

The State of Solid Tumor Biopsies : Innovative approaches to address and understand limited pediatric solid tumor samples and data

July 13, 2021

The Journey of a
Post-Mortem Tissue
Donation



Background:

The annual CureSearch Summit serves as a unique platform for driving critical stakeholder collaborations to accelerate the pace of pediatric oncology drug development. The 2021 CureSearch Summit is a series of four virtual sessions focused on addressing the relative paucity of available pediatric cancer tissue and data.

To develop this topic, CureSearch convened a diverse set of stakeholders (Appendix 1) to identify a challenge to efficient pediatric drug development that could be addressed at the 2021 CureSearch Summit. The working group recommended solid tumor biopsies as a timely, relevant and important topic for discussion.

More tumor tissue samples would accelerate the development of new therapies and diagnostics for pediatric solid tumors. Pediatric cancer is a rare disease; a limited patient pool requires concerted efforts towards efficient, effective, and open resource collection and sharing. It is imperative that innovative approaches to sample collection and sharing be identified and implemented with careful construction of pediatric clinical trial protocols.

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The Summit Working Group identified four primary topics of discussion to address the issue of limited and/or inaccessible patient samples to advance pediatric cancer research. Wide ranging experts in the field contributed to session discussions and presentations including thought leaders from academia, the pharmaceutical industry, patient advocacy groups, patient families, and regulatory entities.

Session 1: March 19, 2021 - New Technologies for Maximizing Analysis of Solid Tumors: A set of panelists from academia and industry will discuss the promise and challenges associated with incorporating liquid biopsies into widespread clinical practice.

Session 2: May 14, 2021 - Blurred Lines: Therapeutic vs Research-only Biopsies This panel discussion will explore the factors that differentiate therapeutic biopsies from research-only biopsies and examine how new technologies and biomarkers are increasing the potential for therapeutic benefit.

Session 3: July 13, 2021 - This session focuses on post-mortem tissue donation and the research potential for this tissue. Panelists discussed approaching families about tissue donation: the reasons these conversations are so important, the benefits donation confers to the entire community, and some suggested approaches to having these sensitive but critical conversations. We discussed ethical guidelines for post-mortem donation as well as the collection process and the applications for post-mortem tissue in research.

Session 4: September 14, 2021 - Biorepository Form and Function This session will provide insight into biorepositories, specifically how tissue is acquired, the types of samples and data that biorepositories house, and their accessibility.

This outcome-driven meeting aims to provide resources to the pediatric cancer community aimed at increasing biopsy use and data sharing to support and accelerate research in the field. A white paper will follow each of the four CureSearch Summit sessions. These white papers review the topic, highlight benefits and challenges to implementation of increased biopsy acquisition and data sharing in the pediatric cancer space, and identify future actions to address the challenges and increase pediatric-specific therapy development.

Session 3 - The Journey of a Post-Mortem Tissue Donation

Session three of the 2021 CureSearch Summit addressed post-mortem tissue donation as a potential source of tissue for research purposes. Recognizing the promise of this tissue as well as the barriers to its collection, this meeting explored conversations and ethical considerations surrounding post-mortem tissue donation, as well as infrastructure needs for tissue donation programs and uses for post-mortem tissue donations. Panelists (Appendix 2) were selected based on their expertise with ethical, infrastructure, clinical and technical aspects relating to post-mortem tissue donations.

The session was designed around the individual experiences of each panelist to provide a balanced, inclusive, and informative discussion. This white paper provides an overview of the panel discussion, as well as critical components of a post-mortem tissue donation program and next steps for CureSearch as we aim to promote post-mortem tissue donation as a standard practice.

Introduction

Cancer is the number one cause of death by disease of children and teens in the U.S. [1]. Despite the impact it has on so many young lives and families, we do not fully understand why children get cancer or how children die from it. These two important questions must be answered to improve outcomes. Patient tumor samples are an important source of discovery. As such, biospecimen donation and collection is fundamental for research.

Beginning with one of the most devastating diagnoses in pediatric cancer, diffuse intrinsic pontine glioma (DIPG), efforts to expand tissue sources shifted toward post-mortem tissue donation. It is difficult to fulfill research requests from limited surgical specimens. With brain tumors like DIPG, the location of the tumor can make a biopsy difficult. Even if biopsy collection is possible, a significant proportion of the biopsy, if not all, will likely be utilized for clinical diagnostic and molecular tests, leaving limited sample remaining for research efforts. An alternative source of tissue, post-mortem tissue donation, provides an additional opportunity to collect tumor tissue for research. Investigators and researchers have empowered research and enabled extensive genomic characterization of this fatal cancer through normal tissue and tumor collection at autopsy [2, 3]. As important as this work was, there remains an unmet need to scale these efforts so that post-mortem tissue donation could be offered to all families with cancer diagnoses.

The discussion that took place during session three of this series, The Journey of a Post-Mortem Tissue Donation, explored the many opportunities and barriers to development of a post-mortem tissue donation program. One theme that emerged as a constant was that families should be approached about the option for tissue donation. In 2013, researchers set out to understand the family experience with autopsy. Their manuscript [4] describes the family's reasoning for participating in this mechanism of tissue donation. Among the 33 families who lost a child to brain tumor and were surveyed for their experiences with autopsy, the vast majority donated due to a desire to advance knowledge or find a cure.

Introduction

The desire to help others and recognition that their child would have wanted to help others, drove their decisions. Armed with this knowledge, it is an institutional responsibility to build out the infrastructure to collect tissue donations at autopsy and the treating team's responsibility to share the option of post-mortem tissue donation. This white paper will present the key concepts addressed by experts in the field in relation to the ethics, promise and important considerations around post-mortem tissue donations.

In a more recent survey, conducted by the Gift from A Child Program from January through May 2021 with the support of pediatric oncology departments from research hospitals in the U.S., Canada and Australia, 108 families who had lost a child to brain cancer were invited to complete a survey assessing family preferences as they pertain to being approached about post-mortem tissue donation. Of those that donated, 90% were very satisfied and 8% were satisfied with their decision to donate. Conversely, of those that did not donate, only 20% were either very satisfied or satisfied with their decision while 57% were very dissatisfied or dissatisfied with their decision not to donate. In addition, researchers found that among families who donated, it was the family who requested donation 79% of the time while clinicians only brought it up 21% of the time. Among those families that did not donate, 20% of families discussed donation, but in many instances, were dissuaded by their medical team from donating and 22% of the time clinicians asked; 59% of the time, no one addressed post-mortem donation [unpublished data].

Making the Ask: Approaching Families about Post-Mortem Tissue Donation

One of the main barriers to post-mortem donation is that families simply aren't aware of the need for post-mortem tissue. It is a physician's responsibility to provide timely and understandable information about post-mortem tissue donation. While physicians' foremost goal is to treat or cure a disease, unfortunately that aim is not always achievable. The recognition that a child in one's care will not survive also makes the discussion of post-mortem tissue donation a difficult one to broach. Not every family is going to be open to the discussion, but there are those that will, and it is the family's choice to make. Taking that decision away from the family by not informing them of the option is a disservice to them – unless there's an obvious religious or cultural concern that the physician is aware of.

As far back as the fourth century BC, Hippocrates presented the concept of beneficence – the qualities of charity, mercy and kindness with a strong connotation of doing good to others – within the Hippocratic oath. Beneficence is a fundamental ethic in health care [5]. When a family is facing the death of a child, offering hope or meaning in the tragedy is a gift that is beneficent. Additionally, the families' choice to provide a post-mortem tissue donation is beneficent toward other children who will face pediatric cancer. Post-mortem donation can further patients' and families' values and provides meaning in a terrible tragedy.

"As a physician I will share with you that helping my own patient families through this process has been extremely rewarding. It's given families hope at a time when I knew as a physician, I had no other type of hope to offer." - Dr. Angela Waanders

The most important role for the physician in the post-mortem tissue donation process is to make sure the oncology team is aware of the option for post-mortem tissue donation and that, as a team, they decide who is best to reach out to the family to make the request. From the clinical perspective, this donation request can be a difficult discussion. To be successful, the physician will require practice, support and modeling. This section will review best practices in addressing this subject with families from the perspective of those who do so regularly, as well as from literature exploring the patient perspective on this topic.

One critical factor in a successful ask is to discuss post-mortem options early in the treatment process and ensure that all aspects of the process are outlined in a manner that is easy for the family and patient to understand. Studies that gauge the parent's perspective of the post-mortem tissue donation process provide models for building the conversation to address family needs and questions [4]. Many parents suggest that physicians provide education and anticipatory guidance regarding the process of post-mortem tissue donation. In addition, they recommend having a professional that regularly cares for the patient or someone who has established a trusting relationship with the family discuss post-mortem tissue donation. Finally, sharing the outcomes of the tissue donation – how well the tissue extraction went, if research models could be made with the donation, and how the models would be used for future discovery – provides the family with a feeling of beneficence and meaning when facing the loss of a loved one. A family's ability to identify some good, despite tragedy, can be an important first step in healing from their loss. Families choose to donate post-mortem tissue to contribute to the legacy of their child, receive consolation that their child is contributing to the world after death and acquire a sense of agency at a time when most everything feels out of control. In addition, adolescents and older children who decide to donate can find meaning and purpose at a difficult time. Despite knowledge of the need and process for approaching families about post-mortem tissue donation, the conversations are often challenging and emotional. Programs like Gift from a Child were developed to support physicians and institutions with all aspects of the post-mortem tissue donation process.

Case Study 1: The Swifty Foundation Gift from a Child Program

Shortly after his diagnosis of medulloblastoma, Michael Gustafson recruited his friends to raise money for cancer research by selling golf balls they found on a nearby golf course, and later to recruit teams for the annual Relay for Life. At the end of Michael's battle, with his parent's help, he started the Swifty Foundation. Michael chose to donate his tissue for research after his death to help find a cure for pediatric brain cancer. Post-mortem tissue donation has become a major priority for Swifty as they often hear from researchers about the dire need for donated tissue to study. Even when funding for research is available, without tissue collection the hands of medical researchers are tied. This remains one of the largest obstacles toward finding a cure and Swifty, through the Gift from a Child program, is determined to remove this barrier.

Gift from a Child (GFAC) is a national initiative supported by families who have lost children to brain cancer, private foundations, researchers and medical professionals. The regional autopsy centers within the GFAC work across institutional lines to collaborate in their mission to increase post-mortem pediatric brain tissue donations through advocacy, as well as the education of families enduring the loss of a child. GFAC has formed partnerships with leading researchers and medical providers who value information and data sharing. In 2020, the Swifty Foundation and GFAC, in partnership with the Children's Brain Tumor Network, helped to develop the Children's Oncology Group (COG) autopsy initiative, in which a number of lead COG institutions are helping hospitals and families outside of the GFAC make post-mortem tissue donation possible.

Tissue Navigators- The Secret Sauce of the Gift from a Child Program

The role of a Tissue Navigator was born out of hearing so many families say, "We want to donate but we have no idea where to start or how to make it happen. We know researchers need the tissue but how do we get this precious gift to them?" Because children typically pass away at home, the logistics of coordinating these donations within the small viable time frame is difficult and each donation provides unique challenges. Gift from a Child Tissue Navigators work across institutional lines to meet these challenges so that no matter where in the country a child dies from brain cancer, donation is an option. Navigators are a committed, resourceful team coordinating their work so that no matter the day or time, GFAC will work to make donation a possibility.

The Ethics of Approaching Families

Though current regulations do not require protocol reviews by an institutional review board if post-mortem tissue is collected for research, approaching families about post-mortem tissue donation is such an important concept that a multi-disciplinary review board should be employed. Maintaining ethical interactions and ensuring that the consenting process is optimal, from both the research and family perspectives, are paramount contributors to the success of a post-mortem tissue donation ask. A multidisciplinary expert Consensus Panel on Research with the Recently Dead (CPRRD) was convened to craft ethics guidelines for research with the recently dead [6]. A non-exhaustive overview of some of the recommendations pertinent to pediatric patients is provided below and should be considered prior to setting up a post-mortem tissue donation program.

- Receive scientific and ethical review and oversight. As noted above, it is important to employ a review board that includes representation from ethics, parents/advocates, and researchers to ensure that both the science and ethics associated with the sample procurement are optimal. Not only does this create confidence in the process, but it also promotes the success of the donation process.
- Involve the community of potential research subjects. Aside from playing an oversight role, the patient/family community can provide insight into how the procurement and research process, as described in the consent, are explained to families. In the consent and discussion, the advocate must use appropriate words, lay language and avoid medical or research jargon. When writing the consents, it helps to employ a family advisory committee to look over the consent and ensure it is written at the appropriate level to be understood by the general population. Different institutions and localities have different comprehension levels. It is often suggested to use eighth grade language to ensure complete understanding for the families involved.
- Use procedures respectful of the dead. Procedures performed on the deceased must be respectful. The procedures may not be identical to requirements for a living human but should be respectful and described thoroughly in the consent. The consent and discussions with the patient or family should share how the person's body will be respected; for example, by keeping the deceased covered, keeping disfigurement low and making the autopsy duration short.
- Acquire consent. The consenting process for post-mortem donation and autopsy is well-defined in adults. Consent should be granted by the patient before death or the next of kin after death. For children under 18, parental permission is required. If the patient is developmentally mature, it is also appropriate to get assent from the patient. The adolescent perspective was assessed in a cross-sectional, interview-based study [7] of twenty adolescents recently discharged from an intensive care unit. Participants were asked if they would like to be included in the tissue donation decision; nineteen of the twenty did. In addition, more than half of 75 parents surveyed thought that adolescents should provide assent. Of course, the decision to request assent from a pediatric patient is dependent on age and situation. If the child is developmentally mature and the situation is appropriate, the child should share in the discussion. This respects his/her developing autonomy.

- Protect confidentiality. When patient tissue is procured for research purposes, it is essential that the sample or data used in research cannot be traced back to the donating patient. Having strict processes established that appropriately anonymize the samples and data collected.
- Do not impose cost on subjects or families. The donation of tissue for research will not directly benefit the patient, so it is important that the patient's family does not incur any cost from the collection of post-mortem tissue for research purposes.
- Clearly explain the ultimate disposition of the body. Provide a very careful description of what the tissue donation is going to look like. Describe any disfigurement and how it will be addressed. Also, share the timing of when the body will be returned. Making this information clear and openly discussing it will enable the family to make an informed decision.

Uses for Donated Tissue

The decision to donate tissue after death may be one of the last steps in a child's life. The aim of this decision is to advance the field and hopefully, produce knowledge that will enable other families to avoid suffering in a similar way. As such, it is important to understand how donated tissue can be used to promote discovery. In addition to making cell and/or animal models from the patient tissue that can be used to test new therapies, tissue is banked and available for future research requests, and the tumor can be genetically sequenced to understand the molecular changes that may have driven the tumor's growth or resistance to therapy. The discoveries that may result from post-mortem tissue donation can drive drug development and are important as targeted therapy continues to become more prevalent.

It is important to have the conversation about post-mortem tissue donation early because it enables the donation collection team to prepare for tissue collection so that samples can be collected as soon after the patient's death as possible. As the tissue sits, either in the body or in collection tubes prior to its processing, (called the post-mortem interval) its utility for certain techniques is reduced due to degradation. Short post-mortem intervals enable development of cell lines as well as collection of nucleotides, like DNA and RNA. It is important to note that even if rapid autopsy is possible, DNA is relatively stable and can often be collected and analyzed even after longer post-mortem intervals. Even in this case, there is still a lot of useful information – such as metabolites and other volatile, short-lived molecules that can be garnered, and downstream research applications that can be accomplished with the tissue.

The process of tissue procurement through post-mortem tissue donation is optimally conducted by a pathologist. The process first proceeds with submission of tissue for clinical purposes to document the diagnosis and extent of disease. Though this is usually known while the patient is alive, this is a good confirmatory step. Pathologists also observe any histological changes that may be related to treatment in both the tumor and the uninvolved brain. For research purposes, the pathologist will map the tumor in six to nine regions and assign them to approved research projects that assess tumor characteristics such as heterogeneity – the variety of cells and mutations within the cells that comprise the tumor. These types of characterizations are usually DNA- and/or RNA-based. In addition, the pathologist will collect the tissue that can then be used to develop cell lines and mouse models which will be included in future investigations to identify new therapies. For example, Dr. Xiao-Nan Li's laboratory is well-versed in the development of tumor models from post-mortem tissue and is able to establish new animal models at a rate comparable to those that are produced from fresh surgical samples. Approximately 50% of tumor tissue samples from post-mortem brain can be grown in animals. The reason for this is that many of the same biological pathways in humans are also present in animals. However, it may be the case that the tumors that have contributed to the death of a patient are highly malignant tumor cells; they have developed resistance to all the therapies administered and, because of their progression and evolution, they have acquired an extraordinary survival ability.

These are some of the best models to assess treatment resistance. Cell lines are more challenging to develop because they are initiated outside of an environment that closely mirrors the one from which they came. A plastic cell culture dish is not as permissible an environment as a mouse brain. Further studies with model development will continue to improve on the process and enable more diverse models to be used for research and discovery.

It is important to note that just because a patient's family consented to the post-mortem tissue donation, it does not mean that anyone who wants the tissue can use it. Tissue from pediatric cancer patients is a vital and rare resource to discovery and is well-protected. Groups of researchers requesting tissue need to have protocols approved by institutional review boards (IRBs) that have insured that the requested tissue, and the amount, will be used to its fullest potential to address the scientific question for which it will be used. The amount of tissue requested is limited to what is needed for the methods described in the protocol, and this is ensured by the IRB, allowing more qualified groups to make good use of these post-mortem tissue samples.

Tissue Alone is not Sufficient

The tissue samples from post-mortem tissue donations are critically important to scientific discovery, but when they are collected with the appropriate patient clinical and treatment data, they are even more substantial resources. Writing a consent allows for the collection of additional data related to the patient's cancer journey and captures the context of the biospecimens or resulting cell models. It also helps researchers to understand exactly what happened to that patient and how that might have contributed to the changes that occurred in the tumor.

Case Study 2: The Children's Brain Tumor Network

The Children's Brain Tumor Network's (CBTN) mission is to drive innovative discoveries, pioneer new treatments, and accelerate open science to improve the health of every child, adolescent and young adult diagnosed with a brain tumor. The CBTN supports the research of new prognostic biomarkers and therapies for children with pediatric brain tumors. This collaborative research effort consists of 25 primary member institutions and has enrolled more than 3,900 subjects and collected more than 45,000 tubes of specimens since its formation. They have also developed important partnerships with groups such as Gift from a Child to progress mutual goals. An important objective of the CBTN has been to develop research platforms that allow scientists to interact with the clinical data, biospecimen data and research data generated from the biospecimens in a manner that will promote sharing and discovery. To progress this aim, the CBTN team developed a comprehensive process and workflow for biospecimen and clinical data collection. This means that for any child enrolled, they collect diagnostic information, what kind of treatments they received and if they responded to those treatments. Collecting these data and ensuring that scientists with the appropriate permissions have access to them will enable further discovery in the most prevalent solid tumor diagnosed in children and teens.

Critical Factors for a Post-Mortem Tissue Donation Program

If you are looking to develop a post-mortem tissue donation program at your institution, refer to the below critical factors for post-mortem tissue donation or contact the Swifty Foundation Gift from a Child Program:

- ✓ Due to the number of logistical challenges that can make post-mortem donation difficult, each donation requires significant planning and foresight.
- ✓ A team approach that integrates multiple key stakeholders and a team that can be available 24-7 are important. Include the other medical providers such as social workers, palliative care teams and hospice workers.
- ✓ Ideally, the post-mortem tissue donation discussion should occur well before the time of the patient's death to ensure the process goes as smoothly as possible for the family and to allow for time for any parent or provider questions to be answered.
- ✓ Parents should be provided with the details of the donation process and options available for the donated tissue, such as designation of where tissue can be shared.
- ✓ Ideally, the autopsy is performed in a hospital with a skilled pathologist.
- ✓ Provide accountability and transparency regarding what happens with the child's tissue to provide the stewardship that the family deserves.
- ✓ Establish a flexible process and workflow that can adjust to family needs and unforeseen challenges to sample procurement
- ✓ Develop a research protocol consent and a research-based autopsy consent. Ensure that the patient community, ethicists and the institutional review board are involved in the review of the consent language.
- ✓ Assure patient families that their concerns are the most important to the care team.

- ✓ Allow families to have as much time with their child after death as is needed but ensure that the social worker and physician – through their therapeutic alliance with the family – share at the time of consent that the post-mortem interval impacts the quality of the tissue donated and support the family at the time of death as they navigate tissue donation.
- ✓ Ensure that the donation has no negative impact on the funeral of the child. Arranging for open-casket funerals are possible after donating and families need to know this.
- ✓ Do not associate a cost with the donation and ensure that families know that they will have no financial requirements associated with their donation.
- ✓ Share with families that they can change their minds about donating tissue at any time as the consent to autopsy is not a binding contract.
- ✓ Use an autopsy procurement kit with clear instructions for tissue handling and storage as well as all the necessary equipment for collecting the sample so that collection and shipment can occur efficiently.
- ✓ Develop an educational program that teaches providers how to speak with families about post-mortem tissue donation to increase provider comfort in the process.
- ✓ Discuss post-mortem tissue donation early and ensure the consent is completed at least 24 hours prior to the patient passing.
- ✓ Perform quality control checks and evaluate the viability of the tumor tissue after collection.
- ✓ Provide emotional and mental support to staff that contribute to making post-mortem tissue donation possible.

Next Steps

By convening a community of stakeholders in the pediatric cancer ecosystem, CureSearch provides a platform to think strategically and work collaboratively. CureSearch is in a unique position to compile information across stakeholders and disseminate outcomes and lessons learned to the broader community. Scientific and drug discovery opportunities lie in providing platforms for discussion amongst academia, industry, patient families, advocacy groups and regulatory bodies. After the annual Summit, CureSearch works collaboratively with meeting participants and contributors to identify action items and move the topic toward resolutions of the challenges discussed.

The optimal scenario for promotion of post-mortem tissue donation would be the development of a network of regional centers throughout the US that are set up within a 500-mile radius of large academic centers to reduce time constraints concerns. For this significant goal to be achieved, education amongst all stakeholders, as well as devoted financial support for the development of the procurement centers (for a review of the requirements for establishment of an autopsy procurement program, see [8]), is necessary. There are already groups such as GFAC and CBTN that have developed protocols and infrastructure; leveraging their resources is an optimal way to proceed with the development of additional centers.

In addition, courses that offer continuing medical education (CME), credits and address education of clinicians on the techniques of sharing post-mortem tissue donation as an option for families would be highly beneficial. Such courses would improve the rate at which families learn about post-mortem tissue donation and are able to consider and consent to donation.

CureSearch's hope is that the distribution of this white paper and associated resources will initiate the important discussion about post-mortem tissue donation to investigators and families around the world. For true progress to be made, we must engage and draw from an array of expertise. CureSearch proposes collaborating with GFAC to develop a working group that will explore mechanisms by which education about post-mortem tissue donation can be expanded and further formalized. Through combination of networks and expert contributions, we hope to provide additional mechanisms by which post-mortem tissue donation is prioritized, until it is considered standard of care.

Updates on working group progress will be provided to 2021 Summit participants in 2022 in the form of a list of action items that are updated quarterly to demonstrate progress.

CureSearch would like to thank panelists and attendees for their contributions to this session of the 2021 virtual CureSearch Summit. The success of this meeting would not have been possible without the engagement of all participants.

Works Cited

1. Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death 1999-2019 on CDC WONDER Online Database, released in 2020. Data are from the Multiple Cause of Death Files, 1999-2019, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at <http://wonder.cdc.gov/ucd-icd10.html> on May 6, 2021 2:30:38 PM <https://wonder.cdc.gov/controller/datarequest/D76.jsessionid=888833ACB8CC3535EBF24EA9EEA8>
2. Broniscer A, Baker JN, Baker SJ, Chi SN, Geyer JR, Morris EB, Gajjar A. Prospective collection of tissue samples at autopsy in children with diffuse intrinsic pontine glioma. *Cancer*. 2010 Oct 1;116(19):4632-7. doi: 10.1002/cncr.25405. PMID: 20589749; PMCID: PMC2989604.
3. Angelini P, Hawkins C, Laperriere N, Bouffet E, Bartels U. Post mortem examinations in diffuse intrinsic pontine glioma: challenges and chances. *J Neurooncol*. 2011 Jan;101(1):75-81. doi: 10.1007/s11060-010-0224-7. Epub 2010 May 16. PMID: 20473723.
4. Baker JN, Windham JA, Hinds PS, Gattuso JS, Mandrell B, Gajjar P, West NK, Hammarback T, Broniscer A. Bereaved parents' intentions and suggestions about research autopsies in children with lethal brain tumors. *J Pediatr*. 2013 Aug;163(2):581-6. doi: 10.1016/j.jpeds.2013.01.015. Epub 2013 Feb 19. PMID: 23433673; PMCID: PMC3664241
5. Kinsinger FS. Beneficence and the professional's moral imperative. *J Chiropr Humanit*. 2009 Dec;16(1):44-6. doi: 10.1016/j.echu.2010.02.006. Epub 2010 Apr 1. PMID: 22693466; PMCID: PMC3342811.
6. Pentz RD, Cohen CB, Wicclair M, DeVita MA, Flamm AL, Youngner SJ, Hamric AB, McCabe MS, Glover JJ, Kittiko WJ, Kinlaw K, Keller J, Asch A, Kavanagh JJ, Arap W. Ethics guidelines for research with the recently dead. *Nat Med*. 2005 Nov;11(11):1145-9. doi: 10.1038/nm1105-1145. PMID: 16270065.
7. Paquette ED, Derrington SF, Shukla A, Sinha N, Oswald S, Sorce L, Michelson KN. Biobanking in the Pediatric Critical Care Setting: Adolescent/Young Adult Perspectives. *J Empir Res Hum Res Ethics*. 2018 Oct;13(4):391-401. doi: 10.1177/1556264618782231. Epub 2018 Jun 14. PMID: 29900801; PMCID: PMC6146019.
8. DeWire M, Erker C, Hummel TR, Chow LML, de Blank P, Salloum R, Pillay-Smiley N, Hoffman L, Gilger E, Gallagher M, Driver L, Meister D, Ward H, Drissi R, Kumar SS, Sengupta S, Kikta B, Meriwether W, Jelinek S, Asher A, Jones B, Leach J, Miles L, Fuller C, Fouladi M. Overcoming barriers to establishing autopsy procurement programs in pediatric patients with central nervous system tumors: a call to develop regional centers. *J Neurooncol*. 2021 Mar;152(1):107-114. doi: 10.1007/s11060-020-03679-2. Epub 2021 Jan 27. PMID: 33502679

Appendix 1. Summit topic working group members.

WORKING GROUP MEMBER	DESIGNATION	AFFILIATION
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Su Young Kim, MD, PhD	Senior Medical Director	AbbVie
Donald Very, PhD	President and CEO	Naviter Bioanalytics, LLC
	Parent	Stage IV osteosarcoma survivor

Appendix 2. Panelist representation for the CureSearch Summit session Blurred Lines: Therapeutic vs Research-only Biopsies.

PANELIST	DESIGNATION	AFFILIATION
Angela Waanders, MD	Executive Board Chair	Children's Brain Tumor Network
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	Max Lacewell Endowed Brain Tumor Research Scholar	Ann & Robert H. Lurie Children's Hospital of Chicago
Sanda Alexandrescu, MD	Staff Pathologist, Department of Pathology; Assistant Professor of Pathology	Harvard Medical School
Patti Gustafson	Executive Director	The Swifty Foundation, Gift from a Child
	Parent	Mom of Michael Gustafson, Developer of his "Master Plan" University
Xiao-Nan Li, MD, PhD	Rachelle and Mark Gordon Endowed Professorship in Cancer Research; Professor, Pediatrics (Hematology, Oncology, and Stem Cell Transplantation)	Northwestern University Feinberg School of Medicine
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