



NICO Corporation Neurosurgical Clinical Areas of Interest or "AOIs"

High Level Tumor AOIs

- 1. Areas of interest in tumor include all primary and secondary tumors.
- 2. Evaluating the clinical impact of NICO technologies in the following surgical approaches:
 - a. Minimally Invasive Parafascicular Surgery "MIPS"
 - b. Endoscopic
 - c. Expanded Endo Nasal/Skull base
 - d. Open
- 3. Evaluating the clinical impact of NICO's technologies in combination with other technologies such as imaging, tissue differentiation technologies and drug delivery etc.

High Level Enabling NeuroOncology and Precision Medicine AOIs

- 1. Areas of interest in NeuroOncology include:
 - a. Evaluating the impact of immediate intraoperative biological tissue and microenvironment preservation in the preanalytical phase on the quality and value of tissue obtained
 - b. Evaluating the impact of increased volume and regionalized sampling to improve the viability of heterogeneous tissue collected for research, assay testing & novel therapeutic development/testing
 - c. Evaluating the benefit of standardizing the tissue collection and biological process from a scientific and operational impact

High Level Vascular AOIs

- 1. Areas of interest in vascular include ICH, IVH, and Cavernous Malformations.
- 2. Evaluating the clinical impact of NICO technologies in the following surgical approaches:
 - a. Minimally Invasive Parafascicular Surgery "MIPS"
 - b. Endoscopic
- 3. Evaluating the clinical impact of NICO's technologies in combination with drug delivery
- 4. Clinical investigation toward advancing intervention and care for traumatic ICH
- 5. For post-ENRICH related AOIs, please visit the ENRICH Investigator Initiated Study Page (link)

High Level Economic and Operational Efficiency AOIs

- 1. Surgical treatment conversions via the use of NICO technologies:
 - a. Non-operable to operable
 - b. Conventional to MIPS, Endoscopic or EEA
 - c. Elimination of secondary procedures (no cranioplasty)
- 2. MIPS surgeon's value to the healthcare system & impact to practice & patient
- 3. Surgical efficiencies as an economic measure

High Level Future and Miscellaneous AOIs

- 1. Development of new teaching or practice models for neurosurgery
- 2. Novel uses or applications for brain access or therapeutic delivery using NICO's technologies
- 3. Evaluating the long-term impact of MIPS surgery versus conventional on cognitive recovery
- 4. Evaluating the impact of the reduction or elimination of post corticosteroids with MIPS





NICO Corporation Neuro Pre-Clinical Areas of Interest or "AOIs"

Intracranial, Extracranial, Malignant or Benign Investigation

High Level AOIs for Various Tumors and Abnormalities

- 1. Progress of disease, biological changes, or therapeutic response without animal sacrifice measuring:
 - a. Metabolic profiles, stability of individual metabolites, and global metabolic function
 - b. Chemokines/cytokines
 - c. Drug levels of intact abnormality throughout disease intervention
- 2. Standard of maintaining tissue quality and microenvironment/immune environment to advance research:
 - a. Volume of tissue/cells obtained
 - b. Accuracy of needle placement and subsequent regions
 - c. Tumoral cellular yield
- 3. Identification of potential therapeutic targets for post-resection intracavity delivery beyond the blood brain barrier and cellular architecture
- 4. Biologically preserved regionalized tissue collection and annotation confirmed by molecular/genetic measures

High Level Enabling Oncology and Precision Medicine AOIs

- 1. Standardized method for tissue transfer cross-institutionally while maintaining biological integrity of samples for increased collaboration
- 2. Development of live tissue/new-age biobanking against historical techniques and challenges
- 3. Investigation of unique markers from active biological tissue toward enhanced methods of tissue differentiation via imaging, fluorescence, or other novel concept
- 4. Variety of high-quality fresh tissue PDX models or avatars enabling research to increase understanding in molecular biomarkers and tissue microenvironment/immune environment
- 5. Longitudinal genomic profiling to understand impact of initial treatment at molecular level providing information on mutation of primary disease and impact on treatment adjustment
- 6. Intracavity delivery and/or evaluation of novel therapeutics

High Level Vascular AOIs

- 1. Potential pathophysiological targets in tissue (obtained via APS) for attenuating secondary injury
- 2. Options in development and intracavity delivery of neuroprotective agents or other therapeutics following ICH removal based on biomarker observation
 - a. Toxicity and dosing
 - b. Delivery beyond the blood brain barrier and cellular architecture

High Level Economic and Operational Efficiency AOIs

- 1. Extended survival of pre-clinical models from patient derived tissues
 - a. Efficient, reproduceable, standardized methods of serial biopsy over disease progression in one animal
 - b. Evaluate economic impact of long-lasting tissue models
- 2. Measure of operational differences of APS versus traditional laboratory techniques and correlation to economic impact
 - a. Tissue harvest
 - b. Sample preparation/processing
 - c. Growth and culture
 - d. Animal model survivability

High Level Future and Miscellaneous AOIs

- 1. Observations matched to scientific data on impact of instrumentation and other environmental factors on key protein and genetic information
- 2. Projects related to facilitating direct delivery or placement of:
 - a. Targeted therapeutics bypassing blood brain barrier/cellular architecture
 - **b.** Brain computer interface