Enter the Matrix

Appendix 2

Valorization

Chronic kidney disease (CKD) remains an important cause of morbidity and mortality worldwide. Incidence and prevalence numbers increase or at least plateaued both nationally and internationally. Patients with advanced stages of CKD rely on renal replacement therapy, of which hemodialysis is the predominantly used modality.
A vascular access is required to facilitate hemodialysis – the artificial kidney needs access to the patient's bloodstream. The arteriovenous fistula (AVF) is the access of choice over arteriovenous grafts and central venous catheters despite its risk of failure to mature (FTM).
Failure to mature describes the unsuccessful adaptation of the native vessels to the altered hemodynamics after the creation of an arteriovenous anastomosis, and occurs in 20-40% of all surgically created AVFs for hemodialysis. Consequently, FTM is an important issue that receives clinical and scientific attention. This thesis reports on the results of probably one of the most innovative approaches to date to reduce FTM rates.
In this chapter we will discuss the valorization opportunities that originate from the work presented in this thesis. Valorization can be subdivided into two aspects. First, knowledge can be me made available for economical and societal exploration. Second, this knowledge can be translated into new products, services, processes, and businesses.

MAKING KNOWLEDGE AVAILABLE AND SUITABLE FOR ECONOMIC AND SOCIETAL EXPLORATION

The society of today increasingly asks academia to perform relevant research that will benefit the society, either through direct implementation of the results or (indirectly) through communication of studies and results thereof to academic peers. Additionally, scientific training of medical PhD candidates results in physicians with improved skills to critically acclaim scientific studies – well needed trait in the era of evidence based medicine, with a worldwide, ever increasing scientific output.
Many of the chapters are or will be published in peer-reviewed journals, therewith distributing the acquired knowledge to the academic/clinical community. In addition, parts of this thesis and other related work is presented on (inter)national conferences.

Direct valorization

The first and foremost direct result was the implementation of a more standardized duplex ultrasonography scanning protocol in several Dutch hospitals. For participation in the Shunt Simulation Study a predefined and uniform duplex scanning protocol was necessary. Although clinical guidelines recommend duplex examination to be a routine

part of AVF creation work up, surprisingly there was large variation in how this duplex examination was performed. This heterogeneity was observed for both pre- and postoperative examination. Measurement standardization (input) was necessary to guarantee accurate flow predictions (model output).
Protocol standardization proved to be well received in several centers where physicians were accustomed to summarily duplex protocols. Our more elaborated protocol was advantageous since it provided them with more information for surgical planning or a better indication of the possible anatomical substrate in case of AVF dysfunction. Consequently, in these centers the now standardized duplex protocol was retained, even after patient inclusion or follow-up visits were finished.

Indirect valorization

Other results of this thesis will be beneficial more indirectly. Chapter 2 for example aims to inform the relative lay reader with the pros and cons, and the necessary preconditions for computational modeling, it identifies the accomplishments to date, and it suggests improvements for further research. It was observed that patient-specific modeling is gaining momentum, also in AVF research. It therefore is also increasingly being published in clinical journals. Unfortunately, in many of the studies methodological difficulties are identified. Increasing the understanding of such studies will lead to a more critical appraisal of the methodology and/or results.
In Chapter 4 it was shown that duplex ultrasonography is a reliable imaging modality to support decision-making in AVF creation. Internationally there is an ongoing debate whether or not duplex scanning should be performed routinely during surgical planning. With the findings from this chapter, additional arguments are provided that the unequivocal results of previous studies are primarily due to methodological difficulties.
Chapter 5 adds to the (hemodynamical) understanding of arteriovenous fistula maturation. Currently, the *Rule of Sixes* for AVF maturation is questioned by the international scientific community in many peer-reviewed publications. Researchers and physicians increasingly recognize the relatively anecdotal evidence of the Rule of Sixes. The study described in this chapter was the first to investigate the postoperative hemodynamical changes for a relatively long period in a large cohort of patients. It therewith provides a better hemodynamical understanding of AVF maturation.
Chapter 6 most importantly confirms the potential benefit of adding patient-specific flow predictions to AVF surgery planning. Until now, it was only known that the patient-specific flow predictions were accurate, but if and to which extent they could influence clinical outcomes was still undetermined. In a way this adds to the valorization of the

previous research that was performed in designing the computational model. Additionally, the findings of this chapter might also spark future interest for or confidence in patient-specific computational modeling.

TRANSLATING KNOWLEDGE INTO PRODUCTS, SERVICES, PROCESSES, AND NEW BUSINESSES

The most obvious possibility to translate the knowledge described in this thesis is to convert the computational model into (stand-alone) software or web-based application. Here, the physician can enter the relevant patient-specific data, and a flow prediction will be calculated or sent to the physician in a timely manner. Till the moment that desktop computers have the computational power of nowadays servers with parallel computing, the major potential to translate the knowledge is probably to provide an integral AVF surgical planning service. This service would then include training of vascular technicians, standardization of duplex examination, and training physicians in clinical decision-making, including how to interpret duplex measurements, which may be with or without the incorporation of patient-specific flow predictions.