

Postmortem Tissue Donation: Giving Families the Ability to Choose

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Postmortem tissue donations can represent a driving force toward progress in brain tumor research, particularly malignant and recurrent tumors where current survival is dismal. In addition to the scientific value, there are benefits to postmortem tissue donation from the parental perspective.¹⁻³ However, several real and perceived barriers exist, which have limited the rate of autopsy including discrepancies between clinician, patient, and parental views.^{4,5} To identify and address these barriers, a consensus conference of advocates of children who died of brain cancer was held in December 2018 at the Children's Hospital of Philadelphia. Major barriers to obtaining autopsy were identified with an emerging theme that a cultural shift is urgently required where families and patients with terminal brain cancers are uniformly provided with the option of postmortem donation.

Summarizing the opinions collected from more than 120 parents whose children died of brain cancer and leveraging the experience of the multi-institutional postmortem CNS tumor collection program, Gift from a Child (GFAC), we seek to inform medical professionals of the need to approach families about this sensitive topic and to demonstrate how barriers to donation can be overcome. A central theme among parent advocates is that families and patients ultimately do want to be asked and provided the opportunity. Specifically, there was broad consensus that processes need to be embedded that require clinicians to broach the topic and ask all families, and a failure to ask robs them of an important opportunity.

Why CNS Tumor Families Consent to Postmortem Donations

A strong consensus emerged that families and patients chose to donate to further research and help future patients. This is consistent with prior research in the area in which parents indicated the desire to advance knowledge and find a cure for other children.^{1,3,6} Ultimately, choosing donation can be a first step in the grieving process. According to one mother, "Being able to donate something that may prevent another child from suffering how our daughter did was crucial to our closure. It was beneficial to our family to know

she was contributing even after death: to know there was one last thing she could do after she'd taken her last breath."

Many adolescents suggest donation themselves. Struggling to find purpose when their life is being cut short, knowing they can be part of cancer studies, new treatment protocols, possibly improving outcomes for future children, can create meaning and offer a balm to their anxiety and grief. As Michael Gustafson said when he described his Master Plan, "I'm going to give up my life and they can use me to find a cure for cancer ... I want my donation to help as many people as I can."⁷

Parents struggle with that same loss of dreams for the life they envisioned for their child. One mom describes donating as part of her daughter's legacy, "Being able to take this shining light and donate her tumor so she could continue to shine is our gift to her and hers to us. She's still a driving force in the world and she's going to make the world a better place. Whether she's here physically or not it's important to know that."

Overcoming Donation Obstacles and Misconceptions

To overcome difficulties preventing postmortem tissue donation, a cultural shift is needed within the pediatric brain tumor community, much like the one that occurred for organ donation, with the goal to offer every family, anywhere in the world, the option to donate. Although donation will not be right for every family, asking families to consider postmortem donation should no longer be the exception because families deserve the right to choose for themselves. Better outcomes for children with cancer depend on more families contributing to cancer research.

Asking families: The clinician's influence. A major obstacle to donation is many families are not made aware of the benefits of tissue donation. Clinicians can overcome this barrier by educating themselves and families on the impact tissue donation has had on medical advances. Families made it clear that many clinicians remain uninformed. As one surveyed mom said, "We asked to donate and our doctor didn't encourage us, in fact he talked us out of it."

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on July 15, 2022 and published at ascopubs.org/journal/jco on August 26, 2022; DOI <https://doi.org/10.1200/JCO.21.02839>

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For families who did donate, almost three quarters initiated the donation conversation with their clinician. Among those who did not donate, more than half report they had not been asked by their health care team. For both groups, the health care team initiated the donation conversation only 20% of the time. One surveyed mom lamented, “I really wish I could have given my son this option. The opportunity was never presented ... I envy the parents that were able to donate.” Furthermore, nearly all families who donated were satisfied with their decision, strikingly, whereas most families who did not donate were unsatisfied with their decision, consistent with previous studies.⁸

A 2011 survey found 93% of families surveyed would have donated if asked to, but asking families remains an obstacle because many doctors admit to being uncomfortable broaching this subject.⁸ Families look to their oncologists for a cure and some physicians find it difficult to accept there are medically no more options. There is a preconceived notion among many neuro-oncologists that families would be upset if approached about postmortem donation. However, our experience suggests the opposite, that withholding this option can be distressing for families.

How families are asked affects whether families will in fact proceed with donating. Presenting donation as impactful for science, helping the next child, and helping a family's grieving process are important factors in a family's decision. A comparative study in *The American Journal of Medicine* found clinicians who seek consent conveying a low level of interest while presenting the option can negatively influence the family's decision.⁹

When and how to ask. Although many oncologists overcome the discomfort of broaching this subject with families, the question of timing remains. Parent interviews and our survey demonstrate that most families are open to this conversation once it is clear a child will not survive or when they transition to hospice care. Ideally, families would be given enough time to contemplate whether the decision is right for them, but asking at a less-than-ideal time is better than not asking at all. Families may fear donating will interfere with time they can spend with their child after death. In practice, families are given as much time as they need with their child and donation should have no bearing on funeral arrangements. Hospitals and philanthropies bear the cost of donation, and consent for postmortem donation is not a binding contract and can be rescinded.

Viable tissue can be obtained even several hours after death or the next day. Although there is a push toward rapid or warm autopsies to obtain viable cells and RNA including the application of single-cell technologies, this has created a perception that later autopsies are of lesser value.¹⁰ Even when viable tissue cannot be stored, DNA is extremely stable for hours to days beyond the time of death and is extremely valuable in understanding the somatic evolution of a tumor.

To ensure families do not miss the opportunity to donate, a regional program was created in the United States with the goal to facilitate brain tissue donation. The program GFAC handles all aspects of a donation, answers questions, and explains the process to both providers and families. To assist families, GFAC has trained parents who have lost children to brain cancer to companion families currently considering donation. To our knowledge, this is the only dedicated consortium providing postmortem donation resources for children with brain tumors.

GFAC has resources available for clinicians and ancillary health professionals to help introduce and educate families about donation. These resources include a website, video testimonials, and printed materials specifically tailored to families.

Oncologists practice informed consent for clinical trials, and similar approaches are warranted with postmortem donation. When informing families, they also need to know there is no financial cost to them as either the hospital, research funds, or philanthropy typically pay for the donation. Furthermore, families can change their mind at any time about donating.

Overcoming postmortem donation logistics. Once a family has consented, there are significant logistical challenges to overcome. In our experience, a higher proportion of children with brain tumors die at home or in hospice, outside of business hours of their treating hospital, contrary to other pediatric cancers, where hospital death is more common, and where further brain tumor-specific studies are needed.¹¹⁻¹⁵ Irrespective of the location of death, however, each donation is unique and requires vigilance, flexibility, and thoughtful planning.

Thoughtful planning includes detailed workflows, dedicated staff to coordinate the donation process, and rapid autopsy kits. Distribution of rapid autopsy kits provide outside agencies everything needed to procure and transport tissue to research laboratories for processing, giving families, wherever they live, the option to donate. A sample workflow highlights postmortem donation for children who die in hospital or at home (Fig 1).

Single institutions can use these workflows to provide the option of postmortem donation to families. However, single institutions will always be limited by their resources and catchment area. A multi-institutional approach to postmortem donation provides the greatest opportunity for any family to choose donation. Tissue coordinators from regional autopsy centers can work across institutional lines coordinating donations wherever they occur, and children need not be treated at these centers to participate in the donation program. GFAC models this approach.

Whether single- or multi-institutional efforts, successful programs in the United States where insurance does not cover autopsy will have:

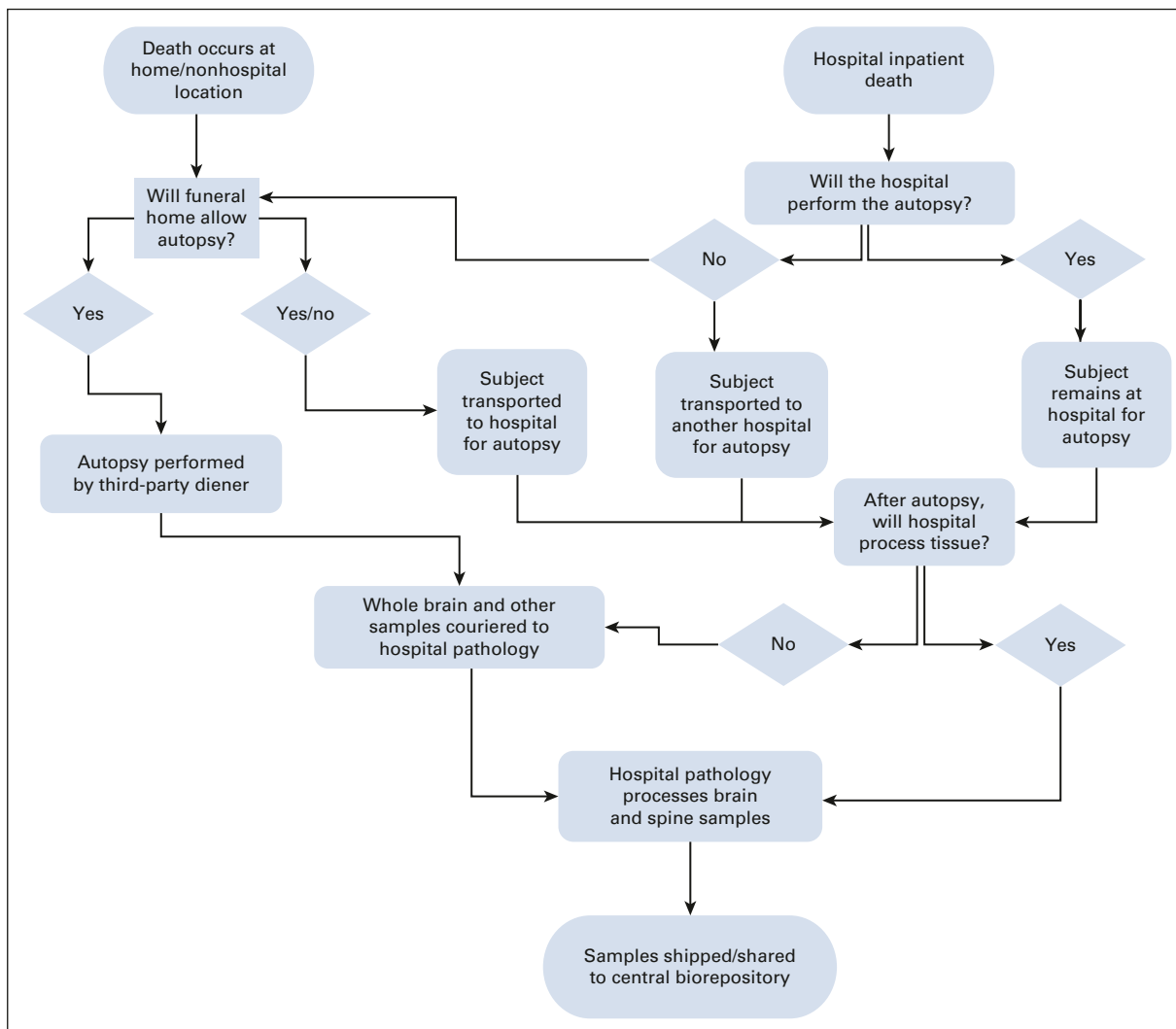


FIG 1. Sample postmortem tissue donation workflow.

- Support from hospital leadership and philanthropies
- Pathology's philosophical buy-in. Demonstrating the pathologist's value in this endeavor and stipends for extra work are beneficial to cooperation
- Consenting processes and material transfer agreements in place between cooperating institutions.

Families enduring the journey of postmortem donation want assurance tissue will be processed in a way that allows for all types of downstream analysis and that the tissue, subsequent cell lines, models, and data are shared across the research community. Transparency and accountability are keys to ensuring good stewardship of donated tissue is being practiced. At the Hospital for Sick Children in Toronto, the practice is to conduct an exit interview with families after postmortem has been conducted.¹ A minimum postdonation standard procedure is required to guarantee transparency. Once this precious gift is given, families have key expectations and most want to be notified:

- When the processing of postmortem tissue has been completed?
- Whether cell lines or mouse models were successfully created?
- Was their child's tissue used in research that was published?

Addressing religious considerations. The world's major religions have prescriptions around postmortem donation. While some do not expressly advocate for it, most do not object. Their views about autopsies are similar to their positions on organ and tissue donations.^{16,17} Although there are variations in recommendations, many religions encourage tissue donations, which are lauded as life-giving gifts and genuine acts of love. The principle of beneficence, which in medical ethics has been closely associated with the maxim, *primum non nocere* (first, do no harm), would direct clinicians to initiate postmortem tissue donation conversations with families to benefit pediatric brain

cancer research. By inviting the family to consider donation, they open the door for a loving act commensurate with the aspirations of world religions.

The clinician's role is not to pressure families to donate but to empathetically provide them information they need to make informed decisions following the dictates of their consciences. Clinicians can also solicit the support and expertise of chaplains or pastoral care teams from various religious traditions to accompany the family while tissue donation conversations are initiated. The presence of clergy from the donor family's religious tradition may ease their concerns.

In conclusion, families facing the unimaginable loss of a child to brain cancer believe that each family has the right to decide whether postmortem donation is right for their

family. If clinicians do not ask, they are depriving families of the benefits cited above: something good coming from their tragic loss, furthering research, a legacy for their child, meaning/purpose for an adolescent patient, and help in a family's grieving process. Clinicians have a responsibility to these families and to their current patients to provide this avenue for furthering research. This gift can only be given by these families.

Clinicians guide families/patient throughout their treatment journey to facilitate informed decision making; therefore, by failing to ask for postmortem, they are deciding for the family not to donate. In a journey where so much has been taken from families, families deserve the opportunity to make a thoughtful decision about this potentially life-giving choice.

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SUPPORT

V.R. has operating funds from the Canadian Institutes for Health Research and the Canadian Cancer Society Research Institute.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI <https://doi.org/10.1200/JCO.21.02839>.

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Manuscript writing: All authors

Final approval of manuscript: All authors

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ACKNOWLEDGMENT

The authors thank the families who participated in the consensus meeting.

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No other potential conflicts of interest were reported.