

Imperial College
London

Fetal Medicine

Christoph Lees



Studies on applied & translational imaging in obstetrics

Lecturers

Dr Ed Mullins

Dr Caroline Shaw

Research Fellows

Dr Anna Clark

Dr B Mylrea Lowndes

Dr Raj Jaspal

Dr Sana Usman

Dr Harsha Shaw (with Professor Tom Bourne)

Research Midwife

Dr Olive Adams



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Dr Ed Mullins
NIHR ACL O&G

Hypertension and Fetal Growth Restriction Studies:

- **First trimester blood pressure in normal range and birthweight (PI)**
- **Postnatal exercise interventions** – systematic review for adherence and effect (PI)
- **Health in Pregnancy** feasibility study; app-based home monitoring (Co-I, NIHR BRC Funding)
- **TRUFFLE 2 – RCT** management of late pre-term Fetal Growth Restriction (local investigator)

Diabetes Studies:

- **Guar gum to prevent recurrent gestational diabetes (GDM)** pilot study (co-I, G Frost)
- **NW London Practice-level GDM data** incidence of T2DM after GDM (PI, Genesis Funding)
- **Ophelia Study** – autoimmunity in GDM (site PI, Diabetes UK Funding)

Recruitment Status

- **Guar gum** (soluble fibre supplement) to prevent Gestational Diabetes Mellitus **n=55/80**
- **Health in pregnancy (originally EiT with Philips)** – Recruitment commences w/c 7th October
- **OPHELIA study** (autoimmunity in Gestational Diabetes) – Recruitment commences next 28 days
- **Database studies**
 - First trimester blood pressure in normal range and birthweight awaiting IG
 - NW London Practice-level GDM data – data analysis in process



Outputs & Funding

Presentations

Diabetes UK Professional conference 19-21/3/19, Liverpool

- Invited speaker– ‘Can we accurately predict macrosomia and should it affect timing of birth?’
- Invited oral presentation, ‘A waiting game, Progression of Autoantibody Positive Gestational Diabetes to Type 1 Diabetes.’

RCOG Annual Congress 17-19 June 2019, London

- Poster presentation, ‘Sweet success, Intensive management of gestational diabetes reduces risk to the background rate.’

Royal Society, London, 5 October 2019 (Professor Dame Sally Davies, Chief Medical Officer, Festschrift)

- Invited talk, ‘The Impact of the Women’s Health Report, 2015,’ (Based on my time as editor-in-chief, Chief Medical Officer’s Women’s Health report).

Funding: Imperial BRC grants

- £1500 – PPI grant (PERC)
- £4000 - CL grant



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Research Studies:

- Using ultrasound-guided High Intensity Focused Ultrasound to treat early gestation twin-twin transfusion syndrome (MRC-DPFS funding £2.2M, awarded 2017).
- Investigating the feasibility of using Doppler ultrasound imaging to map placental vasculature and anastomoses in monochorionic diamniotic twin pregnancies (Wiseman Trust funding £115K)

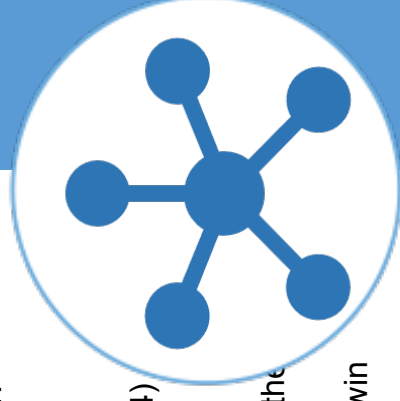
Dr Caroline Shaw

Recruitment Status

- **Using ultrasound-guided High Intensity Focused Ultrasound to treat early gestation twin-twin transfusion syndrome**
 - Aims to develop a non-invasive treatment for early onset TTTS, where other treatment modalities are severely limited
 - In pre-clinical development phase
 - First human treatments planned April 2020
 - Anticipated 13 participants
- **Investigating the feasibility of using Doppler ultrasound imaging to map placental vasculature and anastomoses in monochorionic diamniotic twin pregnancies**
 - Aims to determine the feasibility of using early-pregnancy assessment of monochorionic placental vasculature to predict pregnancy outcomes
 - 30 participants recruited (target 30), feasibility demonstrated
 - Currently amending study to recruit 160 further participants over next 2 years



Outputs & Funding



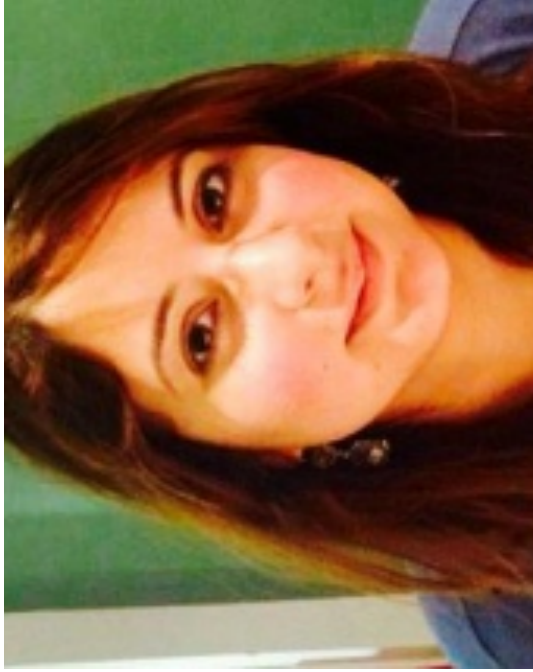
Presentations

1. Shaw C J, Rivens I, Civale J, Botting K J, Ter Haar G, Giussani D A, Lees C C. Trans-abdominal in vivo placental vessel occlusion using High Intensity Focused Ultrasound. *Sci Rep.* 2018; 8(1):13631. (IF 4.1)
2. Shaw C J, Rivens I, Civale J, Botting K J, Allison, BJ, Brain KL, Niu Y, Ter Haar G, Giussani D A, Lees C C. Maternal and fetal cardiometabolic recovery following ultrasound-guided high-intensity focused ultrasound placental vascular occlusion. *J R Soc Interface.* 2019; 16(154):20190013. (IF 3.4)
3. Mylrea-Foley B, Shaw C J, Harikumar N, Legg S, Meher S, Lees C C. Early Onset Twin-Twin Transfusion Syndrome: Case Series and Systematic Review. *AJUM*, in press June 2019.
4. Shaw CJ, Lees CC, Kilby MD. Monochorionic twins and twin to twin transfusion syndrome: the rationale of non-invasive 'mapping' of placental angioarchitecture and treatment. *Placenta*, in press
5. Girardelli S, Shaw C J, Lees C C. Mapping of the placental angioarchitecture in monochorionic twin pregnancies using different colour Doppler filters (oral presentation), ISUOG, Berlin, October 2019
6. Girardelli S, Shaw C J, Lees C C. Antenatal prediction of increased twin-twin transfusion syndrome (TTTS) risk at 14 weeks using different Colour Doppler filters (poster presentation), ISUOG, Berlin, October 2019

Funding:

- TTTS Project: £2.2m from MRC
- Placental Mapping: £115k from Wiseman Trust

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Dr Sana Usman

The sonopartogram:

Developing a predictive model for labour outcome
from transperineal ultrasound



Norwegian University of
Science and Technology

KU LEUVEN

The Sono VE Study (2014-2018)

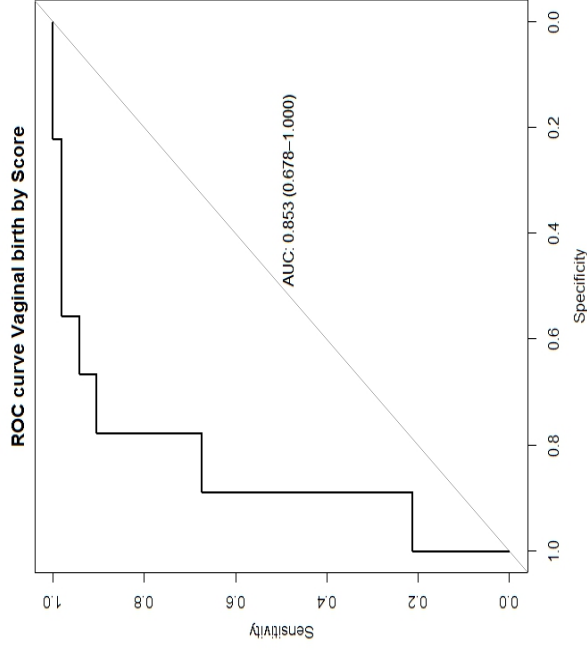
- Repeat assessments in labour
- Test & validate previous model
- Assess Acceptability & Feasibility
- Utility of cerebral Doppler
- **270 women with repeat measurements**
 - **Completed Feb 2018**

Study Design: 122 nulliparous women in the first stage of labor. Covariates included HPD, Caput and OP position, dichotomised respectively into: “40mm, 40 mm”, “10 mm, ≥10 mm” and “No, Yes”. Maternal age, gestational age and maternal BMI included as continuous covariates.

Results: Continuous score did not significantly predict vaginal delivery ($p=0.10$) however dichotomised score is significantly associated with vaginal delivery ($p=0.03$). Women with a score more than median had > 10 x odds of vaginal delivery compared to those with a score below the median. ROC curve showed AUC of 0.853 (95% CI, (0.678, 1.000))

Conclusions: A risk score based on maternal characteristics and intrapartum findings can predict vaginal delivery in nulliparous women in the first stage of labor.

Am J Obstet Gynecol 2015



Acceptability

Study Screens

Feasibility

Second Stage Prediction

Intrapartum app

PPI



Publications

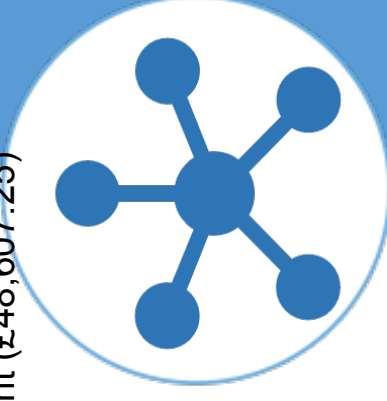
- Prediction of mode of delivery using the first “intrapartum app”. Usman S, Kahrs B, Wilhelm-Benartzi C et al. AJOG 2019
- The views of pregnant women, midwives and a women’s panel on intrapartum ultrasound research: a pilot study. Wilkinson M, Usman S, Alojado M, Barton H, Lees CC. AJUM 2019
- Ultrasound is better tolerated than vaginal examination in and before labour. Usman S, Barton H, Wilhelm-Benartzi C, Lees CC. Aust N Z J Obstet Gynaecol. 2018
- The feasibility and accuracy of ultrasound assessment in the labor room. Usman S, Wilkinson M, Barton H, Lees CC. J Matern Fetal Neonatal Med. 2018
- A model to predict vaginal delivery in nulliparous women based on maternal characteristics and intrapartum ultrasound. Eggebo TM, Wilhelm-Benartzi C, Hassan WA, Usman S, Salvesen KA, Lees CC. AJOG 2015.

Collaborative Papers

- Time to delivery based on sonographic assessment prior to forceps and vacuum. Usman et al/Australasian Journal of Medicine, 2019
- Descent of the fetal head during active pushing: a secondary analysis of a prospective cohort study investigating ultrasound examinations before an operative vaginal delivery. Kahrs & Usman. UOG 2019
- Fetal rotation during vacuum extractions for prolonged labor: a prospective cohort study. Kahrs et al/Acta Obstet Gynecol Scand. 2018
- Sonographic prediction of outcome of vacuum deliveries: a multicenter, prospective cohort study. Kahrs et al/AJOG 2017

Funding

- Imperial Healthcare Charities (£60,546.60) Dec 2015
- Imperial Confidence in Concept Grant, MRC and BRC funded (£47,748) May 2015
- BMA Helen Lawson Grant (£48,607.25) June 2014



Presentations

- ISUOG 2018/2017/2015: 11 abstracts Expert Fetal Medicine 2017 BMFMS
- 3rd European Congress on Intrapartum care
- RCOG world congress 2016 2 abstracts and a workshop

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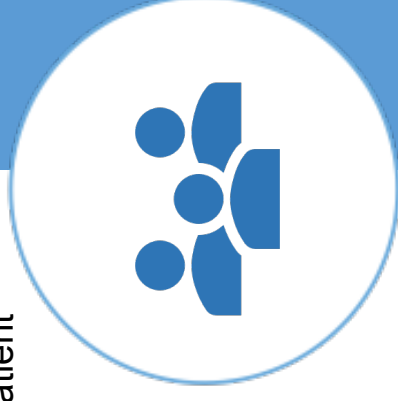
Dr Anna Clark

- Prenatal facial and brain analysis from 3D Ultrasound
- Ultrasound Simulation



Objectives & Recruitment

- **Prenatal facial & brain analysis from 3D Ultrasound**
 - **Objective:** To develop a statistical modelling technique for the analysis of 3D ultrasound volumes of the fetal face and brain in order to provide an objective means to identify patient with facial dysmorphisms and distinguish normal from abnormal brain development
 - **Inclusion criteria:**
 - Women referred to the Centre for Fetal Care, QCCH
 - Maternal age >18 years
 - Gestational age between 24 and 34 weeks
 - Good quality 3D facial and brain volumes (subjectively determined)
 - Signed informed consent
 - **82 patients recruited**



Ultrasound Simulation

- **Objective:** to examine the impact of an optical simulator with fully automated web-based metrics on ultrasound training

Outputs & Funding

- **Funding:**
 - NIHR Imperial Biomedical Research Centre (BRC)
- **Poster presentations** accepted at ISUOG World Congress October 2019, Berlin:
 - *'Assessment of inter-operator variability of manual segmentation for analysis of the fetal face from 3D ultrasound scans'*
 - *Towards fully automated segmentation for the computed assessment of the fetal face from 3D ultrasound scans.*
 - *'The Impact of optical ultrasound simulation using automated metrics on skill acquisition in obstetric ultrasound'*
 - *'The contribution of optical ultrasound simulation and automated metrics on skill acquisition in transvaginal ultrasound'*
- **Oral presentation:** 'Ultrasound Training using an Optical Simulator', Expert Pregnancy Imaging Conference, BMA
- **Papers for submission October 2019:**
 - *'Developing and testing an algorithm for 3D facial segmentation'*, For J Royal Soc Interface (A collaboration with University College London GOS Institute of Child Health & Great Ormond Street Hospital for Children)
 - *'The impact of ultrasound simulation with fully automated metrics on ultrasound training'*. For Ultrasound in Obstetrics & Gynaecology Journal



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Dr Bronacha Mylrea-Lowndes

TRUFFLE 2 Study:

Perinatal and 2 year neurodevelopmental outcome in late preterm fetal compromise: The TRUFFLE 2 Randomised Trial

Imperial Health Charity Research Fellowship Grant,
started July 2019



Project Plan and Recruitment

- Multicentre European randomised control trial led by Imperial College
- Aim is to determine if delivery based on cerebral redistribution reduces adverse outcome in late onset fetal growth restriction
- Primary outcome: reduction in composite neonatal outcome
- Secondary outcome: no worsening of neurodevelopment at 2 years
- **Target: 1558 women**
- **Recruitment June 2020 – June 2022**

P I C O



Project Progress

- **NIHR Award £2.5M May 2019**
- **51 study centres confirmed:**
 - 11 in the UK
 - 40 across Europe
- **Protocol, PIS and consent forms finalised**
- **Study centre visits completed**
 - 4 in Italy
 - 4 in Germany
- **IRAS submission October 2019**
- **Meeting Klagenfurt April 2020**
- **Study centre visits planned:**
 - November: Sweden, Norway
 - December: Belgium, Czech Republic, Austria
- **Applications for parallel studies:**
 - Biomarkers, perinatal mental health, CV function, Cost economics, U/S standardization



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Dr Raj Jaspal

Trust Clinical Research Fellow

CAST study:

Cardiovascular function in IVF **stimulation**

Grant income £8K for CV consumables

Loan of NiCAS cardiovascular monitoring equipment

The CAST study: A longitudinal prospective observational study

Primary Hypothesis:

Controlled ovarian stimulation (COS) with exogenous gonadotrophins has a significant impact upon maternal cardiovascular function during the acute phase of stimulation.

Aims:

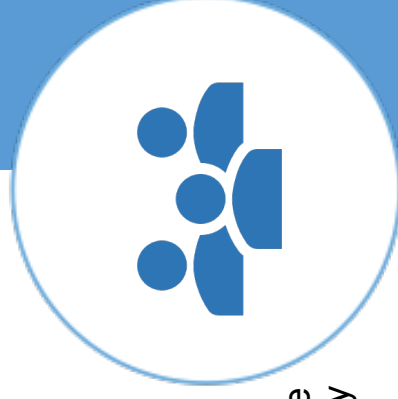
1. Longitudinal changes in CO: comparison of Fresh Vs. Frozen cycles
2. Longitudinal changes in arterial function
3. Comparison of Agonist Vs. Antagonist protocols
4. A comparison of three non-invasive methods of measuring CO

Protocol Outline:

Fresh (ovarian stimulation) IVF cycles will be compared to those undergoing frozen IVF cycles (no ovarian stimulation).

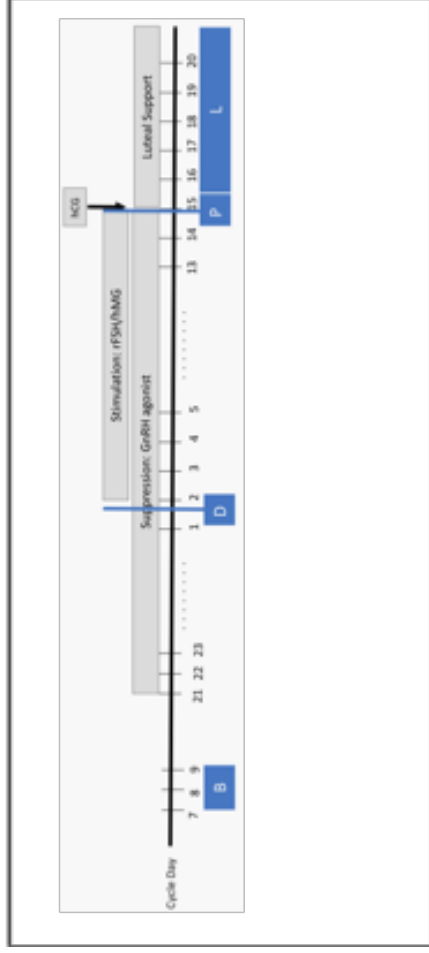
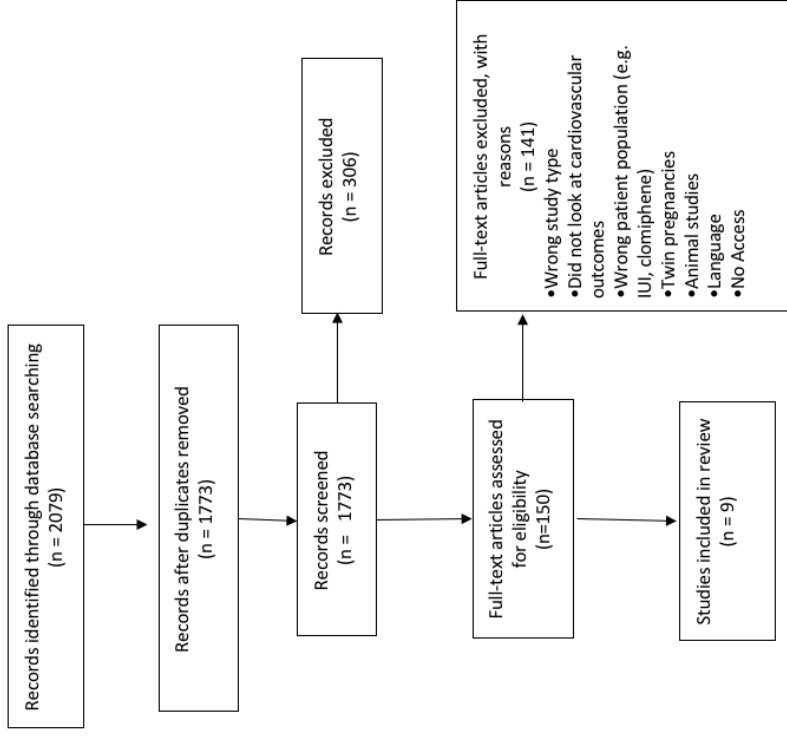
Cardiac and Arterial function measured at: baseline, during ovarian stimulation and pre/post embryo transfer to see if there are any significant longitudinal changes during in vitro fertilisation (IVF) protocols.

We will be measuring serum oestradiol and progesterone at the same time points as cardiovascular parameters to determine if there is any correlation.



63/80 women recruited to CAST undergoing IVF (fresh & frozen cycle)

Systematic review



Current Status and Ongoing Work

- **Ethical approval:** IRAS ID 234271, NRES (East of England /Cambridge East) favourable opinion (5/8/2019)
- **Funding:** awarded Imperial Charity cardiovascular grant (December 2018)
- **Presentations:**
 - Protocol presented at ISUOG maternal haemodynamics meeting (Sept, 2018)
 - Systematic review presented at Expert Pregnancy imaging (May, 2019)
 - Systematic review accepted for oral presentation at ISUOG (Oct, 2019)
- **Publications:** Systematic review submitted to EJOGRB (Sep 2019)





Olive Adams

Research Midwife

TRUFFLE 2 Perinatal and 2-year neurodevelopmental outcome in late preterm fetal compromise: The TRUFFLE 2 Randomised Trial

Health in Pregnancy Conceive 2 feasibility study

The CAST Study Cardiovascular assessment during assisted reproductive technology

Patient and Public Involvement (PPI)

Positively influenced our ability to obtain grants and we ensure to incorporate PPI as a key component into all our ongoing research.

PPI

TRUFFLE 2

- Patient feedback and responses incorporated into grant application.
- Feedback was positive from reviewers- PPI activity considered relevant and well thought out.
- Provides added value to research, Women discussed how and why they felt happy to be randomised.
- Review on study documents; PIS
- Named Member of the Trial Management Group.

Preconception "Beet It" & lifestyle intervention to reduce incidence of hypertension in pregnancy

- Sought opinion on recruitment and design of the study.
- Changes to the design- reduced number of interventions/ advised on engagement by research team.

HIFU-High Intensity Focused Ultrasound, Developing a non-invasive treatment for twin to twin transfusion syndrome

- Specific questions on experience of TTTS and sought opinion of the research design
- Gained ideas on study roll out stage and how experience of TTTS can be improved.
- Education sessions incorporated into study design



Funding and Outputs

- NIHR Imperial Biomedical Research Centre (BRC): PPI Project Grant (Round 4) £1500, October 2018
- **Presentations**
 - Maternal Cardiovascular Working Group. March 2019, Rotterdam
 - Expert Pregnancy Imaging conference, May 2019, BMA London
- **Publications**
 - Imperial Patient Experience Centre, Case study report, September 2019
 - <http://wwwf.imperial.ac.uk/blog/perc/2019/09/>

