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Rapid autopsy program in Japan: how we ethically use cadaveric tissues for research in the absence of legal regulations

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Abstract

Fresh tissue samples have become increasingly important in a broad range of biological and medical areas, such as research on human degenerative and malignant diseases and genomic research. In view of the background, biologists and bioethicists at ASHBi, Kyoto University started a fusion research project aiming to build a platform for rapid autopsies in 2021. In this presentation, first, I will summarize the legal situation concerning the possible operation of rapid autopsy program (RAP) in Japan. Second, I would like to examine ethical and social issues of RAP, particularly in the context of Japan and Kyoto University. Finally, I will describe the current efforts and future challenges of our project.

Background

- In recent years, using fresh human tissues for research in biology and medicine has become increasingly important due to the development of genetic analysis technology and other factors (Hooper & Duregon 2019).
- Still, the data from conventional approaches using surgical leftover specimens have been limited. In recent years, several universities and institutions in the U.S. and other countries have established **rapid autopsy programs (RAPs)**, where autopsies are performed within a few hours after a patient's death for tissues to be collected in an undegraded state. Research using such early postmortem tissues is becoming more active.
- ASHBi at Kyoto University also aims to build a platform for such rapid autopsies and is conducting a three-year **fusion research project** starting in 2021. In the project, biologists and bioethicists collaborate to discuss related practical and ethical issues.

This presentation

✓ summarizes the legal situation and actual operation of RAP in Japan
✓ examines ethical, legal and social issues (ELSIs) of RAP in Japan
✓ describes the current efforts and future challenges of our project.

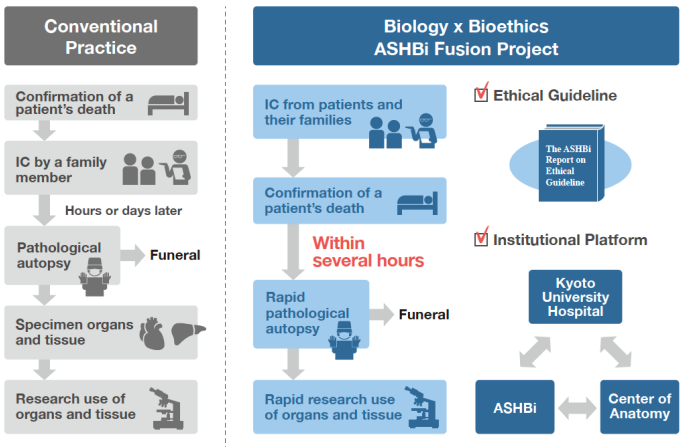

Figure 1. Conceptual illustration of our RAP

Discussion

Legal Status in Japan concerning research use of postmortem tissues

- The Postmortem Examination and Corpse Preservation Act (1949) stipulates conditions in which medical autopsies can be conducted. However, the law has no clear provisions for the research use of postmortem tissues for purposes unrelated to the elucidation of the cause of death.
- Thus, there are **no governmental guidelines** that uniformly define the research use of cadaveric tissues.
- Voluntary guidelines issued by research organizations, such as the Japanese Tissue Culture Association and the Japanese Society of Pathology, have opened the door to the research use of cadaveric tissues.

Current situation of rapid autopsies in Japan

- One of the first RAPs in Japan was the **Akita Rapid Autopsy Program (ARAP)**, which aimed to clarify the clonal evolution of cancer by comprehensive genetic analysis of metastases and residual lesions after treatment. Since 2014, frozen specimens have been sampled at almost all pathological autopsies (Takai et al. 2020). However, since it is conducted as an extension of the elucidation of the cause of death, the procedure for specimen sampling is identical to the conventional one, and consent is taken by the bereaved family after the patient's death.
- Unlike Japanese cases, many RAPs in the U.S. have basically adopted **first-person antemortem consent** considering ELSIs.

Ethical, legal and social issues arising from RAPs

- While a normal pathological autopsy is performed approximately 7-8 hours to several days after the patient's death, a rapid autopsy requires that the autopsy be performed **within a few hours of death**, and the conversation about the autopsy will be forced to begin before the bereaved family is ready. Such a sensitive topic should be discussed at the right time to take their emotions into consideration. It would be better for the bereaved family to discuss the topic while the patient is still alive (Bacon et al. 2020).
- From the perspective of **patient autonomy and the principle of respect for persons** (Pentz et al. 2005), consent by the patient himself/herself is desirable. In particular, when various organs are to be used for research, it would be ethically required that the patient fully understand and agree to the research before giving his or her own consent to tissue donation (Figure. 1).
- Currently, research use of postmortem tissue is regulated by voluntary guidelines by groups of researchers. However, there is no even voluntary guideline for rapid autopsies. Therefore, to implement RAP in Japan, voluntary guidelines must first be developed by researchers, taking into consideration of ELSIs, such as the issue of consent in particular.
- In addition, **stakeholder (public) engagement** will play an important role in making the program ethically and socially robust, considering that openness, public consensus, and public trust are essential for self-regulation by professional groups.

Issues specific to our project

- Pathological autopsies at **Kyoto University Hospital** are carried out after transporting the body to the **Autopsy Center** at the School of Medicine campus. Since the transportation must pass through public roads, the body is transported by car with the cooperation of a funeral service company after the appropriate procedures. Therefore, the time required to start the autopsy tends to be longer than at other facilities.
- The purpose of the RAP at ASHBi is to contribute to **basic biological research**, and it is unique in that tissues from various parts of the body will be used for various studies that might be unrelated to the elucidation of the cause of death. Most of the RAPs overseas have been conducted for cancer research, and the program participants have often been limited to cancer patients. The challenge for ASHBi is how to recruit participants and from which groups.

Current efforts and future challenges

- ◆ Already conducted online and on-site **interviews** at five facilities in the U.S. to learn RAPs, and established our **website** (https://ashbi.kyoto-u.ac.jp/cwl/en/) to disclose information to the relevant stakeholders. We plan to further engage with the public by holding public lectures and events.
- ◆ In addition to the autonomy issue, **psychological aspects** for patients and patients' families, and practical issues of obtaining consent are at stake. As well as the theoretical study by the ethics team, we are preparing to conduct questionnaires and interviews with stakeholders, including healthcare professionals and the general public to examine these aspects further.

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