

STU#:00095863

PROTOCOL TITLE: Nervous System Tumor Bank

PRINCIPAL INVESTIGATOR:

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VERSION NUMBER:

9

VERSION DATE:

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STUDY SUMMARY:

Indicate Special Population(s)	<input type="checkbox"/> Children <input type="checkbox"/> Children who are wards of the state <input checked="" type="checkbox"/> Adults Unable to Consent <input type="checkbox"/> Cognitively Impaired Adults <input type="checkbox"/> Neonates of Uncertain Viability <input type="checkbox"/> Pregnant Women <input type="checkbox"/> Prisoners (or other detained/paroled individuals) <input type="checkbox"/> Students/Employees
Sample Size	Indefinite
Funding Source	Department of Neurological Surgery
Indicate the type of consent to be obtained	<input checked="" type="checkbox"/> Written <input type="checkbox"/> Verbal/Waiver of Documentation of Informed Consent <input checked="" type="checkbox"/> Waiver of HIPAA Authorization <input type="checkbox"/> Waiver/Alteration of Consent Process
Site	<input checked="" type="checkbox"/> Lead Site (For A Multiple Site Research Study) <input type="checkbox"/> Data Coordinating Center (DCC)
Research Related Radiation Exposure	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

OBJECTIVES:

1. To bank human central nervous system (brain and spinal cord) tumor and tumor-mimicking tissues (e.g. arteriovenous malformations and hematomas) resected from patients treated at Northwestern Memorial Hospital (NMH) for use in research. Tissue from each patient will be stored as frozen tissue, paraffin-embedded tissue, and dissociated tumor cells. Peripheral blood mononuclear cells and plasma extracted from peripheral blood obtained at the time of surgery will also be frozen. Cerebrospinal fluid (CSF) from tumor patients will be frozen when drainage of CSF is performed as part of routine clinical care.
2. To bank nonneoplastic (i.e.noncancerous) brain tissue and peripheral blood from patients undergoing brain resections for epilepsy at Northwestern Memorial Hospital for use as control materials in future biomedical research. Tissue from each patient will be

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stored as frozen and paraffin-embedded tissue. Peripheral blood will be separated into peripheral blood mononuclear cells and plasma and store frozen.

3. To collect cerebrospinal fluid from patients undergoing CSF diversion for hydrocephalus or lumbar puncture. CSF extracted as part of routine clinical care in non-tumor patients will be frozen to serve as control materials in future tumor research.
4. To collect blood and clinical information from brain tumor patients presenting to Northwestern Memorial Hospital in the neuro-oncology clinic.
5. To bank post-mortem tissue from patients who have previously been treated at Northwestern Memorial Hospital for nervous system malignancies.
6. To process and bank deidentified pediatric blood, brain tumor, and non-cancerous brain tissues collected from Lurie Children's Hospital.
7. To provide laboratory researchers with fresh deidentified tissues, so as to develop cell cultures and xenograft models of nervous system tumors.

BACKGROUND:

Basic and translational research in cancer relies heavily on the use of human tumor tissue to understand the mechanisms of tumor formation and identify targets for new therapy. Tumor tissue banks that process and store biospecimens from patients during routine clinical care provide an unparalleled resource for cancer researchers to study human tumors and test new therapies. The ability to match tumor tissue to clinical outcomes information is of great importance to understand the implications of characteristic differences among patient's tumors. Heterogeneities in protein and gene expression can be compared to clinical information about response to therapy and survival to determine the true impact of these factors. To facilitate meaningful research, a tumor bank must contain specimens from a sufficient number of patients to allow appropriately powered analyses across samples, and sufficiently preserved specimens from each patient to allow the relevant genomic and proteomic analysis. Additionally, nontumor human tissue is necessary to differentiate neoplastic changes from nontumor variants.

The purpose of the Nervous System Tumor Bank (NSTB) is to establish a repository of brain and spinal cord tumors, as well as conditions mimicking tumors (such as vascular diseases, demyelinating disease, and infections), from human patients for biomedical research across Northwestern University and outside entities that partner with Northwestern investigators (e.g. multi-institutional projects, pharmaceutical companies in clinical trials, etc.). Tissue from consenting patients will be obtained during surgery performed for routine clinical care and will be banked as paraffin-embedded tissue for histopathology, frozen tissue for genomic, proteomic, and metabolic analysis, and dissociated tumor cells for cytometric analysis and cell culture. To improve experimental models of nervous system neoplasms, fresh tissue may be used to develop cell cultures and xenografts in mice. Such models most closely mimic real tumors in patients, and are therefore most optimal for evaluating potential new therapies. Additionally, peripheral blood will be obtained through either the arterial line or by venipuncture at the time of surgery, and extracted peripheral blood mononuclear cells (PBMC) as well as plasma, will be frozen. Patients who undergo placement of a ventricular or lumbar subarachnoid catheter for drainage of cerebrospinal fluid (CSF) either during their surgery or as post-operative care may also have CSF stored as a frozen sample.

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To establish nonneoplastic (i.e. noncancerous) tissue controls, consenting patients undergoing brain resections for epilepsy or other non-neoplastic mimickers, such as vascular malformations, will have tissue obtained at the time of surgery stored as frozen and paraffin-embedded samples, as well as peripheral blood stored frozen as PBMC and plasma. Patients with hydrocephalus undergoing CSF diversion procedures will have nonneoplastic (i.e. noncancerous) CSF drained during the operation stored as a CSF control.

Furthermore, additional tissue will be collected post-mortem from consenting patients to expand the bank's collections, involving detailed analysis of end-stage CNS tumors in a way that is not possible in living patients. Ante-mortem and post-mortem matched tissue of patients undergoing surgery for CNS tumors is rare and valuable for research, because many nervous system tumors recur and are lethal after initial therapy yet we still do not understand why. In each situation, clinical data will be collected, including all relevant demographic variables, to match to the samples. Samples will be coded for storage and all matched data will be de-identified.

Pediatric brain tumor tissue is rare, and there is a new initiative to foster more pediatric-adult brain tumor collaborations between Lurie Children's Hospital and the Feinberg School of Medicine, under the aegis of the Malnati Brain Tumor Institute. Therefore, the Nervous System Tumor Bank will receive deidentified biospecimens from pediatric brain tumor patients (including bone marrow, peripheral blood, brain tumors, etc.), as directed by pediatric neurosurgeon Dr. Michael DeCuypere. Each specimen will be logged into the NSTB database with a numerical code. Most of the fresh specimens will then be transferred to the DeCuypere team, working within the Heimberger lab on SQ-6. Leftover specimens will be stored in the NSTB for potential future use by the DeCuypere/Heimberger group. Dr. DeCuypere will use the NSTB-developed linkage codes to re-identify his patients as needed, according to his separate IRB protocol. At no point will the NSTB team store or handle PHI on any of the pediatric cases.

PROCEDURES INVOLVED:

Study Design: Prospective tissue specimen collection from patients undergoing surgical treatment as part of standard clinical care.

Intra-operative collection of specimens: Patients will undergo surgery for resection of their tumors or tumor mimickers according to standard clinical practice. Once the tumor or tumor mimicker is removed and adequate tissue has been sent to pathology for clinical diagnosis, any remaining tissue will be collected directly from the operating room for banking at the discretion of the surgeon. In addition to tissue, a maximum of 60 milliliters of peripheral blood will be collected in the operating room while the patient is under anesthesia. The maximum volume of blood drawn will be at the discretion of the anesthesiologist attending physician. Blood will be drawn by the anesthesiologist from an arterial line, central venous line, or peripheral IV placed as part of routine anesthesia care. In patients who have a lumbar puncture, ventriculostomy, or lumbar subarachnoid catheter placed as part of the operation or as post-operative care, 10-15 milliliters of CSF will also be collected for banking. All specimens will be collected directly from the operating room by an authorized NSTB staff member and taken to the laboratory immediately for processing and storage.

Neuro-oncology clinic blood collection: Patients who present to the neuro-oncology clinic will have the option to contribute clinical data as well as a blood sample. The blood collection will be performed by a trained technician or nurse in the neuro-oncology clinic. A maximum of 30 milliliters of peripheral blood will be collected via venipuncture.

Specimen processing and storage: Tissue specimens will be divided into multiple pieces for

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processing. Tissue pieces will be dehydrated and embedded in paraffin, snap frozen and stored in liquid nitrogen, mechanically dissociated for generation of a primary tumor cell culture, or distributed fresh to researchers with approved protocols as tissue quantity permits. Peripheral blood will be centrifuged on a Ficoll gradient for separation of the peripheral blood leukocytes and plasma, which will be individually collected and frozen separately. CSF will be centrifuged to remove any cellular debris and frozen in liquid nitrogen. Each patient will be assigned a unique coded identifier and specimen tubes will be marked with this coded identifier only. Each tube will also be labeled with a printed barcode in order to readily identify the specimen from the database records using a barcode scanner.

Postmortem tissue collection. Nervous system tumor patients for whom all therapeutic options have been exhausted and death is imminent will be consented to donate their treated tissues in a postmortem study (i.e. autopsy). In such cases, when the patient expires, the body is transported to the morgue at NMH. The NSTB Director will then perform a postmortem study of the brain and spinal cord, banking both tumor and nontumor tissue for future research into mechanisms of therapy resistance. All specimens will be stored in containers with barcoded labels, similar to the surgical specimens described above. In all cases a clinical autopsy report will be issued by the NSTB Director, necessitating access to PHI for the generation of the report. However, once tissues are banked, they will be coded by the NSTB honest brokers and the Director will not retain or have access to the linkage codes.

Pediatric processing and storage. Pediatric patients who are undergoing surgery at Lurie Children's Hospital (LCH) will be asked to consent for research collection under Lurie Children's IRB 2021-4677. Tissue is allowed for transfer from LCH to the NSTB under material transfer agreement JNN SP0070770. The NSTB staff will receive deidentified samples only from the LCH study's honest broker. The NSTB staff, study personnel, and principal investigator will not have access to personal health information for patients consented under the LCH protocol. Processing of blood and tissue will mirror the sample processing described above under "specimen processing and storage." Only the physical location, number of vials, patient deidentification number, and suspected diagnosis of the specimens from LCH will be logged and kept within the NSTB. No other data will be stored within the NSTB.

Archival pathology requests. In some NSTB-supported projects, preexisting archival pathology material will be obtained from the Pathology Department to complement biospecimens collected by the NSTB. Such material will only be acquired when deemed no longer needed for clinical care by the NSTB Director (a board-certified neuropathologist who has an active clinical practice at NMH) and the appropriate Pathology Department committee.

Database. Specimen information and location will be tracked using Biological Specimen Inventory (BSI) II software and REDCap. Access to PHI within the BSI-II database and REDCap will be limited to the NSTB laboratory personnel who serve as honest brokers. BSI-II is a commercially available specimen database licensed and maintained on a secure server managed by the Robert H. Lurie Comprehensive Cancer Center. REDCap is a secure web application supported by NUCATS and the Feinberg School of Medicine (FSM) that will allow researchers access to the NSTB's deidentified biospecimen repository, in order for them to determine the feasibility of their proposed studies.

Specimen requests and distribution. To obtain materials from the NSTB, investigators will complete and submit a form that describes the project, the number and type of specimens requested, and documentation of IRB approval for their specific project. All requests are promptly reviewed by

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the NSTB Director and Lab Manager. Once their IRB approval is verified, requests deemed easily met (e.g. a small number of unstained slides from preexisting paraffin blocks) will be fulfilled promptly. More complicated requests (e.g. large number of fresh tissues, or something that would exhaust the bank's collection of a rare tumor) will be discussed at the monthly NSTB Committee Meeting. This multidisciplinary committee consists of the following members:

- 1.) Craig Horbinski, NSTB Director
- 2.) Priya Kumthekar, adult neurooncologist
- 3.) Atique Ahmed, NBTI Researcher
- 4.) Hui Zhang, biostatistician
- 5.) Dan Brat, Chair, Department of Pathology
- 6.) Michael DeCuyper, pediatric neurosurgeon

Once the committee approves a request, coded samples and matching de-identified clinical variables will be made available. The NSTB staff and clinical coordinators will maintain access to protected health information (PHI), serving as honest brokers. They will also annotate specimens with therapy and outcome data through linkage with the Northwestern Enterprise Data Warehouse (EDW). Neither the NSTB Director nor the investigators supplied by the NSTB will have access to PHI.

DATA AND SPECIMEN BANKING

Written informed consent will be obtained from patients prior to entering the operating room. Consent will be obtained for patients presenting in the neuro-oncology clinic at the time of their appointment. Post-mortem autopsy consent will either be obtained from the patient during end of life care at Northwestern Memorial Hospital or obtained from the next of kin, as described above. The original signed consent for each case will remain in the patient's medical record and a copy will be kept in a secure file cabinet in the NSTB laboratory. Additionally, consent to participate in the study will be logged in NOTIS.

Tissue, blood, and CSF specimens will be processed as described and stored in the secure laboratory located in the Simpson Querrey building. Stored samples will only be accessed by NSTB staff members. All specimens will be labeled with unique barcodes and identified with a coded patient identifier. Each individual specimen will be logged in the BSI II database. Basic patient demographic data will also be logged in the REDCap database for each specimen including patient name, patient age, patient gender, race and ethnicity, results of clinical molecular and genetic testing, date of specimen procurement, histopathological diagnosis, primary or recurrent tumor, treatments, and tumor location. Clinical variables will be obtained from the medical record by authorized NSTB staff. Please see Appendix A for a complete list of data regularly collected for the annotation of biospecimens. Access to PHI will be limited to the NSTB honest brokers. Investigators from Northwestern may be granted access to REDCap, but will only have access to deidentified information. All samples and sample information will be stored indefinitely.

When specimens are accessed for research under IRB approved protocols, only the de-identified information in the REDCap database will be available to investigators. If more clinical information is necessary, clinical data can be requested from the EDW and authorized NSTB personnel will provide authorized EDW personnel the decoded patient list to obtain the approved clinical data. EDW will then provide de-identified results matched to the tissue code to the requesting investigator. If highly specific data is requested that is outside the abilities of the EDW, the NSTB honest brokers will perform patient chart reviews and only share the deidentified data with the researcher. This data would then be collected under the HIPPA release of "all information in a

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medical record” and would be in addition to the standard data collection logged in REDCap as previously described.

Samples arriving from LCH will not have PHI stored or shared with staff in the NSTB. The consent process and all data is managed under Lurie Children’s IRB 2021-4677.

SHARING RESULTS WITH PARTICIPANTS

Patient family members of patients who participate in the autopsy donation portion of this protocol will have the option to discuss the results of the autopsy procedure with members of the NSTB team.. The option for a phone call will be provided to go over the findings of the autopsy in detail with the family and address any questions that may arise.

INCLUSION AND EXCLUSION CRITERIA

- All adult patients with a tumor (benign or malignant) or tumor mimicker in the nervous system who are undergoing surgical resection as part of routine clinical care will be eligible to contribute tumor tissue and blood
- All adult patients presenting to the neuro-oncology clinic with a tumor (benign or malignant) in the nervous system will be eligible to contribute clinical data and blood
- All adult patients with nervous system lesions that either have a preoperative suspicion of being neoplastic, or are suspected of being a non-neoplastic mimicker (e.g. vascular malformations, infection, autoimmune) who are undergoing surgical biopsy and/or resection as part of routine clinical care will be eligible to contribute brain or spine tissue, tissue, and blood
- All adult patients with epilepsy who are undergoing a brain tissue resection for routine clinical management of their epilepsy will be eligible to contribute resected brain tissue and blood
- All adult patients with hydrocephalus undergoing a CSF diversion procedure as part of routine clinical care will be eligible to contribute CSF
- Age ≥18 years
- Female patients who are sexually active and of childbearing potential will be screened for pregnancy per standard pre-operative protocol. If pregnant and surgical intervention is still clinically indicated, patients will be eligible to participate in the current study
- Adults unable to consent will be allowed to participate in the research if a legally authorized representative is present and able to provide consent.

Pediatric patients who consent under Lurie Children’s IRB 2021-4677.

All subjects must have given signed, informed consent prior to registration on study.

PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Study-wide	Adults	Indefinite	10,000

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Total:			10,000
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RECRUITMENT METHODS

Patients presenting for a neurosurgical procedure for the treatment of a nervous system tumor, a tumor mimicker, epilepsy, or hydrocephalus will be screened for inclusion in this study. Patients who meet the inclusion criteria will be consented for participation in the tumor tissue bank at the time of consent for the surgical procedure.

Patients who present to the neuro-oncology clinic at Northwestern Memorial Hospital as part of an outside consult, seeking additional treatment, or who otherwise have not undergone surgical intervention at NMH will also be screened for inclusion in this study. Consent will be presented to these patients by the neuro-oncology attending physician at the time of the clinical appointment.

Patients returning for end of life care who have previously participated in the tumor tissue bank or received treatment at Northwestern Memorial Hospital will be consented for participation in the post-mortem procedure using a separate, postmortem tissue donation, consent form. If the patient is unable to give consent due to diminished cognitive ability, the patient’s POA or next of kin may act on their behalf.

All recruitment practices for pediatric brain tumor samples is housed within Lurie Children’s IRB 2021-4677.

WITHDRAWAL OF PARTICIPANTS

If a patient wishes to withdraw from this research, a written request must be sent to the primary investigator as described in the consent form. The NSTB staff will then review the distribution and use of the patient’s tissue samples, if any, and work with the patient to meet their wishes. If requested, stored samples will be destroyed.

RISKS TO PARTICIPANTS

There are no additional physical risks to patients undergoing standard of care surgical procedures if they choose to participate. This research does not require any additional procedures to take place for surgical patients. There is a minimal risk of discomfort during the venous blood draw for patients presenting in the neuro-oncology clinic. Patients seen in the clinic will have the option to opt-out of the blood draw. There is a chance of loss of confidentiality with the collection of personal health information, but measures are in place to minimize this risk.

The autopsy donation procedure will not affect any funeral plans that may be in place.

POTENTIAL BENEFITS TO PARTICIPANTS

There are no direct benefits to participants in the research.

DATA MANAGEMENT AND CONFIDENTIALITY

There is no data analysis plan for this research.

As previously described, all electronic PHI will be tracked and stored on the secure FSM servers, NOTIS and REDCap. Access to PHI and the linkage code for deidentification within the FSM folder for the NSTB and the NSTB REDCap project will be limited to the NSTB honest brokers. Additionally, all patients have been given a secondary case ID for upload to NOTIS since other clinical

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coordinators are able to view this information. The linkage code for this secondary case ID to the NSTB ID is only accessible to the honest brokers of the NSTB.

As described previously, samples arriving from LCH will not have PHI stored or shared with staff in the NSTB.

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS

The consent form describes the groups that may have access to PHI and sample information collected from each patient. Only appropriate groups or individuals, such as the EDW, will ever be given PHI for the purposes of research or data collection. No one, other than the NSTB honest brokers, will be given or have access to the linkage code for deidentification.

The research team has been granted access to the Northwestern Memorial Hospital facilities as well as EPIC for the collection of patient samples and patient data. The appropriate EDW exemptions are on file for each NSTB staff member with EPIC access.

CONSENT PROCESS

Consent for this study will be obtained by a physician (attending or resident) or advanced practice nurse who is part of the clinical treatment team. The consent form will be discussed with the patient and any questions will be addressed immediately. Consent will be obtained during pre-operative care, prior to the scheduled procedure for surgical patients or in the neuro-oncology clinic for patients who have not yet presented for surgical intervention at NMH. If a patient is unable to give consent due to diminished cognitive ability, the standard hospital procedures for allowing a healthcare agent to act on their behalf will be utilized. This determination will be made by the physician obtaining consent who is trained on the hospital's standard procedures of consent. Patients returning for additional neurosurgical procedures will not require re-consenting so long as subsequent biospecimen collections are from surgical procedures related to the procedure for which consent was initially obtained (e.g. re-resection of a recurrent glioma after therapy). The patients are informed that they may withdraw their consent at any time.

Patients returning for end of life care who have previously participated in the tumor tissue bank or received treatment at Northwestern Memorial Hospital will be consented for participation in the post-mortem procedure using a separate, postmortem tissue donation and consent form. If a patient expires outside of Northwestern Memorial Hospital without an opportunity to obtain consent for postmortem tissue donation, the option to consent will be presented to the next of kin as per standard clinical practice. However, if the patient had been asked to consent but declined, the next of kin will not be asked and no postmortem tissue will be banked. Consent will be obtained either by a physician (attending or resident), advanced practice nurse who is part of the clinical care team, or a member of the NSTB staff. In most cases, study documents and consent paperwork is provided to the patient and the family prior to the patient expiring. Patients and their family are given time to consider the option of donation, however the patient may pass prior to the completion of the paperwork. In these instances, the POA or next of kin may act on behalf of the patient.

All consent practices for pediatric brain tumor samples is housed within Lurie Children's IRB 2021-4677 and will be done by their study personnel.

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)

HIPPA Authorization will be obtained from all participants at the time of consent. This study will collect and store the following PHI:

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- Names
- Date(s) of birth, admission, discharge, surgery, age, and death
- Medical record numbers
- Results of molecular or genetic testing performed on the tumor tissue as part of standard of care
- Treatment dates and forms of treatments

NON-ENGLISH-SPEAKING PARTICIPANTS

If a translator is provided to the patient per standard hospital practice, that translator may act along with the physician to obtain consent. This is aligned with the hospital's standard practice of providing a translator fluent in the patient's preferred language for the completion of health documents.

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE

The Nervous System Tumor Bank employs experienced lab staff as well as a histology technician. New staff members are trained by the lab manager and director to ensure understanding of the protocols and procedures.

The NSTB is located in the Simpson Querrey building and includes equipment required for the collection and processing of patient samples. This includes three biological safety cabinets, several work benches, three centrifuges, two -80°C freezers, two liquid nitrogen freezers, two 4°C refrigerators, two -20°C freezers, and an assortment of other laboratory supplies and shared equipment.

Appendix A

Characteristics of data

Specimens are collected and then immediately de-identified by the honest brokers of the NSTB. Unique identifiers are assigned to each specimen as NUXXXXX, for example NU00787, NU01253, etc. Some data points are collected on a routine basis from the medical record and logged in REDCap. These variable are as follows:

Patient Information and demographics: name, DOB, age, surgical date, gender, race, ethnicity

Clinical information: diagnosis, treatment received, available molecular panels (i.e. IDH status, HR/PR/ER status, Next Generation Sequencing, methylation profiling, etc.)

Internal data: Number of cryovials collected from blood processing, tumor or vascular tissue, CSF processing, establishing cell cultures, and/or, the creation of fixed formalin paraffin embedding tissue blocks

All data is stored on the FSM secure servers in access protected folders. The linkage code for deidentification is only accessible to the honest brokers of the NSTB. Data is then uploaded to the NSTB REDCap project where PHI is only accessible to the NSTB honest brokers.