthesia for uterine relaxation and fetal risks such as hypoxic brain damage or death if the airway is not secured in a timely manner. Appropriately case selection and surgical planning are pivotal for optimizing outcome and depend on comprehensive preoperative imaging. Ultrasound is the initial imaging method of choice due to its low cost and real-time capability. However, the fetal airway is not always easily seen due to suboptimal fetal position. Therefore, magnetic resonance imaging (MRI) is often used in addition as it provides superior anatomic soft tissue visualization and definition due to multiplanar imaging with a larger field of view. MRI, however, is compromised by the effects of fast unpredictable fetal motion, which affects imaging quality and geometric integrity. Some fetal magnetic resonance advances, such as ultrafast acquisition of thick 2-dimensional (2D) slices while maintaining a high signal-noise ratio, are still not enough to mitigate these challenges. Super-resolution reconstruction (SRR) is an example of postacquisition image processing based on rigid motion correction of 2D slices combined with robust outlier detection to reconstruct an isotropic high-resolution volume. It has been found to enhance anatomic evaluation of fetal brain structural anomalies. We investigated the clinical utility of SRR of the fetal trachea as compared with standard 2D MRI for airway patency diagnosis and anatomic assessment of fetal neck masses.

Methods

Participants

This study is based on 7 consecutive singleton pregnancies with fetal tracheal-laryngeal obstruction with antenatal MRI that were managed in the fetal surgical EXIT program at University College London Hospitals (2013-2019). All cases initially had ultrasonography, which identified fetuses with large neck masses (n = 6) or CHAOS syndrome (n = 1), with referral to our tertiary fetal medicine unit for further assessment and management. All MRI data were analyzed under the study entitled “Guided Instrumentation for Fetal Therapy and Surgery (GIFT-Surg): Fetal MRI to Improve Prenatal Diagnosis and Therapy for Fetal Abnormality” (Hampstead Research Ethics Committee, 15/LO/1488). Women provided written informed consent for fetal MRI research. All images were transferred with Caldicott Guardian approval from University College London Hospitals to collaborators at partner academic institutions (University College London, King’s College London, and Katholieke Universiteit Leuven) via the secure GIFT-Cloud platform, which ensures complete anonymization through XNAT technology. Case outcome data were collected from neonatal records, including laryngoscopy at EXIT, postnatal magnetic resonance and x-ray imaging, and postmortem examination where performed.

Technical and Experiment Information

All MRI examinations were performed on a 1.5-T magnet (MAGNETOM Avanto; Siemens Healthcare). Women were placed in the supine or left lateral decubitus position. The gravid uterus was imaged in at least 3 orthogonal planes (axial, coronal, and sagittal) relative to the fetal body. The protocol consisted of T2-weighted fast acquisition spin echo sequences, typically HASTE (half-Fourier acquisition single-shot turbo spin echo), or gradient echo sequences, such as T1-weighted spoiled FLASH (fast low-angle shot) or T2-weighted TRUFI (true fast imaging with steady state–free precession). For HASTE sequences, the following parameters were applied: echo time (68-112 ms), repetition time (887-1460 ms), flip angle (90°), refocusing flip angle (80°-107°), slice thickness (2-4 mm), slice gap (0%-10% of slice thickness), field of view (260-360 mm × 195-315 mm), and voxel size (1-1.4 mm × 1-1.4 mm). For TRUFI the following parameters were applied: echo time (2.66 ms), repetition time (5.31 ms), flip angle (62°), slice thickness (4 mm), no gap, field of view (320 mm × 320 mm), and voxel size (1.4 mm × 1.4 mm). All patients were scanned in a normal specific absorption rate mode. Total acquisition time did not exceed 40 minutes.

A novel SRR algorithm was then applied to reconstruct an isotropic 3-dimensional volume of the trachea with native 2D MRI stacks. At least 3 orthogonal T2-weighted image stacks, acquired in at least 3 orientations, were used for the algorithm in each case. A region of interest in 1 stack around the trachea was manually segmented and automatically propagated to the remaining stacks with rigid volume-to-volume registration. Afterward, robust SRR involving iterative motion correction and volumetric reconstruction steps was deployed, guided by the respective trachea masks. Iterative 3-dimensional reconstructions were estimated from motion-corrected slices through outlier-robust SRR methods to account for image artifacts as part of the motion correction step. Each SRR generation did not exceed 15 minutes.

Experiments were separated into 3 rounds. The first 2 rounds involved a selection of individual SRR and 2D MRI scans, which were assessed by 3 senior pediatric radiologists (M.A., P.D.H., and T.G.) with specialist fetal MRI expertise who were blinded to case outcomes. The selection was randomly assigned such that each radiologist had a different set of independent SRR and 2D MRI scans in each of the first 2 rounds. Each radiologist read all the images by the end of the second round. In the third round, the radiologists each examined all the 2D MRI scans paired with their corresponding SRR images alongside. The first 2 rounds were separated by 1 week; 2 weeks after this, the third round was performed (Figure 1).
In every round, the assessment contained a set of clinical questions that had 3 themes: diagnosis and confidence of airway patency, anatomic clarity, and characteristics of mass and extent of head and neck involvement (Supplemental Table S1, available online). The time taken to answer these questions was measured. Airway patency was scored on a confidence scale of 0 to 5, ranging from no confidence at all to completely confident. Anatomic clarity was subjectively scored 0 to 4, where 0 = structure was not seen, 1 = poor depiction, 2 = suboptimal visualization, 3 = clear visualization of structure but reduced tissue contrast (image-based diagnosis feasible), and 4 = excellent depiction (optimal for diagnostic purposes).

Figure 1. Flowchart of experimental design. 2D, 2-dimensional; MRI, magnetic resonance imaging; SRR, super-resolution reconstruction.
The presence of various anatomic markers was evaluated, including description of the mass causing displacement, compression, and encasement of the trachea. Extent of neck, facial involvement, and intrathoracic extension was also rated. Further mass characteristics were assessed, such as cystic, septated, solid, and vascular. Radiologists were asked to evaluate SRR quality, which was dependent on the amount of fetal motion artifact remaining where 0 = substantial artifact/blur, 1 = little artifact/blur, and 2 = no artifact/blur. 2D MRI quality was not quantitatively examined, as there was no predefined marking that is comparable to our quality scoring for SRR. Radiologists additionally provided a subjective preference in the third round, to indicate whether 2D MRI, SRR images, both, or neither was more superior in answering the clinical questions. The NASA Task Load Index (TLX) was performed at the end of each round to quantify user cognitive load of evaluating 2D MRI, SRR images, and those 2 modalities combined. The TLX is a subjective multidimensional tool that measures observed workload to assess a task. This has been used before in the context of new medical technology. It scores different task aspects on a graded scale from 0 to 20, including effort, frustration, and performance (Supplemental Table S2, available online).

**Statistics**

Statistical analysis was performed with Excel (Microsoft 365) and SPSS Statistics for Mac version 27 (IBM Corp). Kruskal-Wallis 1-way analysis of variance with correction for multiple comparisons was used to assess data among all imaging modalities. Results are documented as test statistic (degree of freedom) and the P value. For illustration of differences among modalities, a Bland-Altman analysis was used, with the mean difference as a bias measure and the 2.5th and 97.5th percentiles as the 95% limits of agreement. Statistical significance was set <.05.

**Results**

**Cases**

There were 7 cases of tracheal-laryngeal obstruction: 4 lymphatic malformations, 2 teratomas, and 1 CHAOS syndrome. All cases were diagnosed by ultrasound, with an average gestational age at MRI of 31 weeks + 4 days (SD, 1 + 1; range, 29 + 1 to 37 + 6). Average gestational age at delivery was 36 weeks + 3 days (SD, 2 + 2; range, 33 + 1 to 38 + 6). One case was not suitable for an EXIT procedure due to severe lung hypoplasia. The mother had an emergency cesarean section due to a pathologic cardiocograph in her local hospital. Securing of the airway was impossible due to tracheal obstruction, and although a tracheostomy was performed, there was early neonatal death secondary to pulmonary hypoplasia. Six cases had an EXIT procedure, all of which had functional airways created by means of either a tracheostomy or endotracheal intubation. In 1 case there was an early neonatal death due to significant hemorrhage into a teratoma. There was additionally a left-sided pneumothorax that, despite airway security, resulted in poor response to ventilation causing grade 3 hypoxic ischemic encephalopathy. The fetus with CHAOS syndrome had a tracheostomy at EXIT, with a diagnosis of laryngeal atresia fully obstructing the airway at the subglottis. Further details of the cases are illustrated in Figure 2 and Table 1.

**Super-resolution Reconstruction**

An average of 8 stacks (SD, 2.5; range, 3-11) in at least 3 anatomic orientations were used for SRR. Average slice rejection was 1 (SD, 4; range, 0-15), indicating the degree of fetal motion in the acquired data. Of 7 SRR images, 3 (43%) scored >1 quality. Fewer than 5 stacks are typically insufficient for obtaining good SRR quality. This is shown for cases 4 and 6 (Table 2).

**Diagnosis and Confidence of Airway Patency**

With 2D MRI alone, airway patency was correctly diagnosed by each radiologist in 4 of 7 cases (57%). When provided with SRR images alone, however, radiologists were less often correct in their diagnosis (2 of 7 cases, 29%). The combination of 2D MRI with SRR imaging did not improve diagnostic accuracy above 2D MRI scans alone (2 of 7 cases, 29%). In 2 of 7 cases where 2D MRI yielded the correct diagnosis, the addition of SRR made some radiologists change their minds to an incorrect diagnosis (Figure 3).

**Confidence Regarding Airway Patency**

Radiologists were more confident (test statistic [5] = 12.737, P = .026) in assessing airway patency with 2D MRI alone (mean, 3.76; 95% CI, 3.22-4.30) in comparison with SRR images alone (2.81; 95% CI, 2.10-3.52; Figure 4). There was no significant improvement in airway patency confidence between paired data and 2D MRI and SRR data alone (Supplemental Figure S1, available online).

**Anatomic Clarity**

Subjective anatomic clarity was higher with paired data (mean, 3.05; 95% CI, 2.4-3.7; test statistic [3] = 8.251, P = .041) or SRR images alone (2.43; 95% CI, 1.67-3.18; test statistic [4] = 10.995, P = .027) in comparison with 2D MRI alone (2.33; 95% CI, 1.61-3.06; Figures 5 and 6).

**Characteristics of Mass and Extent of Head and Neck Involvement**

Anatomic findings were significantly more likely to be detected with paired data (mean, 12.1; 95% CI, 7.71-16.5) than with 2D MRI alone (11.3; 95% CI, 7.56-15.04; test statistic [3] = 51.907, P < .001; Figure 7).

**Time Taken to Answer Clinical Questions and Subjective Preference**

The average time taken by radiologists to answer the clinical questions was not different between 2D MRI alone (mean, 306.71; 95% CI, 208.21-405.22) and paired data (314.43; 95% CI, 224.35-404.51). On average, 1.5% (4/273) of all clinical questions could not be answered with 2D MRI scans alone and 6.23% (17/273) SRR images alone. In contrast, all clinical questions could be answered by all radiologists using...
paired data. Additionally, the radiologists rated their preference toward using paired imaging (57% = 12/21) versus SRR (0%) or 2D MRI (38% = 8/21) images alone.

**NASA TLX**

The NASA TLX was used to determine radiologist cognitive load in answering the clinical questions. Mental, physical, temporal demand, effort, and frustration levels were all higher with SRR images alone or paired imaging in comparison with 2D MRI alone. Performance was lower with paired images and SRR data alone than with 2D MRI. This was improved by using paired imaging over SRR data alone. Physical demand was significantly increased with paired data (mean, 4.1; 95% CI, 2-6.2) than with SRR images alone (1.61; 95% CI, 0.23-3; test statistic [6] = 16.297, P = .012; Figure 8).

**Discussion**

**Main Findings**

We compared the clinical utility of a novel SRR of the trachea with standard 2D MRI for diagnosis of airway patency and anatomic assessment of fetal neck masses. We found that airway patency was more likely to be correctly diagnosed with 2D MRI alone in comparison with SRR alone or paired data sets. However, anatomic clarity was significantly better with paired or SRR images alone than with 2D MRI scans alone. As SRR quality improved, airway patency confidence increased, as did anatomic clarity (Supplemental Figures S2 and S3, available online). Anatomic markers and mass characteristics were additionally detected significantly more with paired data in comparison with 2D MRI alone, with no increase in time taken to make a clinical assessment.
| Characteristic | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 |
|---------------|--------|--------|--------|--------|--------|--------|--------|
| **Pregnancy** |        |        |        |        |        |        |        |
| GA at MRI, wk + d | 29 + 6 | 29 + 4 | 31 + 1 | 30 + 5 | 37 + 2 | 32 + 3 | 31 + 6 |
| GA at delivery, wk + d | 37 + 5 | 34 + 2 | 36 + 6 | 37 + 3 | 38 + 2 | 34 + 1 | 33 + 4 |
| **Tumor** |        |        |        |        |        |        |        |
| Final diagnosis | Lymphatic malformation | Teratoma | Teratoma | Lymphatic malformation | Lymphatic malformation | Lymphatic Malformation | CHAOS |
| Lesion/obstruction size on MRI, mm | 55 × 35 | 145 × 110 | 45 × 36 | 83 × 42 × 46 | 80 × 60 × 76 | 88 × 122 × 87 | 7 × 5 |
| **Delivery** |        |        |        |        |        |        |        |
| EXIT | No | Yes | Yes | Yes | Yes | Yes | Yes |
| Airway patent | No | No | Yes | Yes | Yes | Yes | No |
| Tracheostomy | No | No | Yes | No | No | No | Yes |
| ET tube | No | No | Yes | Yes | Yes | Yes | No |
| Successful intubation | No | Yes | Yes | Yes | Yes | Yes | Yes |
| Outcome | Emergency caesarean section, cardiac arrest and neonatal death | Neonatal death due to significant hemorrhage into teratoma. Pulmonary hypoplasia, pneumothorax, and HIE grade 3 | Alive | Alive | Alive | Alive | Alive |
| Abbreviations: CHAOS, congenital high airway obstruction; ET, endotracheal; EXIT, ex utero intrapartum treatment; GA, gestational age; HIE, hypoxic ischemic encephalopathy; MRI, magnetic resonance imaging. |
| aDark gray, no; light gray, yes. |
| bET tube placed directly into the trachea. |
Interpretation

For anatomic marker analysis in the presence of fetal airway abnormalities, use of 2D MRI and SRR imaging in combination appears to provide optimum anatomic clarity while taking a similar amount of time as with 2D MRI alone. Although cognitive load is increased when SRR imaging is added, this may be a worthwhile compromise when considering the more comprehensive anatomic assessment of the fetal neck structures required for surgical planning of EXIT procedures. Reduced performance of paired imaging in terms of airway patency and confidence of diagnosis in comparison with 2D MRI alone may be explained by a natural learning curve that radiologists encounter when interpreting SRR images, given the different texture and visualization against the original MRI. Our study suggests the clinical potential of volumetric reconstruction in aiding anatomic clarity where original stacks are of good image quality. It can provide exquisite definition of fetal neck anatomy and potential involvement of the airway in the neck mass, which may facilitate surgical planning and improve perinatal outcome. A high-quality SRR crucially depends on precision of the established spatial correspondences among slices with at least 3 stacks in 3 orientations required for sufficient anatomic detail. Nevertheless, the underlying rigid motion reconstruction model limits the ability to compensate for complex motion of tissue surrounding the trachea. This highlights the importance of optimizing 2D MRI data acquisition, as the quality of the reconstruction is reliant on this.

Case selection for an EXIT procedure is important given the significant maternal and fetal risks that exist with surgery. Choosing to perform EXIT should be balanced against the likelihood of fetal airway obstruction and poor neonatal prognosis. Planning an EXIT procedure is complex as it requires collective efforts of multiple disciplines, such as fetal medicine, anaesthetics, neonatology, pediatric anaesthetics, otolaryngologic surgeons, and radiologists to manage the surgery and neonatal resuscitation. Surgical planning is dependent on imaging findings, such as the level of obstruction in CHAOS, extent of the fetal neck mass, degree of tracheal compression, and displacement of the tracheoesophageal complex. CHAOS is a rare form of tracheal or laryngeal obstruction due to atresia or stenosis. MRI has been used to localize the level of obstruction in CHAOS, aiding determination of the likelihood of EXIT procedure success, as low tracheal obstruction has been associated with failed access of the fetal airway. In our CHAOS case, 2D MRI and SRR helped define that the posterior communication

| Case | Sequence for SRR | Slice rejection, mean ± SD (range) | No. of stacks for SRR | SRR quality |
|------|-----------------|----------------------------------|----------------------|------------|
| 1    | T2 HASTE        | 1 ± 1 (0-2)                      | 5                    | 1.5        |
| 2    | T2 HASTE        | 3 ± 4 (0-10)                     | 8                    | 0.7        |
| 3    | T2 HASTE        | 1 ± 1 (0-3)                      | 8                    | 1.5        |
| 4    | T2 HASTE        | 4 ± 3 (0-6)                      | 4                    | 0³         |
| 5    | T2 HASTE        | 3 ± 2 (0-7)                      | 9                    | 0³         |
| 6    | TRUFI           | 0 ± 1 (0-1)                      | 3                    | 0³         |
| 7    | T2 HASTE        | 7 ± 4 (2-15)                     | 11                   | 1.5        |

Abbreviations: SRR, super-resolution reconstruction; T2 HASTE, T2 half-Fourier acquisition single-shot turbo spin echo; TRUFI, true fast imaging with steady state-free precession.

³Average obtained across 3 radiologists whereby 0 = lots of artifact/blur, 1 = little artifact/blur, and 2 = no artifact/blur.

³Fewer than 5 stacks are typically insufficient for obtaining good SRR quality.
of the obstruction was at the laryngeal level—detail that was not available on ultrasound examination.

**Strengths and Limitations**

Our SRR algorithm is limited, as a sufficiently small mask around the trachea is chosen to assume the approximate rigid motion in that area. This limits the region of interest, which might have affected the radiologists’ ability to identify its spatial location and assessment within the larger anatomic context. Super-resolved images may be improved in the future with a wider FOV or whole body SRR. The small number of patients in our case series may have affected comparison between SRR and 2D MRI. However, complex neck masses and CHAOS are rare, and any single tertiary institution’s experience is likely to be small. There is a possibility of bias in the third round of interpretation by radiologists. Although it is separated by a 2-week interval, it is plausible that providers had image recall, which may have influenced their speed and

![Figure 4. Bland-Altman plot illustrating differences in airway patency confidence of 3 radiologists using 2D MRI alone vs SRR imaging alone, whereby 0 on the y axis = equal confidence. 2D, 2-dimensional; LOA, limits of agreement; MRI, magnetic resonance imaging; SRR, super-resolution reconstruction.](image)

**Figure 4.** Bland-Altman plot illustrating differences in airway patency confidence of 3 radiologists using 2D MRI alone vs SRR imaging alone, whereby 0 on the y axis = equal confidence. 2D, 2-dimensional; LOA, limits of agreement; MRI, magnetic resonance imaging; SRR, super-resolution reconstruction.

![Figure 5. Anatomic clarity average of the 3 radiologists (y-axis). This is illustrated for each of the 7 cases of airway obstruction and the total average (x-axis). Values are presented as mean (95% CI). 2D, 2-dimensional; MRI, magnetic resonance imaging; SRR, super-resolution reconstruction.](image)

**Figure 5.** Anatomic clarity average of the 3 radiologists (y-axis). This is illustrated for each of the 7 cases of airway obstruction and the total average (x-axis). Values are presented as mean (95% CI). 2D, 2-dimensional; MRI, magnetic resonance imaging; SRR, super-resolution reconstruction.

![Figure 6. Bland-Altman plots illustrating anatomic clarity average differences with 2D MRI alone vs SRR alone (left) and 2D MRI vs paired imaging (right). 0 on the y-axis = equal confidence. 2D, 2-dimensional; LOA, limits of agreement; MRI, magnetic resonance imaging; SRR, super-resolution reconstruction.](image)

**Figure 6.** Bland-Altman plots illustrating anatomic clarity average differences with 2D MRI alone vs SRR alone (left) and 2D MRI vs paired imaging (right). 0 on the y-axis = equal confidence. 2D, 2-dimensional; LOA, limits of agreement; MRI, magnetic resonance imaging; SRR, super-resolution reconstruction.
preference for combined SRR and 2D MRI. It is additionally important to note that the involved radiologists had no prior background in interpretation of SRR MRI volumes of the fetal neck and airway. The inevitable learning curve associated with use of this novel technology may therefore have an impact on study results.

**Conclusion**

For fetal neck mass assessment, the addition of SRR to 2D MRI does not increase fetal airway patency diagnostic accuracy but does provide improved anatomic information. This may improve case selection for EXIT procedures and enhance surgical planning by ensuring that appropriate clinical teams and equipment are available. Additional validation with a larger data set is necessary to support the reconstruction fidelity, and SRR images should be considered supportive information and not a replacement of the original 2D MRI stacks.

**Acknowledgments**

We thank all the patients who participated in this research.

**Authorship Contributions**

Nada Mufti, designed the study, analyzed the data, wrote the first draft, and corrected the final version of the manuscript; Michael Ebner, developed the super-resolution reconstruction algorithm and assisted in the experimental design; Premal Patel, refined the study design and randomization of data for experiments; Michael Aertsen, trained radiologist who carried out all 3 experimental rounds and helped in refining the study design and determining the field of view prior to commencement of the experiments; Trevor Gaunt, trained radiologist who carried out all 3 experimental rounds; Paul D. Humphries, trained radiologist who carried out all 3 experimental rounds; Fonteini Emmananouella Bredaki, assisted in the clinical care and data collection; Richard Hewitt, provided advice on otolaryngologic surgical content and laryngoscopy images;
Disclosures

Competing interests: None.

Sponsorships: None.

Funding source: This work was supported by the Guided Instrumentation of Fetal Therapy and Surgery project, funded by the Wellcome Trust (203148/Z/16/Z, 203145/Z/16/Z, WT101957) and Engineering and Physical Sciences Research Council (NS/A000049/1, NS/A000050/1, NS/A000027/1, EP/L016478/1). Sebastien Ourselin is the principal investigator on this grant, and Anna L. David, Jan Deprest, Tom Vercauteren, and Andrew Melbourne are coinvestigators. Nada Mufti is funded with support from Anna L. David, Jan Deprest, Sebastien Ourselin, and Andrew Melbourne. Nada Mufti, supported and supervised this work since conception; Sebastien Ourselin, supported and supervised this work since conception; Jan Deprest, supported and supervised this work since conception; Tom Vercauteren, supervised this work since conception; and Andrew Melbourne, supported and supervised this work since conception; Anna L. David, supported and supervised this work since conception.

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Supplemental Material

Additional supporting information is available at http://journals.sagepub.com/doi/suppl/10.1177/2473974X18[article ID]

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