The latest on perinatal post-mortem ultrasound

G. Gorincour, A. Bouachba, L. Tuchtan, MD Piercecchi-Marti, **M. Ducloyer**

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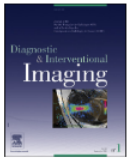

ORIGINAL ARTICLE / *Forensic medicine*

Diagnosis of congenital abnormalities with post-mortem ultrasound in perinatal death

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KEYWORDS
Post-mortem imaging;
Fetal ultrasound;
Termination of pregnancy;
Intrauterine fetal death;
Autopsy

Abstract
Purpose: To determine the sensitivity and specificity of post-mortem ultrasound in the diagnosis of major congenital abnormalities of fetuses using conventional autopsy as the standard of reference.
Material and methods: All fetuses coming from terminations of pregnancy or intrauterine fetal deaths in a single institution were included. A total of 75 fetuses were included during the study period. The results of post-mortem ultrasound examinations were compared to those of conventional autopsy that served as standard of reference.

- Prospective study
- Single referral institution
- 11 months
- Consecutive cases of TOP and IUFD
  - Body storage 4°C, < 60 hours
  - Whole-body US
  - Full autopsy as Gold Standard
  - US / Autopsy blinded to each other

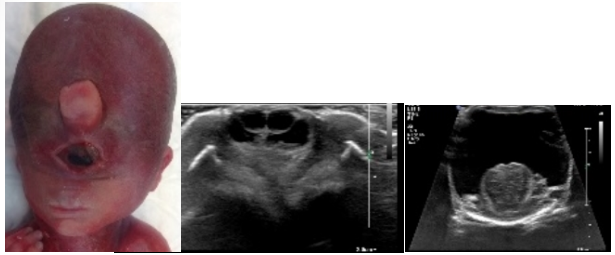
- Whole-body US (average 20 min)
  - One experienced perinatal radiologist
  - Blind form prenatal data
  - Supine position
    - Brain / fontanelles
    - Chest, abdomen, pelvis
    - Bones
  - Prone position
    - Kidneys, adrenals, spine

- Autopsy
  - 3 experienced perinatal pathologists
  - SOFFOET recommendations
  - Aware of prenatal data
  - Full
    - External
    - Macro
    - Micro

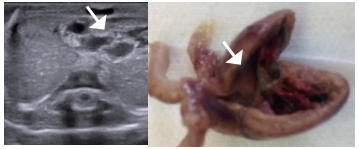
- Autopsy
  - 3 experienced perinatal pathologists
  - SOFFOET recommendations
  - Aware of prenatal data
  - Full
    - External
    - Macro
    - Micro

- 75 cases included
  - TOP 79 %
  - IUFD 21 %
  - Mean GA : 24,4 (15-39)
  - WBPMUS feasible 100 %

Abnormal organ	US	Autopsy
Brain	22	27
Lung	6	8
Heart	3	24
Digestive	2	3
Urinary	9	10
Spine	10	10
Bones	5	5
TOTAL	**57**	**87**

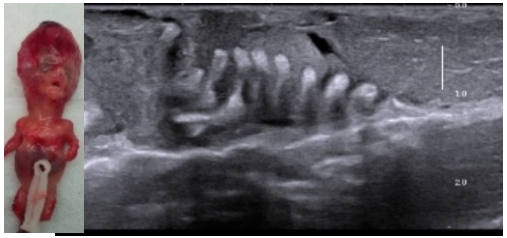


25 WG, holoprosencephaly, cyclops

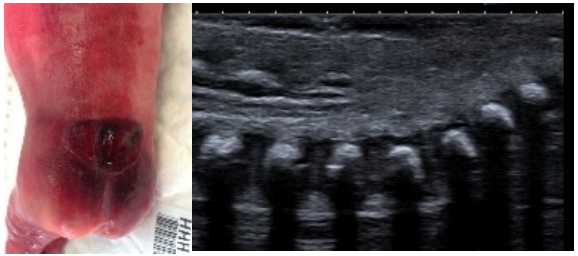


21 WG, VSD

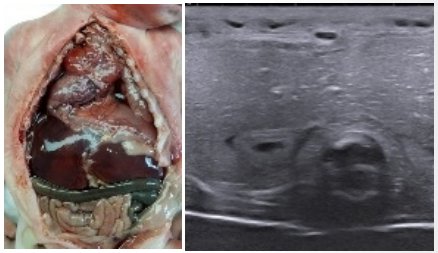
BRAIN		
	Se	95.24 %
	Sp	88.89 %
	PPV	76.92 %
	NPV	97.96 %



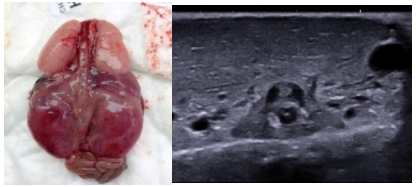
16 WG, osteogenesis imperfecta



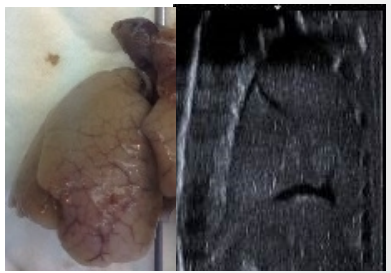
24 WG, spina bifida



30 WG, right isomerism



16 WG, polycystic kidney disease



24 WG, bilobed right lung

- Feasibility 100 %
- Variable difficulty
  - Maceration
    - +++ Brain
  - Small GA
- Lack of contrast resolution : +++ Brain

WB-PM-US as a first line screening tool in perinatal death ?

- NPV 100 %
  - Except Brain 97 %
    - Dedicated MRI for brain ?
- Very low PPV for Heart
  - 15% … Dedicated Angio CT ?

And then ?

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Postmortem fetal imaging: prospective blinded comparison of two-dimensional ultrasound with magnetic resonance imaging

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Conclusions *PM-MRI performed significantly better than PM-US in this unselected population, due mainly to a lower non-diagnostic rate. PM-MRI should remain the first-line imaging investigation for perinatal autopsy, but PM-US could be considered if MRI is not available, albeit with a higher non-diagnostic rate. Copyright © 2019 ISUOG. Published by John Wiley & Sons Ltd.*

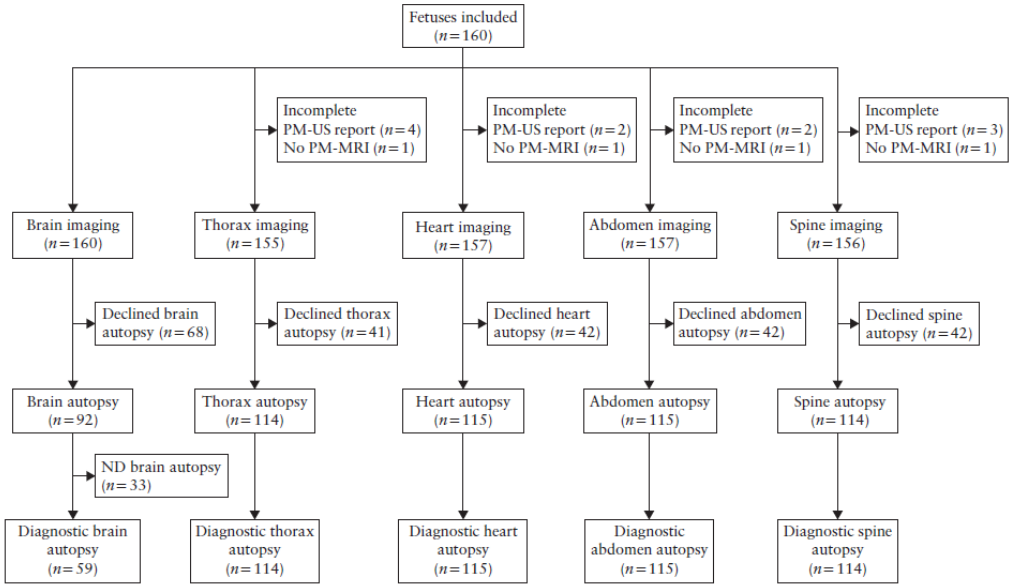

Figure 1 STARD flow diagram summarizing cases included in study which underwent both postmortem ultrasound (PM-US) and postmortem magnetic resonance imaging (PM-MRI). ND, non-diagnostic.

Table 2 Comparison of diagnostic accuracy between postmortem ultrasound imaging (PM-US) and postmortem magnetic resonance imaging (PM-MRI) when both techniques were diagnostic, using autopsy as gold standard

	PM-US	*PM-MRI*	P
Brain ($n=49$)			
Sensitivity	70.8 (17/24) [48.9–87.4]	79.2 (19/24) [57.9–92.0]*	NS
Specificity	100.0 (25/25) [86.3–100]*	84.0 (21/25) [63.9–95.5]*	NS
Concordant with autopsy	85.7 (42/49) [72.8–94.1]*	81.6 (40/49) [68.0–91.2]*	NS
Discordant with autopsy	14.3 (7/49) [5.9–27.2]*	18.4 (9/49) [8.8–32.0]*	NS
Thorax ($n=93$)			
Sensitivity	31.8 (7/22) [13.9–54.9]*	40.9 (9/22) [20.7–63.7]*	NS
Specificity	98.6 (70/71) [95.9–100]*	98.6 (70/71) [95.9–100]*	NS
Concordant with autopsy	82.8 (77/93) [75.1–90.5]	84.9 (79/93) [77.7–92.2]	NS
Discordant with autopsy	17.2 (16/93) [9.5–24.9]	15.1 (14/93) [7.8–22.3]	NS
Heart ($n=80$)			
Sensitivity	69.6 (16/23) [47.1–86.8]*	65.2 (15/23) [42.7–83.6]*	NS
Specificity	93.0 (53/57) [83.0–98.1]*	100.0 (57/57) [93.7–100]*	NS
Concordant with autopsy	86.3 (69/80) [78.7–93.8]	90.0 (72/80) [81.2–95.6]*	NS
Discordant with autopsy	13.8 (11/80) [6.2–21.3]	10.0 (8/80) [4.4–18.8]*	NS
Abdomen ($n=88$)			
Sensitivity	61.5 (16/26) [40.6–79.8]*	57.7 (15/26) [38.7–76.7]	NS
Specificity	85.5 (53/62) [74.2–93.1]*	91.9 (57/62) [82.2–97.3]*	NS
Concordant with autopsy	79.5 (70/88) [71.1–88.0]	81.8 (72/88) [73.8–89.9]	NS
Discordant with autopsy	20.5 (18/88) [12.0–28.9]	18.2 (16/88) [10.1–26.2]	NS
Spine ($n=113$)			
Sensitivity	83.3 (5/6) [35.9–99.6]*	83.3 (5/6) [35.9–99.6]*	NS
Specificity	97.2 (104/107) [92.0–99.4]*	100.0 (107/107) [96.6–100]*	NS
Concordant with autopsy	96.5 (109/113) [91.2–99.0]*	99.1 (112/113) [95.2–100]*	NS
Discordant with autopsy	3.5 (4/113) [9.7–8.8] *	0.9 (1/113) [0.0–4.8]*	NS

Data are given as % (n/N) [95% CI of %]. *Exact CI. NS, not significant.

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Table 1 Comparison of rates of non-diagnostic examination between postmortem ultrasound imaging (PM-US) and postmortem magnetic resonance imaging (PM-MRI)

Variable	Fetuses	Non-diagnostic PM-US	Non-diagnostic PM-MRI
Brain			
Overall	160 (100)	43 (26.9)**	7 (4.4)**
Cause of death			
Stillbirth	28 (17.5)	17 (60.7)**	5 (17.9)**
TOP	109 (68.1)	21 (19.3)**	1 (0.9)**
Miscarriage	23 (14.4)	5 (21.7)	1 (4.3)
Maceration			
Yes	36 (22.5)	16 (44.4)*	7 (19.4)*
No	124 (77.5)	27 (21.8)**	0 (0)**
Gestational age			
< 20 weeks	27 (16.9)	10 (37.0)*	3 (11.1)*
≥ 20 weeks	133 (83.1)	33 (24.8)**	4 (3.0)**
Thorax			
Overall	155 (100)	27 (17.4)**	8 (5.2)**
Cause of death			
Stillbirth	26 (16.8)	8 (30.8)	5 (19.2)
TOP	106 (68.4)	17 (16.0)**	2 (1.9)**
Miscarriage	23 (14.8)	2 (8.7)	1 (4.3)
Maceration			
Yes	32 (20.6)	10 (31.3)*	3 (9.4)*
No	123 (79.4)	17 (13.8)*	5 (4.1)*
Gestational age			
< 20 weeks	27 (17.4)	10 (37.0)	7 (25.9)
≥ 20 weeks	128 (82.6)	17 (13.3)**	1 (0.8)**
Heart			
Overall	157 (100)	48 (30.6)**	6 (3.8)**
Cause of death			
Stillbirth	27 (17.2)	13 (48.1)	1 (3.7)
TOP	107 (68.2)	31 (29.0)**	1 (0.9)**
Miscarriage	23 (14.6)	4 (17.4)	1 (4.3)
Maceration			
Yes	34 (21.7)	19 (55.9)**	4 (11.8)**
No	123 (78.3)	29 (23.6)**	2 (1.6)**
Gestational age			
< 20 weeks	27 (17.2)	11 (40.7)	5 (18.5)
≥ 20 weeks	130 (82.8)	37 (28.5)**	1 (0.8)**
Abdomen			
Overall	157 (100)	37 (23.6)**	5 (3.2)**
Cause of death			
Stillbirth	27 (17.2)	10 (37.0)	3 (11.1)
TOP	107 (68.2)	20 (18.7)**	1 (0.9)**
Miscarriage	23 (14.6)	7 (30.4)*	1 (4.3)*
Maceration			
Yes	34 (21.7)	9 (26.5)	3 (8.8)
No	123 (78.3)	28 (22.8)**	2 (1.6)**
Gestational age			
< 20 weeks	27 (17.2)	9 (33.3)	4 (14.8)
≥ 20 weeks	130 (82.8)	28 (21.5)**	1 (0.8)**
Spine			
Overall	156 (100)	2 (1.3)	0 (0.0)

Table 3 Abnormalities identified at autopsy not seen on diagnostic postmortem ultrasound imaging (PM-US) and/or postmortem magnetic resonance imaging (PM-MRI)

Anatomical region	Diagnosis missed at: Both PM-US and PM-MRI — n	Diagnosis	PM-US but not PM-MRI — n	Diagnosis	PM-MRI but not PM-US — n	Diagnosis
Brain	1	Thin lateral ventricular wall from probable ventriculomegaly	2	Tumor	0	—
	2	Increased folding by gyri without sign of micropolygyria				
	1	Olfactory bulb agenesis				
	1	Thin corpus callosum				
Thorax	10	Abnormal lung lobulations	1	Absent thymus	0	—
	1	Enlarged thymus	1	Esophageal atresia with fistula in trachea		
	2	Hypoplastic lungs				
Heart	1	Atrial septal defect	1	Tetralogy of Fallot	1	Small rhabdomyoma confirmed by histology
	1	Transposition of the great vessels with ventricular septal defect			1	Pulmonary artery stenosis
	3	Dilated cardiac cavities				
	1	Increased cardiac weight				
Abdomen	3	Meckel's diverticulum	1	Volvulus	1	Asplenia
	2	Malrotation				
	1	Abnormal organ volume				
	3	Polysplenia/asplenia				
	1	Bowel agenesis/absence of anus				
Spine	1	Open spina bifida	0	—	0	—

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ORIGINAL ARTICLE

Impact of the delay between fetal death and delivery on the success of postmortem ultrasound following termination of pregnancy

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ABSTRACT

Objective: To evaluate the impact of the delay between fetal death and delivery on the non-diagnostic rates of post-mortem ultrasound (PM-US), following the termination of pregnancy (TOP).

Methods: We reviewed 204 cases of fetal two-dimensional PM-US performed in our center as part of a post-mortem imaging research program, over the last 5 years. Informed consent was obtained from the parents for all cases. PM-US was performed and reported according to a pre-specified template with operators blinded to the prenatal diagnosis. In order to calculate the precise delay between the fetal death and the delivery, we included 107 fetal TOP's $\geq$ 20 weeks of gestational age (GA), where feticide was performed using an injection of lidocaine 2% prior to induction of labor. Logistic regression analysis was conducted to analyze the impact of delay between fetal death and delivery (in hours), the GA at TOP (in weeks) and the method of feticide (intracardiac versus intraumbilical injection) on the PMUS nondiagnostic rates.

Results: The delay between fetal death and delivery increased the nondiagnostic rate of PM-US for cerebral examinations (OR: 1.04, IC 95%: 1.01–1.08, $p < .05$). For PM-US cardiac examination, the delay did not influence the nondiagnostic rate. However, GA (OR: 1.25, IC 95%: 1.10–1.46, $p < .01$) and feticide with intracardiac injection (OR: 4.29, IC 95%: 1.68–12.02, $p < .01$) were associated with higher nondiagnostic rates. For noncardiac thoracic and abdominal examinations, none of the studied variables influenced the nondiagnostic rate.

Conclusion: The success rate of cerebral PM-US was influenced by the delay between fetal death and delivery, suggesting a possible advantage of performing the feticide closer to the delivery where the examination of the brain is planned. For cardiac abnormalities, feticide by intraumbilical, rather than intracardiac injection improves diagnostic rates of cardiac PM-US.

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KEYWORDS
Postmortem; postmortem-ultrasound; termination of pregnancy; virtual autopsy; maceration

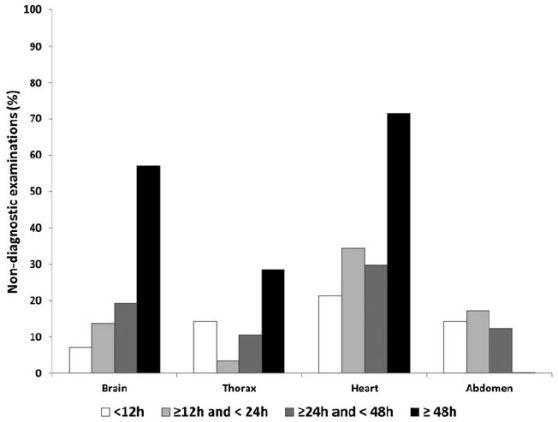

Figure 2. Correlation of PM-US nondiagnostic rate and time interval between fetal death and the delivery for each anatomical region. The time interval was arbitrarily divided into 4 groups: < 12 h, ≥ 12 h and < 24 h, ≥ 24 and < 48 h, and ≥ 48 h between fetal death and delivery.

Table 1. Logistic regression analysis evaluating various factors associated with nondiagnostic rate of PM-US.

	Univariate analysis		Multivariate analysis	
	OR (CI 95%)	*p*	OR (CI 95%)	*p*
Brain				
Delay	1.04 (1.01–1.08)	<.05	1.04 (1.01–1.08)	<.05
GA	1.16 (1.01–1.33)	<.05	1.14 (0.99–1.33)	NS
Feticide method				
Intracardiac injection	1.68 (0.63–4.52)	NS		
Intraumbilical injection	1			
Thorax				
Delay	1.03 (0.99–1.07)	NS		
GA	1.10 (0.93–1.30)	NS		
Feticide method				
Intracardiac injection	1.25 (0.36–4.38)	NS		
Intraumbilical injection	1			
Heart				
Delay	1.02 (0.99–1.05)	NS		
GA	1.18 (1.05–1.33)	<.01	1.25 (1.10–1.46)	<.01
Feticide method				
Intracardiac injection	2.68 (1.16–6.22)	<.05	4.29 (1.68–12.02)	<.01
Intraumbilical injection	1		1	
Abdomen				
Delay	1.00 (0.99–1.01)	NS		
GA	1.06 (0.91–1.24)	NS		
Feticide method				
Intracardiac injection	0.52 (0.16–1.67)	NS		
Intraumbilical injection	1			

OR: odds ratio; CI: confidence interval; GA: gestational age; NS: not significant.

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Feasibility of INTACT (INcisionless TArgeted Core Tissue) biopsy procedure for perinatal autopsy

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Results *Thirty fetuses underwent organ sampling. Mean gestational age was 30 weeks (range, 18–40 weeks) and mean delivery-to-biopsy interval was 12 days (range, 6–22 days). The overall biopsy success rate was 153/201 (76.1%) samples, with the success rates in individual organs being highest for the heart and lungs (93% and 91%, respectively) and lowest for the spleen (11%). Excluding splenic samples, the biopsy success rate was 150/173 (86.7%). Histological abnormalities were found in 4/201 (2%) samples, all of which occurred in the lungs and kidneys of a fetus with pulmonary hypoplasia and multicystic kidney disease.*

Conclusions *Incisionless ultrasound-guided organ biopsy using the INTACT procedure is feasible, with an overall biopsy success rate of over 75%. This novel technique offers the ideal combination of an imaging-led autopsy with organ sampling for parents who decline the conventional invasive approach.* © *2019 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of the International Society of Ultrasound in Obstetrics and Gynecology.*

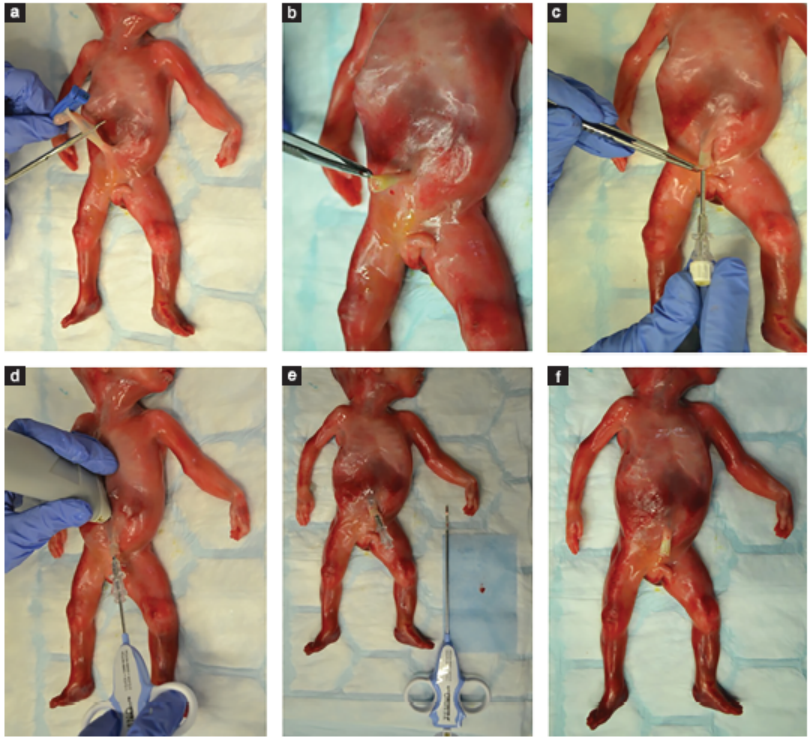

Figure 1 Images demonstrating steps of INcisionless TArgeted Core Tissue (INTACT) biopsy procedure, performed in 20-week fetus. (a) After review of autopsy consent form, case identification and ultrasound examination, umbilical clamp is removed if possible, and umbilical cord cut to length of < 2 cm. (b,c) 13.5-G coaxial needle and trocar are inserted via umbilical cord. (d) Once needle is identified on ultrasound to be intra-abdominal, ultrasound is used to guide it towards intended target organ; trocar is then removed and 14-G Temno biopsy needle is inserted through coaxial needle. (e) Three cores are obtained per target organ, and tissue samples are placed on blue blotting paper. (f) After procedure, there are no incisions or visible damage to body.

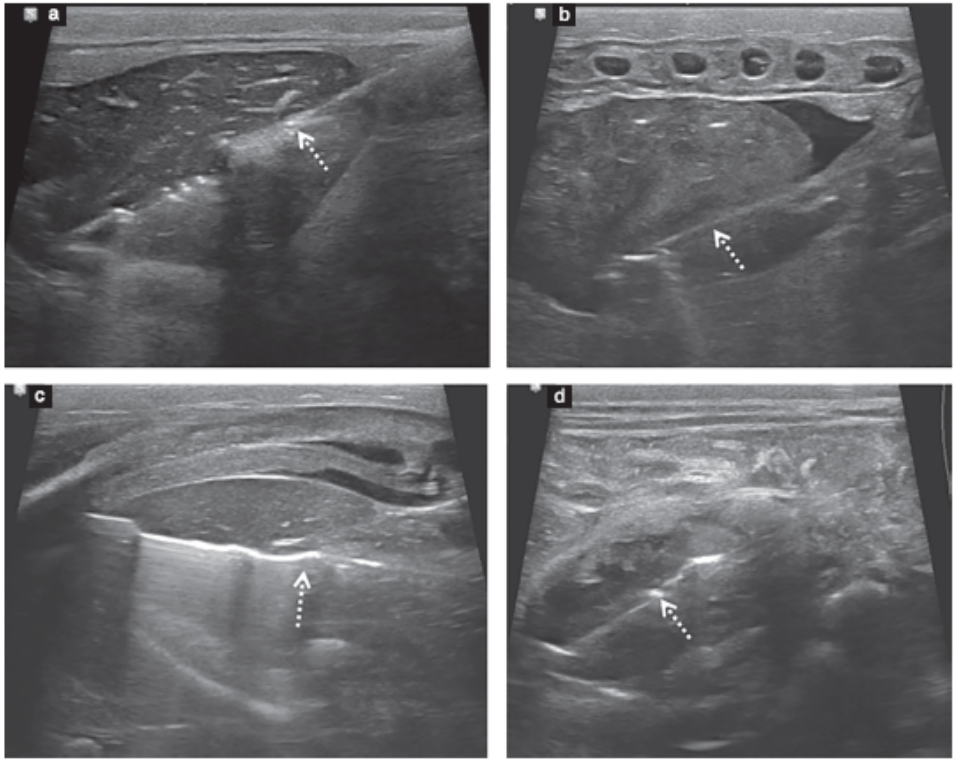

Figure 2 Postmortem ultrasound images in 35-week fetus during INcisionless TArgeted Core Tissue (INTACT) biopsy procedure. (a) Longitudinal view of liver. (b) Longitudinal view of heart. (c) Longitudinal view of spleen. (d) Transverse view of right kidney. Biopsy needle (dotted arrow) is seen clearly on all images.

The latest on perinatal post-mortem ultrasound / Gorincour / ESPR 2022

Fetal postmortem imaging: an overview of current techniques and future perspectives

Xin Kang, MD, PhD; Andrew Carlin, MD; Mieke M. Cannie, MD, PhD; Teresa Cos Sanchez, MD; Jacques C. Jani, MD, PhD

Fetal loss owing to miscarriage, stillbirth, or termination of pregnancy is tragic for any family. Therefore, determining the cause of death or diagnosis of fetal disease is essential to better understand and prevent such events, in addition to evaluating the risk of recurrence for future pregnancies.[1,2] Routine prenatal diagnosis has developed rapidly in the past 10 years because of improvements in prenatal imaging[3–12] and invasive and noninvasive prenatal genetic testing,[13–28] which has led to earlier and more frequent diagnoses of fetal structural abnormalities and syndromic diseases.[4,29–33] Consequently, the current usefulness of fetal postmortem examinations could be questioned. However, although the importance of the educational role of autopsy is undervalued,[34] recent series have shown that invasive autopsy provided additional findings in 16%–22% of cases in developed countries,[29,30,35] including 1% of major findings, and revised the prenatal diagnosis in 40% of cases in developing countries,[36] indicating that fetal post-

Fetal death because of miscarriage, unexpected intrauterine fetal demise, or termination of pregnancy is a traumatic event for any family. Despite advances in prenatal imaging and genetic diagnosis, conventional autopsy remains the gold standard because it can provide additional information not available during fetal life in up to 40% of cases and this by itself may change the recurrence risk and hence future counseling for parents. However, conventional autopsy is negatively affected by procedures involving long reporting times because the fetal brain is prone to the effect of autolysis, which may result in suboptimal examinations, particularly of the central nervous system. More importantly, fewer than 50%–60% of parents consent to invasive autopsy, mainly owing to the concerns about body disfigurement.

Consequently, this has led to the development of noninvasive perinatal virtual autopsy using imaging techniques. Because a significant component of conventional autopsy involves the anatomic examination of organs, imaging techniques such as magnetic resonance imaging, ultrasound, and computed tomography are possible alternatives. With a parental acceptance rate of nearly 100%, imaging techniques as part of postmortem examination have become widely used in recent years in some countries.

Postmortem magnetic resonance imaging using 1.5-Tesla magnets is the most studied technique and offers an overall diagnostic accuracy of 77%–94%. It is probably the best choice as a virtual autopsy technique for fetuses >20 weeks' gestation. However, for fetuses <20 weeks' gestation, its performance is poor. The use of higher magnetic resonance imaging magnetic fields such as 3-Tesla may slightly improve performance. Of note, in cases of fetal maceration, magnetic resonance imaging may offer diagnoses in a proportion of brain lesions wherein conventional autopsy fails. Postmortem ultrasound examination using a high-frequency probe offers overall sensitivity and specificity of 67%–77% and 74%–90%, respectively, with the advantage of easy access and affordability. The main difference between postmortem ultrasound and magnetic resonance imaging relates to their respective abilities to obtain images of sufficient quality for a confident diagnosis. The nondiagnostic rate using postmortem ultrasound ranges from 17% to 30%, depending on the organ examined, whereas the nondiagnostic rate using postmortem magnetic resonance imaging in most situations is far less than 10%. For fetuses ≤20 weeks' gestation, microfocus computed tomography achieves close to 100% agreement with autopsy and is likely to be the technique of the future in this subgroup. The lack of histology has always been listed as 1 limitation of all postmortem imaging techniques. Image-guided needle tissue biopsy coupled with any postmortem imaging can overcome this limitation.

In addition to describing the diagnostic accuracy and limitations of each imaging technology, we propose a novel, stepwise diagnostic approach and describe the possible application of these techniques in clinical practice as an alternative or an adjunct or for triage to select cases that would specifically benefit from invasive examination, with the aim of reducing parental distress and pathologist workload. The widespread use of postmortem fetal imaging is inevitable, meaning that hurdles such as specialized training and dedicated financing must be overcome to improve access to these newer, well-validated techniques.

Key words: autopsy, congenital anomalies, diagnosis, management, micro-CT, minimally invasive, MRI, postmortem, stillbirth, termination, ultrasound, virtual autopsy

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The authors report no conflict of interest.

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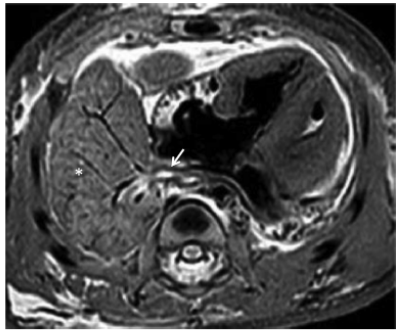
FIGURE 5
Pulmonary hypoplasia at 31 weeks



Axial views of 3-T postmortem magnetic resonance imaging of the thorax of a fetus of 31-week gestational age terminated for pulmonary hypoplasia showing normal right lung (*) with right main bronchus (*arrow*) and agenesis of the left lung and left main bronchus.

Kang. Fetal postmortem imaging. Am J Obstet Gynecol 2020.

demonstrates higher quality imaging with better tissue contrast than 1.5-T MRI. This enabled 3-T MRI to provide a higher success rate of about 60% than success rate of less than 10% for 1.5-T.[104] However, the overall accuracy obtained is only 55%, and the diagnostic rate for fetuses ≤16 weeks GA is even worse. Furthermore, our experience of staining fetuses with gadolinium-based 3-T MRI was also unsuccessful.[112] These results suggest that spatial resolution is suboptimal when using 1.5-T and 3-T MRIs for the examination of small fetuses. High-field MRI at 9.4-T or 7-T has shown higher sensitivity and specificity in small sample studies.[78,83,111] However, access to these machines is currently restricted because they are only available in relatively few centers for research purposes only. The US Food and Drug Administration and the European Union have recently approved a 7-T MRI device (Magnetom Terra, Siemens Medical Solution Inc) for examination of the head and extremities. We anticipate that access to these newer 7-T MRI machines will progressively improve, making their use in routine clinical practice a realistic possibility in the future. However, further studies with large sample sizes are needed to explore the use of these powerful machines for fetal postmortem examination, as all previously published data on fetal high-field MRI used experimental machines with small-bore diameters of 20–30 cm.[78,83,111]

Postmortem Ultrasound

Ultrasound is less expensive and more widely available even in developing countries compared with MRI. High-frequency transducers provide high-resolution images particularly when the targeted organ is near, as is the case in the postmortem setting, wherein the fetus is examined by direct contact with the transducer (Figure 1).

Furness et al[124] first described almost 30 years ago a technique for performing postmortem ultrasound on fetal viscera in a water bath or after gelatin preparation. Only recently has a feasibility study been conducted on fetuses. This single-reporter unblinded study showed a sensitivity of 86%–91% and a specificity of 87%–95% for postmortem ultrasound using transducers at a maximum of between 9 and 18 MHz.[125] However, when postmortem ultrasound was performed blindly and by multiple operators, it demonstrated lower accuracy with overall sensitivities and specificities of 67%–77% and 74%–90%, respectively (Table 3).[110,126,127]

Abdominal organs, in particular the kidneys, are the easiest to assess with postmortem ultrasound, which encourages its use for future ultrasound-guided postmortem biopsy studies (Figures 2–4). Conversely, cardiac anatomy is more difficult to assess because postmortem intracardiac blood clots have echogenicities very similar to those of the myometrium, and artifacts arising from the presence of air in the cardiac chambers are frequently encountered after feticide by intracardiac injections (Figure 6).[128,129] An additional limitation of postmortem ultrasound is its higher nondiagnostic examinations rate of 17%–30% than the 3%–5% nondiagnostic rate of postmortem MRI for fetuses >20 weeks GA.[110] Finally, discrepancies between single-operator and multiple-operator studies may indicate that postmortem ultrasound performance is operator dependent and that the learning effect should be investigated in further studies.

Postmortem Computed Tomography Scan and X-Ray Examination

Routine fetal postmortem x-ray examinations or babygrams are routinely performed as an adjunct to invasive autopsy in many centers. However, this practice has been proven to be neither diagnostically useful nor cost-effective in a retrospective study.[130] It should only be used in selected cases of prenatally suspected skeletal abnormalities or when a pathologist needs to include or exclude

Postmortem Ultrasound

Ultrasound is less expensive and more widely available even in developing countries compared with MRI. High-frequency transducers provide high-resolution images particularly when the targeted organ is near, as is the case in the postmortem setting, wherein the fetus is examined by direct contact with the transducer (Figure 1).

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Diagnostic accuracy of postmortem ultrasound *vs* postmortem 1.5-T MRI for non-invasive perinatal autopsy

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Results *During the study period, 136 cases underwent both PM-US and PM-MRI, of which 88 (64.7%) also underwent autopsy. There was no significant difference in the rates of concordance with autopsy between the two modalities for overall diagnosis (PM-US, 86.4% (95% CI, 77.7–92.0%) vs PM-MRI, 88.6% (95% CI, 80.3–93.7%)) or in the sensitivities and specificities for individual anatomical regions. There were more non-diagnostic PM-US than PM-MRI examinations for the brain (22.8% vs 3.7%) and heart (14.7% vs 5.1%). If an 'imaging-only' autopsy had been performed, PM-US would have achieved the same diagnosis as 1.5-T PM-MRI in 86.8% (95% CI, 80.0–91.5%) of cases, with the highest rates of agreement being for spine (99.3% (95% CI, 95.9–99.9%)) and cardiac (97.3% (95% CI, 92.4–99.1%)) findings and the lowest being for brain diagnoses (85.2% (95% CI, 76.9–90.8%)).*

Conclusion *Although there were fewer non-diagnostic cases using PM-MRI than for PM-US, the high concordance rate for overall diagnosis suggests that PM-US could be used for triaging cases when PM-MRI access is limited or unavailable.* © *2020 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

Table 2 Postmortem ultrasound (PM-US) and magnetic resonance imaging (PM-MRI) diagnostic accuracy for individual body systems, all body systems summated and overall diagnoses, using autopsy as reference standard

	TP	*FP*	*FN*	*TN*	*ND imaging*	*ND autopsy*	*No imaging*	*No autopsy*	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*Concordance (%)*
Brain PM-US	7	0	1	11	31	5	3	105	87.5 (52.9–97.8)	100 (74.1–100)	100 (64.6–100)	91.7 (64.6–98.5)	94.7 (75.4–99.1)
Brain PM-MRI	10	0	2	14	5	5	0	105	83.3 (55.2–95.3)	100 (78.5–100)	100 (72.2–100)	87.5 (64.0–96.5)	92.3 (75.9–97.9)
Cardiac PM-US	4	1	4	64	20	3	0	48	50.0 (21.5–78.5)	98.5 (91.8–99.7)	80.0 (37.6–96.4)	94.1 (85.8–97.7)	93.2 (84.9–97.0)
Cardiac PM-MRI	9	1	2	69	7	3	1	48	81.8 (52.3–94.9)	98.6 (92.3–99.7)	90.0 (59.6–98.2)	97.2 (90.3–99.2)	96.3 (89.7–98.7)
Thoracic PM-US	6	1	9	71	0	1	0	48	40.0 (19.8–64.3)	98.6 (92.5–99.8)	85.7 (48.7–97.4)	88.8 (80.0–94.0)	88.5 (80.1–93.6)
Thoracic PM-MRI	11	3	4	68	0	1	1	48	73.3 (48.0–89.1)	95.8 (88.3–98.6)	78.6 (52.4–92.4)	94.4 (86.6–97.8)	91.9 (84.1–96.0)
Abdominal PM-US	14	3	0	68	0	3	0	48	100 (78.5–100)	95.8 (88.3–98.6)	82.4 (59.0–93.8)	100 (94.7–100)	96.5 (90.1–98.8)
Abdominal PM-MRI	14	5	0	65	1	3	1	48	100 (78.5–100)	92.9 (84.3–96.9)	73.7 (51.2–88.2)	100 (94.4–100)	94.0 (86.8–97.4)
Total body systems PM-US	31	5	14	214	51	12	3	249	68.9 (54.3–80.5)	97.7 (94.8–99.3)	86.1 (71.3–93.9)	93.9 (90.0–96.3)	92.8 (89.0–95.3)
Total body systems PM-MRI	44	9	8	216	13	12	3	249	84.6 (72.5–92.0)	96.0 (92.6–97.9)	83.0 (70.8–90.8)	96.4 (93.1–98.2)	93.9 (90.4–96.1)
Overall diagnosis* PM-US	32	3	9	44	0	0	0	48	78.0 (63.3–88.0)	93.6 (82.8–97.8)	91.4 (77.6–97.0)	83.0 (70.8–90.8)	86.4 (77.7–92.0)
Overall diagnosis* PM-MRI	37	6	4	41	0	0	0	48	90.2 (77.5–96.1)	87.2 (74.8–94.0)	86.0 (72.7–93.4)	91.1 (79.3–96.5)	88.6 (80.3–93.7)

Values in parentheses are 95% CI. There were no statistically significant differences in diagnostic accuracy between two imaging modalities.
*Overall diagnosis refers to major pathology identified as cause of perinatal death. FN, false negative; FP, false positive; ND, non-diagnostic; NPV, negative predictive value; PPV, positive predictive value; TN, true negative; TP, true positive.

Original Investigation

Postmortem Assessment of Isolated Congenital Heart Defects Remains Essential Following Termination of Pregnancy

Pediatric and Developmental Pathology
2021, Vol. 24(5) 422–429


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Camilla Struksnæs[1], Harm-Gerd K Blaas[1,2], Sturla H Eik-Nes[1,2], Eva Tegnander[1,2], and Christina Vogt[1,3]

Abstract

Objectives: To investigate the correlation between prenatal ultrasound (US) and autopsy findings in pregnancies terminated due to isolated congenital heart defects (CHDs), including CHDs associated with heterotaxy syndrome.

Materials and methods: The material consists of 67 fetuses with prenatally detected isolated CHDs or CHDs associated with heterotaxy syndrome at a tertiary center in Norway between 1985 and 2014. The main CHDs were categorized into subdiagnoses of CHDs in accordance with ICD-10. The US and autopsy findings were categorized according to degree of concordance.

Results: Gestational age at termination was 12 + 0–22 + 6 weeks. Hypoplastic left heart syndrome was the most common main diagnosis among the 67 fetuses (32.8%). There was full agreement between US and autopsy findings in 97.4% (222/228) of all subdiagnoses. The discrepant findings in three fetuses had no influence on the decision to terminate the pregnancy.

Conclusions: The correlation was high between prenatal US and postmortem findings in fetuses with isolated CHDs. Meticulous assessment of cardiac anatomy is particularly necessary when the decision to terminate relies on isolated CHDs. The trend of earlier termination challenges verification of diagnoses at autopsy. Consequently, the fetus should be examined at a tertiary center with fetal medicine specialists, pediatric cardiologists and perinatal pathologists.

Table 2. Main Diagnosis Based on Autopsy Results in 67 Pregnancies Terminated due to Isolated CHDs.

Main Diagnosis	n	%
HLHS	22	32.8
Left atrial isomerism	6	8.9
DORV simple	5	7.4
Tricuspid atresia complex	5	7.4
Truncus arteriosus	4	6.0
TGA complex	3	4.5
DILV complex	3	4.5
HRHS	2	3.0
AVSD simple	2	3.0
TGA simple	2	3.0
Mitral atresia/stenosis simple	2	3.0
Pulmonary stenosis simple	2	3.0
Tricuspid atresia/stenosis simple	2	3.0
Right atrial isomerism	2	3.0
Other CHDs with heterotaxy	2	3.0
TGA, corrected	1	1.5
DIRV complex	1	1.5
Mitral atresia complex	1	1.5
Total	**67**	**100**

Table 5. Correlation Between Prenatal US and Autopsy Findings in All Subdiagnoses of CHDs in 67 Fetuses.

Categories	N	%
1: Full agreement between US and autopsy findings	222	97.4
2: Minor autopsy findings not seen or recorded at US examination	1	0.4
3: Major autopsy findings not detected at US examination	3	1.3
4: None of the autopsy findings suspected at US examination	–	–
5: US findings not confirmed or not possible to confirm at autopsy	2	0.9
1-5: Total	228	100

CHDs, congenital heart defects; US, ultrasound.

Table 6. Cases With Disagreement Between Ultrasound and Postmortem Findings.

Case	Year	GA	Ultrasound Diagnosis	Final Diagnosis After Autopsy	Disagreement
1	2004	18	Tricuspid atresia, hypoplastic RV, suspected truncus arteriosus	HRHS with tricuspid atresia, hypoplastic RV, complete TGA, VSD and LVOTO	VSD not seen at US (category 2). Suspected truncus arteriosus at US was diagnosed as complete TGA (category 3), VSD and LVOTO at autopsy (category 3)
2	2011	17	HLHS with mitral atresia, VSD, DORV, hypoplastic aorta with preductal coarctation	HLHS with mitral atresia, VSD, hypoplastic aorta with preductal coarctation	DORV not verified at autopsy (category 5, false positive)
3	2014	21	TOF with VSD, overriding aorta and pulmonary artery smaller than aorta. Suspected DORV variant	DORV, aortic stenosis, VSD, interrupted aortic arch, left subclavian artery rising from pulmonary artery	Aortic stenosis, interrupted aortic arch, left subclavian artery rising from pulmonary artery were not seen at US (category 3). Overriding aorta and pulmonary artery smaller than aorta were not confirmed (category 5, false positive)

GA, gestational age; RV, right ventricle; HRHS, hypoplastic right heart syndrome; TGA, transposition of the great arteries; VSD, ventricular septal defect; LVOTO, left ventricle outflow tract obstruction; US, ultrasound; HLHS, hypoplastic left heart syndrome; DORV, double outlet right ventricle; TOF, Tetralogy of Fallot.

Open access Original research

BMJ Paediatrics Open

Diagnostic accuracy of perinatal post-mortem ultrasound (PMUS): a systematic review

Susan Shelmerdine ,[1,2] Dean Langan,[2] Neil J Sebire,[2,3] Owen Arthurs[1,2]

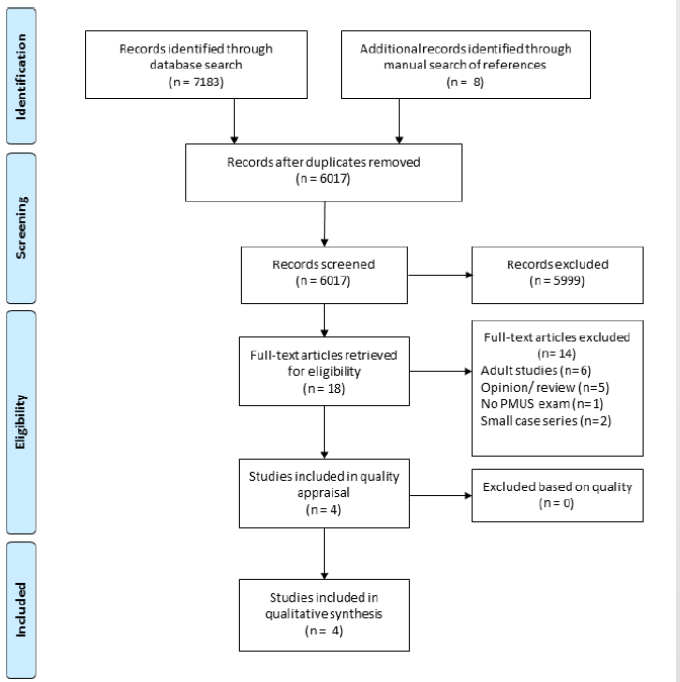

Table 1 Demographic details of population studied for all articles

Author, year	Country	Sample size, n	Patient group	Median gestation at death	Gestational age range (weeks)	Median post-mortem weight (g)	Weight range (g)	Mode of death
Prodhomme *et al*, 2015[10]	France	169	Fetuses	27 weeks	15–38	Not stated	Not stated	97% (164) terminations 3% (5) intrauterine deaths
Tuchtan *et al*, 2018[19]	France	75	Fetuses	Not stated, however 42 cases were<24 weeks; 33 were>24 weeks	15–38	Not stated	Not stated	79% (59) terminations 4% (3) miscarriages 17% (13) intrauterine deaths
Votino *et al*, 2018[20]	Belgium	88	Fetuses	21 weeks	11–40	702	7–4020	66% (58) terminations 17% (15) miscarriages 17% (15) intrauterine deaths
Kang *et al*, 2019[17]	Belgium and UK	163 imaged, 123 with reference test	Fetuses	23 weeks	13–42	Not stated	Not stated	50% (82) terminations 21% (34) miscarriages 29% (47) intrauterine deaths

Table 2 Study characteristics for articles included in systematic review

Author, year	Country	Sample size	Study design	Number of centres	Patient selection	Study period	Index test	Reference test
Prodhomme *et al*, 2015[10]	France	169	Retrospective	Single	Unclear	4 years (2009–2013)	2D whole-body ultrasound	Conventional autopsy
Tuchtan *et al*, 2018[19]	France	75	Prospective	Single	Consecutive	1 year (2014)	2D whole-body ultrasound	Conventional autopsy
Votino *et al*, 2018[20]	Belgium	88	Prospective	Single	Consecutive	19 months (2012–2013)	2D and 3D whole-body ultrasound	Conventional autopsy
Kang *et al*, 2019[17]	Belgium and UK	163	Prospective	Multiple, two centres	Consecutive	2 years (2014–2016)	2D whole-body ultrasound	Conventional and minimally invasive autopsy

2D, two-dimensional; 3D, three-dimensional.

Table 3 Details of index test for studies included for systematic review

Author, year	Ultrasound machine	Ultrasound transducers/ probes	Imaging time (min)	Patient preparation	Ultrasound operator, experience	No. operators	Blinded to clinical history	Time between delivery to imaging	Diagnostic accuracy subgroup measures
Prodhomme *et al*, 2015[18]	Philips iU22	5–8 MHz microconvex 5–12 MHz linear 5–17 MHz linear	Not stated	No additional preparation over cold storage of body	Paediatric radiologist, >10 years of experience	Single	No	Not stated	Agreement with final autopsy diagnosis. List of diagnoses given
Tuchtan *et al*, 2018[19]	Toshiba Aplio 500; Supersonic Aixplorer; GE Voluson E8	Toshiba: 7–10 MHz curved 10–15 MHz linear Supersonic: 6–10 MHz curved 11–15 MHz linear GE: 5–10 MHz curved 10–14 MHz linear	20	No additional preparation over cold storage of body	Paediatric Radiologist, 15 years ultrasound and 6 years post-mortem imaging experience	Single	Yes	Not stated	Anatomical structures were divided into seven categories: brain, spine, lung, heart, skeletal, gastrointestinal and genitourinary. Overall and individual body organ accuracy rates given
Votino *et al*, 2018[20]	GE Voluson E8	6–18 MHz linear, 6–12 MHz curved, 5–9 MHz curved	15	Fetuses either fixed in formalin (>15 weeks gestation), otherwise no additional preparation.	Fetal medicine doctor, 10 years of ultrasound experience	Single	No	Median time 2 days (1 hour–4 days)	Diagnoses categorised into three body systems: neurological (brain/ spine), thorax (including heart) and abdomen. Individual body system accuracy rates given
Kang *et al*, 2019[17]	GE Voluson E8; GE LOGIQ E9; Samsung HM70A	GE Voluson: 6–18 MHz linear 6–12 MHz curved 5–9 MHz curved GE Logiq: 2.5–8 MHz linear 1–5 MHz curved Samsung: 7–16 MHz linear	Not stated	No additional preparation over cold storage of body	Fetal medicine doctor or paediatric radiologist (>5 years experience each)	Two (one from each centre)	Yes	Median time 2 days (0–39 days)	19 internal organs assessed and grouped into four anatomic regions for analysis: neurological (brain/ spine), thorax, heart and abdomen. Overall and individual body system accuracy rates given

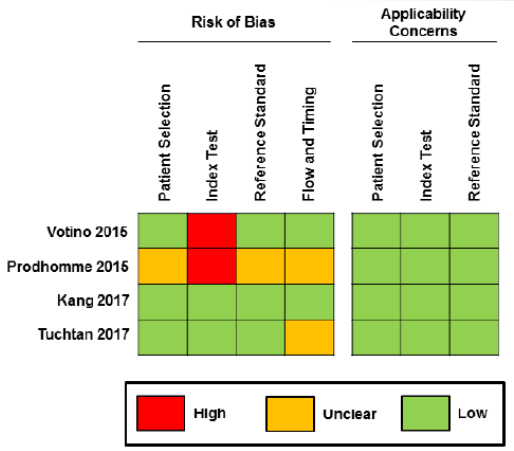

Table 6 Estimates of mean sensitivity and specificity (with 95% CIs), overall and split by different body systems

Body system	Mean sensitivity (95% CI)	Mean specificity (95% CI)
Overall	73.3 (59.9 to 83.5)	96.6 (92.6 to 98.4)
Neurological	84.3 (70.8 to 92.2)	96.7 (86.5 to 99.3)
Cardiothoracic	52.1 (27.6 to 75.5)	96.6 (86.8 to 99.2)
Abdominal	78.4 (61.0 to 89.4)	97.3 (88.9 to 99.4)
P value (neuro vs cardio)	0.010	0.916
P value (neuro vs abdom)	0.498	0.819
p-value (cardio vs abdom)	0.059	0.731

diagnostic accuracy rates are highest for neurological and abdominal abnormalities (mean sensitivity rates of 84.3% and 78.4%, respectively), but less effective for cardiothoracic abnormalities (mean sensitivity rate of 52.1%). There were no studies reporting the PMUS accuracy rates in neonates and older children.

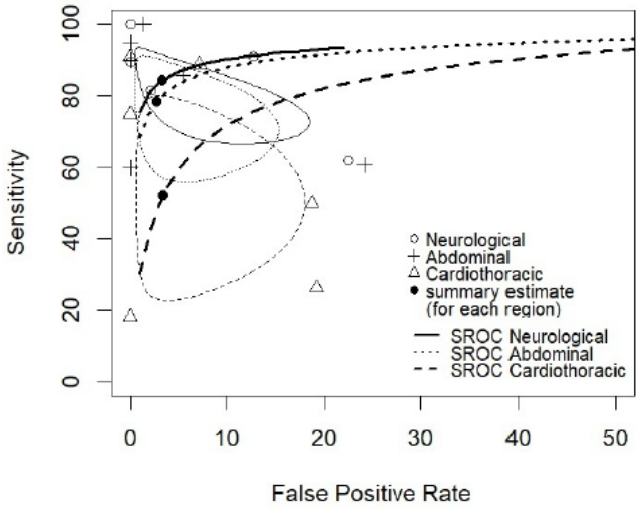

Figure 4 Receiver operating characteristic plot of sensitivity against false positivity rate (1, specificity) of 19 studies from table 5 separated by body system. Bivariate overall summary estimates of sensitivity and false positivity rate for each body system are overlaid with corresponding 95% confidence ellipses. SROC, summary receiver operating characteristic

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REVIEW ARTICLE

Post-mortem perinatal imaging: what is the evidence?

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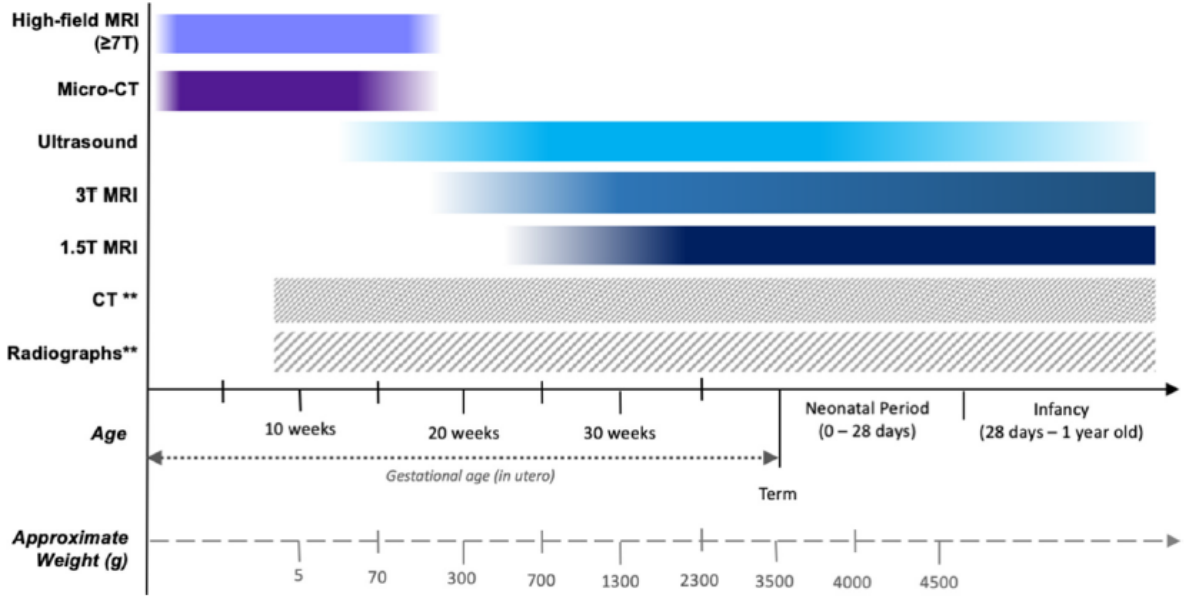
Table 1. Benefits and drawbacks of different post-mortem imaging modalities for perinatal loss

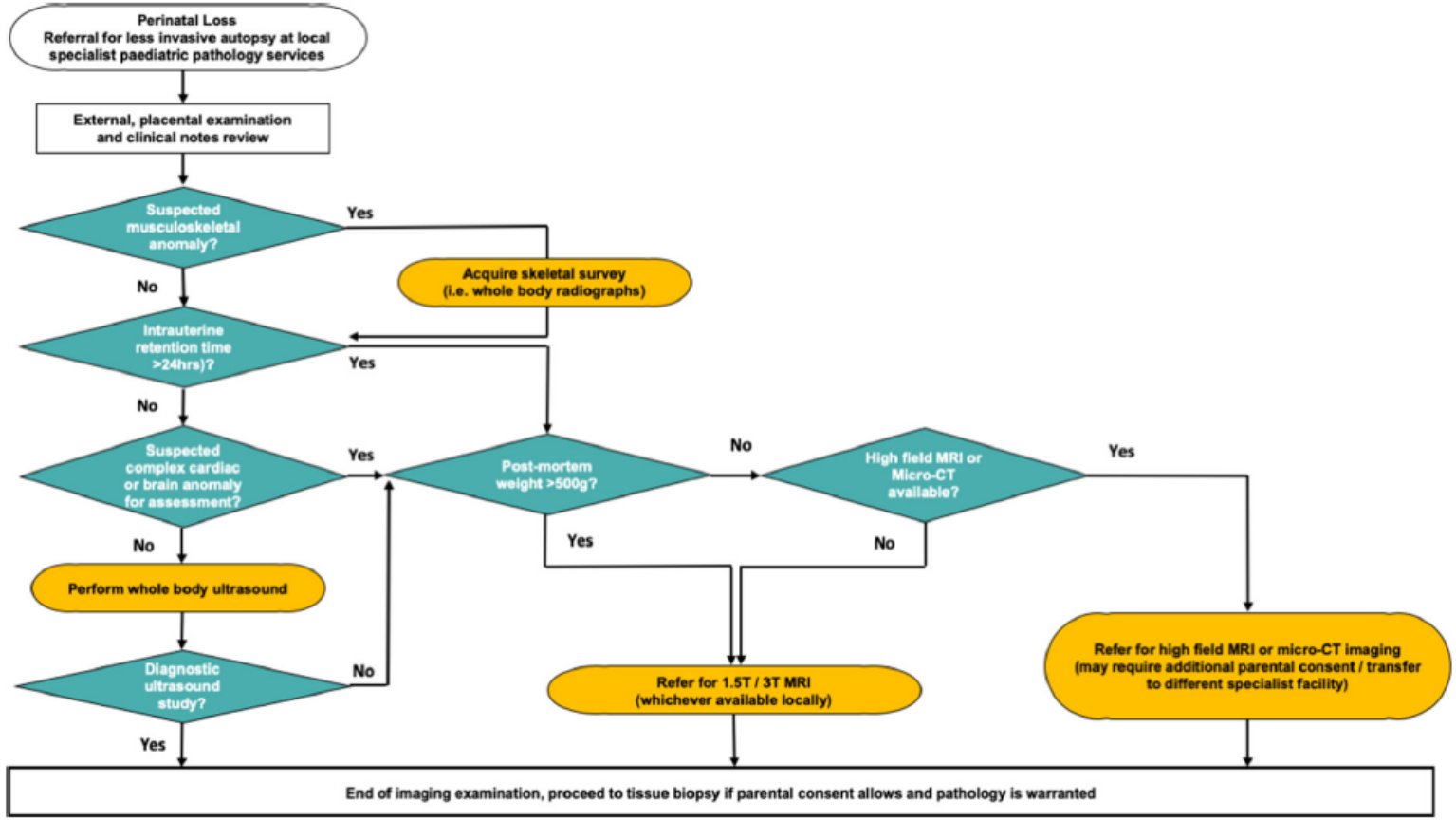
	Radiographs	Ultrasound	CT	MRI (3 T or 1.5 T)	Micro-CT	High Field MRI (7 T+)
Availability	Easily available	Easily available	Easily available	Moderate	Limited: few select centres/research facilities	Limited: few select centres/ research facilities
Cost	Cheap	Cheap	Cheap	Expensive+	Same cost as CT scanner.	Expensive+ +
Size of foetus	Any size	Any size – although intrauterine retention time may affect image quality.	Technically feasible, but poor diagnostic accuracy and lack of internal contrast from lack of body fat.	Better for larger foetuses, poorer for body weight <500 g.	Up to 30 cm in length, limited by scanner bore.	Similar to micro-CT
Advantages	Easy to perform, already part of routine autopsy service.	Ease of access, cheap and portable. Facilitates image-guided biopsies.	Highest accuracy for intracranial and musculoskeletal trauma (older children; trauma)	Multiple sequences, multiplanar reconstructions	Excellent resolution & soft tissue detail. Excellent bone detail without exogenous contrast.	Excellent resolution & soft tissue detail No need for exogenous contrast
Drawback	No internal soft tissue detail. Only useful in minority (<5%) of cases	Operator-dependent Requires a hands-on approach (radiologist).	Poor soft tissue detail due to lack of internal body fat.	Availability/access may be limited Poorer resolution in smaller foetuses.	Iodine contrast is required for soft tissue detail, which can cause tissue discoloration.	Expensive, limited access, long scanning times (hours).
Indication:	Estimation of foetal gestational age, diagnosis of skeletal dysplasias and limb anomalies	Assessment of soft tissue/internal organ detail	Bony injuries; trauma; consider for skeletal dysplasias or trauma (although radiographs better and cheaper)	Assessment of soft tissue/internal organ detail	Small foetuses (<20 weeks gestation) where ultrasound and 1.5 T/3 T MRI non-diagnostic.	Currently research tool only.

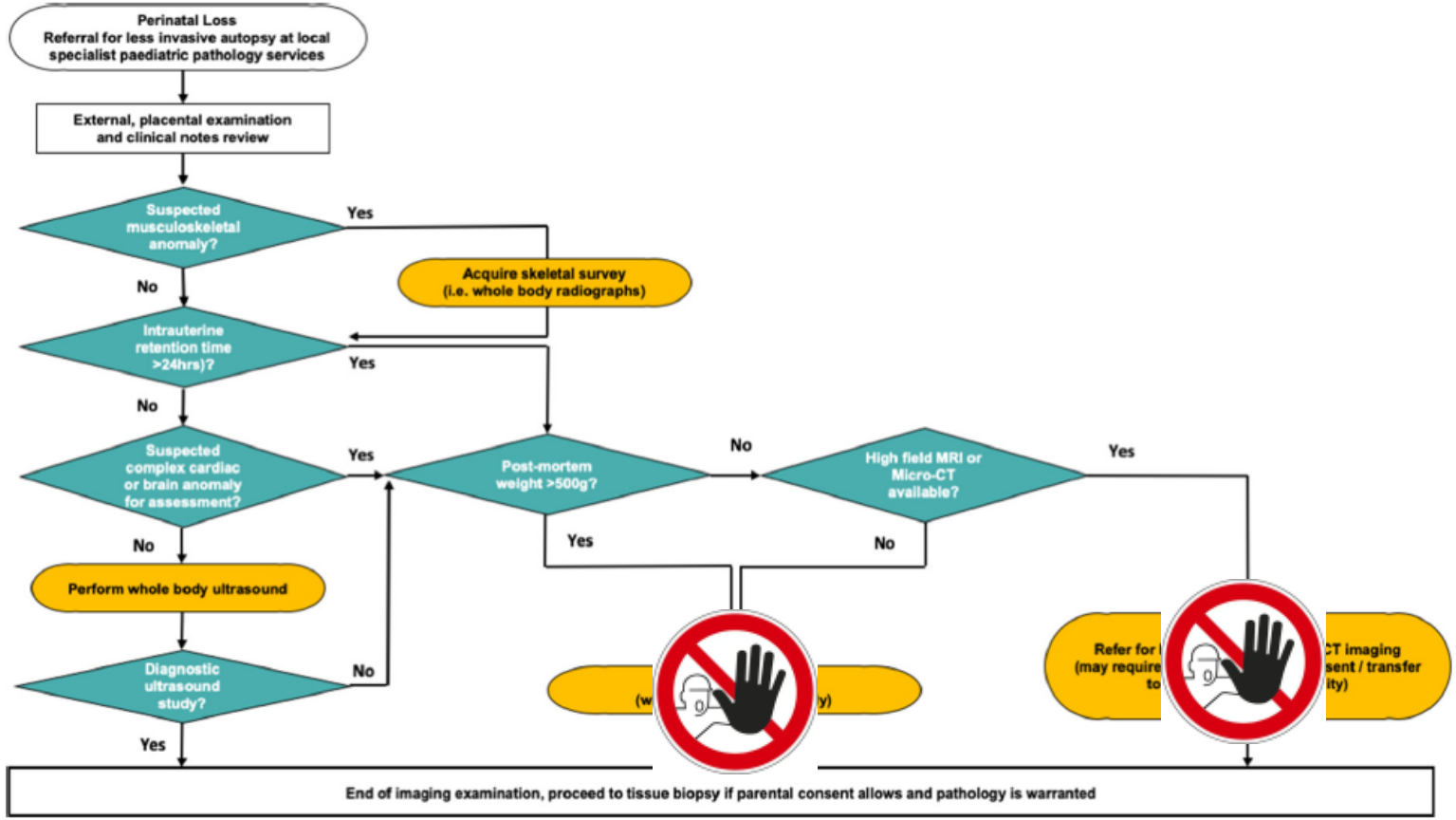
Reproduced from Shelmerdine SC et al, Insights into Imaging 2021.[13]

The latest on perinatal post-mortem ultrasound / Gorincour / ESPR 2022

Figure 2. Typical estimated gestational ages and the approximate post-mortem weights (g) at which various post-mortem imaging modalities would provide diagnostic quality examinations. ** Technically, radiographs and CT can be performed at any age after 8 weeks gestation (when the foetal skeleton beings to ossify), but in practice they are best reserved for specific clinical situations, such as for suspected skeletal abnormalities or trauma.[14] *Reproduced from Shelmerdine SC et al, Insights into Imaging 2021.*[13]




Perinatal Loss
Referral for less invasive autopsy at local specialist paediatric pathology services
External, placental examination and clinical notes review
Suspected musculoskeletal anomaly?
Yes
No
Acquire skeletal survey (i.e. whole body radiographs)
Intrauterine retention time >24hrs)?
Yes
No
Suspected complex cardiac or brain anomaly for assessment?
Yes
Post-mortem weight >500g?
No
High field MRI or Micro-CT available?
Yes
No
Yes
No
Perform whole body ultrasound
Diagnostic ultrasound study?
No
Yes
Refer for 1.5T / 3T MRI (whichever available locally)
Refer for high field MRI or micro-CT imaging (may require additional parental consent / transfer to different specialist facility)
End of imaging examination, proceed to tissue biopsy if parental consent allows and pathology is warranted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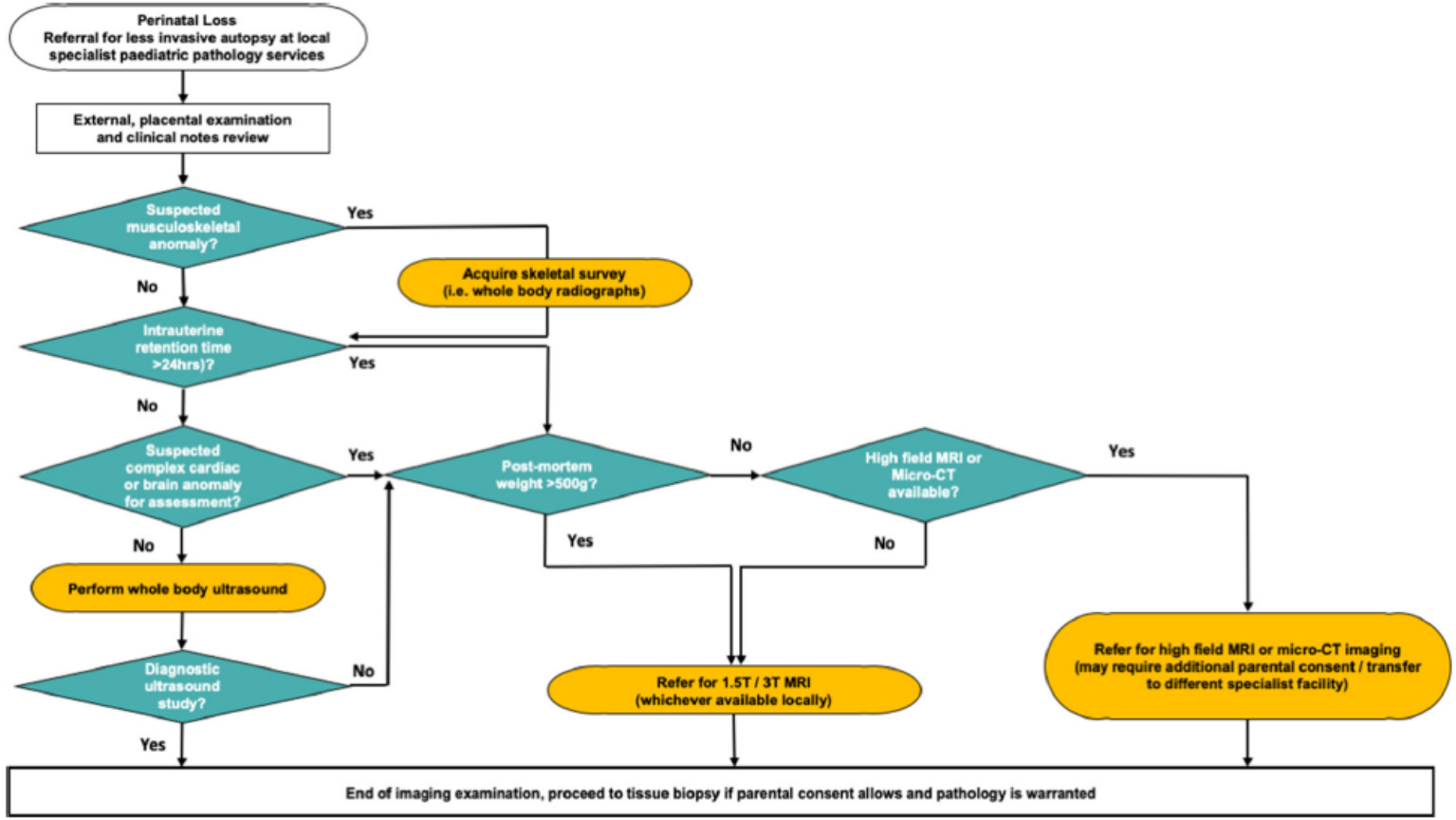
Le projet soutenu par la Fondation LUMIÈRE a permis la création de

LA PLATEFORME LUMIÈRE

à l'Hôpital Necker-Enfants Malades.

http://fondation-lumiere.org/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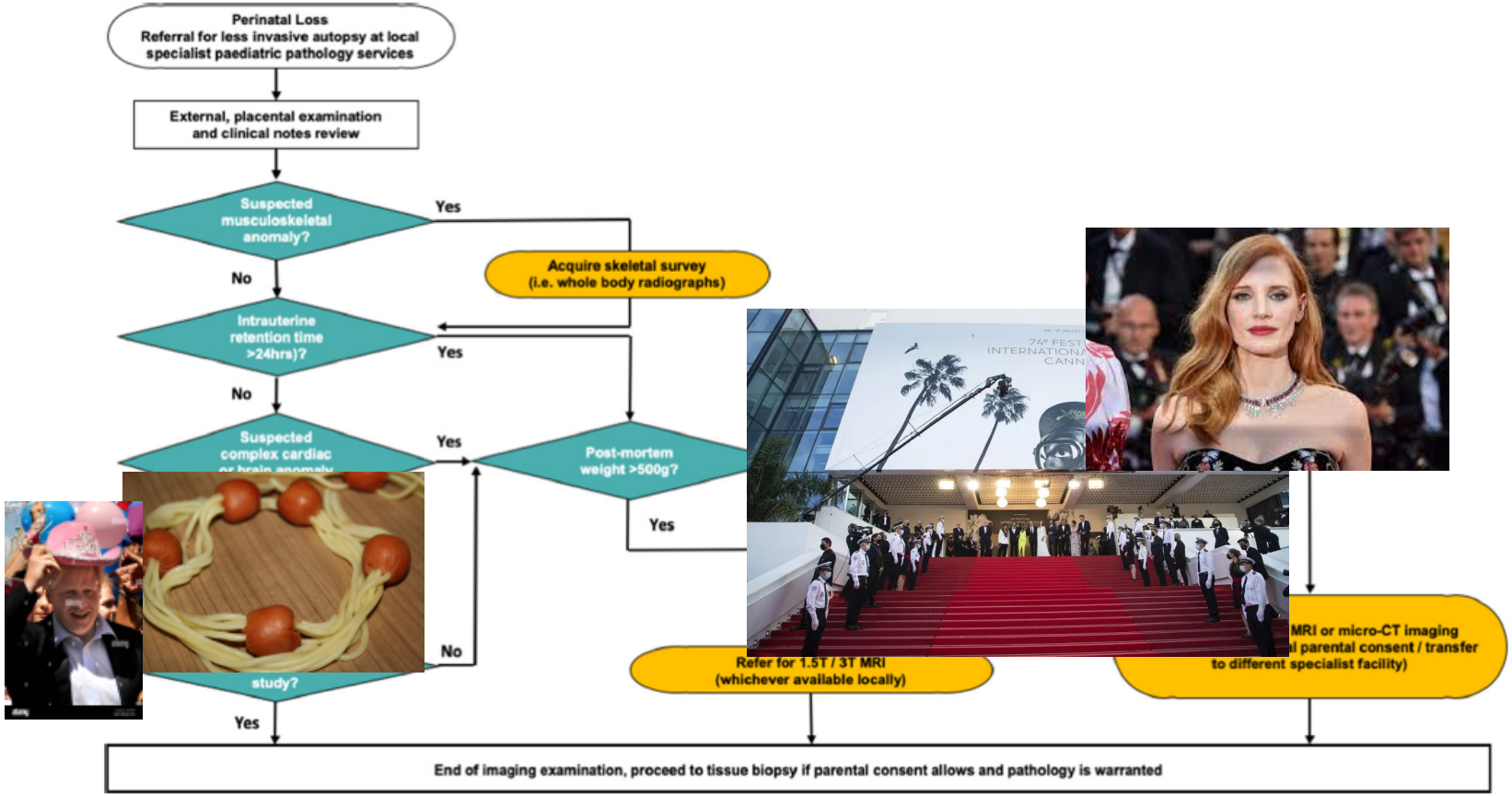
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The latest on perinatal post-mortem ultrasound

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IMAGE
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