Consent in crisis: the need to reconceptualise consent to tissue banking research

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Abstract

The issues surrounding consent to tissue banking research in Australia are complex and have created a forum of intense debate, thus providing a window of opportunity to critically appraise and challenge standard models of consent for research in general and for tissue banking research in particular. The usual practical difficulties associated with meeting the criteria for valid consent to research (including adequate information provision and voluntariness) are amplified in the case of tissue banking research. A number of models, based on widely accepted ethical principles, have been proposed to improve the process of obtaining consent to tissue banking research, all of which assume that the consent of *individual* tissue donors is needed to meet the criteria for valid consent. Feminist and communitarian theories use many of the same criteria for valid consent but interpret these criteria differently and de-emphasize the importance of individual autonomy as the central criterion for valid consent. An enriched model of consent incorporating feminist and communitarian ideas could satisfy the currently accepted criteria for valid consent while also furthering a broader range of community values.

Keywords: tissue bank; consent; research; bioethics; epidemiology

Emergence of the "consent to tissue banking" debate

Tissue banks are thought by many scientists to be an essential resource for medical research in the postgenomic age. 1-3 Collections of tissue, usually removed in the course of diagnostic or therapeutic procedures, enable laboratory-based epidemiological studies to be carried out, linking abnormalities in the tissue to disease aetiology, prognosis and treatment responsiveness. Moreover, storage over time enables laboratory findings to be correlated with disease progression and patient response to treatment, as well as enabling as-yet undiscovered techniques to be applied in the future to previously collected samples. Evolving laboratory techniques such as tissue microarrays, laser capture microscopy and adaptations of mass spectrometry, together with new information technology tools, give tissue banking research its power.

Until recently consent to tissue banking was obtained (if at all) in a blanket fashion that permitted researchers to carry out unspecified research on tissue left over after necessary diagnostic tests were completed. It was also thought to be acceptable to access tissue archives for research, even if consent to research had not been obtained at the time of collection. 3, 4

Recent scandals surrounding the non-consensual retention of organs at post-mortem examinations in the United Kingdom (e.g. Alder Hey, Bristol)5 and Australia (e.g. Glebe),6 along

with the emergence of increasing concerns about information—particularly genetic—privacy,3 have led to a number of inquiries that have, in turn, led to amendments in human tissue and privacy legislation. Although areas of uncertainty remain (particularly in relation to accessing archival tissues and obtaining consent to unspecified future research), these amendments have generally resulted in ever-more stringent consent requirements such that it is no longer acceptable to assume the probity of blanket (open-ended) consent to research or the acceptability of accessing tissue archives without recontacting the original donors.

Although increasingly stringent consent requirements often satisfy those who are concerned about research subject autonomy,7 human rights8-9 and respect for persons,10 these requirements might create an untenable workload and reduce sample sizes—a concern that has been prominently aired in the bioethical and biomedical literature. 2, 3, 11-18 Far less attention has been paid to the possibility that standard models of consent, although appropriate for clinical trials, might be simply inappropriate for laboratory-based epidemiological research that uses tissue banks.

Practical challenges of obtaining valid consent to tissue banking research

According to the National Health and Medical Research Council's *National Statement on Ethical Conduct in Research Involving Humans,* two important criteria need to be met for consent to be ethically and legally valid:

(1) Participants need to be provided, at their level of comprehension, with information about the purpose, methods, demands, risks, inconveniences, discomforts, and possible outcomes of the research (including the likelihood and form of publication of research results) and

(2) The exercise of a voluntary choice to participate.4

These criteria are difficult to meet in any research context but are particularly difficult to achieve when obtaining consent to tissue banking research.

In particular, it is frequently impossible to satisfy these criteria when carrying out research using tissue archives that contain samples collected over many years. In many cases, consent to research has been obtained, if at all, in a “blanket” fashion, such that donors were not informed of the potential for future uses of their tissue. In addition, although donors should ideally be recontacted regarding further research using their tissues, researchers have often noted that this is practically difficult and often impossible because many will have died or moved, and it is potentially harmful to remind people of previous illnesses.

Laying aside the problems with archival material and supposing that only prospectively collected tissue samples are used, there are still many challenges to meeting the criteria for valid consent. First, participants cannot be provided with comprehensive *information about the purpose* of research because this is often not known at the time of collection. Although information about the purpose and nature of research is relatively easy to give in time-limited and well-defined clinical trials, tissue banking research is often not time-limited and the purposes of future research projects cannot always be predicted at the time of collection and original consent. Consent that is completely open-ended may not be acceptable to patients who would not want their tissue to be used for certain types of research. People may object to participating in projects with particular aims. Some people may, for example, object to participating in research that is aimed at developing diagnostic or prognostic tests for conditions for which there is no treatment. Others may object to research with potentially stigmatizing outcomes, such as research linking ethnicity to behavioural characteristics. People may also object to participating in projects in which researchers aim to make financial profits.

Second, participants cannot be provided with *information about the demands, risks, inconveniences or discomforts* of the research because, like the purpose of the research, these are often not known at the time of tissue donation. In clinical trials, risks (both physical and psychological) are usually more easily predictable on the basis of information gained from earlier phases of research (e.g. toxicological studies) and participants are generally closely monitored for the development of adverse effects. The risks associated with tissue banking research relate primarily to the potential for unauthorized disclosure of health (especially genetic) information to third parties, leading to potential stigma or discrimination.2 In addition, tissue banking research, like clinical research, may reveal health information about participants, their families or communities that they themselves may not wish to know. Aside from issues of privacy, such information may have reproductive or therapeutic implications.

Third, participants cannot be provided with meaningful *information about the possible benefits* of the research because these are not known. The possible benefits associated with the knowledge gained from a randomized controlled trial (even one with a negative result) are relatively easy to articulate to patients—although even here there is evidence that patients fail to grasp the notion that it is not the goal of a clinical trial to be of direct benefit to participants.19 It is far more difficult to articulate the likely outcomes of tissue banking research. There is, for example, an ongoing debate about the strength of the link between physical (tissue) abnormalities—particularly involving genes—and the cause/behaviour of disease.20 At a more technical level, there are concerns that typical molecular epidemiological techniques fail to capture important molecular information that may be contained in what has mistakenly been categorized as "junk DNA"21 or in inherited non-genetic (epigenetic) systems.22 Moreover, the methods of tissue banking research are highly technical and not necessarily accessible to tissue donors or even to clinicians who are often charged with both procuring tissue and obtaining consent for its use in research.

Fourth, tissue banking research raises difficulties not only with the provision of information but also with the voluntariness of research participation. For research to be voluntary, participants must be free to refuse to take part in research altogether and must also be free at any time to withdraw consent to further involvement in the research. Patients are often ill and frightened at the time of tissue collection for diagnostic or therapeutic purposes. It may, therefore, be difficult for them to understand the issues at stake, and they may be reluctant to refuse their clinician's request that they participate in research. Withdrawal from research is a challenge even in clinical trials because patients may discontinue the experimental therapy but cannot necessarily have their clinical data withdrawn from the study database. This is a particular problem in the tissue banking setting because it is not always the case that samples (or associated data) can or should be removed at a participant's request.10 This needs to be made clear on consent forms but, as discussed above, tissue banking research is open-ended, and it would be difficult to ensure that donors are truly willing to waive the right to withdraw.

Possible approaches to obtaining consent to tissue banking research

There is an extensive debate in the bioethical2, 7, 8, 11-18 and law reform literature3 about the way in which consent to tissue banking should be obtained. Three models are commonly proposed. The first model, which prioritizes individual autonomy and human rights over scientific progress, permits the use of archival materials only when the original donors can be recontacted and requires that individual donors be recontacted to provide consent for each new project. The second model allows consent to be (at least partially) open-ended and allows archival tissues to be used even if the original donors cannot be contacted. A "middle ground" approach uses consent models in which participants are given the opportunity to decide under

what circumstances they would like to be recontacted or whether they are willing to give open-ended consent.

There is, however, a fourth, more radical, approach that examines the ideological assumptions underpinning all of the standard models of consent. This approach uses the insights of communitarian and feminist scholars who privilege different values, have different interpretations of the criteria for valid consent and, therefore, endorse fundamentally different models of consent.

Both feminist and communitarian scholars have recognised that the standard model of consent is highly individualistic, reflecting western liberal value systems. Communitarian scholars have argued that such models of consent may lead to a lack of social cohesion,23-24 inappropriate de-emphasis of the 'common good',25 threats to identity and social roles25-26 and moral relativism.25-26 Feminist scholars have challenged the notion that maximizing 'rationalistic, atomistic and individualistic'27 autonomy should be the primary goal of human interaction. Instead, many feminist theories tend to emphasize the importance of care, relationships, altruism and shared responsibility.27

An alternative model of consent which draws shared insights from communitarian and feminist theories may therefore look very different and provide a means for reframing processes for obtaining consent to tissue banking. This model would require extensive involvement of communities in (1) setting research priorities, (2) determining procedures for obtaining consent (including the possibility of proxy consent being given by community representatives) and (3) determining the ways in which the results and products of research will be disseminated. This would entail ongoing contact between researchers and communities28 in a relationship that encourages trust and aims for mutual benefit.29-30

Application of an enriched consent model to tissue banking research

The failure of standard approaches to consent to tissue banking research demands consideration of alternative models of consent. This is not only because standard consent procedures "fail" in the tissue banking context or because regulation is currently ambiguous and potentially open to interpretation but also because tissue banks are, by definition, collections of materials from communities, be they disease communities, geographical communities or ethnic communities. Tissue banking research is thus the perfect exemplar of research that could benefit from community involvement at all stages of the research endeavour.

One could envisage a situation in which communities are directly involved in setting research priorities for and administering a local tissue bank. In its most extreme form, such a model might allow for communities to 'own' their tissue bank, with researchers and ethics committees acting more as consultants than as decision-makers.

Despite the de-emphasis of the individual as the sole decision-maker, such models would not be incompatible with western liberal values. Indeed, by involving communities at all stages of the research endeavour in a contextually sensitive and ongoing manner, participant autonomy—albeit indirect—may be respected even more than it is in standard models of consent. In addition, community-based processes may enhance the quality of consent by focusing on the values that underpin the rationale for consent and may ensure that scientific progress will not be stalled by the arguably impossible task of individually informing all research participants of all research projects.

This model may also be relevant to other forms of epidemiological research, that is any kind of research in which information is collected and stored for long periods of time in the form of

medical records (paper or electronic) and computer databases (genetic or non-genetic). Community engagement could also be considered in relation to clinical trials which, at present, are evaluated, authorized and discontinued only on the basis of decisions made by human research ethics committees.

Streamlining of these research ethics processes might have the added benefit of simplifying regulation, which is currently extremely complex, requiring tissue bankers (in New South Wales) to be cognizant of:

- the common law relating to assault and confidentiality;
- legislation such as the *Privacy Act 1988* (Cwlth); the Privacy and *Personal Information Act 1998* (NSW); the *Health Records and Information Privacy Act 2004* (NSW); and the *Human Tissue Act 1983* (NSW);
- National guidelines such as the NHMRC's National Statement on the Ethical Conduct of Research Involving Humans;
- organizational policies such as the Royal College of Pathologists of Australia (RCPA) policy statement on the secondary use of human tissue samples collected for diagnostic purposes, the 'Guidelines for Human DNA Banking' from the Human Genetics Society of Australasia and the National Pathology Accreditation Advisory Council 'Guidelines for the Retention of Laboratory and Diagnostic Material';
- New South Wales Health Department policies such as the 'Information Privacy Code of Practice' and 'Requirements of the *Human Tissue Act 1983* in Relation to Research Utilising Human Tissue: Guidance for Human Research Ethics Committees'.

There is no doubt that this model would pose its own practical and ethical challenges. Its implementation would be resource-intensive (as consent procedures typically are) and it would raise issues such as dissent within communities. This does not mean that efforts to change consent procedures would be futile. Rather, changes would need to be resourced adequately and planned carefully. At the very least, minimum standards for community engagement could be established, and efforts could be focused on communities for whom involvement is most important and with whom community engagement is most likely (e.g. parents of children whose organs have been removed during autopsies).

From a philosophical perspective, communitarian ethics would not, and should not, simply override libertarian values and practices. But a community-based model could better account for the ways in which individuals exist within communities and the social contexts in which people make decisions about their health and their bodies.

Conclusion: an attempt to reconceptualise tissue banking consent is warranted

Given the fundamental ethical and sociocultural issues that arise where standard models of consent are applied to tissue banking, there is reason to consider a different approach to tissue banking consent. Such approaches could generate a process that both satisfies the criteria for valid consent (albeit interpreted somewhat differently) and also engage with a wide range of broadly shared community values.

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