The Future of Brain Monitoring with Acoustocerebrography

Our Health Care System is confronted with serious changes worldwide. Cost and care structures are changing, not least in part due to the growing disruption by new business models. Demographically, many countries are faced with the greatest challenges in centuries, and technologically, we are experiencing with digitization just the beginning of a development that offers such revolutionary potential that its full extent can only be imagined. Health Care, health policies and health administrations are only partially or not at all prepared and only occasionally capable of adapting. This emerging vacuum allows innovative, agile actors to reorganize the system according to their own rules.

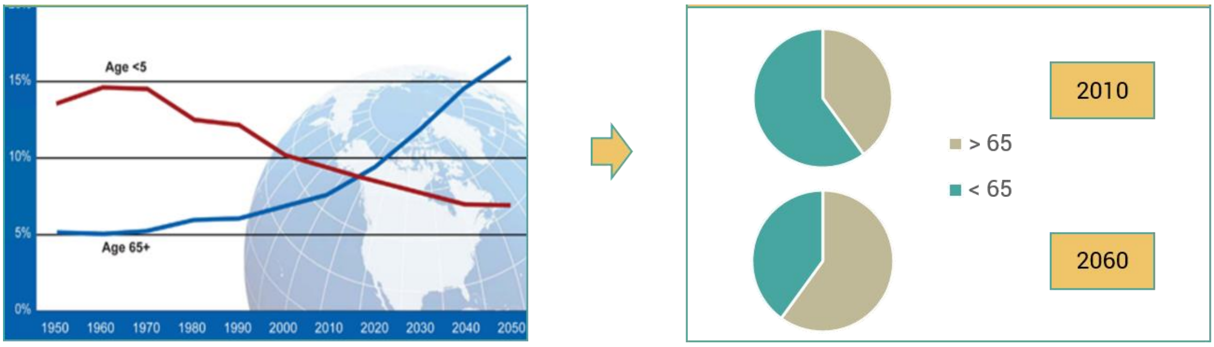

Figure 1, left: Percentage of under five-year-olds and over 65-year-olds in World Population; right: Health Care Spendings for those age groups

The United Nations estimate that by around 2018, for the first time in the history of population development, the percentage of the world's population which is over 65 years old will be greater than the percentage of those under 5 years of age. This means for the costs resulting from the care of an increasingly older and multi-morbid world that the ratio of expenditure will flip in the long term. In 2010, the majority of costs (60%) were caused by a patient population under 65 years of age. 50 years from now, it will be the other way around: The population group over 65 years of age will make up this percentage – and the trend will continue (see Figure 1).

Simultaneously, the health care cost's percentage of GDP in the OECD nations has increased tenfold between 2010 and 2015. We will have to care more and more for age-related illnesses and have to find appropriate diagnosis and therapy solutions to properly address this challenge – whereby "appropriate" in this context means especially cost-effective and specifically customized for this segment of the population.

Although this will not be a surprise for most of our readers, it is curious that such solutions, particularly in the area of brain monitoring, i.e. exactly the part of the body that is particularly affected by old age, are not available on a broad scale. The reasons for this, among others, lie in the complexity of the brain as well as the inertia of the health care system as a whole, and not just in this country. Additionally, this challenge is not uniformly shared across the geographic landscape. For the first time since the turn of the millennium, the percentage of people who live in cities has surpassed the percentage of those who live outside of cities (see Figure 2).

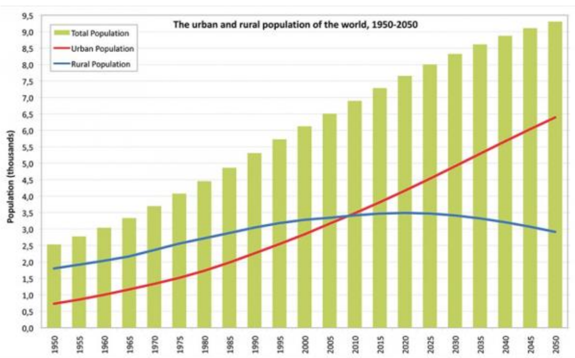

Figure 2: World Population by location

What at first may sound like good news with regards to health care, at second glance turns into another challenge: The areas of concentration outside of the cities are getting smaller and the distances between these hubs are getting larger. This puts additional pressure on the existing system, which is evident in rising health care expenses per capita. These expenses can be seen in the OECD mean between 1970 and 2010 with an increase from $200 to $4000 (see Figure 3). These developments mean that treatment and care must be structured significantly more efficiently with the help of organizational and technical solutions. Since by far the largest portion of all health care costs during one's life occurs in the last years of life, the preservation of independent living represents the largest relief for the health care system, both mentally and physically.

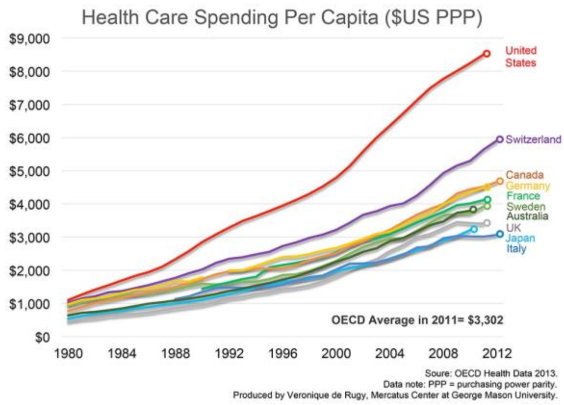

Figure 3: Health Care Spendings per capita for selected regions

When considering all these aspects, the impairments of the brain, in particular, are a burden for patients and their families as well as for the system itself.

Shortening the time between detection of any illness affecting the central nervous system and the treatment represents a significant contribution in supporting the entire system. This includes two aspects: on the one side, improved stroke and lesion diagnostics of acute changes in the brain, on the other side, the ability of general practitioners with the support of a system of experts to recognize subtle changes in the brain structure at an earlier point in time.

Until only recently, this gap could not be narrowed, since brain diagnostics were missing the capability to recognize pathological changes in the brain tissue in a fast, cost-effective and simple manner. The most popular methods include Magnetic Resonance Imaging (MRI, also called Magnetic Resonance Tomography). This is a commonly used imaging procedure, which allows for the creation of precise, high-resolution sectional views of the body, in particular organs and tissue. These images are based on the physical principles of magnetic resonance. Another method used often, Computer Tomography (CT), is a radiographic procedure that creates a computer-aided assessment of a multitude of x-ray images taken from various directions in the form of sectional images, which are then evaluated. These investment-intensive devices are still used for diagnostics, although they lack mobility – and are less than suitable for simple operation by general practitioners. A significant disadvantage is the exposure of patients to radiation or similar issues, which always subjects the procedure to the consideration of necessity (particularly in the case of small children).

Potential of Acoustocerebrography

With the help of a new ultrasound procedure, this situation may be significantly improved.

The Acoustocerebrography (ACG) is a non-invasive, transcranial ("going through the skull") acoustic spectroscopy, which utilizes the research results of Molecular Acoustics, referring to the science of transmission mechanisms of acoustic energy via molecules in liquids and gases.

This scientific field was already subject to research more than 100 years ago. During WW II, this research helped create, among other things, the first "stealth" submarine with a coating that made the vessel "inaudible" for enemy sonar. After the war, this field experienced a notable increase in research activity, which laid the ground work for standard literature that is still valid today (Schaaffs, 1963) and was recognized with a Nobel Prize awarded to Manfred Eigen in 1967.

In the following twenty years, the research intensity subsided in favor of the emerging laser spectrography. Important reasons were the requirements for the evaluation of enormous data volume, which computers were not capable of fulfilling until the turn of the millennium, as well as the fact that electromagnetic spectra are more easily separable than acoustic ones, making their analysis significantly simpler.

Since the late 1980s, research and associated patents have picked up again in this area. Kosugi et al. (1987) and Sekhar et al. (1990) looked at the acoustic signatures of blood circulation and aneurysms. Wrobel (1994) simulated the bio-sonar system of bats to derive practical applications for the construction of a device that would enable the acoustic signature of brain tissue to be made audible. In the subsequent years, the analysis and usage of signal processing in the neural networks with the help of ultrasound (1999), the first description of the method (2001) as well as the classification of the stroke risk factors (2015) followed. In 2015, Bogdan et al. describe the foundation for the construction of a diagnostic device for brain tissue.

In essence, the novelty of this diagnostic technology is the fact that multi-frequent ultrasound measurements were not specifically used until now to measure tissue attributes in medicine. Additionally, the collected data is recorded by a self-learning system, which could lead to incredible possibilities in the field of medical diagnosis.

The combination of these two factors allows for comparatively fast measuring. Through its mobile use, a significantly faster treatment can occur within a few minutes which does not require radioactive exposure or contrasts, and does not have any contraindications when compared to other methods.

A probe sends an ultrasound signal in a certain frequency which is then received by a second probe. Depending on which angle is applied and what type of obstruction the signal must overcome, the captured values vary reflecting pass-through time and absorption. Considering these two values and supported by interferometry – a measuring method to determine the changes of an amplitude by overlaying two or more waves – the ratio of sound frequencies to each other can be calculated. Since the measuring is continuously performed with different frequencies, a multi-dimensional image of the processes in the brain tissue emerges as a whole.

The first clinical results were presented by Dobkowska-Chudon et al. (2016) and Olszewski et al. (2016), who applied the method in patients with lesions in the white tissue. For instance, this finding can be caused by atrial fibrillation, which the affected patients might not even be aware of.

But if the coagulated blood which is caused by the heart's irregular pump activities (= fibrillation) begins moving again as soon as the regular rhythm resumes, it may lead to embolisms, which are present in the brain with these lesions. Because of their tissue changing attributes, these lesions are, among others, suspected to promote dementia.

Dobkowska (2016) and Olszewski (2016) were able to show that the number of lesions, which are normally counted out in the image of an MRI, can be clustered with the help of Acoustocerebrography. The result provides valuable insight by showing if the patient exhibits less than five (L0), between five and ten, ten to thirty, or more than thirty (L30) lesions. Consequently, these values allow an assignment of risk classifications. Figure 4 shows such a differentiation of clusters.

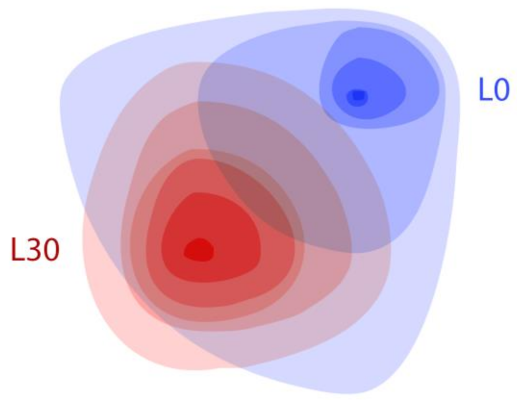

Figure 4: Clusters of White Matter Lesions

Although this method does not replace CTs and MRIs, it enables the attending medical staff to make a timely and immediate, low-cost pre-diagnosis to determine further therapy paths. These benefits are not possible with CT and MRIs, basically "due to their design." Furthermore, ACG can be applied in a series of other research areas:

Neurosurgery In this field, ACG offers a continuous, non-invasive monitoring of patients with subarachnoid hemorrhage (i.e. blood flows into the space filled with brain fluid between the medial and inner meninges) and traumatic brain injury. Today, these patients are being multimodal monitored, i.e. blood pressure, pulse, temperature, oxygen saturation and intracranial pressure are continuously measured, in order to adequately respond if they move into the critical range.

These parameters are measured by different devices and need to be time-synchronized in order to obtain a meaningful comprehensive picture. The intracranial pressure is usually measured invasively with an intracranial probe, which is introduced through a hole in the skull.

Pediatrics ACG offers great benefits particularly in aiding with brain diagnosis in children, for instance, after a fall on the head. Contrary to a CT, ACG works without x-rays, and allows a first diagnosis already in the pediatrician or general practitioner's office, and, in special cases, can be used even at home. Additionally, when bleeding of the brain is detected in premature babies, real-time monitoring is possible.

Intensive Care ACG makes a continuous monitoring of the brain tissue possible, before, during and after an operation. This allows for a more exact and faster diagnosis of patients. However, this does not only apply in the OR. It can even be used during the ambulance transport, which significantly shortens the time before the initial diagnosis. Especially with strokes, this reduction in time is pivotal for the subsequent treatment success.

Telemedicine During a routine checkup, primary care providers can quickly and without complications assess patients with the help of ACG and pass on the measured values to a specialist. As a result, patients do not need to be unnecessarily referred to a CT or/and MRI. This application is particularly beneficial with older people or people who live in areas that are underserviced by the medical community.

Geriatrics The (multi-) morbidity in older patients requires a higher degree of monitoring as well as a more intensive need for care. With regularly recurring measurements, ACG can help detect changes in brain tissue over time without putting patients through strenuous and complicated procedures.

Veterinary Medicine In the veterinary field, ACG can be used to monitor the brain of animals beginning with the size of a mouse; for instance, to observe the effect of sedation and other medications as well as monitoring the brain functions of animals in general.

Biopharmacology/Animal Testing

In the course of developing new medications, tests on living animals are necessary, whereby ACG can be used in test series to detect desired and undesired effects (side effects) in the brain in real-time as part of continuous monitoring.

Other Application Areas In general, the physical basics of Molecular Acoustics allow with the help of computer-aided analysis of data the use of ACG everywhere organic matter is interfused with microorganisms, since those trigger biochemical changes or a maturation or fermentation process, respectively. Here the food sector with its monitoring of small and big quantities of valuable consumer goods such as wine and spirits comes to mind. In the pharmaceutical industry, products manufactured in bioreactors such as insulin can be monitored for quality assurance without introducing any contact with the produced substance. In the above mentioned products, a biochemical process occurs, whereby its progress must be verified in regular intervals. However, each check comes with the possibility of contamination with foreign germs, viruses and bacteria and represents, depending on batch size, a potentially significant financial risk. With ACG technology, this risk could be reduced to zero, since on the one side already the smallest undesirable development during production could be detected and necessary steps to avoid any hazard could be taken; and on the other side, quality control would occur without any direct contact with the produced goods. This way, any danger of contamination would be eliminated from the start.

Benefits of Acoustocerebrography

Ultrasound is nothing new. New, however, is its use in the hereby described context as well as the linkage of the ultrasound principle to the idea of establishing parameters of the brain tissue. In the past, this only took place via a CSF-puncture (analysis of the cerebrospinal fluid, i.e. the fluid that surrounds the central nervous system), with overlapping magnetic fields (MRI) or with x-rays (CT). All these methods have serious disadvantages: They take time and are cost-intensive. Additionally, they only offer a momentary snapshot and expose patients to significant physiological stress (noise, magnetic fields, drilling into the skull and an elevated cancer risk). For children, MRIs and CTs are not suitable due to the necessity to remain completely still or the exposure of x-rays, respectively.

The benefits for the patients are clear: Users of ACG are continuously provided an overview of their brain tissue condition and could be warned when a certain danger threshold is reached –without wait time and also ambulatory.

Medical staff could benefit as well: Lower expenditure in the office as well as better patient care through observation and prevention.

Finally, also the health insurers receive a benefit, since the costs of unnecessary procedures such as MRI, CT and cranial pressure measurements would be eliminated. Instead, ACG can now provide a continuous image of biochemical changes in the brain, when, for instance, parameters like cranial pressure cannot be established due to their invasive nature and complexity. Suspected cases can be evaluated at a much earlier point in time. Patients with risk factors can be preventively identified and, if needed, referred to a specialist. Thus, expensive examinations with MRI or CT scans can benefit patients who really need them.

With the use of ACG, hospitals can expect a significant process optimization due to uninterrupted monitoring. In addition, any time saving until or during treatment means an improvement of their cost position, which – considering the economic situation of hospitals – should be good news for any hospital operator in this country and elsewhere.

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