Version 1 (17th April 2013)

Invasive Procedures

Group members

Dr John O'Hara; Costas Tsakirides; Dr Andy Pringle; Dr Karen Hind

Other Contributors

Professor Rod King (author of the University Human Tissue Act Report)

Contents

Introduction

Within the areas of sport science and sport medicine the use of invasive procedures on participants is required, so clinical and biological samples can be acquired to address specific research questions. The invasive procedures presently being used within the Carnegie Faculty include:

1) Finger Tip Blood Sampling
2) Phlebotomy and Cannulation
3) Muscle Biopsy
4) Ingestion of Food and Supplements (e.g ^{13}C Stable Mass Isotopes)

Each of these invasive procedures will be commented on in detail below, with regards best practice and any ethical implications. However, it is worth noting that collection and storage of clinical and biological samples falls within the scope of the Human Tissue Act (The Human Tissue Act 2004, http://www.hta.gov.uk/legislationpoliciesandcodesofpractice/legislation/humantissueact.cfm), which needs to be considered alongside the use of invasive procedures.

Human Tissue Act

All practice that involves human tissue sampling is subject to the jurisdiction of the Human Tissue Act, 2004. Thus the identification of what constitutes "Relevant material" is Germaine to any assessments on proposals made to Faculty Research Ethics Committee (and University Research Ethics Committee). Current guidance would indicate that certain samples typically collected during sports science trials, (but not exclusively so) are "Not Relevant material" whilst others are. This is of importance in the processing and storage of such samples due to the time and condition imposition

within the act. The following is a simple guide to “Relevant” and “Not-Relevant” material. “Relevant material” is that deemed to contain human cells.

Relevant Material includes:

Stem Cells

Bone marrow

Blood

Faeces

Urine

Sweat

Not Relevant Material includes:

Hair (living person)

Nails

Plasma

Serum

It follows that samples that are “Not Relevant” may be stored on University premises (subject to compliance with standard ethical clearance for trials in which such samples are collected). Whilst this is a clear factual demarcation, this does not necessarily exclude the collection and storage of samples that are relevant. For example, if samples undergo procedures that render it acellular then it need not be considered “Relevant material”. In this case proposals for ethical clearance should state fully the collection and procedures which render a “Relevant” sample “Not Relevant”. This is sufficient to enable storage on University premises.

The issue for our Faculty (and University) would be the approval of proposals that include “Relevant” samples and the way in which such samples are to be analysed and stored. Thus samples which we consider to primarily be “Relevant” could be made, by procedure “Not Relevant” (e.g. urine after centrifugation or filtration). If storage is an issue then under the Human Tissue act such storage must be licensed by the Human Tissue Act. At present the Faculty and University does not have such license. Nevertheless, storage may be possible for a specific research project provided approval has been made by a designated ethics committee. In this instance this would be by a designated National Research Ethics Committee (NRES). Although the details of the act are published, several

"grey" areas remain, for example what constitutes "storage", this could be interpreted as batching of a sample set over a time period or otherwise. Clearly collection of samples over several hours and subsequent analysis or dispatch to a laboratory for which a license has been granted may be deemed acceptable by a specific interpretation of the Human Tissue Act. After consultation (by Professor Rod King) with Dr Andrew Rawnsley (Research Governance and Training Manager, Teeside University) some of these points have been resolved (see below), but if the extent and nature of research in the University changes then we should consider application for a license under the Human Tissue act to facilitate the authorisation of research in which relevant samples are an issue. The inclusion or exclusion of samples from the Human Tissue act is of course also dependent on qualifying consent and assurance about processing of tissue with the participant of any trial.

Storage of Samples

1) *Standard Conditions pertaining to ordinary University ethical consideration (no site license in force)*

Samples that are "Relevant material" should be collected and analysed as soon as possible but not more than 24 hours after collection. Samples should then be discarded.

2) *Permitted Conditions pertaining to extraordinary University ethical consideration*

    a. *Joint Ethical Proposal*

Samples that are "Relevant material" should be collected and dispatched to a licensed laboratory as soon as possible but not more than 48 hours after collection. Such would apply for example when there is a joint protocol with another establishment at which a site license is in force at their premises. Faculty (University) ethical consideration would have been made on such an understanding.

    b. *NRES Approval*

Samples that are "Relevant material" should be collected and stored in suitable University premises. Such would apply for example when special approval has been given to a specific proposal and project by an external NRES ethical committee. Such may be granted where the proposal and project is purely for scientific research purposes. It is unlikely that more than two such approvals would be granted at any one time for the University. Faculty (University) ethical consideration would also be made on such an understanding.

    c. *Standard Conditions pertaining to ordinary University ethical consideration (site license in force)*

Samples that are "Relevant material" should be collected and stored in suitable university premises.

Notes

The following descriptors have relevance to the Human Tissue Act and should be considered if appropriate, as associated guidelines and legislation may apply to the sampling and storage of samples.

i) Mental Health/Mental Capacity
ii) Tissue
iii) Dangerous Materials
iv) Radiation
v) Child Protection
vi) Insurance
vii) Clinical Trials (Regulations 2006, Medicine for Human Use)
viii) Consent form inclusion

Invasive Procedures

Blood Sampling

Finger Tip Blood Sampling

Obtaining fingertip blood samples, when conducted by a trained and competent person and in accordance with the guidelines of our professional association (BASES), is a low risk activity. Under the conditions stipulated below this should be approved as part of a research ethics application at a local level.

The applicant (if an undergraduate or post-graduate student) must demonstrate experience of using this procedures during taught modules, as well as undergoing a physiology laboratory induction and the specific training for fingertip blood sampling in preparation for their research project. This training is delivered at various times throughout the year by the Learning Support Officers.

As part of that process they will be assessed by the Learning Support Officer delivering the training. They need to be signed off as competent by the Learning Support Officer and Supervisor for this specific skill and have that evidence attached to their ethics application. On that basis the Major Independent Study supervisor will then be able to sign the ethics forms (as long as they are trained and competent in fingertip blood sampling) and forward to the relevant Local Research Ethics Co-ordinator for their approval.

Phlebotomy and Cannnulation

Phlebotomy procedures are regularly used within Carnegie Faculty research, however, they are invasive and of higher risk. Phlebotomy (venous blood sampling) is a technique used when bloods are required to be drawn on a single occasion. This is where a small needle is inserted into an appropriate vein, which remains *in situ* until the bloods have been drawn and then it is immediately removed. Cannulation is a technique used when bloods are required at regular intervals over a set period of time. This is where a catheter is inserted in an appropriate vein. This procedure requires a small needle to be inserted into the selected vein, once the needle is in the vein a small plastic tube

is gentle pushed into the lumen of the vein. The needle is then withdrawn and the remaining part of the catheter is secured in place for the set time period. Both of these techniques should only be undertaken by a trained and competent person, which is usually an academic, a learning support officer, or a post-graduate research student.

The Faculty employ a phlebotomy consultant and assessor (Mr Ran Kurvits). He oversees and develops our best practise, as well as delivering all our training requirements. He also supervises trainees and confirms their competency, against national bench marks, following a period of assessment. Once competency has been confirmed and ethical approval is in place, blood sampling can be carried out.

Under certain circumstances an ethics application could be signed off by the Local Research Ethics Co-ordinator, as long as the following criteria are met, even though this is an invasive procedure:

1) The researcher has been deemed competent and can provide the relevant supporting evidence (i.e. signed assessment log).
2) The lead researcher has previously received Faculty Ethical Approval to use these techniques on more than two research studies (this acts as way of confirming their experience).

If criteria 1 can be satisfied, but criteria 2 cannot be met, then any ethics applications should be referred to the Faculty Research Ethics Committee for consideration using the published timetable. It is important to note that there may be other elements of the ethics application which need to be approved by the Faculty Research Ethics Committee.

Muscle Biopsy

Taking a muscle biopsy enables a range of biological analyses to be performed to inform specific research questions. The muscle biopsy procedure involves the removal of a small piece of muscle tissue (typically 50-100 mg) typically taken from the *vastus lateralis* using a small sterile hollow needle. Prior to the taking the biopsy, and following skin cleaning, a small amount of local freezing (anaesthetic) should be injected into and under the skin. There is an extremely low risk of allergic reaction to the local injection (1 in 1 million). The chance of a local skin infection in less than 1 in 1000. Participants are likely to experience some soreness in the muscle and some local bruising following each biopsy.

Using muscle biopsy procedures in research is a high risk activity, but under the conditions stipulated below should be approved as part of a research ethics application at Faculty level:

Muscle biopsies should be taken by a competent and trainer professional. Presently this is a visiting Professor (Ernest Schilders) to the University who is a licensed orthopaedic surgeon who has significant experience in using this method. Further, prior to participation all volunteers should be screened to diagnose any underlying pathology, or any medication, that could increase the risk of excessive bleeding, allergic reaction, infection or any other medical condition associated with the procedure.

Ingestion of Food and Supplements

^{13}C Stable Mass Isotopes

^{13}Carbon stable mass isotope tracer techniques are used in research that needs to quantify carbohydrate (exogenous and endogenous (liver and muscle) and fat oxidation, following the ingestion of a carbohydrate beverage. ^{13}C is naturally occurring in the diet (~1%) and is less abundant than the naturally occurring ^{12}C in the diet (~99%). It is a non-radioactive isotope. A trace amount is used to enrich typically carbohydrate beverages (~>1.5%), which is a safe increase.

This technique allows researchers to evaluate the ratio of ^{13}C/^{12}C in expired air and plasma glucose typically during exercise, to ascertain the rates at which the exogenous source of carbohydrate is being used as a fuel, and the rate at which pre-existing stores of glycogen (liver and muscle) are being used.

Approved suppliers should always be used and products should be stored and used in a safe and secure manner. Trained and experienced lead researchers should oversee the use and administration of ^{13}C stable mass isotopes.

This technique is low risk and there is no reason why this cannot be signed off at a local level, by the Local Research Ethics Co-ordinator.

Dual X-Ray Absorptiometry

Please see separate guidelines