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Does magnetic resonance imaging (MRI) improve the accuracy of diagnosis of brain abnormalities in the unborn fetus?

Submission date
01/03/2011

Recruitment status
No longer recruiting

Registration date
14/03/2011

Overall study status
Completed

Last Edited
23/09/2019

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims:
Ultrasound scanning is routinely used during pregnancy to identify babies who appear to have abnormal brain development; no medical test is perfect however, and the information provided by ultrasound is occasionally incomplete or inaccurate. The purpose of the initial study was to find out if magnetic resonance imaging (MRI) improves the accuracy of diagnosis of brain abnormalities. Between July 2011 and August 2014 the study recruited over 900 pregnant women whose ultrasound showed abnormal development of the baby's brain. Following on from this, MERIDIAN was extended to incorporate additional follow-up of its participants, which allows us to update and improve the MERIDIAN primary outcome data using updated postnatal information available when the children are aged 2-3 years and to refine the information given to pregnant women by collecting developmental outcome data on children in MERIDIAN.
Who can participate?
Pregnant women over the age of 16 who were carrying a baby with a suspected brain abnormality following a specialist ultrasound examination. Both single and multifetal pregnancies were eligible and all participants were at least 18 weeks gestational age. All surviving children from the MERIDIAN cohort, whose mother underwent MR imaging during her pregnancy will be invited to participate in the follow up study.

What does the study involve?
All pregnant women recruited to the study are invited for an MR scan and the information from the scan then used by their doctor to help with their medical care. MRI results are compared with the results of scans and other tests performed after delivery. We also look at whether using MRI changes the counselling and information about the baby's development given to the women, and whether this extra information is helpful for participants in how they come to their decision about continuing with the pregnancy or not. The women and the health professionals that care for them are asked by questionnaire and interview for their opinions about MRI and how helpful it is. Finally, the cost of using MRI is estimated and evaluated against the number of times it has a direct impact on antenatal counselling. The follow up study involves a medical case note review in which the research team review the child's medical records to collect information about the child's development, postnatal diagnoses and postnatal imaging or investigations

until the age of 2-3 years. Participants are also invited to participate in a development assessment called the Bayley's Scale of Infant Development. The results from the assessments allow us to classify the developmental status of the child. This is compared to the prognosis given based on antenatal ultrasound and MRI.

What are the possible benefits and risks of participating?
Potential benefits for study participants included the possibility of additional or more accurate diagnostic information relevant to their pregnancy, additional clinical contact (both with staff at the MR centre and also with clinical staff at the referring centre) and the chance to view and discuss the MR images acquired with a relevant health professional. The risks to the pregnant woman in performing in utero MR are exceptionally small. The greatest risk to the woman was from the recognised general contraindications to MR examination (e.g. cardiac pacemaker). The absolute risk to the fetus of performing MR imaging in the second and third trimesters is not certain, but no definite health risks are currently known. The potential benefits of participating in the follow up study are that they may gain additional information about their child's development. There may also be opportunity for participants to be signposted towards additional support where required. A potential risk to participation is that occasionally, children become tired or are unwilling to take part in the developmental assessment. The assessment will always be conducted with parents present which is usually enough to put the child at ease and most children enjoy completing the tasks. There is a small chance that we might identify a previously unrecognised developmental problem. This would be very unusual at the 2-3 year age window we are using. Where this occurs we will speak to parents about future actions.

Where is the study run from?
The work is centred at the Academic Unit of Radiology, University of Sheffield. Women were recruited from 15 specialist Fetal Medicine Units into the initial study. These units cover a large area of England, Scotland and Northern Ireland. MRI scans were carried out in Sheffield, Newcastle, Leeds, Birmingham, Nottingham QMC and Belfast. For the follow up study participants will be approached by the hospital site in which they were first recruited to the initial MERIDIAN study.

When is the study starting and how long is it expected to run for?
April 2011 to November 2017.
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Who is funding the study?
NIHR - Health Technology Assessment Programme - HTA (UK)

Who is the main contact?
Professor Paul Griffiths
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Study website
http://www.sheffield.ac.uk/meridian/studysummary

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 09/06/01

Study information

Scientific Title
Magnetic resonance imaging to enhance the diagnosis of fetal developmental brain abnormalities in utero

Acronym
MERIDIAN

Study objectives
1. Null Hypothesis - The diagnostic accuracy achieved by in utero magnetic resonance (MR) imaging following detailed ante-natal ultrasound examination for suspected developmental brain abnormalities is no greater than that achieved by ultrasound alone.
2. Alternative Hypothesis - The diagnostic accuracy achieved by in utero magnetic resonance (MR) imaging following detailed ante-natal ultrasound examination for suspected developmental brain abnormalities is greater than that achieved by ultrasound alone.

More details can be found at http://www.hta.ac.uk/project/2289.asp

On 10/09/2015 there was a substantial update of this record in order to include details of a follow-up phase of the study. This included added extra information in the interventions, outcome measures, inclusion/exclusion criteria, ethics and sponsor details fields. No changes to the initial study details were requested.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Initial study:
South Yorkshire Ethics Committee, 04/04/2011, ref: 11/YH/0006
Follow-up study::
South Yorkshire Ethics Committee, 28/09/2015, ref: 15/YH/0398

Study design
Multicentre observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Congenital disorders

Interventions
Initial study:
MERIDIAN is a multicentre study recruiting from 13 sites within the UK incorporating a wide geographic and socioeconomic base. Participants will be recruited by a fetal medicine specialist following an ultrasound scan which has identified a known or suspected brain abnormality in their fetus. The patient will be consented into the study and referred within five working days where possible for an MRI examination at one of six scanning centres (Sheffield, Newcastle, Leeds, Birmingham, Edinburgh or Manchester). A form outlining diagnosis, prognosis and intended management is filled out during the consultation and sent to the radiologist. When the participant attends the MRI scan, a report on the in utero MRI examination will be issued to the referring clinician giving details of the radiologist's diagnosis and diagnostic confidence. The participant will then attend a follow up fetal medicine consultation where the specialist will be in a position to counsel the parents with respect to clinical management (termination or continuation of pregnancy). Within 12 months of the initial fetal medicine consultation the fetal medicine specialist will request relevant medical and maternity records for the collection of outcome data. In some cases the participant herself will be contacted in order to follow up the data where case notes have not been located.

Follow-up study:
The follow up study will follow up the children born from MERIDIAN when they are aged 2-3 years old. The family of all surviving, eligible children will be approached regarding participation in the follow up study. The study has three projects; participants have the option to participate in project 1 or project 1 and 2. Project 3 does not require any participant involvement. Consent

for projects 1 and 2 will be obtained via post.
1. Project 1 is a medical case note review, in which details of postnatal imaging, diagnoses or assessments regarding the child's development which were not collected as part of the original MERIDIAN or have been completed since then will be collected and recorded by the research midwife at the site.
1. Project 2 - if If participants also consent to this part of the study then they will be invited to attend a developmental assessment. The assessments will be performed at the local research hospital site or in the child's home. The Bayley Scales of Infant Development (BSID) will be used to assess developmental outcome along with the Gross Motor Function Classification System (GMFCS) and Strengths and Difficulties Questionnaire (SDQ). Where it is not possible to arrange a face to face appointment, or if for any reason the questionnaires are not completed during the appointment then there will be the option for the GMFCS and SDQ to be posted out or given to parents for them to complete and return to the research team. Alternatively the questionnaires can be completed over the telephone with the child's parent.
3. Project 3 - this part of the study does not require input from the MERIDIAN participants or research sites, and will be completed by the central study team at the University of Sheffield. The information for project 3 will come from the assessments described in project 2. We will identify all cases of isolated mild ventriculomegaly diagnosed on iuMR and define their developmental outcome at 2-3 years as severely impaired, mild-moderately impaired or normal as per project 2. In MERIDIAN, the most common information given to women on the basis of isolated mild VM on USS is "favourable (90%)" followed by poor or intermediate and the remainder as normal. We will calculate the prevalence of severe and non-severe impairments in isolated mild VM cases.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Initial study:
1. Absolute diagnostic accuracy of MRI as assessed by percentage of cases where in utero MR diagnosis agrees with post-mortem autopsy/MRI or postnatal imaging
2. Absolute diagnostic accuracy of ultrasound scan as assessed by percentage of cases where ultrasound diagnosis at the time of referral for MRI agrees with post-mortem autopsy/MRI or postnatal imaging. Agreement between prenatal diagnosis and outcome diagnosis will be judged independently by two fetal medicine experts and a third expert will arbitrate if there is a discrepancy in opinion.

Follow-up study:
1. Project 1
The primary outcome measure will be a refined estimate of diagnostic accuracy of in utero MR compared to antenatal US. This will be measured by:
1.1. Measurement of diagnostic accuracy of antenatal US alone (i.e. prior to in utero MR) relative to updated reference diagnosis at 2-3 years of age (postnatal imaging or post-mortem examination)
1.2. Measurement of diagnostic accuracy of in utero MR (following antenatal US) relative to the updated reference diagnosis at 2-3 years of age (postnatal imaging or post-mortem examination).
2. Project 2

The primary outcome measure will be to quantify the value of prognoses based on MR and USS by:
2.1. Assessing the concordance between severe neurodevelopmental impairment (defined by BSID <70 on either index) and poor prognosis, based on MR and on USS
2.2. Comparing the relative prognostic accuracy of USS and MR
3. Project 3
We will assess the clinical significance of isolated, mild ventriculomegaly through:
3.1. Identification of all isolated, mild ventriculomegaly cases diagnosed on in utero MR in the MERIDIAN cohort and defining their developmental outcome at 2-3 years
3.2. Comparison of developmental outcome to the prognoses made based on USS. Prognoses were made on a 5 point categorical scale (poor – less than 50% chance of normal neurodevelopmental outcome, intermediate – 50-90% of normal outcome, favourable – greater than 90% chance of normal outcome, normal – no abnormality found, or unknown).

Secondary outcome measures

Initial study:
1. Effect of including the MRI scan on diagnostic confidence - Change in diagnostic confidence will be measured before and after the scan as assessed by a 5 point likert scale
2. Effect of including the MRI scan on prognosis - Change in prognosis will be measured before and after the MRI scan as assessed by a 4 point categorical scale (poor - less than 50% chance of normal neuro-developmental outcome, intermediate - 50-90% chance of normal outcome, favourable - greater than 90% chance of normal outcome, normal - no abnormality found after detailed fetal medicine investigation)
3. Effect of including MRI scan on management - Change in management will be measured before and after the MRI scan as asssessed by a 2 point categorical scale. This scale will record whether termination of pregancy was discussed on the basis of poor neuro-developmental prognosis
4. A sociological study to include - survey questions to assess participants levels of anxiety and depression at stages of the care pathway (Hospital Anxiety and Depression Scale - HADS), participant views on the care package they have encountered and in-depth interviews on a subsample of participants and involved health professionals
5. A health economics study will be completed to assess the cost effectiveness of including MRI scans

Follow-up study:
Project 2
1. Qualitative assessment of the cases for which the USS prognosis and MR prognosis differed, in relation specifically to the original diagnoses. Prognosis was measured on a 5 point categorical scale (poor – less than 50% chance of normal neurodevelopmental outcome, intermediate – 50-90% of normal outcome, favourable – greater than 90% chance of normal outcome, normal – no abnormality found, or unknown).
2. The concordance in the subgroup of children for which the MR scan was performed within 24 weeks.
3 Subdividing the children without severe impairment into the categories 'mild-moderate impairment' and 'normal' to assess the ability of antenatal imaging to predict non-severe impairment.

Overall study start date

01/04/2011

Completion date

30/11/2017

Eligibility

Key inclusion criteria
Initial study:
1. Participant is in the late second or third trimester of pregnancy (18 weeks gestational age and onwards)
2. Participant is thought to be carrying a fetus with a developmental brain abnormality following detailed specialist ultrasound examination
3. Participant has a singleton or multifetal pregnancy

Follow-up study:
1. Participated in MERIDIAN and has a surviving child aged 2 years old or more*
2. Underwent an iuMR scan during pregnancy as part of MERIDIAN

*If the child is no longer alive then data will be collected and recorded on date of death and cause of death. No contact will be made with the family.

Children who are over 38 months (term corrected) will not be eligible for a developmental assessment but will be included in project 1 (case note review), additional data will only be collected up until the child was 42 months.

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
750

Total final enrolment
570

Key exclusion criteria
Initial study:
1. Participant is unable to give informed consent.
2. Participant has a cardiac pacemaker, intraorbital metallic foreign body or recent surgery with metallic sutures or implant
3. Participant has previously experienced or is likely to suffer severe anxiety or claustrophobia in relation to MR imaging examination
4. Participant is unable or unwilling to travel to Manchester, Edinburgh, Birmingham, Leeds, Newcastle or Sheffield for specialist MR imaging
5. Participant is unable to understand English (except where satisfactory translation services are available)
6. Participant is under the age of 16 years

Follow-up study:
1. If the child born from MERIDIAN is no longer alive (*see above)
2. If the child is no longer in the care of the biological mother who consented to the original MERIDIAN study
3. Is unable to give informed consent
4. Is unable to understand English (except where another parent/guardian of the child can translate and provide consent)
5. If they were withdrawn at any stage of MERIDIAN
6. If they did not attend for fetal MR as part of MERIDIAN

Date of first enrolment
01/04/2011

Date of final enrolment
31/07/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Academic Unit of Radiology
Sheffield
United Kingdom
S10 2JF

Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Foundation Trust (UK)

Sponsor details
Clinical Research Office
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
We intend to publish the study results in peer reviewed scientific journals and at clinical and academic conferences. We intend to publish the primary papers in early 2016

Intention to publish date
01/04/2016

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2019	23/09/2019	Yes	No
HRA research summary			28/06/2023	No	No