

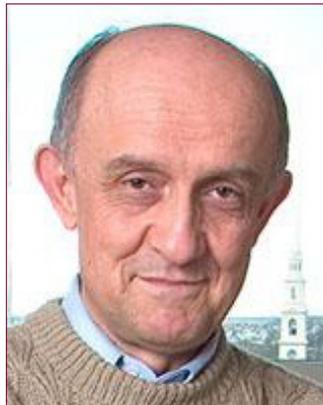
Brown experts to lead statistical analysis of nationwide \$100M dementia study

PROVIDENCE – **CONSTANTINE GATSONIS**, professor and chair of biostatistics at Brown, will lead the statistical analysis for a new national study on whether having the results of a diagnostic scan for amyloid plaques in the brain can affect the care and medical outcomes of people with dementia or mild cognitive impairment.

To help find the answers, the \$100-million, four-year “Imaging Dementia — Evidence for Amyloid Scanning” (IDEAS) study will assemble a registry of more than 18,000 people who have had PET scans and will select a control group who have not. Researchers will then gather data for two aims:

1. assessing whether having a scan result affects how care is managed — for instance whether the scans result in changes in the therapies or counseling offered patients; and
2. determining whether patients who have scans are less likely to have adverse outcomes that require visits to the hospital or the emergency room in the following 12 months.

“The purpose of the IDEAS study is to examine how brain imaging, specifically an amyloid PET scan, helps guide doctors in diagnosing and treating Alzheimer’s and other dementias in cases where the cause of cognitive impairment



Constantine Gatsonis

is difficult to diagnose,” said **DR. GIL D. RABINOVICI, MD**, IDEAS study chair and associate professor of neurology at the University of California–San Francisco. “We believe the study will show that, in diagnostically uncertain cases, knowledge of amyloid status will lead to significant changes in patient management — such as earlier counseling and prescription of more appropriate drugs — that will translate into improved long-term outcomes.”

Brown researchers have direct experience with the kind of data in the study. The University’s Center for Statistical Sciences, which Gatsonis directs, hosts the biostatistics center for the studies of the National Oncology PET Registry.

The new study will generate a huge amount of data, and tasks such as identifying appropriate matches to make meaningful comparisons will be difficult, Gatsonis said. He and Brown School of Public Health colleagues Roe Gutmann and Ilana Gareen, who collaborated to help design the study, will lead the complex statistical analyses needed to answer the questions.

“The study poses major methodological challenges,” he said. “[They] require innovation in both statistics and computation.”

The study will be funded by the Centers for Medicare & Medicaid Services and various private sources. ❖

School of Public Health holds annual research day

PROVIDENCE – The Brown School of Public Health held its annual research day on April 20th, which featured 59 poster presentations of research projects by undergraduates, graduate students, postdoctoral researchers, partner hospitals, and the Department of Health.

At the end of the poster presentation, awards were given to the best undergraduate, master’s, and doctoral or postdoctoral presenters. The winners in those respective categories were **LAUREN COLWELL**, **JOSEPH SERVADIO**, and **LIANGYUAN HU**. The runners up in each category were Katherine Caine, Brady Bennett tied with Elizabeth Kinnard, and Yi Zhao.

TERRIE FOX WETLE, dean of the School of Public Health, praised the “exceptional posters showcasing just a

tiny portion of the exciting public health research being done by Brown students, faculty, and community partners.”

Public health figures honored

Dean Wetle concluded the event with a reception honoring three leading figures in public health: **STEPHEN BUKA**, chair of epidemiology; **WILLIAM RAKOWSKI**, associate dean for academic affairs; and **DR. MICHAEL FINE**, former director of the Rhode Island Department of Health.

In honoring them, Dean Wetle acknowledged their importance in the formation and continued success of the School of Public Health. She outlined their vital contributions, including their ability to recruit outstanding faculty to the School, their interdisciplinary and



internationally recognized research, their dedication to students, their valued leadership within the University, and their tireless service to the health and well-being of the public.

Buka, who is stepping down from his role as chair of the epidemiology department, describes Public Health Research Day as part of the “magic of conducting public health research at Brown University.” It’s a reminder, he says, “of the breadth and talent of the faculty and students.” As proud as he is of his tenure as chair, he has “even greater expectations” for the future.

In addition, Public Health Research Day “generates a lot of enthusiasm

among students and faculty,” says Rakowski, who is retiring this summer. And while the research on display demonstrates wide-ranging interests, there is also coherence. “It is something the School does as a unit. That makes it important.” Rakowski especially enjoys the combination of socializing and academics. “It’s fun to talk to the students about what they’ve done, and sometimes throw them a tough question or two,” he adds. “They kind

of expect it from me.”

In honoring Dr. Fine, Dean Wetle highlighted the important relationship between the School and the Department of Public Health, which had several of their own posters on display. When policy-makers and academics present side-by-side, particularly at an event such as Public Health Research Day, it drives home the School’s mission of learning public health by doing public health. ❖

ED team at RIH publishes results of Google Glass to diagnose skin conditions

Patients liked remote access to specialists not normally available in emergencies



LIFESPAN

PROVIDENCE – One enterprising team of physicians at Rhode Island Hospital experimented with Google Glass to gauge the effectiveness, security and patient acceptance of a real-time, video dermatological consultation. The research results were published today in *JAMA Dermatology*.

Skin problems account for 3.3 percent of emergency department visits, and most patients wait months to see a dermatologist. For the patients who qualified for the trial, the emergency department physicians at Rhode Island Hospital used Google Glass – a pair of eyeglasses with a computer, camera and microphone built into the frame – to contact a dermatologist through a video link using Glass and running a third-party, Health Insurance Portability and Accountability Act (HIPAA)-compliant video platform. Later, patients were surveyed about their experience with teledermatology.

“While the patients prefer in-person visits, they said they preferred the video consultation over a more widely practiced telephone consult,” said **PAUL S. PORTER, MD**, the principal investigator and a physician in the emergency department of Rhode Island, Hasbro Children’s and The Miriam hospitals. “For patients, a fast and accurate diagnosis means a faster path to satisfactory treatment. A device

like this democratizes telemedicine because a hospital can start a program for a few thousand dollars and gain access to an experience that was only previously available at a much higher price point.”

Because of the interactive nature of the device, the teledermatologists were able to appreciate both the gestalt of nonspecific skin eruptions and specific dermatoses, or skin diseases. Additionally, the off-site doctors were able to interact with the on-site doctors by asking questions and requesting additional skin locations to examine. During the process of informed consent, medical staff explained to patients that no information was stored, and the live transmission was encrypted. The participants overwhelmingly believed that their privacy was protected.

Rhode Island Hospital was the first hospital in the U.S. to test Google Glass in an emergency department setting. The study began in March, 2014 and concluded after six months.

The study had several limitations: Because of the small size and single-site status, results cannot be generalized to other institutions; the accuracy of the diagnosis in the cases wasn’t measured; and the financial and workflow effects of the device weren’t addressed.

The study was funded by the University Emergency Medicine Foundation.

Dr. Porter, the principal investigator, is a physician in the emergency department of Rhode Island, Hasbro Children’s and The Miriam hospitals and assistant professor of emergency medicine at The Alpert Medical School of Brown University. Other researchers involved in the study were Jayne Bird, MD, and Sandy Chai, MD, of the department of dermatology, Rhode Island Hospital; Roger Y. Wu, MD, MBA, Megan L. Ranney, MD, MPH, and Brian Zink, MD, of the department of emergency medicine, Rhode Island Hospital; and Peter R. Chai, MD, MMS, of the University of Massachusetts School of Medicine. ❖

Hasbro study finds link between adverse childhood experiences and pediatric asthma

Children who experience violence, substance abuse at home report significantly higher rates of asthma

PROVIDENCE – **ROBYN WING, MD**, an emergency medicine physician at Hasbro Children’s Hospital, recently led a study that found children who were exposed to an adverse childhood experience (ACE) were 28 percent more likely to develop asthma. The rate of asthma occurrence further increased in children with each additional ACE exposure. The study, recently published in the *Annals of Allergy, Asthma & Immunology*, suggests that psychosocial factors may contribute to pediatric asthma.

“Asthma is one of the most common chronic childhood conditions, currently affecting 7 million, or 9.5 percent, of children in the U.S.,” said Dr. Wing. “The biological risk factors for asthma onset and severity, such as genetics, allergens, tobacco smoke, air pollution and respiratory infections, have been well established by previous studies. But, psychosocial factors, such as stress, which we know can be physically harmful, are now being examined as a risk factor for asthma in children.”

Dr. Wing’s team analyzed data from nearly 100,000 children and teens in the 2011-2012 National Survey of Children’s Health and compared parent or guardian reports of a child having asthma to whether a child had experienced an ACE at home. An ACE is classified as whether a child has ever:

- Lived with a parent or guardian who got divorced or separated while child was present.
- Lived with a parent or guardian who died.
- Lived with a parent or guardian who served time in jail or prison while child was present.
- Lived with anyone who was mentally ill or suicidal, or severely depressed for more than a couple of weeks.
- Lived with anyone who had a problem with alcohol or drugs.
- Saw or heard parents, guardians or any other adults in the home slap, hit, kick, punch or beat each other up.

Children exposed to one ACE had a 28 percent increase in reported asthma compared to those with no ACEs. These rates increase with each additional ACE, with children exposed to four ACEs having a 73 percent increase in reported asthma.

Most prior asthma studies have focused on neighborhood and urban-related issues, such as family poverty, poor quality housing and access to community resources. But, disruptive family relationships within the home can be a significant source of psychosocial stress for children.

“Psychosocial stressors activate the sympathetic nervous system, which

controls our ‘fight or flight’ responses when we experience stressful situations,” said Dr. Wing. “Increased activity of this system releases cortisol, a stress hormone, which has been shown to affect the activity of immune cells. Occasional increases in these hormones are protective, but excessively high or prolonged exposures, such as those experienced by children exposed to ACEs, can be harmful.”

Dr. Wing hopes this study, and others like it, will underscore the complex causes of asthma, enabling clinicians to better target preventative medications and other interventions. “Physicians taking care of children with asthma should take the time to ask about the child’s home situation,” said Dr. Wing. “For children experiencing stressors at home, encouraging efforts to increase the child’s capability of handling stressors, using methods such as individual or family therapy, may help target pediatric asthma.”

She continued, “Stress should be viewed as a risk factor for asthma development and asthma exacerbations, much like tobacco smoke and dust mites. At the very least, clinicians can share with parents the impacts of ACEs on their child’s asthma, perhaps acting as a motivating factor for parents to remove or shield a child from a stressful home situation.” ❖

Compassion unleashed with Memorial Hospital’s new Pet Therapy Program

PAWTUCKET – The Center for Rehabilitation at Memorial Hospital of Rhode Island has launched a pet therapy program to enhance the environment of care for patients of all age levels.

KEITH RAFAL, MD, MPH, chief of rehab and medical director of the Center for Rehabilitation, said, “Memorial Hospital’s pet therapy program is a special way we show compassion for our patients, their families and hospital staff.”

Pet therapy is a guided interaction between a patient and a trained animal. It also involves the animal’s handler. Therapy dogs are family pets, not service dogs like those that assist the disabled. These dogs are obedient and deal well



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with different situations and enjoy meeting people. Memorial's program is offered to patients on the Center for Rehabilitation, both in the therapy area and patient rooms. Susan Higgins, owner/handler of her pug dog, Bridget, currently visits Memorial's rehab patients once a week for one hour. Bridget has been a therapy dog for the past six years.

Dr. Rafal adds, "You can feel the joy and see the smiles that our lovable volunteers bring to all."

The owners ensure their animals meet all the standards set by Therapy Dogs International, Inc. for medical pet therapy, including providing licensing, credentialing and general liability insurance. ❖

Pictured left to right in The Center for Rehabilitation at Memorial Hospital, Susan Higgins, owner/handler of Bridget, therapy dog, visiting with William Black, a rehab patient and Providence resident, and Keith Rafal, MD, MPH, chief of rehab and medical director of the Center for Rehabilitation.

URI engineering students develop wristband to measure tremors in PD

KINGSTON – For the 4 million people worldwide with Parkinson's disease, a smart wristband invented by a team of University of Rhode Island engineering students could let them lead healthier lives.

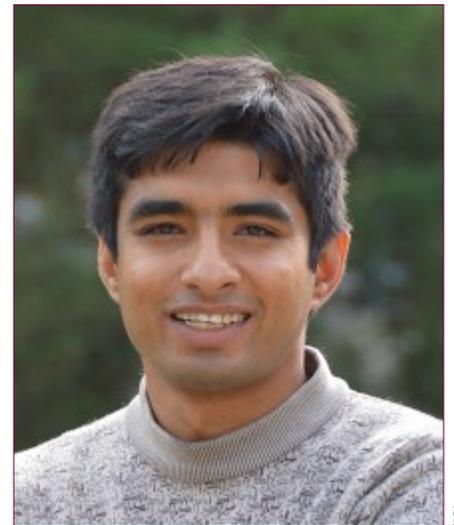
Known as TeleTremor, the wristband uses high-quality motion sensors to detect tremors and movement difficulties in people with Parkinson's disease and send the information over a secure Internet connection to doctors. Though

innovative visualizations, TeleTremor enables neurologists to make more informed decisions by measuring the effect of prescribed medications and progression of the disease.

Biomedical engineering student **TREVOR BERNIER**, computer engineering student **JOSEPH TUDINO** and electrical engineering student **AKINTOYE ONIKOYI** teamed up to design the system and build a prototype.

In March 2015, they garnered international exposure as one of 23 finalists at the International Undergraduate Global Health Technologies Design Competition at Rice University in Houston.

"TeleTremor is a product of URI's continuous efforts toward nurturing excellence, leadership, innovation and real-world experience through collaboration in our next generation of engineers who are acquiring the right skills for today's highly dynamic marketplace," says **KUNAL MANKODIYA**, an assistant professor of biomedical



URI's Kunal Mankodiya, an assistant professor of biomedical engineering, supervised the team.

engineering who supervised the team.

It's not the first time Mankodiya and his students have leveraged smart technology to improve patient care. Another team of students is working on a smartphone system that can monitor vital signs and send the information to doctors over the Internet. It's all part of the college's push to connect education with improving lives. ❖



URI engineering students showcase TeleTremor at the International Undergraduate Global Health Technologies Design Competition.

Gold by special delivery intensifies cancer-killing radiation

KINGSTON – Researchers from the University of Rhode Island and Brown University have demonstrated a promising new way to increase the effectiveness of radiation in killing cancer cells.

Building on research by URI Physics **PROFESSORS YANA RESHETNYAK** and **OLEG ANDREEV**, the new approach involves gold nanoparticles tethered to acid-seeking compounds called pHLIPs. The pHLIPs (pH low-insertion peptides) home in on the high acidity of malignant cells, delivering their nanoparticle passengers straight to the cells' doorsteps. The nanoparticles then act as tiny antennas, focusing the energy of radiation in the area directly around the cancer cells.

In a paper published April 13 in the Proceedings of the National Academy of Sciences, the research team shows that the approach substantially increases the cancer-killing power of radiation in lab tests.

"This study was a good proof of concept," said Michael Antosh, assistant professor in Brown's Institute for Brain and Neural Systems and the paper's lead author. "We're encouraged by our initial results and we're excited to take the next step and test this in mice."

The team is hopeful that the approach could ultimately improve radiation treatment for cancer patients. By increasing the effectiveness that a given dose of radiation has on cancer, the technique could reduce the overall radiation dose a patient requires, which would in turn reduce side effects. It could also increase the effectiveness of radiation at doses currently administered.

Reshetnyak and Andreev, along with Yale University Professor Donald Engelman, invented the pHLIP technology. They had previously developed pHLIPs as a potential delivery system for cancer drugs and diagnostic agents. Cancer cells are generally more acidic than healthy cells, and pHLIPs are natural acid-seekers.

"We previously demonstrated that

pHLIP-nanogold particles could find and accumulate in tumors established in mice," Reshetnyak said. "Now our task is to test if we can treat cancer by irradiating tumors with nanogold particles more efficiently in comparison with traditional radiation treatment."

Both theoretical and experimental work had shown that gold nanoparticles could intensify the effect of radiation. The particles absorb up to 100 times more radiation than tissue. Radiation causes the particles to release a stream of electrons into the area around them. If the particles were in close proximity to cancer cells, that stream of electrons would inflict damage on those cells.

"The idea here was to bring this all together, combining the nanoparticles with the delivery system and then irradiating them to see if it had the desired effect," said Leon Cooper, the Thomas J. Watson Sr. Professor of Science at Brown and one of the study's co-authors. Cooper, who shared the Nobel Prize in 1972 for explaining the behavior of electrons in superconductors, has been working for the last several years to better understand biological responses to radiation.

Gold is an especially good choice for amplifying radiation. When matter

is hit by radiation at certain energies, electrons are released through a process known as the photoelectric effect. But gold has an additional source of electron emission, known as the Auger effect, that results from the particular arrangement of electrons orbiting gold atoms. It's the effect of the Auger electrons that the researchers were working to maximize. Working out the quantitative details of the process involved a complex series of calculations and simulations.

Experiments showed that cancer cells irradiated in the presence of pHLIP-delivered gold had a 24-percent lower survival rate compared to those treated with radiation alone. The pHLIP samples had a 21-percent lower survival compared to irradiation with just gold but no pHLIPs. That suggests that the pHLIPs were effective in getting the gold close enough to the cells to do damage.

The next step, the researchers say, is to test the approach in a rodent model, which the team is planning to do soon.

"This work is a great example of successful collaboration between Brown and URI," Andreev said. "We hope that the results of this research moving forward will lead to clinical application of pHLIP-based nanotechnology." ❖

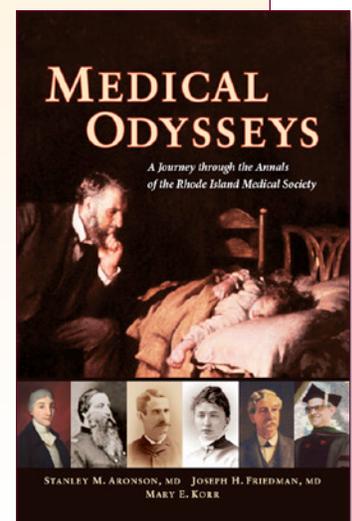
Medical Odysseys Available!

Medical Odysseys: A Journey through the Annals of the Rhode Island Medical Society, was published for the Society's Bicentennial in 2012.

A limited number of copies remain. Readers of Dr. Stanley Aronson's uniquely erudite and entertaining essays on medicine, medical history, language and forensic folklore will cherish this compilation, which also includes commentaries by Dr. Joseph Friedman, executive editor of the *Rhode Island Medical Journal*, as well as essays on aspects of RIMS' history by RIMJ managing editor Mary Korr.

The cost is \$15 and includes postage.

Please contact Sarah at the RIMS office:
[ssstevens@rimed.org](mailto:sstevens@rimed.org) or 401-528-3281.



Borderline Personality Disorder as Debilitating as Bipolar Disorder

Mark Zimmerman, MD, compared psychiatric disorders to predict morbidity

PROVIDENCE – The deterioration of psychiatric and physical health caused by borderline personality disorder (BPD) rivals that of bipolar disorder, according to **MARK ZIMMERMAN, MD**, a researcher at Rhode Island Hospital. His research was published online in the *British Journal of Psychiatry* last week.

“The level of psychosocial morbidity and suicidality associated with BPD is as great, or greater, than that experienced by patients with bipolar disorder,” said Zimmerman, director of outpatient psychiatry at Rhode Island Hospital and director of the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project. “From a public health perspective, improving the detection and treatment of BPD is as imperative as diagnosing and treating bipolar disorders.”

The National Institute of Mental Health estimates that 1.6 percent of the U.S. population is diagnosed with BPD, compared with 2.6 percent of those with bipolar disorder.

This is the largest comparison of patients who have been diagnosed with BPD or bipolar disorder. Persons with BPD have difficulty regulating emotions and thoughts, often teetering at extremes. They engage in impulsive and reckless behavior, and their relationships with other people are rocky. While persons with bipolar disorder experience the same mood for weeks, those with BPD cope with intense bouts of anger, depression and anxiety that are short in duration. According to Zimmerman’s study, clinical experience suggests that BPD is as disabling as bipolar disorders. In psychiatric patient samples, BPD is as frequent as bipolar disorder.

Like bipolar patients, persons with BPD are likely to also suffer from depression, anxiety disorders, substance abuse, eating disorders and suicidal behaviors. These co-occurring mental illnesses may have symptoms that overlap with BPD, making it difficult to recognize BPD in patients with these other mental illnesses.

“Despite the clinical and public health significance of both of these disorders, it sometimes seems as if BPD lives in the shadow of bipolar disorder,” said Zimmerman. “Bipolar disorder is a widely researched, well-publicized, well-funded topic. By contrast, BPD is seldom discussed and it is not included in the Global Burden of Disease study, a comprehensive registry that quantifies diseases by cost, mortality, geography, risk and other factors.”

This study was a component of the MIDAS project, which is an ongoing clinical research study at Rhode Island Hospital involving the integration of research assessment methods into routine clinical practice.

No external financial support was provided for this research study. Zimmerman’s principal affiliation is Rhode Island Hospital and The Miriam Hospital, members of the Lifespan health system in Rhode Island. He also has an academic appointment at the Alpert Medical School of Brown University, department of psychiatry and human behavior. Other researchers from that department involved in the study were **WILLIAM ELLISON, PhD, THERESA A. MORGAN, PhD, DIANE YOUNG, PhD, IWONA CHELMINSKI, PhD, and KRISTY DALRYMPLE, PhD.** ❖

Sandra Salzillo to speak at international trauma treatment conference

PROVIDENCE – **SANDRA SALZILLO, MA, CAGS, LMHC, APA**, a licensed mental health clinician with the Program in Women’s Oncology at Women & Infants Hospital, was invited to serve on the faculty for an international conference on trauma treatment.

“After the Storms: Psyche’s Response to Trauma, Resilience and Healing” will take place June 18 to 21, at The Assisi Institute, an international psychological organization founded in 1989 and located in Mystic, CT. Salzillo joins some of the world’s leading scholars, psychologists and trauma experts on the faculty.

“The psychological, emotional and

physical impact of trauma is a daily reality for millions of Americans,” Salzillo says. “About 70 percent of us have experienced some type of traumatic event at least once in their lives. Of these people, at least 20 percent, or about 44 million people, will develop post-traumatic stress syndrome or PTSD as a result.”

The conference will highlight the need for a more nuanced approach in working with people who struggle with the daily realities of PTSD, and will offer some of the latest research in neurological and somatic studies. In addition, presentations on innovative approaches to helping integrate

and work with the ongoing effects of trauma are planned.

Salzillo is a nationally-acclaimed visual artist, expressive arts facilitator and archetypal pattern analyst. She is a senior faculty member at the Assisi Institute and an adjunct professor in the holistic counseling master’s program at Salve Regina University. At Women & Infants, she facilitates groups and workshops, and provides individual counseling to patients. Her work is based on connecting women to their imaginative abilities, which allows for a deeper understanding of their personal process. ❖