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RC PSYCH Royal College of Psychiatrists

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RCGP Royal College of General Practitioners

IPEM

The Royal Society of Medicine

BIR The British Institute of Radiology

MS Multiple Sclerosis Society

Management of Incidental Findings Detected During Research Imaging

A report by Representatives of Research Imaging Centres, Professional Societies, Regulatory Bodies, Funding Organisations, Royal Colleges involved in research imaging and Patient Organisations, in the UK

Participating Imaging Research Centres

- Aberdeen Biomedical Imaging Centre
- Aston Brain Centre
- Bangor University Imaging Centre
- Bristol Oncology Centre
- Birmingham University Imaging Centre
- Cambridge, Wolfson Brain Imaging Centre and Neurosurgery
- Cambridge, University of, Department of Radiology
- Cardiff University Brain Imaging Centre
- Dundee Research Imaging Centre
- University of Edinburgh Research Imaging Centre
- Glasgow Clinical Neuroradiology
- Glasgow, Centre for Cognitive Neuroimaging
- Hull Imaging Centre (Centre for MR Investigations)
- Liverpool Magnetic Resonance And Image Analysis Research Centre (MARIARC)
- London UCL, Queens Square
- London King's College, the Institute of Psychiatry
- London Imperial College, London, MRC Clinical Sciences Centre, Hammersmith
- London, Wellcome Trust Centre for Neuroimaging, UCL
- London, Hammersmith, GSK Imaging Centre
- Manchester, University of
- Newcastle Magnetic Resonance Centre
- Norfolk and Norwich (Norwich Radiology Academy)
- Nottingham, University of
- Oxford Centre for Functional Magnetic Resonance Imaging of the Brain
- Sheffield, Royal Hallamshire Hospital
- York Neuroimaging Centre
- Switzerland, University Hospital, Basel
- The Netherlands, Erasmus MC/Rotterdam Scan Study Group

Acknowledgements and disclaimer

This report has been prepared by representatives from several UK Royal Colleges, professional interest groups, funders of imaging research in the UK, regulatory bodies, National Research Ethics Service, ethicists, patient representatives and imaging research centres in the UK and Europe. It draws on material prepared in advance of the meeting on Ethical Management of Research Imaging by the meeting organisers and speakers, The Royal College of Radiologists' Research Committee (now the Academic Committee), UK Biobank Ethics and Governance Council, Research Imaging Centres, the British Chapter of the International Society for Magnetic Resonance in Medicine, as well as the discussions among participants, feedback on the day and comments received during preparation of the report. The Summary, Conclusions and Recommendations are intended to reflect the range of views expressed by participants, as well as a consensus on acceptable current practice, to highlight areas where more evidence is required and aspirations for the future management of ethical aspects of incidental findings arising during imaging research.

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We are also grateful to the Wellcome Trust which provided the venue and funding for the meeting, The Royal College of Radiologists and the SINAPSE Collaboration which both provided funding and whose members initiated, organised and co-ordinated the meeting and writing of the report.

The contents are a record of the views expressed at the meeting by the individual participants and do not necessarily reflect the views of, or endorsement by, all individual bodies whose representatives attended the meeting. Several other organisations and centres, considered likely to have an interest in this topic, were contacted but no response was received. The organisers apologise for any omission on their part. Debate on the management of incidental findings in several types of research, not just imaging, is continuing through several activities (National Research Ethics Service, UK Biobank Ethics and Governance Council, Wellcome Trust) providing considerable further opportunity to achieve an optimum agreed strategy in the UK.

Contents

1. Context

Medical imaging, including magnetic resonance (MR), computed tomography (CT), ultrasound and radioisotope imaging, is used increasingly in research involving normal participants, as well as patients with many different sorts of disorders. This has highlighted a problem arising through the discovery of *incidental abnormalities or findings*.

An *incidental finding* may be defined as 'a finding that has potential health or reproductive importance, unknown to the participant, which is discovered unexpectedly in the course of conducting research, but is unrelated to the purpose and beyond the aims of the study'.[1,2] Such findings raise ethical and legal issues that are not currently addressed explicitly in guidelines. There is little consensus in the UK (or elsewhere) as to how these consequences of the use of imaging in research should be handled. Guidance from regulatory bodies is ambiguous.[3]

Medical research leads to many benefits for society. Part of good research practice is recognising and having in place mechanisms for dealing with all aspects of the conduct of that research. Imaging research, as with all research on human participants, is carefully ethically regulated to safeguard the interests of research participants. However, the wider use of imaging in research is making incidental imaging findings more common, and recent academic[4] and popular press editorials[5] have highlighted the need for greater awareness, clarity and uniformity of approach among research imaging centres on how these should be managed. Research using imaging could risk falling into disrepute if the public were to perceive that the research, in some way, disregarded the needs of research participants.[2] In general, the researcher has a duty of care to the participant. Hence, there is a need for greater awareness of the issues raised by incidental findings in research imaging, and for discussion of management options, with a view to establishing acceptable standards for practice in the UK. Such proposals should take account of current ethical principles, be considerate of the level of duty of care a researcher has to the research participant and be proportionate to the likely risk of failing to recognise and act on any serious incidental finding, or of incorrectly diagnosing inconsequential incidental findings, while at the same time being feasible and practical within the resourcing, workload and financial constraints that affect imaging research. Any future recommendations on incidental findings should promote trust in research imaging without unduly encumbering the scientific process.[2] While the focus of the present work was on research using medical imaging technologies such as MR, CT, ultrasound, radioisotope imaging, and so on, the principles are transferable to other research methods that involve collection of biological samples or related material from people.

2. Aims and objectives

The aims of this symposium and report were to:

- Engage all stakeholders including research imaging centres, professional organisations whose members use imaging in research, ethicists, research funders, regulatory bodies including ethics committees and patient organisations
- Identify the magnitude and potential implications of incidental findings in research imaging
- Highlight the issues related to ethics and good practice in managing incidental findings in research imaging of both 'normal' participants and patients
- Summarise current opinions on and concerns about practical aspects of managing incidental findings among those involved in research using imaging
- Produce a position statement and guidance to encourage best imaging research practice in the UK, taking account of practical limitations, to facilitate management of incidental findings within a defined ethical framework for imaging research in the future
- Develop practical guidance for research ethics committees
- Make the information from this meeting as widely available in as open access as possible, including examples of information sheets and templates for use in research imaging centres.

The meeting programme and list of participants are available in Appendices 1 and 2.

3. Summary

- Imaging with magnetic resonance, computed tomography, ultrasound and molecular imaging is used with increasing frequency in research in the UK and elsewhere.
- Incidental findings arising in the course of imaging research are common – around 3–12% in neuroimaging and up to 30% in body imaging (especially abdominal or chest imaging) depending on the population being studied.
- In general, even when the research participant is told that the scan is not for medical purposes, is not a diagnostic scan and that the scan will not be examined by a radiologist and reported, the limited evidence available suggests that research participants associate *medical imaging equipment* with the process of *diagnosis* which risks raising the *expectation* that their images will be reviewed by a competent professional.
- Similarly, limited available evidence suggests that many research participants, including those who are researchers themselves, expect that they will be told of any potential life-threatening abnormality that shows up on a research scan and that there will be some guidance as to what to do about it.
- A survey of existing ethics and regulatory guidance shows that there should be mechanisms in place for managing the consequences of *research procedures*, including (although not currently explicitly stated) incidental findings upon/in imaging. However, the guidance is not explicit, is ambiguous and is hard to find in ethics and regulatory instructions.
- A survey of current UK research imaging centres suggests that existing standards, such as they are, are not being applied consistently. Practice for recognising, interpreting and managing any medical or other consequences of incidental findings varies widely from no strategy through to reporting of all research images with any diagnostic content by a radiologist, careful discussion with the research participant about any incidental finding and its likely implications, and referral to an appropriate specialist for advice on requirement for treatment.
- A framework to help standardise understanding of the issues and options for management of imaging research to deal with incidental findings across research ethics committees, NHS research and development (R&D) departments and between NHS and university research and ethics committees would be beneficial. This applies to other research findings not just those from imaging.
- At present, resources in imaging research centres to identify incidental findings routinely, and manage them, vary from none (for example, in a centre geographically and administratively remote from any medical input) to comprehensive (such as in a hospital radiology department with specialist radiologists available to report scans and relevant clinical specialists involved in the research).
- The extent and scope of the researchers' duty of care to the research participant is not well defined or tested (in litigation), but a researcher is expected to exercise reasonable care towards their participants, including to feed back information on any incidental finding of a treatable condition.
- Research imaging is designed to address specific scientific questions. Its primary function, particularly in normal participants, is not as a diagnostic test for a clinical condition, nor as a screening test. Indeed, the detection of incidental abnormalities as a consequence of research imaging that may be of suboptimal diagnostic standard (in some situations) risks exposing the research population to a non-evidence-based use of imaging when, in addition, evidence is lacking on how to manage at least some of the potential findings. Therefore, in general, there should be no expectation on the side of the participant or obligation on the side of the researcher that diagnostic images will be obtained routinely in addition to the research imaging.
- While accepting that having a qualified radiologist review all research images would be the most sensitive and specific method for identifying incidental findings, there would be serious practical implications were this to be implemented universally for various reasons including some shortage of radiologists in the UK and many research imaging centres appearing not to be linked with radiological expertise, making it difficult for radiologists to provide input to research imaging.
- Many research imaging protocols include only limited or no diagnostic images. The addition of diagnostic to research sequences would increase the duration of research imaging, might also reduce participant tolerance, impair research image quality and (especially in the case of CT scanning) expose participants to potential harm from the additional ionising radiation. The primary purpose of imaging used in research is to answer the research question not to provide a diagnostic service. Enhancing all research protocols to a diagnostic standard would add significantly to research costs, would risk increasing the frequency of incidental findings without clear benefit, and might hinder or delay the results of much-needed publicly funded research.

- It is noted that, by analogy with experimental laboratory research, there may be circumstances where diagnostic scanning of the participant *prior* to their participation in certain types of imaging (such as detailed neuroimaging of networks underlying complex cognitive functions) may be considered to reduce variation between participants (including that due to incidental findings), thus reducing 'noise' in the research results. This approach has been suggested in some circumstances; for example, in neuroimaging in psychology research outside the UK.
- Several research imaging centres provided examples of information sheets and documents describing workflows and policies regarding identification of incidental findings based on their own experience in their populations, aimed at improving transparency of how research images would be handled. These are available in Appendix 3.
- Further thought is required to clarify which findings require referral for specialist advice +/- treatment, which require some observation without immediate intervention, which could be ignored indefinitely and what to tell the participant to avoid undue alarm. In part, this reflects lack of information on the long-term natural history of some disorders that are increasingly detected in asymptomatic individuals. Management decisions should be based on the best evidence, where available, from epidemiology studies and treatment trials and in many cases this will require referral to the appropriate medical expert.
- Many, though not all, of those present felt that individuals who were not prepared to have their results fed back to them or their GP/responsible doctor should not participate in the research as this placed the scanner operator or researcher in a difficult ethical and professional dilemma should they notice an incidental finding of potential importance to health. However, it was also recognised that excluding participants in such a way might be a breach of their human rights. Further focused discussion on this point, perhaps by **a specific working group** (and this might apply to other, non imaging, research findings) is required.
- There is a **lack of evidence on which to base practice** – on the balance of harm versus benefit in telling research participants about findings; on false-positive rates; on how often it might cause a serious problem if research participants were not told anything or were told about inconsequential findings; on pick-up rate of radiographer/researcher versus specialist radiologist; on whether examples of common incidental findings would help less specialist researchers differentiate which incidental findings might require closer specialist scrutiny or not; on how many participants might refuse to take part if they were not going to get any feedback or if they were going to get feedback even if they did not wish it; about whether individuals who do not wish to be told the results of their scan should be barred from participating in the research or not; on whether there are ways in which participants can be told with greater clarity about what will happen to their images; about the burden of work created by reporting all scans; about mechanisms for streamlining access to specialist opinions; etc, etc. Research to clarify these issues is vital for developing evidence-based policies for the management and feedback of incidental findings.
- The meeting attendees (Appendix 2) showed overwhelming agreement that incidental findings present a difficult problem, while agreeing that there was no clear present consensus on many aspects of how they should be managed (Table 1, overleaf). The uncertainties raised may not be possible to resolve from first principles and may differ between studies and centres for good reasons. Hence a series of processes that will judge and deliver an opinion on how to manage a particular study, through a process that is accountable, inclusive and transparent, is required.
- A sliding scale of options reflecting current *minimum acceptable* to *optimum practice*, that would take account of research participants' expectations, the potential health implications of incidental findings, the particular circumstances of the study and ensuring that the research participant understood the practice in that centre when consenting, is required. Best practice is hard to define as it is a balance between providing appropriate imaging and management strategies for potential incidental findings while still facilitating research projects. Section 7 summarises these options.
- An interim framework agreed as a result of this meeting would require regular review as the understanding and awareness of incidental findings mature, expectations evolve and evidence on the clinical course, treatment and resources to deal with incidental findings become more widely available. Further progress in imaging techniques is likely to lead to the detection of previously undiscovered findings that may need to be dealt with.

4. Background

Medical imaging – much of it with magnetic resonance (MR) or computed tomographic (CT) scanning – is used increasingly in research involving normal participants, as well as patients. This leads to a range of important social benefits but also to a problem arising through the discovery of *incidental abnormalities or findings*. An *incidental finding* may be defined as 'a finding that has potential health or reproductive importance, unknown to the participant, which is discovered in the course of conducting research, but is unrelated to the purpose and beyond the aims of the study'.[1] Incidental findings are not a new problem, having been a consequence of many types of clinical research with many different laboratory or physiological measures for many years,[6] but the increasing use of imaging has thrown the issue into prominence. Advances in imaging techniques, both higher spatial resolution and new techniques with greater sensitivity, enable the detection of even more subtle abnormalities that would have previously gone unnoticed. Incidental findings raise ethical and legal issues that are not currently addressed explicitly in guidelines.[3] There is little consensus or clarity in the UK (or elsewhere) as to how these consequences of the use of imaging in research should be handled.[3,7]

The problem is not trivial

For example, on brain imaging, around 3% of apparently normal participants will have important unexpected abnormalities, although the prevalence may be quite a bit higher in some populations (Table 1, overleaf).[8,9] This translates to a 'number needed to scan' of 37 to find one unexpected abnormality. On body imaging, incidental findings occur with similar or greater frequencies during whole-body CT or MR imaging[10] and during specific organ imaging, especially cardiac CT[11] and colonography[12] (Table 2, overleaf).

It is also not uncommon for completely unremarkable physiological features, normal variants, minor developmental anomalies and imaging technique artefacts to be misidentified as pathology by untrained observers, leading to unnecessary worry for the participant if they are informed. Examples are listed in the footnote to Table 1. In general, radiological expertise is required to recognise and interpret these abnormalities appropriately, but for several reasons, the bulk of imaging research is conducted without any input from radiologists (and is likely to continue in this way).

The effects of incidentally discovered pathology on the individual can be complex and far-reaching.[13–15] Some may require medical intervention and many need to be handled sensitively to avoid causing unnecessary alarm.[16,17] The personal financial implications, including loss of insurance, may be huge. Indeterminate incidental findings may trigger further investigations which may carry further expense and risk for the participant.[15,18] In the case of cardiac CT imaging, this has initiated a debate as to whether the imaging field of view should be restricted deliberately to avoid detecting non-cardiac abnormalities and the associated cost of their investigation.[11]

What does current regulatory guidance state?

A recent systematic review of all UK, European and international humanitarian, legal and ethical agencies' guidance as applied to research imaging indicates that guidance on management of incidental pathology is inconsistent between agencies and difficult to find.[3] Where given, guidance on management of research imaging was inconsistent, limited and did not address the interests of participants. Both the UK Department of Health (DH) and the National Research Ethics Service (NRES) state that the research participant *'should be made aware of possible disadvantages and risks of taking part in research',* that *'the risks should be outlined including the discovery of another condition of which they were unaware'* that *'might have medical or insurance implications'* and what the arrangements would be for dealing with this.[3] However, there is little to indicate the frequency or implications of incidental imaging findings, nor that some degree of expertise is required to interpret and manage these. Much research imaging (as much as 43% in a recent survey of UK practice),[19] particularly neuroimaging, is undertaken by research scientists without medical training, often in research centres that are remote from radiology departments or even hospitals, potentially leading to variation in awareness and understanding of the issue and consequently in management of findings.[4] Furthermore, the legal obligations to disclose findings and the associated liability may vary depending on whether the relationship between the researcher and the research participant is viewed as similar to that of a physician/patient or rather as one involving researcher/participant – as participants', researchers' and regulators' expectations may differ in this respect, so may their respective expectations about the standard of care required in the case of an incidental finding.[13] In the absence of a clear indication of what does or does not count as a reasonable standard of care, the courts will take ordinary and common practice and the views of a responsible body of professionals into account. Thus, there is a potential for the behaviour of the profession to influence where the bar is set.[13]

Table 1. Some common incidental findings in descending order of their prevalence on brain MR imaging, and details of their potential complications and treatment[8]

Incidental finding	Prevalence (%)	Most common potential complications	Treatment of asymptomatic findings
Arachnoid cyst	0.5	Pressure on adjacent brain structures	Neurosurgical decompression is not indicated for asymptomatic cysts (no RCTs).
Aneurysm	0.35	Haemorrhage (risk influenced by aneurysm site and size)	Endovascular coiling or neurosurgical clipping are available, but there is uncertainty about their use because of the lack of published RCTs comparing treatment with conservative management for asymptomatic aneurysms.
Meningioma	0.29	Pressure on adjacent brain structures	Neurosurgical excision and radiotherapy tend to be used when meningiomas cause symptoms (no RCTs).
Cavernous malformation	0.16	Haemorrhage and epileptic seizure(s)	Neurosurgical excision and stereotactic radiosurgery are available, but there are no case series or RCTs supporting their use for asymptomatic cavernous malformations.
Hydrocephalus	0.1	Headache and drowsiness	Shunting is not indicated for people without symptoms.
White matter lesions suggestive of an inflammatory disorder	0.06	Later development of multiple sclerosis	Immunological treatments are not indicated. Cautious medical review and advice may be needed.
Low grade glioma	0.05	Pressure on adjacent brain structures and epileptic seizure(s)	Neurosurgical excision may be used, but who to treat and when are uncertain (no RCTs). Occasionally more malignant primary brain tumours like glioblastomas have been reported as first presenting during scanning for other purposes.
Arteriovenous malformation (AVM)	0.05	Haemorrhage and epileptic seizure(s)	Endovascular embolisation, neurosurgical excision and stereotactic radiosurgery are available. There is an ongoing RCT comparing treatment with conservative management for unruptured AVMs.
Common developmental variants, rarely of medical importance	Precise unknown		May alarm non-expert

RCT = randomised controlled trial

Additional common developmental or normal variants that are of little health relevance but may alarm the untrained observer include mega cisterna magna, callosal lipoma, asymmetrical ventricles, enlarged perivascular spaces. Other anomalies that may sometimes be of health relevance and that are not listed above include Arnold Chiari malformations, cerebellar atrophy and pineal cysts.

Table 2. Common incidental findings on body imaging and their potential implications for medical management[10–12,15]

Body imaging: examples of incidental findings		
Major	**Moderate**	**Minor**
Aortic aneurysm >5 cm	Gallstone in common bile duct	Left-sided inferior vena cava (IVC)
Aortic dissection	Splenomegaly	Gallstones in gallbladder
Solid liver mass	Indeterminate liver lesion	Hepatic cysts
Solid renal mass	Abdominal wall hernia	Diverticulosis
Ovarian cyst >5 cm	Uterine mass	Calcified pulmonary nodule
Solid pancreas mass	Absent kidney	Calcified pleural plaques
Undescended testis	Pelvic kidney	Lipoma
Gall bladder mass	Adrenal mass	Bladder diverticulum
Bilateral small kidneys	Ureteric calculus	Renal calculus
Pneumothorax	Bowel inflammation	Degenerative spine changes
Pulmonary embolism	Emphysema	Bone infarct
Deep vein thrombosis	Bronchiectasis	Fatty liver
Gastric mass	Irregular nodular margin liver	Renal cysts
Oesophageal mass	Air in the biliary tree	Appendicolith
Solid pulmonary mass	Pancreatic cystic lesion	Muscle atrophy

Note: It is often difficult to determine the significance of a finding (major, moderate, minor) in the absence of a full relevant clinical history for the research participant. Major – always requires further investigation and likely to have adverse health effects; Moderate – usually requires further investigation but health effects unclear; Minor – rarely requires further investigation and unlikely to have adverse health effects.

How variable is management of incidental findings in research in the UK?

The RCR Academic Committee (formerly the Research Committee) recently completed a survey of imaging researchers who had performed a study using 'healthy' participants between 2006 and 2009.[19] Briefly, of 146 investigators surveyed, 63 (43%) responded. Although most had local guidelines on incidental findings, the most common current practice was to rely on the researcher (frequently non-medical) recognising that *something was not right* and asking a radiologist to review the scan. However, many recognised that this was not ideal. Consent, reporting and disclosure varied widely depending on whether the researcher was medical or non-medical, radiologist or not, and their seniority (Figure 1 and Table 3).

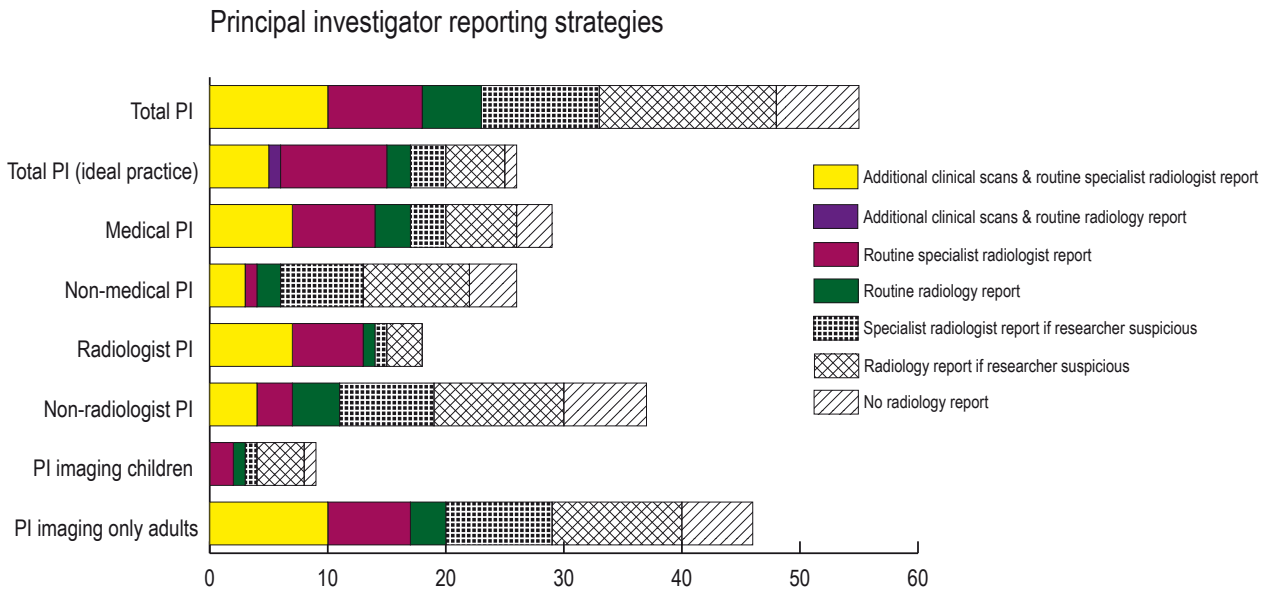

Figure 1. Research image reporting strategy. Bar charts demonstrating principal investigator (PI) reporting strategies (current practice unless shown otherwise). The degree of shading reflects how proactive a reporting strategy is (darker more proactive). Adapted from Booth *et al.*[19]

Table 3. Principal investigator (PI) incidental finding (IF) management strategy subgroup analysis, showing how management strategies relating to consent, reporting and disclosure differed depending on whether the researcher was medical or non-medical, a radiologist or not, and their duration as a PI[19]

Management	Practice*	Strategy	Principal investigator subgroup difference	P value
Consent	Current	Indicate that incidental findings would be disclosed to the participant by a member of the research team	Medical more likely than non-medical	<0.0001
Consent	Current	Indicate whether incidental findings were likely to be treatable	Medical more likely than non-medical	=0.047
Consent	Current	Indicate if there would be potential future recontact if the data were to be reanalysed	Medical more likely than non-medical	=0.017
Consent	Current	Discuss potential benefits of identifying any incidental lesion	Radiologists were more likely than non-radiologists	=0.048
Consent	Ideal	Opt for discussion with participants regarding the investigator's responsibility to provide medical services should any IF be found	Medical more likely than non-medical	=0.036
Reporting	Current	Take a proactive approach (ie, radiologist reporting of all scans, obtaining additional scans routinely, specialist reporting or combinations thereof) to identify incidental findings	Medical more likely than non-medical	=0.041
Reporting	Current	Tend towards proactive image review and specialist reporting	Medical more likely than non-medical	=0.007
Disclosure	Current	More likely never to disclose incidental findings to the participant	Non-medical more likely than medical	=0.003
Disclosure	Current	Disclose incidental findings routinely to the participant	PIs for a shorter period of time	=0.042
Disclosure	Current	Disclose incidental findings to the participant, if felt to be relevant	PIs for a longer period of time	=0.020
Disclosure	Current	Use research team physician to disclose IF to the participant	Medical more likely than non-medical & radiologists were more likely than non-radiologists	<0.001
Disclosure	Current & ideal	Use the participant's own GP to disclose IF to the participant	Non-medical more likely than medical	<0.001

*Practice can be current or ideal. Ideal practice defined as 'practice without funding or time constraints'.

A previous survey of research imaging centres, mostly in the USA, found that the primary responsibility for MR scanning in neuroimaging research was by students in 41%, professionals and postdoctorates in 21% and professional staff only in 38% and in about two-thirds, the handling of any incidental findings would depend on a junior researcher recognising it.[20]

What do research participants think?

The little information that exists on expectations of imaging research participants for their research images suggests that most participants would want to be informed of any incidental finding. Among research participants surveyed in the USA in 2005, 90% of 105 respondents said that they would want the findings communicated to them and that 60% preferred this to be done by a physician in the research team, with no difference in response from participants scanned in medical to non-medical settings.[21] Students taking a module on ethics of research imaging on a Neuroimaging MSc course, between 2007 and 2010, unanimously indicated that they wanted their research scan read by an expert, to be informed of important (but not of inconsequential) findings and that these would be acted upon. In 2008–09, virtually all (98%) research participants participating in the Lothian Birth Cohort 1936 study (all aged around 70 at the time of scanning) indicated that they would prefer that an abnormality that might affect their health be identified and acted on, but two-thirds had not considered that this might affect their life insurance or have other implications. A study of 45 participants in the National Child Development Study (1958 Birth Cohort), of whom 16% had previously experienced an MRI for clinical reasons, found that while 43% of the group said they were prepared to take part in a functional (fMRI) study regardless of whether feedback was provided, 41% would only do so if they received feedback about all potential problems and 11% would only participate if feedback was provided on problems considered to be both serious and treatable.[22]

Interestingly, the preference expressed by most lay research participants for being informed of any incidental abnormality that might affect their health, was mirrored by imaging researchers when asked for their preferences should they volunteer for a research scan – all said that they would want to be informed of any incidental finding of medical importance and to know that it would be acted upon.[23]

Researcher's duty of care

The ethical argument for feedback of incidental findings to research participants is based on the duty of care that researchers have toward their research participants. While a clear and well-established duty of care exists for doctors in relation to patients, at least for findings of relevance to health, it is less well defined in research relationships[13,24] and with findings that are not of direct relevance to health[14] and may be held to vary across research settings related to such considerations as the invasiveness of the research, the extent of data being collected and the duration of the research relationship. Indeed, the extent and scope of this researcher/participant duty has not been defined and tested (in litigation) unlike the clinician/patient duty which has been extensively defined and refined over many years of legal precedent. Nevertheless, a duty of care of a more limited scope between researcher and participant is likely to exist.[13]

While doctors are required to act in the best interests of their patients, a researcher is expected to exercise reasonable care towards their participants, and to respect them as people. On this basis, there is a broad consensus, reflected in most guidelines,[3] that researchers should provide their research participants with information generated through research procedures that may be expected to be beneficial to them and for their health. Thus, there is a case that part of the researcher duty of care is to feed back an incidental finding of a treatable condition so that a research participant may experience the benefit of earlier and perhaps more effective treatment than might have been the case if diagnosis had occurred at a later time following the development of overt symptoms.[13] An incidental finding could also indicate that preventative action is required to avoid the development of a serious condition. However, the precise role that a particular researcher might take in this process is at present unclear but is probably informed by their professional status and experience. Thus if findings were observed by radiographers during the imaging visit, it would probably not be appropriate for the radiographer to give their view directly to the participant, as this would not occur in clinical practice. Rather the scan should be reviewed by a radiologist (as it would be in a clinical setting) and if necessary (that is, the finding was serious), reported back to the participant and the GP or other clinically responsible individual involved in the study. The treatability or otherwise of a 'serious' finding should probably not influence the feedback to the participant.

However, while a duty of care can mean that a researcher should feed back beneficial information they may come across as they pursue their research protocol, there is no duty to seek out such information beyond the research protocol.[13] It has been suggested that in MRI research using relatively limited sequences (in terms of their diagnostic capability), clinical standard scans should be added to the protocol because they are more likely to reveal incidental findings. For example, sequences that are of limited diagnostic utility (often used in fMRI studies) may make the interpretation of potential incidental findings difficult, creating (in some circles) an argument to include higher grade diagnostic scans in research studies, so that incidental findings may be disambiguated and potential false-positives reduced. While we might regard this as a researcher simply doing the participant a (potential) favour, there can be no requirement for a

researcher to adopt a clinical standard of scanning for a research study: that would both redirect the purpose of the study and move beyond researchers' duty of care.

In research studies, it is very important that participants' expectations are appropriately managed and that they do not regard the research procedures as health checks,[13] because they are not being taken in a healthcare setting, the scans may not be optimised for clinical diagnosis and they should know whether the scans will be routinely reviewed by a radiologist, because otherwise the participants could be falsely reassured that all is well if they do not receive any feedback, or that feedback will indicate all potential problems. This is especially important when using research procedures (like MRIs) that are similar to clinical assessments which participants may assume are clinical assessments.

Despite these significant issues, many may in practice be resolvable in light of practical experience.[4,14] For example, the issues around a particular study may crystallise once the actual participant population and imaging routine is known and that would clarify, in many cases, the extent of the duty of care between researcher and participant.

What practical solutions to this mismatch between current imaging research practice, research participant expectations and ethical principles have other organisations suggested?

In 2005, a wide range of neuroimaging researchers discussed management of incidental findings in imaging research at a meeting at the USA National Institutes of Health (see http://accessible.ninds.nih.gov/news_and_events/proceedings/ifexecsummary.htm).[2] Although they did not reach a final consensus, they did at least highlight the problem and achieve an agreement around a minimum standard for handling of research scans.[25] They also recognised that *'Any future official recommendations on incidental findings should promote trust in research without unduly encumbering the scientific process'*.[2] Further recommendations were made by Wolf and colleagues (Table 4, overleaf).[1]

Experience from the Rotterdam Scan Study, a large population-based study in persons aged over 45 years in The Netherlands,[26] shows that over 95% of study participants would want to have *relevant findings* communicated to them and their general practitioner. In this study, all research brain MR scans are read within a week after acquisition by physicians (clinical PhD students in the Rotterdam Scan Study), who have been trained on detection of *'non-normality'* by supervised reading and whose performance has been evaluated on a training set of 100 scans. Potential *'non-normal'* findings (approximately 10% of all scans) are subsequently evaluated by one of the collaborating neuroradiologists. The Rotterdam Scan Study protocol for management of incidental findings incorporates the view of an expert panel, distinguishing a priori *relevant* (that is, to be communicated to the individual) from *irrelevant* (that is, not to be revealed to the participant) findings. This distinction is based on the best available evidence regarding natural history of these abnormalities. This expert panel meets every two years to make necessary adaptations based on new evidence. Potential relevant findings that are not on any of the a priori defined lists are evaluated by (members of) the expert panel on a case-by-case basis. Relevant findings are communicated to the participants by telephone, by one of the neuroradiologists involved in the Rotterdam Scan Study. An appointment with a relevant medical specialist is scheduled within two weeks after this telephone conversation. Consent to inform the participant's GP is explicitly checked during this telephone conversation, as well as approval to transmit the research MRI scan to the hospital database.

A research imaging group at the University of California, Irvine, USA, created a web-based system whereby investigators performing brain MRI on healthy participants could refer images with suspected concerns to a board-certified neuroradiologist for an expert opinion.[27] Among 27 scans referred for further opinion, one was considered to be of clinical significance and the others were of no consequence. The increasing availability of national picture archiving and communication systems (PACS) with research imaging centres linked to PACS may make this approach feasible much more widely.

UK Biobank is a prospective cohort study that aims to build a resource of information and samples that will support a diverse range of health-related research intended to improve the prevention, diagnosis and treatment of illness and the promotion of health throughout society. Having completed recruitment of 500,000 participants, the project is developing ways to enhance the phenotyping data, including through the use of MRI on 100,000 cohort members.

In this context, the UK Biobank Ethics and Governance Council has been considering the problem of incidental findings from imaging since 2009 (UK Biobank Ethics and Governance Council Review 2009).[28] Recognising that the possibility of an incidental finding was much higher with MR imaging than with the less intrusive research technologies used by UK Biobank during the recruitment phase, but that some findings would turn out to be false-positives and conversely that there was little information on what to do about some findings whose natural history was poorly characterised, the Council considered four options. These range from:

1. Not collecting any imaging data at all (for example, if the balance between the potential benefits and potential harms is considered to be unacceptable in the context of UK Biobank)

Table 4. Recommended classification of incidental findings by Wolf *et al* in the USA.[1] Note that these recommendations were designed for genetic as well as imaging research. These actions assume other recommendations – that the research protocol and consent forms anticipate incidental findings and indicate the management plan.

Category	Relevant incidental findings	Recommended action
Strong net benefit	■ Information revealing a **condition likely to be life-threatening** ■ Information revealing a **condition likely to be grave that can be avoided or ameliorated** ■ Genetic information revealing significant risk of a condition likely to be life-threatening ■ Genetic information that can be used to avoid or ameliorate a condition likely to be grave ■ Genetic information that can be used in reproductive decision-making: (1) To avoid significant risk for offspring of a condition likely to be life-threatening or grave or (2) To ameliorate a condition likely to be life-threatening or grave	**Disclose** to research participant as an incidental finding, unless s/he elected not to know
Possible net benefit	■ Information revealing a non-fatal **condition that is likely to be grave or serious but that cannot be avoided or ameliorated, when a research participant is likely to deem that information important** ■ Genetic information revealing significant risk of a condition likely to be grave or serious, when that risk cannot be modified but a research participant is likely to deem that information important ■ Genetic information that is likely to be deemed important by a research participant and can be used in reproductive decision-making: (1) to avoid significant risk for offspring of a condition likely to be serious or (2) to ameliorate a condition likely to be serious	**May disclose** to research participant as an incidental findings, unless s/he elected not to know
Unlikely net benefit	■ Information revealing a **condition that is not likely to be of serious health or reproductive importance** ■ Information whose **likely health or reproductive importance cannot be ascertained**	**Do not disclose** to research participant as an incidental finding

2. Collecting imaging data with full clinical feedback
3. Collecting the imaging data but providing no feedback at all with explicit consent of participants
4. Collecting the data and providing feedback on any potentially serious findings made during the imaging visit (possibly including whether participants should have the right to decide for themselves whether to receive the feedback).

At the time of writing, discussions are ongoing but three options have been discounted by UK Biobank and these decisions were endorsed by the Ethics and Governance Council.

1. UK Biobank's Board of Directors is enthusiastic about the potential of the imaging and about the value of moving to a pilot phase. However, the Board has informed the Ethics and Governance Council that it would consider the results of any such pilot before making a decision regarding the full-scale launch of the imaging visits.
2. Full clinical feedback because the purpose of UK Biobank is to create a research resource for the benefit of future generations and, like many research initiatives, it does not aim to give participants routine health information or a health check.
3. No feedback. This was considered to be ethically problematic in relation to not only participants but also to radiographers who may feel morally or professionally compelled to inform the participant in the case of noticing an abnormality during scanning. Also, UK Biobank received legal advice that an irreducible duty of care might be found to exist between the radiographer and the participant, which would likely require feedback of serious incidental findings resulting from MRI.

Under option 4, a two-stage process is being considered whereby a radiographer would identify scans that revealed potentially serious findings and that these scans would then be clinically reviewed by a radiologist who would decide whether there were significant clinical findings which should be reported to the participant and their GP.[28] UK Biobank intends to submit a funding application for the MRI survey late in 2011. If funded, a pilot phase will inform the further development of the feedback protocol.

The Nuffield Council on Bioethics addressed the issue of incidental findings identified through increasing use of commercially operated 'health screening' using several forms of imaging, and published their report in September 2010. Several of those involved in the present workshop (Wardlaw, Al-Shahi Salman) also provided evidence to the Nuffield Council and commented on their draft report. This provided useful additional insights into the frequency and implications of incidental findings and data protection arising through non-research uses of medical research technologies, not just imaging.[29]

The British Chapter of the International Society for Magnetic Resonance in Medicine has also prepared a discussion document on incidental imaging findings for the research community, which is included in full in Appendix 4.

The recent systematic review of legal and ethical agencies' guidance as applied to research imaging suggested possible approaches to UK best research imaging practice.[3]

Various research imaging centres have their own guidelines,[30] which were shared at the meeting. These are available in Appendix 3.

5. Methods

We used several methods to assess the magnitude of the problem of incidental findings in imaging research in the UK, debate the topic among a broad cross section of imaging research centres, professional organisations whose members are involved in imaging research, funding organisations, regulatory bodies, ethicists and patient representatives, gather a consensus opinion, identify areas for future research and prepare this report and guidance.

The following key issues were addressed in the meeting:

- What are the practical and logistical barriers to delivery of an ethical framework to manage incidental findings in research imaging?
- What would constitute ideal practice, and what are the reasonable alternatives that can be achieved if expertise and funding are limited?
- Should, and if so how can non-medical, non-radiological imaging researchers be guided in recognising important abnormalities?
- What do the stakeholders in the meeting feel are the minimum acceptable arrangements for research imaging in the UK?
- Are there efficient ways that research imaging centres could better access radiological expertise if this is felt to be the ethical imperative?
- What should research participants be told about handling of the images, the possibility of an incidental finding and its potential implications?
- If incidental findings are to be disclosed to the participant, how should this be handled?
- Should all imaging modalities and organ systems be handled in the same way or are there important differences in the frequency and nature of the incidental findings that require different standards?
- Should research participants be able to opt out of being told about any finding no matter how serious, or should such participants be excluded from participating in the research?
- What are the legal and professional obligations of investigators in identifying and reporting abnormalities, particularly where an abnormality may pose a risk to others (such as a bus driver with a cerebral aneurysm)?
- Should there be a guideline on management of incidental findings in research imaging in the UK? If so, how should this be put into practice?
- What are the gaps in current knowledge on this topic and how can these be overcome?
- Should funding organisations and ethics committees require that applications for research including imaging demonstrate their plans for dealing with incidental findings?

Prior to the meeting, the literature on frequency of incidental findings in imaging research was reviewed in body[10,11,31] and neuroimaging including the publication of a systematic review of the frequency of incidental findings in neuroimaging.[8]

We reviewed the current guidance on management of incidental findings that was available in all UK and international ethics and regulatory guidance.[3]

We collected and reviewed the published literature reporting the discussions that had taken place in the last ten years on this topic in other countries,[1,2,13,16,18,20,21,25,32-34] in part summarised in the Background above.

We conducted a survey of UK research imaging centres and researchers identified as principal investigators of imaging research studies involving normal participants.[19]

We devised a one-day meeting (see Appendix 1 for the programme) at which representatives from all UK (and some non-UK) research imaging centres, professional organisations whose members are likely to be involved in imaging research, lawyers, regulatory bodies, the National Research Ethics Service, R+D offices, ethicists, the different disciplines involved in imaging research and patient groups could participate in a structured discussion on specific key questions about management of incidental findings. The full list of participants is provided in Appendix 2.

Before this meeting, we circulated background materials including a summary of the problem, to all participants to prepare them for discussions on the day. Several centres kindly agreed to share their standard operating procedures (SOPs), research participant information sheets and consent forms and these were also circulated prior to the meeting (Appendix 3). UK Biobank Ethics and Governance Council and the British Chapter of the International Society for Magnetic Resonance in Medicine had been working on this topic for their respective members and their most recent reports were also circulated to the meeting attendees.[28]

At the meeting, seven speakers gave brief presentations to summarise: the purpose of the meeting (A Jackson), the frequency and type of incidental findings in neuroimaging (R Al-Shahi Salman) and in body imaging (D Lomas) research, the results of the survey of current

practice in UK centres for dealing with incidental findings (T Booth), the current debate on management of incidental findings from the wider European perspective (R von Kummer, Germany), current UK and international guidance from a legal perspective (G Laurie), and expectations of research participants from the Ethics Committee perspective (H Davies).[†]

The participants were divided into four groups, each with a chairperson, and asked to discuss a specific question and provide bullet point recommendations. These were fed back to the entire meeting, with further discussion by the entire group and a summing up of the main points derived from the meeting.

Senior neuroradiologists and imaging researchers from Germany (Professor R von Kummer, Professor F Hentschel), Switzerland (Dr S Ulmer) and from the Netherlands (Dr M Vernooij) attended the meeting and/or commented on the draft report and thus provided insights from their practice and from debates on the subject of incidental findings that are ongoing elsewhere in Europe.

Group discussion topics and chairpersons were:

1. What are the practicalities and logistic barriers to delivery of ethical research imaging? *Dr Adam Waldman*
2. Consent and what research participants should be told *Dr Chris Freeman*
3. What is ideal practice and what is acceptable minimum practice? *Professor Martin Leach*
4. How should a guideline be put into practice? *Professor Alastair Compston*

Groups were encouraged to consider:

- The size of the problem
- The expectations of research participants
- The current regulatory framework
- What imaging centres are currently doing in the UK about incidental findings
- Practical issues
- Some example guidelines that several centres have kindly agreed to share with the meeting delegates
- What is happening in other countries, and so on, while considering the tensions and questions that needed to be resolved, which included:
  - The many existing regulations that cover conduct of research and the perception that more regulations will 'stifle' research
  - Whether the existing regulations are being interpreted correctly with respect to incidental findings
  - Whether additional regulations are required, or rather clarifications of existing regulations would be enough
  - Problems with who checks imaging for abnormalities – trained or untrained staff checking imaging for abnormalities
  - Resources for having trained staff checking imaging for abnormalities
  - Dealing with perceived abnormalities – true and false-positives
  - Should extra scans be performed routinely if the planned research sequences are not of diagnostic quality, or is it acceptable if the participant is told that the scan will not include any diagnostic scans?
  - Should research participants simply be told that no one will look at their scan from a diagnostic point of view, either for any information that might be clinically useful if they are a patient being scanned in a disease-focused research study or to exclude incidental findings, and therefore no report will be provided at all?
  - Should research participants be able to refuse to be told if an abnormality shows up on their scan, or should such individuals be excluded from research studies?
  - Should funding bodies ask for brief information on how centres manage incidental findings as part of any funding application involving imaging?
  - Should local and regional ethics committees and R+D departments ask specifically for information on managing incidental findings on investigations done in research or should this appear in existing sections of the ethics form?
  - Should ethics form completion guidance be edited to include specific advice on where to enter details on handling of incidental findings?

Chairs were advised of the importance of making sure that the tensions were well aired, as they will be different in different centres depending on the background of staff and research interests; that any guideline would have to take account of this 'one size does not fit all' problem; that this is likely to be an evolving process as more information becomes available, technology develops and attitudes change; and that something achievable is better than something aspirational that is beyond the reach of most centres.

[†] Video recordings of the talks are available at: http://www.sinapse.ac.uk/media/events/ethics_management.asp
Question and answer sessions followed the talks. See above link for video and transcripts.

6. Main analyses

Dr R Al-Shahi Salman summarised the findings of a recent systematic review of incidental findings in neuroimaging (Figure 2).[8] Incidental findings increase with age and higher resolution of MR; and occur at the rate of one for every 37 participants scanned, not counting markers of cerebrovascular disease. Treatment of incidental findings may result in benefit or harm but for most incidental findings the overall balance of benefit and harm is not known.

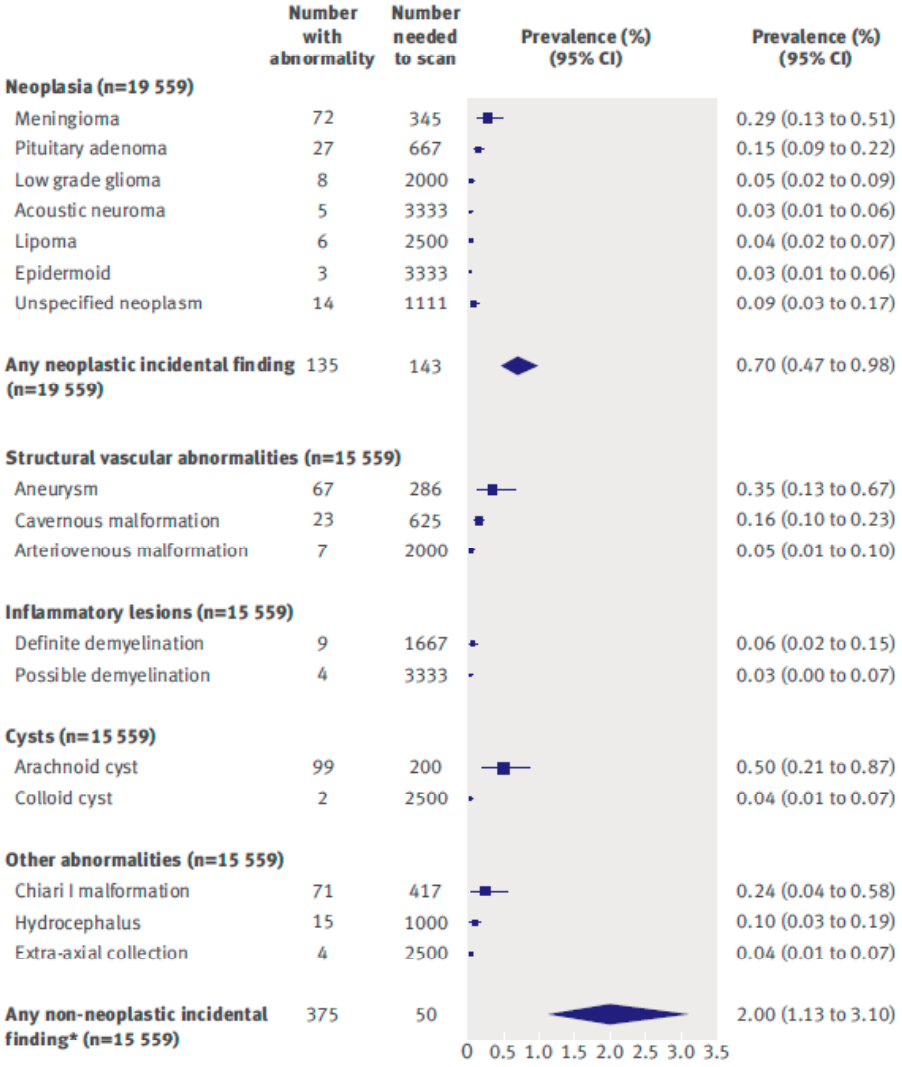

Figure 2. Incidental findings on imaging in normal participants by lesion type. From Morris *et al*[8] published in the *BMJ* as Open Access under a Creative Commons licence.

Professor D Lomas summarised the common incidental findings in body imaging as major (such as large aortic aneurysm), moderate and minor; these are more common than on brain imaging, occurring at the rate of 4% major and 15–20% minor (Table 2, page 10). They frequently present in the absence of any clinical information, access to any previous imaging or medical history, often require further investigation and nearly always create new workload. The CI/PIs of the research projects often have highly subspecialised clinical interests and as a result, limited or no experience in managing incidental abnormalities across a wide range of organ systems. Figure 3, overleaf, illustrates an incidental finding identified during a research scan in a body fat study (a small filling defect in the common bile duct). This subtle finding would most probably be missed by an untrained observer and is most likely a gallstone but in this location may cause infection and obstructive jaundice and in clinical practice would usually be removed.

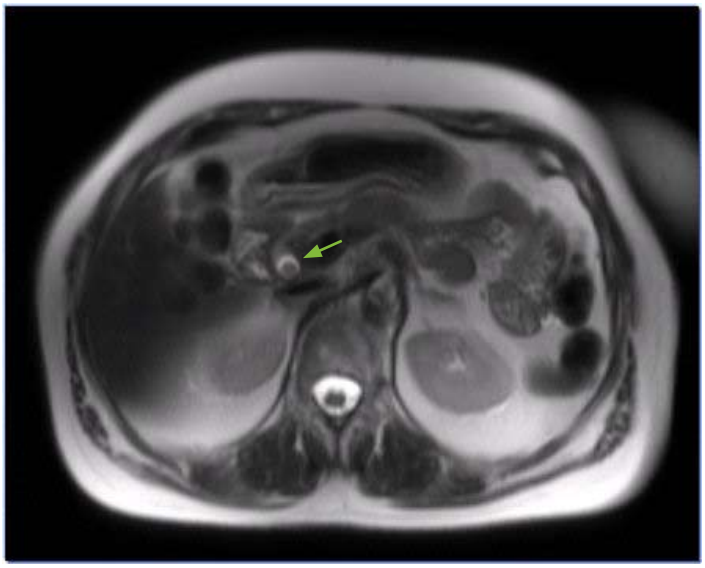

Figure 3. A snapshot of a T2-W image obtained during a body fat study which demonstrates a small filling defect in the common bile duct (green arrow). This is a subtle finding likely to be overlooked by the untrained observer. The filling defect is most likely a gallstone, which in this location usually causes infection or intermittent billiary obstruction (ie, jaundice) and in normal clinical practice would be investigated and removed

Dr T Booth summarised the results of a survey of current UK research imaging practice on incidental findings.[19] Principal investigators (n=160) of imaging studies involving normal participants were surveyed of whom 63 researchers (43%) responded. Practice regarding consent, identification and reporting of findings and disclosure of important medical findings to participants varied widely (Figure 1, page 11 and Table 3, page 12). Full details in Booth *et al*.[19]

Professor R von Kummer summarised practice in Germany where the management of incidental findings has become a controversial topic of debate between the German Neuroradiological Society and the Bonn Neuroethics Working Group. The latter took the view that research imaging would not be examined for incidental findings in general, that participants could opt in or out of being told about any research findings and then opt in or out of receiving any treatment. The former group preferred that research images be examined by a neuroradiologist because participants expect that images will be evaluated properly,[35] and went further to suggest that participants should be screened with imaging before participation to exclude those with anatomical variants or incidental findings as their variation would mean that they would be excluded from the analysis. A parallel was drawn with the usual practice in laboratory research of using genetically identical laboratory animals to reduce heterogeneity in many typical lab experiments.

Professor Graeme Laurie summarised the current relevant international and national guidance, human rights and common law regarding research imaging findings, contrasting consent and care, data protection and access and issues related to duty of care. Four general options were discussed, from 'provide no feedback whatsoever' to 'the right not to know'. Currently there is no consistency or clarity in guidance, the legal issues need to be separated from the ethical issues, and there is no single solution for all eventualities. Rather, a range of solutions is required to match various study circumstances.

Dr Hugh Davies summarised the expectations of research participants and how the problem of incidental findings is currently viewed by ethics committees. Ethics committees are particularly concerned about the potential harms of research, for the participant's autonomy; informed consent is seen as central to the participant's protection and the patient/participant information sheet is examined in detail. Ethics committees regard the researcher as having a duty of care to the participant and expect sensitive, comprehensive management of any affected participants. They are sensitised to researchers who either try to trivialise the problem or exaggerate the benefits of their research. In summary, ethics committees have difficulties in this area, vary in their comments and remedies and would appreciate guidance on how to manage incidental findings perhaps in the form of frequently asked questions and exemplar scenarios.*

General observations during question and answer session discussions

It was clear that, among the participating organisations, there were significant differences in outlook and understanding regarding the role and expectations of research participants, the duty of the investigators, the level of care to be extended to the participants and the appropriateness of additional investigations focused on care rather than the scientific question (Table 5, overleaf). In Table 5, the full range of topics that were discussed, the degree of consensus and the availability of evidence to underpin proposed practice is indicated. 'Unclear' indicates that there is currently insufficient evidence to inform practice and more information is needed from new research; 'consensus' indicates that the considerable majority agreed; 'moderate agreement' indicates that around half of attendees agreed; and 'no agreement' indicates that opinions differed widely. The absence of consensus on some of these underlying concepts meant that

* A summary of the talks (note video recordings of the talks and a transcript of the questions and answers that followed) are available at: http://www.sinapse.ac.uk/media/events/ethics_management.asp

while there was some progress in terms of the *minimum requirement*, there was considerable caution regarding defining best practice for all parties, as implicitly anything less than this would be considered, if not immediately then in the near future, as unacceptable.

Table 5. Problems identified in Summary and recommendations from discussions

Guiding principles		
Topic	*Explanation*	*Status among meeting attendees*
EU Human Rights Legislation	Guidelines should be consistent with EU Human Rights legislation	Consensus
EU Clinical Trials Directive	Guidelines should be consistent with the EU directive	Consensus
Transparency	Guidelines should be clear and transparent for both researcher and participant	Consensus
'Duty of Care' definition	The participant–researcher relationship is different from that of patient–doctor	Moderate agreement
'Duty of Care' for medical staff engaged in research	The participant–researcher relationship is always the same as patient–doctor if the researchers are qualified medical professionals	No agreement
Participant expectations	Research participants should not be subject to any unexpected surprises through taking part in an imaging research examination	Consensus
Research governance	Guidelines should be consistent with the current UK guidance on research governance	Consensus
Risks to UK research	Any related guidelines should seek to minimise the bureaucratic and regulatory burden for researchers as much as possible	Consensus
The right 'not to know'	Is it acceptable not to inform a patient or their GP/Care team of an imaging finding that may be harmful to their health?	No agreement
Risks to non-clinical researchers	Is it an unacceptable stress for a researcher to identify a harmful finding knowing the participant will not be informed?	Unclear
Risks to non-clinical researchers	Non-clinical research staff should hold liability insurance to cover litigation related to incidental findings	Unclear
Risks to clinical researchers	It is an unacceptable professional conflict for a doctor or other healthcare professional to identify a potentially harmful finding knowing that the participant will not be informed	Moderate agreement
Risks to clinical researchers	Does conventional medical insurance cover the risk of litigation related to problems arising from incidental findings?	Unclear
Informed consent		
Topic	*Explanation*	*Status*
Incidental findings	Information about health significant incidental findings should be included in the consent process	Moderate agreement
False-negative and -positive findings	Information on false-negatives and -positives should be provided	Unclear
Reporting competency	Competency information on whoever reviews and reports the imaging study should be included	Unclear
Health risks of further investigations	Information on the health risks related to further investigation of an incidental finding should be provided	Unclear
Financial cost of further investigation	Information on the financial costs related to further investigation of an incidental finding should be provided (this may include ability of participant to obtain insurance in future, etc, as well as direct costs of further care)	Unclear
Informing the participant's GP/ care team	Explicit agreement to inform the participant's GP or clinical care team of a potentially harmful incidental finding should be obtained as part of the consent process	Moderate agreement
Research imaging examination protocols		
Topic	*Explanation*	*Status*
Research only images	Imaging examination protocols should not include any additional diagnostic imaging to aid interpretation of potential incidental findings	Unclear
Recording of images	Research imaging examinations should be recorded and retained in a way that allows them to be used by their GP/care team in the further investigation of an incidental finding	Unclear
Research imaging examination review and reporting		
Topic	*Explanation*	*Status*
No reporting	Research imaging examinations should not be reported at all in respect of incidental findings	Unclear
Reporting in non-clinical research environments	It is acceptable not to review and report research imaging examinations performed in a non-clinical research setting; eg, a university science centre	Unclear
Reporting in clinical research environments	All research imaging examinations performed in a clinical research setting should be reviewed and reported; eg, a hospital-based imaging centre	Moderate agreement
Reporting style	Any report issued should concentrate only on the likely significant findings	Consensus
Reporting by researchers	It is acceptable for researchers to identify and report potential incidental findings	Unclear
Reporting by radiographers	It is acceptable for radiographers to identify and report potential incidental findings	Unclear
Reporting by radiologists	Only radiologists are competent to reliably identify and report potential incidental findings	Unclear
Consequences of detecting an incidental finding		
Topic	*Explanation*	*Status*
Informing the participant	There should be a plan for who will inform the participant of any incidental finding	Moderate agreement
Informing the GP/care team	The principal investigator is responsible for informing the GP/care team of any incidental findings in a timely fashion	Unclear
Transition of participant to patient	If an incidental finding is identified that requires further investigation the research participant effectively becomes a patient	Consensus
Responsibility to investigate	There should be clarity regarding who bears the responsibility for further investigating any incidental finding	Moderate agreement
Guidance on further investigation	Who and how should guidance regarding further investigation be provided?	Unclear

Unclear = insufficient evidence to inform practice; consensus = majority agreed; moderate agreement = around half of attendees agreed; no agreement = opinions differed widely.

For many centres and experimental questions where imaging plays a central role, hypothetical best practice could impose major constraints or operational problems. Agreement on a high level of 'care' is unlikely without a clear consensus on the moral, legal and ethical responsibilities of research investigators in relation to research participants in this context.

Within the meeting, while we had presentations on the legal and ethical views from the expert speakers and those experts among the participants, we did not have detailed discussion with large panels of experts on those topics. The message from the speakers was that a clear statement of the ethical, moral and legal position does not exist as such at present, although there are boundaries within which to operate. Several other bodies, such as UK Biobank Ethics and Governance Council, individual imaging centres and bodies outside the UK[1,35] have struggled with these problems, in some cases over many years, and while they may have thoroughly aired the issues and arrived at a working solution that fits their population, research questions and resources, there were differences between centres (see Appendix 3) and these policies would not necessarily be directly translatable to all other centres. It was clear that there was a spectrum of views among the meeting attendees regarding the responsibilities and duties of investigators and of physicians who are investigators.

The extremes range from the following.

Extreme 1: Experiments are designed to address important scientific questions, potentially increasing medical and scientific understanding, within the framework of an ethically approved protocol. The investigator is responsible for conducting this in accordance with the ethical permission (which should relate the risks and benefits and process for incidental findings). A process for dealing with incidental findings should be in place (minimum standard to be defined but providing clinical referral). The study is not designed to detect abnormalities but any abnormality obvious to the investigating team will be acted upon (not currently clear whether this is always the case). No additional imaging or expert scrutiny will be included in the process during the research protocol itself. This embodies a view that it is not the responsibility of the research study to search (screen) for abnormalities, the participant has agreed to participate on the basis of no harm (other than approved by the ethics committee) and of no personal benefit (in terms of most studies). The research question does not involve detection of potential abnormalities and staff are not trained to detect them. If in the course of the experiment something obviously unusual is detected, the investigator has a duty to the participant to act on it (unless the participant has specifically excluded that). Reducing the volume of research as a result of increased burden or cost might in itself be unethical as it could reduce medical advances. This responsibility to society needs to be balanced against the responsibility to the individual participant. Many of these issues could be solved by ensuring greater transparency so that research participants' expectations matched the practices in the particular research imaging centre.

Extreme 2: Experiments are designed to address important scientific questions, potentially increasing medical and scientific understanding, within the framework of an ethically approved protocol. The investigator is responsible for conducting this in accordance with the ethical permission (which should relate the risks and benefits and process for incidental findings). The investigator is responsible for the care of the participant while participating in the experiment. As there is a risk that incidental abnormalities may be detected, the protocol should provide (at least at baseline) a comprehensive survey of (at least) the part of the body to be examined, of diagnostic quality. These should be evaluated by an expert reviewer to identify any abnormalities, which should then be referred through an appropriate clinical pathway. The participant may determine that they or their GP should not be informed. This may exclude the participant from the study and/or these wishes may be overridden in certain circumstances.

Set against these, there are concerns:

- That many investigators may not be sufficiently competent to identify important abnormalities
- Non-clinically trained researchers, including radiographers, may lack the knowledge to interpret the significance of an incidental finding
- Recognition of incidental findings is related to the sequences used. For example, in brain imaging, some centres may only use functional imaging and T1-weighted volume sequences, so are more likely to see congenital incidental lesions but not to see white matter lesions which would be seen on T2-weighted sequences, for example. The rate of incidental findings on different sequences is difficult to extract from current data as most studies in the meta-analyses include T2-weighted sequences
- Participants' expectations may not match the conditions to which they have consented. They may not understand the scope (anatomical) and potential of the imaging examination. Investigators and physicians may have undefined liabilities in relation to a non-detected abnormality.

There could be important benefits from detecting incidental findings in some cases. Failing to detect an abnormality could represent a missed opportunity to benefit the health of the individual by acting before acute symptoms occurred. Not only that, but the law is quite clear about so-called 'loss of a chance' cases. If the harm would have resulted even if there was disclosure and if the chances of preventing it are below 50% – that is, less probable than not – a successful negligence action will not arise.

The implication for the participant and researcher where the participant elects not to receive any feedback is unknown and requires further study.

However, some participants who do not wish to be told about incidental findings may be putting the researcher at odds with their professional responsibility should an incidental finding be noted, particularly if the incidental finding is potentially fatal and/or treatable. Should participants that refuse to be told about any combination of potentially fatal/not fatal and/or treatable/not treatable incidental findings be excluded from imaging research? Some would argue that exclusion from research could in fact be an affront to the right **not** to know information about one's self. Advance refusals – as this would be, are recognised and protected in law. It is ethically questionable whether the protection of professional interests – which seems to be the main motivation here – is a sufficient basis for this policy. Further evidence is required on the balance of benefits and harms of research participants refusing any feedback of incidental findings arising in research.

Participants and researchers, young and old may find it difficult to estimate risks and benefits and think through the possible consequences. It may be difficult to expect young research participants to make informed decisions about whether they do or do not want to be informed about non-fatal, non-treatable incidental findings and expecting inexperienced non-clinical researchers to be able to judge the seriousness and treatability of any such findings, is unrealistic. Non-clinical researchers (including radiographers and senior non-clinical researchers) have insufficient knowledge in general to judge the seriousness and treatability of most incidental findings.

In order to make good, informed choices, research participants and non-clinical researchers would need guidance on the seriousness of common incidental findings and when to refer for further opinion.

Screening for abnormalities is no longer the incidental detection of abnormalities but is putting in place an unproven, non-evidence-based medical investigation that is beyond the remit of a research investigation, and is not the subject of the research question – in many cases, a research study is not a health screening service.

Setting a defined standard of best practice approaching the second extreme (as outlined above) would be of major difficulty for important research centres and areas, would significantly inhibit research and would place a major financial and regulatory burden, where research has proceeded effectively to date without major adverse effects.

There is a driver towards defensive measures to minimise potential future difficult legal cases. Accepting and incorporating steps to better detect incidental findings will result in an irreversible change in the researcher/participant balance.

Significant harm can accrue from mistaking an artefact or normal feature for an incidental finding. However, the incidence of false-positives, and the distress that feedback on these might cause to research participants and the implications for unnecessary use of clinical time, is unknown.

There are also important questions to be considered.

- What is the reasonable expectation of a participant in a research study involving imaging? Is this absolute or does it depend on context, type of research centre (clinical or non-clinical), part of the body investigated, type of assessment, research question? Note that this MUST be context-specific because the law requires a REASONABLE standard of care and what is reasonable always depends on all of the specific facts and circumstances.
- What is the legal position? It appears this is undefined, but can be influenced by best practice, guidelines, consent and may only be established by case law.
- Should standards for one part of the body differ from those for other parts – while there may be practical issues, are there any moral or ethical reasons?
- Is it appropriate to specifically design a study to reduce the likelihood of incidental findings (such as poor image quality, reduced field of view, avoiding certain body parts)?
- What is the moral and ethical driver to subject one part of the body to an intense diagnostic survey, while excluding other parts, just because the research question (which is completely independent of the medical implications of an incidental finding) applies to one body part?
- Should information on incidental findings be fed back to a responsible clinician or to the GP to act on? While the representative from the Royal College of General Practitioners (RCGP) stated that all GPs would expect to be informed of their patient's participation in a research study so as to be able to discharge their medical duty of care (within the approvals of the Ethics Committee), it may be placing an undue burden on and add to the workload of the GP to sort out any implications of an incidental finding when this may require the knowledge of a specialist. Should a clinician with relevant specialist knowledge for the particular study be encouraged to provide support to the study to deal with incidental findings?

- The liability of a radiologist undertaking review of research scans may be covered by their malpractice insurance but this may differ in different research scenarios (for example, outside NHS). This point was not aired at the meeting but was raised during the report writing.

These questions indicate that while the ethical principles may be clear, there remain many unanswered issues that need to be addressed, either through discussion to reach a consensus or through future research. Any official future recommendations on incidental findings should promote trust in research without unduly encumbering or damaging the scientific process.†

Comment from a participating patient representative. *'Several personal experiences were aired during the meeting, or afterwards during the writing process. These were both from the perspective of researchers' experiences on dealing with incidental findings found in research participants during research in their centres and from the perspective of research participants in whom an incidental abnormality had come to light as a result of their or a relative's participation in research or imaging for another purpose. Both clinician/researchers and lay representatives reported personal experiences of having an incidental finding on their own or a close relative's scan. All were unexpected and provoked anxiety (in some cases considerable). Some had adverse effects on the research participant, for example, inability to obtain insurance, including travel insurance, to certain countries. There were also benefits, such as initiation of early treatment to prevent progression of serious life-threatening disorders.'*

One representative experience, contributed during the report preparation, is paraphrased as follows: *'To sum up, I find it difficult to give a conclusive view on the ethical management of research imaging, particularly in respect of incidental findings. There are a number of patient and lay considerations most of which have been touched on in the draft report. Firstly, diagnosis and treatment advances are largely dependent on research and this must be supported on the assumption that patients are fully briefed, and made aware of the potential risks in participating. Patients require assurance that research proposals have been approved by an ethical research governing body and that the supervision of the research is properly managed. There are major concerns about a research participant's awareness of what this all entails and they bring into question patient capacity issues. Individuals with vulnerable personalities; mental health needs; 'research tourists'; individuals who only participate for reward, are examples of groups who all require special consideration, especially where incidental findings occur. While this may be covered by the 'ethics governance committee' these groups are particularly vulnerable. I did not get the impression that* [the particular vulnerability of some research groups] *is on the radar of approving bodies or research supervisors. Incidental findings are controversial for all participants, irrespective of whether they are vulnerable or not. My colleague* [diagnosed and treated for an inner ear tumour about six years ago] *recently had a small shadow on a follow-up CT scan which may be a vein or alternatively could be a regrowth of the tumour. My colleague had previously come to terms (I think) with the uncertainty surrounding* [the long-term prognosis of] *his condition. He had some support to deal with this recent unclear follow-up scan report. However, such an unclear finding in a 'cold' research participant would be devastating. Like most, he would want to know that support would be available* [to explain and manage the consequences of the finding and that such measures would be] *robust. I believe that each research proposal must include a pathway for the individual should some incidental findings emerge. I noted at the event last year that many male participants may never see their GP and GPs do not necessarily follow up reports of incidental findings. It is essential that someone 'holds the reins' and this must be addressed in the research proposal. The issue of life insurance must be fully explained and the implications made. The clinician who described his own experience of finding something untoward on his own research scan almost by accident emphasises why the risks must be explained to the participant. This may however increase the risk of individuals withdrawing from research but this is the risk which has to be taken. I am still trying to square all of this with the fact that some clinicians make judgements not to inform patients of unclear findings on images which are very unlikely to be anything untoward* [and of some research participants' desire not to be told of any finding, especially those that are unlikely to have health consequences]. *This must occur in other diagnostic fields and explaining the remote possibility of an unclear finding will be counterproductive.'*

Discussion group summaries

The following summaries were prepared by the discussion group chairs following the discussion in their respective groups, and fed back to all meeting participants at the end of the day. They reflect the comments made within each discussion group. Participants were divided equally among the discussion groups to encourage an even distribution of representatives from research imaging centres, professional bodies, ethicists, funders, regulatory bodies and lay representatives.††

Group 1. Practicalities and logistic barriers to delivery of ethical research imaging *(Dr Adam Waldman)*

Discussion structured around consent/reporting/disclosure but it was apparent that they were interrelated.

† Video recordings and transcripts of the question and answer sessions following each talk are available at: http://www.sinapse.ac.uk/media/events/ethics_management.asp

†† Video recordings and transcripts of the discussion group feedback are available at: http://www.sinapse.ac.uk/media/events/ethics_management.asp

Consent

Expectations of research participants regarding handing of incidental findings (especially review of images) differ from what they are told. There is no information on whether expectations vary depending on imaging environment such as university hospital versus non-clinical research institute. Reactive reporting strategy may be difficult to express when obtaining informed consent; for example, how to communicate that the images will not be formally reviewed by an expert, but abnormalities may be detected if someone else 'notices' them. There was discussion on how this added 'serendipity' or 'randomness' that would be difficult for participants to manage.

Possible solutions:

- Research on how participant expectations differ between imaging environments
- Clear and explicit description at time of obtaining consent.

'Reporting'

Strategies for looking for (or not looking for) incidental findings was the main area of debate. Pro-active versus reactive strategies were discussed. Reporting is often limited by resources/access to radiologists. Many non-clinical researchers who don't have reporting access would like it. But there is some variation in opinions on ideal practice (some did not think routine radiological review of images was necessarily appropriate or desirable, even if practicable). Implications of reporting structure on the consent process were discussed. Potentially, there are huge resource implications (cost, availability of radiologists).

Possible solutions to radiological/expert reporting access:

- Central/telereporting
- Payment for governance reporting incorporated into grants and involvement of radiologists in research teams
- Stratified reporting could be routine review of images by junior radiologists, neurologists, trained radiographers? Selected secondary radiologist review.

Disclosure

There was some discussion on means of disclosure; however, there was no complete consensus on participants' right 'not to know' or researchers' right 'not to tell'. Some felt that it was acceptable not to disclose findings in any circumstance. It was noted that disclosure was difficult for groups not including clinicians who are not always qualified to answer questions that might arise. Confidentiality of incidental findings was also discussed. Should the PI know or should it be managed purely in a clinical pathway? At what point involve GPs? Issues for clinical and non-clinical groups are different.

Conclusions

There is wide variation in practice with a strong divide between approaches of clinical and non-clinical researchers. It was also concluded that participants are not patients (but may become patients).

Points of consensus: defined pathways needed and clear guidance through NRES/university ethics service.

Group 2 – Consent and what research participants should be told *(Dr Chris Freeman)*

It was clear from the discussion that some research groups have no medical input or support and no system for medically reporting scans or providing feedback or advice, nor do they have any ability to refer on for further investigation. They rely entirely on informing the participant's GP. There was much discussion about how research would be impeded if any other protocol were to be recommended. Many in the group were unhappy with this way of working, and no overall agreement was reached. The group felt that the options for consent included:

- The participant would not be told anything regardless of whether any IF had been noticed [but with a safety clause in case of public safety issue]
- The participant would be told that the results had been sent to their GP
- The participant would be told if there was any significant finding
- The participant would be told of any finding regardless of significance.

The following were agreed.

- Participants must be told that the research scan is not a clinical investigation.
- Balance of information is important – don't want excessive patient information as this leads to misinformation. It must be clear and concise.

- Investigators should consider the use of scenarios as examples of incidental findings and their potential impact to reduce requirement for text and increase clarity.
- Participants should be told the rate of incidental findings.
- Participants should be told that there might be a period of uncertainty while the implications and next steps are considered, during which the participant will need to cope while awaiting the final outcome.
- Participants should be told about the process for managing research scans in relation to incidental findings, including:
  - That there is a wide range of practice
  - That the participant understands, if and how the scan will be reported and by whom, and
  - What will happen if there is an IF, in detail, including who will deal with any medical aspects?
- Some centres just inform the GP, but this was felt to be risky in case the result was not acted on.
- Minimum standard: if relying on GP then the participant must be told that the GP will be informed:
  - The Group felt that informing the participant's GP of the participant's participation in the research and of any findings was the **minimum standard**
  - The group considered that it was acceptable for participants to opt for non-disclosure if the centre was prepared to accept this, but these centres would be in the minority (many of those present indicated that they would not accept a research participant who was not prepared to have their results passed to their GP)
  - The group also felt that it would be necessary to override this (that is, go against the participant's wishes) for public safety; for example, in the case of a research participant who was a bus driver and was found to have a brain tumour.
- Best practice: While it is still necessary to define the gold standard, the group felt that best practice would include having a radiologist with relevant experience in the area being researched reviewing the images. Additionally, there should be a clear system for performing and issuing the report, having a physician or neurologist involved in the study who could further evaluate the significance of any incidental findings and advise on action, and medical disclosure to the participant by a clinician with relevant experience. The group felt that this best practice model should be encouraged, while recognising difficulties in resourcing.
- On further discussion, it was noted that GPs would want to know both that their patient had been in a research study and the results particularly if any significant incidental finding had been found.

Group 3 – What is ideal practice and what is acceptable minimum practice? *(Professor Martin Leach)*

The group discussed what they felt was the ethical and moral duty of care to a participant and found widely varying views without clear agreement.

- The group felt that a common standard was required but were unable to determine this in the short time available. They questioned whether we should be interested just in incidental findings that occur as a side-effect of the study or whether we should be screening for abnormalities by using more extensive sequences than were required for the research.
- This led to wide ranging discussion on what the standard procedure for 'incidental finding' detection should be – what is the level of competence required to review research scans for incidental findings? Is it necessary for a radiologist to review the research imaging? This evoked a wide range of views.
- It was clear that a standard procedure for identifying and managing incidental findings, with a defined action plan, should be defined as a common standard.
- The procedure needs to be incorporated into ethics applications, consent forms and patient information sheets.
- Ethical committees need guidance to understand the implications of the type of imaging and the qualifications of people reviewing them (if not radiologists).
- Research participants would need to be clear about the limitations of the imaging review and of the sequences/images obtained in terms of their diagnostic capability.
- Research participants need to be given information about both the positive and the negative implications of incidental findings.
- There needs to be clarity about the disclosure procedure.
- The group agreed that radiologists were best able to identify abnormalities (within the limitations of the imaging available within the study), but acknowledged the serious financial and practical implications of requiring a radiological review of all research studies.
- The group noted the need for research on the impact of incidental findings and the balance of benefit and harm. The short- and long-term consequences of incidental findings have not been systematically researched, most literature reports are anecdotal, and therefore the consequences are not known.

Group 4 – How should a guideline be put into practice? *(Professor Alastair Compston)*

The group agreed the following key principles in formulating any guidance.

- Any guidance would need to recognise that incidental findings are a potential medical issue and deal with the transition from research participant to patient.
- There should be no surprises: the guidance should cover all possible scenarios to protect the participant and the researcher.
- The guidance should be within and above law and ethics – it should recognise both legal and ethical principles but (as this is new territory) may need to rise above these where necessary.
- It should embrace autonomy, capacity, societal responsibilities, hidden consequences (for example, insurance and its possible compromise, and so on).
- The group raised the issue of whether a participant should be questioned about their motivation for participating in the research but were unable to agree on whether the guidance should ask why a participant wants to be involved. It was felt that most UK research participants would be motivated by altruism, with less risk of people with specific symptoms volunteering for what they perceive to be a 'free' scan. However, the language used discussing the research with the prospective participant in information sheets and consent forms should be neutral and not leading.
- Another key issue is the commitment to maintaining involvement beyond the research and address consequences for individuals with incidental findings and the associated financial implications.
- The group suggested the following mechanisms for implementing the guidance:
  - Embedded in research governance systems
  - Embedded in ethical review systems
  - Included in mentoring/appraisal and training of researchers
  - Generic across different stakeholder institutions regardless of whether they were hosted in the NHS, universities or industry
  - The guidance should be simple, with a clear core plus options reflecting particular circumstances
  - The guidance should be generalisable across all imaging modalities, not just MR, and potentially be adopted outside the UK.
- It should be clear that the researchers take the responsibility for the care and costs of managing any incidental finding until responsibility can be devolved at an appropriate point; for example, if the research participant were to come under the care of a specific clinician who would manage their incidental finding thereafter.
- There should be a compulsory field in research ethics and R+D applications where details of strategy for managing incidental findings would be entered. The guidance document should be available on all relevant professional bodies' and societies' (in addition to those present) websites and disseminated to all members.
- The guidance should be written up as a citable publication so as to be easily found on PubMed, and related search engines.
- The publication and society guidance should be cast in such a way as to come at the top of Google searches.

7. Recommendations

The participants agreed that guidance regarding management of incidental findings in research imaging should follow these principles.

Transparency

Research participants, in general, want to know what their research imaging shows; existing guidance suggests that there are circumstances under which it is appropriate to feed back these findings; ethics committees want to know that the research participant's interests are protected and risks minimised.

Expectations

Available studies (albeit limited) indicate that research participants expect that an appropriately experienced individual will look at their scan; even when told that the scan is not a diagnostic scan, most want to know if any potentially serious condition shows up regardless of treatability; The Council for International Organizations of Medical Sciences and the National Research Ethics Service state that everyone is entitled to know of findings related to health.

Duty of care

Researchers have some duty of care to research participants, although it is not clear if this is the same as a doctor–patient relationship. Nonetheless, the law expects a 'reasonable standard of care' in research, but there are no test cases so the research community and the courts are likely to be guided by what a responsible body of relevant professionals would consider to be an appropriate standard of care. This means that the practices of the profession, current and future, will likely influence the nature and the scope of the duty of care owed by researchers to their research participants. In law, determination of a successful action in negligence would rest on proof of failure to deliver a reasonable standard of care and that harm had been suffered as a result.

Resource

Researchers, hospitals and universities face a considerable regulatory burden already. There is little enthusiasm for anything that might add to this burden. There is far more research imaging being done than there are trained radiologists to review all the scans (in the UK anyway), there are few academic radiologists in the UK (or elsewhere) and a chronic shortage of NHS consultant radiologists, so there are unlikely to be sufficient radiologists ever to report all research images. Many scans performed for research use non-diagnostic sequences; there is unlikely to be time to perform additional diagnostic images on all scans performed for research. The associated financial resource requirements for radiologist reporting and obtaining additional images are substantial. The research purpose should be clearly differentiated from any clinical diagnostic intent and any lack of diagnostic sequences and implications thereof for recognising incidental findings of relevance to health made absolutely clear. Note, however, that in the case of harm arising from an incidental finding, a researcher who was also a clinician would likely be held to the higher standard of clinical care and certainly it should be a matter of good practice that they behave in this way. There are additional financial, workload and data protection issues.

Lack of evidence on some key areas

Research is needed about how best to manage this ethical aspect of imaging research. There are multiple areas where there is no information to inform practice. In particular, robust evidence is lacking on the course of indeterminate incidental findings and whether intervention benefits the participant.

Ethics committees

There is perhaps some variation in how ethics committees interpret, understand or are aware of issues related to incidental findings in imaging research – clarification and guidance for ethics committees, both NHS and university-based, local and multicentre, would be helpful.

Flexibility

One size does not fit all; research questions differ; populations differ; researchers' backgrounds differ; location of scanner with respect to clinical infrastructure differs.

Evolving field

The technology, aspects of rights of the individual, medical knowledge, legal framework, skills and awareness of researchers and availability of tools to support management of incidental findings in imaging centres are all evolving. Guidance should be flexible and responsive to this changing environment.

Given these principles, the participants felt that the following guidance should be adopted as widely and as soon as possible.

Expected risks of incidental findings

1. Imaging research centres should acknowledge the problem of incidental findings in research and assess the frequency and type of incidental findings that they are likely to encounter given the type of research participants and imaging research performed in their centre.
2. Ignoring the issue of incidental findings is not acceptable. Guidance on their management is required that protects the research participant, society and the researcher.
3. Incidental findings are a medical issue, as identification of one marks a transition from research participant to potential patient, including a different set of responsibilities, priorities and professional standards and requirements for the participant.

Informing the participant

4. Researchers must provide a reasonable standard of care to research participants. They should aim to give feedback on health information that is likely to result in avoidance of significant harm to the participant.
5. In general, most people when acting as research participants would prefer to be told about potentially life-threatening incidental findings, but not necessarily about minor 'normal variants' or findings that are unlikely ever to cause symptoms or affect their health. Hence, it is important that someone who is able to judge the potential health implications of an incidental finding is available to advise on what information to give the participant and whether they should be referred for formal medical assessment. Imaging centres should review how they would access such support and where remote from medical advice, consider establishing links with interested clinicians or radiologists in the appropriate specialty.
6. The majority opinion was that telling the research participant that they would receive no feedback whatsoever on their imaging, regardless of what the images showed, was not acceptable.
7. The majority opinion was also that participants who are not prepared to have information from research imaging fed back to them if an incidental finding were to be noted should probably not participate in research imaging studies as conducted in most centres. This is because the noting of an abnormality by a radiographer or other professional performing the scan would place that professional at variance with their professional duty of care to the participant and in a personal professional dilemma in the event that they knew the participant had a potentially serious but treatable abnormality but were not able to act on the information. However opinion was not unanimous on this point, particularly as there is so little evidence on the balance of benefit and hazard of such a policy, and individual centres may wish to include participants who refuse to be told about even potentially life-threatening unexpected findings, but the consent procedure should reflect this.

Consent

8. Information should be made more easily available to ethics committees on the prevalence and risks of incidental findings through central information sources such as NRES and also for individual studies where there may be a specific context that affects the risk and types of incidental findings. This will facilitate the ethics committee's role in minimising the risk to study participants.
9. Imaging centres should explain clearly to their ethics committees, for each study, how they will identify incidental findings particularly those that have significant health implications, how they will deal with such findings, and how they will explain the problem of false-positives and false-negatives to research participants, to the best of their knowledge, ability and resources.
10. Imaging centres should review their research participant information sheets and consent forms to ensure that these provide clear and unambiguous information regarding whether the research imaging will include images with diagnostic content and how this is related to clinical imaging of the same area, if the images will be reviewed for medical content and by whom, where the images will be stored, the procedure should an incidental finding be observed, and what information will be fed back to the participant. They should ensure that participants understand the limitations of the research imaging and of the image review process.
11. The precise content of this information will vary between centres depending on the research participant population case mix, the type of research imaging, the organ system, the ease of availability of experts to review medical content of images and the ease of

access to specialist medical advice to advise on management of any incidental finding. Examples of procedures adopted in some research imaging centres, participant information sheets and consent forms are provided in Appendix 3.

12. Research participants should be fully informed about the likelihood of an incidental finding in the particular type of imaging research in which they are participating, the likelihood that this finding will be a serious threat to their health, and any implications for insurance, or employment. An indication of the procedure, including the duration of any period of uncertainty about the diagnosis while obtaining further opinions, should be provided, possibly with worked examples, to facilitate research participants' comprehension.
13. Possible benefits of taking part; how their confidentiality will be safeguarded during and after the study and the procedures for handling, processing, storage and destruction of their data should be clear. It should also be clear if the data are to be retained for use in future studies and whether further ethics committee approval will be sought.

Imaging acquisition and reporting issues

14. At present, it is not possible to implement a single optimum standard strategy for recognition and management of incidental findings in imaging research across the UK. Rather, a range of strategies is possible at present with an acceptable minimum standard. However, as knowledge and resources evolve, research imaging centres should continue to review their practice to see whether they could achieve a better standard as circumstances and available resources change.
15. In general, the diagnostic content of any research imaging should be reviewed by an observer who is competent in that field. Centres should review their current image review procedures and make best use of available skills in image interpretation, including by linking with other imaging centres or research groups to enhance access to better expertise where necessary. Requirements will vary with the research question, population being studied and type of imaging being used.
16. Those without current access to more expert image interpretation should see whether, for example through collaboration with a local radiology department or interested clinician, they could improve their access to expert image interpretation for the proportion of cases in which an incidental finding is suspected.
17. Standard operating procedures (SOPs) that give guidance on when doubtful cases should be escalated to professionals with more expertise would be useful to help overcome the knowledge gap between the radiologically inexperienced researcher and expert.
18. While the participants agreed that the optimal method for detecting incidental findings was review by a radiologist, the possibility of establishing examples of common incidental findings in commonly imaged organs, their seriousness, and whether they are likely to require referral for further management; for example, on the web, should be considered as an aid for imaging centres without radiology on site. Training in how to recognise common incidental findings, and what to do if a possible incidental finding is seen, should be considered as part of Good Clinical Practice training or through specialist professional organisations (see Rotterdam Scan Study above).[26] This would be intended to help to raise awareness among non-clinical, non-radiological researchers but NOT to replace expert review where needed. Issues regarding liability and several other factors would require consideration should this approach be developed.
19. The possibility of establishing ways of overcoming limited access to radiological resources for imaging research should be explored. This might include extended collaboration, for example a network of radiologists who could review research images remotely and provide quick advice to non-medically qualified researchers seeking information on the importance of a particular finding, as described in California.

Procedure for handling incidental findings

20. As a minimum standard, within the ethics approvals and where necessary with the participant's consent, information on incidental findings should be provided to the research participant and to their GP or clinically responsible physician linked to the study in a timely fashion. In general, while the GP will be kept informed within the confines of the ethics agreement, many incidental findings with the potential to adversely affect health will require specialist medical advice. Therefore, research imaging centres should endeavour to identify relevant medical specialists able to provide informal advice for the type of incidental findings that they are likely to encounter and referral pathways for more formal assessments.
21. Researchers should avoid feeding back unverified results with no action plan to the participant as these may simply result in greater anxiety.

General points

22. Imaging research centres should ensure that research staff (both their own and any researchers from other departments using the centre) receive training in ethical aspects of research imaging, including awareness of the magnitude of the problem posed by incidental findings and basic knowledge of management of incidental findings. This is particularly important among staff who are likely to be obtaining consent for imaging procedures, particularly those who are not medically qualified, so that they are able to inform participants about the likelihood of a finding, how their research images will be handled, and the mechanisms in place for managing any incidental finding, in a particular study.
23. Training in awareness of incidental findings in research imaging should be considered as part of the routine of good clinical practice training and noted, for example, on curriculum vitaes and in annual appraisals of research imaging staff, so as to provide a record of training in awareness and management of incidental findings.
24. Guidance should be provided for research ethics committees to assist them in understanding the scope of the problem, raise awareness of the likely frequency and implications of incidental findings in different types of imaging research, and help them to identify whether appropriate mechanisms for managing incidental findings are in place in individual research ethics applications, taking account of the population being studied and resource implications.
25. Ethics applications (and by inference, where appropriate, NHS R+D office applications) should include a section where the approach to managing incidental findings for each study for which approval is sought can be recorded. This would help to standardise practice across the UK and to raise awareness of the need to have reasonable standards in place to cope with the ethical issues raised by incidental findings.
26. Funding organisations should consider including a section in their application forms where applicants could indicate the approach to be adopted in the proposed study for managing incidental findings, or perhaps provide a 'tick box' to indicate that they have a mechanism in place for managing them. This would require further consideration on the part of funding organisations but might encourage awareness of the problem and help promote better practice in much the same way that requesting information about dissemination of the research results or involvement of the lay public has improved practice in those two areas.
27. Similarly, research co-ordinating and facilitating organisations, such as DH-funded comprehensive national and local research networks, should think about whether study-appropriate methods for managing incidental findings should be considered as part of the procedure for assessing new studies for adoption and subsequently in their feasibility assessment prior to their implementation in local centres.
28. Other methods to help standardise the approach to incidental findings across the UK; for example, through raising awareness of where to find information on incidental findings through publication of discussion papers in peer-review scientific journals, by individual societies and open-access internet access to this document would be beneficial.
29. Research imaging centres should consider ways that they can collaborate with each other or with specific research groups or organisations to reduce duplication, improve access to clinical expertise or fill other resource gaps that restrict their ability to optimise their management of incidental findings.
30. Research into the cost implications of different strategies for handling incidental findings, on the psychological effects of different strategies, to obtain a much broader and more representative sample of opinions from research participants on how incidental findings should be handled, on health and secondary (such as insurance) effects of common incidental findings, of how the validity of any incidental finding would be established, and on the material significance of different incidental findings incorporating the 'relevance', 'seriousness' and possible 'treatability', should be encouraged. Research to obtain a much broader and more representative sample of opinions from research participants on how incidental findings should be handled would also be valuable. Issues such as the liability of healthcare professionals and researchers in identifying and acting on incidental findings, in the absence of information on a normal diagnostic standard, in all areas of research should be clarified. Collating the results of this research and interpreting whether and how it should influence the ethical, medical or legal framework around research imaging practice, may require commissioning of a further multidisciplinary report.
31. While many of the opinions expressed and principles that came out of the discussions during the meeting on 1 July 2010 and the subsequent report preparation were in agreement with those expressed by representatives from other parts of Europe (specifically Germany and the Netherlands), it should be noted that the potential solutions and resource limitations may be more UK-specific and should not be taken to represent the situation in other countries.

8. Conclusions and future direction

This work has highlighted that the present situation regarding ethical management of research imaging including incidental findings in the UK is unsatisfactory on many counts. Practice in research imaging centres around the UK is very varied. Current ethics and regulatory guidance is ambiguous and difficult to find. Ethics committees vary in their awareness and approach to the problem. Resources in imaging centres, populations studied, body regions studied and imaging methods used all vary, meaning that the likelihood of detection and the seriousness of any incidental findings will also vary in magnitude. Research participants, who have volunteered to participate in the research usually for no personal gain, not unreasonably expect that their images will be inspected and any abnormality with the potential for adverse effects on health will be brought to their attention and medical advice offered. The challenge is to strike the correct balance between answering the research question and the welfare of the participant – recommendations on incidental findings should promote trust in research without unduly encumbering the scientific process.[2]

There are many areas in this field where there is little or no evidence on which to build a more transparent, consistent and ethically justifiable framework for dealing with incidental findings, or which could help to determine what level of resource is cost-effective for managing incidental findings.

While many researchers who are familiar with imaging recognise that incidental findings are common, and that health benefits may result from their early recognition, opinions differ as to whether research images should be routinely inspected for clinically relevant abnormalities and by whom, how this information should be acted on, what the research participant should be told and by whom and what should happen after that. Current procedures largely reflect historical factors such as location of the research imaging centre with respect to medical services, interests of imaging researchers, awareness of the issue, attitudes and available resources. Most of these are modifiable or can be circumvented with heightened awareness, modern technologies and a willingness to collaborate.

These points apply in the UK as well as elsewhere, although it is important to be aware that the availability of the NHS providing health services to all, free at the point of delivery, brings subtle but important differences to the consideration of incidental findings compared with healthcare systems where medical services are not free at the point of delivery. In the UK, research imaging studies may be less vulnerable to the risk that participants, who are worried about their symptoms, agree to participate in a research imaging study as a way of getting a ‘free scan’. Therefore, evidence on incidental findings derived from research imaging in other countries without state provided ‘free at the point of delivery’ healthcare systems may not be relevant in the UK. Resource-specific factors, such as availability of radiologists to provide expert opinion on research imaging findings, or of radiographers with suitable training and accreditation, also differ between countries and should be interpreted in that light.

This meeting has already raised awareness, provoked national debate and achieved a degree of consensus on minimum acceptable practice, even if it has identified many more questions that require more work to answer. It has brought together a large group of key organisations, allowed them to air the issues from their own perspective, and to hear others’ views, identified gaps in knowledge and improved communication between organisations involved in imaging research. It has encouraged and increased discussion and awareness of the problem within key organisations. It has highlighted the need for better:

- Awareness of the issues among imaging researchers
- Information on incidence and common types of incidental findings (Tables 1, 2 and Figure 2)
- Guidance from ethics committees for prospective researchers and from central ethics agencies for local and national ethics committees on how to handle research studies using imaging (NRES, in preparation)
- Guidance for funders of research imaging studies to ask questions in grant applications about what measures are in place to manage incidental findings
- Training of imaging researchers in the recognition of common abnormalities and artefacts
- Transparency of study information sheets and consent procedures to increase understanding of research participants of the risk of and procedures for managing incidental findings (for examples see Appendix 3; NRES guidance in preparation)
- Information on several aspects of incidental findings for which there is currently no evidence base.

All of this is helpful and is already leading to improved guidance for ethics committees (H Davies, NRES, in preparation). Identification of acceptable minimum practice raises the minimum standard and facilitates further incremental steps towards better practice. Examples of current practice in individual centres are available as templates for other centres (Appendix 3). There are practical suggestions on how to improve research participants’ understanding of the risks of incidental findings, what to expect should one be found and how long it

might take to resolve. There is a common purpose now to create a framework of good practice for imaging research in the UK to safeguard both research participants and research imaging centres through better knowledge of the problem, and to avoid research imaging falling into disrepute through practices which could disadvantage research participants. Addressing the issues which the present workshop and report raised but were not able to solve, as well as interpreting the results of further research on issues for which there was an insufficient evidence base (outlined in the report) and whether and how these should influence the ethical, medical or legal framework around research imaging practice, may require commissioning of further multidisciplinary reports.

This document will be published as open access and made as widely available as possible to facilitate dissemination of information and improvements in practice.

Approved electronically by the Board of the Faculty of Clinical Radiology: April 2011

9. Contributors

The following people either assisted in preparation of background materials for the meeting, in drafting of the report or provided comments on the near final version of the report.

Professor JM Wardlaw, Brain Research Imaging Centre, Edinburgh, and SINAPSE Collaboration

Dr H Davies, National Research Ethics Committee

Professor D Lomas, The Royal College of Radiologists' Academic Committee and University of Cambridge

Dr T Booth, The Royal College of Radiologists' Academic Committee and University of Cambridge

Dr A Waldman, The Royal College of Radiologists' Academic Committee and Imperial College, London

Professor A Jackson, Chair, The Royal College of Radiologists' Academic Committee (to July 2010)

Professor M Leach, British Chapter, International Society for Magnetic Resonance in Medicine

Dr C Freeman, Ethics Committee, Royal College of Psychiatrists

Professor A Compston, President, Association of British Neurologists

Professor Graeme Laurie, Chair, UK Biobank Ethics and Governance Council, and University of Edinburgh

Ms Rowena Lamb, Research Ethics Administrator, Kings College London,

Dr A P Toms, Norwich Radiology Academy, NIHR Clinical Research Networks

Professor Richard Ashcroft, MRC Ethics Committee (ERPIC)

Professor Martin PM Richards, UK Biobank Ethics and Governance Council

Mr J Sellors, UK Biobank

Professor Rory Collins, UK Biobank

Professor R Dolan, Wellcome Trust Neuroimaging Laboratory, Queen Square, London

Dr Catherine Moody, MRC

Dr Catherine Elliot, MRC

Dr Beth Thompson, Wellcome Trust

Ms Adrienne Hunt, UK Biobank Ethics and Governance Council

Ms Sheelagh McGuinness, UK Biobank Ethics and Governance Council

Dr Erika Denton, Department of Health, National Imaging Board

Professor David Gadian, British Chapter, International Society for Magnetic Resonance in Medicine

Mrs F Crabbe, Centre for Cognitive Neuroimaging, University of Glasgow, British Association of MR Radiographers,

Dr Klaus Kessler, Centre for Cognitive Neuroimaging, University of Glasgow

Professor David Misselbrook, Royal Society of Medicine

Professor Robert Jefferson, Committee for Ethical Issues in Medicine, Royal College of Physicians. London

Professor G Barker, Professor of Magnetic Resonance, Kings College London

Mr D Brown, Multiple Sclerosis Society,

Mr P Kelly, Clinical Radiology Patients' Liaison Group, The Royal College of Radiologists

Mrs Moira Heath, Clinical Radiology Patients' Liaison Group, The Royal College of Radiologists

Dr Graham Kemp, Magnetic Resonance and Image Analysis Centre, Liverpool

Dr Glynn Coutts, MR Special Interest Group, Institute of Physics and Engineering in Medicine

Dr Paul Mullins, Bangor University Imaging Centre

Dr J Thai, Aston Brain Centre

Dr P Gowland, Nottingham Imaging Centre

Professor P Matthews, Imperial College, London and GSK Clinical Imaging Centre, Hammersmith Hospital, London

Professor F Gilbert, Aberdeen Biomedical Imaging Centre, Chair, The Royal College of Radiologists' Academic Committee (from August 2010)

Dr M Vernooij, Erasmus MC/the Rotterdam Scan Study

Professor Dr Frank Hentschel, German Society of Neuroradiology

Professor Dr Rüdiger von Kummer, German Society of Neuroradiology

Dr Stephan Ulmer, Geneva

Dr Janet De Wilde, SINAPSE Executive Director

Dr Duncan Martin, Brain Research Imaging Centre, University of Edinburgh

Dr Rustam Al Shahi Salman, University of Edinburgh

Professor A Blamire, Newcastle Magnetic Resonance Imaging Centre

Professor John D Pickard, Wolfson Brain Imaging Centre, Cambridge,

Professor Donald Hadley, Department of Clinical Neuroradiology, Glasgow

Dr John Perrins, Committee on Safety of Devices

Group comments were also received from UK Biobank Ethics and Governance Council, The British Chapter of the International Society for Magnetic Resonance in Medicine, The Royal College of Radiologists' Academic Committee. Comments were also received on the final draft from Professor Audrey Paterson, College of Radiographers. All comments from all parties have been incorporated, wherever possible.

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Appendix 1. Meeting Programme, 1 July 2010, Wellcome Trust, London

10:00–11:00 ***Chair: Professor Alan Jackson***	Welcome and Introduction ***Professor Alan Jackson, Chair, RCR Research Committee***
	Frequency and type of incidental findings in neuroimaging ***Dr Rustam Al Shahi Salman, MRC Clinician Scientist (UK)***
	Frequency and type of incidental findings in body imaging ***Professor David Lomas (UK)***
	Results of The Royal College of Radiologists' survey of ethical aspects of research imaging ***Dr Thomas Booth (UK)***
11:00–11:30	**Coffee Break**
11.30–12.30 ***Chair: Professor Tarek Yousry***	Ethics of Research Imaging in Germany. Expectations of Researchers and Patients ***Professor Rüdiger von Kummer/Professor F Hentschel (Germany)***
	Current UK legal and regulatory framework for research imaging ***Professor Graeme Laurie, Director SCRIPT (UK)***
	Expectations of research participants and patients – The Ethics Committee perspective on how imaging should be handled in research ***Dr Hugh Davies, National Research Ethics Committee (UK)***
12:30–14:30	**Working Lunch and Break-Out Discussion Groups** Small group discussions: 1. Practicalities and logistic barriers to delivery of ethical research imaging – ***Dr Adam Waldman*** 2. Consent and what research participants should be told – ***Dr Chris Freeman*** 3. What is ideal practice and what is acceptable minimum practice? – ***Professor Martin Leach*** 4. How should a Guideline be put into practice? – ***Professor Alastair Compston***
14:30–15:00	**Tea break**
15:00–16:00 ***Chair: Professor Joanna Wardlaw***	**Feedback from discussion groups. Final discussions.** **Preparation of draft statement** Statements from discussion groups by respective chairs Formulation of a consensus draft statement.
16:00	**End**

Appendix 2. Participating organisations and representatives

This is a list of those participating organisations and representatives who were invited and from whom an initial response was received and representatives that attended on 1 July 2010

Organising Committee

- Professor Joanna Wardlaw, Western General Hospital, Edinburgh. Director, Brain Research Imaging Centre and SINAPSE
- Professor Alan Jackson, Wolfson Molecular Imaging Centre, University of Manchester
- Professor David Lomas, Addenbrooke's Hospital, Cambridge
- Professor Adam Waldman, Imperial College NHS Healthcare Trust. London.
- Dr Thomas Booth, Royal Free Hospital NHS Trust, London
- Mrs Nan Parkinson, RCR, London

Speakers

- Professor Alan Jackson, Professor of Radiology, Imaging Science, Wolfson Molecular Imaging Centre, University of Manchester
- Dr Rustam Al Shahi Salman, MRC Clinician Scientist and Honorary Consultant, Division of Clinical Neurosciences, Western General Hospital, Edinburgh
- Professor David Lomas, Professor of Clinical MRI, Department of Radiology, School of Clinical Medicine, Addenbrooke's Hospital, Cambridge
- Dr Thomas Booth, Specialist Registrar in Radiology, Royal Free Hospital NHS Trust, London
- Professor Rüdiger von Kummer, Head of the Department of Radiology, University Hospital Carl Gustav Carus, University of Technology, Dresden, Germany
- Professor Graeme Laurie, Professor of Medical Jurisprudence, HRC/SCRIPT, Law and Technology Centre, School of Law, University of Edinburgh
- Dr Hugh Davies, Research Ethics Adviser, National Research Ethics Service, National Patient Safety Agency, London

Imaging Research Centres

- Aberdeen Biomedical Imaging Centre (Dr Alison Murray and Professor Fiona Gilbert)
- Aston Brain Centre (Professor Stefano Seri and Dr Jade Thai)
- Bangor University Imaging Centre (Dr P Mullins)
- Bristol Oncology Centre (Dr Diane Crawford and Dr Chiara Bucciarelli-Ducci)
- Birmingham University Imaging Centre (Ms Nina Salman)
- Cambridge, Wolfson Brain Imaging Centre and Neurosurgery (Professor J Gillard and Professor J D Pickard)
- Cardiff University Brain Imaging Centre (Professor Richard Wise)
- Dundee Research Imaging Centre (apologies received from Professor G Houston)
- Edinburgh, Brain Research Imaging Centre (Professor Joanna Wardlaw, Dr Duncan Martin)
- Glasgow, Clinical Neurosciences (Professor Donald Hadley and Dr Celestine Santosh)
- Glasgow, Centre for Cognitive Neuroimaging (Dr Klaus Kessler and Mrs Frances Crabbe)
- Hull Imaging Centre (Centre for MR Investigations) (Dr Ian Holland)
- Liverpool Magnetic Resonance and Image Analysis Research Centre (MARIARC) (Dr Graham Kemp)
- London UCL, Queens Square (Professor Tarek Yousry and Professor Patrick Haggard)
- London King's College, the Institute of Psychiatry (Professor Gareth Barker and Dr Rowena Lamb)
- London Imperial College, London, MRC Clinical Sciences Centre, Hammersmith (Professor David Brooks)
- London, Wellcome Trust Centre for Neuroimaging, UCL (Professor Ray Dolan)
- London, Hammersmith, GSK Imaging Centre (Professor P Matthews)
- Manchester, University of (Professor Alan Jackson)
- Newcastle Magnetic Resonance Centre (Professor Andy Blamire)
- Norfolk and Norwich (Norwich Radiology Academy) (Dr Andoni Toms)
- Nottingham, University of (Dr Rob Dineen, Dr Penny Gowland and Ms Carolyn Costigan)
- Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (Dr Stuart Clare)

- Sheffield, Royal Hallamshire Hospital (Dr Nigel Hoggard)
- York Neuroimaging Centre (Professor Tony Morland)
- Switzerland, University Hospital, Basel (Dr Stephan Ulmer)
- The Netherlands, Erasmus MC/Rotterdam Scan Study Group (Dr Meike Vernooij)

Medical Ethicists and Lawyers

- Oxford Centre for Neuroethics (Dr Mark Sheehan)
- UK Biobank Ethics and Governance Council (Professor Martin Richards, Mr Jonathan Sellors, Professor Rory Collins and Ms Adrienne Hunt)
- National Research Ethics Committee (NRES) Advisory Panel (Dr Hugh Davies, apologies received from Dr David Neal)
- British Medical Association, BMA Medical Ethics Committee (apologies received from Dr Julian Sheather)
- MRC Ethics Committee (ERPIC) (Professor Richard Ashcroft)

Research Funding Organisations

- Wellcome Trust – WT Policy Unit; (Dr Katherine Littler, Dr Gary Wilson, and Dr Beth Thompson)
- Medical Research Council (MRC) (Dr Catherine Moody)
- National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Commissioning Board, NIHR Comprehensive Clinical Research Network (CCRN) (Professor Sallie Lamb)

Regulatory and Guidelines Groups

- Committee on Safety of Devices (Dr John Perrins, Committee Chair)
- National Institute for Health and Clinical Excellence (NICE), NICE Board (Dr Jane Adam)
- Department of Health (DH), Research Governance Framework, National Imaging Board (Dr Erika Denton, Dr Pete Cavanagh)
- National Health Service (NHS) Research and Development (R+D) Offices (Dr Ian Holland)

Professional Societies and Special Interest Groups

- Academy of Medical Sciences (Acad Med Sci) (Miss Catherine Luckin)
- Association of British Neurologists (ABN) (Professor Alastair Compston)
- British Association of MR Radiographers (BAMMR) (apologies received from Ms Rebecca Vosper; Mrs Frances Crabbe represented BAMMR)
- British Chapter, International Society for Magnetic Resonance in Medicine (ISMRM) (Professor Martin Leach)
- British Institute of Radiology MRI Committee (BIR) (Professor David Lomas)
- British Psychological Society (BPS) (Professor John Oates)
- British Society of Neuroradiologists (BSNR) (Dr Adam Waldman, Professor JM Wardlaw, Professor Alan Jackson)
- Institute of Physics and Engineering in Medicine (IPEM), MR Special Interest Group (Dr Glyn Coutts)
- Royal College of General Practitioners (RCGP) Health Informatics Group (Dr Bob Milne)
- Royal College of Physicians (RCPL), Committee for Ethical Issues in Medicine (Dr Bob Jefferson)
- Royal College of Psychiatrists (RCPsych) Ethics Sub-committee (Dr Chris Freeman)
- The Royal College of Radiologists (RCR) (Professor Alan Jackson)
- Scottish Imaging Network, A Platform for Scientific Excellence (SINAPSE) (Dr Janet De Wilde)

Research imaging administrators and business managers

- Brain Imaging Research Centre, Edinburgh (Dr Duncan Martin)

Patient representatives

- RCR, Clinical Radiology Patients' Liaison Group (Mr Pat Kelly)
- RCGP, Patient Partnership Group, RCGP (Ms Stephanie Shepherd)
- Multiple Sclerosis (MS) Society (Dr Douglas Brown)

Public relations/press officers

- British Medical Association (A Davis)
- Wellcome Trust (P Bailey)
- The Royal College of Radiologists (D Garbutt)

Note that several other organisations and centres considered likely to have an interest in this topic were contacted but no response was received. The organisers apologise for any omission on their part.

Appendix 3. Examples of information sheets and operating procedures from research imaging centres. These may be used as templates by other centres

Brain Research Imaging Centre, Edinburgh

Centre for Cognitive Neuroimaging, Glasgow

Institute of Neurological Sciences, Glasgow

Institute of Psychiatry, King's College London

Liverpool University

University College London

Wolfson Brain Imaging Centre, Addenbrooke's Hospital, University of Cambridge

BRAIN RESEARCH IMAGING CENTRE

Clinical Neurosciences
SCHOOL OF MOLECULAR AND CLINICAL MEDICINE
The University of Edinburgh
Western General Hospital
Crewe Road
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INFORMATION SHEET

ASSESSMENT OF MAGNETIC RESONANCE IMAGING PROTOCOLS WITH HEALTHY VOLUNTEERS

Thank you for your interest in this important work.

Medical researchers need to know more about how normal healthy brains work so that they can continue to improve the treatment of people who become ill, and work towards prevention of brain diseases.

Magnetic Resonance Imaging (MRI) uses a combination of powerful magnets and radio waves to create very high quality pictures of particular parts of the body. MRI does not use X-rays, and no drugs or injections will be involved if you agree to be scanned.

Although MRI techniques are already very well developed for taking pictures of the brain structure, less is known about how our body chemistry behaves during illness, how blood flows through our brains, and how our brains actually work. This Centre's scanner is dedicated to finding out more about these things and also to improve existing techniques.

If you agree to join the study, **we will check that it is perfectly safe for you to be scanned.** Although MRI is normally a very safe method of taking pictures, we do not scan people who have a heart pacemaker or who have had surgery involving the insertion of metal clips into the brain or hearing implants, or people who have metal fragments in their eyes, perhaps as a result of their job. Neither will we scan you if there is a chance that you might be pregnant. On the other hand, the metals used in operations such as hip replacements are very rarely a reason not to undergo scanning. The Radiographers will check if you are in any doubt.

When you come to the Centre for your scan, a changing cubicle will be provided. You will be asked to place any metal objects, such as keys, watches, coins and credit cards, in a locker. Please do not wear any make-up or talc, and be prepared to remove contact lenses if you use them. You may be asked to wear a wrap-around gown while you are in the scanner.

You will be asked to lie on the scanner bed for up to one hour. Usually it takes less time. While you are in the scanner, a series of pictures will be taken. Most volunteers coming to this Centre will have pictures taken of their brain, but many will have scans of their spine or heart, or another area of their body.

If you have volunteered for a *functional MRI* scan, pictures will be taken of how parts of the brain begin to 'work harder' during certain activities. You will be asked to carry out a simple task while lying in the scanner so that pictures can be taken while you are performing the activity. The task may involve listening to things, looking at images, or doing simple arithmetic, for example.

The scanner makes quite loud noises while it operates. For your comfort, you will be provided with ear plugs or headphones, and it may be possible to play music into the Scanner Room if you wish.

If at any stage shortly before or during your scan, you become worried, or wish to ask a question, you will be able to speak to one of the Radiographers, who will use an intercom to keep in touch with you.

Of course you do not have to take part in this study, and **you may withdraw from it at any time**. We are, though, very grateful to you for offering to help us and, if you are willing, you may be asked to come back for extra scans.

As part of this study we may obtain limited diagnostic scans of your brain. Our research studies are designed to improve knowledge of how the brain works, not for diagnostic or clinical purposes. However, a consultant Radiologist will examine these scans and a report will be sent either to your GP or the Principal Investigator of the study in which you are participating if they are clinically trained (or a nominated clinically-trained deputy if not) to document the examination. You may therefore need to give your GPs name and address to the person who has recruited you into the study. We may not be able to scan you unless we have your GPs name and address in some situations.

You should be aware that there is a small possibility (about 3%) of a significant abnormality being detected in your scan, which may need to be acted upon, or your GP told about, in case of any future illness. The study investigator or the research centre Radiologist will be happy to discuss this further with you if you wish.

Further information on magnetic resonance imaging is available, if you require it, from Dr. David Summers, a Consultant Neuroradiologist in the Hospital (Tel: 0131 537 2475).He is not involved in this study, and so will be able to give you independent advice.

Otherwise, the Superintendent Radiographer or the centre's Radiologists will be happy to try to answer any other questions that you might have. They can be contacted at the address shown at the top of the front of this information sheet.

Once again, many thanks.

Study Information Sheet - MRI

Title of Project: Standard Functional Magnetic Resonance Imaging (fMRI) Study

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. If there is anything that is not clear or if you would like more information, please ask us. Take time to decide whether or not you wish to take part.
Thank you for reading this.

What is the purpose of this study?
This study will use functional magnetic resonance imaging (fMRI) to take pictures of the activity of your brain while

Why have I been chosen?
You have been chosen because you have already volunteered to participate in the Centre for Cognitive Neuroimaging Research Panel, coordinated at Psychology Department, or you volunteered to participate in research studies using functional magnetic resonance imaging.

Who is organizing this study?
This study is organized by one of the Principle Investigators within the Psychology Department.

What will happen to me if I take part?
Before you take part a member of staff will ask you some questions to ensure that you have no metal within you before you enter the strong magnetic field of the MRI scanner. You may be asked to remove coloured contact lenses and to change (we provide training suits in case there is metal on your clothes). You will then be asked to lie in the scanner and the scanning will start. The scanning can be noisy so we shall give you headphones or earplugs to reduce this noise. If you are very claustrophobic, that is if you feel very uncomfortable in small closed environment, then it may not be appropriate for you to be scanned.
During the scan you will be asked different things (eg, to listen to sounds/voices, watch images…) Whatever the nature of the task, it will always be explained to you before you sign the consent form, and will never involve any painful stimulation. We will repeat the instructions before each task. At all time you will remain in contact with us through the intercom and you will have a buzzer in your hand, in case you want us to stop the scan and come in the scanner room.
We will ask you in all cases to try to keep your head as still as possible. To help you do so, we will place foam pads under your neck and on the side of your head.
The scanning session will take about one and a half hours, although you will not actually be scanned for more than 60 minutes of this time.

What is the device involved?
We can learn a great deal about how the brain works by looking at the blood flow to different parts of the brain whilst the brain performs different tasks. We measure brain function using

images taken with a magnetic resonance imaging scanner. This scanner uses a strong magnetic field to create detailed images of brain structure and function. By taking a series of images whilst you perform a task we can build up a picture of the brain areas activated by this type of task. The scan does not involve any injections or X-rays.

What are the possible risks/side effects of taking part?

The scanner can be loud when it takes images, and you will be given earplugs and/or headphones to block out some of the sound. Also, the scanner space is quite reduced, and people who are uncomfortable in small or confined spaces may not be able to participate. If this applies to you, remember that you may withdraw from the study at any time without explaining why. MRI is generally thought to be a safe, non-invasive imaging technique. There are no known risks or side effects, except that in less then 5% of people the scanning might induce a peripheral nerve stimulation (felt as small twitches); this is not dangerous but might induce discomfort. In some very rare cases, being in the magnetic field may also trigger vertigo (dizziness). In the unlikely case you experience one of these feelings, please alert us and withdraw from the study, should you wish to do so. Although there is no evidence of danger, as a natural precaution we do not wish to include any women who may either be pregnant or have any reason to believe they may be pregnant.

What are the possible benefits of taking part?

We will reimburse you for your time and travel, and you will have the pleasure of knowing that you have made a contribution to our understanding of the relationship between brain and behaviour. However, there will be no direct benefits accruing in terms of your treatment.

What happens at the end of the study?

The results of this study may be published in a journal or used for teaching purposes. The results may also be presented at scientific meetings, or in talks at academic institutions. Results will always be presented in such a way that data from individual volunteers cannot be identified.

Confidentiality - who will have access to the data?

The data will be stored on a secure network and only members of the Centre for Cognitive Neuroimaging (CCNI) of the Psychology Department at University of Glasgow will have access to the data. It is possible that the data may be used by researchers working with CCNi for other similar ethically approved research protocols, where the same standards of confidentiality will apply. In all cases your name will not be used and your data will be identified only by a 5 digit code.

Will my General Practitioner (GP) be informed?

This is not a diagnostic scan. Your GP will not be routinely informed if your participation in this study has been as a normal volunteer. Brain images will NOT be routinely examined for abnormalities by a trained neuro-radiologist. Like faces, brains come in all shapes and sizes, however, so that there are many normal variations of what the scan shows. There is a chance of less than 1:100 that your scan may, by chance, show a significant abnormality of which you are unaware.

There is no guarantee that abnormalities will be picked up. It is possible, however, that an abnormality is detected, by chance, in the scan of a normal volunteer by the radiographer or one of the investigators. This is referred to as incidental finding. If this happens, your brain scan will be examined by a trained neuro-radiologist who will provide an expert opinion on the importance of the incidental finding for your health, and on the potential health benefit of disclosing this information to you. There are three possible cases:

- Unlikely net benefit: If the incidental finding is a condition not likely to be of serious importance for your health, or whose likely health importance cannot be ascertained, that finding will not be disclosed to you or your GP.

- Possible net benefit: If the incidental finding consists of a nonfatal condition that could possibly be grave or serious but that cannot be avoided or improved, then when you are likely to deem that information important, that finding will be disclosed to you with appropriate guidance. You may also choose not to be informed should such an unlikely finding apply to you. In that case, please tick the appropriate box on the consent form.
- Strong net benefit: In the very unlikely case of a life threatening condition or a condition likely to be grave and that can be treated or improved, this information will be disclosed to you and you will be appropriately advised. Further action will be decided which could involve further imaging and/or a discussion between you and your GP or an appropriate clinician.

What if new information becomes available?
If the new information pertains specifically to the health of the volunteer, the volunteer may be informed (see previous paragraph). Otherwise, new information will be published through traditional scientific channels (journal articles, conference presentations).

What will happen to the study results?
In accordance with good research practice, they will be kept securely for a minimum of 10 years and possibly indefinitely in the CCNi data archive.

Will I receive a financial compensation?
Yes; You will receive £6 per hour for your participation in this study.

Can I ask questions about the research project?
Yes; We will answer all questions you may have that are related to the research project to which you agree to participate (see contact details below)

Can I withdraw from the study?
Yes. You participation to this research project is voluntary, and you may withdraw from the research at any time and for any reason, without explaining why, and this will not affect your medical care or legal rights.

Can the investigators interrupt the study?
The research may be interrupted by the researchers at any time, and for several possible reasons such as new requirements for the selection of participants, for example.

Are there compensation arrangements if something goes wrong?
In the unlikely event of anything untoward happening, the University of Glasgow provides insurance for claims.

This research study has been approved by the Ethics Committee of the Faculty of Information and Mathematical Sciences at University of Glasgow.

Contact details
Name
Address
Telephone Email

Thank you for considering taking part in this study. Our research depends entirely on the goodwill of potential volunteers such as you. If you require any further information, we will be pleased to help you in any way we can.

Department of Clinical Neuroradiology, Institute of Neurological Sciences Glasgow

Policy for Reporting in NeuroImaging Research

The Department of Clinical Neuroradiology recognises the vital role of approved research within the Institute of Neurological Sciences and is committed to supporting that research.

All scans carried out for the sole purpose of research will be reported by a Consultant Neuroradiologist.

A "Responsible Neuroradiologist" will be identified for all research studies and their involvement will be as described in one of the following three categories.

A. Academic. The "Responsible Neuroradiologist" will be a full part of the research team and will provide academic input to the study as well as reporting the scans.
B. Supportive. The "Responsible Neuroradiologist" will support the research by reporting the scans but will not take any further part in the research study.
C. Funded. The "Responsible Neuroradiologist" will be fully compensated through research funds for the task of reporting the scans. Compensation will be on a per scan or fee for study basis.

It is expected that the vast majority of studies will come into category A and indeed this category of involvement will be actively encouraged. The department will regularly review the number of studies in each category and assess whether there are resource implications that need to be addressed. Following accepted authorship guidelines the Neuroradiologist would be an author on a scientific paper if involved as in Category A.

Ethics application

The "Responsible Neuroradiologist" must be named in all Ethics Applications.

The following phrase will appear in the "Information for Patients" form in all Ethics applications:

"The (MRI/CT/SPECT) scan being done is designed to answer research questions, not examine your brain medically. This (MRI/CT/SPECT) scan is not a substitute for one a doctor would request. It may not show problems that would be picked up by a full medical (MRI/CT/SPECT) scan. However, your scan will be reviewed by a specialist radiologist, and if we believe that an abnormality may be present we will contact you and your health team and help you get a more detailed assessment and medical follow-up where necessary. There is a possibility that detection of an abnormality may be a false alarm that might cause you unnecessary concern.

The report on the scan will become part of your hospital record."

Dr. K Forbes, Clinical Lead
Prof. DM Hadley, Research Programme Leader

January 2010

Incidental Findings

Our standard policy for (research) scans at the IoP is that a radiologist will look at any appropriate structural scans and, while they will not issue a formal report if the scan is normal, we/they will ensure that the subject's GP is notified if there is any abnormality which may warrant follow up. Although we will ask research participants to sign a form giving consent to this, is important that you mention this in the information sheet for your study, so that the participant is fully informed when they consent to be part of the study. (Note that the best way to deal with incidental finding, and in particular whether or not participants should be able to 'opt out' of knowing if anything unexpected is found, can be controversial. Members of the CNS and the relevant ethics committees will continue to monitor the situation, and this page will be updated if 'best practice' guidelines change. Currently, however, CNS policy is that participants who are not willing for their GP to be contacted if necessary **CANNOT BE SCANNED**).

Note that while our standard procedures ensure that the subject's GP will be notified if necessary, confidentiality issues mean that the radiologist will not (cannot!) inform the researchers of any such cases. It also makes it very hard for the radiologist to discuss such issues even if raised directly by the researcher, and makes giving advice on exclusion of abnormal scans impossible. If you want to have a radiologist involved in your study we therefore strongly advise that:

- you approach the radiologist in advance of submitting a grant that requires them to comment/scan/report on/... lots of scans!
- where appropriate (and after discussion as point a, above!) you include a statement in your information sheet detailing the radiologists involvement in the study.

Examples of sentences you might include in your information sheet can be found below:

As CNS policy is to inform a research subject's GP if any significant abnormality that might require medical intervention is seen, it is important that Patient/Subject Information Sheets reflect this. Additionally, if you (the researcher) will be informed of any abnormalities, this should also be stated on the information sheet. There are a number of possible situations, for each of which a slightly different wording will be suitable.

1. If you simply want the subject's GP to be informed, then a suitable wording (agreed with <NAME DELETED>, our main radiological contact) would be something like:

   "A limited assessment of the MRI scans will be performed by a neuroradiologist and identification of a major abnormality that requires action will be reported to the doctor you specify on your MRI consent form."

   Note that while you are free to modify this wording if necessary (e.g. to simplify for studies involving children, or to match the style of the rest of your info sheet), you should take care not to change the basic meaning. In particular, be careful not to imply that the scans we take are in any way a replacement for a full clinical scan; if participants have any worries about their health they should always talk to their own GP. Also note that what <NAME DELETED> or the other radiologists will be able to

do on research scans will only be a limited assessment, intended to identify gross abnormalities; they will **NOT** generate a formal report, as would be the case for a clinical scan.

2. If, in addition to the subject's GP being informed, you (the investigator) would also like to be informed if an abnormality is found (for example in order to exclude that subject's data from further analysis) then a suitable wording would be something like:

   "A limited assessment of the MRI scans will be performed by a neuroradiologist and identification of a major abnormality that requires action will be reported to the doctor you specify on your MRI consent form, and to the study investigators."

   Please let <NAME DELETED> know as early as possible if you are intending to include a statement like this in your info sheet, so that they can confirm that it is appropriate, and work out a suitable way to inform you as/if/when necessary.
3. Finally, if your study needs specific radiological input (e.g. because the inclusion criteria or the proposed analyses are anatomically/radiologically based), then it is essential that you talk to <NAME DELETED> as early as possible during project planning. After discussing everything with <NAME DELETED> you should (assuming they are able to be involved in the study), include in your info sheet a statement such as:

   "MRI scans will be reviewed by a neuroradiologist and identification of a major abnormality that requires action will be reported to the doctor you specify on your MRI consent form; in addition major abnormalities relevant to the particular study and its specified inclusion/exclusion criteria will be reported to the study investigators."

UNIVERSITY OF LIVERPOOL

Magnetic Resonance & Image Analysis Research Centre (MARIARC)

MARIARC
Pembroke Place
Liverpool
L69 3GE
UK

www.liv.ac.uk/mariarc

Recommended standard text for Patient Information Sheets in magnetic resonance research studies:

What will happen to me if I take part?

You will be asked to fill in a short safety screening form to make sure there are no reasons why you would not be suitable for magnetic resonance scanning. You will be asked to wear a gown (changing rooms are provided) and remove items which are affected by the magnetic field (e.g. hearing aids, mobile phones, keys, coins, pens, credit cards (secure lockers are provided). While inside the scanner, you will be asked to wear earplugs to protect your hearing from the noise of the scanner.

What are the possible disadvantages and risks of taking part?

There are no known risks in properly conducted magnetic resonance scanning. As it involves a strong magnetic field, certain standard precautions will be observed. Most importantly, we will NOT study you if you are fitted with a heart pacemaker, mini-defbrillator or a neurostimulator ; if you have surgical clips in your head; if you have suffered injuries which may have left metal particles in your eye or head, or elsewhere in your body; or if you have an artificial heart valve. We will also ask about other kinds of surgery and metal implant which might affect your suitability. Some people find the scanner a claustrophobic or uncomfortable environment, and we will ask you about this.

Occasionally research studies using magnetic resonance imaging reveal significant unexpected abnormalities which require medical follow-up, either for further investigation or (more rarely) treatment. The scans we do are for research purposes, but we review them carefully to avoid missing such an abnormality. We will spend a few extra minutes taking high-quality images which we will routinely have reviewed by a consultant radiologist. If any significant abnormality is found, we will send the report to your GP, who will be able to take it further with you.

Please note that this is not a substitute for a 'medical' magnetic resonance scan that a doctor might order to make a diagnosis. It should therefore not be seen as a 'health check'.

Text used on obligatory screening form for research scans:

Our policy on unexpected abnormal findings in research studies

Occasionally research studies using magnetic resonance imaging (MRI) reveal significant unexpected abnormalities which require medical follow-up, either for further investigation or (more rarely) treatment. The MRI scans we do are for research, but we review them carefully to avoid missing any such abnormality. For studies of brain, we take a high-quality image (which adds a few minutes to the research study for which you have volunteered) and have them reviewed by a consultant radiologist. If any significant unexpected abnormality is found we will send the report to your GP, who will be able to take it further with you. Studies of organs other than brain are dealt with slightly differently, but in any case a health professional will review an MRI scan and report any significant unexpected abnormality to your GP.

Graham Kemp

Director, MARIARC
5 April 2011

UNIVERSITY OF LIVERPOOL

Scan Date ..... Area..... Report Date.....

Date of Screening.....

Magnetic Resonance and Image Analysis Research Centre

SAFETY SCREENING FORM FOR RESEARCH SCANS

Surname..... Forenames.....

Address.....

E-mail address..... Telephone number.....

Date of Birth ..... Sex ..... Weight ..... Height .....

G. P.'s Name & Address .....

.....

It is very important that you give full and accurate answers to the questions on this form.
The information you give will be treated in strict confidence.

Our policy on unexpected abnormal findings in research studies

Occasionally research studies using magnetic resonance imaging (MRI) reveal significant unexpected abnormalities which require medical follow-up, either for further investigation or (more rarely) treatment. The MRI scans we do are for research, but we review them carefully to avoid missing any such abnormality. For studies of brain, we take a high-quality image (which adds a few minutes to the research study for which you have volunteered) and have them reviewed by a consultant radiologist. If any significant unexpected abnormality is found we will send the report to your GP, who will be able to take it further with you. Studies of organs other than brain are dealt with slightly differently, but in any case a health professional will review an MRI scan and report any significant unexpected abnormality to your GP.

WARNING Do NOT enter the scan rooms with ANY metal objects such as:-

Glasses	Jewellery/piercings	Safety pins
Coins	Removable Dentures	Hairpins/hairclips
Keys	Eye make-up	Mobile phone
Watch	Hearing aid	Magnetic strip cards e.g. credit cards

Lockers are provided in the waiting area for the safe-keeping of your belongings. Do not take anything through to the scanning area. A changing area is provided where you can change out of your clothes into a gown. Underwear with metal fastenings must be removed and left in the changing room. You may wear a t-shirt under the gown as long as it has no metal. If you have an inhaler or other emergency medication please alert the researcher and leave it in the changing room where it can be located in an emergency.

The following are <u>hazardous</u> during an MR scan.
You should <u>not</u> undergo an MR scan if these apply.

Please tick YES or NO boxes as appropriate:

Yes	No	
		Cardiac Pacemaker or mini-defibrillator
		Brain clips (cerebral aneurysm clips)
		Metal fragments in the eye or head
		Artificial heart valve
		Neurostimulators
		Shrapnel

Yes	No	
		Do you have any internal metal at all?

If YES, where, is it?

The following may interfere with and in some cases preclude an MR scan

Please tick YES box if any of these apply:

Yes	
	Surgical Clips
	Vascular clips or stents
	Shunt, spinal or ventricular
	Insulin Pump
	Electrodes
	Hearing aids or cochlear implant
	Orthopaedic Surgery
	Prosthetic limb
	Metal mesh implants
	Wire sutures
	Tattoos
	Colostomy , ileostomy or drainage bag
	Any history of injuries to the eyes
	Other implants, including dental work

Yes	No	Please tick YES or NO boxes as appropriate	If YES, please give details
		Have you had any operations or procedures in which metal may have been implanted in your body?	
		Have you suffered from any back or neck pain?	
Are you suffering, from or receiving treatment (e.g. medication) for any disease, illness or medical condition?			
		• Epilepsy, fits/faints/dizzy spells or migraine	
		• Renal (kidney) disease	
		• Cardiac (heart) disease	
		• Hypertension (high blood pressure)	
		• Chest (lung disease), including asthma	
		• Diabetes	
		• Other illness	
		Do you carry any emergency medicine with you?	
		Have you had symptoms in the region we are scanning ?	
		Is there any possibility you could be pregnant? Do you have an IUD? Are you breast feeding?	
		Do you suffer from claustrophobia (fear of tight spaces)?	

If you have any queries or concerns please ask.

If you are willing to continue please tick the boxes and sign below:

I confirm that the information given by me on this form is complete and accurate, to the best of my knowledge	☐
If an unexpected significant abnormality is discovered I consent to my GP being contacted	☐
I understand that I must not take any metal objects into the scan room with me.	☐

Signature…… **Date**……..

To be completed by authorised MARIARC staff

Proceed with MR? YES / NO

Name……..…… Signature: .....

Position at MARIARC……..…..... Date:…….

When more than one study is scheduled, the table below **MUST** be filled in for all MR scan dates subsequent to the first. If there have been no changes to any conditions above since the previous screening including operations, metal in the eye or likelihood of pregnancy then tick **NO CHANGE** and sign as indicated.

NO CHANGE	Signature of volunteer *To confirm that the answers to the questions asked on this form are unchanged*	Signature of screener	Date

THE WELLCOME TRUST CENTRE FOR NEUROIMAGING
(Inc LEOPOLD MULLER FUNCTIONAL IMAGING LABORATORY)
12 QUEEN SQUARE
LONDON WC1N 3BG, UK

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version_1: 25/02/10
UCL Ethics Project ID number:
3 pages

Participant Information Sheet

Study title: **Minimum risk magnetic resonance imaging studies of healthy human cognition**

Invitation:
You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the research?
This research is trying to understand how the adult human brain works – for example, how it allows us to see, pay attention, read and speak, learn and remember, imagine, navigate around in the world, interact with other people, solve problems, and experience emotions. If we can understand how these vital functions are supported by the healthy brain, in the future we may be able to do more to help patients who have difficulties in these domains.

Do I have to take part?
It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep, and asked to sign consent forms, copies of which you will also get to keep. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?
It you agree to participate, you will be invited to come to the Wellcome Trust Centre for Neuroimaging in Queen Square in central London. To cover your travel and meal expenses, you will receive £10 for every hour or part of an hour spent in the department. A researcher will welcome you, explain the exact procedures of the study, and will answer any questions you may have. None of the tests are invasive, and there is no need to restrict your lifestyle in any way. Although it is likely that we can complete all the tests during one visit, it may be necessary for you to return for a second visit. If this is likely, we will advise you in advance and you can take this into account before deciding if you want to take part.

What do I have to do?
Before scanning, you will be shown exactly what you have to do, and given time to practise. Tests typically involve looking at visual information presented on a screen and/or listening to information presented via headphones. You might be asked to respond using a simple keypad. Having practised on the task, and having asked any questions, you will then be asked to perform the same task while your brain is being scanned. Our research is done using Magnetic Resonance Imaging (MRI). It is like an X-ray machine, but it does not use X-rays or any ionising radiation. It uses magnets instead. MRI is painless and safe, as long as people with any magnetic metal implants (such as pacemakers)

are excluded. Before being invited to the Centre a researcher will check that you are suitable for scanning using MRI. Once you have removed any metal you are wearing or carrying, you will be asked to lie on a table inside the scanner for up to 60 minutes while the images of your brain are made. The researcher will be able talk to you between scans while you are inside the scanner. One sort of brain scan involves taking detailed anatomical images of your brain – a structural scan. While structural images of your brain are made, you will be asked to relax and keep still. During another type of scan, known as a functional MRI (fMRI) scan, you will do the cognitive tasks you practised before entering the scanner, e.g. looking at pictures (on a special screen set up in the scanner so you can see while lying down), listening to information via headphones, and using a simple keypad to respond. After scanning, we may ask you a number of questions about your experience of doing the tasks during the scan. Depending on the exact task, and including breaks, your visit to the Centre (including practise, scanning and debriefing) may take about 2-3 hours.

Are there any side effects?
During scanning, the scanner is very noisy. To reduce the noise, you will either wear ear plugs, or headphones that are designed to reduce the noise impact of the scanner. Some people find the enclosed space of the scanner uncomfortable. You will have access to a panic button at all times and can press this to stop the scan and you will immediately be removed from the scanner. An infrequent side effect of MR scanning in higher (3 Tesla) magnetic fields is a tingling sensation in the peripheral parts of your body. If this occurs, you will be trained in advance to press the panic button, and the scan will immediately be stopped.

Recording your testing session:
In some circumstances it may be necessary to make video, audio or digital recordings of your practice/debriefing sessions. This will help us to score your performance accurately after testing is complete. If this is necessary, you will be informed in advance. You will also be asked to sign a separate consent form relating to the use of the recorded material. The recordings will be kept confidential, will not have your name or details associated with them, and will be kept in secure accommodation.

Are there any benefits to taking part?
There will be no direct benefit to you from taking part in this research. However your data may contribute important theoretical information to our understanding of how the brain works, and in the future may aid attempts at rehabilitation in patients with brain injury or disease.

If I have a complaint:
If you are unhappy with how you have been treated during your participation, information about how to make a complaint is given on the signed consent form, a copy of which you will be given to keep. The department is covered by UCL/UCLH liability insurance.

Will my taking part be kept confidential?
All information that is collected from you during the course of the research will be kept strictly confidential, anonymised, and will be collected and stored in accordance with the Data Protection Act 1998. Data will be kept in secured accommodation and on secured computers in the Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL. The data will be used only for the purpose of informing the research questions in this study, and only accessible by the relevant research teams at the Centre. The data will be retained indefinitely and securely, and may be accessed by the research teams for comparison with future data relating to the research question.

Will my GP be informed?
Your GP will not be notified of your participation in this research. However, for our records, we may request you provide the name and address of your GP. Should the MRI scan unexpectedly reveal any clinically relevant abnormality, we would like your permission to notify your GP.

What will happen to the results of the research study?
Once the study is complete, has been written up, peer-reviewed and accepted in a scientific journal, you will be contacted by post with a summary of the findings, and can elect to receive a full copy of the report if you wish. You will not be identified personally in any publication.

Who funds this research?
Our work is funded by medical charities such as the Wellcome Trust, and government bodies such as the Medical Research Council, and the European Union.

Who has reviewed this research?
A Research Ethics Committee reviews all proposals for research using human participants before they can proceed. This research has been approved by the University College London Research Ethics Committee.

Contacts for further information:
If you have any questions after reading this information sheet please ask the researcher you have been dealing with, who will provide you with their telephone number/email address on initial contact. Other members of the research team include:

Mr Peter Aston, Laboratory Manager (020-78337472)
Mr David Bradbury, Head of Imaging Support (020-78337463)
Professor Ray Dolan, Centre Director (020-78337456)

Thank you for taking the time to consider participating in our research.

UNIVERSITY OF CAMBRIDGE

[relevant department headed paper]

INFORMATION SHEET
VOLUNTEERS

Version Number:
Date:

Title of Project:

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.

Part 1 tells you the purpose of this study and what will happen to you if you take part.
Part 2 gives you more detailed information about the conduct of the study.

Please ask if anything is not clear or if you would like more information. Take time to decide whether or not to take part.

Part 1.
What is the purpose of this study?

Do I have to take part?

What will happen to me if I take part?

What are the possible disadvantages and risks of taking part?

Will my GP be informed
Your GP will not be routinely informed if your participation in this study has been as a normal volunteer. However, like faces, brains come in all shapes and sizes, so that there are many normal variations of what the scan shows. There is a chance of less than 1:100 that your MR scan may show a significant abnormality of which you are unaware. In such circumstances, you will be appropriately counselled. You will be referred to the appropriate specialist in consultation with your General Practitioner if that is what you would like. Such early detection has the benefit of starting treatment early but, in a small number of cases, may have implications for future employment and insurance.

What are the possible benefits of taking part?

What if there is a problem?

Will my taking part in the study be kept confidential?
Yes. We will not inform anyone of your participation in the study without your consent. All information gathered about you during the study will be kept confidential. The details are included in Part 2.

Contacts for further information.

This completes part 1 of the Information sheet.

Part 2

What will happen if I don't want to carry on with the study?

What if I am unhappy with things or something goes wrong?

Are there compensation arrangements if something goes wrong?
In the unlikely event of anything untoward happening, insurance has been taken out with Royal Sun Alliance to cover this study.

Who is organizing and funding the research?

Who has looked at and approved the study?

Confidentiality – who will have access to the data?
Imaging data will be stored on a secure network and only members of the Wolfson Brain Imaging Centre (WBIC) and members of the research group will have access to the data. It is possible that the data may be used by researchers working with the WBIC for other similar ethically approved research protocols, where the same standards of confidentiality will apply. It may also be disclosed to researchers working outside the EEC, when that person is working in close collaboration with researchers scanning within the Wolfson Brain Imaging Centre. In that case that person has signed a Code of Conduct guaranteeing that the data will be kept confidential & securely. The University is deemed to be the Data Controller and all enquiries concerning access to the data should be addressed to him. The Administrator of the Centre will be able to tell you the name and address of this officer.
Research data will be …..

What will happen to the study results?
Imaging data will be kept securely for a minimum of 10 years and possibly indefinitely in the WBIC data archive in accordance with good research practice. Research data will be….

You may withdraw from the study at any time without explaining why.

This research study has been approved by the Local Research Ethics Committee.

Contacts for further information

Contact address: Name
Address

Contact No

Thank you for considering taking part in this study. Our research depends entirely on the goodwill of potential volunteers such as you. If you require any further information, we will be pleased to help you in any way we can.

Sebastian:Users:innov8gd:Public:CURRENT WORK:RCR:461 Ethics Document:client supply:Wolfson.doc

Appendix 4. Discussion paper on Incidental Findings prepared by the British Chapter of the International Society for Magnetic Resonance in Medicine

British Chapter of the International Society for Magnetic Resonance in Medicine

Discussion Paper on Incidental Findings During MRI Research

Background – A brief look at the literature

There is considerable background literature to the topic of incidental findings on MRI (for example *Katzman et al, 1999; Illes et al, 2006; Illes et al, 2008; Wolf et al, 2008; Wolf et al, 2008a; Illes et al, 2009; Hoggard et al, 2009; Morin et al, 2009;Pierce et al 2009*). A working group was established in the US in 2004 which has eloquently considered the ethical problems associated with performing MRI in healthy volunteers and treatment of unforeseen abnormalities. This group, consisting of medical ethicists, clinical and non-clinical MR researchers, have reported their deliberations (*Illes et al, 2006; Illes et al, 2008; Illes et al, 2009*). The key finding of that group states:

"Further research is needed to evaluate the costs and benefits of identifying incidental findings and referring subjects for follow-up. How the burden of false-positives, combined with the burden of testing for incidental findings, weighs against the problem of missed incidental findings must be assessed. We must understand the downstream financial cost on the investigative process, and the psychological and financial burden that discovery of an incidental finding might have on subjects, in parallel with thinking about incidental findings upstream. …determining the frequency of confirmed and false-positive findings and developing age-appropriate and even disease specific databases is imperative". (*Illes et al, Science, 2006*)

In the UK a recent meta-analysis of neuroimaging studies worldwide was reported (Morris *et al*, BMJ, 2009). This analysis suggests the incidence of :

neoplastic brain lesions is 0.7%

- most common findings being meningioma (0.29%), pituitary adenoma (0.15%).

non-neoplastic brain lesions (excluding markers of cerebrovascular disease) is 2.0%,

- most common findings being arachnoid cysts (0.5%), aneurysms (0.35%).

In general incidence varied with subject age and detection of abnormalities was dependent on image resolution.

Data on incidence of abnormalities in non-neuro scanning is minimal. A recent UK study (*Morin et al, Eur J Radiol, 2009*) analysed the research group's own database of liver MRI from 148 healthy controls. Incidence of abnormality was 29%, with 12.8% being clinical significant findings. These numbers increased with subject obesity (BMI).

Summary of Ethical Considerations

The main areas of concern can be summarised.

i. Does the MR research community have a duty to formally review research scans for incidental findings?

ii. Does the MR research community have a duty to routinely acquire additional scans as part of all research protocols for the sole purpose of formal review?

iii. By whom should any review be performed and reported – in MR research sites ranging from psychology groups through to radiologist led teams it is not possible to adopt a single approach under current arrangements.

iv. If an abnormality is found, who should that information be communicated to (subject directly or via their GP) and by whom?

v. Making an incidental observation can have a profound effect on a subject's wellbeing and future life plans. For example it may be seen as a positive benefit in early diagnosis, or equally as a negative impact on ability to drive, obtain life, health or travel insurance etc.

vi. What are the implications of MR research scans becoming a health screening device?

vii. Risk associated with subsequent treatment may not be clear, or may be significant leading to mental stress on subjects in determining their course of action post diagnosis.

viii. Identifying an abnormality may lead to invasive and aggressive treatment, with concomitant morbidity, in some cases for disease that if left untreated would not have been life threatening (overdiagnosis and overtreatment).

ix. What is the appropriate advice to be given to volunteers, and what consent is required?

Suggested Stance

The British Chapter of the ISMRM (BC) recognises the need for careful deliberation on the issue of incidental finding in healthy controls. The BC would welcome guidelines in this area but urges a cautious approach in developing such guidelines.

MR-related research and development is an important area of UK science and taking action which stifles innovation and understanding, or places an unreasonable additional burden on research activities and funds, should be avoided. Obtaining improved demographic data on the levels of incidental findings should be a matter of priority.

Radiological review of all research scans does not seem an appropriate approach, raising many issues itself:

a) *Risk/Benefit to volunteers* – as discussed above, although there may be potential benefit to the subject of reviewing all scans, there are also significant risks and costs involved in this for the volunteer, although these may be harder to quantify. In short, it is not clear whether in general we would be helping our subjects by reviewing all scans.

b) *Liability* – If it is stated that data are being screened for abnormalities, the PI (or individual screening the images) must be accepting liability in the case that they miss any lesion. Given that **most** research protocols will fall short of a full clinical investigation, may be restricted to certain body areas and will not be optimised for all potential abnormalities would a radiologist assume such liability when only a small subset of a clinical scan has been collected? This situation should be contrasted with the situation when subjects are informed at the time of obtaining consent that they are not having a clinical scan, that the measurements will not be designed to screen for abnormalities, but that there is a chance of incidental observations which would be handled in a specific way.

c) *Capacity* – Many units do not have access to radiology input (indeed do not need it for their research objectives), while those that do would quickly arrive at a backlog of data to review. Additional scans to assure adequate clinical standard for detection of abnormalities would increase research costs and reduce research volume. Further, Centres investigating multiple body areas would require access to specialist radiologists to cover all body areas.

d) *Cost* – Estimated total cost to the UK research budgets may exceed £1m/annum assuming a scan review charge of £50/scan. If additional scans are required this cost would be even greater and would make many research protocols impossible.

e) *Effects on subject recruitment:* If we review all research scans, this may act as an inducement for some people to volunteer to participate in research studies. Ethics committees may consider this to be inappropriate, particularly for more invasive studies. Furthermore this will bias the population that is recruited, and this in turn will bias the research.

Researchers using MRI as a tool to study any subjects (whether patients or healthy volunteers) have a duty of care to take action if abnormalities are identified. All sites involved in studying volunteers for research must have a clear policy on the process to apply in the event of an incidental finding, which should be applied across all research projects undertaken at that site and should be agreed by their ethics committee. Information regarding potential incidental findings should be included in patient information. In framing this policy and the related information, it would be desirable to indicate to volunteers the limitations of image information acquired in any particular study, the limitations of any evaluation of the images, the process to be applied should there be incidental findings, and the likely risks and benefits resulting from such findings. It may be desirable, as part of consent, to ascertain whether the volunteer wishes to be informed of incidental findings. The process must protect the subject's anonymity and must allow for the subject to be given appropriate information in a controlled manner. However the purpose of research studies is not to provide a mechanism for screening subjects for disease, and this should be made clear to subjects at recruitment.

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