The Use of AI in Pediatric Congenital Heart Disease: How Far Have We Come?

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OBJECTIVES/GOALS: Artificial Intelligence (AI) is gaining popularity in a variety of disciplines. While clinical applications for AI have increased in recent years, the use of AI in pediatric congenital heart disease (CHD) is limited. The goal of this systematic review was to assess how AI is currently used in this patient population and to describe knowledge gaps. METHODS/STUDY POPULATION: A systematic search was performed up to July 2023 using PubMed and Scopus databases and revealed 814 articles. Upon initial screening, 161 duplicates, 76 non-AI articles, and an additional 318 irrelevant articles were removed. A total of 259 full-text articles were reviewed for relevance. Articles that did not include a retrospective or prospective review of human subject data were excluded. Articles that had only results in the adult, prenatal, or non-CHD population were excluded. The remaining 68 articles were included in this review. RESULTS/ANTICIPATED RESULTS: Of the 68 articles in this review, 19 were performed within cardiac surgery, 41 were within cardiology, and the remaining 8 included articles were combined cardiac surgery and cardiology. Upon initial review, 24 used AI for diagnostic purposes, 40 for predicting survival or adverse outcomes, 2 for developing training tools, and 2 for surveillance of CHD trends. We anticipate that upon further review of these 68 articles, there will be a wide variety in the types of AI models that were used. The results will reveal a multitude of challenges and limitations that future studies will need to further address. DISCUSSION/SIGNIFICANCE: While technical innovations in pediatric CHD have dramatically improved survival rates, we have hit a plateau in improving the complications of these patients. AI has created an opportunity to build new diagnostic, predictive, teaching, and surveillance tools for advancing CHD care, but it seems we still have a long way to go.

Exploring the Iterative Clustering for Subtype Discovery (iKCAT) Algorithm for Robust Computer-Aided Diagnosis of Lung Cancer

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OBJECTIVES/GOALS: With a growing interest in tailoring disease diagnosis to each individual as opposed to a "one-size-fits-all" approach, our aim is to enhance the robustness of the Iterative Clustering for Subtype Discovery (iKCAT) algorithm in characterizing lung cancer subtypes for individualized treatment. METHODS/STUDY POPULATION: Our method explores the robustness of the previously developed iKCAT algorithm. This 323

iterative clustering method finds robust-homogeneous and differentiable-subtypes of lung nodules through iterative K-means clustering that helps classify them and leaves some data unclustered. This set of unclustered or "hard" data represents images that cannot confidently be assigned to any subtypes and may require more resources (e.g., time or radiologists) to diagnose. We explore the robustness of iKCAT across multiple feature spaces, including designed image features (which are engineered to capture some properties such as level of elongation, eccentricity and circularity), reduced designed image features using Principal Component Analysis (PCA) and Uniform Manifold Approximation and Projection (UMAP). RESULTS/ ANTICIPATED RESULTS: When running our experiment on the 64 image features, our results consistently carved out a single pure, homogeneous cluster over the course of 30 iKCAT runs. From an initial dataset of 1490 data points, 1430 points were left unclustered in this feature space. When conducting the 30 iKCAT runs on the PCA feature space with 10 components, we found it did not produce any distinct cluster above the defined homogeneity threshold. The 2D UMAP feature space consistently generated 8 clusters with an average homogeneity of 87. 22% over 30 runs, and only left 9 points unclustered. Over 30 iKCAT runs, we identified 8 persistent clusters or subtypes, 3 mostly malignant and 5 mostly benign clusters. DISCUSSION/SIGNIFICANCE: Through our experiment using the iKCAT algorithm, we found that iKCAT's clustering functionality produced the most persistent results on the 2D UMAP feature space due to its high average homogeneity scores and consistency in identifying clusters/ subtypes, helping improve tailored disease diagnosis.

Applying MeSH Tree Structures and Condition-to-MeSH Mapping to Catalog and Characterize Clinical Trials Research Focus Areas

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OBJECTIVES/GOALS: Characterizing and analyzing research studies presents several challenges given the various ways studies may be labeled or organized. The Medical Subject Headings (MeSH) thesaurus is a hierarchical vocabulary that can index and organize research foci using common business intelligence tools to enable rapid exploration of research portfolios. METHODS/STUDY POPULATION: Metadata from ClinicalTrials.gov on 455,437 trials were downloaded and all MeSH terms associated with trials in the condition_browse section were loaded into a database. The corresponding MeSH trees for each term were then identified and mapped to their ancestor terms within the tree. Trials were then indexed based on top four hierarchical levels for each associated MeSH term. Trials performed at the University of Miami (UM) were identified based on locations associated with the trial as well as matching National Clinical Trial

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(NCT) numbers identified from internal research administration systems. Business intelligence software (Microsoft PowerBI) was applied to the corresponding dataset to enable end user exploration and analysis of the trials within ClinicalTrials.gov. RESULTS/ ANTICIPATED RESULTS: A total of 3,271 studies associated with UM were identified, of which, 3,054 (93.3%) had at least one condition MeSH term linked. A total of 7,711 MeSH terms were associated with the trials overall, representing 1,112 unique MeSH terms; the most common terms were carcinoma (164), lymphoma (155), HIV Infections (139), neoplasms (136), and leukemia (122). Utilizing MeSH hierarchy, trials were characterized were categorized into 36 different trees. The most common top tree nodes were neoplasms (1,181), followed by pathological conditions/signs and symptoms (913), immune system diseases (574), nervous system diseases (513), and digestive system diseases (483). Within trees, a total of 184, 681, and 1057 different MeSH terms were specified at the second, third, and fourth nodes in the hierarchy respectively. DISCUSSION/SIGNIFICANCE: Utilizing existing metadata from trials posted on ClinicalTrials.gov and MeSH tree structures can enable organizations to readily explore the foci of clinical trials research. High rates of MeSH term association to research study conditions are necessary to ensure adequate representation of research foci.

An umbrella protocol that establishes an enterprise-wide framework for the operation of a Clinical Data Warehouse

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OBJECTIVES/GOALS: To streamline the standards and procedures for operating a research-specific, clinical data warehouse, acheived by defining roles, introducing a common language, and categorizing dataset types to provide transparency regarding data security risks inherent in the use of patient data. METHODS/STUDY POPULATION: We established a Bioethics committee responsible for ensuring clinical data is securely procured, maintained, and extracted in a manner that adheres to all federal, state, and local laws. We created an operational framework in the form of an umbrella IRB protocol and shared it with the bioethics committee for feedback and approval. The protocol was approved first by the bioethics committee and subsequently by the IRB. It was then disseminated across the institution and published online for continuous reference and use by committee members, researchers, and the data warehouse service team. RESULTS/ANTICIPATED RESULTS: The resulting framework defined the roles of researchers, data warehouse service team members, and honest brokers; explains the procedures for accessing and securely delivering data; and lists six categories of datasets according to type and implicit risks: datasets that are preparatory for research/aggregate counts, anonymized datasets, coded datasets, limited datasets, identified datasets for recruitment purposes, and defined identified cohort datasets. The protocol is approved and in use enterprise-wide, has reduced the number of questions from stakeholders, and has given researchers, IRB members, and informatics staff confidence in the use of the clinical research data warehouse. DISCUSSION/SIGNIFICANCE: We offer our framework to CTSAs interested in streamlining their data warehouse operations. We believe the adoption of this framework will establish strong procedures for ensuring compliance with IRB requirements, data privacy, and data security while reducing barriers to clinical research.

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Other

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Tyrosine kinase inhibition reduces pathological markers of Alzheimer's Disease*[†]

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OBJECTIVES/GOALS: Alzheimer's Disease (AD) displays numerous pathological features, including amyloid-beta deposition, extensive neuroinflammation, and vascular fibrosis. However, putative therapeutic options for alleviating these features remain limited, emphasizing the need to develop comprehensive treatments for patients with AD. METHODS/STUDY POPULATION: CSF from human AD patients treated with nilotinib (n=12), a tyrosine kinase inhibitor, or placebo (n=11) was collected and sequenced, and significantly altered miRNAs were identified and analyzed for alterations to disease-associated genes via gene ontology analysis. TgAPP mice were injected intraperitoneally with one of two novel tyrosine kinase inhibitors, BK40143 or BK40197, or DMSO (n=12 per group) daily for six weeks, during which memory deficits between groups were measured, before brains were harvested for analysis of amyloid-beta load via ELISA, microglial activation via Sholl analysis, and vascular collagen levels via immunohistochemistry. RESULTS/ANTICIPATED RESULTS: CSF obtained from AD subjects treated with nilotinib revealed significantly increased (p<0.05) levels of miRNAs regulating autophagy, neuroinflammation, and collagen production compared to placebo. These results were validated in vivoin TgAPP mice, who displayed improved recall on the novel object recognition test and Morris water maze following treatment with our drugs, correlating with decreased levels of brain amyloid-beta (30% decrease, p=0.002), decreased microglial reactivity and activation (40% decrease, p=0.01), and decreased vascular fibrosis (50% decrease, p=0.005) along small brain blood vessels compared to controls. DISCUSSION/SIGNIFICANCE: These data identify tyrosine kinase inhibition as a valid therapeutic strategy for alleviating various pathological features associated with AD and warrant further investigation as a treatment option for human patients as a means of slowing cognitive decline.

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Maternal hypertension results in a decreased number of glial cells in offspring during early development

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OBJECTIVES/GOALS: Preeclampsia, a hypertensive disorder in pregnancy, disrupts immune cell profiles at birth in both mice and humans. In mice, it affects offspring's memory and behavior. This study aimed to investigate whether preeclampsia induces lasting immune cell changes after birth and its impact on astrocyte and microglia cell counts in offspring. METHODS/STUDY POPULATION: Preeclampsia was induced in C57BL/6 females by infusion of vasopressin (24 ng/hr) or saline throughout gestation via osmotic minipump. Parturition was allowed to occur naturally. Offspring were euthanized at various timepoints post-delivery for experimental measures. Total urine protein was determined via bicinchoninic acid assay. Single cell suspensions were prepared from thymus spleen, and brain tissue and separated via density gradient.