

## Aim and outlines of this thesis

The aim of the research described in this thesis is to investigate male steroid hormone metabolism at castration levels in prostatic carcinoma using ID-LC-MS/MS, in order to gain more insight in the process of prostate cancer progression, and to improve and to personalize (hormonal) treatment of prostate cancer. Furthermore, this study is a critical appraisal of current clinical methods for analysing serum testosterone and advocates the use of more accurate techniques in basic science as well as in clinical research.

In **chapter 2** we describe the current literature about intraprostatic concentrations of testosterone and dihydrotestosterone and the currently available analytical methods for measuring androgen levels. In **chapter 3** we describe the current literature about intraprostatic testosterone and DHT after androgen hormonal manipulation in patients with benign prostatic hyperplasia or prostate cancer. In **chapter 4** we evaluate the serum testosterone concentrations in men on androgen deprivation therapy using ID-LC-MS/MS, an ultrasensitive method of serum testosterone measurement. We compare the concentrations in subjects that underwent surgical castration with men that received luteinizing hormone-releasing hormone agonist therapy for prostate cancer. This is followed by an evaluation of serum testosterone concentrations in men that received treatment with a luteinizing hormone-releasing hormone antagonist in **chapter 5**.

In the **6<sup>th</sup> chapter** we describe the effect of obesity/body mass index on the efficacy of LHRH-agonist therapy in patients with prostate cancer. In **chapter 7** we describe the role of serum testosterone in the progression and process of formation of metastases in CRPC. LHRH-agonists are known to cause a peak in serum testosterone levels in the first weeks after the start of the treatment, and prevention of the clinical effects of this testosterone flare by anti-androgen therapy is recommended. **Chapter 8** describes the absence of evidence for the need of flare prevention.

This thesis is concluded in **chapter 9** where we discuss the presented data and describe future perspectives of these subjects.