PROTOCOL TITLE: Nervous System Tumor Bank

PRINCIPAL INVESTIGATOR:
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VERSION NUMBER:
5

VERSION DATE:
April 19, 2018

STUDY SUMMARY:

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

OBJECTIVES:

1. To bank human nervous system (brain and spinal cord) tumor and tumor-mimicking tissues (e.g. vascular malformations) resected from patients treated at Northwestern Memorial Hospital 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 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 tumor research. Tissue from each patient will be stored as frozen and paraffin-embedded tissue. Peripheral blood will be separated into...
peripheral blood mononuclear cells and plasma and frozen.

3. To collect cerebrospinal fluid from patients undergoing CSF diversion for hydrocephalus. 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 bank post-mortem tissue from patients who have previously been treated at Northwestern Memorial Hospital for nervous system tumor resection.

5. 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 cancer, 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 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 will also have CSF stored as a frozen sample. 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.

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 according to standard clinical practice. Once the tumor 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, 40 mL of peripheral blood will be collected in the operating room while the patient is under anesthesia. 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 ventriculostomy or lumbar subarachnoid catheter placed as part of the operation or as post-operative care, 10-15 mL of CSF will also be collected for banking. All specimens will be collected directly from the operating room by an authorized technician from the NSTB and taken to the laboratory immediately for processing and storage.

Specimen processing and storage: Tissue specimens will be divided into multiple pieces for 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 autopsy suite 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.
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 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 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.) C. David James, NBTI Research Director
3.) Orin Bloch, adult neurosurgeon
4.) Rintaro Hashizume, NBTI Researcher
5.) Priya Kumthekar, adult neurooncologist
6.) Atique Ahmed, NBTI Researcher
7.) Denise Scholtens, biostatistician
8.) Dan Brat, Chair, Department of Pathology

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. 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 Tarry 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, and tumor location. Clinical variables will be obtained from the medical record by authorized NSTB staff. Access to PHI will be limited to the NSTB honest brokers. Investigators from Northwestern as well as outside institutions 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.

**INCLUSION AND EXCLUSION CRITERIA**

- All adult patients with a tumor (benign or malignant) 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 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.

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

**PARTICIPANT POPULATION(S)**

<table>
<thead>
<tr>
<th>Accrual Number:</th>
<th>Category/Group: (Adults/Children Special/Vulnerable Populations)</th>
<th>Consented: Maximum Number to be Consented or Reviewed/Collected/Screened</th>
<th>Enrolled: Number to Complete the Study or Needed to Address the</th>
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**IRB #: STU00095863-MODCR0001 Approved by NU IRB for use on or after 5/21/2018 through 5/20/2019.**
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 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.

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 if they choose to participate. This research does not require any additional procedures to take place. There is a chance of loss of confidentiality with the collection of personal health information, but measures are in place to minimize this risk.

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 in NOTIS and REDCap. Access to PHI within REDCap will be limited to the NSTB honest brokers.

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. PHI will only be shared with those who have appropriate need to know and approval.

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. 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 by a physician (attending or resident), advanced practice nurse who is part of the clinical treatment team, or the NSTB Lab Manager.

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:
- 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

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.

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 Tarry building and includes equipment required for the collection and processing of patient samples. This includes two biological safety cabinets, several work benches, three centrifuges, a -80°C freezer, two liquid nitrogen freezers, two 4°C refrigerators, one -20°C freezer, and an assortment of other laboratory supplies and shared equipment.