Transforming Lives Through Research

Spectrum Health Research Report 2014
**Table of Contents**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Letter from the Vice President of Research</td>
<td>Page 3</td>
</tr>
<tr>
<td>Leading the Region in Research</td>
<td>Page 4</td>
</tr>
<tr>
<td>A Collaborative Spirit</td>
<td>Page 8</td>
</tr>
<tr>
<td>Featured Research Initiatives</td>
<td>Page 9</td>
</tr>
<tr>
<td>Research Funding and Administration</td>
<td>Page 20</td>
</tr>
<tr>
<td>Fiscal Year 2014 Grant Awards</td>
<td>Page 21</td>
</tr>
<tr>
<td>Fiscal Year 2014 Publications and Presentations</td>
<td>Page 24</td>
</tr>
</tbody>
</table>
In this report, we highlight exciting Spectrum Health research focused on cardiovascular, cancer, neurosciences, pediatrics, women’s health and musculoskeletal sciences work. These researchers, who represent the more than 100 physician-scientists throughout Spectrum Health, offer hope and transform lives through their research. We are proud of their efforts.

Research supports our institution’s four key strategies in the following ways:

**Drive Exceptional Value** – Peer-reviewed, investigator-initiated research that brings novel treatments and/or care to our patients, their families and the community. This research will drive a healing experience that is safe, of high quality and at the forefront of patient care.

**Transform the Care Model** – An environment where interdisciplinary teams of physicians, other patient care providers and researchers work together to drive patient-centered research, ultimately influencing how best to deliver local, evidence-based care to our patients.

**Grow With Purpose** – We are committed to supporting and developing areas of research emphasis, as well as providing a means for investigator-initiated research.

**Lead New Health Solutions** – Through new research initiatives, our physicians will lead the discovery of innovative health solutions.

In the past year, our portfolio expanded beyond clinical research to include basic and translational research initiatives. We opened the Spectrum Health Basic and Translational Research Laboratories to support this important work. For the first time, we received investigator-initiated research funding from the National Institutes of Health, raising the academic stature of our institution.

Academic, protected-time positions now exist for our physicians, and we extended the first appointments for assistant, associate and senior scientist positions. We also created adjunct research positions to encourage association and enhance collaboration with community research institutions, and offered our first adjunct appointments.

We continue to push research forward and promote life sciences education throughout our region through strong inter-institutional commitments and community partnerships. By collaborating with others in medical research, biomedical research and education, we can make an even greater impact on our community and clinical care.

In these and countless other ways, research embodies Spectrum Health’s mission to improve the health of the communities we serve. The momentum of 2014 continues as we focus on transforming lives, one discovery at a time.

Sandra A. Rempel, PhD
Vice President of Research
Leading the Region in Research

At Spectrum Health, our mission is to improve the health of the communities we serve. We understand that future breakthroughs in medical treatments are founded on the clinical, basic and translational research of today.

Clinical Research
Spectrum Health continues to be a champion of clinical research since launching clinical trials in the late 1970s. Many of those early studies—surfactant for premature infants whose lungs are not fully developed, platinum-based chemotherapy and lasers for treatment of coronary artery disease—are now routinely used.

More than 97 percent of research at Spectrum Health is clinical, of which 81 percent is patient-oriented research. Thousands of patients each year choose to participate in Spectrum Health’s clinical trials. The clinical research is led by cardiovascular, hematology/oncology, pediatric, clinical neurosciences, orthopedics, women’s health, emergency medicine and many other specialties.

Spectrum Health is home to West Michigan’s largest and only fully accredited health system-based clinical research program. More than 90 percent of Grand Rapids-area clinical studies are connected to Spectrum Health.

Fiscal Year 2014 Facts:
- $20.7 million portfolio
- 863 clinical studies
- 116 published articles
- More than 100 researchers

Epidemiologic and behavioral studies. Epidemiologic studies investigate factors that determine the presence or absence of diseases and disorders, and their societal and economic impact. Behavioral studies systematically analyze and investigate human behavior through controlled and naturalistic observation, and disciplined scientific experimentation.

Outcomes and health services research. This type of research measures the changes that occur in people’s health and satisfaction due to specific medical and health interventions. It is the study of the delivery and consequences of health care on outcomes from the perspectives of patients, providers and the health care system.

Patient-oriented research. Our physician scientists conduct research with human subjects, such as clinical trials, or on material of human origin such as tissues and other specimens. Clinical trials are used to determine whether new biomedical or behavioral interventions are safe and effective, such as drugs, treatments and devices, or new ways of using known drugs, treatments or devices.
The Spectrum Health Basic and Translational Research Laboratories, located in the Cooper’s Landing Building at 1345 Monroe Avenue, opened in August 2013 with more than 9,000 square feet of dedicated research space.
Basic and Translational Research
Through basic research, we aim to understand the biologic basis of disease so that we can design effective therapies and new treatments. Recently, Spectrum Health’s focus has broadened to include translational research—the development of laboratory discoveries into potential diagnostic tools, drugs or medical devices—for use at the bedside.

The following novel clinical initiatives were announced in fiscal year 2014, supported by research at Spectrum Health’s Basic and Translational Research Laboratories. These efforts brought National Institutes of Health Investigator-Initiated Research (R01) funding for basic and translational research to Spectrum Health for the first time, raising the academic stature of our institution.

Helen DeVos Children’s Hospital Pediatric Urology Program
The program cares for children with urinary and reproductive tract anomalies. It is complemented by the pediatric urology research laboratory, directed by Kirstan Meldrum, MD, to discover new approaches to repair the damaged kidneys of children.

The Neuroblastoma and Medulloblastoma Translational Research Consortium
Headquartered at Helen DeVos Children’s Hospital, the Neuroblastoma and Medulloblastoma Translational Research Consortium is an association of 22 universities and children’s hospitals offering a nationwide network of childhood cancer clinical trials. It is complemented by the neuroblastoma translational research laboratory, directed by Giselle Sholler, MD, to identify new and individualized therapies for children with tumors of the nervous system.

The Adult Bone Marrow Transplant Program
The program focuses on transplants for patients with lymphoma, leukemia, multiple myeloma and myelodysplastic syndrome (MDS), performing both autologous and donor transplants. It is complemented by the laboratory of blood and marrow transplantation research, directed by Samer Al-Homsy, MD, to explore new avenues to prevent graft-versus-host disease.

The Brain and Spine Tumor Center
The center is a partnership between Spectrum Health Medical Group neuroscience experts and the Spectrum Health Cancer Center. It provides advanced and effective brain tumor and spine tumor treatments with individualized care plans. It is complemented by the molecular neuro-oncology laboratory, directed by Sandra Rempel, PhD, to discover novel therapeutic targets for the treatment of brain tumors based on the genetics of a patient’s tumor.
A Collaborative Spirit

One-of-a-Kind Community Partnerships
Grand Rapids, Michigan, is home to several institutions for medical research, biomedical research and education of the life sciences. These institutions include Spectrum Health, Van Andel Institute, Michigan State University College of Human Medicine and Grand Valley State University.

The collaborative spirit of Grand Rapids is reflected in the strong inter-institutional commitments to promote research and education. By working together, these institutions promote stronger research programs than any one institute could develop on its own. Examples of Spectrum Health’s collaboration with our community colleagues include the following:
- Partnership with Michigan State University College of Human Medicine in support of collaborative research programs in orthopaedics, women’s health, neurodegenerative disease and pediatric neurosciences
- Spectrum Health Frederik Meijer Heart & Vascular Institute and the Van Andel Institute partnered to build an inter-institutional program in cardiovascular basic and translational research and clinical trials
- Partnership with Grand Valley State University to support the launch of a new executive MBA program, designed to educate professionals with a focus on health care for Grand Rapids
- Partnership with Michigan State University College of Human Medicine and Grand Valley State University to provide medical and science students with much-needed research fellowships and internships, benefiting both the students and the laboratories they serve

National Recognition
In addition to investigator-initiated research, Spectrum Health’s research portfolio supports national research ranging from consortia to national tissue-based initiatives.

Headquartered at Spectrum Health, the Cancer Research Consortium of West Michigan (formerly the Grand Rapids Clinical Oncology Program) offers new and unique national cancer clinical trials through a community-based clinical research program. The consortium is funded through a competitive award from the National Cancer Institute.

The Spectrum Health Universal Biorepository Program is dedicated to the collection and storage of patient specimens used for academic and industrial research. The program participated as a tissue and data source site for The Cancer Genome Atlas project, which is a nationwide initiative funded by the National Institutes of Health to map the cancer genome. Involvement in this project is limited, and selected sites must meet strict criteria for inclusion.
Cardiovascular Research Highlights

Spectrum Health has an established strength in cardiovascular research. Highlights in fiscal year 2014 include the following.

The Frederik Meijer Heart & Vascular Institute
The Institute brings together cardiovascular expertise in clinical care, research and education. The institute oversees more than 60 scientists and students in the areas of tissue engineering, myocardial regeneration, stem cell biology, end-stage heart failure and transplant immunology. Annually, about 50 active cardiovascular clinical trials have Institute physicians as principal investigators.

Minimally Invasive Cardiac Surgery Clinical Trial
Physicians in the Spectrum Health Frederik Meijer Heart & Vascular Institute have participated with other institutions on a clinical trial to evaluate an alternative to open-heart surgery for patients with severe aortic stenosis. The Medtronic CoreValve® System is designed to provide a minimally invasive, transcatheter treatment option for patients with symptomatic, severe aortic stenosis who are at high risk or who are ineligible for open-heart surgery.

Discover Magazine’s “Top 100 Stories of 2013”
Discover Magazine selected original cardiovascular research conducted at Spectrum Health as one of the “Top 100 Stories of 2013.” Spectrum Health cardiologist Ryan Madder, MD, used near-infrared spectroscopy to identify the characteristic makeup, or signature, of arterial plaque. Arterial plaque blocks arteries and causes heart attacks. The study was ranked 53rd among the top science stories of 2013.

Photo above: Angiogram and corresponding chemogram of a patient with an ST-segment elevation myocardial infarction. Arrow indicates a large lipid core plaque.
Getting to the heart of it: New device seals area to prevent leaks

International clinical study evaluates safety and efficacy of aneurysm sealing system for endovascular repair

Spectrum Health is participating in an international clinical trial for a new investigational device designed for the repair of some abdominal aortic aneurysms (AAA).

The EVAS FORWARD trial, sponsored by Endologix, Inc., evaluates the safety and efficacy of the Nellix™ EndoVascular Aneurysm Sealing System (EVAS). The device is not commercially available in the United States, and is available only at selected clinical study sites for investigational use. It is only for infrarenal AAAs, which occur below the renal arteries, the blood vessels that lead to the kidneys.

The trial is designed to determine if a new stent graft procedure that seals the AAA repair in a polymer will result in reduced leaks and surgical repairs. The trial enrolled 179 patients at 29 centers in the U.S. and Europe. Spectrum Health physicians performed the Nellix procedure on 19 patients.

Spectrum Health Medical Group vascular surgeon Robert Cuff, MD, leads the trial at the Spectrum Health Fred and Lena Meijer Heart Center.

The aorta is the body's main artery, carrying blood from the heart to the rest of the body. An AAA is an enlarged and weakened section, or “ballooning” of the aorta, that is prone to rupture and often results in death. According to the Centers for Disease Control and Prevention, approximately 13,000 Americans die each year from thoracic and abdominal aortic aneurysms. Most of the deaths result from rupture or dissection, a kind of splitting of the aorta.

A stent-graft can be used to repair an AAA. A stent-graft is a long, cylinder-like tube made of a thin metal stent frame covered with a graft material such as polyester. The stent helps to hold the graft in place. The stent-graft is inserted into the aorta and placed at the site. Once in place, the stent-graft is expanded, attaching to the wall of the aorta and supporting it. The aneurysm eventually shrinks down onto the stent. Most times two or more stent pieces are combined to repair the aneurysm.

Dr. Cuff explained two common complications with this procedure. One is blood from small vessels leaking back into the aneurysm sac, the space created between the stent and the damaged aorta. The other complication is shifting of the stent-graft, which can cause the pieces to separate. This can cause the stent-graft to leak, requiring a surgical repair. These complications can occur in up to 20 percent of cases and require additional surgeries to repair.

“This Nellix system includes an additional step in performing a minimally invasive AAA repair,” said Dr. Cuff. “Once the stents are in place, special endobags surrounding the stents are filled with a resin-like polymer material that fills the remaining aneurysm sac to protect the aorta while excluding and sealing the aneurysm from blood flow. By sealing the aneurysm sac, we hope to learn if this will significantly reduce these complication rates.”

Enrollment under an extended investigation phase is anticipated to begin shortly, and will continue during the pivotal trial follow-up period and premarket access reparation/review process.
Before and after pictures of a recent case. Note the large AAA with bilateral iliac artery aneurysms and large secondary (lumbar vessels) still patent on the aneurysm. After being treated with the Nellix device, there is complete sealing and exclusion of the aneurysm sac and iliac aneurysm with no backfilling from the lumbar vessels.
Using a cancer’s genetic profile to guide treatment

Multidisciplinary teams explore an infrastructure for personalized cancer care

The landscape of cancer care is evolving due to the increased availability of information about biomarkers (alterations in DNA or protein expression) present in a patient’s tumor, which make each individual’s cancer unique. New biomarkers, drugs and clinical trials are discovered on a weekly basis. Biomarker-targeted therapy for a patient’s specific cancer represents the new era of cancer treatment.

Personalized medicine is defined as an “emerging practice of medicine that uses an individual’s genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease. Knowledge of a patient’s genetic profile can help doctors select the proper medication or therapy and administer it using the proper dose or regimen” (ghr.nlm.nih.gov/).

Next-generation sequencing (NGS) is a technology that may be used to identify certain biomarkers in a patient’s cancer tumor. This can now be performed in real time, with the potential to impact therapeutic decisions in patients with complex, advanced or recurring cancer. Early efforts at major academic centers suggest personalized cancer care can be delivered; however, substantial institutional resources are required to get started. With the availability of biomarker testing in referral laboratories such as Foundation Medicine and Caris Life Sciences®, clinicians in a wider number of centers can pursue such testing by sending it outside their centers.

Another approach is to perform biomarker testing in-house through the center’s Clinical Laboratory Improvement Amendments (CLIA)-approved Spectrum Health Advanced Technology Laboratory. This offers the benefits of quicker turnaround times and confirmation of test results with standard sequencing technologies, all at a reduced cost compared to biomarker testing available at referral laboratories. Although the cost and availability of biomarker testing are becoming less problematic, the integration of such testing into clinical care remains a challenge and has largely been left up to the treating physician. Several questions remain regarding the feasibility of providing personalized cancer care using biomarker results in non-university cancer centers where the majority of patients receive their care.

Once biomarker results are obtained, major academic centers have convened molecular tumor boards that include broad participation of clinical experts, translational scientists and others in their initial efforts in this space. Brian Lane, MD, PhD, chief of urology, Spectrum Health Medical Group and Spectrum Health Betz Family Endowed Chair for Cancer Research, wanted to determine if a regional Center for Personalized Cancer Care could employ the same options for patients. A pilot trial exploring the feasibility of convening an institutional multispecialty tumor sequencing advisory board (TSAB) of professionals to evaluate
biomarker results at Spectrum Health was recently completed. During the course of the 15-patient trial, the team outlined and expanded the roles, functions and interaction of the various stakeholders, forming a cohesive and multidisciplinary board averaging 16 or more members per meeting.

The pilot study involved analysis of cancer tumor tissue from 15 patients using a biomarker test (Ion Torrent AmpliSeq Cancer Hotspot Panel v2) performed in-house by the CLIA-approved Spectrum Health Advanced Technology Laboratory. Cancer tumor samples were obtained from Spectrum Health’s biorepository and analyzed at 2,800 frequently mutated sites in 50 genes. The primary outcome of interest was the proportion of multidisciplinary TSAB discussions regarding biomarker results and corresponding therapies occurring in a clinically meaningful time frame. Secondary outcomes included TSAB function and processes, biomarker test turnaround time, and proportion of reports with biomarker results associated with a targeted therapy. The study results will be submitted for publication in early 2015.

“From this pilot study, we developed the essential components of a Center for Personalized Cancer Care, which can provide decision support for clinicians utilizing NGS [biomarker testing] in this era of genomic medicine,” said Dr. Lane. “Clinically significant mutations were identified in 73 percent of patients, identifying potential druggable targets in patients who may also be eligible for innovative clinical trials.”

After proof of feasibility, the Hotspot Panel is now offered as a clinically available test at Spectrum Health Advanced Technology Laboratory, with a turnaround time of 10 to 14 days on average. Spectrum Health Advanced Technology Laboratory remains the only CLIA-approved laboratory in West Michigan performing clinical biomarker testing on a next-generation sequencing platform.

“Our laboratory continues to work with physicians to develop additional clinically useful biomarker panels in order to provide affordable, state-of-the-art, personalized cancer care for patients in this quickly progressing field,” said Kim Collison MSA, MT (ASCP), Spectrum Health Advanced Technology Laboratory manager. “In addition to the Hotspot Panel, we also offer the National Comprehensive Cancer Network (NCCN)-recommended extended mutation testing (NRAS and KRAS). This testing provides information to assist the physician in the determination of effective drug therapy for metastatic colon cancer.”

Other biomarker testing currently in development includes a non-small cell lung cancer panel and a hematology oncology panel.

References

5. Sweeney et al., “Impact on overall survival (OS) with chemotherapy versus hormonal therapy for hormone-sensitive newly metastatic prostate cancer (mPCa): An ECOG-led phase III randomized trial,” (2014) Chicago, IL, pp. 5s.
Clearer picture of the brain helps pinpoint seizures

The gold standard for identifying the source of epileptic seizures is to place electrodes in specific areas of the brain to map the location of the seizure onset and its impact. Brain mapping is the process of directly stimulating the brain through the same implanted electrodes to determine areas of the brain that cannot be removed, because their loss would result in permanent dysfunction. Often once the source of the disturbance is identified, that section of the brain is surgically removed if possible.

Although these methods are considered the most accurate way to localize seizures and map brain function, many are attempting to design a noninvasive technological process that can complete these tasks without actually having to directly place electrodes on the brain surface. Functional MRI (fMRI) is the most frequently utilized technology to map brain function noninvasively. But to determine its true accuracy, this data in many cases still has to be directly compared to direct electrical recordings.

In recent years, it has become clear that there are networks in the brain that may be causing seizures rather than a single, discrete location. With the use of functional MRI technology (fMRI), we are able to see these networks in action and track how signals are traveling in the brain. Now it is possible to combine these two techniques for a comprehensive view of epileptic focal points. This dual approach provides a non-invasive, big picture perspective from the fMRI along with results from small electrodes implanted for brain mapping. Spectrum Health is one of the few centers in the country that is mapping networks in the brain using both electrical and MRI approaches to more clearly pinpoint the location of seizures.

Spectrum Health Medical Group neurosurgeon Kost Elisevich, MD, PhD, and epileptologist Brien Smith, MD, along with researchers from Henry Ford Hospital, Wayne State University, Michigan State University and Grand Valley State University, are collaborating on studies in this area. They are evaluating the broader perspective that can be gained by combining fMRI with the traditional electrode approach of localizing the source of seizures.

Two clinical trials are under way, with patients enrolled in both. One study is using a special imaging protocol to segment, quantify and characterize
Spectrum Health is one of the few centers in the country that is mapping networks in the brain using both electrical and MRI approaches to more clearly pinpoint the location of seizures.

Brain structures on both magnetic resonance imaging (MRI) and Single Photon Emission Computed Tomography (SPECT) and determine how these attributes may relate to the underlying source of epileptic tissue in the temporal lobe. As patients are acquired in this database, the findings from imaging analysis will be compared to the clinical diagnosis, surgical intervention and outcomes. The ultimate goal of this study is to develop methods and systems that facilitate and improve diagnosis, treatment planning, treatment evaluation and prognosis while reducing risk and cost.

The second study attempts to undertake a comprehensive picture of focal epilepsy (seizures coming from one specific area of the brain) using sophisticated imaging and intracranial electrographic recording (measured electrical brain activity with electrodes implanted into the brain or placed on the surface). This study will attempt to analyze multiple characteristics about epileptic tissue, including electrical characteristics, altered cellular makeup, brain morphology, extent of the abnormal network and consequences of inflammatory changes.

Further understanding of the anatomical, electrical, cellular, genetic and inflammatory characteristics that alter brain networks and result in epileptic circuits may allow us to design interventions that modify this pathological process.
Just as every child is different, every tumor can be different

Clinical studies explore a personalized approach to treating childhood cancer

In 2003, the first human genome was sequenced after 13 years of work. Today we can sequence a patient’s DNA and their tumor’s DNA in less than a month, opening new possibilities and informing new ways of treating children with cancer. We can personalize treatment by understanding what genes make a tumor grow and divide, and what genes make a tumor resistant to therapy. This makes it possible to determine specific treatment for each child based on their genetic information.

Giselle Sholler, MD, Haworth Endowed Director of Pediatric Oncology Innovative Therapeutics at Helen DeVos Children’s Hospital, is leading the Pediatric Oncology Research Program. This includes our Molecularly Guided Therapy Clinical Trial, Signatures Program and Early Phase Clinical Trials Program. The goal of the personalized medicine studies is to profile the genetic makeup of all tumors for each child diagnosed with any type of cancer at Spectrum Health Helen DeVos Children’s Hospital.

One example of this personalized approach is Tristin’s treatment on our Molecular Guided Therapy Trial funded through our Dell Grant. Now an 18-year-old boy, he was diagnosed with Stage 4 neuroblastoma at 13 years of age. He received an initial high dose of chemotherapy and his tumor remained. He then traveled from his home in Tennessee to a medical center in New York City, where he was treated with more high-dose chemotherapy for three years.

Tristin came to Helen DeVos Children’s Hospital in February 2013. He was one of the first patients we were able to treat in this completely new way of caring for children using personalized medicine. Following his tumor profile and adjusting his treatment as it changes has brought hope, allowing Tristin to graduate from high school and even start college.

The Signatures Program involves the collection of normal and malignant patient tissues to determine the molecular makeup of these tissues and correlate with clinical data. This will be used to identify diagnostic markers that could be used to detect disease progression and response to therapy, and identify optimal molecularly informed treatment options (both novel targets and targets of existing drugs). These new agents will be tested in laboratory models of patients and development of phase I clinical trials.

“Identifying an important gene in neuroblastoma targeted by a drug called DFMO, we created the first clinical trial to target cancer stem cells and prevent children from relapsing,” said Dr. Sholler. “This trial is showing great promise, and children are staying in remission. Our goal in this study is to increase the rate of children staying in remission from 60 to 80 percent.”

Tissue samples are collected from new and relapsed childhood cancer patients at Helen DeVos Children’s Hospital and at 22 other children’s hospitals within the Spectrum Health-led national consortium, the Neuroblastoma Medulloblastoma Translational Research Consortium. Every one of these samples will be analyzed using the latest molecular profiling technologies and computational techniques to identify molecular biomarkers and targeted drug interventions, which can be used by doctors to look for the best treatment options for their patients.
Blood transfusions could harm children with traumatic injury

Study finds pediatric blood conservation results in better outcomes

The pediatric critical care team at Spectrum Health Helen DeVos Children’s Hospital has been focused on blood management during the past 16 years and is recognized nationally for optimizing patient outcomes by minimizing blood product utilization.

One study published in 2014 examined the outcomes of transfused trauma patients. RBC Transfusions in Children Requiring Intensive Care Admission After Traumatic Injury was published in the June 2014 edition of Pediatric Critical Care Medicine.

Trauma is a frequent occurrence in the pediatric population. The Centers for Disease Control and Prevention reports that trauma is a leading cause of death for individuals ages 1 to 44. It is estimated that 10 – 15 percent of children hospitalized after trauma have life-threatening injuries that demand an expedient and systematic approach to their care. Packed red blood cell (PRBC) transfusions to critically injured patients are considered life-saving therapy, especially when administered in response to hemodynamic instability after hemorrhage. However, studies show that after significant injuries, the patient may deteriorate into a generalized body inflammation and compromised body immunity. In these situations, transfusions may worsen the patient’s condition.

“Our analysis was intended to define the characteristics of transfused pediatric trauma patients compared with the non-transfused patients and to evaluate the frequency, timing, quantity and storage age of PRBC transfusions received during their PICU stays,” said Nabil Hassan, MD, lead author of the study and medical director of pediatric blood management at Helen DeVos Children’s Hospital. “We also examined the relationship of these factors to clinical course and eventual outcomes to improve the quality of care offered to trauma patients.”

In this retrospective review, PRBC transfusions of pediatric trauma patients were associated with worse clinical outcomes independent of the severity of injury. Frequency and volume of transfusions, as well as blood older than 28 days, seem to be contributing factors to these outcomes. This pediatric study, as well as other studies in adults, adds to the body of evidence that PRBC transfusions, particularly of increased storage age, may be harmful to patients after traumatic injury.

“Given this evidence, it may be appropriate to reexamine indications for transfusions, and consider implementing blood conservation strategies to minimize transfusion needs,” said Dr. Hassan.

Additional authors include James M. DeCou, MD; Dianne Reischman, PhD; Todd A. Nickoles, RN, BSN; Emily Gleason, RN, BSN; Diana L. Ropele, RN, MSN; Dominic Sanfilippo, MD; Alan T. Davis, PhD; David Alters, MD; Surender Rajasekaran, MD, MPH.

Helen DeVos Children’s Hospital physicians have published several studies, with more under way, examining the results of blood management in critically ill children, premature newborns, patients with cancer and blood disorders, and those undergoing surgery. Those who have collaborated on blood management efforts and research include Brian Boville, MD, Philip Nowicki, MD, John Kampinen, MD, Jeffery Cassidy, MD, Deb Cloney, MD, Harold Conrad, MD, Deanna Mitchell, MD, and Beth Kurt, MD.

References


A rare cancer of the placenta, gestational trophoblastic neoplasia (GTN), affects about one in 1,000 pregnant women in the U.S. each year. While rare, this disease can become malignant and fatal. Julian Schink, MD, Spectrum Health Medical Group chief of women’s health, is principal investigator of an international phase III randomized trial comparing two chemotherapy drugs used to treat the disease.

This study (Gynecologic Oncology Group Study 275) tests the hypothesis that treatment with multi-day methotrexate is inferior to treatment with a regimen known as pulse actinomycin-D, administered once every two weeks, in low-risk gestational trophoblastic disease.

The abnormal growth in the placenta occurs in women of reproductive age and can be benign or malignant. The disease can be fatal but is curable if diagnosed early. The cure rate approaches 100 percent and fertility preservation is usually possible with individualized care based on careful staging and multidisciplinary team planning.

In the U.S., pregnant women commonly have ultrasounds, so this condition is often diagnosed early. Other cultures, particularly in the developing world, do not use ultrasound as widely, and therefore pregnant women in those countries are often diagnosed with widely metastatic disease.

The condition is so rare that it needs to be studied worldwide to attract enough patients. This National Cancer Institute-funded study currently has 29 patients enrolled. The goal is to accrue 381 patients.

This trial builds on a previous international study of Dr. Schink’s (Gynecologic Oncology Group Study 242), which determined that second curettage (surgical removal of uterine tissue) is a safe, simple alternative to immediate chemotherapy for patients with newly diagnosed, non-metastatic, low-risk GTN.

That study showed that second curettage could be safely offered to patients regardless of hCG (human chorionic gonadotropin hormone) level and the amount of intra-uterine disease. Immediate chemotherapy is still preferred and more effective for patients with a WHO (World Health Organization) risk score of 5 or 6 and for patients at the extremes of reproductive life, specifically under 19 and over 39 years of age. In this study, 46.8 percent of patients derived significant benefit from immediate second curettage and avoided chemotherapy.

“We know that surgical treatment is effective, and now we are investigating chemotherapy drugs to determine which offers the most promise for women with GTN,” said Dr. Schink. “Our goal is to identify the treatment that is the most convenient and best tolerated by patients. This disease affects young women in the prime of their lives and can be very disruptive.”

References
1. American Cancer Society (www.cancer.org)
New hope for people suffering from chronic bone infections

Evaluating the safety and efficacy of new bone graft substitute for musculoskeletal repair

Osteomyelitis or bone infection is a major patient problem where prolonged, long-term antibiotic therapy, multiple surgical interventions and the threat of amputation are the current standard of care. Rising prosthetic infections, diabetic ulcers, war injuries, sports injuries and an increasing resistance to antibiotics contribute to this growing condition. Current treatment options include the use of a product, such as Cerament™, a bone void filler used to remodel the bone. This treatment is combined with prolonged systemic antibiotic therapy. Studies have been undertaken to determine whether antibiotic treatment is more efficacious when locally administered. Initial investigations show remarkable outcome when the antibiotic is locally administered at the time of applying the cement (Fig. 1). However, local administration of the antibiotic can be very difficult, and new devices or methodologies are needed.

Jason Calhoun, MD, chief of musculoskeletal sciences, Spectrum Health Medical Group, has more than 170 peer review publications, 57 chapters and three books mainly on musculoskeletal infection. Dr. Calhoun was The Cierny Mader International Visiting Professor at the Oxford Bone Infection Conference on April 3, 2014, where he presented his research regarding bone infection treated with antibiotic orthopaedic implants.

While at this conference, Dr. Calhoun first heard Dr. Martin McNally, lead surgeon of the bone infection unit at the Nuffield Orthopaedic Centre in Oxford, United Kingdom, present on a clinical trial of 41 patients with osteomyelitis who were treated with a new product, Cerament™|G, which is the bone void filler combined with the antibiotic gentamicin. The study showed no recurrence of infection, no late wound leakage, no toxicity and no renal complications, with more than 75 percent of patients having complete bone remodeling at six months.

In a news release about the UK study results, Dr. McNally stated, “Local antibiotic management of osteomyelitis provides a much-needed treatment option for people who suffer from chronic bone infections. We are pleased by early results and are optimistic that CERAMENT™|G offers the potential to improve health outcomes, lower healthcare costs and deliver a higher quality of life for patients suffering from this devastating disease.”

“I have been treating bone infections for many years with the implanting antibiotic devices to treat bone infection and had never seen such a remarkable outcome,” Calhoun said.

Calhoun has approached the company to bring its device to the U.S. and is one of three leading U.S. orthopaedic surgeons developing an international clinical trial. He was part of a group that convened in Washington, D.C., to discuss developing a multimillion-dollar grant to study this treatment in the U.S., with Spectrum Health as one of the three supervisory sites.

References
Research Administration and Funding

Fiscal 2014 Federal Award Funding (% of funding by organization)

Spectrum Health’s Office of Sponsored Programs in the Offices of Research Administration partners with physicians, clinicians, researchers, employees and administrators to develop competitive funding proposals and manage sponsored awards. The office is the central coordination point for all sponsored programs, including government-funded and industry-sponsored grants, contracts and subawards. The office also partners with the Spectrum Health Foundation in the development of internal grants and privately sponsored research grants.

In fiscal year 2014, 105 proposals were submitted, a 13 percent increase over proposals submitted in fiscal year 2013. The office administered 166 awards for total funding of $20.7 million from state and federal government, private sponsors and philanthropic grants in fiscal year 2014. This represents a 65 percent increase over awards managed in fiscal year 2013.

Spectrum Health Office of Sponsored Programs is administering a portfolio that is gradually increasing in federal and state awards, despite the decreasing federal and state funds available to support research. This past year, research was significantly supported by increases in private Foundation and philanthropic support.
Grants

**CANCER RESEARCH**

**Adult Brain Tumor**
- **Principal Investigator:** Rempel, Sandra, PhD
- **Project Title:** HSP27: A Modulator and Therapeutic Target of SPARC-Induced Glioma Invasion
- **Sponsor:** National Institutes of Health
- **Award Total:** $774,853
- **Department:** Spectrum Health Brain Tumor Research Lab
- **Award Period:** 1/4/2011 – 12/31/2015

**Adult and Pediatric BMT**
- **Principal Investigator:** Abdel-Mageed, Aly S., MD
- **Project Title:** A Multi-Center Study of Hematopoietic Stem Cell Donor Safety and Quality of Life (Subcontract)
- **Sponsor:** National Institutes of Health (Subaward)
- **Award Total:** N/A (Per-Patient Reimbursement)
- **Department:** Department of Pediatric Bone Marrow Transplant
- **Award Period:** 10/1/2009 – open

**Adult and Pediatric Orthopaedic Oncology**
- **Principal Investigator:** Foley, Jessica, MD
- **Project Title:** Targeting Chemo-Resistant Subpopulations in Human Osteosarcoma: Development and Implementation of a Novel Therapeutic Strategy
- **Sponsor:** Hyundai Hope On Wheels
- **Award Total:** $75,000
- **Department:** Helen DeVos Children’s Hospital Department of Pediatric Hematology and Oncology, and Spectrum Health Department of Orthopaedic Oncology
- **Award Period:** 8/29/2013 – 4/30/2015

**Canine and Pediatric Urologic Oncology**
- **Principal Investigator:** Kahonski, Richard, MD
- **Project Title:** Cancer of the Prostate Strategic Urologic Endeavor (CaPSURE) (Subcontract)
- **Sponsor:** U.S. Department of Defense (Subaward)
- **Award Total:** N/A (Per-Patient Reimbursement)
- **Department:** Spectrum Health Department of Urology
- **Award Period:** 7/1/2012 – 9/30/2015

**Biobank and Laboratory**
- **Principal Investigator:** Cottingham, Sandra, MD, PhD
- **Project Title:** The Cancer Genome Atlas (Subcontract)
- **Sponsor:** National Institutes of Health (Subaward)
- **Award Total:** $101,500
- **Department:** Spectrum Health Laboratory and Universal Biorepository
- **Award Period:** 12/9/2013 – 12/31/2014

**Colorectal Cancer**
- **Principal Investigator:** Hoedema, Rebecca, MD
- **Project Title:** A Phase III Prospective Randomized Trial Comparing Laparoscopic-Assisted Resection vs. Open Resection for Rectal Cancer (Subcontract)
- **Sponsor:** National Institutes of Health (Subaward)
- **Award Total:** N/A (Per-Patient Reimbursement)
- **Department:** Spectrum Health Department of Colon and Rectal Surgery
- **Award Period:** 1/15/2009 – open

**General Oncology**
- **Principal Investigator:** Dougherty, Mary, MSN, RN, AOCNS
- **Project Title:** Determining Severity, Interference and Number of Days of Symptoms From Side Effects in Cancer Patients Prescribed Oral Chemotherapy Agents, How Comorbid Conditions May Influence (Subcontract)
- **Sponsor:** Walther Cancer Foundation Behavioral Cooperative Oncology Group (BCOG) (Subaward)
- **Award Total:** $1,650
- **Department:** Department of Oncology and Medical-Surgical Nursing Administration
- **Award Period:** 5/1/2012 – 10/31/2013
**Head and Neck Cancer**
Principal Investigator: Padula, Gilbert, MD
Project Title: A Phase III Prospective Randomized Trial of Acupuncture for Treatment of Radiation-Induced Xerostomia in Patients with Head and Neck Cancer (Subcontract)
Sponsor: National Institutes of Health (Subaward)
Award Total: N/A (Per-Patient Reimbursement)
Department: Helen DeVos Children’s Hospital Department of Hematology and Oncology
Award Period: 4/1/2013 – 3/31/2015

**Pediatric Oncology**
Principal Investigator: Dickens, David, MD
Project Title: Children’s Oncology Group (Subcontract)
Sponsor: National Institutes of Health (Subaward)
Award Total: N/A (Per-Patient Reimbursement)
Department: Helen DeVos Children’s Hospital Department of Hematology and Oncology
Award Period: 4/13/2012 – open

**Lung**
Principal Investigator: Patzelt, Lawrence, MD
Project Title: Managing Fatigue Using Virtual Reality for Postoperative Lung Cancer Patients (Subcontract)
Sponsor: National Institutes of Health (Subaward)
Award Total: $47,701
Department: Department of Cardiology
Award Period: 9/1/2012 – 8/31/2014

**Cardiovascular Research**

**Cardiovascular**
Principal Investigator: Wohns, David, MD
Project Title: Risk Stratification in Older Persons with Acute Myocardial Infarction SILVER-AMI (Subcontract)
Sponsor: National Institutes of Health (Subaward)
Award Total: N/A (Per-Patient Reimbursement)
Department: Department of Cardiology
Award Period: 8/18/2012 – 5/31/2015

**Interventional Cardiology**
Principal Investigator: McNamara, Richard, MD
Project Title: Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) (Subcontract)
Sponsor: National Institutes of Health (Subaward)
Award Total: N/A (Per-Patient Reimbursement)
Department: Department of Surgical Specialties
Award Period: 2/26/2008 – 12/31/2016

**Vascular Surgery**
Principal Investigator: Mansour, MA, MD
Project Title: Persistent Pain and Associated Physical Function Decline Among Elderly Individuals (Subcontract)
Sponsor: National Institutes of Health (Subaward)
Total: $1,500 (Subaward)
Department: Spectrum Health Emergency Department
Award Period: 12/1/2013 – open
<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Project Title</th>
<th>Sponsor</th>
<th>Award Total</th>
<th>Department</th>
<th>Award Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oostema, Adam, MD</td>
<td>Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke Trial (POINT)</td>
<td>National Institutes of Health (Subaward)</td>
<td>$36,500</td>
<td>Spectrum Health Emergency Department</td>
<td>9/1/2013 – 8/31/2014</td>
</tr>
<tr>
<td>Pastyrnak, Steven, PhD</td>
<td>Neurobehavioral and Medical Effects of Single-Family Room Design for the Care of High-Risk Neonates: A Randomized, Controlled Study</td>
<td>The Gerber Foundation</td>
<td>$196,630</td>
<td>Helen DeVos Children's Hospital Department of Psychology</td>
<td>11/18/2010 – 8/31/2015</td>
</tr>
<tr>
<td>Elisevich, Kost, MD</td>
<td>Decision Support Systems for the Lateralization of Medial Temporal Lobe Epilepsy</td>
<td>National Institutes of Health (Subaward)</td>
<td>$58,935</td>
<td>Department of Neurosciences</td>
<td>9/1/2012 – 8/31/2015</td>
</tr>
<tr>
<td>DeRoos, Steven, MD</td>
<td>Feasibility Clinical Trial Evaluating a Personalized Medicine Approach for Patients with Tuberous Sclerosis Complex</td>
<td>Van Andel Research Institute</td>
<td>N/A</td>
<td>Helen DeVos Children's Hospital Department of Neurology</td>
<td>5/1/2013 – 4/30/2016</td>
</tr>
<tr>
<td>Pastyrnak, Steven, PhD</td>
<td>Neonatal Neurobehavior and Outcomes in Very Preterm Infants (NOVI)</td>
<td>National Institutes of Health (Subaward)</td>
<td>$70,690</td>
<td>Helen DeVos Children's Hospital Department of Psychology</td>
<td>9/3/2013 – 8/31/2015</td>
</tr>
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</table>

**PULMONARY RESEARCH**

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Project Title</th>
<th>Sponsor</th>
<th>Award Total</th>
<th>Department</th>
<th>Award Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girgis, Reda, MD</td>
<td>Long-Term Oxygen Treatment Trial (LOTT)</td>
<td>National Institutes of Health (Subaward)</td>
<td>$43,599</td>
<td>Pulmonary Department</td>
<td>3/6/2014 – 12/31/2014</td>
</tr>
<tr>
<td>Pastyrnak, Steven, PhD</td>
<td>Neurobehavioral and Medical Effects of Single-Family Room Design for the Care of High-Risk Neonates: A Randomized, Controlled Study</td>
<td>The Gerber Foundation</td>
<td>N/A</td>
<td>Helen DeVos Children's Hospital Department of Psychology</td>
<td>3/3/2012 – 2/28/2015</td>
</tr>
</tbody>
</table>

**NEONATAL RESEARCH**

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Project Title</th>
<th>Sponsor</th>
<th>Award Total</th>
<th>Department</th>
<th>Award Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pastyrnak, Steven, PhD</td>
<td>Neonatal Biomarkers in Extremely Preterm Babies Predict Childhood Brain Disorders (ELGAN-2)</td>
<td>National Institutes of Health (Subaward)</td>
<td>$437,513</td>
<td>Helen DeVos Children's Hospital Department of Psychology</td>
<td>9/15/2011 – 8/31/2014</td>
</tr>
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</table>

**NEUROSCIENCE RESEARCH**

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Project Title</th>
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<th>Department</th>
<th>Award Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elisevich, Kost, MD</td>
<td>Decision Support Systems for the Lateralization of Medial Temporal Lobe Epilepsy</td>
<td>National Institutes of Health (Subaward)</td>
<td>$58,935</td>
<td>Department of Neurosciences</td>
<td>9/1/2012 – 8/31/2015</td>
</tr>
</tbody>
</table>

**PEDIATRIC DIABETES/ENDOCRINE RESEARCH**

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Project Title</th>
<th>Sponsor</th>
<th>Award Total</th>
<th>Department</th>
<th>Award Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cemeroglu, Ayse, MD</td>
<td>TrialNet Natural History Study of the Development of Type 1 Diabetes</td>
<td>National Institutes of Health (Subaward)</td>
<td>N/A</td>
<td>Helen DeVos Children's Hospital Department of Endocrine Diabetes</td>
<td>4/27/2010 – 5/31/2015</td>
</tr>
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</table>

**PEDIATRIC NEPHROLOGY RESEARCH**

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Project Title</th>
<th>Sponsor</th>
<th>Award Total</th>
<th>Department</th>
<th>Award Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cai, Yi, MD</td>
<td>CureGN: Cure Glomerulonephropathy</td>
<td>National Institutes of Health (Subaward)</td>
<td>N/A</td>
<td>Helen DeVos Children's Hospital Department of Pediatric Nephrology</td>
<td>6/1/2014 – 5/31/2015</td>
</tr>
</tbody>
</table>
PEDIATRIC PULMONOLOGY RESEARCH
Principal Investigator: Millard, Susan, MD
Project Title: Baby Observational and Nutritional Study (BONUS) (Subcontract)
Sponsor: Cystic Fibrosis Foundation (Subaward)
Award Total: N/A (Per-Patient Reimbursement)
Department: Helen DeVos Children’s Hospital Department of Pediatric Pulmonology
Award Period: 2/1/2011 – 4/30/2016

Principal Investigator: Millard, Susan, MD
Project Title: G551D Observational Study (GOAL) (Subcontract)
Sponsor: Cystic Fibrosis Foundation Therapeutics (Subaward)
Award Total: N/A (Per-Patient Reimbursement)
Department: Helen DeVos Children’s Hospital Department of Pediatric Pulmonology
Award Period: 2/6/2012 – 12/31/2020

Principal Investigator: Millard, Susan, MD
Project Title: The EPIC Observational Study: Longitudinal Assessment of Risk Factors for and Impact of Pseudomonas Aeruginosa Acquisition and Early Anti-Pseudomonal Treatment in Children With CF (EPIC-002)
Sponsor: Cystic Fibrosis Foundation Therapeutics
Award Total: N/A (Per-Patient Reimbursement)
Department: Helen DeVos Children’s Hospital Department of Pediatric Pulmonology
Award Period: 9/1/2013 – 8/31/2018

PEDIATRIC UROLOGY RESEARCH
Principal Investigator: Meldrum, Kirstan, MD
Project Title: IL-18 Mediates Obstruction-Induced Renal Injury via TLR4 Signaling
Sponsor: National Institutes of Health
Award Total: $578,076
Department: Helen DeVos Children’s Hospital Department of Pediatric Urology

Publications
The Research Department received the following publications for inclusion in the fiscal year 2014 Annual Report. The names of Spectrum Health researchers are boldface in each listing.

CANCER RESEARCH
Adult Brain Tumor
Publications

Adult and Pediatric BMT
Publications


Publications


Adult and Pediatric Urologic Oncology

Publications


Awards


Adult Surgical Oncology

Publications

**Adult Uterine and Ovarian Cancer**

**Publications**

**Imaging**

**Publications**

**Pediatric Radiology**

**Book Chapters/Reviews/Essays**
CARDIOVASCULAR RESEARCH

Cardiovascular

Publications

Cardiothoracic Surgery

Publications


Electrophysiology

Publications


Book Chapters/Reviews/Essays

Heart Failure

Publications

Interventional Cardiology

Publications


Pediatric Congenital Heart Disease

Publications


Book Chapters/Reviews/Essays


Patents

Vascular Surgery

Publications


CRITICAL CARE RESEARCH

Critical Care

Publications


Book Chapters/Reviews/Essays

Pediatric Critical Care

Publications


EMERGENCY MEDICINE RESEARCH

Publications


Book Chapters/Reviews/Essays


GENERAL SURGERY RESEARCH

Publications


Book Chapters/Reviews/Essays


NEONATAL RESEARCH

Publications


NEUROSCIENCE RESEARCH

Adult Stroke and Traumatic Brain Injury

Publications

Epilepsy

Publications

Book Chapters/Reviews/Essays

ORTHOPAEDICS/SPORTS MEDICINE RESEARCH

Publications


Book Chapters/Reviews/Essays

PEDIATRIC DIABETES/ENDOCRINE RESEARCH

Publications


PHARMACY RESEARCH

Publications

WOMEN’S HEALTH RESEARCH

Obstetrics and Gynecology

Publications


