Summary

This study deals with the acoustic detection of intracranial aneurysms. Clinical investigations, model studies and a clinical decision analysis were performed to investigate the possibility of recording aneurysmal sounds over the eyes and the possibility of the application of an acoustic detector as a screening device for intracranial aneurysms.

Chapter 1 reviews the literature concerning the clinical backgrounds of screening for intracranial aneurysms: the natural history of unruptured aneurysms, surgical morbidity and mortality, the available methods for screening for intracranial aneurysms and the identification of groups at risk. Subarachnoid hemorrhage (SAH) is a serious clinical condition caused by rupture of an intracranial saccular aneurysm in 70% of cases. The incidence of aneurysmal SAH is about 1:10,000 persons per year. The prognosis for patients with an aneurysmal SAH is poor, with an overall mortality of 55% and a morbidity of 15%. Aneurysms can be treated surgically: they are excluded from the circulation by means of clipping. Early recognition and treatment, i.e. before rupture has occurred, might considerably improve the prognosis. The benefit of early detection depends on the balance between the risk of aneurysmal rupture during a patient's life time on the one hand and surgical risks on the other hand. The rate of hemorrhage of an unruptured aneurysm is 1 - 2% every year. The outcome of surgery has improved greatly with recent advances in microsurgical and anesthetic techniques and are even better for unruptured aneurysms. The mortality and morbidity have been reported to be approximately 1% and 3½% respectively, influenced by factors including the size and location of the aneurysm and the skills of the neurosurgical team. Most authors agree nowadays that early treatment of unruptured aneurysms, i.e. before rupture has occurred, can considerably improve the prognosis for most patients. If early treatment can improve the prognosis, early detection seems rational. For proper screening for intracranial aneurysms in groups at risk, a suitable test should be available. Such a test should be simple and non-invasive, acceptable for the patient, reproducible, have a good test performance and have low costs and low risks. The available methods for detecting aneurysms are angiography (conventional, arterial DSA and iv DSA) and computed tomography, none of which are appropriate for application on a large scale. A promising method that has been developed recently is magnetic resonance angiography (MRA), but at the moment it is expensive and scarcely available. Most benefit is to be expected from screening groups at risk. Many patients with aneurysmal SAH have suffered warning symptoms. A typical warning symptom is a sudden, severe and unusual headache. Most symptoms however are very specific. Another group at risk, probably the most important one, consists of members of a family with multiple cases of aneurysmal SAH or unruptured aneurysms, especially with 3 or more. Finally, some pathologies are associated with intracranial aneurysms. The most important of these diseases is autosomal dominant polycystic kidney disease.

Chapter 2 reviews the literature concerning observations of bruits related to intracranial aneurysms and theories regarding the etiology of aneurysmal sounds. Aneurysms have been mentioned in a few case reports as a possible cause of cranial
bruits and especially of orbital bruits, perceived with a conventional stethoscope. In some of the experimental studies which were performed to investigate the hemodynamic behavior of aneurysms, the phenomenon of bruits they produced received attention. Vibrations have been observed in some animal aneurysm models as well as in some in vitro models. In one study, bruits were recorded from aneurysms during surgery. On the basis of these observations, the idea was put forward that it might be possible to record aneurysmal sounds noninvasively with sensitive stethoscopes. This resulted in the development of a few electronic recording methods for the acoustic detection of intracranial aneurysms. With these methods some aneurysms could be detected but they demonstrated problems concerning their sensitivity and reliability. Several theories have been postulated concerning the etiology of aneurysmal bruits. The most common theory is that of an aneurysm acting as a resonator, driven by pulsatile flow, turbulence or vortices.

This study was performed in order to investigate the possibility of recording aneurysmal sounds over the eyes and the possibility of using an acoustic detector as a screening device for intracranial aneurysms.

In chapter 3 the instrumentation and recording method used for the clinical measurements are described. A new method for recording intracranial sounds was developed, which was based on the methods of Olinger et al and Kosugi et al. A number of adjustments were made in order to improve the signal-to-noise ratio and to reduce artificial noise. The most important adjustments were: using hydrophones, a 200 Hz high pass filter, ECG-triggering with a delay of 200 ms, clipping and sufficient averaging. The measuring procedure was automated to a considerable extent. Sounds were measured over the left and right eyes; the measurements resulted in power spectra with a frequency range of 200 - 1250 Hz. Preliminary measurements were performed in healthy control subjects and patients with intracranial pathology. These measurements showed that in the control subjects a "normal spectrum" could be found with a smoothly descending pattern, whereas in patients with intracranial aneurysms power spectra were found that deviated from this normal spectrum. The deviation consisted of the presence of peaks, with varying dominant frequencies, widths and heights. In patients with an arteriovenous malformation or vasospasm, abnormal power spectra could also be measured.

In chapter 4 the results of a clinical study on 73 control subjects and 89 aneurysm patients are presented. For the control subjects, most power spectra showed the typical normal spectrum without significant peaks, whereas for the aneurysm patients most spectra showed abnormal peaks. Characteristics of these peaks were described and compared with peaks that were found in control subjects. Aneurysm patients in whom normal power spectra were found had smaller aneurysms than the patients in whom the power spectra showed peaks. No relationship could be established between the dominant frequencies of the peaks and the size of the aneurysms, between the side of the peak in the spectra and the side of the aneurysm (left or right), nor between the presence of a peak in the power spectra and the location of the aneurysm. In order to find an objective, simple parameter that can be used to establish whether a measurement is normal or abnormal, the power-median was evaluated and its test accuracy was determined. A suitable combination of the sensitivity and the specificity that could be found for the power-median was 0.79 and 0.75. A second parameter was the power-mean. These were calculated for the left and right eyes of the 73 control subjects and 89 aneurysm patients. A significant difference was found between control and aneurysm patients, although the test accuracy was not as high as for the power-median.
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parameter, the mean difference error, led to similar results, but combining both parameters improved the results slightly. For control subjects, the variability of the power-median within subjects was small compared to the variability between subjects, meaning that the reproducibility was good for control subjects.

Chapter 5 deals with the findings of transorbital acoustic measurements in patients with other intracranial pathologies than aneurysms. Measurements were performed in patients with AVMs, SAH of unknown pathology, vasospasm and intracranial tumors in order to evaluate if abnormal power spectra are found in patients with these pathologies, and, if so, whether these power spectra can be distinguished from those found in aneurysm patients. A substantial number of abnormal power spectra were indeed found in patients with AVMs, vasospasm and gliomas and patients with non-perimesencephalic hemorrhages of unknown origin, but not in patients with perimesencephalic hemorrhages, hemorrhages of unknown origin but negative CT, and patients with meningiomas. The peaks that were found in the patients with the pathologies mentioned could not be distinguished from peaks as seen in aneurysm patients because of the large variation in all groups.

In chapter 6 acoustic recordings directly from the surface of intracranial aneurysms during surgery are described. Sounds with frequencies between 200 and 1250 Hz could be detected in 41% of cases (12 out of 29), which was less often than expected. Five more bruits were detected with frequencies below 200 Hz. The power spectra and the time course of the bruits with energy above 200 Hz were analyzed, and these were related to the transorbital measurements. After clipping, bruits were recorded as well. These probably originated within the vessels. A relationship between the power spectra detected with the transorbital method before or after surgery and the bruits recorded directly from the surface of aneurysms and afferent vessels could not be established.

In chapter 7 and 8 aneurysm models used for the study of the characteristics and etiology of aneurysmal sounds are described.

At first, an attempt was made to record sounds from a simple aneurysm model in a rat (chapter 7). We chose the venous patch model, which is a relatively simple and reliable model. The technical result was good in 5 out of 6 cases. The sounds that were recorded over these aneurysms did not differ from the sounds that were recorded over the carotid artery; we did not succeed in recording aneurysmal sounds from this rat model.

Model studies were continued with an elastic in vitro aneurysm model (chapter 8). Starting from the hypothesis that an aneurysm has a specific resonant frequency which is determined by the inertia of the fluid in the neck and the elasticity of the aneurysm, a basic formula was derived for this resonance frequency. It was verified experimentally that the frequencies were related to the wall thickness \( f \sim \sqrt{\frac{\rho}{\mu}} \), effective neck length \( f \sim \frac{1}{\sqrt{H}} \), and size \( f \sim \frac{1}{R^2} \). For in vivo aneurysms, size is expected to be an important factor determining the resonant frequency. Experiments were performed with the aneurysm models connected to a flow circuit. As a result of steady flow through the circuit, sounds were emitted by the model at its resonance frequencies above a threshold value for the flow velocity; above this threshold value
the energy of the sounds increased exponentially with increasing flow velocity. The findings supported the hypothesis of an aneurysm acting as a resonator, which can be brought to vibration by flow induced turbulence.

In Chapter 9 a clinical decision analysis was applied to the problem of screening for intracranial aneurysms with the transorbital acoustic measurements (ADA), which is a non-invasive, risk-free test. The strategies of "no screening", "screening with ADA" and "screening with DSA" were compared to obtain more insight in the factors that determine which strategy is preferable for certain situations. The outcome in terms of quality adjusted life years (QALY) was in favor of screening for most patients. For low prevalences and low life expectancies, the results of "screening with ADA" were better than of "screening with DSA"; for higher values, DSA resulted in more QALYs than ADA, but the differences were relatively small. In general, the results of ADA were influenced more by the sensitivity than by the specificity. The calculations were performed assuming a sensitivity and specificity of 0.75; with higher figures, the acoustic screening test would lead to even more benefit.

Chapter 10 discusses the outcomes of the transorbital investigations and the experimental results in relation to the application of transorbital sound recordings for the acoustic detection of intracranial aneurysms. An appropriate screening method could be useful for the prevention of aneurysmal subarachnoid hemorrhage. The acoustic transorbital recording method is a non-invasive, risk-free, low-cost test with a high acceptability for the patients. With the acoustic transorbital recording method it is possible to detect abnormal sound patterns in patients with intracranial aneurysms. The sensitivity and specificity for patients admitted to the clinic, obtained with a simple parameter, are limited but would be high enough for a useful application of the recording method as a screening test. The performance of the recording method as a test has to be assessed for unruptured aneurysms before it can be applied. Other intracranial pathological conditions such as an AVM, glioma or vasospasm can cause abnormal sound patterns as well. Bruits can be detected directly from the surface of a part of aneurysms exposed during surgery. The experimental findings support the hypothesis of an aneurysm acting as a resonator which can be brought to vibration by flow. The resonance frequency of an aneurysm is expected to have a strong relationship to its size. Suggestions for improving the recording method and for further research are made.