Development of Micro-CT for Human Fetal Post-mortem Imaging

Background

Every day in the UK it is estimated over 500 babies are miscarried and 8 are stillborn. Following this loss, many parents want to know why their baby died, but do not want a standard autopsy (or post-mortem) that involves cutting into the body. However, if an autopsy is not carried out, parents and clinicians may miss out on valuable information about why the baby died and which can influence future pregnancies. There may also be religious reasons why a standard autopsy is unacceptable.

Recent work

Research demonstrates that medical imaging can provide much of the information that a post-mortem would provide and is acceptable to more parents. Three-dimensional imaging techniques (computed tomography, magnetic resonance imaging, and ultrasound) have all been developed as part of less invasive post-mortem imaging techniques, together with laparoscopic techniques, where tissue sampling of specific organs can sometimes provide additional information on the cause of death. This type of post-mortem imaging gives the same information as a standard invasive post-mortem technique for nine out of ten babies and is more acceptable to parents than current techniques.

Why was this research needed?

Ideally, parents would have a range of choices for the investigation of their loss, from less invasive techniques to the standard invasive post-mortem, with reliable information about the likelihood of getting helpful information about their baby with each option. One area where current imaging techniques are not able to provide diagnostic information is for fetuses lost in the early part of pregnancy (below 22 weeks gestation). This project developed and optimised a new imaging technique called micro-focus computed tomography (micro-CT) to provide diagnostically useful information on fetuses from this gestational range.

What I did?

Micro-CT is able to take high-resolution images of very small objects. However, for biological tissue, a contrast agent is required to enable soft tissue structures to be imaged. Potassium tri-iodide (I2KI) is ideal as it can penetrate several centimetres of tissue once the fetus is immersed within this fluid. Dependant on the biological tissue, the x-ray beam will be differentially attenuated, providing information on the density and atomic number of this tissue.

I identified the optimal I2KI concentration for these fetuses and determined an equation to accurately predict the immersion time required for a range of fetal weights, providing parents and professionals with information on when the scan can be completed.

Optimal imaging parameters were also identified to ensure that maximal signal-to-noise and contrast-to-noise was achieved within a clinically relevant timeframe of 30 minutes. Additionally, maceration, frames-per-projection and specimen size were all identified as being factors which determined the overall image quality possible.

This work culminated in a published “How to” guide (Nature Protocols, 2021), where three individual high-resolution scans are described for each fetus within a 90 minute scanning time, providing high-quality imaging for diagnosis of any fetal anomalies.

In addition, an animation was developed (<https://www.youtube.com/watch?v=nV16GazlcGA>), in conjunction with radiologists, pathologists, behavioural scientists and two pregnancy loss charities (the Miscarriage Association, and Stillbirth and Neonatal Death Society), detailing the autopsy options available for parents following a pregnancy loss.

Together, this work led to me being awarded the Great Ormond Street Hospital STAR Award for “Research Success of the Year, 2021”.

Why is this important for parents?

Many parents say they cannot bear the thought of their baby being ‘cut open’, but do not mind non-invasive tests being carried out, such as imaging and keyhole post-mortem techniques. Micro-CT can provide the same answers with less disturbance to the body than in a traditional post-mortem and is welcomed by parents and pregnancy loss charities.

Why is this important to the NHS?

Parents state that they want the ‘minimum necessary’ disturbance to their baby’s body in a postmortem. Developing new techniques such as micro-CT means that the most suitable tests for individual babies are offered. Families will have more choice, supported by appropriate counselling, giving them the best chance of finding out why their baby has died and whether future children might be affected. This technique has the potential to become the standard imaging technique offered to parents who have suffered a miscarriage, because there is no other technique that can provide this diagnostic information non-invasively. This would avoid the need for standard post-mortem, change the way that pregnancy loss is dealt with in the NHS, and help counsel parents for possible future pregnancies. These are key priority areas for the NHS’ “5-year forward view”, and the Department of Health.

Key papers published from this work

**1, Simcock IC**, Shelmerdine SC, Langan D, Anna G, Sebire NJ, Arthurs OJ. Micro-CT yields high image quality in human fetal post-mortem imaging despite maceration. BMC Med Imaging. 2021 Aug 24;21(1):128. doi: 10.1186/s12880-021-00658-5.

2, Shelmerdine SC, Hutchinson JC, Lewis C, **Simcock IC**, Sekar T, Sebire NJ, Arthurs OJ. A pragmatic evidence-based approach to post-mortem perinatal imaging. Insights Imaging. 2021 Jul 15;12(1):101. doi: 10.1186/s13244-021-01042-1.

**3, Simcock IC**, Shelmerdine SC, Hutchinson JC, et al., Human fetal whole-body postmortem microfocus computed tomographic imaging. Nat Protoc. 2021 May;16(5):2594-2614. doi: 10.1038/s41596-021-00512-6. Epub 2021 Apr 14.

4, Lewis C, **Simcock IC**, Arthurs OJ. Improving uptake of perinatal autopsy. Curr Opin Obstet Gynecol. 2021 Apr 1;33(2):129-134. doi: 10.1097/GCO.0000000000000691.

5, Novo Matos J, Garcia-Canadilla P, **Simcock IC**, et al., Micro-computed tomography (micro-CT) for the assessment of myocardial disarray, fibrosis and ventricular mass in a feline model of hypertrophic cardiomyopathy. Sci Rep. 2020 Nov 19;10(1):20169. doi: 10.1038/s41598-020-76809-5.

6, Hutchinson JC, Shelmerdine SC, Lewis C, Parmenter J, **Simcock IC**, et al., Minimally invasive perinatal and pediatric autopsy with laparoscopically assisted tissue sampling: feasibility and experience of the MinImAL procedure. Ultrasound Obstet Gynecol. 2019 Nov;54(5):661-669. doi: 10.1002/uog.20211.

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9, Hutchinson JC, Shelmerdine SC, **Simcock IC**, et al., Early clinical applications for imaging at microscopic detail: microfocus computed tomography (micro-CT). Br J Radiol. 2017 Jul;90(1075):20170113. doi: 10.1259/bjr.20170113. Epub 2017 May 4.