



The Montlake Cut

A Publication of the Department of Neurological Surgery
UW Medicine Health Care

A View From Puget Sound



Richard G. Ellenbogen
M.D., F.A.C.S.

Welcome to the winter 2014 issue of 'The Montlake Cut'. In this issue we are pleased to bring you news of an intriguing research effort to develop a robotically driven flexible endoscope for neurosurgical procedures, as well as provide an overview of our substantial clinical and research involvement in understanding and treating concussion. In addition, we profile a new medical school clerkship developed by Assistant Professor Amy Lee with able assistance from Aubriana Ard and our faculty, and give some insight into our CME efforts in Central Washington. Further, we cite some of our basic scientist's most recent publications and share news of a recent award to our longtime colleague Pat Blissitt, Neuroscience Clinical Nurse Specialist at HMC. We are also delighted to introduce several new staff members to our administrative core and especially pleased that Dr. Minku Chowdhary invigorates this 2014 New Year edition with a brand new puzzler.

Please enjoy this edition and remember, as always, we welcome your feedback and thank you for your support.

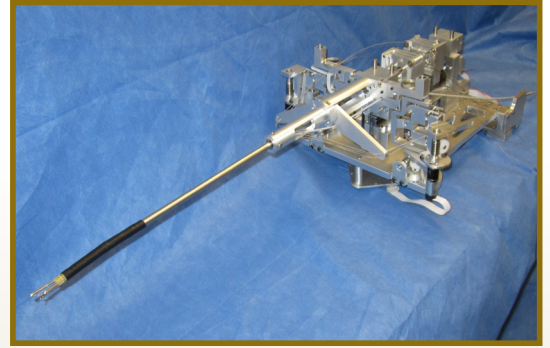
Sincerely,

Richard G. Ellenbogen, MD, FACS
Professor & Chairman, Department of Neurological Surgery

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Ender's Game - Science Fiction & Science Future



What does the film *Ender's Game* have to do with robotics and the Department of Neurological Surgery? Plenty, as it turns out. The 2013 film, based on the classic 1980's novel of the same name by Orson Scott Card, features a scene showing one of the main characters undergoing robotic neurosurgery. Rather than science fiction, that surgical robot (Raven II) not only turns out to be real but also has significant connections to our Department through its developers, Drs. Blake Hannaford, UW Electrical Engineering, and Jacob Rosen, UW Santa Cruz Computer Engineering. Raven II was developed with NSF funding and is now used by research universities across the country, principally for procedural design and testing of new hardware. The eventual goal is to use Raven II in clinical settings. Drs. Hannaford and Rosen are directly connected to the UW Neurological Surgery through extensive collaboration on a flexible, robotically-driven endoscope and surgical control console - the "Roboscope" - that will feature 3D visualization and a suite of surgical tools.

Drs. Hannaford and Rosen have joined with Neurological Surgery faculty (Laligam Sekhar, Louis Kim, James Pridgeon) and several other School of Medicine Faculty (Kristen Moe and Thomas Lendvay) to develop a robotically controlled, bendable robotic sheath, an introducer device, and a surgical control cockpit. The combined system, known as the Roboscopic Surgical System (RSS), is designed to leverage existing complementary technologies and improve the quality and cost-effectiveness of surgical care. In combination, the RSS will enable surgery to be performed on a smaller scale (microsurgery), increase accuracy and precision (stereotactic surgery), access small corridors through natural orifices (minimally invasive surgery), enable the processing of large amounts of data (image-guided surgery), create opportunities for telesurgery and reduce the surgeon's physiological tremor 10-fold. The investigators have formed an outside company, Spi Surgical, that has received more than \$1M in federal funding to develop the prototypes for what they hope will become the first working neurosurgical robotic system.

Traditional neurosurgical approaches to the skull base have concentrated on craniofacial translocation procedures (displacement or removal of bone for the surgical approach). While these approaches can achieve access to pathology, they can also generate significant morbidity to adjacent bone and neurovascular structures. To overcome some of these drawbacks, neuroendoscopy was introduced in 1992. Since then, the endoscope has been used in the management of intracranial tumors, hydrocephalus, intracranial hematomas, pituitary tumors, and other neurological problems. Some of central corridor pathology (between the orbits) can now be accessed and treated with transnasal endoscopic surgery, such as the resection of pituitary adenomas and the repair of skull base CSF leak.

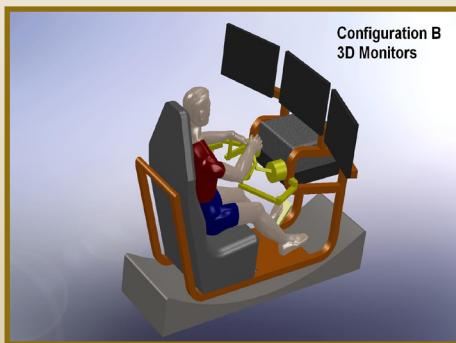
A critical problem with current endoscopic techniques concerns the devices themselves: present technology allows only a straight line from the point of entry to the surgical site often creating a suboptimal access trajectory for many surgical procedures. Due to the complex curved geometries within the skull, this is particularly true for neurosurgical procedures. Lesions that cannot be reached in a straight line from the point of entry cannot be treated effectively with currently available straight, rigid endoscopes. Lesions located away from the midline, or obstructed by essential brain structures are even more problematic. With better scopes and robotics, the surgeon will be able to operate at the end of a curvilinear path and navigate around vital structures such as eloquent areas and blood vessels. Further, a flexible endoscope with a curved path enlarges the range of endoscopic operations in several key specialties such as neurosurgery, otolaryngology - head and neck surgery, urology, obstetrics and gynecology.

Science Fiction or Science Fact? *Ender's Game* and our colleagues are showing us Science Future.

- Jim Pridgeon, MHA, Lecturer

Read the November 2013 article published on the University of Washington site:

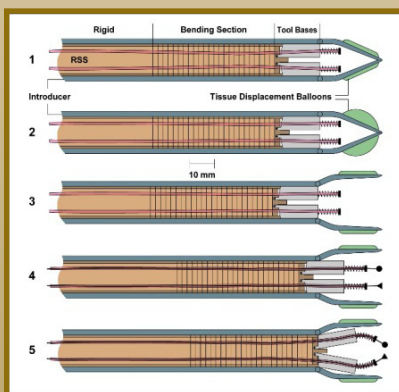
<http://www.washington.edu/news/2013/11/01/uw-surgical-robot-featured-in-2013-movie-enders-game/>



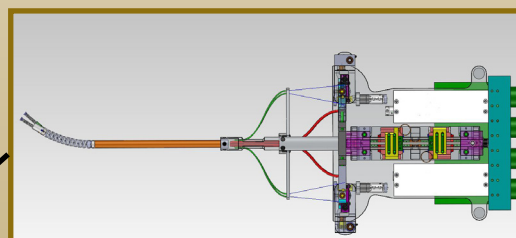
Control Console Drawing



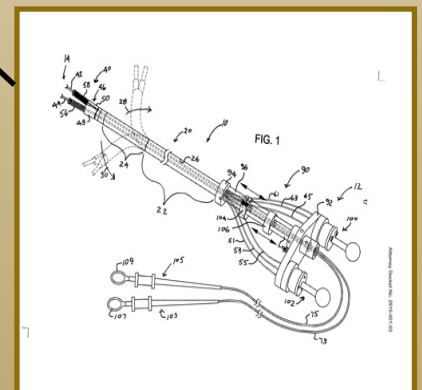
Control Console Prototype



Introducer Drawings



Roboscope Drawing



Roboscope Drawing

New Respect For An Old Problem



Concussion is a serious but long neglected public health problem. In addition to our lack of fundamental understanding about mechanisms and long-term outcomes, concussion has been plagued by a culture of disregard. Significant symptoms have too often been discounted and athletes encouraged to “shake it off and get back in the game”.

A concussion is a type of Traumatic Brain Injury (TBI) caused by the forceful shaking of the brain in the skull from a blow, fall or collision. (*see sidebar*). An injury to the body that causes the head and brain to move quickly back and forth may produce the same changes. The annual incidence is not precisely known because most injuries do not result in ER visits or hospitalizations. However, the Center for Disease Control (CDC)

estimates that there are several million sports and recreation-related concussions in the US each year. ER visits among children and adolescents for sports and recreation-related TBI, including concussions, increased by 60% during the last decade. This may have resulted from an increased awareness on the part of coaches, trainers and parents that these injuries can be significant. UW faculty are providing national and international leadership for optimal concussion care and improving future treatment through research. Drs. Stan Herring from Rehabilitation Medicine and Rich Ellenbogen from Neurological Surgery are Co-Directors of the UW Medicine Concussion Program and Clinic.

Immediate Concussion Symptoms Include:

- headache
- confusion/disorientation
- difficulty concentrating
- slow or incoherent speech
- sensitivity to light
- nausea
- amnesia
- memory loss
- ringing in ears
- dizziness
- double vision

Delayed Concussion Symptoms Include:

- headache
- memory difficulties
- fatigue
- anxiety
- light & noise intolerance
- poor concentration
- foggiess
- sleep disturbance
- depression

The ‘perfect storm’ of soldiers returning from Iraq and Afghanistan with TBI and PTSD, plus the increased recognition of concussion in youth and professional sports, has required neuroscientists to better understand the consequences of TBI. There is heightened concern about these injuries in children and teens both because they are at greater risk and may take longer to recover than adults. This increased awareness has resulted in revised injury guidelines and substantive rule changes in youth, college and professional sports, as well as increases in research funding by the NFL, NIH and DOD.

UW faculty in Neurological Surgery collaborate with UW faculty experts in several departments as well as other universities to help define both best practices and better understanding of concussion. The UW faculty provided support in passage of the Zackery Lystedt Law in Washington state (*see below*). The NFL has encouraged the adoption of this legislation nationwide and it is now law in all states except Mississippi.

The Zackery Lystedt Law in Washington state requires education of athletes, parents and coaches about concussions, removal from practice or play if an athlete is suspected of having suffered a concussion and return to practice or play only with the written clearance of a licensed healthcare professional knowledgeable about concussions. The law is named after Zackery Lystedt, a Maple Valley teenager who returned to play after suffering a concussion while still having symptoms. As a result, he suffered a severe traumatic brain injury that could have been avoided. Zackery Lystedt's life was saved at Harborview Medical Center/UW Medicine by the neurological surgery team.

Concussion and TBI Research Awards

Research collaborations on concussions are increasing. In mid-December, the NIH announced eight grants to address some of the most fundamental problems including improved diagnosis and a better understanding of the long-term effects of repeated head injuries. Funded largely by a \$30M NFL donation to the NIH Foundation, two of the eight projects involve Neurological Surgery faculty. Richard Ellenbogen is Site PI for a multi-center effort entitled “Neuropathology of CTE and Delayed Effects of TBI: Toward In Vivo Diagnostics.” This study will identify and describe the chronic effects of mild, moderate and severe TBIs compared with features of Chronic Traumatic Encephalopathy. We aim to identify potential markers that may eventually be used to diagnose and treat the degenerative effects of TBI.

Neurological Surgery Professor Jeffrey G. Ojemann was awarded another of the grants to study *Cortical GABA in Pediatric Sports Concussion*. MR spectroscopy will be employed to monitor GABA levels in adolescents who have sports-related concussions and compare those levels to uninjured controls. Dr. Ojemann’s group will also compare GABA levels with existing cognitive measures such as memory tests and structural brain imaging. Diagnostic tools that can detect brain injury and recovery reliably following concussion are essential for determining when it is safe to resume normal activities. Neurological Surgery faculty members are involved with two additional collaborative projects of concussion and other TBI. One is a Paul G. Allen Family Foundation award with colleagues in the Departments of Medicine and Pathology/NeuroPathology in collaboration with Group Health Cooperative and the Allen Brain Institute. A second award is for the UW’s clinical site participation in the NIH-funded TRACK-TBI study. (*see below*)

-Richard G. Ellenbogen, MD, Professor and Chairman

Paul G. Allen Family Foundation Award

In November 2013, the **Paul G. Allen Foundation** awarded a new \$2.37 million grant to help Seattle-area researchers embark on an important research effort designed to investigate the lasting effects of TBI in people - an area that has long been filled with question marks for physicians and scientists. The grant, awarded over two years to the University of Washington, Group Health Cooperative and the Allen Institute for Brain Science, will help fill in the gaps about the unknown lasting structural and biological effects of TBI. The proposal entitled *Structural and Biological Changes in TBI-Related Neurodegeneration* address effects of TBI that are largely unknown. We expect the results of our neuropathologic and molecular analyses of brains from TBI and control cases will illuminate neurodegenerative phenotypes of TBI, identify relationships between TBI-related neurodegeneration and other neurodegenerative diseases and foster future research into mechanisms, diagnostic strategies and therapeutic targets.

UW Neurological Surgery is pleased to announce its participation in **TRACK-TBI**, a major TBI research initiative funded by the **National Institute of Health**. UW is one of 20 UW institutions participating in the International Traumatic Brain Injury Initiative study coordinated by UC San Francisco. Three thousand US TBI cases and trauma controls will be followed from injury to 1 year after injury. Neurological Surgery Professor Nancy Temkin is Co-Principal Investigator of the overall study, Professor Randy Chesnut is the UW Site Principal Investigator, and Professor and Chair Richard Ellenbogen is Co-Investigator. Rehabilitation Medicine Professor Sureyya Dikmen (Adjunct Professor of Neurological Surgery) is a major collaborator on Neurological Surgery TBI research teams and is also a Co-Investigator. Sara Wellnitz will be the study coordinator for UW-based projects.

Read the UCSF Press release here:

<http://www.ucsf.edu/news/2013/10/109851/traumatic-brain-injury-research-advances-188-million-nih-award-administered-ucsf>

New Clerkship in Neurological Surgery Offered

This Fall, the School of Medicine offered UW medical students the opportunity to elect a Neurological Surgery rotation. While for many years the Department has hosted final year Sub I's on-service at one of our centers for as much as a month (with their eyes on the Match), there has not been a formal elective for UW students. Now our own fourth-year medical students may choose either neurology or neurosurgery as a clinical rotation.

Assistant Professor Amy Lee managed to formalize the more-than-a-little daunting expectations required to create the *de novo* course, and Aubriana Ard, our remarkably talented Graduate Medical Education Program Administrator, helped put it in motion. Then they had to round up faculty members to participate!

This clerkship provides an introduction to Neurological Surgery and features a faculty lecture series surveying the main components of our specialty. Students learn to do a proper neurological exam, the fundamental anatomy and physiology of the nervous system, as well as concepts in the diagnosis, pathophysiology and treatment of neurosurgical disorders. This 4-week rotation includes inpatient rounds and outpatient neurosurgical clinics, OR exposure and weekly conferences/didactics. Some of medicine's most common problems - TBI, hydrocephalus, stroke, back pain, hemorrhage and tumors - are illnesses often first seen by non-neurosurgeons in offices, clinics and emergency departments. All of us hope that the students also learn a little bit about what it means to be a good doctor as well as a skilled surgeon. - So far, the elective has been popular with students, residents and faculty. At least no one has yet been flamed on the internet!

Lectures:

The Neurological Exam: Drs. Richard Rapport & John Howe

Tumors: Dr. Manuel Ferriera

Hydrocephalus/Pediatric Neurosurgery: Drs. Sam Browd & Amy Lee

Spine: Dr. Eric Chang

Neurovascular: Dr. Louis Kim

Epilepsy: Dr. George Ojemann

Traumatic Brain Injury: Drs. Richard Rapport & John Howe

Pain: Dr. John Loeser

Concussion Treatment: Dr. Richard Ellenbogen



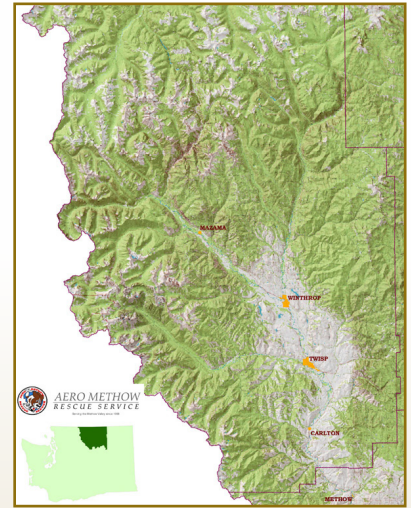
Dr. Amy Lee



Aubriana Ard

UW Neurological Surgery Again Provides CME in Twisp

For the fourth consecutive year, the Department of Neurological Surgery and UW Medicine has taken specialized training to the staff at Aero Methow and the community of Twisp. This year, Chief Residents Michelle Chowdary and Ryan Morton used a weekend to make the four-hour trip from Seattle and talked to about 25 EMTs and paramedics. Dr. Morton discussed TBI and vascular neurosurgery and Dr. Chowdary spoke about cervical spinal injuries. Dr. Rapport was there too and talked about the biological basis of memory, although what this has to do with emergency management in the field, he didn't specify.



Aero Methow Rescue Region

Aero Methow has served the people and communities of the geographically vast Methow Valley as its only nonprofit ambulance and rescue service since 1968. From the end of Gold Creek (south) to the Canadian line, and west from Rainy Pass on the North Cascades Highway to Loup Loup Summit headed east, they are dedicated to serving others by providing urgent medical care and transportation of sick and injured residents and visitors in the valley. A secondary mission is to promote injury prevention through education. While there are doctors in the Central Valley, their offices are closed at 5 PM and on weekends, so often these dedicated medics are the only health

care available in this entire region. Many of their evacuated patients wind up at HMC.

Cindy Button, herself a Paramedic, is the Aero Methow Director of Services. Her father, the late Dr. William Henry, was the only physician in the Methow Valley from 1960-1990. Bill Henry helped Mike Copass establish the state-wide emergency transportation system when Mike directed the Harborview ED. - **Richard Rapport, M.D.**



Aero Methow Group



Director, Cindy Button & her mother Ann Henry



Aero Methow Rescue Service



Dr. Michelle Chowdary & Dr. Ryan Morton

Department Basic Scientists at Work

While some of the older neurosurgical faculty remember when it was part of an academic career to do one's own bench research, basic science as applied to neurological surgery is now far too complex to be part-time work. That is why we are blessed to have full-time researchers as a part of our Department. These basic investigators run sophisticated laboratories aimed at investigating problems with translational elements that have both clinical application or in other ways overlap with the clinical interests of the Department. Some highlights of their very recently published work are shown here.



Robert Hevner in *Journal of Neuroscience*, **Dynamic Interactions between Intermediate Neurogenic Progenitors and Radial Glia in Embryonic Mouse Neocortex: Potential Role in Dll1-Notch Signaling.**

There are different populations of progenitors in the CNS and these inter-communicate via Notch signaling to maintain pool density and identity. High-resolution, live-cell multi-photon microscopy has revealed the involvement of short and long-range anatomic processes.

Phil Horner in *Journal of Neuroscience*, **Differential Progression of Structural and Functional Alterations in Distinct Retinal Ganglion Cell Types in a Mouse Model of Glaucoma.**

A principal risk factor for glaucoma is elevated intraocular pressure. In mice, this leads to early changes in the light-response of specific (not all) retinal ganglion cell types, before detectable dendritic loss and cell death.

Forrest Kievit (with Richard Ellenbogen, Miqin Zhang) in *World Neurosurgery*, **Targeted Cell Uptake of a Non-Internalizing Antibody Through Conjugation to Iron Oxide Nanoparticles in Primary CNS Lymphoma (PCNSL).**

It is difficult to deliver therapeutically-effective doses of drugs to the intracellular site of the target PCNSL. However, iron oxide nanoparticles coated with a copolymer and conjugated with antibody showed higher binding (and internalization) to PCNSL as compared with control cells.

Richard Morrison (with Yoshito Kinoshita) in *Journal of Neuroscience*, **Declines in Drp1 and Parkin Expression Underlie DNA Damage-Induced Changes in Mitochondrial Length and Neuronal Death.**

It is important to maintain the proper mitochondrial length for normal function. Neuronal DNA damage results in more elongated mitochondria, and this correlated with declining expression prior to cell death of a fission protein (Drp1) and of the ubiquitin ligase, parkin.

Pierre Mourad in *Autism Research*, **Mice Exposed to Diagnostic Ultrasound in Utero are Less Social Yet More Active in Social Situations Relative to Controls.**

Pregnant animal studies show a link between clinically-relevant doses of ultrasound, structure and function in the brains of the offspring. Fetal ultrasound resulted in more active mice, but who were less interested in social interaction.

Sean Murphy (with Richard Morrison) in *Journal of Neurochemistry*, MS-275, A Class I Histone Deacetylase Inhibitor, Protects hte p53-Deficient Mouse against Ischemic Injury

Histone deacetylase inhibitors are highly neuroprotective in animals. To see if this depended on an important acetylation target, p53, CNS cells and tissues from p53-deficient mice were made ischemic. Interestingly, benefits of the drug were most pronounced in the absence of p53.

John Silber in *Chemical Research Toxicology*, Synthesis and Characterization of DNA Minor Groove Binding Alkylating Agents.

Toxicity was evaluated in cells under-and over-expressing the enzyme that excises N3-Methyladenine from DNA. This was inversely related to enzyme expression, suggesting that unrepaired N3-Methyladenine is toxic due to its ability to directly block DNA polymerization.

Complete Citations

Nelson, Hodge, Bedogni, **Hevner** (2013) *J Neurosci*. 33:9122-9139

Santina, Inman, **Horner**, Wong (2013) *J Neurosci*. 33:17444-17457

Wang, **Kievit**, Veiseh, Arami, Stephen, Fang, Liu, **Ellenbogen**, **Zhang** (2013) *World Neurosurgery*. 80:134-141

Wang, Garden, Kinoshita, Wyles, Babazadeh, Sopher, **Kinoshita**, **Morrison** (2013) *J Neurosci*. 33:1357-1365

McClintic, King, Webb, **Mourad** (2013) *Autism Res*. - In Press

Murphy, Lee, McClean, Pemberton, Uo, **Morrison**, Bastian, Baltan (2013) *J Neurochem*. - In Press

Iyer, Srinivasan, Singh, Mascara, Zavitova, Sidone, Fouguerel, Svilar, Sobol, Bobola, **Silber**, Gold (2013) *Chem Res. Toxicol*. 26:156-168

Pat Blissitt, RN Honored



Harborview's Pat Blissitt, RN has been named the **March of Dimes Nurse of the Year** for Western Washington in the Education Category. She is currently the Neuroscience Clinical Nurse Specialist at HMC, as well as Assistant Professor in the UW School of Nursing where she instructs both undergraduate and graduate students. Pat is a familiar figure to all of us on the wards and in the NCCU. She was a member of the team that helped to create the Comprehensive Stroke Program at HMC last year, and has developed Web-based training modules to meet staff educational needs. In addition to her regular teaching duties, she organizes the "Chalk Talks" in the unit, and is always around to explain the newest developments, changes in algorithms, alterations in rules - or lead a new befuddled RN, resident, or medical student to figure out which end is up.

UW Department of Neurological Surgery Welcomes Two Hew Hires and Announces a Promotion

Christina Buckman joined our department on August 26th and will be responsible for all publications, social media, records retention, departmental events, observational privileges and providing administrative support for the summer student program. Christina comes to us from the Daily Journal of Commerce, where she worked as Layout/Design Specialist and Assistant Editor. She also has prior experience as Event Planner at The Ruins (a high-end exclusive dining and event club) and was Administrative Support and Assistant Editor/Content Contributor at Encore Media Group/City Arts Magazine. Welcome Christina!



Christina Buckman



Jackie Chapman

Jackie Chapman joined our team on October 11th and is serving as our Appointments and Promotions Specialist. She will also take the lead on processing all staff hiring and HR paperwork, handle all visitor and visa requests, manage Jana Pettit's calendar and facility requests at NJB and serve as a Project Manager for all facility/lab projects in all of our departmental locations. Jackie was a Business Organizer/Productivity Consultant, Research Assistant, an English teacher in South Korea and Manager of an Australian B&B. Welcome Jackie!

We are pleased to announce that Kris Lewis has been promoted to Senior Computer Specialist. Kris has a degree in Computer Science, specializing in IT security and cryptography and has held positions as a Database Developer and Web Administrator. Kris will be responsible for building departmental databases, running queries from existing UW Medicine databases and supporting all data requests, providing support for Mac users, working closely with faculty and staff to understand user needs. In addition he will develop and maintain a disaster and recovery plan for all of the department hardware and software and provide the technical expertise to keep our website and social media platforms up-to-date. Congratulations Kris!



Kristofer Lewis



Yvette Kieu

Yvette Kieu joined our department on December 2nd as our new fiscal specialist. She will be working on purchasing, travel arrangements, reimbursements and payroll. Yvette recently graduated from the UW majoring in Communications with a double minor in Business Administration and Diversity. As a student, Yvette worked with the Seattle Preservation and Development Authority to help with grant writing and sponsorship opportunities. In addition, she worked with Seattle MESA developing and implementing outreach programs and providing counseling to under-represented students. Welcome Yvette!

Births

Congratulations to our resident Chibawayne Ene and his wife, Rachel Elizabeth Ene. They welcomed Ian Joseph Chidera Ene on December 23rd. He came into the world at 4:25 pm and both Mom and Ian are doing great, and big brother Ben is adjusting very well to the new “boss” in town!



Dr. Minku Chowdhary
Chief, Neurosurgery
Overlake Hospital

Puzzler



Puzzler: Jay Cutler and Barry Bonds are two famous athletes who owe success to the discoveries of this man, who is so unique, that there are only 3 other people in the world like him.

Answer to October's Puzzler

October's Puzzler: This man's most famous book had to be rewritten due to protests from other researchers in the field along with some adoptive parents and some feminists. His other research included studies on the role of a group of people whose name derives from Ancient Greek and translates as “female slaves.” Who was he, and what role did he play in modern healthcare?

Answer: John H. Kennell, role of immediate maternal infant bonding which changed hospital procedures that gave new mothers more private time with their infants, let fathers into the delivery room and allowed young children to visit new siblings in the hospital. Read the NYTimes September 2013 article about Dr. Kennell.

http://www.nytimes.com/2013/09/22/health/john-kennell-advocate-of-infant-bonding-dies-at-91.html?ref=science&_r=0

We remain eager to publish stories and photos about all aspects and activities of the Department. Please share your memories, ideas and suggestions for stories and news items that expand our common ground. Please contact us at these email addresses:

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