
An empirical study of tissue banking in Australia: Navigating regulatory and ethical challenges

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Collections of tumour samples can be an invaluable resource for medical research. There are, however, numerous ethical and legal challenges associated with tumour banking. While there has been extensive discussion of these issues in the legal and ethical literature, there are few available empirical data in relation to the activities of tumour banks in Australia, their practices around ethically charged issues, and their success in implementing complex regulatory guidelines. The aim of this study was to gain more information about the activities of tumour banks in New South Wales, Australia, with a particular focus on their management of, and attitudes towards, ethical and regulatory issues. A survey of 27 tumour collection and research facilities was conducted using a 55-item questionnaire. There is significant heterogeneity of research methodologies as well as of methods for gaining consent and ensuring donor privacy, and there is general concern among the research community about ethical and regulatory issues related to tumour banking. Heterogeneity of practice and uncertainty about ethical and regulatory requirements is problematic in its potential to hinder research and its potential to generate the space for unethical practice, whether intentional or unintentional. There is a pressing need to address these issues so that tumour banks can be used in the most ethical and efficient way possible.

INTRODUCTION

Collections of stored tumour samples removed during diagnostic or therapeutic procedures are an invaluable resource for medical research. These collections or “tumour banks” are particularly valuable for molecular, genetic and immunopathological investigation of the aetiology, prognosis and management of cancer.¹ Molecular techniques involving tissue micro-arrays, laser capture microscopy and adaptations of mass spectrometry, together with new information technology tools, have the potential to shed light on tumour aetiology, classification (in relation to other neoplasms), and

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¹ Australian Law Reform Commission, *Essentially Yours: The Protection of Human Genetic Information in Australia, Report 96* (Commonwealth of Australia, Canberra, 2003); Oosterhuis J, Coebergh J and Veen EV, “Tumour Banks: Well-guarded Treasures in the Interest of Patients” (2003) 3 (1) *Nature Reviews Cancer* 73.

treatment responsiveness. Whilst the above techniques can be applied to single samples, tissue banking of specimens greatly enhances the power of translational research. The banking of numerous samples enables epidemiologically sound correlations to be made. Moreover, storage over time enables laboratory findings to be correlated with tumour progression and patient responses, as well as enabling as yet undiscovered techniques to be applied to samples collected today.

The collection, storage and use of tissue for research presents a number of technical, ethical and regulatory challenges. While it is important to facilitate the progress of research, it is also important to protect the interests of tissue donors and of the communities of which they are a part. This may require that the tissue is used only with the donor's consent and only for research that is acceptable to them.² In addition, it may also be necessary to protect donor privacy,³ particularly as advances in genomic research allow greater insight into a donor's present and future health risks as well as the health status of the donor's family and community. Protection of donor interests in these ways not only satisfies contemporary ethical and legal standards but encourages public trust in the research process and can be an important element of ongoing public commitment to research efforts, and willingness to donate tissue. The fragility of public trust in the research endeavour, and in research involving retained tissue, in particular, has been highlighted by the impact of recent national and international "tissue retention scandals".⁴

While few would argue against the need for regulation of research involving human tissue, the increased public scrutiny of tissue research practices, along with more stringent personal privacy and human tissue legislation, have created an increasingly complex network of regulations around tissue banking. For example, tumour banks in New South Wales must comply with numerous legislative and regulatory requirements, including the following:

- the common law relating to assault and confidentiality;
- *Privacy Act 1988* (Cth);
- *Privacy and Personal Information Act 1998* (NSW);
- *Health Records and Information Privacy Act 2004* (NSW);
- *Human Tissue Act 1983* (NSW);
- National Health and Medical Research Council's *National Statement on the Ethical Conduct of Research Involving Humans*;
- Royal College of Pathologists of Australia (RCPA) policy statement on the secondary use of human tissue samples collected for diagnostic purposes;
- National Health and Medical Research Council, *Guidelines for Genetic Registers and Associated Genetic Material*;
- Human Genetics Society of Australasia, *Guidelines for Human DNA Banking*;
- NSW Health, *Information Privacy Code of Practice*;
- Human Genetics Society of Australasia and Royal Australasian College of Physicians, *Policy Statement on the Retention, Storage and Use of Sample Cards from Newborn Screening Programs*;
- NSW Health, *Requirements of the Human Tissue Act 1983 in Relation to Research Utilising Human Tissue: Guidance for Human Research Ethics Committees*; and

² Ashcroft R, "The Ethics of Reusing Archived Tissue for Research" (2000) 26 (5) *Neuropathology and Applied Neurobiology* 408; Van Diest P, "No Consent Should be Needed for Using Leftover Body Material for Scientific Purposes. For" (2002) 325 *BMJ* 648; Salvulescu J, "No Consent Should be Needed for Using Leftover Body Material for Scientific Purposes. Against" (2002) 325 *BMJ* 648.

³ Gaze B, "Privacy and Research Involving Humans" (2003) 10 *JLM* 410; Caulfield T, "Tissue Banking, Patient Rights and Confidentiality: Tensions in Law and Policy" (2004) 23 *Medicine and Law* 39; Korn D, "Dangerous Intersections: New Proposals to Protect Genetic Privacy May Collide With the Public Interest in Fostering Medical Research" (1996) 13 *Issues in Science and Technology* 55.

⁴ Trouet C, "New European Guidelines for the Use of Stored Human Biological Materials in Biomedical Research" (2004) 30 *Journal of Medical Ethics* 99.

- National Pathology Accreditation Advisory Council, *Guidelines for the Retention of Laboratory and Diagnostic Material*.⁵

The concern that many researchers have is that this regulatory complexity may adversely impact upon the progress of cancer research in Australia. At present, however, there are few empirical data about the impact of the regulatory environment on tumour banking research. Furthermore, there is little information about how scientists and administrators perceive and address the ethical and legal challenges associated with tumour banking. This aim of this study was to provide an overview of tumour banking research in New South Wales and to describe the practical, ethical and regulatory concerns expressed by researchers.

PARTICIPANTS AND METHODS

There is currently no comprehensive registry of tissue banks in Australia. Consequently, the authors compiled a list of tumour banks through internet searches, from existing lists of tissue banking facilities collated by previous Australian researchers, through listings of identifiable health services' tumour banks, through listings of the Australasian Biospecimens Network membership, and through snowball sampling. Twenty-seven appropriate tumour banks were identified. While the intention was to develop as comprehensive a list of tumour banks as possible, in the absence of an existing register of tumour banks it is likely that some banks may have been inadvertently excluded from the sample. Nonetheless, it is the authors' belief that this list is representative of the range of research institutions involved in tumour collection and research, including public research institutions, cancer institutes, pathology laboratories and private research institutions.

A 55-item survey tool was developed by the research team at the Centre for Values Ethics and the Law in Medicine (CVELIM). This was based on a taxonomy of tumour banking activities developed previously at the Centre.⁶ The survey included questions about demographics, research activities, data storage and donor privacy, consent procedures, administrative and regulatory processes, funding, and the difficulties that researchers reported in relation to meeting ethical and regulatory standards. The survey instrument was developed in consultation with tumour bank researchers to ensure coherence, content validity and scope, and was piloted with representative stakeholders to clarify format, wording and face validity.

The self-response surveys were mailed in July 2005 to 27 research groups known to be involved in cancer research and to have tumour sample collections. Surveys were addressed to senior members of the research organisation who were likely to have an understanding of both the scientific and managerial aspects of tumour bank practice. A follow-up survey was mailed to non-responders one month later and follow-up reminder calls were made, where necessary. A total of 17 responses were received, representing a response rate of 63%.

RESULTS

Tumour bank demographics and activities

All groups surveyed use their tumour sample collections for research. Additionally, 12% of respondents used their collections for educational purposes. No respondents reported using their collections for development of commercial products, and no respondents reported being involved in non-medical testing (eg law enforcement, insurance).

All of the tumour research collections were established post-1983. Half were established since 1998, and more than a third were established in the last two years.

There was a wide range in the size of collections, from those with less than 10 samples to those with up to 20,000 samples. The median number of samples was 350. There was also a wide range in the rate of collection, with one bank collecting about 2,000 samples a year. The average collection rate was 111 samples per year.

⁵ See Lipworth W, "Navigating Tissue Banking Regulation: Conceptual Frameworks for Researchers, Administrators, Regulators and Policy-makers" (2005) 13 JLM 245 at 247-248.

⁶ Lipworth, n 5.

A variety of tissue types were collected, including adrenal gland, bladder, bone, breast, brain, cervix, colorectal, endometrium, fallopian tube, glioma, head and neck, kidney, leukaemia, liver, lymphomas, ovary, pancreas, prostate, pituitary, skin, testes and thyroid. The most commonly reported type of tumour samples were leukaemia and breast, brain, colorectal and ovarian cancers. A total of 47% of respondents collected tissue samples of diseases other than cancer in addition to tumour samples and 88% of respondents collected normal (non-pathological) tissue. Most commonly, this normal tissue consisted of blood samples or non-pathological correlates of tumours of interest (eg normal breast for breast cancer studies).

Research activities

A range of different types of research were conducted using the banked samples. A total of 82% of respondents conducted research into the aetiology of cancer, 53% into diagnostic methods and tools, 41% into treatments, and 18% into normal biology and physiology. The majority of this research used molecular, proteomic and cytogenetic techniques, with histopathological and immunophenotypic research methods being utilised less often.

A total of 65% of respondents reported performing genetic/genomic studies using their banked samples. These included:

- linkage studies, to identify the gene sequences associated with inherited diseases (n=12%);
- association studies, to find correlations between a disease and a genetic change where there is no obvious pattern of inheritance (n=47%);
- genetic epidemiology studies, to identify the interaction between genes and environment (n=12%); and
- pharmacogenetic studies, to determine if there is a genetic basis for responsiveness to drugs or to adverse drug reactions (n=24%).

Privacy and data storage

All tumour banks surveyed had mechanisms in place to protect data privacy. The vast majority of research facilities de-identified tumour samples with 82% retaining a coded link between the sample and the donor, making re-identification possible. A small number (6%) of facilities did not de-identify or anonymise tumour samples at any point.

A total of 65% of respondents said that their bank linked samples to a health record database to track donor patient outcomes. Third-party access to written and/or computer records relating to samples was reported by 18% of respondents, although in no case did third parties include insurance companies, law enforcement groups or financial sponsors.

Research groups reported collecting the following information about samples and/or donors:

- demographic information (77%);
- diagnostic information (71%);
- exposure and lifestyle information (24%);
- family history data (41%);
- histopathological data (65%);
- recurrence data (59%);
- research results (47%);
- genetic profile (eg genomic information) (41%); and
- treatment data (53%).

Consent

In relation to current practice, all respondents reported obtaining consent for the collection, storage and research use of samples. However, 47% of respondents reported that there were samples in their collections that had been collected in the past without consent being obtained for research purposes (eg in archival collections).

Respondents were asked to identify what model of consent was commonly used in their facility. They were asked indicate which of the following models of consent they used:

- blanket consent, where a donor gives consent for the use of their tissue sample for research in general, ie the exact research uses are unspecified, and it is therefore generally understood that the consent allows for the use of the sample in almost any type of research at the discretion of the tissue bank;
- project-specific consent, where a donor gives consent for the use of their tissue sample for a single specific research project, ie for investigating a specified research question at a specified research facility; or
- categorical consent, where a donor gives consent for the use of their tissue sample in a specific category of research, eg the donor may give consent to research into a particular disease, or research for a particular treatment, or research by a particular group, but not to research in general and not only to a single specified project.

Table 1 lists the types of consent given.

TABLE 1 Types of consent given

Type of consent	Percentage of respondents
Blanket consent only	47%
Project-specific consent only	24%
Categorical consent only	29%
Donors have the opportunity to decide whether they would like to give blanket consent, project-specific consent or categorical consent	6%

Over 70% of respondents reported that their donors are not given the opportunity to specify whether they would like to be recontacted in future, should the tumour bank wish to obtain further consent for new projects.

A total of 59% of respondents reported that their donors are informed of how long samples will be stored. Only 29% of respondents said donors are informed of who owns the sample once it is donated. Less than half (47%) of respondents reported that donors are given an indication of whether or not they will receive a portion of profits should research lead to a commercial product. A total of 88% of respondents reported that their donors are given information about the likelihood, or lack thereof, of direct benefits from involvement in research, while 82% of respondents said donors are given information on the potential risks associated with donation (eg possibility of breach of confidentiality). A total of 82% indicated that donors are informed that samples might be used in genetic research.

Respondents reported using a number of different approaches for dealing with situations where researchers sought access to samples where consent for future research had not explicitly been obtained from the donor. These include:

- recontacting the donor and obtaining consent for the research project under consideration (35%);
- presuming consent (24%); and
- seeking consent from a third party (18%).

In cases where consent was gained from a third party, this was most often from a close relative (47%) or from an institutional research ethics committee (24%). No respondents reported obtaining third-party consent from a community representative. The most common reason for seeking consent from a third party was:

- the donor was deceased (29%);
- the donor could not be located or contacted (18%);
- the donor was a minor (12%); and
- the donor was judged to be too ill to give consent (6%).

A total of 24% of banks reported not using samples for research purposes unless consent to future research had been explicitly obtained at the time of tissue donation.

Disposal and ownership

In relation to perceived ownership of tissue samples, 77% of respondents stated that tissue samples were the property of the tumour bank or the hospital while 12% reported that the samples were owned by the donor. In no case did respondents believe that samples were owned by financial sponsors of research.

Respondents reported a number of different approaches to the disposal and return of tissue samples:

- 41% reported that samples were discarded or destroyed following the completion of research;
- 6% of samples were retained in long-term storage;
- 6% were returned to diagnostic pathology services; and
- 35% had no specified management plan for the return or disposal of tissue samples.

No respondents reported returning samples to donors.

Disposal/return most commonly occurred when there was no longer sufficient tissue to carry out further research (53%) or when the research project was completed (12%).

Ethical oversight of research involving banked specimens

All respondents reported that research done within their institution using tumour samples was subject to the approval of the relevant Human Research Ethics Committee (HREC).

In the majority of cases, samples were accessible to researchers from other institutions (n=71%). Where researchers from external institutions sought access to samples for research, in all cases respondents indicated that this research had to be approved by a HREC, either at the institution where the bank was located (n=6%), at the external researcher's institution (n=41%), at either institution (n=12%) or at both institutions (n=41%).

Administration and community participation

Tumour banks had a range of administrative structures and frequently were linked to multiple institutions including universities and hospitals:

- 94% of tumour banks reported were located within a larger research institution;
- 35% were linked to a hospital or health service; and
- 41% were linked to a university.

No respondents reported being part of a commercial/private enterprise.

A total of 65% of respondents had an advisory committee. The composition of advisory committees included researchers (59%), clinicians (59%), lawyers (12%), and community representatives (12%). No advisory boards included ethicists.

A total of 41% of tumour banks had a process for community participation (eg feedback to donors about the research activities of the bank). The most common forms of communication with the "community" were newsletters and websites, while 18% of banks had in place processes whereby community representatives could provide input into the direction or mission of the tumour bank, including having advocacy or consumer group representation on the advisory board.

Funding

The vast majority of tumour banks reported receiving funding from federal (53%) or State (41%) government grants. Other sources of funding included hospital funds (47%), university grants (29%), and less often cancer foundations, benevolent foundations, trust funds and philanthropic donations. No funding support was received by 6% of respondents.

Attitudes towards regulation

A total of 71% of respondents felt that there is an appropriate amount of ethical oversight of tumour banking practice. The remainder felt that there was too much ethical oversight of tumour banking practice and no respondents felt that there was insufficient regulation.

A total of 59% of respondents felt that ethical oversight of tumour banking practice is sufficiently informed, while 71% reported that in their experience, HRECs varied in their interpretation of ethical and/or legal requirements around gaining consent for research involving tumour bank samples.

Tumour banks used a variety of sources for advice on how to navigate tumour banking regulatory obligations. Most commonly accessed sources were:

- HRECs (94%);
- the research community (59%);
- advisory boards to tumour banks (53%); and
- the National Health and Medical Research Council (NHMRC) (59%).

Other sources included administration research offices, the Australasian Biospecimens Network, lawyers, the Department of Health Ethics Branch, and the Australian Health Ethics Committee (AHEC).

When asked what they believe would be most helpful in facilitating tumour bank research, the most common suggestions were:

- simplification of legislation governing tumour banking (71%);
- increased provision of funding to tumour banks (82%); and
- establishment of a centralised ethics committee for consideration of research involving tumour banks (71%).

A total of 53% advocated the provision of more information, education and guidance on regulatory requirements from bodies such as AHEC and NHMRC, while 29% supported consolidation of samples within larger banks or facilities and 29% advocated the establishment of professional advisory boards to provide guidance on processes for administration of tumour banks. Some respondents advocated greater cooperation between tumour banks.

DISCUSSION

This study confirms that tumour banking is extensively practised in New South Wales and that there has been an exponential growth of tumour banking in the last 10 years. These banks collect a range of tissues and perform important research into aetiology, diagnosis, prognosis and management of cancer using a number of established and emerging methodologies. There is, however, significant variation in the administration of tumour bank research and it appears that there is ongoing uncertainty regarding the processes necessary to meet ethical and legal requirements for appropriate conduct of research.

This research is valuable because it provides the first detailed, descriptive, account of tumour bank activity in New South Wales. The high response rate and self-report nature of the survey suggest that the results are likely to provide an accurate insight into research using stored tissues. There are, however, a number of limitations to this research. First, since this study used a self-report instrument, this research is open to the possibility of social desirability bias and interpretive error. Second, the generalisability of the data is open to contest as the sample was limited to New South Wales and it is possible that some tumour banks were inadvertently excluded due to the absence of a comprehensive register of research facilities. Finally, as this research reports only the results of a survey, it cannot adequately capture the complexity of the ethical and legal issues surrounding consent, privacy, community participation and appropriateness of regulation. This would require the use of qualitative methodologies such as in-depth interviews or focus groups. This is the focus of ongoing research.

It is reassuring to note that all tumour banks seek consent for storage and use of samples in research. There is, however, significant heterogeneity in consent processes, suggesting that there may be a need for clearer guidance as to which consent processes are most appropriate in a range of situations. While the lack of consistency regarding consent methods is not necessarily a problem, it is of some concern that a large number of donors do not appear to be informed about the ownership of samples, the commercial utilisation of samples, the retention and disposal of samples, and the risks associated with the research, particularly related to potential breaches of confidentiality. This is particularly important given that 82% of tumour banks have processes whereby samples could conceivably be re-identified. It is worth noting, however, that the results of the research suggest that the risks associated with donating tumour samples for research are likely to be small because samples

are almost always de-identified (coded), no banks provide access to third parties who do not have a direct research interest and, in all cases, access to samples for research purposes is overseen by research ethics committees.

While all tumour banks reported an administrative structure that involved scientific and advisory groups, few banks provide opportunity for community involvement and participation. Also, many banks do not have processes for communicating with donors, communities of donors and the wider community. Given the fragility of public trust in science and medical research, the authors believe that the lack of serious attention paid to community participation and the failure to establish adequate processes for providing information represent serious failures in the current organisation of tumour banking research and offer real opportunities for improvement.

In general, respondents to this survey indicated that they felt that there was an appropriate amount of ethical oversight of tumour banking. While this suggests that researchers recognise the need for ethical and legal oversight, there are concerns about regulatory processes. The present results suggest that regulation of tumour banking research may be improved and made less burdensome by the provision of simple, clear and uniform guidance regarding ethical and legal requirements and through consideration of means to simplify and streamline existing privacy and human tissue legislation. The results also suggest that there may be significant support for specific measures, such as the establishment of centralised ethics committees for the consideration of tumour banking research.

CONCLUSION

It is apparent that there is ongoing uncertainty regarding the appropriate processes by which tumour banks should be established and administered. This is highly problematic for researchers, donors, administrators and sponsors as it has the potential to hinder research, entrench unethical practice and thus threaten the entire cancer research endeavour. There is a pressing need to clarify the ethical and regulatory issues surrounding tumour banking and to place tumour banks within a broader research and social context. Tumour banking research does not occur in isolation either from health care or from other types of medical research, and as such all members of the community have an interest in its conduct and outcomes.

It is widely anticipated that the recently established Human Genetics Advisory Committee (HGAC), which has been formed to advise government on the social, ethical and legal implications of human genetic and related technologies, will review the processes of tissue banking, particularly those related to consent.⁷ It is the authors' hope that the HGAC will also consider some of the other issues raised by tumour banking research, particularly the means by which communities can engage in both determining the direction of research and in the construction of policies regarding its conduct and organisation.

⁷ See NHMRC website brief on the Human Genetics Advisory Committee: <http://www.nhmrc.gov.au> viewed 1 May 2006.