Computer Aided Diagnosis system for prostatic biopsy guidance and follow-up fusing multi-modal imaging.

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Abstract

Put your abstract or summary here, if your university requires it.

To ...

Acknowledgements

I would like to acknowledge the thousands of individuals who have coded for the LaTeX project for free. It is due to their efforts that we can generate professionally typeset PDFs now.

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CaP prostate cancer

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Chapter 1

Introduction

1.1 Prostate Cancer

1.1.1 Anatomy

prostate cancer (CaP)

The prostate is an exocrine gland of the male reproductive system and possesses an inverted pyramidal form. Its mensurations are usually about 3 centimetres in height by 2.5 centimetres in depth. Its weight is estimated between 15 and 25 grams for an adult. The size of the prostate increases at two moments during development: initially at puberty to reach its normal size then after 60 years of age leading to benign prostatic hyperplasia (BPH [1]).

The prostate is located below the bladder and in the front of the rectum and the urethra goes through the prostate as shown on Fig. 1.1. The urethral sphincter is located at the apex of the prostate around the prostatic urethra in order to drain the glands. The prostate is also composed of a muscle which allows the expulsion of the sperm during the ejaculation.

The prostate has an inverted pyramidal form. The base is the upper part and closest to the bladder while the apex is lower down and further from the bladder (Fig. 1.1 and 1.2). The seminal vesicles are located above the base of the prostate localized between the rectum and the bladder (Fig. 1.1).

[1] For all abbreviations see the glossary on page **??**.

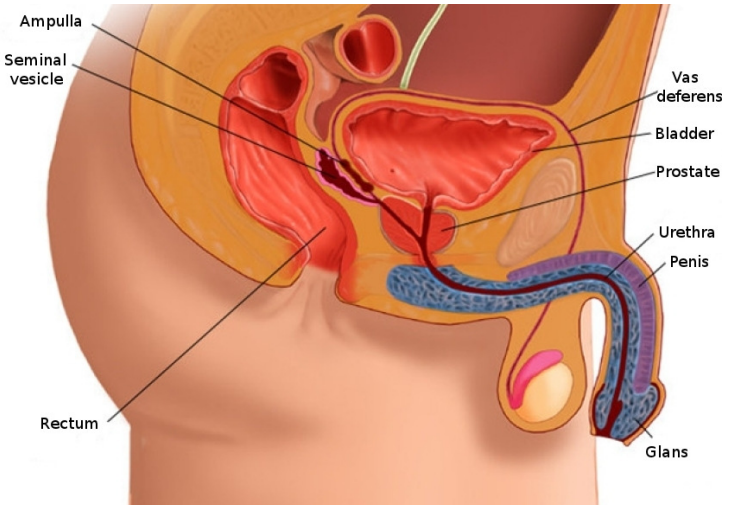


Figure 1.1: Sagittal anatomy scheme of the male reproductive system (**?**).

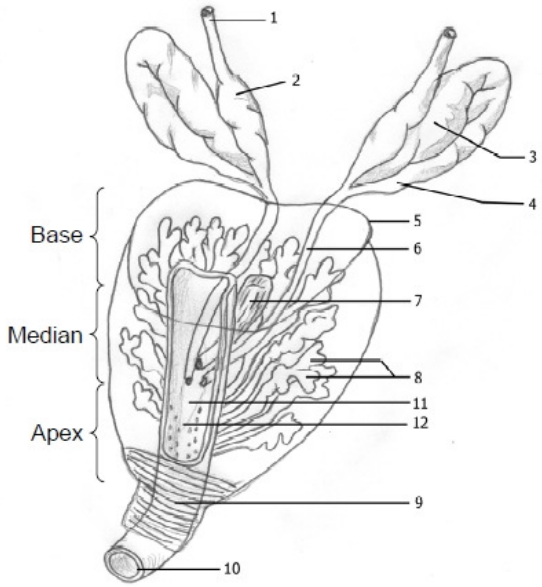
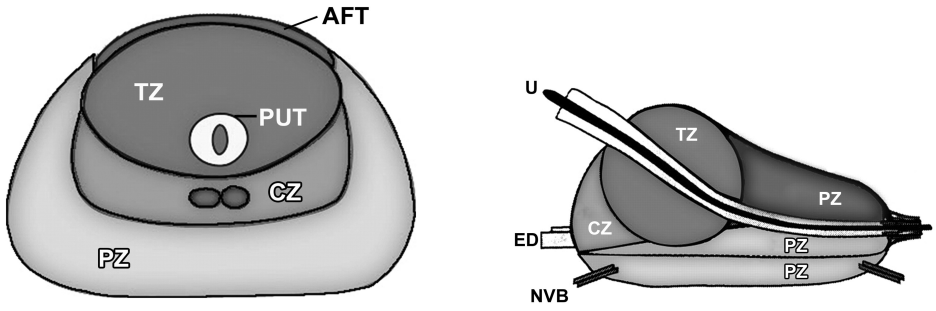


Figure 1.2: Representation of the prostate. 1: Vas deferens, 2: Ampulla, 3: Seminal vesicle, 4: Excretory duct of seminal vesicle, 5: Prostate contour, 6: Ejaculatory duct, 7: Prostatic urticle, 8: Glandular tissue, 9: Urethral sphincter, 10: Urethra, 11: Seminal colliculus, 12: Urethral crest (**?**).



(a) Transverse anatomy of the prostate.

(b) Sagital anatomy of the prostate.

Figure 1.3: Presentation of the different zones of the prostate. *AFT:* anterior fibromuscular tissue, *CZ:* central zone, *ED:* ejaculatory duct, *NVB:* neurovascular bundle, *PUT:* periurethral tissue, *PZ:* peripherical zone, *U:* urethra, *TZ:* transitional zone (**?**).

The prostate can be divided in different zones (Fig. 1.3) as proposed by McNeal (**?**) and widely accepted in the literature (**? ? ? ?**): central zone (CZ[1]), transitional zone (TZ[1]) and peripheral zone (PZ[1]).

The PZ which represents about 70% of the prostate is composed of glandular tissue. Roughly 70% of prostate cancers (PCa[1]) originate in this zone.

The CZ which accounts for about 20-25% of the prostate is composed of stromal tissue. The excretory ducts of the seminal vesicles and ampulla go through the base and join to form the ejaculatory duct.

The TZ is composed of two symmetric lobes localized on each sides of the urethra. The TZ represents 5% of the prostate. The size of this zone increases with age and with the development of a pathology known as benign prostatic hyperplasia.

Approximately 30% of PCa are found in these two zones.

On MRI images, the CZ and TZ are usually difficult to distinguish.

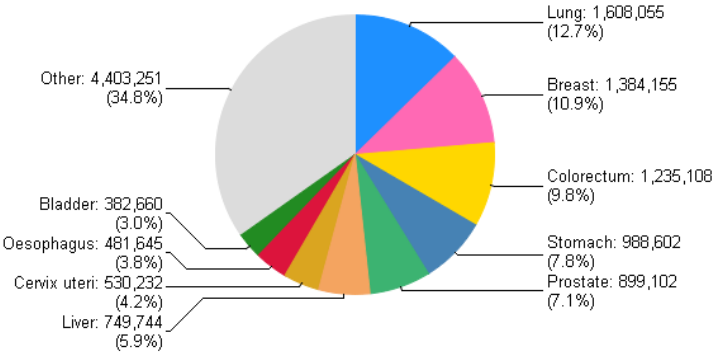
The PZ accounts for about 70% of glandular tissue. 70% of PCa arise in this zone.

1.1.2 Statistics

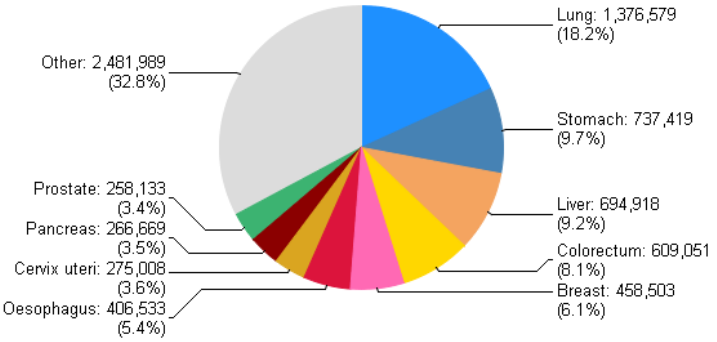
1.1.2.1 Overview

The World Health Organization (WHO) published in 2008 that PCa was the second most frequently diagnosed cancer of men and the fifth most common cancer overall (**?**

[1]For all abbreviations see the glossary on page **??**.



(a) Estimated number cancers cases for both sexes and all ages.



(b) Estimated number cancers deaths for both sexes and all ages.

Figure 1.4: Cancer estimations in 2008 by the World Health Organization (WHO) (**?**).

). No less than 899,000 new cases where detected worldwide in 2008 (**?**). As presented on Fig. 1.4, PCa accounts for approximately 7.1% (Fig. 1.4(a)) of all cancers diagnosed in 2008 and 3.4% (Fig. 1.4(b)) of all cancers deaths in 2008 (**?**).

1.1.2.2 Risk Factors

The risk factors can be categorized in three different classes:

- Age: age is the most important risk factor for PCa. The diagnosis of PCa for men over 50 years old. PCa rate increases upto about 70 and declines thereafter (**?**).
- Genetic factors: it has been shown that the probability to have a cancer is higher when a member of the family has been already diagnosed (**?**).

- Race: in the United States, the Africo Americans have a higher probability of developing a PCa than European American and Hispanic men (**?**).

1.1.3 Diagnosis and Medical Exams

The presence of PCa may be suggested in several ways: digital rectal examination, Prostate Specific Antigen (PSA[1]) test, biopsy using transrectal ultrasound (TRUS[1]) and magnetic resonance imaging (MRI[1]-MRSI[1]).

1.1.3.1 Digital Rectal Examination

Both benign prostatic hyperplasia and cancer may lead to an increasing size of the prostate. A rectal examination may allow detection of harder nodules within the softer prostatic tissue. The advantages are that this method is very fast and does not need any special equipment.

1.1.3.2 PSA test

The PSA is a protein secreted by the prostate. A higher-than-normal level of PSA can indicate an abnormality of the prostate: a benign prostatic hyperplasia or a cancer. However, other factors can lead to an increasing level of PSA such as prostate infections, irritations, a recent ejaculation or a recent rectal examination, etc.

The PSA can be found in the blood in two different forms: free PSA (about 10%) and linked to another protein (about 90%).

A level of PSA higher than 10 $ng.mL^{-1}$ is considered as pathologic (**?**). If the PSA level is between 10 $ng.mL^{-1}$ and 4 $ng.mL^{-1}$, the patient is considered as suspicious (**?**). In that case, the ratio free PSA over total PSA is computed. If the ratio is higher than 15%, the case is considered as pathologic.

1.1.3.3 TRUS

As described in Sect. 1.1.1, the prostate is localized in front of the rectum. Hence, its position allows one to carry out a biopsy using transrectal ultrasound (TRUS) in order to localise more precisely an eventual cancer (Fig. 1.5).

Add example of images of TRUS PCa and not

[1]For all abbreviations see the glossary on page **??**.

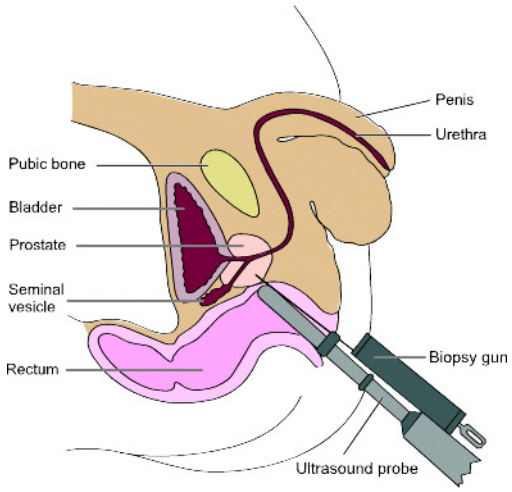


Figure 1.5: Biopsy of the prostate using TRUS

Add information about protocol: manipulation of the patients, which equipment (see Jhimli thesis) The biopsy is usually prescribed when the PSA level is higher-than-normal or abnormalities were detected during a rectal examination. At least six different samples are taken from the right and left parts of the three different zones: apex, median and base. The samples are analysed in order to determine the presence of a cancer. **Add more information on the specificities and accuracy of the techniques. Add also what are the advantages (real-time)**

1.1.3.4 MRI

MRI is a relatively recent technique. This exam allows one to obtain a better spatial resolution and a more precise localization and aggressiveness of the cancer compared with the previous methods. We refer the reader to Sect. 1.2 in order to have complete explanation of the different MRI modalities.

The MRI modalities used in PCa diagnosis are: (i) T2-weighted imaging, (ii) diffusion-weighted imaging (DWI[1]), (iii) dynamic contrast-enhanced imaging (DCE[1]) and (iv) magnetic resonance spectroscopy imaging (MRSI[1]).

- T2-Weighted Imaging: T2-weighted imaging provides a spontaneously high contrast image and a good spatial resolution (Fig. 1.6) depicting precisely the prostate

[1]For all abbreviations see the glossary on page **??**.

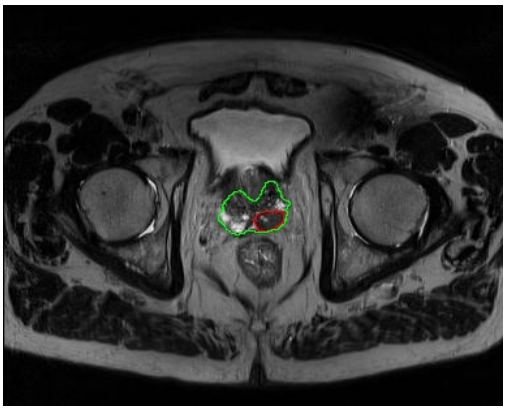


Figure 1.6: T2-Weighted Imaging. The prostate is highlighted in green. The cancer is highlighted in red. Cancer tissue is characterized by a very low-signal intensity allowing to distinguished it easily in the PZ.

anatomy. Fat, muscles and prostate can easily be differentiated through the contrast between each tissue. The PZ is mainly glandular, which implies a high-signal intensity enclosed by a thin border of low-signal intensity (**?**). The CZ and TZ are fibrous zones and give a lower signal than that of the PZ (**?**). Tumours are characterized by very low signal intensity (**?**) implying an easily distinction in PZ. However, note that low signal intensity can be also characteristic of different benign conditions such as haemorrhage, prostatitis, hyperplastic nodules or post-treatment relapses (**?**).

- Diffusion-Weighted Imaging: Diffusion-weighted imaging (DWI[1]) represents the degree of diffusion of the water molecules inside the tissue. On DWI images, the prostate can be divided in two parts. The glandular nature of the prostate zone means that tissue. Water is able to move freely and gives a hyper intense signal. The CZ is more chaotic and inhibits the motion of the water. Thus, the signal of CZ will be lower and more heterogeneous than that of the PZ. Tumours imply a greater density of membranes. These membranes also inhibit water motion. Hence, cancer tissue will appear to be darker on DWI images as shown on Fig. 1.7.

- Dynamic Contrast-Enhanced MR Imaging: Dynamic contrast-enhanced MR imaging (DCE[1]) provides a cinetic study. This technique consists to acquire a series

[1]For all abbreviations see the glossary on page **??**.

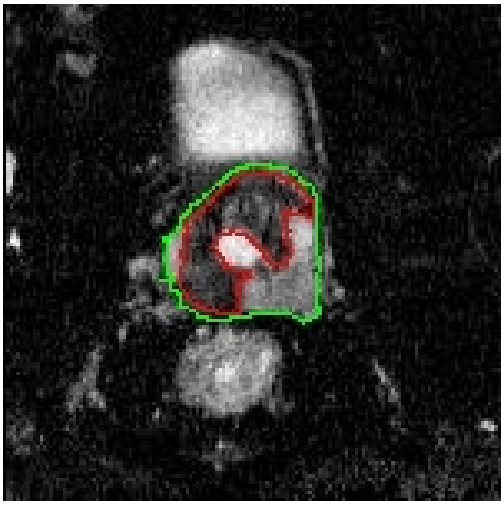


Figure 1.7: Diffusion-Weighted Imaging. The prostate is highlighted in green. The cancer is highlighted in red.

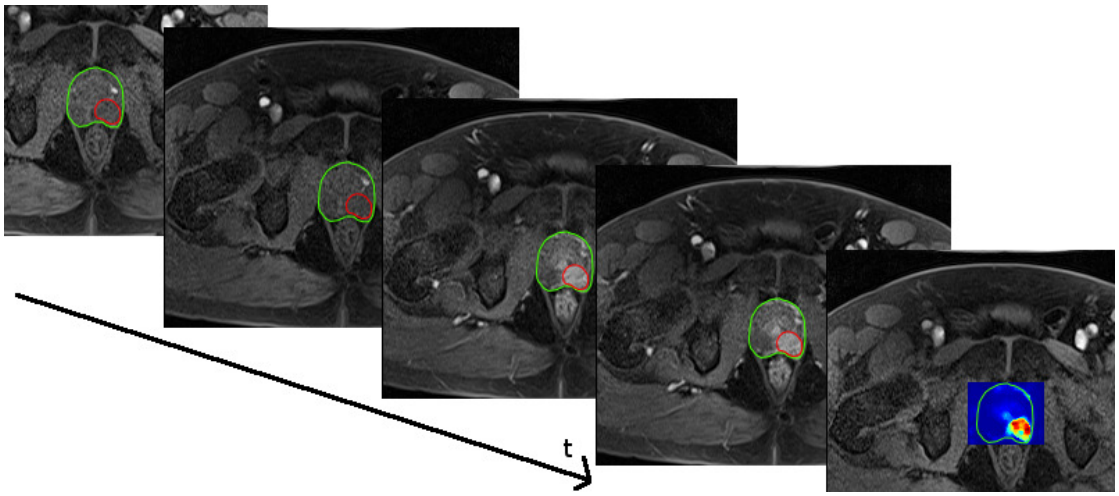


Figure 1.8: Dynamic Contrast-Enhanced MR Imaging. The prostate is highlighted in green. The cancer is highlighted in red. The image contrast changes over time will be studied in order to create a cancer map image (bottom right image).

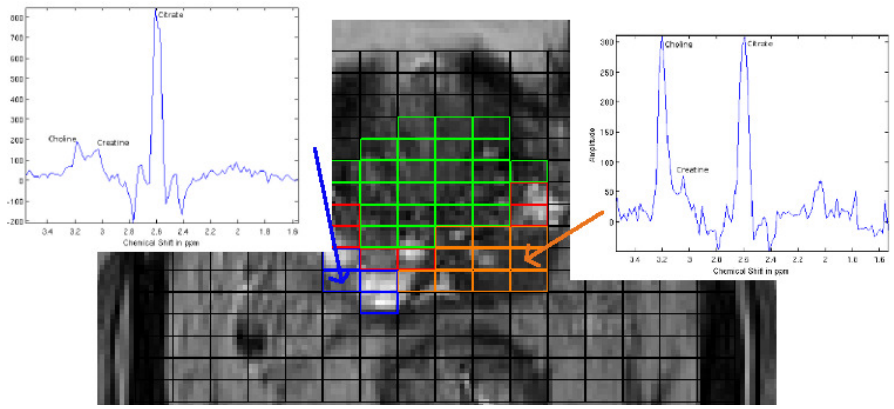


Figure 1.9: MR Spectroscopic Imaging. The prostate voxels are highlighted in color: (i) green - CZ ; (ii) red - TZ ; (iii) blue - PZ ; (iv) orange - PCa. Examples of healthy tissue spectrum (left) and cancer tissue spectrum (right) are given.

of images in both space and time during the passage of contrast agent (Fig. 1.8). The arrival and departure of the contrast agent will be studied in order to determine the type of tissue. The PZ being mainly composed of glandular tissue the amount of interstitial space is limited involving restricted exchanges and a limited abundance of contrast agent. The signal over time neither rise quickly nor fall off quickly. The CZ has a more disorganised structure which allows easily the arrival of contrast agent. The signal intensity over time will have a rapid increase followed by a plateau. Tumours, due of a high vascularity, will have high exchange in input and in output. Thus, the signal observed during time will have a rapid increase and rapid fall.

- Magnetic resonance spectroscopic imaging: MRSI is a technique that allows the study of metabolite concentrations. The difference in metabolism between healthy and cancer tissues allows one to find a pattern in the concentrations observed. The resolution of the spectroscopy is inferior to the other techniques (Fig. 1.9) but this technique is particularly sensitive and bring some information about the aggressiveness of the PCa.

1.2 Magnetic Resonance Imaging Principles

Chapter 2

Aims of the project

2.1 Final aim

Our ultimate goal is...

2.2 Preliminary aims

There will be several preliminary scientific targets to be accomplished on the way...

Chapter 3

State of the art in multi-modal magnetic resonance imaging

3.1 Magnetic resonance imaging techniques

3.1.1 Anatomic T2-weighted magnetic resonance imaging

3.1.1.1 Imaging characteristics

As previously mentioned in Sect. 1.1.3.4, T2-weighted MRI modality allows to clearly differentiate the prostate anatomy (**?** **?**). Indeed, high-intensity-signal of PZ is highly contrasted with low-signal-intensity of CZ or TZ (**?**) (see Fig.**Add figure healthy T2**), while PCa is usually characterized by a very low-signal-intensity (**Add figure PCa T2**).

Thus, T2-weighted MRI signal could be enough discriminative in order to highlight PCa tissue from healthy tissue in PZ (see Fig.**Add PCa T2**). However, low-signal-intensity is not always synonym of PCa tissue and can be consecutive to benign abnormalities (e.g., chronic prostatitis, atrophy, scars, post-examination effects, post-treatment side effects and BPH) (**?**) (see Fig. **Add figure with BPH**). With an eye to reduce false positive detections due these abnormalities, several studies provided a way to characterized them. Thus, Cruz et al. associated wedge shape and diffuse extensions without mass effect in T2-weighted MRI with highly benign area (**?**). Haemorrhage due to post-examination (i.e., TRUS biopsy) can be differentiated using T1-weighted MRI (**?**). Indeed, haemorrhage is characterized by high-signal-intensity on T1-weighted MRI as depicted in Fig. **Add T1** (**?**). With the intention of decreasing artefacts, a delay of

eight weeks should be observed between a biopsy examination and a MRI examination (**?**).

PCa detection and localization in TZ and CZ are more challenging tasks. The signal intensity in these zones are very similar to that representing PCa tissue. However, Akin et al. characterized PCa in CZ and TZ as an homogeneous low-signal-intensity, ill-defined margins, and lack of capsule (see Fig. **Add PCa in TZ**) (**?**).

3.1.1.2 Medical facts

3.1.2 Dynamic contrast-enhanced magnetic resonance imaging

3.1.3 Diffusion weighted imaging

3.1.4 Proton magnetic resonance spectroscopic imaging

3.2 Fusion of magnetic resonance imaging techniques

Chapter 4

Discussion

Chapter 5

Materials & methods

Declaration

I herewith declare that I have produced this paper without the prohibited assistance of third parties and without making use of aids other than those specified; notions taken over directly or indirectly from other sources have been identified as such. This paper has not previously been presented in identical or similar form to any other German or foreign examination board.

The thesis work was conducted from XXX to YYY under the supervision of PI at ZZZ.

CITY,