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

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Abstract

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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.

Contents

List of Abbreviations

BPH benign prostatic hyperplasia

CaP prostate cancer

CG central gland

CZ central zone

Fig. figure

MRI magnetic resonance imaging

PZ peripheral zone

TZ transitional zone

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Chapter 1

Introduction

1.1 Prostate Cancer

1.1.1 Anatomy

The prostate is an exocrine gland of the male reproductive system having an inverted pyramidal shape, which is located below the bladder and infront of the rectum (see Fig. 1.1). It measures approximately three centimetres in height by two and half centimetres in depth and its weight is estimated to be between seven and sixteen grams for an adult ((3)). The prostate size increases at two distinct stages during physical development: initially at puberty to reach its normal size, then again after sixty years of age leading to benign prostatic hyperplasia (BPH) ((4)).

A zonal classification of the prostate, depicted in Fig. 1.2, was suggested by Mc-

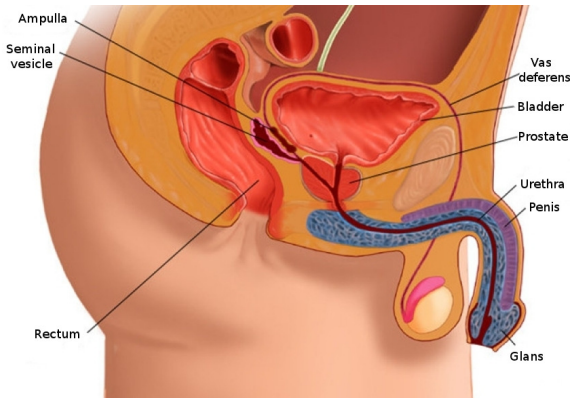
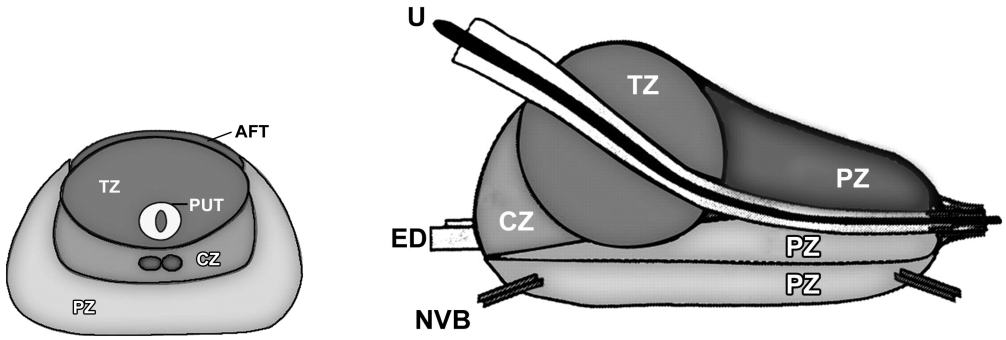


Figure 1.1: Sagittal anatomy scheme of the male reproductive system



(a) Transverse anatomy of the prostate.

(b) Sagittal anatomy of the prostate.

Figure 1.2: Prostate anatomy with division in different zones. *AFT:* anterior fibromuscular tissue, *CZ:* central zone, *ED:* ejaculatory duct, *NVB:* neurovascular bundle, *PUT:* tissue, *PZ:* peripheral zone, *U:* urethra, *TZ:* transitional zone, *B:* base, *M:* median, *A:* apex (copyright by (1)).

Neal ((5)). Subsequently, this categorization was widely accepted in the literature (cf., (4, 6, 7, 8)) and is used in all medical examinations (e.g., biopsy, magnetic resonance imaging (MRI) screening). The classification is based on dividing the gland into three distinct regions: (i) central zone (CZ) accounting for 20-25% of the whole prostate gland, (ii) transitional zone (TZ) standing for 5% and (iii) peripheral zone (PZ) representing the 70%. In MRI images, tissues of CZ and TZ are difficult to distinguish and are usually merged into a common region, denominated central gland (CG). As part of this classification, the prostate can be divided in three longitudinal portions depicted in Fig. 1.2(b): (i) base, (ii) median gland and (iii) apex.

1.1.2 Prostate Carcinoma

prostate cancer (CaP) has been reported on a worldwide scale to be the second most frequently diagnosed cancer of men accounting for 13.6% ((2)). Statistically, in 2008, the number of new diagnosed cases was estimated to be $899,000$ with no less than $258,100$ deaths ((2)). In United States, aside from skin cancer, CaP was declared to be the most commonly diagnosed cancer among men, implying that approximately one in six men will be diagnosed with CaP during their lifetime and one in thirty-six will die from this

disease causing CaP to be the second most common cause of cancer death among men ((9), (10)).

Despite active research to determine the causes of prostate cancer, a fuzzy list of risk factors has arisen ((11)). The etiology was linked to the following factors ((11)): (i) family history ((12, 13)), (ii) genetic factors ((14, 15, 16)), (iii) race-ethnicity ((12, 17)), (iv) diet ((12, 18, 19)), (v) obesity ((12, 20)). This list of risk factors alone cannot be used to diagnose CaP and in this way, screening enables early detection and treatment.

CaP growth is characterized by two main types of evolution ((21)): slow-growing tumours, accounting for up to 85 % of all CaPs ((22)), progress slowly and usually stay confined to the prostate gland. For such cases, treatment can be substituted with active surveillance. In contrast, the second variant of CaPs develops rapidly and metastasises from prostate gland to others organs, primarily the bones ((23)). Bone metastases, being an incurable disease, significantly affects the morbidity and mortality rate ((24)). Hence, the results of the surveillance have to be trustworthy in order to distinguish aggressive from slow-growing CaP.

CaP is more likely to come into being in specific regions of the prostate. In that respect, around 70-80 % of CaPs originate in PZ whereas 10-20 % in TZ ((25, 26, 27)). Only about 5 % of CaPs occur in CZ ((26, 28)). However, those cancers appear to be more aggressive and more likely to invade other organs due to their location ((28)).

1.1.3 Statistics

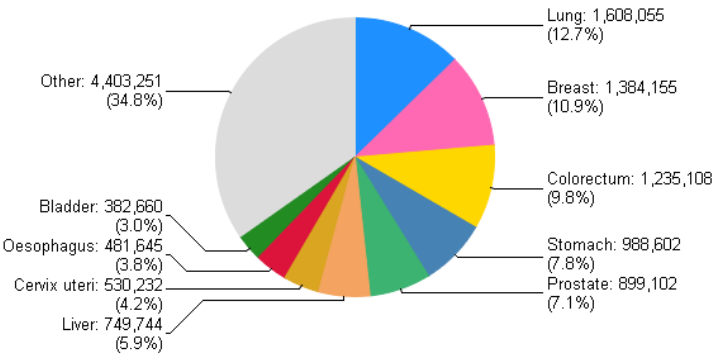
1.1.3.1 Overview

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 (2). No less than 899,000 new cases where detected worldwide in 2008 (2). As presented on Fig. 1.3, PCa accounts for approximately 7.1% (Fig. 1.3(a)) of all cancers diagnosed in 2008 and 3.4% (Fig. 1.3(b)) of all cancers deaths in 2008 (2).

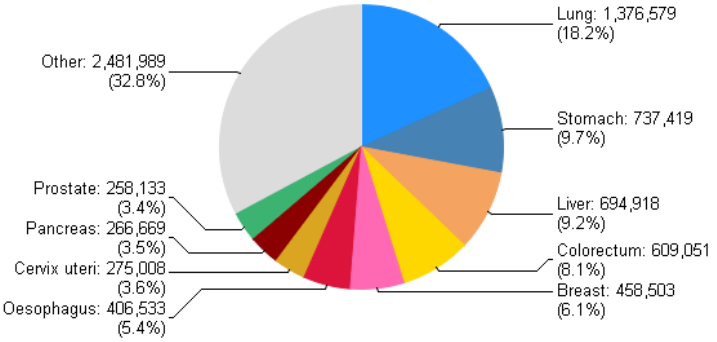
1.1.3.2 Risk Factors

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 (**?**).



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



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

Figure 1.3: Cancer estimations in 2008 by the World Health Organization (WHO) (2).

- 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 (**?**).

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. **??**, T2-weighted MRI modality allows to clearly differentiate the prostate anatomy (6, 29). Indeed, high-intensity-signal of PZ is highly contrasted with low-signal-intensity of CZ or TZ (29) (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) (30) (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 (31). Haemorrhage due to post-examination (i.e., TRUS biopsy) can be differentiated using T1-weighted MRI (32). Indeed, haemorrhage is characterized by high-signal-intensity on T1-weighted MRI as depicted in Fig. **Add T1** (32). 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**) (33).

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

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