RESEARCH ETHICS

Consent gained from patients after breast surgery for the use of surplus tissue in research: an exploration

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Objectives: (1) To investigate the quality of consent gained for the use in research of tissue that is surplus after surgery. (2) To compare the use of two consent forms: a simple locally introduced form and a more complex centrally instigated form. (3) To discuss the attitudes of patients towards the use of their surplus tissue in research.
Design: Data were collected through interviews and analysed with a combination of quantitative and qualitative analytical techniques.
Participants and setting: Patients of the breast care unit at a teaching hospital were interviewed at home or in a quiet room at the hospital.
Results: 57 people were interviewed out of 81 approached, between October 2003 and March 2004. Most participants had a poor level of knowledge about the consent they had given, but reported being happy about having given it. The patients who had signed the locally introduced form had considerably more knowledge than those who had signed the centrally instigated form ($z = -2.56$; $p < 0.05$). Participants considered being well informed to be less important than believing that their opinions were valued and respected.
Conclusions: The findings suggest that traditional models of informed consent are not universally applicable and, in this case, seem to overstate what people wish to know. The simple consent form achieved a better quality of informed consent and provided a better model of practice than the complex form, and it seemed that a focused approach to consent seeking is more effective and acceptable than more complex approaches.

This study deals with human tissue that has been removed for diagnostic or therapeutic purposes, and is considered surplus after such procedures. This resource was considered a waste product and hence was retained, stored and used, often for several research, quality control and teaching purposes without patients' consent.[1] The Human Tissue Bill,[2] published for consultation in 2003, before the Human Tissue Act[3] was passed in 2004, suggested that any use of this tissue without the ''appropriate consent'' of the patient from whom it was taken should be a criminal offence, although what was meant by appropriate consent was not specified. The Human Tissue Act[3] reversed this requirement, stating that this tissue could legitimately be used without consent for quality control and teaching purposes and for research so long as the research has been ethically approved, or the tissue anonymised.

Before the introduction of the bill, but after the Alder Hey Inquiry,[4] the Breast Cancer Research Group, St James' Hospital (SJUH), Leeds, UK, in consultation with patients and other interested groups, introduced a locally designed consent form. This was a simple A4 sheet, which was given to patients as early as possible, preoperatively. It requested consent for the retention and use of any tissue removed during surgery that was not required for diagnostic or other medical reasons. Signing of this form indicated that consent had been given. The Department of Health introduced a new surgical generic consent form to be used nationally, 18 months after the introduction of this consent-seeking procedure. This new, more detailed and complex A3 form was modified locally to include a section requesting consent for the retention and use of surplus tissue. With this form no specific signature was required for the consent for tissue retention; instead, a box was ticked at the same time and on the same form that was signed to give consent for the surgical procedure. This generic consent form superseded the locally developed one (copies of both are available from the authors on request).

The local research ethics committee at SJUH commissioned the current piece of research, against the backdrop of the suggested restrictions of the Human Tissue Bill, with the aims of investigating the quality of the consent gained, of comparing the two forms and of investigating attitudes and views of patients on this issue.

METHOD

Design

This was a descriptive study of the knowledge and attitudes of patients whose consent to tissue retention had been sought using one of two different consent forms. The study protocol was subject to peer review as well as local research ethics committee approval. Data were collected through interview, and analysed with a combination of quantitative and qualitative techniques.

This study required some measure of participants' knowledge of the consent; however, despite the Human Tissue Bill[2] having stipulated that ''fully informed consent'' should be sought, no clear criteria were given for what constitutes ''fully informed consent''. Medical Research Council (MRC) recommendations[5] predating the Bill (box 1) provided some basic requirements; however, it was considered that the bill seemed to go further than these. Therefore, it was considered important to be able to elicit knowledge scores, which helped to describe and compare the levels of knowledge in individual participants, but it was not considered possible to set ''pass'' or ''fail'' levels with respect to this. Sixteen items of knowledge that participants might have known were identified from three sources: MRC recommendations (box 1),[5] a patient information sheet created by staff at SJUH, and other facts mentioned by participants but

Abbreviations: DCIS, ductal carcinoma in situ; MRC, Medical Research Council; SJUH, St James' Hospital

Box 1 MRC recommendations on the consent required for the use of surplus tissue[5]

''At the very least patients should be made aware in any surgical consent form that they sign that surplus material may be used for research, and be given the opportunity to refuse.''

not covered by either of these previous sources. Table 1 lists these items of knowledge with their respective sources.

The interview was conducted in two parts. The first part was structured, and consisted of questions probing factual knowledge about the consent, as well as questions aimed at assessing the attitudes of participants towards the consent. The second part was designed to be less structured, to enable participants to explain in more detail their thoughts about the consent and the process by which it was sought. Between these two parts of the interview, participants were asked to reread an SJUH-designed information sheet used in conjunction with the consenting process, describing the ways in which their breast tissue could be used (both the interview schedule and the information sheet are available from the authors on request).

Participants

Potential participants were categorised into one of four different condition groups. Participants in three of these condition groups had undergone surgery for the removal of either an invasive cancer, a ductal carcinoma in situ (DCIS) or a benign lump, and had given their consent on one of the consent forms for the retention and use of any surplus tissue. Participants in the fourth condition group had undergone a core biopsy investigation, which had indicated no further need for treatment and so had not been subject to surgery and had not had any tissue retained. Participants from these condition groups were included, as it was thought that the different perceived levels of threat from cancer in the different groups may have had an effect on the attitudes.

Participants were recruited through SJUH into the breast care unit. Initially, potential participants were identified by selecting alternate patients of clinic lists from certain months, who belonged to the appropriate condition groups. Those who had had a recurrence of illness or those for whom there was reason to believe that re-contact may have been overly upsetting (a condition stipulated by the local research ethics committee) were excluded. In total, 88 people were initially identified and 7 were excluded (recurrence of illness ($n = 2$); death($n = 1$); and potentially upset ($n = 4$), as judged by the individual's breast care nurse). The remaining 81 people were sent information sheets about the study and were followed up over the telephone by SJUH, asking whether they would be willing to participate. If they agreed, an appointment was arranged, during which the study was further explained and written consent obtained.

Of the people approached, 60 agreed to be interviewed either in their own homes or in a quiet room at the hospital, and 57 datasets were obtained (3 interview tapes were corrupted). A breakdown of these is as follows: 28 had had invasive cancer, 8 had had DCIS, 8 had had a benign lump and 13 had undergone a core biopsy. Except for the last group, all participants had given their consent to tissue retention: 27 had signed the specific SJUH-designed form and 17 had ticked the appropriate box on the generic form. The form they had consented with depended only on the timing of their treatment. The possibility of retaining surplus tissue does not arise for patients having a core biopsy so they had not encountered either of the consent-seeking processes for tissue retention. This group, as far as was practical, was asked the same questions as the other groups in a prospective manner (eg, ''If you had had to have had surgery, would you have been happy to give your consent?'').

Analysis

The sociodemographic status of participants was found using the ACORN geodemographic classification tool.[6]

Each interview was transcribed and the two parts of the interview were analysed separately. The first part of the interview was analysed according to the descriptive coding method recommended for survey data by Moser and Kalton.[7] This included devising a coding booklet based on the literature and the aims of the study and then testing and modifying it on 12 of the transcripts. This process meant that the final codebook, which was used to score all of the transcripts, coded for the presence, or absence, of responses predicted by the researchers, as well as coding the respondents' own chosen terms of reference, unpredicted by researchers. This allowed frequencies of particular responses to be measured, which was the dependent variable used in the analysis.

In coding the knowledge scores, participants were given a point merely for mentioning or demonstrating knowledge of one of the codable facts; each participant was therefore given a score out of 16. The scoring process necessarily included interpretation of lay language, which may have been open to bias. An independent colleague, otherwise unassociated with the study, was trained in the use of the coding frame and recoded a selection of the transcripts. The two sets of assigned codes were compared and 69% agreement was found. This was considered to indicate sufficient reliability for the exploratory purposes of the study; therefore, the original codes were used. In coding, credit was given as much as possible, so any coding bias is likely to have led to an overestimation of knowledge rather than underestimation.

In addition to these knowledge scores, whether participants actually remembered giving their consent was used as a secondary measure of whether informed consent had been obtained.

The second part of the interview was analysed with the ''framework analysis'' qualitative approach,[8] chosen because it uses a matrix approach that allows themes to be developed that are grounded in the complete dataset and also allows for comparisons between cases. Framework analysis has successfully been applied to projects of a similar nature—for example, a study investigating information needs and information-seeking behaviour of patients with cancer.[9] The software NUD*IST N6[10] was used to facilitate the analysis.

RESULTS

Response rate

The overall response rate was 70% (57 participants of 81 approached). A small variation was found here for the different groups approached, with the cancer and DCIS groups having higher response rates (78% and 80%, respectively) than the benign and core biopsy groups (72% and 65%, respectively). Additionally, the response rate of those who had signed the locally produced consent form was higher than that of those who had indicated consent with the tick-box on the generic consent form (80% and 63%, respectively).

Sample demographics

The ages of participants ranged from 20 to 79 years, with the mean age being 54.7 years. The cancer group was found to be significantly older than the core biopsy group (one way analysis of variance: $F(3,56) = 9.05$; $p<0.01$ and Tukey's reanalysis test, $p<0.01$). Other than this, there were no significant differences between the mean ages of the groups. Only two participants were men.

Analysis of sociodemographic groups suggested that an even spread was achieved across the different condition and consent form groups.

Knowledge about the consent

Table 1 shows the 16 items of knowledge in rank order according to the number of participants who scored a point for each, and the sources of these items.

This shows that most participants (80%) knew that consenting would not have affected their treatment. Around half of the participants knew that the consent was something about science or research (59%), that it had to do with their tissue being used in some way (52%) and that everyone would be asked for their consent (48%). A more detailed inspection of these response patterns shows that most participants who had signed the locally produced consent form had known that the consent they had given was to do with tissue (70%) and its use in research (74%), which is in contrast with those who had signed the generic consent form, of whom only a small proportion had knowledge of these facts (24% and 35%, respectively).

The mean overall knowledge score of all the participants was 2.9 of a possible 16, with the lowest score being 0 and the highest being 7. The mean scores of those who had signed the different consent forms were 4 ($n = 27$) and 2.6 ($n = 17$). These data were found to be non-normally distributed; therefore, a Mann–Whitney non-parametric statistical test was used to compare them. This showed that the knowledge scores of the locally produced consent form group were significantly higher than the scores of the generic consent form group ($z = -2.56$; $p<0.05$).

Thirteen people (30%) initially reported not being able to remember having given consent. This was heavily weighted towards those who had consented through the tick-box on the generic form, with 65% of these having no recollection of having given their consent, compared with only 7% of those who had signed the locally produced form. This was despite the generic consent form group having given their consent more recently.

Table 1 Facts that participants could have known about the consent they had given

Point scoring fact	Participants who had knowledge of this n (%)
Consenting did not affect treatment†	35 (80)
Consent given was to do with science or research*	26 (59)
Removed tissue to be used in some way†	23 (52)
Everyone is asked‡	21 (48)
Tissue frozen or refrigerated‡	13 (30)
Research conducted could be with a microscope†	10 (23)
Stored for an indefinite time period‡	8 (18)
Research conducted may include testing new treatments†	4 (9)
Tissue used was surplus to clinical requirements*	4 (9)
Consent is about a small amount of tissue†	3 (7)
Could be used as a comparison or control in research‡	3 (7)
Research conducted could include growing cells†	3 (7)
Stored as slices†	1 (2)
Something about storage†	1 (2)
Research involved molecules†	0 (0)
Stored in a wax or paraffin block†	0 (0)

*From Medical Research Council recommendations.
†From St James Hospital information sheet.
‡From participant responses.

Attitude towards the consent

Participants in the surgical groups, all of whom had given their consent for their tissue to be retained and used, were asked whether they were happy to have done so. In response to this, all 44 (100%) stated that they were, and 43 (98%) stated that they could think of no downsides to giving their consent. Only 1 (2%) participant reported a specific use that she would object to, stating that she would not like the researchers to grow the cancerous tissue (however, after having read on the information sheet that sometimes cells are grown, she stated that she did not really mind, and that it was up to the hospital to do with it as they liked). In all, 31 (70%) stated that they could think of no uses of their tissue that they would object to and 8 (18%) stated that it should be put to a good use, but did not specify what they meant by this.

A total of 35 (80%) thought that consent should be sought, 16 (36%) thought that they would not have minded if their consent had not been sought and 4 (9%) stated that they did not think consent should be sought at all; 12 (27%) participants believed that giving their consent was of benefit to them and helped them feel better about the operation they would undergo.

Core biopsy group

Participants in the core biopsy group showed a level of knowledge about the consent equal to those who had signed the generic consent form (mean score = 2.6, $n = 13$), despite not having been through the process of having their consent sought. Overall, attitude responses from these participants were similar to those of the other groups and all but one of these participants stated that they would have been happy to have given their consent if they had had surgery.

Framework analysis results

The framework analysis led to three key themes being developed from the data: ''personal aspects''—a theme that contained comments made by the participants about their own responses and feelings towards the issue; ''process''—a theme that contained comments made by the participants about the way in which consent was sought; and ''knowledge''—a theme that contained comments about information they had been given or knew already about the issue.

Under the theme ''personal aspects'', a sense was gained that the participants viewed the experience of giving consent as secondary to their experience of the illness or the surgery they were to undergo. Therefore, for most participants, giving consent for tissue use and retention was not an issue about which they felt overly concerned. Examples of such comments were ''As I say it is a very traumatic time and well that is all I can tell you because I signed it because I just thought, I mean I don't mind them using it or care about them using it. As I say it doesn't make any difference they have got it'' and ''… I cannot imagine how anybody would be affected by it really, if it is helping somebody else then why worry.''

Under the ''process'' theme, it was highlighted that what was considered important to the participants for giving their consent was to feel valued and respected by the hospital staff—for example, ''So I had probably an understanding and I know it was the Registrar that he asked me and then he popped in at night and I think he said thank you for letting them use it'' … ''I deal with things my own way, probably not in a professional way I would deal with it at home with the family but maybe some women would prefer to feel that they are valued''. This value and respect was described as being conveyed by their general experience of the time spent and treatment received at the hospital, as well as by the way in which they were approached for their consent—for example, ''I

mean I feel that you can take it and do what you want because we have had such good treatment but there are a lot of people who are not like that''. On this issue, a number commented that it was important that they had been asked nicely, that they had been given time to think about it or that it had been emphasised that they should feel under no pressure to agree—for example, ''She made it quite clear, I wasn't pushed or rushed into anything it was a genuine question that she asked''.

Under the ''knowledge'' theme, different levels of information needs were identified. However, a large proportion of the participants stated that they only felt a need to be informed of the basic information that their tissue would be used in research—for example, ''To be honest I could have asked for more information but they literally just said it was to go for research but to be honest I was not interested. As long as they could do something with it I was not really bothered about what they did with it.'' Further, many stated that although any extra information was interesting to them, they did not consider it essential to give their consent and that too much information could actually be detrimental to the consent process rather than helpful. Finally, across both the themes of ''process'' and ''knowledge'', the timings of the consent being sought and information given were identified as being important. There were different views as to the best time, but it was generally acknowledged that the closer to the operation, the less able the person is to properly consider the issue and make a decision—for example, ''It would have been better if I had been given it a lot further in advance. I was actually given it in the hospital the night before the operation and obviously with the nature of the operation I was not in the right mind to consider it''.

DISCUSSION

Although, as stated previously, it was not possible to set ''pass'' or ''fail'' knowledge scores, it was considered that the study showed that participants from all groups had a generally low level of knowledge about the consent they had given and yet overwhelmingly seemed to have a positive attitude towards giving it. The findings of the framework analysis suggest that the consent was viewed by participants as being important, as it showed that their opinions were valued and treated with respect, but that overall most had a low level of concern for the issue and did not feel a need to know too much about it.

A comparison of the responses of the two consent form groups showed that participants who had signed the old locally produced form were significantly more informed than those who had consented through the new generic form. As the group who signed the locally produced consent form had consented longer ago than the group who signed the generic consent form, the difference in knowledge at the time of signing may actually have been much larger. Further, as the mean knowledge score for the group signing the generic consent form was the same as that of the core biopsy group, who had not been through the consenting process, it suggests that the group signing the generic consent form had not gained any knowledge through the consent-seeking process.

A question raised by these findings is whether the fact that participants had a low level of knowledge about the consent renders the consent invalid. Participants were overwhelmingly positive about having given their consent, but this in itself cannot be taken as indicating that the consent is valid. Most of those who had signed the locally produced consent form did at least seem to have fulfilled the MRC criteria as set out in box 1.[5] Although this level of knowledge would probably not be considered sufficient in a traditional understanding of informed consent—that is, for receiving a treatment—it could reasonably be argued on the basis of the current findings that this is sufficient for the type of consent necessary for the use of surplus tissue. If this is the case, then the fact that a substantial proportion of those who had consented through the generic consent form did not seem to have even this limited knowledge could be argued to indicate that the consent gained through the generic form is not always sufficiently informed to be valid. To further unpick this question of how much knowledge is required for a valid consent, further research is required to investigate public opinion.

No other studies known to the authors discuss the quality of consent gained for the retention and use of surplus tissue and, clearly, more research is needed to establish a more complete understanding of the public views about this complicated subject. Additionally, there is a considerable gap in this study, as, for ethical reasons, those who had not given consent for the use of their tissue were not contacted and interviewed and so were unable to contribute. Unfortunately, no data are available as to exactly how many patients refused their consent, although from breast care staff reports it was thought that most participants who were asked for their consent gave it. Despite these drawbacks, the following conclusions can be drawn. Firstly, the new generic consent form seems to do a poor job of gaining the type of consent that public (MRC) guidelines suggested as being minimally required for the retention and use of surplus tissue. Secondly, from the patient's point of view, giving informed consent is secondary to feeling valued and respected. This is an important finding and perhaps highlights the difference between the traditional concept of informed consent—that is, that which is required for treatment and consent for tissue retention for research. Simplistically, in consent for treatment, one of the primary reasons for informed consent is that the patient can understand and make a choice about any risks to which they are subjecting themselves, whereas in tissue use the potential risks to the patient are small, and are arguably better managed by researchers and ethics committees. Despite this, it was not that participants thought that no consent was necessary, so while the study would not support the quite extreme position suggested by the Human Tissue Bill,[2] neither would it seem to support the Human Tissue Act[3] in placing no legal requirement on consent being gained. Finally, traditional views of informed consent may overstate what people wish to know, particularly in relation to tissue use. Alongside the findings of studies dealing with consent for medical treatments, it seems that a focused approach, providing a small amount of simple information, is a more effective and acceptable approach to consent seeking, than approaches that attempt to provide patients with more complex information.

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