# Image Analysis to Provide Computer-Aided Detection for Pediatric Diseases

Center for Childhood Cancer, Biopathology Center Imaging Core, The Research Institute at Nationwide Children's Hospital & Research Informatics Core, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio

## Background

The Research Institute at Nationwide Children's Hospital is organized into Centers of Emphasis that allow traditional academic boundaries to be crossed and merged. Scientific and clinical interests prevail in this model which encourages collaboration and the free flow of ideas. Interdisciplinary teams develop novel approaches to common and often serious childhood diseases.

Each of the Centers has a thematic focus, ranging from the most basic molecular biology to applied, patient-oriented research. The Center Directors are leaders in their respective fields, and the individual faculty members have been selectively recruited to help achieve their Center's mission.

The initial focus has been pediatric cancers. The Biopathology Center (BPC) is largely a government funded organization whose primary objective is the long-term acquisition, storage and distribution of a large number of both cancerous and normal biological specimens and related data for the purpose of supporting cutting edge research. The BPC currently houses over 1.4 million biological specimens which are received from over 500 hospitals. The BPC receives and processes over 1000 aliquots daily and distributes over 25,000 specimens annually to over 130 academic and commercial researchers.

## Solution

Working with pathologists, the team developed a software package to enable the automated electronic scanning and analysis of digital pathology images to detect and measure markers for both pediatric and adult cancerous diseases. This software enhances the pathology workflow by providing time-saving tools for pathologists. Similarities and differences between cancerous diseases were analyzed, providing the ability to search across multiple specimens representing multiple cancer protocols from various cancerous diseases.

## Biomedical Imaging Team

The Biomedical Imaging Team is a multidisciplinary team consisting of healthcare and informatics professionals working together to provide high quality digital images to our customers.

Services provided include:

- Pathology Imaging
- Automated Pathology Review Applications
- Image Architecture Analysis & Development
- Online capture of pathology review data
- Image Analysis
- Slide Conferencing
- Digitized Pathology Reports

http://imaging.nchresearch.org

## Research Informatics Core

The Research Informatics Core is a multidisciplinary informatics application development team dedicated to enhancing and expanding research through the scientific application of information management and informatics innovation.

The Core is an award winning, service-oriented group which possesses the following capabilities in these diverse areas:

- Custom computer application development
- Data and environment integration
- Development of data mining and reporting tools
- Systems Architecture
- Project management
- Database design and development
- Development of expert systems
- Image analysis
- Informatics consulting

http://informatics.nchresearch.org

## Acknowledgements

- Children's Oncology Group
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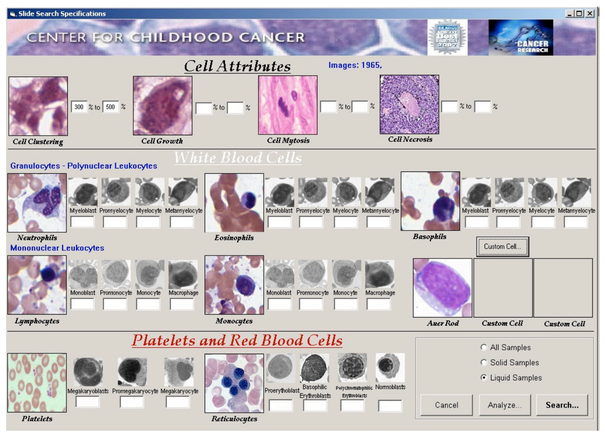
- Gynecologic Oncology Group
- Aperio Technologies

## Technology & Design



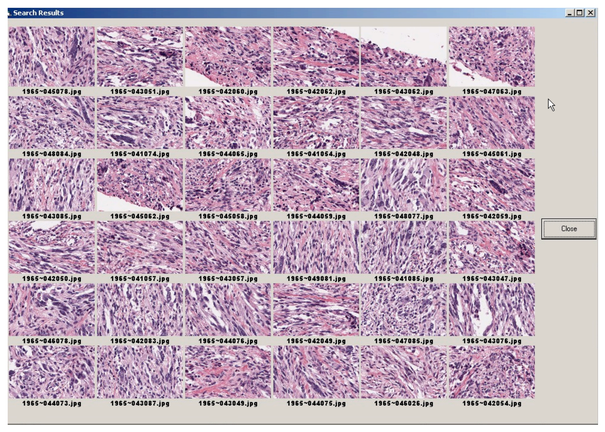

The Image Analyzer utilizes the .NET technology and integrates with the virtual microscopy software to store values related to the efficient location, persistence, and indexing of key areas of interest in a Microsoft SQL Server 2005 database. The Image Analyzer is designed to run both as a web-enabled application and a Microsoft Windows compiled application.

The image analysis application was designed from a use case developed within the Children's Oncology Group (COG). The use case included defining a pediatric cancer protocol and scanning all cases in the protocol with associated slides. Consultation was conducted with both solid tumor (sarcoma) specialists and hematology and leukemia experts.

To allow for the efficient analysis of large datasets, the Ohio Supercomputer Center (OSC) installed the Microsoft Windows High Performance Computing (HPC) Server 2008 on ten nodes. The heart of this system is an IBM x3455 1U server featuring 1 dual-core AMD 2.4GHz Opteron processor, with 2GB of main memory, and a pair of 70 GB mirrored SATA drives for system software and swap space. The motherboard is capable of being upgraded to quad-core, quad-socket configuration, for a total of 16 cores. A link to the DDN 8500 provides storage for application executables and data.

## Results

The first release of the software focused on the electronic location of abnormal nuclei diffusion within cancerous tumors. An advanced algorithm highlights areas of interest for pathologists and cancer researchers by performing the analysis on an individual slide specimen image, subset, or entire image archive.




## Future Iterations

Future software iterations are being designed to provide pathologists and other cancer researchers the algorithms necessary to specify criteria across additional cancerous diseases, including solid and liquid infections. These tools will search on nuclei or white blood cell clustering, cellular mitosis and infectious cellular growth. Additional algorithms will detect and measure solid tumor necrosis levels and search cancerous blood infections by white blood cell maturation stages and platelet and red blood cell levels. The tool also can search for custom cells known to be definitive markers in certain cancers, such as Auer Rods in Acute Myelogenous Leukemia.

Computational and analytical sophistication is increasingly critical for drug discovery, research and development, and patient treatment. Extensive and increasing interdisciplinary studies and integration of laboratory process are common in the evolvement of bioinformatics, driving up the demands for computing and data management capabilities. The acquisition of the high performance analytics computing cluster is essential to enhancing the health of children by engaging in high-quality, cutting-edge research.

In addition to pediatric cancers, the team is interested in introducing image analysis and high performance computing to biobehavioral health, Duchenne muscular dystrophy (DMD) and gynecologic cancers. Biobehavioral health research involves examining the integration of randomized clinical trial data and large, administrative, observational datasets to examine biases for examining drug safety and effectiveness. For example, we are using cross-design synthesis, which involves Bayesian meta analyses of trial data and propensity methods for observational data, to examine the association between adolescent and young-adult use of newer types of antidepressants and suicidal thoughts and behaviors.

Research into DMD, a lethal, X-chromosome linked recessive muscle-weakness disorder affecting 1 in 3,500 live male births in the United States, includes studying the efficacy and safety of various gene modifications and gene therapies. Patients are severely challenged with wheelchair dependency by age 10-12 and death anytime after age 18 due to the inability of muscle to protect itself from contraction-induced injury due to an absence of structural protein, dystrophin, at sarcolemma resulting from a mutation of the gene-encoding dystrophin.

These studies and workflows combine biology, chemistry, imaging, and statistical analysis, together driving up the demands for computing and data management capabilities. The acquisition of the high performance analytics computing cluster is essential to our commitment to enhance the health of children by engaging in high-quality, cutting-edge research meeting the highest scientific and ethical standards.