Fetal post mortem imaging:
Congenital malformations

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Consultant Paediatric Radiologist
GOSH, London UK
PM imaging may be ...

- **Diagnostic**
  - Skeletal dysplasia
  - PMMR for intracranial abnormalities

- **Contributory**
  - Evaluate for associated abnormalities
  - Identify unsuspected abnormalities (e.g. NAI)
  - Guide pathologist to areas of abnormality

- **Reassuring**
  - Confirms antenatally suspected abnormalities
  - Document (store / preserve) changes prior to autopsy
  - Lack of associated abnormalities
  - 3D visualisation – models
Congenital malformations

- Fetal congenital malformations
  - Skeletal anomalies
  - Skeletal anomalies as part of wider spectrum
  - Brain, cardiac, kidney anomalies

- What is the best imaging modality to use?
- How good is e.g. CT vs MR?
- What are the limitations of each technique?

- Developing research areas
  - Other imaging techniques, PM US, micro CT
  - Rapid prototyping
- Our step wise approach to minimally invasive autopsy
Congenital = common
Types of imaging?

• Radiographs
• PM CT
• PM MR
• PM Ultrasound
• Micro CT
All skeletal surveys: 1027

- Babygrams: 739
  - Normal: 665
    - Required: 41
    - Dysplasia: 20
    - Contributory: 16
    - Non contributory: 5
  - Abnormal: 74
    - Not required: 33
    - Unexpected findings: 2
- Full Skeletal surveys: 288
  - Normal: 236
    - Not required: 33
    - Unexpected findings: 2
  - Abnormal: 52
    - Non contributory: 28
    - False positive: 3
    - Non contributory: 50

72% required, 28% not required.

90% Normal, 10% Abnormal.

55% Required, 45% Not required.

82% Normal, 18% Abnormal.

55% Required, 45% Not required.
Cost of workload?

• What is our current workload?
  • 410 cases / yr, 75% babygrams / faxitrons

• Add value?
  • Make diagnosis e.g. dysplasia - 20 / 739 = 2.7%
  • Give additional information - 19 / 739 = 2.6%

• Net cost? £72 / babygrams = £ 21,283
  only 39 were useful (£ 2,808)

• Is there a potential cost saving?
  • Stop routine babygrams, selected cases = save £18,500
  • Use CT (£400) in suspected abnormalities = £ 7,500
PM CT

• CT used widely in adults
• Usually needs IV contrast to define soft tissues
• Used to show bone detail

• PM CT now becoming popular in adults
  • Vascular, coronary artery, stroke

• Children have different causes of death
  • Sepsis, trauma, sudden unexplained death
Skeletal abnormalities
Skeletal abnormalities
PM CT vs XR
PM CT vs XR
Un-enhanced PMCT

Whole-body post-mortem computed tomography compared with autopsy in the investigation of unexpected death in infants and children

Mara Preisy, Antoine Jérôme Marchand, Philippe Lege, Renaud Blouet, Michel Roussey, Fabienne Pelli, Coline Rozel, Catherine Treguier, Pierre Damaull, Bertrand Bruaou
Un-enhanced PMCT
Comparison of diagnostic performance for perinatal and paediatric post-mortem imaging: CT versus MRI

Owen J. Arthurs¹,² - Anna Guy¹ - Sudhin Thayil³ - Angie Wade⁴ - Rod Jones⁵,⁶ - Wendy Norman⁵,⁶ - Rosemary Scott⁷ - Nicola J. Robertson⁸ - Thomas S. Jacques¹,² - W. K. ‘Kling’ Chong¹ - Roxanna Gunny¹ - Dawn Saunders¹ - Oystein E. Olsen¹ - Catherine M. Owens¹,⁵,⁶ - Amaka C. Offiah⁸,¹⁰ - Lyn S. Chitty¹,⁷,¹¹ - Andrew M. Taylor⁵,⁶ - Neil J. Sebire¹,² - for the Magnetic Resonance Imaging Autopsy Study (MaRIAS) Collaborative Group

Eur Radiol
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PAEDIATRIC
Contrast-enhanced PMCT
Ventilated PMCT
PMCT in children

• Unenhanced PMCT has limited diagnostic accuracy

• Excellent for bones – fractures, dysplasias
• Useful in NAI

• PMCT needs
  • either contrast – cardiac
  • or ventilation – lungs

• Very poor in small fetuses
PMMR = MARIAS study

- DoH funded 2 large trials in 2007
  - Oxford – 180 adults, PMCT and MR
  - GOSH / UCL, London – 400 fetuses and children, PMMR

- Magnetic Resonance Imaging in Autopsy study (MARIAS)
  - 400 unselected fetuses and children, blinded reporting
  - All underwent PM MRI
    + ancillary investigations (placental analysis, external examination, no histology)
    + full autopsy

Accuracy of PM MRI alone vs full autopsy
Accuracy of MIA (PM MRI + Ix) vs full autopsy

Thayil S et al., Lancet 2013
**Organ-specific PMMR**

- PMMR very good at neuro, cardiac, renal, MSK
- PMMR poor for bowel and lung pathology esp infection

<table>
<thead>
<tr>
<th></th>
<th>FP/TP</th>
<th>FN/TN</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Concordance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEURO (n=336)</td>
<td>58 / 98</td>
<td>14 / 166</td>
<td>87.5% [80.1, 92.4]</td>
<td>74.1% [68.0, 79.4]</td>
<td>62.8% [55.0, 70.0]</td>
<td>92.2% [87.4, 95.3]</td>
<td>78.6% [73.9, 82.6]</td>
</tr>
<tr>
<td>CARDIAC (n=361)</td>
<td>12 / 33</td>
<td>12 / 304</td>
<td>73.3% [58.9, 84.0]</td>
<td>96.2% [93.5, 97.8]</td>
<td>73.3% [58.9, 84.0]</td>
<td>96.2% [93.5, 97.8]</td>
<td>93.3% [90.3, 95.5]</td>
</tr>
<tr>
<td>CHEST (n=373)</td>
<td>38 / 44</td>
<td>67 / 224</td>
<td>39.6% [31.0, 48.9]</td>
<td>85.5% [80.7, 89.2]</td>
<td>53.7% [42.9, 64.0]</td>
<td>77.0% [71.8, 81.4]</td>
<td>71.8% [67.1, 76.2]</td>
</tr>
<tr>
<td>ABDO (n=373)</td>
<td>28 / 50</td>
<td>19 / 276</td>
<td>72.5% [61.0, 81.6]</td>
<td>90.8% [87.0, 93.6]</td>
<td>64.1% [53.0, 73.9]</td>
<td>93.6% [90.2, 95.8]</td>
<td>87.4% [83.6, 90.4]</td>
</tr>
<tr>
<td>MSK (n=385)</td>
<td>6 / 23</td>
<td>22 / 334</td>
<td>51.1% [37.0, 65.0]</td>
<td>98.2% [96.2, 99.2]</td>
<td>79.3% [61.6, 90.2]</td>
<td>93.8% [90.8, 95.9]</td>
<td>92.7% [89.7, 94.9]</td>
</tr>
</tbody>
</table>
Neuro PM MRI

Arthurs OJ et al., 2015
Cardiac PM MRI
Chest PM MRI

Arthurs OJ et al., 2014
Chest PM MR
Abdominal PM MRI

Arthurs OJ et al., 2014
### Table 2. Sequence parameters for post-mortem MRI (PMMR) in a neonate or infant

<table>
<thead>
<tr>
<th>Sequence</th>
<th>FOV (mm)</th>
<th>Slice thickness (mm)</th>
<th>Matrix</th>
<th>Voxel size (mm)</th>
<th>TR (ms)</th>
<th>TE (ms)</th>
<th>Flip angle (°)</th>
<th>Averages (NEX/NSA)</th>
<th>Number slices and gap</th>
<th>Approximate length of sequence (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brain imaging</strong></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3D FLASH T1-w (seg)</td>
<td>256</td>
<td>1</td>
<td>256/256</td>
<td>1.0 × 1.0 × 1.0</td>
<td>11</td>
<td>4.9</td>
<td>15</td>
<td>3</td>
<td>60 per slab</td>
<td>5.44</td>
</tr>
<tr>
<td>2D DESTIR T2-w (axial and coronal)</td>
<td>100</td>
<td>2</td>
<td>172/256</td>
<td>0.4 × 0.4 × 2.0</td>
<td>5400</td>
<td>16 and 115</td>
<td>150</td>
<td>6</td>
<td>18 (1 mm)</td>
<td>13.46</td>
</tr>
<tr>
<td>2D GRE T1, HEME (axial)</td>
<td>100</td>
<td>4</td>
<td>120/256</td>
<td>0.5 × 0.4 × 4.0</td>
<td>800</td>
<td>26</td>
<td>20</td>
<td>4</td>
<td>18 (0 mm)</td>
<td>6.25</td>
</tr>
<tr>
<td>DWI (axial) (b-values 0,500,1000)</td>
<td>230</td>
<td>5</td>
<td>128/128</td>
<td>1.8 × 1.8 × 5.0</td>
<td>2700</td>
<td>96</td>
<td>90</td>
<td>3</td>
<td>19 (0 mm)</td>
<td>1.06</td>
</tr>
<tr>
<td><strong>Spine imaging</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3D CISS T2-w (seg)</td>
<td>150</td>
<td>1.5</td>
<td>128/256</td>
<td>0.6 × 0.6 × 1.5</td>
<td>9.1</td>
<td>4.5</td>
<td>70</td>
<td>8</td>
<td>12 per slab</td>
<td>4.21</td>
</tr>
<tr>
<td>3D FLASH T1-w (seg)</td>
<td>150</td>
<td>1.25</td>
<td>128/256</td>
<td>0.6 × 0.6 × 1.3</td>
<td>11</td>
<td>5.3</td>
<td>15</td>
<td>10</td>
<td>16 per slab</td>
<td>3.19</td>
</tr>
<tr>
<td><strong>Body imaging</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3D T2-w TSE (cor)</td>
<td>200</td>
<td>0.8</td>
<td>160/256</td>
<td>0.8 × 0.8 × 0.8</td>
<td>3500</td>
<td>275</td>
<td>Variable</td>
<td>2</td>
<td>72 per slab</td>
<td>6.20</td>
</tr>
<tr>
<td>3D T1-w VIBE (cor)</td>
<td>200</td>
<td>0.8</td>
<td>160/256</td>
<td>0.8 × 0.8 × 0.8</td>
<td>5.9</td>
<td>2.4</td>
<td>25</td>
<td>8</td>
<td>72 per slab</td>
<td>5.32</td>
</tr>
<tr>
<td>3D CISS T2-w (axial) (cardiac)</td>
<td>150</td>
<td>0.6</td>
<td>192/256</td>
<td>0.6 × 0.6 × 0.6</td>
<td>5.6</td>
<td>2.5</td>
<td>54</td>
<td>10</td>
<td>Adjust to cover heart and entire lung fields</td>
<td>29.25</td>
</tr>
<tr>
<td>2D T2-w TIRM (axial) (T1 = 150)</td>
<td>180</td>
<td>5</td>
<td>160/256</td>
<td>0.7 × 0.7 × 5.0</td>
<td>5000</td>
<td>109</td>
<td>150</td>
<td>5</td>
<td>Adjust to cover body and extremities</td>
<td>6.58</td>
</tr>
</tbody>
</table>

2D, two-dimensional; 3D, three-dimensional; Cor/Sag, coronal or sagittal acquisition, respectively; CISS, constructive interference in steady state; Diffusion-weighted Imaging; FLASH, fast low angle shot; FOV, field of view; GRE, gradient recalled echo; HEME, T2- weighted echo time average; T1-w, T1 weighted; T2-w, T2 weighted; TE, echo time; TIRM, turbo inversion recovery magnetization prepared gradient echo; *Volumetric interpolated breath-hold examination.*

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**REVIEW ARTICLE**

**Perinatal and paediatric post-mortem magnetic resonance imaging (PMMR): sequences and technique**

1. WENDY NORMAN, DCR(R), DRI, 1,2NOORUHUDA JAYAM, MBBCh, FRCP, 1,3ROD JONES, DCR(R), MSc, 1,3ANDREW M TAYLOR, FRCP, MD, and 1,3GWEN J ARTHURS, FRCP, PhD
1. Cardiorespiratory Division, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK
2. Centre for Cardiovascular Imaging, UCL Institute of Cardiovascular Science, London, UK
3. Department of Radiology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK
4. Institute of Child Health, UCL, London, UK
PMMR in fetuses

• PMMR feasible, high diagnostic accuracy

• Particularly in fetuses >90%, even at 1.5 T

• PMMR very good at neuro, cardiac, renal, MSK
• PMMR poor for bowel and lung pathology esp infection

• **Problems:**

• Understanding normal PM change
• Antenatal vs post mortem ischaemia
• Understanding imaging changes of prolonged in utero death (maceration)
• Small fetuses – non diagnostic imaging
Understanding PM change

• Several artefacts

• Pericardial effusion
• Pericardial air
• Pleural effusion
• Subcut oedema
• Ascites

• Slumping

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Normal perinatal and paediatric postmortem magnetic resonance imaging appearances

Owen J. Arthurs · Jay L. Barber · Andrew M. Taylor · Neil J. Sehrie
PM MR – stillbirth?

Barber J et al., 2015
Small fetuses

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Percentage of PMMR diagnostic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>84g (22,125)</td>
</tr>
<tr>
<td>Neurological</td>
<td>90g (53,119)</td>
</tr>
<tr>
<td>Abdominal</td>
<td>63g (16,90)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>53g (16,89)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Not estimable</td>
</tr>
<tr>
<td>All 5 areas</td>
<td>156g (122,190)</td>
</tr>
</tbody>
</table>

Jawad N et al., 2015
PM US

- Good at renal lesions
- Good at intracranial lesions
- More operator dependent
PM US

- Good at renal lesions
- Good at intracranial lesions
- More operator dependent
Micro CT
Micro CT
Rapid prototyping

Schievano S et al., Insights 2010
Acceptability of MIA

Published online 22 May 2012 in Wiley Online Library (wileonlinelibrary.com). DOI: 10.1002/uog.10079

Acceptability, reliability and confidence of diagnosis of fetal and neonatal virtopsy compared with conventional autopsy: a prospective study

M. CANNIE*††, C. VOTINO§¶, PH. MOERMAN***, R. VANHESTE††, V. SEGERS††, K. VAN BERKEL§¶, M. HANSSSENS††, X. KANG§, T. COS§, M. KIR*, L. BALEPA§, L. DIVANO*, W. FOULONG§, J. DE MEY† and J. JANI§

69 mothers approached (102 fetuses/neonates)

TOP chromosomal/structural abnormalities (n = 66)
Unexplained IUF (n = 4)
Expected IUF (n = 20)
Postnatal death (n = 12)

Classical autopsy offered

59 mothers consented to classical autopsy (64 fetuses/neonates)

37 mothers declined classical autopsy (38 fetuses/neonates)

Virtopsy (MRI/CT) offered

All 59 mothers consented to virtopsy (64 fetuses/neonates)

9 fetuses had MRI and CT

33 fetuses/neonates ≥ 20 weeks of gestation

14 autopsies excluding brain

19 full body autopsies including brain

Figure 3 Flow chart summarizing the recruitment process of the 96 mothers included in the study.
Perinatal PM imaging

• Will it replace the autopsy?
  • No – but will allow optimal invasive management

• Stepwise approach

• In some cases, PM imaging will be sufficient
• In others, imaging-guided targeted biopsy will be needed
• In some, minimally invasive evisceration will be needed
• Full autopsy will occasionally be required
Stepwise approach

Clinical history
- Gestation
- Presentation
- History

External examination
- Radiographs

PM MRI
- Confirm / refute

Other imaging tests
- PM US
- PM CT

Full autopsy

Targeted biopsy

Endoscopic
- Or traditional

Tissue sampling

Diagnosis
- Cause of death
Training in PM imaging

• What skills are needed?
  • Imaging techniques and interpretation?
  • Perinatal pathology?
  • Fetal medicine?

• Pathologist as central point
• Writing death certificates
• Liaise with coroner
• Referrals via pathology for “PM examination”

• Image as necessary
Conclusion

• Post mortem perinatal imaging is rapidly developing

• PMCT – bone detail, good in suspected NAI
• PMMR – better soft tissue contrast, high diagnostic yield

• PM CT and PM MR not currently widely available
• Careful interpretation, training issues

• Providing a “better service” for bereaved parents
THANK YOU

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