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Experts' attitudes towards 'targeted autopsies' using qualitative interviews in a medical network in Germany

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ABSTRACT

Objectives The behaviour of tumour metastases and the different responses to therapies are still not fully understood. The project 'targeted autopsies' of the Universities of Regensburg and Erlangen aimed to further uncover the metastatic behaviour of malignant tumours by scientifically processing different tumour samples. To initiate such a programme, the concerns of all possible stakeholders must be analysed so that the programme can be set up accordingly and the highest possible level of approval can be achieved.

Design This study investigated the basic attitude toward a targeted autopsy programme for patients with tumours and possible criteria for such a programme using qualitative interviews. Focus group discussions were held to explore the opinions and views regarding ethical aspects of various professional groups (experts) involved in this project. An interview guideline was prepared beforehand by the supervising project group. Semistructured interviews were conducted, transcribed and analysed through qualitative content analysis according to Mayring.

Setting University of Regensburg, Germany and cooperating medical partners.

Results Altogether, 15 experts were interviewed. The experts described the project as interesting and feasible. They assumed a sufficient participation rate in this autopsy programme from the population; however, they recommend giving importance to providing sufficient and professional education to all persons involved. Preserving the dignity of the donor and providing appropriate care for relatives is of great importance. Good organisation is considered imperative for the success of the project.

Conclusion Generally, experts favour the implementation of a targeted autopsy programme. However, some hurdles must be overcome. Challenges similar to those in general or rapid autopsy and organ donation programmes exist, such as donor recruitment, staffing shortages and financial constraints. People involved must be well informed before the project.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first structured qualitative interview study on the design of the proposed autopsy programme.
⇒ Despite the seemingly small number of participants (n=15), numerous insights into the topic were gained.
⇒ One of the study strengths is the very broad spectrum of disciplines involved.
⇒ The study aimed to identify relevant aspects from the experts' point of view to obtain a more comprehensive understanding of the opinions of patients and their relatives, which need to be added in a further step.

INTRODUCTION

Metastatic disease accounts for approximately 80% of cancer-related deaths.[1] Still, we fail to predict whether a potentially effective antiproliferative therapy will lead to successful tumour mass reduction in a patient with metastases.[2] Metastases from the same tumour may respond differently even within the same patient. Some may remain stable or even regress, whereas others progress simultaneously. For instance, although some metastases remain stable or even regress, others exhibit progressive behaviour at the same time point. Ongoing advances in biomedicine have improved understanding of the spread of metastases[3] and potential therapy resistance of malignant tumours and the establishment of effective treatments owing to the development of specific therapies.[4]

Such therapy optimisation requires molecular examinations on metastases, among other things.[5] Appropriate tissue samples are also required; accordingly, the model called 'targeted autopsies' was developed by project group Z02 within the framework of SFB TRR 305 (Special Research Area Transregio Regensburg–Erlangen). This project is conducted by the University of Regensburg in cooperation with the University of Erlangen and research groups. The project aims to further gain an even better understanding of the metastatic pathways and mechanisms and the different response rates of different metastases to antiproliferative tumour therapy. Targeted autopsy involves taking samples from different locations based on imaging findings to draw conclusions

about the potentially different tumour biology of the metastases. 'Targeted autopsies' bear a strong resemblance to 'rapid autopsies' established, for example, in America, Australia and Europe.[6–9] In principle, efforts are made to preserve tissue specimens from various kinds of solid tumours within a period as short as possible after a patient's death to facilitate appropriate pathological and molecular analyses. Adherence to this narrow time window after death is crucial because the quality of the samples decreases with increasing time due to autolytic processes.[10] 'Rapid autopsies', already established in other countries, reportedly have the highest ethical and moral demands, and major organisational difficulties are expected.[6 7 11 12]

To our knowledge, the 'targeted autopsy' is the first nationwide project of this kind in Germany. This study aimed to explore the basic perspectives of experts regarding a targeted autopsy programme for patients with metastatic solid tumours through a postmortem study. It also aimed to identify potential criteria for designing and implementing such a programme from organisational, communicative and ethical standpoints in Germany.

METHODS

Consent to participate

Participants were informed in detail about the objectives and specific study procedures, including recording and analysing the interviews and for the transfer of their data to IMIG Munich, the participating Institute for Market Research in healthcare, which conducted the interviews. This carried out the temporal coordination of the interviews. All participants provided written informed consent before participation. All methods were conducted in accordance with relevant guidelines and regulations.

Preparation of an interview guideline

The interdisciplinary project group, comprising scientists from pathology, oncology/haematology and palliative medicine fields, developed the interview guideline (table 1). This guide was used to conduct the interviews and was validated during multiple pretests. The guideline covered the following core aspects of the issue of 'conducting postmortem studies':

- What is your attitude towards postmortem studies, particularly when an autopsy is performed after death

Table 1 Guided interview with corresponding questions

1	**Entry questions**
1.1 1.2 1.3	How long have you been in the profession? What are your personal expectations of the discussion topic? Do you have prior experience with such studies?
2	**Discussion**
2.1	What are the ethical aspects to be considered in the project?
2.2	What moral/social aspects are important?
2.3	What are the internal requirements for conducting such a research project?
2.4	How could/should the process/organisation of such a project take place?
2.5	How are the issues of recruitment/education/inclusion viewed?
2.6	What are the hurdles and challenges (eg, timing of education, education with whom, involvement of relatives, when and how to involve relatives)?
2.7	Value of the position/handling of the subject: permission to pass on data or results of the autopsy to third parties, such as relatives, family doctor and specialist.
2.8	For all persons involved in the project: concrete procedure/checklist (?) or formula for transfer to pathology: needs of referring physicians (of patients with metastatic tumour disease).
2.9	How involved do internal/external referring physicians want to be?
2.10	What should be the content and organisation of the aftercare for relatives?
2.11	What is important, particularly in family follow-up care? Clarify cost issues, such as repatriation and funeral.
2.12	Communication processes/stages
2.12.1 2.12.2 2.12.3	Communication/phase I (before the patient is admitted to the study). Communication/phase II (after the inclusion and end-of-life situation). Communication/phase III (after the inclusion and the patient died).
3	**Closing questions**
3.1	What additional issues/procedures or requests have not yet been discussed to you?
3.2	What is your basic attitude towards the research project on postmortem studies based on targeted autopsies?
3.3	How would you personally evaluate the research project that we have talked about in detail today?

to better understand (metastatic severe) disease by a laboratory analysis?
- With an approving attitude to postmortem studies (targeted autopsies on patients with tumours), what are your requirements on this topic and what should/must be considered?

Semistructured qualitative guided interviews were conducted because these are based on open conversations. This approach created an atmosphere that allowed the interviewed persons to freely express opinions and ideas on the topic. Moreover, this method helped in achieving meaningful results for the respective target group.[13–16]

Participants

The project group invited experts from previously defined disciplines related to postmortem studies by telephone to voluntarily participate in the survey.

None of the authors actively participated in the interviews.

The questions relevant to the project were very broad, as suggested by the literature on similar projects. Therefore, participants were carefully selected from various professional groups and different settings (eg, outpatients vs. inpatients).

The experts also provided written consent to interviews. The IMIG Munich has the contact details of the experts interviewed. Data protection guidelines have been followed. As the project progressed, participants were assigned unique identification numbers (indicated in brackets below).

Data collection and analysis

In October 2022, the qualitative survey was conducted based on three focus group discussions with 4–5 participants each and (due to scheduling reasons) two individual interviews. All were conducted online through protected online video conference meetings in cooperation with the IMIG Institute. The focus group discussions and individual interviews were audio-recorded and subsequently transcribed verbatim. This was followed by an analytical evaluation of the contents according to Mayring.[16]

Patient and public involvement

None.

RESULTS

Altogether, the following 15 individuals agreed to participate in the study: 2 palliative care physicians (outpatient and inpatient), 1 inpatient palliative care nurse, 1 SAPV (Specialised outpatient palliative care) palliative care nurse, 1 inpatient hospice administrator, 2 family physicians (urban and rural), 1 patient representative spokesperson, 1 lawyer, 2 oncologists (outpatient and inpatient), 1 psycho-oncologist, 1 study coordination specialist, 1 pathologist and 1 chaplain.

The respondents' opinions were as follows.

Prior experience/expectations on targeted autopsies

Among the 15 participants, only one reported having experience with postmortem studies. The participants expressed that their expectations for 'targeted autopsies' on patients with tumours were very interesting, curious and exciting; however, they were also sceptical about its implementation, as indicated in the responses below:

> Quote: I find that this topic is quite interesting, and I thought of how do I bring it to the customer, to the patient. (Expert 6)

> Quote: …And that would certainly help in the long run. That's one of the hopes. That you can gain knowledge and of course improve therapy accordingly…. (Expert 11)

Ethical/moral/social aspects

According to the respondents, 'ethics' must be safeguarded, as in all research projects, and it holds particular importance in the present topic. In this context, 'advance care planning' was highlighted as being very important by one interview participant. The challenge of discussing the topic of postmortem tissue removal with the patient during his or her lifetime is already practised to a certain extent at other levels, such as '…at Body Worlds, for example…' (Expert 2) and is ethically justifiable.

> Quote: So ethically, if the patient consents, I have to say, so I do not find that reprehensible now. It does not cause any harm to the patient. (Expert 9)

The patients' dignity must be preserved. 'The human being or the person to be autopsied must not become an object or be objectified too much'. (Expert 15). It is considered useful '…for sick patients to familiarize themselves with the subject even before they die'. (Expert 3). For the experts, first consent by the deceased is the priority, so the relatives are relieved of this decision. Second, the postmortem interval until tissue extraction must be kept as short as possible, so that usable tissues can be obtained immediately.

Regarding society and relatives, no problems were seen, since '…the willingness of the population to be allowed to examine postmortem tissue is actually quite great…' (Expert 14) and '…especially when it comes to tumor diseases, many things are unresolved as far as forms of therapy are concerned, and they understand that immediately and are then also very quickly willing to agree to it'. (Expert 11)

Requirements for project implementation

The interviewees provided a list of prerequisites to meet for a smooth implementation of the planned research project.

A special contact person is considered particularly important for the postmortem process to ensure a problem-free process.

> Quote: …Similar to the transplant bank, they already know that if I call someone there, there's a machinery that just goes on. (Expert 11)

According to the interview panel, the 'targeted autopsies' show clear parallels to the 'rapid autopsies' already established in the USA. In this context, '…there is a team that can be called immediately, that is available 24 hours a day…' (Expert 5), and such a project would require numerous personnel and financial resources. Thus, it should be conducted within the framework of a study.

The experts view the initial information and training of nurses, who are regarded as the 'central occupational group', as crucial, along with those of family physicians to primarily minimise resistance from them. Regarding the timing of information, '…one should start talking to most patients when an advanced tumor with no chance of cure is present…' so that '…the patient has time to think about it…' (Expert 3+5), whereas, according to the experts, '…the initiator of the whole process must be the attending physician, where the primary therapeutic relationship of trust exists'. (Expert 7)

Process, basic organisation, recruitment and information

In principle, the treating family physician or specialist should establish and maintain contact with the patient regarding the subject of consent for autopsy. This was not considered realistic by all respondents because of time and skill constraints.

> Quote: …in oncology, I find it difficult to imagine, as there are a thousand other studies that patients need to be educated about… (Expert 10)

The organisation and timing of the research project across all three phases of communication should be transparent, clear and documented. All persons directly caring for patients with tumours, particularly nursing staff, must be fully integrated. Regarding information and care similar to organ transplantation, trained representatives – who '…do not belong directly to the treatment team to precisely avoid the impression that the treatment team could have a conflict of interest and perhaps terminate the therapy prematurely because they are interested in organ removal' (Expert 2)—must be present.

Patients with tumours for a targeted autopsy must be recruited as early as possible, individualised and free from coercion. Early involvement of relatives is recommended, but only during prior consultation with the patient.

> Quote: … that you approach and try to recruit patients for the study during an illness, not during the time when death seemed imminent, so to speak. But during a considerably earlier phase of the disease,… (Expert 11)

> Quote: Especially with a topic like this, you certainly have to address the relatives, but certainly never before the patient, that is, in terms of time. (Expert 8)

A concept of brief duration that does not incur costs for potential referrers of patients with tumours (such as clinics, family physicians/specialists, hospices and nursing homes) and their relatives must be available.

According to the experts, detailed patient education and a well-defined autopsy protocol are required.

Aftercare for relatives

All participants consider a final discussion with the relatives, as they are also involved in organ transplantation, useful. This can be done not only by the attending physician but also by a trained section assistant.

Three communication phases

Communication is crucial in the autopsy programme. Three phases can be identified, each focusing on necessary discussions: phase I, before a patient and potential study participant is included in the study; phase II, when a patient included in the study is near/at the end of life; and phase III, when an included patient has died.

For phase I (before inclusion in the project), the interview participants again emphasised that they should primarily talk to the patient and then the relatives. Depending on the study, the person who will conduct the interview for obtaining informed consent (study physician, attending physician) must be clarified.

> Quote: …who is authorized to educate. Is this sort of an interventional study requiring GCP-compliant education. (Expert 10)

Phase II (after inclusion and near end-of-life situation) requires, in view of the increasing concreteness of the project and according to the opinion of the experts, staff trained in conducting discussions who can address recurring or new questions for the patients and their relatives without time constraints.

A surprising subsequent rejection of the autopsy by relatives must be expected, despite a prior consent being obtained from the patient. The experts recommend acceptance of the wishes of the relatives.

To reduce uncertainties and fears of patients and relatives, appropriate information should be provided in the primary patient brochure, particularly as it is considered critical '…if afterwards relatives are still persuaded in the mourning phase to join in quickly…' (Expert 8).

However, the experts believe that if conflict occurs, such as relatives objecting to an autopsy even though the patient has given written consent, the patient's decision counts, not that of the relatives.

> Quote: …because only the decision of the patient is considered, not that of the relative. (Expert 12)

In phase III (after inclusion and the patient's death), experts emphasised that the patient's decision is the most important factor in determining whether further procedures should be carried out, not that of the relatives. Thus, a procedure in coordination with the relatives while the patient is still alive must be established.

Dealing with the autopsy results

Regarding sensitive transmission of autopsy results to the relatives, '…it is specified in writing beforehand that they

may have the result and that the treating physicians are included' because '…medical confidentiality does not end with death, but continues beyond death'. (Expert 9). The finding should be '…clear to the medical text, the so-called relative diagnosis, which is then just formulated in understandable language, not medical…' (Expert 2).

Project organisation

A structured checklist or standard operating procedure should be available for the procedure, which contains the organisational steps as well as contact persons and telephone numbers. To avoid misunderstandings regarding the planned 'targeted autopsies', patient education should be provided by the physicians involved in the study.

> Quote: …whether the reluctance to do an autopsy arose from the fact that the communication between the physician and patient was not right at that time. (Expert 12)

The experts called for a clear regulation regarding the transfer costs. Neither relatives nor participating clinics may incur additional costs for the project. As a cost-effective solution, a procedure is recommended, that is, an autopsy on site or at a nearby suitable institution.

Conclusion statements

Overall, the interviews indicated that the participants viewed the implementation of the research project as quite possible or largely unproblematic, as long as the basic requirements could be met.

> Quote: …I think it is scientifically important. I think it has a potential. I think that this general promotion is very important, that patients and relatives are well educated, and that there is an accompanying trusted person. (Expert 14)

> Quote: …that tumor research without autopsy is actually amputated tumor research. (Expert 2)

DISCUSSION

Our understanding of organ-specific metastasis pathways, mechanisms of tissue destruction caused by tumour metastases and causes of tumour-related organ failure remains limited. Moreover, the biological basis for successful anti-tumour therapy in metastatic diseases is still insufficiently understood.[1] The pathology institutes of the universities of Regensburg and Erlangen have developed the model of 'targeted autopsies', which involve taking larger tissue samples from certain defined metastasis sites of the deceased as soon as possible. This method was expected to improve our biological understanding of metastasis, which is an urgent need for more targeted treatment of patients. This is necessary, because tissue samples obtained through pure biopsies during a patient's lifetime often are very small and are used for further investigation, such as for molecular analyses for therapy planning. Moreover, the infiltration patterns of metastases cannot be properly evaluated using biopsy specimens.[17] The number of autopsies performed in Germany has been declining,[18 19] and postmortem tissue removal not only raises significant ethical demands[20] but also entails considerable challenges in recruiting patients who are willing to donate.[6] Therefore, experts from various specialties were asked for their insights on the project's feasibility for further development. During this process, as many opinions as possible should be gathered from specialists who care for patients and, when necessary, initiate or perform autopsies. This approach provides a broad range of opinions on the topic.

For instance, in the 'rapid autopsies', for example, in the USA and Australia, which is a project very similar to the 'targeted autopsies', tissue samples are also taken postmortem with a special purpose.[6 9 11 12 21] Implementing such a programme is ambitious and demands substantial personnel and financial resources, making the realisation of such a project challenging and costly.[6 9 12] Moreover, for the 'targeted autopsies', the experts emphasise the need for corresponding personnel involvement, such as a dedicated continuous contact person, staff for the training of participating physicians and clinics, trained personnel for patient education and support of the relatives and personnel responsible for creating autopsy reports understandable for the relatives. Additionally, an on-call team who performs the necessary tissue removal is required. Other costs include advertising and transfer expenses for the funeral service. The extent to which these requirements can be covered within the framework of a study in Germany remains to be determined.

Good and appropriate communication among the scientists appears to be one, if not the key to the project's success.[22] The experts interviewed highlighted version aspects of successful communication in the context of such a scientific programme, which align with the existing literature. Trust-based communication is an important foundation.[23] Although a lack of communication is a key obstacle, a proactive, empathetic dialogue increases the likelihood of obtaining consent.[24] Furthermore, the belief that relatives are generally opposed to autopsies appears inaccurate; often, it is the hesitation of doctors to initiate the conversation that prevents discussions from taking place.[6 25 26] In addition to scientific questions, these conversations should address widespread misconceptions, such as fear of disfigurement or delaying the funeral.[27]

In organ transplantation, the experts did not see any major problems regarding patient consent, which must be given while the patient is still alive in the case of targeted autopsies. Similar to already running autopsy programmes such as the CASCADE programme (Cancer Tissue Collection After Death), a concern was that insufficiently educated personnel would give the wrong impression or cause uncertainties that could jeopardise the project. Having experience in rapid autopsy allows well-educated and motivated personnel to contribute to the success of such a project.[6 9 28 29]

Given the high expenditure on public relations efforts for organ transplantation programmes, the success of targeted autopsies will likely rely heavily on good patient information, appropriate publicity and suitable access to oncological units. This is also supported by expert opinions and experiences related to brain donations in Alzheimer's research.[30 31] This is also supported by the data obtained in organ donation, which attributes the increasingly low organ donation figures in Germany to recognition and reporting deficits and calls for an improvement in the hospital's internal processes, such as in obtaining well-founded informed consent.[32]

The opportunity for postmortem organ donation, and thereby the chance to 'do good' even after death, is available to everyone. Patients with active tumour disease, who are typically excluded from organ donation due to their disease, are therefore offered a new opportunity to exercise their willingness to contribute to the community even after death. Evidence from the field of rapid autopsy has indicated a clear willingness and urgent desire of patients to participate in such a postmortem study programme.[33] Such a programme can help in providing meaning at the end of life for patients and their relatives.[9] Giving one's life-shortening illness 'meaning' and being able to help others altruistically, even if one cannot benefit from the results of the study, are essential motivators for those in an advanced palliative situation to want to participate in scientific studies.[34]

As is customary for organ donors, dignified treatment of the deceased is the top priority. Experts also considered postmortem conversations as useful for relatives. Similar to organ donation, professional care provided to relatives could increase the donor rates.[35] In the CASCADE programme family members were invited 2 weeks after the death of the patient to meet with the clinical team.[9]

The experts considered a fixed organisational plan and corresponding contact persons as essential for project implementation. They agreed with the corresponding considerations here, similar to rapid autopsies and organ donation programmes. Despite clear organisational guidelines, rapid autopsies (in contrast to organ donation) encountered difficulties in the actual procedure. Local conditions must be adequately considered in the organisation. This is a decisive aspect for successful implementation on site.[12]

As consent for autopsies is best obtained by an experienced clinician with an established relationship of trust, given the high consent rate,[36] the experts emphasised the need for professional independence between the person providing information and the primary clinician to avoid any pressure on the patient or relatives when making a decision. In general, many of the aspects already mentioned from a professional perspective are also ethical issues that must be addressed (such as communication, respecting the patient's autonomy to give consent and altruistic content of consent).[37–40] This once again underlines the high relevance of our findings for concrete project planning.

The targeted autopsy programme was still in development at the time of the interviews. The results have been incorporated into the concrete implementation of the project.

In this study, only subject matter experts were interviewed regarding the planned project. Patients and relatives were not involved. Therefore, generalisation of the study data is limited. Future studies should then gather the opinions and wishes about targeted autopsies from this group of people.

CONCLUSIONS

The innovative concept of targeted autopsies is a new approach in Germany for obtaining postmortem tumour samples - primarius and/or metastases - and may be useful for further analysis of the precise mechanisms of metastasis and the cause of a differential response of individual metastases to tumour therapy. The project requires precise planning, organisation and a trained, empathic and dedicated team. Securing appropriate financing is also necessary. Therefore, the development of this project in Germany remains to be seen with excitement. We believe that the new knowledge gained in this project, supported by the results of these interviews with multiprofessional experts, will benefit patients with cancer and undoubtedly justifies the great effort required to implement this project.

Contributors UK, UV-K, MR and KE conceptualised the study. UK, UV-K and MR carried out the formal analysis. UK, KE and MR carried out the project administration. UV-K and WH carried out the supervision. UK and UV-K wrote the first draft of the manuscript, and all authors provided input on the various versions of the draft manuscript and reviewed and approved the final manuscript. UK is the guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This qualitative study has obtained ethical approval in September 2022 from the ethics committee of the University of Regensburg (Nr. 21–2440_1–101) before it commenced. All approvals were granted in full compliance with the principles of the Declaration of Helsinki. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. All relevant data are within the paper. The transcripts analysed in this study are available from the corresponding author on reasonable request.

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