How has your academic career led to your current research interest in intracranial pressure (ICP)? Can you discuss the main aims of your investigations?

My research on the physics of the inner ear examines how auditory sensory cells – the receptors of sound in the inner ear – are so extraordinarily sensitive to pressure changes that they can detect subatomic vibrations. These changes include the ICP of the cerebrospinal fluid, which communicates with one compartment of the inner ear. The idea that inner ear sensory cells could be used as sensors of ICP has been assisted by the fact that they emit readily detectable signals, which routinely serve for the diagnosis of hearing conditions. Discussions with neurosurgeon colleagues have convinced our team that a new, useful technique might be developed using this concept, and my research endeavours since then have been to probe the method, its sensitivity, robustness and accuracy in different frameworks and experimental setups.

In what ways have your experiments led to the idea of building a hand-held device for measuring ICP through the ear?

Our first proof-of-concept measurements were carried out in operating theatres and intensive care units with rather cumbersome, off-the-shelf equipment and even more worryingly, with off-site data processing. The flexibility of measurements and their immediate interest for the surgeons were lost. The idea to design a hand-held device was inspired by these difficulties. The first design opened new possibilities for physiological measurements, for example in zero-gravity environments and parabolic flights in which the smallest additional pound of equipment is a burden. We have just started a clinical experiment in which patients are given the equipment for a few weeks, with the task of recording themselves at home when an attack of headache occurs.

What role has spin-off company Echodia played in driving your innovations from the laboratory to the market?

We created Echodia five years ago after the necessary steps had been initiated in around 2005. Even with the best technique and the most thorough possible controls with invasive measurements serving as gold standards, we were aware that we would have to demonstrate the utility of the technique to colleagues who had neither the time nor the background in audiology to do more than turn on a user-friendly device and trust its outcome. Furthermore, clinical tests require a professionally designed and European Conformity (CE) marked device that only a company can provide. For the distributed technology to be reliable, it was also designed to perform standard clinical tests that our audiologist colleagues could check, improving the technology by contributing their feedback.

How do you foresee non-invasive ICP systems developing in the future?

We feel that a genuinely simple and reliable device measuring ICP changes whenever needed – several times a day for weeks if necessary – would have a huge impact in neurology and related fields, for a number of conditions. We are, however, charting virgin territory as this dream has been futile with the currently acknowledged invasive ICP methods. Until now, none of the attempts to devise non-invasive ICP monitoring devices has changed the paradigms for neurologists who have to follow up difficult patients in whom excessive ICP may be one cause of their problem. Now that the device is on its way to becoming a simple and reliable tool, we are well aware that we’ll have to validate new protocols in order to conquer novel clinical domains.

Professor Paul Avan describes how his interest in the inner ear is paving the way for the revolutionary observation of long-term intracranial pressure
In an outpatient clinic, patients can be tested in sitting posture and then tilted into supine position, which triggers a mild increase in ICP. The system measures this increase, from which, in some conditions, we have shown that information can be derived as to the level of baseline ICP and whether it is normal or not.
The method typically used to measure intracranial pressure is a risky invasive procedure.

MARKED IMPROVEMENTS

Despite the success Avan has achieved to date, he is still working on improving the efficacy and accuracy of inner ear ICP monitoring. The system is designed for detecting ICP changes in individual at-risk patients over an extended period of time. There are, however, a number of factors that can lead to a drift in readings over time, which would impact accuracy. “One challenge of long-term monitoring, which we have set out to eliminate, is the gradual shift in air pressure in the tympanic cavity,” he explains. “This confounding effect will be automatically detected and compensated for by the next version of the system.”

A second limitation is that it is sensitive to changes in ICP but cannot provide baseline ICP values without an invasive measurement for calibration. Fortunately for patients, Avan has tested several protocols using the non-invasive system that do not require this risky step: “We have developed strategies, such as body tilting, which may unveil abnormal ICP even in the absence of calibration,” he elaborates. “Unfortunately, these tricks do not work universally; they are specific to the situation for which they were designed; but we have already identified several such situations in which our system has proved reliable.” Avan is currently developing similar tricks to use in other categories of patients so that, in future, the protocol will be sensitive enough to diagnose changes in ICP in all situations.

FUTURE APPLICATIONS

Avan and his team are currently testing their latest modifications on patients with interesting ICP variations, for example, those who have undergone surgery to remove a brain tumour. The clinicians involved in the trials can efficiently watch for increases in ICP over time, which might suggest a recurrence of the cancer and highlight the need for further tests. Another interesting potential application will be for use in research into the cause of migraines. The hypothesis that increased ICP causes migraines is controversial, so Avan will be using his non-invasive approach to help probe this contentious issue.

The inner ear NIM-o-PIC system will only ever be able to detect changes in ICP, not absolute values. Despite this, Avan believes it will be a vital tool for monitoring at-risk patients in the near future: “We will never claim to replace invasive ICP monitoring, but whenever the clinical status of patients fluctuates and it would be desirable to repeatedly check whether ICP fluctuates in unison, our system offers an easy, painless insight that can be repeated at will by non-specialists,” he concludes.