بسم الله الرحمن الرحيم

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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: ....

Role of Focal HIFU Prostate Ablation in the Management of Unilaterally Diagnosed Low and Intermediate Risk Prostate Cancer

Thesis

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Mohamed Essam Noureldin

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List of Abbreviations

Abb.	Full term
ADC	Apparent diffusion coefficient
AE	
ASTRO	American Society for Radiation Oncology
BPH	Benign prostatic hyperplasia
BPSA	Benign Prostate-specific Antigen
CAD	Computer aided detection
CI	Confidence interval
DCE	Dynamic contrast enhancement
DRE	Digital rectal examination
DWI	Diffusion weight imaging
EAU	European association of urology
ED	Erectile dysfunction
EDAP	
f/tPSA	Free/total
FFS	Failure-free survival rate
FPSA	Free prostate-specific antigen
FT	Focal Therapy
HEAT	
HIFU	High-intensity focused ultrasound
IIEF-15	15-question International Index of Erectile Function
IPSS	International Prostate Symptom Score
ISUP	International society of urological pathology
LMIC	Low and middle-income countries
MAI	Malignancy Attention Index
MDT	Multi-disciplinary team meeting
MRI	Magnetic Resonance Imaging
PCa	Prostate cancer

PI-RADS 2.0 ..... Prostate Imaging Reporting and Data System Version 2.0

PIVOT .....Prostate cancer Intervention Versus Observation Trial

PRECISION

PROMIS

PSA..... Prostate-specific antigen

RCT..... Randomised controlled trial

SPCG-4..... Scandinavian prostate cancer group

T2WI..... T2-weighted imaging

TPM..... Template prostate mapping

TPM..... Template prostate mapping

TRUS..... Transrectal ultrasound

TWOC..... Trial without the catheter

TZ..... Transitional zone

UCLA..... University of California, Los Anglos

WHO..... World Health Organization

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INTRODUCTION

Prostate cancer (PCa) incidence is steadily increasing worldwide. Current screening strategies have led to earlier diagnosis of PCa at earlier clinical stages, lower grades, and smaller volumes. PCa is also the most frequent cancer among males in Europe. It is more frequent in northern and western Europe (>200 per 100,000), but rates in eastern and southern Europe have increased in the past few years starting to match levels seen in both northern and western Europe.

D'Amico et al., established risk stratification to better understand and classify the biologic behavior of prostate cancer; it includes low-, intermediate-, and high-risk prostate cancer.

The therapeutic choice is very debatable for prostate cancer. Several factors share in decision making including; tumor stage, prostate-specific antigen (PSA) value, Gleason score, patient's age, concomitant diseases, life expectancy, and patient's preference ***(Aus et al., 2005).***

The management strategy for newly diagnosed clinically localized prostate cancer includes radical prostatectomy, radical radiotherapy, and active surveillance. As an alternative, minimally invasive therapies such as cryotherapy and High Intensity Focused Ultrasound (HIFU) have been proposed as iso-effective cancer control with fewer complications and side

effects ***(Berge et al., 2014).*** Since the 1990s, HIFU has been used for the treatment of prostate cancer. Feijoo et al., stated that HIFU constitutes an attractive therapeutic alternative for selected patients with localized prostate cancer. Their results were encouraging by showing the high efficacy rate along with low morbidity rates and minimal functional changes, but longer follow-up is expected to establish further considerations of this novel approach ***(Feijoo et al., 2016).***

In 2008, Muto et al., raised the concept of focal therapy with HIFU in the treatment of localized prostate cancer in low-risk patients ***(Muto et al., 2008).*** But focal HIFU was assigned to have multiple limitations, the most two frequent limitations were the significant shift of the prostate and swelling during treatment ***(Shoji et al., 2013),*** also identification of unilateral disease by means of random biopsy only is difficult as all other means of focal treatment approaches in prostate cancer ***(Roman Ganzer et al., 2013).***

In addition to that most of the disapproval of HIFU in the literature mainly stems from overall lack of data, paucity of evidence concerning improved quality of life and long-term survival, lack of long-term follow-up data, and missing comparisons of HIFU with conventional therapy options ***(Blana et al., 2009).*** Also, the EAU states that focal therapeutic options such as HIFU are currently not standard therapeutic options for localized prostate cancer and should only be performed within clinical trials, but it emphasizes their future

potential. However, in 2010 the EAU has recommended HIFU as an alternative option, in addition to salvage RP, cryosurgery, and interstitial brachytherapy, for the treatment of recurrent prostate cancer following radiotherapy in patients who are well informed about its experimental nature ***(Aus et al., 2005).***

Therefore, the goal of focal HIFU is to achieve treatment of significant prostate cancer while sparing the remaining benign prostate or even prostate tissue harbouring only insignificant cancer. This will potentially minimize the side effects compared to radical treatment approaches. Focal HIFU is an emerging modality of prostate cancer therapy and despite several studies to prove its efficacy, there remains some challenges in achieving the most accurate definition for treatment failure, also a validated follow up protocol after HIFU treatment is still to be established.

In our study we will highlight in a prospective manner the efficacy of this treatment modality on low and intermediate risk focal prostate cancer patients and commenting on the short-term outcome, we will also try to conclude the most appropriate methodology for follow up.

AIM OF THE WORK

The aim of this thesis study is to evaluate focal HIFU prostate ablation in the management of unilaterally diagnosed low and intermediate risk Prostate cancer.

Chapter 1

SETTING THE SCENE FOR FOCAL PROSTATE THERAPY

To achieve satisfactory outcomes for focal prostate cancer treatment; few aspects need to be covered and well digested to pave the way for best focal treatment practice, under-standing the zonal anatomy and respecting anatomical landmarks of prostate within depth knowledge of surrounding structures to achieve good ablation and at the same time minimizing side effects is of utmost importance. Achieving accurate diagnosis to specify tumour location is a corner stone for performing correct focal treatment, this requires multidisciplinary team approach starting from accurate imaging and robust reporting from well-trained radiologist followed by clear mapping biopsies protocols. Ultrasound skills and understanding the different ablative technologies is an integral part of a successful focal treatment. This will be thoroughly discussed in the next review.

Gross anatomy of the prostate

The prostate is a conical pelvic organ surrounding the proximal urethra as it exists from the bladder. It is located just inferior to the neck of the urinary bladder. The base of this cone is superiorly related to the bladder while the apex of the gland rests on the superior surface of the urogenital diaphragm. It