

Neuro-Otology and Auditory Science

Auditory Science Lab

Robert V. Harrison

The Auditory Science Laboratory at the Hospital for Sick Children has been a part of the University Department of Otolaryngology-Head & Neck Surgery for 35 years! Over that period we have enjoyed continuous funding from CIHR (and originally MRC), as well as supplementary grants, large and small, from other agencies. We have generated over 200 peer reviewed research papers, as well as hundreds of conference lectures and posters.

We have employed a range of research tools to probe the structure and function of the normal and pathological inner ear, and the plasticity of the central auditory brain. Functional methods include electrophysiological measurement of single neuron responses and other evoked signals from auditory brainstem, midbrain and cortex. We use otoacoustic emission measures in human subjects and in animal models. In our anatomical studies, we make histological evaluations of the inner ear with light and electron microscopy.

For more information check out our website: <https://lab.research.sickkids.ca/harrison>

Alas, all good things come to an end at some time. As this founder and director of the Auditory Science Laboratory approaches retirement, so too the laboratory ramps down to its final days (in late 2021). No new graduate students or post-docs can be recruited, and existing projects are being finalized. One important ongoing study is a collaborative effort with the University of Utah (Dr. Albert Park) on hearing loss associated with cytomegalovirus infection. We are presently supported by the Barberian Scholarship fund for this work.

For over 10 years the mainstay lab technician (now called a project manager) has been Jaina Negandhi. She has now found a new home with Dr. Karen

Gordon working with human subjects. Children with cochlear implants as opposed to chinchillas and lizards! I wish her much success in that new research area.

Our mission has always been to increase knowledge about the complex biological mechanisms of the auditory system and to understand the exact nature of hearing deficits. This new knowledge may lead to improved strategies for prevention, diagnosis and remediation of hearing disorders. This has been a very productive 35 years and I would like to thank all those graduate students (N>30) and post-docs (n>30) that I have trained in the Auditory Science Laboratory, and the scores of research collaborators who have trained me!

Neurotology and Vestibular Research

John Rutka & Phillip Gerrestsen

The 2019-2020 academic year allowed us to focus on a number of clinical projects that required completion. We were especially pleased that our 25 year clinical experience in assessing systemic gentamicin toxicity was published. We believe this to be the most important paper recently published in the field of clinical ototoxicity and will fundamentally change practice patterns worldwide (ie identifying the differences in vestibulotoxicity patterns between single and multiple daily dosing gentamicin regimens, the role for multidisciplinary in-hospital monitoring of patients receiving aminoglycosides, further insights into the medicolegal aspects of vestibulotoxicity etc). Terence Fu and Paul Douglas-Jones are to be jointly acknowledged for the work they did on this paper.

In February 2021 we expect Dr. Neil Bailie from Belfast, Northern Ireland to join us on staff.

Dr. Bailie's research interests currently involve the use of ceramics in middle ear and mastoid surgery, the development of collaborative multidisciplinary

neurotology models to meet patient demands and the application of endoscopic ear surgery techniques in post graduate training.

We will also be taking part in a number of collaborative research projects with our UHN Centre for Advanced Hearing and Balance Testing through co-workers Kaitlin Harvey and Carolyn Falls.

Our current research projects involve:

1. The prevalence and correlation of Head Shake Nystagmus (HSN) to VEMP, ENG and vHIT testing from the UHN Center for Advanced Hearing and Balance Testing databases.
2. The Burden of Dizziness in the Province of Ontario from OMA/MOHLTC data from 2007-2017.
3. A Substantive Review of our Prospective Workplace Safety and Insurance Board (WSIB) Neurotology Data base of over 4,500 Head Injured Workers.
4. Further analysis of the UHN Multidisciplinary Gentamicin Monitoring Program for the Prevention of Ototoxicity-Does it work?/Where it falls down?
5. Further analysis of the Effects of Vestibular Rehabilitation Therapy in Cerebellar Ataxia and Bilateral Vestibulopathy (CABV).
6. Creation of a Comprehensive Teaching Portfolio from the UHN Neuroradiology and Neurotology Rounds.
7. Creation of a Comprehensive Video Library of Otolaryngology/Neurotology Findings/Procedures.
8. Trends in surgery for chronic ear disease in the Province of Ontario-Data looks at OMA/MOHLTC data in the surgical management of CSOM from 2008-2020 compared to similar data from 1987-2002.

Dr. Philip Gerretsen and his research team have continued to be busy in the clinical management of

cognitive vestibular disorders at UHN. Their hallmark papers describing the Association between Catastrophization and Dizziness and the Interdisciplinary Integration of Nursing and Psychiatry is to be followed by an interesting assessment studying the outcomes of patients with cognitive vestibular dysfunction with/without an insurance/medicolegal action.

Further research activities include:

1. Outcome analysis of patients receiving Cognitive Vestibular Therapy with/without an insurance/medicolegal claim.
2. Reactivity of the Vestibular System to Caloric Vestibular Stimulation in Schizophrenia.

Neurotology/Vestibular Publications for the academic year 2019-2020 included:

- Kraus M, Hassannia F, Bergin M, Al-Zaabi K, Rutka JA. Longterm Outcomes from Blind Sac Closure of the External Auditory Canal: Our Institutional Experience in Different Pathologies. *J Int Adv Otol* 2020; 16 (1):58-62
doi:10.1552/iao.2020.7688.
- Varrino B, Sulway S, Wetmore C, Dillon W, Misquitta K et al. Vestibular Exercises as a Fall Prevention Strategy in Patients with Cognitive Impairment. *C J Neurol Sci* 2019
doi:org/10.10107/cjn.2019.309.
- Hassania F, Carr SD, Rutka JA. Transient Vertigo with Horizontal Nystagmus to Loud Noise and Pressure: Utricular Hydrops or Vestibular Atelectasis? *J Int Adv Otol* 2019 DOI: 5152/iao.219.6238.
- Hassania F, Douglas-Jones P, Rutka JA. Gauging the Effectiveness of Canal Occlusion Surgery: How I do it. *J Laryngol Otol* 2019; 1-5.
<https://doi.org/10.1017/S0022215119002032>.
- Hassania F, Lee J, Rutka JA. Delayed Failure in Tympanoplasty: A 20 Year Study of the Incidents and Reasons for Reperforation in 359 Patients. *Clin Otolaryngol* 2020; 00:1-3
DOI:10.1111/coa.13522.

- Al-Zaabi K, Hassania F, Bergin MJ, Rutka JA. Management of Invasive Intralabyrinthine Cholesteatoma: Can One Realistically Preserve Hearing when Disease is Medial to the Otic Capsule. *Am J Otolaryngol* 2020 1-3 doi.org/10.1016/j.amjoto.2020.102407.
- Fu TS, Douglas-Jones P, Dillon W, Ilan O, Syed IM, Leis J, Gold W et al. Gentamicin Vestibulotoxicity. Further Insights From a Large Clinical Series. *Otol Neurotol* 2020; 41(7): 864-872.

Cochlear Implant, Neurotology & Otology Research

Vincent Lin, Trung Le, Joseph Chen, and Andrew Dimitrijevic

The Sunnybrook Cochlear Implant program is currently funded for 250 implants for the 2019-2020 fiscal year. Our recent submissions to Health Quality Ontario were successful and now we are approved for bilateral adult cochlear implantation, single sided deafness, bone conduction devices and also brainstem implants. Special thanks to Dr. Chen for his hard work with the team at Health Quality Ontario to help pass these important recommendations. The Sunnybrook cochlear implant team continues to grow and this year we have 3 surgeons, 6 full time implant audiologists, 2 admins, 1 communication disorders assistant, 2 clinical fellows, 1 full time researcher, graduate students and post-doctorate fellows.

The electrophysiology lab led by Dr. Dimitrijevic continues to produce clinical relevant research on listening effort and biomarkers for cochlear implant performance. The lab continues to publish and present at major international meetings such as the ARO.

Currently our team is involved with several industry lead clinical trials. The largest being the expanded criteria trial led by Med-EL which is almost finished enrolment with a goal to formally recognize expanded clinical criteria for adult cochlear implant patients. We continue to recruit patients into our genetics study which in collaboration with our

colleague at SickKids is using high powered gene sequencing to hopefully unlock new genetic clues for those with a strong family history of hearing loss. Our single sided deafness trial is continuing to enrol patients and we anticipate this to dramatically increase with the change in funding.

Dr. Vincent Lin continues to utilize the hearing impaired MoCA to better characterize our elderly patients undergoing cochlear implantation and our next major milestone is to expand the HI-MoCA into a more comprehensive test that can be repeated longitudinally in patients pre and post-implantation to determine effects on overall cognition. This is in collaboration with our colleagues in neurology at Sunnybrook.

Our research fellows and residents continue to help tremendously with our clinical outcomes data research looking at quality of life and economics of implantation. All these efforts were essential as they provided evidence for the tremendous benefit of cochlear implantation in our adult population and helped steer Health Quality Ontario towards the funding of our expanded criteria and bilateral implantation.

We are most grateful to our patients who continue to generously donate both time and finances towards our research endeavours and we look forward to another successful year at the Sunnybrook Cochlear Implant program.

Auditory Development & Regeneration

Alain Dabdoub & Trung Le

The Dabdoub Lab continues to make significant progress in discovery science elucidating the biology of the inner ear as well as in translational science thanks to the efforts of a dedicated group of trainees and the vision and support of the Sunnybrook Department of Otolaryngology-Head & Neck Surgery.

For this year, I highlight three areas of innovation:

- We built the first electrochemical immuno-biosensor to detect inner ear biomarkers

circulating in blood. We published the proof of concept study earlier this year and filed a patent for the technology. We have successfully obtained a five year NSERC grant to support this work.

- We have discovered a novel protein expressed in sensory hair cells through our bioinformatics work supported by the Harry Barberian Scholarship. We presented our findings at the International Society of Developmental Biology Meeting and continue to elucidate the function of this protein.
- We are the first to use MRI guided focused ultrasound to systemically and noninvasively deliver gene therapy to the inner ear in collaboration with the Centre for Excellence in Focused Ultrasound at Sunnybrook. We presented this work, funded by a Krembil Foundation grant, at the Federation of European Neuroscience Societies conference.

We are well positioned for transformational advances in basic and translational research for the treatment of inner ear disorders including hearing loss and balance dysfunction.

Follow us on Twitter: @LabDabdoub

Paediatric Cochlear Implant Research Lab

Karen Gordon, Blake Papsin, Adrian James, Sharon Cushing

The Cochlear Implant Laboratory at the Hospital for Sick Children continues to investigate auditory and vestibular development and plasticity. We ask: 1) What aspects of auditory and vestibular development are arrested in children with hearing loss; 2) What changes in the auditory and vestibular system occur during the period of deafness; and 3) To what extent can auditory and vestibular plasticity and development be promoted by cochlear implant use? We are also interested in innovations in cochlear implant design and programming which seek to improve the resilience of the device as well as to preserve residual hearing and binaural cues. Our work is supported by research funding from the

Canadian Institutes of Health Research along with the Cochlear Americas Chair in Auditory Development and generous donations. Specific hypotheses which stem from these questions are tested through a number of studies currently underway.

Our team includes two research project coordinators, Jaina Neghandi and Al Blakeman.

In September 2018, Robel Alemu began his MSc program at the Institute of Medical Science. He is working on a new set up to assess spatial hearing in children with and without hearing loss and is set to defend his research thesis at the end of August 2020. We were joined by Dr. Carly Anderson in February 2019 who, after completing her PhD (2016) and Research Fellowship (2017) at the University of Nottingham, worked as the Research Programme Manager at Action on Hearing Loss, London, UK. She had been working on a collaborative project with Dr. Dimitrijevic assessing brain function in adults and children using bilateral cochlear implants, but this was halted in March due to COVID-19 restrictions. Her work has pivoted to assessment of cortical plasticity in adolescents who receive bilateral cochlear implants. In September 2019, we welcomed Rebecca Benjamin to work on a project examining strategies to balance function in children with hearing loss. This work was also halted by COVID-19 restrictions but we are presently attempting to restart data collection.

We also said farewell to several members of our laboratory. Dr. Hyo-Jeong Lee was a visiting otolaryngologist from Seoul, Korea from October 2018 to December 2019. She worked on brain plasticity in children with single sided deafness who receive a cochlear implant. Claire McSweeney completed her MSc program at the Institute of Medical Science in August 2019. She worked on a project exploring the effects of impaired binaural hearing and vestibular deficits on spatial awareness, memory, and navigation and the implications of these spatial problems on physical activity and academics (reading and mathematics). Dr. Hillary Ganek, a PhD speech-language pathologist,

completed her post-doctoral work on language exposure in children's everyday environments. She compared data recorded with a Language ENvironment Analysis (LENA) device and scene categorization provided by datalogging functions in the cochlear implant processors.

We have enjoyed the opportunity to work with a number of students last summer and were disappointed to have to cancel plans to take on several undergraduate summer students due to COVID-19 restrictions. We continue to have important collaborations both locally (Robert Harrison, Adrian James, Ben Dunkley, James Rutka, Sandra Trehub, Susan Blaser, Frank Russo, Jenny Campos, Andrew Dimitrijevic, Elizabeth Pang), nationally (Sam Doesburg) and internationally (Robert Cowen, Ruth Litovsky, Andrej Kral).

Despite COVID-19 restrictions to our clinic and research, the past year has been very productive: 21 publications came out or are in the press. Between this summer and last, we collectively presented over 30 abstracts at international meetings and gave more than 50 invited talks internationally.

Some highlights from the past year include:

- CIHR funding in the 2019 Spring competition (Novel treatment to promote spatial hearing in children who are deaf: Primary Investigator: Gordon, KA, Co-investigator(s): Papsin BC, Cushing SL; Collaborator(s): Scollie S, Papaioannou V, CIHR Project Grant, Fall 2019 competition, \$559,980).
- Karen Gordon appointed as Chair of IMS Appointments Committee and member of IMS Leadership Committee.
- 6 student/trainee awards including the Canada Graduate Scholarship-Master's Program, Canadian Institutes of Health Research (CIHR) – Frederick Banting and Charles Best Canada Graduate Scholarships to Rebecca Benjamin.
- Open Scholarship Award, Institute of Medical Science, University of Toronto to Robel Alemu and Rebecca Benjamin.

- Summer Undergraduate Research Program 2019, Joint Funding Award, Institute of Medical Science, University of Toronto to Yujia (Joyce) Chen.

OtoSim™ Lab

Paolo Campisi and Vito Forte

Despite the COVID-19 crisis, and by sticking with our innovative mission aligned with that of the department, the OtoSim™ educational platforms continue to be well positioned to satisfy all the learning requirements whether in-person or remote. This success to-date has been made possible thanks to the ongoing efforts of team members and collaborators.

Dr. Vito Forte is still full-time CEO and CTO of OtoSim™ Inc. and he also is an active member in the CIGITI Lab at SickKids. This has resulted in a successful collaborative team involving engineering students from UofT as well as other programs across Canada. This activity continues to stimulate students from the lab and the program to pursue further post graduate degrees.

Product development remains a key component at OtoSim™ Inc. We have introduced advanced self-learning software and remote teaching capabilities and released many upgrades to the software. These software upgrades now permit the creation of instructor image libraries and content creation allowing for even greater collaborations with other centres around the world.

Over 650 universities around the world now use our proven technologies.

This past year, the National Resident Project was successfully completed, spear-headed by Dr. Campisi and all the program directors from across Canada. This voluntary involvement of each center was made possible through the generous support of Mr. Ralph Chiodo, the Department of Otolaryngology-Head & Neck Surgery and OtoSim™ Inc. Every resident across Canada received at no charge their own hardware and software package. The PGY5 cohorts have generously gifted their devices back to the incoming PGY1s in hope of sustaining this valuable

initiative. Independent analysis of data is currently underway for future publication and competency-based planning.

The UofT Clerkship year continues to effectively use the OtoSim™ Mobile and now the OphthoSim™ Mobile for the training of the ear and eye exam during COVID-19 times. This innovative initiative has been led by Dr. Al Vescan and Dr. Stacey Bernstein, Clerkship Director, MD Program, Faculty of Medicine, University of Toronto and made possible through a generous grant to the University of Toronto. Simulation and teaching are carried out through a combined Zoom lecture delivered by Dr. Campisi while students can simultaneously practice their otoscopy or ophthalmoscopy skills using a real scope viewing

pathologies, through the mobile device attached to their smartphone or tablet, either during the virtual lecture or later at the student's leisure. Dr. Vescan has also deployed the mobile simulators in the clinic with students practicing and viewing pathologies prior to the patient encounter to maximize the learning moment. Activities for the students have been coordinated through Andrea Donovan, Education Coordinator, Department of Otolaryngology-Head & Neck Surgery.

Development continues for both smart-phone based mobile simulators bringing another dimension to teaching of otoscopy and direct ophthalmoscopy applying effective, efficient and affordable simulation achieving a global impact.