RESEARCH OPERATIONS AND CLINICAL RESEARCH

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Allina Health, Neuroscience Research

December 11, 2023

Allina Health

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Disclosures

- Employed by Allina Health Research.
- No other disclosures.

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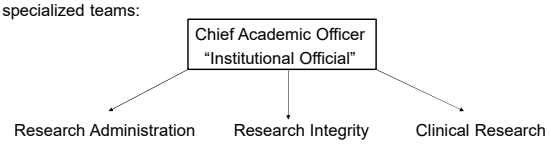
Introduction

Operating a research program within a healthcare organization takes a village of specialized teams:



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Research Administration & Operations

- Contracts: Specialized legal team handling agreements between AH Research, Investigators, and Funding Organizations/Industry Sponsors.
  - examples: NDAs, Clinical Trial Agreements, Intellectual property
- Grants and Finance: Identify federal and state funding opportunities, assist clinical researchers with applications, manages $ spending and cost reimbursement. Negotiates budgets for the cost of carrying out sponsored clinical trials (cost to healthcare organization and patient compensation).
- Research Billing: clinical trial billing is complex, with some activities standard of care – billed to insurance/payors, some covered by sponsors, some as a cost to the healthcare organization.
- Clinical Research Informatics and Analytics (CRIA): data analysts assisting with prep-to-research, large scale data pulls, statistical analyses.

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Research Integrity

- Human Research Protection Program (HRPP).
  - Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected;
  - Provide guidance and support to the research community in the conduct of research with human subjects;
  - Assist the research community in ensuring compliance with relevant regulations;
  - To provide timely and high quality review and oversight of human research projects; and
  - To facilitate excellence in the conduct of human subjects research.
- Allina Health Institutional Review Board (IRB)
  - Appointed by the Institutional Official (IO).
  - Prospectively reviews and makes decisions concerning all human research conducted at Allina Health facilities, by its employees or agents, or under its auspices.
  - Responsible for the protection of rights and welfare of human research subjects at Allina Health, through review and oversight of safe and ethical research.
  - **The IRB functions independently of, but in coordination with, other organizational committees and officials. The IRB, however, makes its independent determination whether to approve or disapprove a research plan based upon whether human subjects are adequately protected.**

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Clinical Research Houses

Partnered with institutes and service lines at Allina Health

- Neurosciences Research ←We are here.
- Mental Health & Addiction Services Research
- Cancer Research
- Courage Kenny Rehabilitation Research
- Orthopedics Research
- Nursing Research
- Care Delivery Research
- Mother Baby Research
- EMS Research
- Cardiology (through MHIF) & Spine (through TC Spine)

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Neurosciences Clinical Research Team

- Director & Manager of Clinical Research: Operational leadership of multiple research houses. Interface with Research Operations and Integrity.
- Project Manager Clinical Research: New study start up through interface with clinical and operational areas, oversight and management of studies/projects throughout the life of the project.
- Regulatory Specialist: all regulatory submissions, communications with IRB, and regulatory documentation management.
- Research Nurse: specialty patient care in accordance with clinical trial protocols as delegated by the principal investigator, including: assessment, care coordination, education, data collection, chart review. ←more on research nursing to follow!
- Research Coordinator: manages and conducts the day-to-day activities of a clinical trial in accordance with protocol as delegated by PI. Liaison with the clinical site, recruiting and consenting participants, maintaining study guidelines, and collecting and/or reviewing the data or review before it is entered into a study database.

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Neurosciences Research Areas

- Stroke Neurology
- Neurophysiology
- NeuroOncology & Neuro Pathology
- Neuro Interventional Radiology
- Neurosurgery

As of November: 21 active studies; 7 pending startup.

Neuro Research Growing with the AHNSP Institute! Looking forward to adding:

- Dementia Neurology
- Epilepsy

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CLINICAL RESEARCH AND RESEARCH NURSING

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Nurse Researcher

Allina Health, Neuroscience Research

December 11, 2023

Allina Health

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Introduction

Researcher Focus

- Neuro-Oncology Clinical Trials & Registry Studies
  - Primary & Recurrent Brain Cancer
    Glioblastoma, Grade 4 Astrocytoma, Gliosarcoma, Meningioma, Brain Mets
  - Adult population

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Disclosures

- We have nothing to disclose

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Objectives

- Types of Research & Research Studies
- Clinical Research & Clinical Research Nursing
- Why is Research Important
- Barriers and Challenges
- Diversity and Inclusion
- Neuro-Oncology Research Trials at Allina

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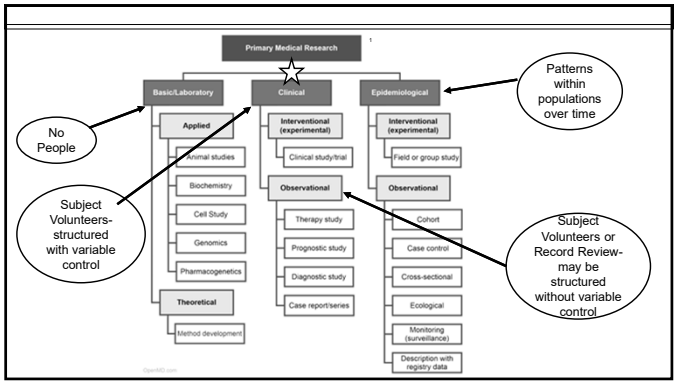

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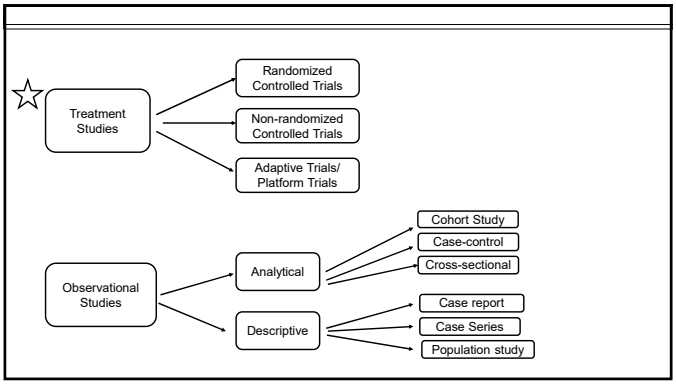

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Clinical Trial

- New ways to prevent, detect, or treat disease [2]
  - New drugs
  - New drug combinations
  - New surgical techniques
  - New medical devices
  - New ways to use existing treatments
  - New ways to change behaviors for health improvement
  - New ways to improve quality of life for people with acute and chronic illness

GOAL: Safety and Effectiveness

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Why is Clinical Research Important?

- Innovation
- Diagnosing, treating, curing, and/orpreventing disease
  - Unsuccessful research contributes to knowledge
- Informs evidence-based practice
- Involves participants in their care
- All treatments must be fully researched before being adopted in practice

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Why Participate?

- Hope
- Helping others
- Science
- Personal
- New treatments
- Financial
- Additional support from research team
- No other treatment options or option preservation

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Barriers and Challenges

- Trials take YEARS to complete[3] (March 2022)
  - Avg 12 years for drugs
  - Avg 7 years for devices
- Drug development-market costs[4] (2020)
  - $1.3 billion- 1.8 billion for drug development to market
- Not guaranteed to work as intended
- Unknown risks and side effects
- Location & transportation
- Insurance/ Finances
- Inclusivity
- Patient support

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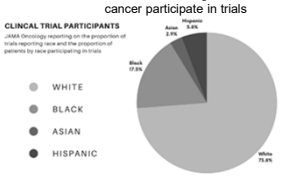
Diversity, Inclusion, and Representation

Greater diversity = Better data ⟹ Better Treatments

- People experience disease differently- research must reflect our population
  - race, ethnicity, gender, age, ability, sexual orientation, socioeconomic status, education, health
- Advancements benefit those with access
- Immense history of unethical research leading to justifiable mistrust in medicine and research

2019

<5% of adults diagnosed with cancer participate in trials



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Phases of a Clinical Trial

Preclinical- Drug/treatment development

Phase 1	Phase 2	Phase 3	Phase 4
Safety & dosage determined	Efficacy & Side Effects- Limited Population	Effectiveness & Comparisons- Larger Population	Post-Approval Effectiveness & Safety- thousands
<100 people	100-300 people	300+ people	

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What is a Clinical Research Nurse?

National Institute of Health:

- "Clinical research nursing is nursing practice with a specialty focus on the care of research participants. In addition to **providing and coordinating clinical care**, clinical research nurses have a central role in assuring **participant safety**, ongoing maintenance of **informed consent**, integrity of **protocol implementation**, accuracy of **data collection**, data **recording** and follow up. Care received by research participants is driven by study requirements and the collection of research data as well as clinical indications. Study procedures may include administration of **investigational drugs**, performance of an experimental or investigational surgical or radiological procedure, detailed **clinical assessment** or phenotyping to characterize the natural history and etiology of a disease, or delivery of a psychosocial intervention. Additional nursing **care may be necessitated by the response of the participant** to the study intervention."

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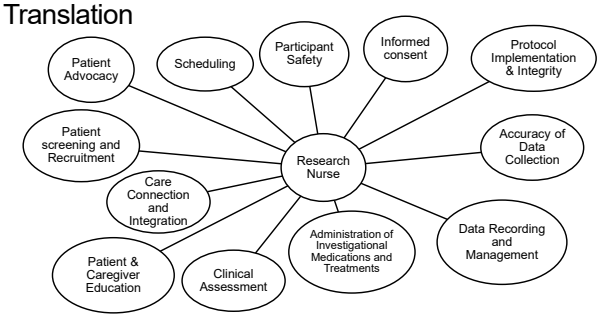
Translation



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How Do We Know What To Do?

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The Protocol!

Detailed plan describing how the trial will be conducted.

- Background Information & Rationale
- Objective
- Study Design
- Drug & Device Information
- **Subject inclusion and Exclusion**
- Treatment of Subjects
- **Study Visit Calendar**
- Evaluation Criteria
- Clinical Assessment
- Efficacy
- **Safety**
- **Adverse Events**
- Discontinuation
- Statistics
- Quality Control
- Ethics
- Data Management
- Supplemental Documents or Appendices

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Eligibility Criteria

Define patient population for reliable, reproducible results, minimizing harm to subjects

- Inclusion Criteria: Objective, consistent, and reliable to target intended study population
- Exclusion Criteria: Characteristics for disqualification including comorbidities, concomitant treatment, medications, or infection

- Age
- Diagnosis & pathology
- Treatment history
- Labs/ tests
- Medication interactions
- Chronic Conditions/Comorbidities
- Ability to give consent
- Extent of disease

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Starting a Patient on a Trial

- Pre-screening
- Provider notification
- Patient discussion
- Subject consent
- Register patient into the study
- Screening procedures
- Subject randomization
- Subject consent (treatment)

Eligibility Criteria

⇨ Begin treatment trial activities

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Screening Procedures

- Clinic Visit & Vitals
- Physical & Neuro Exam
- Karnofsky Performance Score
- Tumor Pathology
- Labs
- EKG
- MRI
- Medical History
- Demographics
- Medication List
- Survey
- Neuro Cognitive Testing
- Adverse Events Profile
- Insurance Coverage
- Financial Assistance

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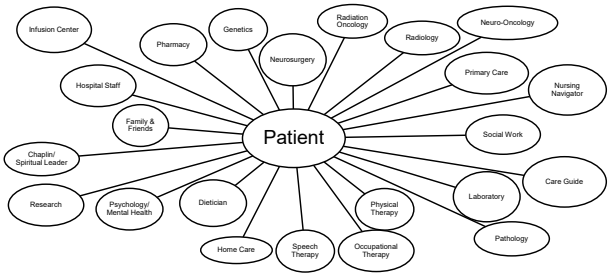
Interdisciplinary Team



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Neuro-Oncology Studies at Allina Health

- Denovo DB-102
- TRIDENT EF-32
- GBM AGILE
- GammaTiles Registry
- GammaTiles ROADS

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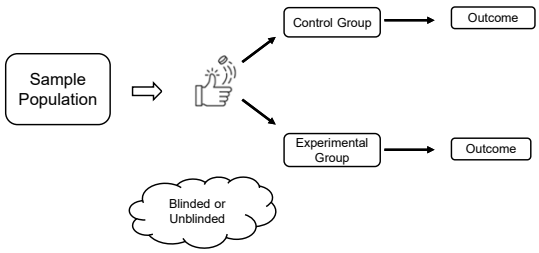
Randomized Clinical Trial



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DENOVO Biopharma ENGAGE DB102-01

DB102-01 : A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Enzastaurin Added to Temozolomide During and Following Radiation Therapy in Newly Diagnosed Glioblastoma Patients Who Possess the Novel Genomic Biomarker DGM1

- Randomized, Double-Blind
- Newly Diagnosed Glioblastoma
- Tumor Biomarker: DGM1
- Phase 3
- Treatment: Enzastaurin (oral) or Placebo + Standard Chemoradiation
- Study Length: 2 years

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Novocure TRIDENT EF-32

A Pivotal Randomized, Open-Label Study of OPTUNE® (TTFields, 200 kHZ) Concomitant with Radiation Therapy and Temozolomide For the Treatment of Newly Diagnosed Glioblastoma

- Randomized, Unblinded
- Newly Diagnosed Glioblastoma
- Phase 3
- Treatment: Optune Device (standard or experimental) + Standard Chemoradiation
- Study Length: 24 months

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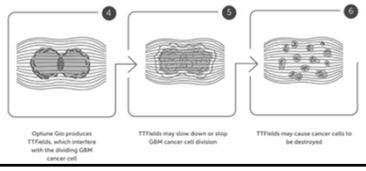
Optune Device

TTFields interfere with GBM cancer cell division

Optune Gio uses TTFields, which are electrical fields that may stop cancer cells from pulling apart. This helps slow tumor growth. Additionally, Optune Gio may even destroy existing cancer cells.

- Portable, noninvasive device
- TTFields are low-intensity (1-3 V/cm), intermediate-frequency (200 kHz), alternating bi-directional electrical fields to disrupt cell division
- Transducer arrays on scalp



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GBM AGILE- Adaptive Global Innovative Learning Environment

GBM AGILE Global Adaptive Trial Master Protocol: An International, Seamless Phase II/III Response Adaptive Randomization Platform Trial Designed To Evaluate Multiple Regimens In Newly Diagnosed and Recurrent Glioblastoma (GBM)

- Randomized, Unblinded
- Adaptive/Platform Trial
- Newly Diagnosed OR Recurrent Glioblastoma
- Seamless Phase 2/3
- Treatment: Experimental or Control- depends on treatment available at time of randomization
- Study Length: 24 months

Treatments: Regorafenib (Oral), Paxalisib (Oral), VAL-083 (IV), VT-1021 (IV), Troriluzole (Oral), ADI-PEG20 (IM)

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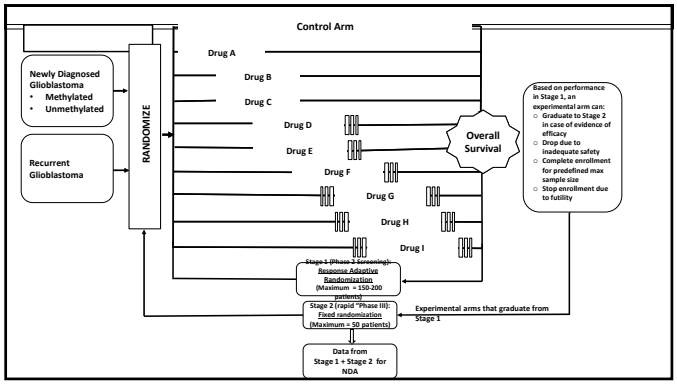

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GammaTiles

STaRT Registry GTM-101: Multicenter Observational Study of GammaTile™ Surgically Targeted Radiation Therapy (STaRT) in Intracranial Brain Neoplasms

- Unrandomized
- Observational Study
- Brain Cancer
- Phase 4
- Treatment: GammaTile
- Study Length: 5 years

ROADS Clinical Trial GTM-102:A Phase 3 Randomized Controlled Trial of Post-Surgical Stereotactic Radiotherapy (SRT) versus Surgically Targeted Radiation Therapy (STaRT) with Gamma Tile for Treatment of Newly Diagnosed Metastatic Brain Tumors.

- Randomized, unblinded
- Clinical Trial
- Metastatic Brain Cancer
- Phase 3
- Treatment: Surgery with radiation or surgery with GammaTile + Standard of care drug therapy
- Study Length: 4 years

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GammaTile Registry

GammaTile ROADS Trial

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NIH STROKENET RESEARCH

Max Klaiman, Project Manager
December 11th, 2023

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What is StrokeNet?

- Trial Network created by the NIH
- Designed to conduct clinical trials in three main Stroke areas:
  - Acute Treatment
  - Stroke Prevention
  - Rehabilitation
- Over 500 hospitals in the US participate in StrokeNet Trials

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StrokeNet within Allina Health

- Allina Health's participation in StrokeNet began in 2018
- StrokeNet has a multi-layered structure:
  - Funded centrally through the University of Cincinnati
  - There are 27 Regional Coordinating Centers (RCCs) which can interact with more local healthcare systems
  - Each of the 500 hospitals participating in StrokeNet studies are part of one of the 27 RCCs
- We are part of the UMN RCC
  - Historically alongside Fairview, Regions, Essentia, MPLS Childrens, KU Medical Center*, and St. Louis University*

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StrokeNet Trials at Allina Health

- Neuroscience Research has participated in 9 StrokeNet trials since joining the network in 2018, at all three Metro Hospitals
  - ARCADIA
  - ARCADIA-CSI
  - ASPIRE
  - CAPTIVA
  - FASTEST
  - RHAPSODY-2
  - SATURN
  - SISTER
  - SLEEP-SMART

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Trial Highlight: ARCADIA

- ARCADIA was a trial looking at aspirin vs. apixaban for secondary stroke prevention in patients with ESUS and evidence of Atrial Cardiopathy
- More than 1000 patients were randomized over 5 years into the trial
- The study completed in early 2023, and it was determined that Eliquis was not more effective at preventing secondary stroke in this patient population
- United Hospital was a top-enrolling site, with over 50 enrolled patients over the life of the trial

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Trial Highlight: FASTEST

- The FASTEST Trial is seeking to establish the first treatment for acute spontaneous ICH, within 120 minutes from stroke onset
- Patients are randomized to rFVIIa infusion vs. placebo and standard therapy for their ICH
- Study-wide, FASTEST is looking to enroll 860 participants across 100 hospitals
- We look forward to opening this trial in early 2024, and offering this treatment to our patients!

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Summary

- StrokeNet continues to grow, and we are expecting to qualify for and open additional studies into 2024 and beyond
- The work done by the NIH-funded research network is the start of offering ground-breaking treatment options to our patients
- Allina Health remains a key contributor in our UMN RCC, and we hope to expand our participation in the network in the years to come

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Questions?

- StrokeNet's Website: https://www.nihstrokenet.org/

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THANK YOU

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