Unboxing the brain

Valorization

8.6 Introduction

CEREBRO vascular pathologies can have a major impact on a patient's quality of life or even result in the death of the patient. Therefore, early diagnosis and adequate monitoring of cerebral diseases is very important. However, performing measurements on the brain is challenging because the accessibility of the brain is limited by the skull and opening the skull is very invasive. To obtain crucial information about the status of the brain and the pathology, new and preferably non-invasive measurement techniques are being developed. Although new non-invasive techniques show promising results, these techniques are often not good enough to be deployed within the clinical setting and, hence, need to be improved. Moreover, risk stratification of some cerebral diseases can not be performed because the associated metrics can not yet be measured. In these cases it might be possible to estimate the diagnostic metrics by using information measured at other locations within the body. Technological advances, such as computer models, can potentially play an important role in the improvement and development of the non-invasive monitoring and assessment methods of the future. In this thesis we showed how technologies can be used to improve the non-invasive assessment of intracranial pressure in patients suffering from traumatic brain injury (Chapters 2 and 3) or to improve the non-invasive assessment of aneurysm rupture risk in patients suffering from cerebral aneurysms (Chapters 4 and 5).

8.7 Clinical and Societal relevance

In **Part I** we aimed to improve the assessment of the optic nerve sheath diameter (ONSD) for the detection of elevated intracranial pressure (ICP). The work performed in **Chapter 2** highlights the influence of measurement inaccuracies on ONSD values which includes the sensitivity of these ONSD values to changes in ICP. Our work makes clinicians (and researchers) aware of the possible intra- and interobserver variabilities present within manual ONSD measurements as well as their corresponding influence on risk stratification. By exposing the discrepancies in manual assessment methods that cause the uncertainties in ONSD threshold values, we show the importance of standardization by methodological guidelines and the need to comply to such guidelines. Our set of ONSD assessment guidelines proposed in Chapter 2 is a first step towards standardization of ONSD assessment. Only by standardized assessment methods we can ensure good quality measurements and achieve accurate discriminative clinical metrics, not only for pathologies and applications discussed in this thesis, but for clinical monitoring and diagnosing applications in general.

The completely automated ONSD algorithm, presented in **Chapter 3**, does not only relieve clinicians from the task of manually assessing the ONSD, but also improves the accuracy of ONSD assessment as it overcomes the intra- and interobserver variability associated with manual ONSD assessment. Our algorithm can easily be applied within the clinical settings because it is applicable to B-mode ultrasound images that are already regularly used to image the optic nerve sheath and because our algorithm requires no additional knowledge or effort from clinicians. In addition, our presented technology can be incorporated fairly easy within the clinical setting by implementing our algorithm on ultrasound scanners. Moreover, our algorithm will be published in journals associated with the field making it widely available and, hence, increasing the number of patients that can benefit from our work even further. Although further research should be performed to validate if the automatic ONSD assessment indeed results in more accurate ONSD cut-off values for the detection of patients with elevated ICP, such a non-invasive ICP assessment brings multiple benefits for both society and patients. First of all, the physiological burden on these already critically-ill traumatic brain injury patients is greatly reduced because the very invasive ICP sensors become redundant. In addition, the hospitalization cost of these patients might be reduced as patients can be treated more effectively. Moreover, non-invasive methods allow ICP monitoring in non-comatose patients normally not subjected to ICP measurements because of its invasive nature, e.g. children with hydrocephalus, also improving clinical care for such patient groups.

In **Part II** we explored the feasibility of a pulse wave propagation model (PWPM) for the estimation of patient-specific boundary conditions for cerebral aneurysm rupture risk models. Most clinical treatments are based on their effectiveness within patient populations. However, these treatments might not be as effective for every individual patient within this population. Individualized treatments would be the pinnacle of clinical practice but require assessment of the multifactorial physiological status of every individual patient. Unfortunately, current measurement methods are not capable of measuring and taking into account all the relevant factors needed for an accurate and detailed assessment of the patient's status. Moreover, even with improved measurement techniques it might still not be possible to directly measure every relevant parameter/process within the human body. In such cases it might be possible to estimate these metrics by using information from other locations within the body. Our PWPM that mimics physiological processes of the human body by combining physical laws and physiological knowledge can be used to simulate these unmeasurable variables using patient data that can be measured at other locations in the human body. This allows for the diagnosis and monitoring of cerebral pathologies that would otherwise not be possible. Moreover, these models can also be used to simulate the effect of certain treatment

options[1] and any possible changes within the patients, hereby aiding in the clinical decision-making. Finally, such computer models might be used to link many of these aspects together, hereby creating a more complete picture of the physiological state of the patient, which allows for a more patient-specific treatment.
In order to simulate patient-specific diagnostic metrics it is important that computer models describe the relevant patient characteristics as closely as possible. Unfortunately, not all model settings can be measured patient-specifically due to for example, technical or ethical limitations. In addition, not all the processes within the human body can be captured within physical equations because some processes will never be completely understood. Therefore, researchers need to deal with the fact that some model parameters have to be set to population-based values and that some processes have to be simplified using model assumptions. Using the framework presented in **Chapters 4 and 5** one can determine the uncertainties within the simulation outputs resulting from the errors present in the model input parameters. Moreover, it enables one to pinpoint those model parameters and model assumptions that have a large influence on the model outputs and should therefore resemble the true patient-specific situation as closely as possible. Identification of such important parameters allows researchers to focus their efforts on measuring these variables more accurately or on developing new technologies that can be used to perform accurate measurements of the necessary parameters within patients. Therefore, our framework contributes to the efficient development of patient-specific models.
Although frameworks for patient-specific aneurysm rupture risk have already been developed[2, 3], complete frameworks that can capture the total physiological state of a patient and assess patient-specific treatment methods are still far from bedside application. In order to incorporate such frameworks into daily clinical practice, a multi-disciplinary collaboration between engineers and clinicians is needed. Hereto, it is important that both clinicians and researchers are aware of the existence and possibilities of the tools and computer models as described in this thesis. The methods presented in this thesis are or will be published in scientific journals and are therefore available for other investigators who are interested in creating model-based frameworks that can support patient-specific decision-making. Hopefully, our work contributes to a future where patient-specific treatment is daily clinical practice.

References

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