GHANA COLLEGE OF PHYSICIANS AND SURGEONS

FACULTY OF SURGERY

DETERMINANTS OF SIGNIFICANT VOIDING DYSFUNCTION AFTER IODINE-125 BRACHYTHERAPY FOR LOCALIZED PROSTATE CANCER AT THE KORLE BU TEACHING HOSPITAL.

BY

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BSc Hum Bio, MB ChB (KNUST – SMS)

SEPTEMBER 2024

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SUBMITTTED TO THE FACULTY OF SURGERY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE CONFERMENT OF A FELLOW OF GHANA COLLEGE OF SURGEONS.

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DECLARATION

I hereby declare that this dissertation is my own work which I carried out under the guidance of my Supervisors.

It has not been submitted before towards the award of a degree or examination of any college.

Dr Jonathan Charles Lamptey

Signature 

Date: 27th March 20244

ATTESTATION BY SUPERVISORS

We attest that this Dissertation titled **"Determinants of significant voiding dysfunction after iodine-125 brachytherapy for localized prostate cancer at the Korle Bu Teaching Hospital.**" is an original research to be undertaken by Dr. Jonathan Charles Lamptey at the Urology Unit of the Department of Surgery, Korle Bu Teaching Hospital under our supervision.

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LIST OF ABBREVIATIONS AND TERMS

ADT …….. Androgen Deprivation Therapy

AROU……Acute Retention of Urine

CaP …….. Prostate Cancer

DRE …….. Digital Rectal Examination

EBRT……. External Beam Radiation Therapy

IPSS ……. International Prostate Symptom Score

I-125 …… Iodine 125

LDR …… Low Dose Rate

LUTS…… Lower Urinary Tract Symptoms

PPB ……... Permanent Prostate Brachytherapy

PSA ……. Prostate Specific Antigen

QoL ……... Quality of Life

RP…….. Radical Prostatectomy

SDM ……. Shared Decision Making

3D- CRT…… Three Dimensional Conformal Radiation Therapy

TRUS …… Trans Rectal Ultrasound

TURP ……. Transurethral Resection of the Prostate

LIST OF TABLES AND FIGURES

ABSTRACT

Background: Prostate cancer is the second most commonly diagnosed cancer amongst men after lung cancer accounting for 14.1% of cancers in men.

Both incidence and mortality vary tremendously across geographic regions and populations reflecting multifactorial impacts of genetic variation; diet, lifestyle, environmental factors, access to care and variations in use of prostate specific antigen (PSA)-based screening policies.

With the increasing use of PSA as a screening tool in Sub Saharan Africa many more cases of localized cancer of the prostate are being diagnosed. Radical prostatectomy and radiation therapy remain the main options for active treatment of localized cancer of the prostate.

Low dose rate brachytherapy has recently (2008) become available in Ghana. Patients are therefore able to participate in the decision making process on which form of treatment they should undergo. With largely similar oncologic outcomes from radical prostatectomy and brachytherapy, the complications associated with each procedure plays a major role in deciding on the treatment option.

Studies in other jurisdictions have pointed at urinary morbidity as the main complication from brachytherapy. Furthermore, some studies point to different factors as predicting which patients are most at risk of significant urinary morbidity after low dose rate brachytherapy. Local data for this sub-region would be important to guide local practice.

Objective: To determine the factors that are associated with significant voiding dysfunction at one month after I-125 prostate brachytherapy of men undergoing the procedure at the Korle Bu Teaching Hospital.

Methodology: Patients presenting for prostate brachytherapy were recruited into this prospective study.

Basic demographic and disease related data were taken including the pre –operative International Prostate Symptom Score(IPSS). Peri-operative data such as u30 and D90 were also documented. The post-operative IPSS were evaluated monthly for 4 months and documented together with any other complaints at one month. Post-operative follow up evaluation was done via phone interviews.

Results: Significant voiding dysfunction at 1month post brachytherapy occurred in 67.7% of the study population. Two persons representing 2.8% had Acute Retention of Urine (AROU) with both occurring within 2 days of the procedure. The most common complaints at 1month were related to the urinary system.

At one month, the median IPSS score had increased from 5 to 11. It gradually declined thereafter but did not reach pre-procedure levels during the four month follow up period.

Digital Rectal Examination ($p= 0.686$), Gleason score ($p= 0.799$), prostate volume ($p= 0.137$), Pre-biopsy PSA ($p= 0.949$), number of needles used ($p= 0.465$), number of seeds implanted ($p=0.724$) and u30 ($p= 0.9310$) all showed no statistical correlation with the occurrence of significant voiding dysfunction at 1month. Pre-operative IPSS and the prior use of tamsulosin both showed statistical significance on bivariate regression analysis with $p= 0.001$ and $p<0.011$ respectively. However these two parameters failed to show statistical significance when subjected to multivariate regression analysis ($p= 0.635$ and $p= 0.069$ for pre-operative IPSS and prior use of tamsulosin respectively). D90 and pre-operative nocturia (as scored on IPSS) were predictive of occurrence of significant voiding dysfunction at one month both on bivariate and multivariate regression analysis. The D90 scores analysis yielded $p=0.009$ and $p=0.037$ on bivariate and multivariate analysis respectively. With regards the pre-operative nocturia score, $p<0.001$ and $p=0.002$ on bivariate and multivariate analysis respectively.

Conclusion: The study confirmed that prostate brachytherapy significantly worsens voiding function at one month. D90 and preoperative nocturia value on IPSS scoring were predictors of significant voiding dysfunction at one month.

Key words: LOW DOSE RATE BRACHYTHERAPY, PROSTATE CANCER, INTERNATIONAL PROSTATE SYMPTOM SCORE, URINARY MORBIDITY.

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND

Prostate Cancer(CaP) is the second most commonly diagnosed cancer amongst men after lung cancer accounting for 14.1% of cancers in men worldover.[1] It was estimated in 2020 that 37.5 per 100,000 men developed prostate cancer. In 2012, it was reported as the most common cancer in men[1]

The incidence, presentation and mortality varies across geographical regions. This may reflect the differences in culture such as food habits, and environmental factors; availability of health care and overall life expectancy.[2] also screening protocols with PSA may contribute to these differences.[2]

The introduction of PSA based screening into Sub Saharan Africa has resulted in higher detection rates of CaP with more of them now being localized prostate cancer.[3] The readily available modes in the sub - region for the active treatment for localised prostate cancer are radical prostatectomy and radiation therapy. Low dose rate (LDR) brachytherapy for localised prostate cancer was started in Ghana in 2008 using Iodine -125. [97] This has afforded patients and clinicians the opportunity to participate in the shared decision making process of choosing which of the modes of treatment to opt for. Whether there are differences in oncological outcomes for RP versus LDR brachytherapy remains controversial with conflicting data from some studies. [37] The complications of treatment therefore become a major factor in the form of therapy that would be applied to each patient.[71]

It has been shown that urinary morbidity is the main complication following LDR brachytherapy.[81] The incidence of acute urinary retention estimated to be about 2-4%.[81] Those patients who

experience urinary symptom flare (defined here as increase in International Prostate Symptom Score by 5 or more points) reported as 35.5% by Cesaretti et al. [88] Furthermore different studies have identified different factors as being predictive of the incidence of significant urinary morbidity. Eriguchi et al in 2015 reported pre-operative IPSS, total number of needles used, and the minimal dose received by 30% of the urethra (u30) were major determinants on IPSS flare. Other studies have also identified, peak urinary flow rate less than 10 mL/s, post-void residual volume greater than 100 ml, or prostate volume > 40g as being predictive of significant urinary morbidity.

This study seeks to evaluate the burden of significant acute voiding dysfunction that occurs in patients who undergo prostate brachytherapy in Korle Bu Teaching Hospital. Furthermore, it would seek to identify factors that can predict these occurrences. This study would provide the literature that is needed in the decision-making process of choosing active treatment for localised CaP for Ghanaian men.

1.2 JUSTIFICATION

Low dose rate prostate brachytherapy has been available in Ghana since 2008.[97] It has therefore become a viable option for patients to choose when deciding on active treatment of localized prostate cancer. For patients who often have a number of similarly effective options for treating their prostate cancer, including radical prostatectomy or radiation therapy, the expected acute and long-term complications become significant factors to be considered in making their choice.[37]

Research has shown that when patients with localized prostate cancer have evidence-based information many more chose brachytherapy as treatment modality.[96] It has been established that urinary morbidity is one of the commonest complications following prostate brachytherapy. It is therefore one of the main factors patients would consider in making their choice of treatment.[81] Since prostate pathologies seems to have a different biology amongst people of different races,[2] it is imperative to get local data to guide counseling and treatment.

The study therefore seeks to assess the burden of urinary morbidity in patient's undergoing brachytherapy in Ghana. It also seeks to identify the key factors that can predict those at risk. This would greatly assist in counseling patients in the shared decision-making process of treatment for localized prostate cancer.

CHAPTER 2

LITERATURE REVIEW

2.1 EPIDEMIOLOGY

The fourth most common cancer worldwide is cancer of the prostate.[1] It is the second most commonly diagnosed cancer amongst men after lung cancer accounting for 14.1% of cancers in men.[1] It is the fifth leading cause of cancer death amongst men.[1]CaP is the most common cancer among men of African descent in the Caribbean, USA, and Sub-Saharan Africa. [2]

The differences in incidences in various parts of the world are due to different screening and diagnostic practices.[3] A study by Seraphin et al reported increasing trends in many sub Saharan countries over the period 1995-2018 with annual increases ranging from 2-10%.[4] Reasons for this are thought to primarily reflect increased awareness and improvements in the health care system, enabling a broader use of PSA testing and possibly increased use of transurethral resections.[4] The exact statistics with regards incidence in the subregion is however unknown. This is due to data gaps and an absence of cancer registries in some regions of the African continent. [5]

The Kumasi cancer register, here in Ghana stated that prostate cancer accounted for 13.1% of all male cancers in 2014. This was reported by Laryea et al.[6] Wiredu et al also reported earlier in 2006 based on hospital autopsy records that prostate cancer accounted for 17.35% of male cancer mortality.[7]

Furthermore, Klufio reported that at the Korle Bu Teaching hospital, prostate cancer formed 63.7% of all genito-urinary cancers seen at the hospital over a 10 year period.[8] PSA screening is becoming more common in Ghana; this is leading to a rise in the incidence of CaP.[9]

2.2 RISK FACTORS

Not much is known about the etiology of CaP.[1] Well established risk factors are positive family history, aging, some genetic mutations (e.g., *BRCA1*) and conditions (Lynch syndrome) as well as race.[1] Studies have confirmed that blacks have a higher incidence of CaP and often present with advanced disease.[10] Blacks in the United States of America and the Caribbean have the highest incidence rates worldwide.[2] Other modifiable risk factors have been implicated in the incidence of prostate cancer. Though data are not entirely consistent, there is some association

with frequent consumption of red meat and dairy products.[11] There is a weak association of prostate cancer onset to smoking and obesity; however these two factors are positively linked with mortality from CaP. [11, 12] It has been shown that exercise, frequent eating of cruciferous vegetables, tomatoes and soy foods may offer some protection from CaP.[11]

2.3 CLINICAL PRESENTATION

CaP patients may be asymptomatic at presentation. An increasing number of asymptomatic patients are being diagnosed in Sub Saharan Africa due to increasing use of PSA as a screening tool.[4] Others may present with lower urinary tract symptoms (LUTS): straining, poor urinary stream, intermittency, feeling of incomplete bladder emptying, nocturia, urgency, and frequency. More advanced disease may present with bone pain, hematuria, pathological fractures, symptoms of obstructive uropathy and anaemia.[13]

Prostate cancer is usually suspected based on abnormal digital rectal examination (DRE) findings and/or raised PSA levels. Definitive diagnosis depends on histopathological examination of prostate biopsy cores. Specimen for histology may also be from transurethral resection of the prostate (TURP) or open prostatectomy.[14]

In a study published in 2014, Tindall et al noted that Blacks in South Africa present with higher PSA levels and histopathological tumor grade compared with Black Americans. This was further marked in men from rural communities. Their data suggested that lack of PSA testing might be leading to an aggressive CaP disease phenotype within these men.[15]

Majority of cancers of the prostate are located in the peripheral zone of the prostate. They may be picked up by DRE when the volume is ≥ 0.2 ml. In about 18% of cases, prostate cancer is detected by suspicious DRE alone, irrespective of PSA level.[16] Okotie et al in 2007 reported that an suspicious DRE findings was associated with an elevated risk of higher Gleason Grade Group at histology.[17]

2.4 DIAGNOSIS

Selley et al in a review of data regarding the diagnosis of CaP found that DRE had a sensitivity that ranged from 44 to 97% and the specificity from 22 to 96%. They also reported that about one-

fifth of the prostate cancers that can be identified by PSA were missed; nearly a third of the cancers with normal PSA values were detectable by DRE.[18] DRE is an examination which is not easily reproducible even when carried out by experienced examiners. Generally, it misses a good number of cancers as compared with PSA. Furthermore it tends to pick up cancers at a more advanced stage.[18] Nevertheless it has the advantage of detecting tumours that do not secrete PSA.[18]

Selley et al further reported that in diagnosing CaP, the PSA has a sensitivity that varied from 57 to 99%; its specificity also ranged from 59 to 97%.[18] The PSA value is directly related to age, and hence it is a more useful marker for men younger than 60 years.[18] With TRUS guided - biopsy of the prostate the sensitivity ranged from 52 to 91% and the specificity from 41 to 97%.[18] PSA screening programs have led to early prostate cancer detection. This has resulted in an increased rate of detecting localised disease.[19] Both the European Association of Urology and the American Urological Association recommend the use of multi parametric MRI in men at risk of habouring prostate cancer before biopsy is done.[14,20]

Histological examination of prostate tissue is necessary for the definite diagnosis of CaP. Biopsies are possible either by the trans-rectal or trans-perineal routes. Systematic biopsy of the prostate is considered as the gold standard for the diagnosis of prostate cancer. When prostate biopsy is used to identify prostate cancer, the TRUS biopsy is regarded as the standard of care.

[21] In 2020, Ortner et al described the trans-perineal biopsy as the modern gold standard in the diagnosis of prostate cancer.[22]

2.5 STAGING

Accurate staging of CaP is necessary to ascertain the extent of the disease. This is useful for prognostication and planning treatment. Several parameters help in assessing extent of the disease. These include DRE, PSA value and its derivatives, histology report from biopsy (especially Gleason Score) and imaging modalities. The 2002 TNM prostate staging classifies the cancer based on the primary tumour (T), lymph node involvement (N) and presence of metastasis (M). This is displayed in table 1.

The T category is based on clinical examination, imaging, endoscopy, biopsy and biochemical tests. The N category is based on clinical examination or imaging. The M category is based on clinical examination, imaging, skeletal studies and biochemical tests.[23]

Table 2.5.1 TNM Classification of prostate cancer

TNM CLASSIFICATION	
Primary tumour	
TX	Primary tumour cannot be assessed
TO	No evidence of primary tumour
T1	Clinically inapparent tumour
T1a	Tumour (non-palpable) as incidental histological finding at TURP in 5% tissue resected;
T1b	Tumour (non-palpable) as incidental histological finding at transurethral resection of prostate in > 5% of tissue resected;
T1c	Tumour (non-palpable) identified by needle biopsy (for elevated serum PSA)
T2	Palpable Tumour confined within prostate
T2a	Tumour involving one-half of one lobe or less
T2b	Tumour involving more than one-half of one lobe but not both lobes
T2c	Tumour involving both lobes
T3	Tumour extends through prostatic capsule
T3a	Extra-capsular extension
T3b	Invasion of seminal vesicle(s)
T4	Tumour fixed or invades adjacent structures: bladder neck, external sphincter, rectum, levator muscles and pelvic wall
Regional lymph nodes	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Regional lymph node metastases within true pelvis, below common iliac artery bifurcation, either unilateral or bilateral
Metastasis	
MX	Distant metastases cannot be assessed
MO	No distant metastases
M1	Distant metastases
M1a	Nonregional lymph nodes
M1b	Metastasis to bone
M1c	Other site(s) of metastasis

Clinical T staging may be done by DRE. DRE however has poor sensitivity and a lack of reproducibility; hence it can overestimate and underestimate the extent of disease. Nevertheless, DRE in conjunction with other modalities can help predict tumor extent.[19] Pathologically staging can be done by examination of radical prostatectomy specimens.[19]

50% of bone density must be replaced by tumour before standard imaging methods can detect the metastasis.[24] This low sensitivity means that x-rays are typically used only to confirm a positive bone scan in men at low risk for bone metastases. In low resource settings, they are often used as a quick and low cost way to detect advanced disease.[24]

Skeletal scintigraphy with labeled phosphonates are useful for assessing of local bone metabolism. This is most useful in identifying metastases when there is significant reactive hyper-metabolism in the bone. Bones scans are traditionally the metastatic imaging of choice for detecting metastatic disease.[25] Current NCCN guidelines recommend the use of technetium-99m bone scan, CT scans or MRI scans among high-risk and unfavorable intermediate-risk men who are at a high risk for occult metastasis on the basis of clinical parameters.[26]

Whole-Body MRI is more useful than skeletal scintigraphy and conventional x-rays in detecting bone metastases. It also performs as well as CT scans for evaluating enlarged lymph node.[27] Whole Body MRI can hence be used as a single modality for metastatic work up in detecting both soft tissue and bone metastasis.[27]

Local staging of prostate cancer assesses presence of extracapsular extension and seminal vesicle involvement. CT scans though widely used and recommended in many guidelines has a very limited role for local staging of high-risk prostate cancer because it generally does not visualize early metastases.[26,28,29] MRI is the imaging of choice for this assessment. Obliteration of the recto-prostatic angle and asymmetry of neurovascular bundles on MRI is often indicative of extracapsular extension .[30]Wang et al in 2004 showed that MRI has a specificity of 95%, a sensitivity of 42% and a positive predictive value of 75% in detecting extra capsular extension. It has a positive predictive value of 78% and a negative predictive value of 94% in detecting seminal vesicle invasion.[31]

The presence of regional lymph node spread is a strong predictor of disease progression.[32] Most guidelines recommend imaging for lymph node metastases for patients who are at higher risk of metastases: at least T2 on DRE, PSA >20 ng/ml or Gleason grade 4 or [28,33] risk of lymph node

metastases can be estimated using nomograms. The gold standard for the detection of lymph node metastases is via lymph node dissection.

Pathological stage is the single most important prognostic indicator for clinically localized prostate cancer. There are well validated nomograms for predicting pathological T stage. They are based on pre-operative clinical staging, PSA and Gleason score.[34]

2.6 LOCALIZED CANCER OF PROSTATE

Currently the management of prostate cancer involves weighing the risk of cancer mortality versus mortality from other risks. Therefore, the mode of management must be tailored to the individual in question. Choosing one method must always be a shared decision making process with the patient. This is done after counseling the patient on the various options, risks, benefits and the effect of individual patient factors like comorbidities and age.[35] Daskivich et al found that depending on the risk category, the ten-year risk of death from prostate cancer ranged from three to eighteen percent.[36] The same study found that for patients with any comorbidity, there was a ten-year mortality rate from the other causes of thirty-three percent or higher.[36] Therefore, decisions regarding the benefit of treatment should be rooted in an individualized assessment that includes age, comorbidities, and risk of cancer mortality.[35,36]

The cancer is classified as localized cancer when after clinical evaluation there are no lymph nodes or metastasis or extension of the cancer beyond the capsule of the prostate: cT1-T2, N0, M0. Several management options are available for management of localized prostate cancer.

2.6.1 MANAGEMENT OF LOCALIZED PROSTATE CANCER

For patients with localized CaP with short life-expectancy, where mortality is expected to be from other competing risk factors, watchful waiting is a reasonable treatment modality. Some patients have good longevity, but risk of disease progression and hence benefit from treatment in improving longevity is unclear. In this group of patients, active surveillance has emerged as a rational means of deferring therapy until more clear evidence emerges for need of definitive therapy.[37]

Active treatment options for localized CaP include external beam radiation therapy, brachytherapy and radical prostatectomy. More modern approaches include partial gland therapy with High Intensity Focused Ultrasound and cryotherapy.

2.7 BRACHYTHERAPY

The standard approaches to treatment for localized prostate cancer are radiation therapy and radical prostatectomy.

Early records of treatment of prostate cancer with radiation is credited to Pasteau and Degrais in 1911. They used an intra-urethral radium source. Between 1930 and 1950, external beam radiation was used to treat prostate cancer with low success rates and significant morbidity to surrounding tissues.[38] Since then there has been rapid improvements in using radiation to treat prostate cancer. The development of linear accelerator for radiation therapy has resulted in less damage to neighbouring structures particularly the skin.[39] Further in-roads were made with development of conformal techniques in the 1980s and 1990s that resulted in less toxicity to rectum, urethra, femoral heads, and bladder neck while delivering higher doses to the prostate. The adoption of CT scan based planning for treatment in the 1990s led to our ability to calculate dose of radiation being received by the target organ and regions of interest. The further advances in using 3D- Conformal Radiation Therapy (3D-CRT) and then later the Image Modulated Radiation techniques have further aided the ability to supply higher radiation doses to the prostate while simultaneously lowering doses to regions of interest.

Brachytherapy is a precise form of targeted radiotherapy. It employs advanced computerized treatment planning and image guided delivery systems to achieve a tailored ablative tumour dose to the prostate.[40] While radiating the prostate, the technology ensures sparing of surrounding organs to minimize potential toxicities.[40] It uses low energy sources and the dose delivered falls rapidly beyond the target volume, and hence a high ratio of target to non-target dose. This rapid fall off, however, means that there must be a high degree of accuracy in the placement of the radiation sources to ensure that no part of the gland is under dosed.[37]

Low dose rate (LDR) brachytherapy is used as a form of monotherapy treatment option for localized CaP. It may also be employed with External Beam Radiation Therapy (EBRT) as a boost. It is not used as a form of palliative treatment. It therefore serves as a curative treatment alternative in patients with organ-confined cancer. [41–43]

2.7.1 History

In 1922 at Johns Hopkins University, Young performed prostate brachytherapy using intra-cavitary radium sources which were positioned in the bladder, rectum, and urethra. These sources then "cross-fired" the radiation into the prostate. Benjamin Stockwell Barrington modified this approach later at Memorial Hospital in New York. He implanted needles containing radioactive radon gas into the prostate transperineally. In the 1970s, Whitmore and colleagues (1972) at Memorial Sloan Kettering in New York performed I-125 implantation. They did this in patients after the patients had undergone lymph node dissection. To do this, the prostate was exposed by the retropubic approach and then implanted with the seeds under direct vision. This in poor placement of the seeds within the prostate. [44]. Currently for brachytherapy sessions, computer programs use algorithms to optimize of dosimetric coverage of the entire gland while minimizing dose to the intra-prostatic urethra and rectum.[45]Holm and colleagues (1983) described closed trans-perineal approach with the aid of trans-rectal ultrasonography. With this approach, the needles are followed on ultrasonography during insertion. This has led to a more precise placement of the seeds as compared with the open retropubic approach.[46]

In 2017, it was reported that Nearly 300,000 patients with prostate cancer receive brachytherapy using I-125 seeds worldwide each year.[47]

Two forms of prostate brachytherapy are recognized. High-Dose-Rate (HDR) and Low-Dose-Rate (LDR) brachytherapy. The HDR delivers high doses of radiation using temporary catheters. It employs Iridium-192 delivered through hollow catheters placed transperineally into the prostate. The radiation dose is delivered in this way over several applications.

LDR brachytherapy involves the deployment of permanent seeds into the prostate. It is also therefore also called permanent prostate brachytherapy (PPB). The seeds deliver low doses (LDR-Brachytherapy delivers ≤2 Gy/h) of radiation over weeks to months depending on the isotope chosen. Several isotopes are available for LDR brachytherapy. I-125 has a half-life of 59.6 days and delivers low energy x-rays at 27 keV. Pd-103 has a shorter half-life of 17days and emits 21-keV x-rays. The recommended monotherapy dose prescription for I-125 is 140 to 160 Gy and for Pd-103 is 110 to 125 Gy. When brachytherapy is combined with EBRT, brachytherapy doses ought to be lower (108 to 110Gy for I-125 and 90 to 100Gy for 103Pd). [40]

Currently, medical data on I-125 and Pd-103 shows that they are equally effective, stage for stage, in providing cancer control.[48]

According to Skowronek's review article in 2013, Brachytherapy is the most cost sparing technique of all prostate cancer treatment options.[48] This is so when all costs including diagnostic, treatment and social expenses after treatment are considered .[48]

Patients with high probability of localized disease or limited extra-prostatic extension are considered ideal candidates for monotherapy .[49]Low-risk patients may also LDR brachytherapy alone without additional external radiation therapy. [49] High-risk patients should be given supplemental EBRT if LDR brachytherapy is employed. For intermediate risk patients, they should be evaluated on a case by case basis. Those intermediate risk patients with favourable features may have brachytherapy as monotherapy.[49]

Androgen Deprivation Therapy (ADT) is a commonly used strategy to downsize the prostate towards brachytherapy. However its contribution in improving cancer control rates in this setting is still unclear. Currently there is little evidence to demonstrate a benefit of adding ADT to brachytherapy for patients in the low or favorable intermediate risk categories.[50,51] The use of three to twenty four months of ADT has been shown to improve biochemical control for patients with unfavorable intermediate risk, high-risk disease or suboptimal post-implant dosimetry. [50,52,53]

2.7.2 Procedure of prostate brachytherapy

Preparation of the rectum is required. This is usually carried out with an the night before and on the day of the procedure.[54] Prophylactic antibiotic is recommended just before surgery. In the operating room, patient is placed in the lithotomy position adapted according to prostate size and the risk of pubic-arch interference.[48,54] A urethral catheter is passed filled with contrast, saline or air filled gel to help identify the urethra and differentiate the bladder and the prostate.[48,54] A trans rectal ultrasound probe is then inserted into rectum and affixed to a mount through a stepping device. This is used to evaluate the size and shape of the prostate. Patient's perineum is cleaned and draped. A template grid is attached to the stepper. This allows for precise and reproducible imaging of the gland throughout the procedure. [48,54]

The template pattern is superimposed over the ultrasound image by computer software. Needles are inserted transperineally through the template into the gland. Sealed metallic seeds containing the radioactive material are implanted as the needle is withdrawn. [37,48,54]

Computer programs which employ sophisticated algorithms are used to optimize dosimetric coverage of the entire prostate while minimizing dose to the intra-prostatic urethra and rectum. Stone et al and Stock (1999) determined the number of seeds to be implanted based on the size of the gland and the nomograms. [37,55] The urethral catheter is kept in-situ post procedure. The patient is discharged post-operative day after successful voiding without a catheter.[48]

2.7.3 Patient selection for brachytherapy

Patient selection involves two main factors. The first is selection of patients who are likely to have a good disease-free outcome. The second is to select patients who will have a good functional outcome.[41] For disease free survival, the key prognostic factors are initial PSA, Gleason Group and the TNM stage. The initial IPSS score and prostate size are the most useful predictors of good functional outcome.[41]

The decision to actively treat or not treat localized prostate cancer and which treatment option to use must always be a shared decision. Shared Decision Masking (SDM) is variably adopted in practice with clinical personnel not applying the same set of criteria in involving patients in the decision making process.[56] SDM is highly recommended when making decisions regarding CaP treatment.[56,57] Martinez- Gonzalez et al showed that SDM improves patient knowledge and perception of being informed. In addition SDM has but short-term effect on patient perceived QoL.[58]

Shared decision-making has several aspects. The clinician and patient must participate deciding on the choice of treatment. Additionally both are required to share information with each other. Thirdly, both clinician and the patient must express their treatment preferences. Fourthly, both of them must reach a consensus on the treatment mode to be adopted.[59]

In best practice, decisions regarding the benefit of treatment should be rooted in an individualized assessment that includes age, comorbidities, and risk of cancer mortality.[37] Estimating the life expectancy is very important to the informed-decision making process in CaP. Many randomized

clinical trials have provided evidence that the risk of death from other causes exceeds the risk of death from prostate cancer.[60] From data collected in the Prostate Cancer Outcomes Study, the risk of death from other causes can be modeled as a function of comorbidity and age.[35] The 10-year risk of death from prostate cancer ranged from 3% to 18% depending on the risk category, whereas men with any comorbidity had a 10-year mortality rate from other causes of 33% or higher.[35] Therefore, persons perceived to have a life of 10years or more are traditionally considered to benefit from therapy. Several tools are available for estimating the life expectancy. Most of these tools employ patient's age and co-morbidity. Men with a high risk of metastatic progression or mortality within 10 years of diagnosis should be considered for aggressive therapy despite the presence of one or more competing risks for mortality within the same period.

Patients with preexisting urinary, sexual or bladder conditions may be at increased risk for either more intense or protracted morbidity. It is therefore important to evaluate these and factor them into treatment choice. Radical prostatectomy offers the added advantage of improving obstructive urinary symptoms compared with radiation therapy that may actually worsen the symptoms. [61,62] The same study showed 40% improvement in baseline urinary symptoms after radical prostatectomy (RP). [62] Patients with urethral catheters from bladder outlet obstruction would benefit from surgical treatment with an added benefit of relieving them of the catheter. [62] The effect of radiotherapy on baseline urinary symptoms has been less well reported but is typically characterized as transient worsening, followed by improvement in symptoms as the prostate regresses. [35] Men with large prostates and obstructive symptoms are likely to be at increased risk of retention after brachytherapy.[35] Therefore, prostate sizes greater than 60g, IPSS scores greater than 20, large median lobe hypertrophy and Qmax of less than 10 are considered relative contraindications for brachytherapy. [37,63,64]

Larger prostate size at radical prostatectomy has been shown to result in longer operative times, higher incidence of urinary incontinence and longer hospital stay.[61] In addition, prostate gland size greater than 60g may pose challenge at brachytherapy due to pubic arch interference.[49] This means that for patients with large prostates, the patients should be well informed of the possible complications with their choice of active treatment. TURP is considered a relative contraindication to brachytherapy. Such patients with previous TURP have been shown by some studies to have higher risk of incontinence and acute urinary toxicity (approximately 50%) after radiation therapy.

[45,65,66] Mansfield et al in 1996 found that a delay of up to 8weeks after TURP before radiation therapy reduced the risk of urinary incontinence. [67] Other studies did not support this position showing that the risk of this type of complication is really less than 10%.[66]

Tyson et al from a study on functional outcomes after active prostate cancer treatment recommended that baseline bowel function should play a role in deciding on the mode of treatment. Men undergoing radiation therapy have an increased risk of bowel dysfunction as compared to those undergoing radical prostatectomy.[68] Men with preexisting fecal frequency, inflammatory bowel disease, tenesmus, or extensive previous rectal surgery may therefore benefit more from surgery in order not to exacerbate these symptoms.[68]

Comparing the oncologic outcomes of radical prostatectomy and radiation treatment for localized cancer of the prostate, Hoffman et al followed up patients for 15yrs. The study revealed that radical prostatectomy was associated with a statistically significant overall (HR = 0.60; 95% CI 0.53–0.70) and disease-specific (HR = 0.35; 95% CI 0.26–0.49) survival advantage.[69] This study and others like it notwithstanding, there is lack of clear evidence comparing the oncologic outcomes of surgery versus radiation therapy due to inherent biases in setting up these studies and hence interpreting these results.

Because differences in oncologic outcomes for individual treatment approaches are controversial at best, patients must thoroughly consider acute and long-term effects on quality of life in choosing treatment modality.[37] There is evidence to show that the kind of primary treatment for localised prostate cancer has clear impact on Quality of Life. Patients should be made aware of this during counseling.[70]

Some important factors are considered in making a choice for prostate brachytherapy. There should be an an estimate of the expected benefit/risk ratio considering the patient's life expectancy and the prognosis of the prostate cancer.[54]. Also brachytherapy is appropriate in patients who are fit for anaesthesia. There should also be no challenge in placing the patient in lithotomy position for extended periods.[47] Thirdly factors relating to the expected results (brachytherapy as monotherapy or in combination with EBRT) in terms of efficacy and safety compared to other alternative treatments such as active surveillance, EBRT or radical surgery.[54]

2.7.3 Complications of brachytherapy

There are a number of similarly efficacious treatment options for treating localised prostate cancer. These include radical prostatectomy and brachytherapy. The expected acute and long-term side effects of these procedures are vital factors to be discussed in the shared decision making process.[71]

Complications in the acute and late period post LDR brachytherapy include urinary tract infections, hematuria, urinary toxicity, gastro intestinal toxicity, urinary incontinence, erectile dysfunction and urethral stricture.[37,72]

Immediate adverse side effects after seed implantation are not frequent. The risk of infection is less than 5%; this is so since the needles are inserted into the prostate trans-perineally and not trans-rectally.[66] Significant rectal complications are quite rare. The reported incidence of this is in the range of 1% to 2%. [73] Mohammed et al in 2012 reported a rate of approximately 1% of rectal bleeding [74]. GI toxicity is less with brachytherapy as compared with EBRT. [75] Fistulation between the rectum and urethra was reported in one study to be as low as 0.3 %. [76]
Barker et al reported an incidence of hematuria in the acute setting with 13% of subjects having at least one episode of gross hematuria.[77] Leapman et al also followed up two thousand four hundred and fifty four patients treated with LDR prostate brachytherapy over a twenty year period. They reported incidence of late gross hematuria occurring in 8.9% of patients. This occurred at a median time of 772.2 days after implantation. [78]. Hematuria tends to resolve spontaneously in all patients. [77,78]. Sexual function is preserved in only 18% of patients after brachytherapy according to analysis of several articles by Burnett et al in 2007.[79] Erectile dysfunction seems to arise from exposure of the neurovascular bundle to the radiation. [80]

2.7.4 Urinary Complications of Brachytherapy

The major acute toxicity of brachytherapy is with the lower urinary tract, with a low but non-negligible risk of need for temporary catheterization. This is a major factor in determining the suitable patient population for LDR brachytherapy. [37]

Urinary complications is common and often temporary after brachytherapy and it remains one of the main considerations patients consider before opting for brachytherapy.[81,82] Kollmeier et al in 2012 showed that incidence of LUTS generally worsened significantly after brachytherapy and then begins to improve at a rate that depends on the isotope used.[83] One study in 2013 showed that

the rate of chronic grade 2 urinary toxicity was about 20% after brachytherapy.[84] Tanaka et al in their study found that the incidence of worsening urinary frequency after LDR brachytherapy was 70%. [81] In another study to assess urinary toxicity after I – 125 prostate brachytherapy, Mallick et al reported the incidence of urinary disorders to be 76% but found severe urinary complications to be rare.[85] Mallick et al also found that the major changes in IPSS occurred during the first and third month after implantation. It then improved during the 6th month. Merrick et al had similar findings in 2002. They reported that the IPSS peaked 1 month after implantation whether the patient received prophylactic alpha-blockers or not.[86] Patients on prophylactic alpha blockers returned to their initial IPSS at a median of three months and mean of four months postoperatively. However the study also found that for those patients not on the alpha-blockers, the IPSS returned to the baseline value at a mean and median of ten months and six months, respectively.[86] A smaller study by Niehaus et al for LDR brachytherapy patients who were on alpha-adrenergic blockers post procedure, the IPSS peaked 1 month after implantation and returned to baseline at a mean of 1.9 months.[87] Mallick et al found that within the first six months the maximum urinary flow rate deteriorated significantly, but the changes in post-void residual volume were less marked.[85]

Cesaretti et al after following up on 172 patients reported a mean pretreatment IPSS of 7.5. They observed a mean peak IPSS of19.4 and occurring at a median time of 1.3 months after surgery.[88] In their study the mean nadir IPSS was 6.7 and occurred at a median time of 14.3 months after the brachytherapy.[88] The same study also showed that 35.5% of patients had an increase of 5 points or more of their IPSS (IPSS flare).

Tanaka et al reported in 2014 that the most common adverse finding among the urinary toxicities affecting about 70% of patients within the first 6months was urinary frequency.[81] The same study found the incidence of retention of urine to be approximately 2-4% after LDR brachytherapy.[81] Another study by Tanaka et al 2019 reported incidence of AROU to be 2.3% with 92.5% recovering from AROU with a median time of 4.3 months during the follow up period. Mabjeesh et al reported an incidence of 3.2% of the incidence of AROU following LDR brachytherapy. This is consistent with the findings elsewhere. They also reported that the median time to retention onset was 1 day post-implantation.[89]

Several factors have been found in some studies to significantly predict which patients are at risk of developing urinary complications. Cesaretti et al in 2003 followed up on 172 LDR prostate

brachytherapy patients. The team evaluated PSA, cancer stage, use of hormone therapy, implanted activity, ultrasound volume, dose, seed number and needle number. They reported that no single one of these had had a significant predict the risk of developing an IPSS flare (i.e. an increase of 5points of the IPSS). [88] Contrary to this, Keyes et al reported in their study of 712 brachytherapy patients that greater baseline IPSS, diabetes mellitus and prostate edema were predictors of urinary flares. [82] Such patients with flares had greater incidence Radiation Therapy Oncology Group (RTOG) grade 3 urinary toxicity. [82] Keyes et al in another report showed that patients with a larger prostate sizes, higher pre-operative IPSS, greater number of needles, and use of hormonal therapy had more acute toxicity. [90] Furthermore, they reported that the IPSS generally returned to the initial preoperative value at a median of 12.6 months. Patients with a high initial IPSS had a quicker resolution of their IPSS. Higher prostate D90 (dose covering 90% of the prostate), maximal post implant IPSS, and retention of urine slowed the return of the IPSS to baseline.[90] In another study, Mallick et al reported that preoperative IPSS of more than eight and previous alpha blocker usage were significant predictive factors of urinary toxicity. [85] Also they found that the radiation dose received by 90% of the target volume(D90) and by 30% of the urethra(u30), and the prostate size receiving 144Gy were predictive of incidence of urinary morbidity[85]. In a large study involving 2,339 patients Tanaka et al reported that age, prostate size, initial IPSS, and drinking status were independent factors predicting acute urinary toxicity Grade ≥2. [91] Another earlier report by Tanaka et al in 2013 showed pre-operative IPSS to be the major predictor for the incidence of Grade ≥ 2 acute urinary toxicity.[92] Combination of LDR brachytherapy with EBRT was also a predictor for the incidence of late urinary toxicity.[92,93] Another study found that patients with IPSS scores greater than 15, peak urinary flow rate less than 10 mL/s, post-void residual volume > 100 ml, or prostate size > 40g have greater incidence of acute urinary toxicity.[94]. These findings are corroborated by a study by Mabjeesh et al in 2007. They reported that prostate size, pretreatment IPSS were significant independent predictive factors for urinary retention after brachytherapy. [94] In another study of 1034 patients who received alpha blockers in peri-operative period, the IPSS reached a maximum at a mean of 0.5 months and resolved at a mean of 1.7 months post brachytherapy. The IPSS resolution after brachytherapy was best predicted by the pretreatment IPSS. [95] Eriguchi and colleagues followed up 1313 patients between 2009 and 2014 to assess their IPSS scores amongst other parameters post LDR brachytherapy. They found out that the pretreatment IPSS, total needles, and the minimal dose received by 30% of the urethra (u30) had the greatest effect on IPSS flare. They also reported that grade 2+ urinary toxicity was most

commonly seen in those patients with larger prostate size (>30g) who received Neoadjuvant ADT.[98]

2.7.5 Post Procedure Radiation Risk

After brachytherapy the risk of radiation induced injury to the people in the patient's immediate environment is considered low. Michalski et al in 2003 evaluated 44 LDR Brachytherapy patients and their families. They concluded that the risk to family with routine precautions is very low and very much below the thresholds set by the U.S. Nuclear Regulatory Commission.[99] Additional study came to a similar conclusion stating that the exposure risks related to brachytherapy with 125-Iodine to operators and public are limited. [100] Seed loss through the urination may however pose a threat to people. Stutz et al evaluated 1794 patients and found that seed loss through the urinary tract is a common event after LDR brachytherapy, occurring in 29.7% of patients.[101] another study found seed loss to occur in 6% of patients and represented 0.13% of total seeds implanted. [102] In order to reduce risk and also following the ALARA (As Low As Reasonably Achievable) principle various post-operative instructions are given to patients. Different protocols exist. Many centres recommend straining urine during voiding in order to recover voided seeds. The seeds are placed in a lead container provided to the patients and later returned to the centre for safe disposal. [101, 103, 104, 105]

CHAPTER 3
AIMS AND OBJECTIVES

3.1 AIM

To determine the factors that predict the occurrence of significant voiding dysfunction after Iodine-125 prostate brachytherapy for localised prostate cancer at the Korle Bu Teaching Hospital.

3.2 OBJECTIVES

1. To find the demographics, clinic-pathological characteristics and procedure related factors of patients undergoing brachytherapy.

2. To evaluate the monthly changes in IPSS score from pre-implant IPSS up to 4months post procedure.

3. To identify the proportion of patients who have significant voiding dysfunction after one month.

4. To determine the association between prostate size, pre-implant IPSS, initial PSA, number of needles used, number of seeds implanted, the radiation dose received by 90% of the target volume (D90) and by 30% of the urethra (u30) and the occurrence of significant voiding dysfunction at one month.

(Patients with Significant Voiding Dysfunction are those patients who have an IPSS flare (an increase of 5 or more compared to pre-brachytherapy IPSS) or who require further medication or medical intervention for their symptoms).

3.3 HYPOTHESIS

3.3.1 Null Hypothesis-

There are no factors that are associated with the occurrence of significant voiding dysfunction in patients after I-125 prostate brachytherapy

3.3.2 Alternate hypothesis-

There are some factors that are associated with the occurrence of significant voiding dysfunction after I-125 prostate brachytherapy.

CHAPTER 4

MATERIAL AND METHODS

4.1 STUDY DESIGN

This is a prospective study of consecutive patients undergoing Iodine-125 prostate brachytherapy and satisfying the inclusion criteria.

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4.2 DESCRIPTION OF STUDY SETTING

The Urology Unit of the Korle Bu Teaching Hospital will be site for conduction of this study. This would include the wards and OPD of the Unit. The Korle Bu Teaching Hospital has evolved from a modest 192-bed capacity hospital to over 2000 beds. It remains the largest referral facility in the West African Sub region.[106] The Hospital, as at 2016 report operated 17 clinical and diagnostic units and departments as well as three "Centres of Excellence". [106]

The Urology Unit currently operates a 27 – bed general male ward with the female patients admitted onto the main surgical wards. Prostate pathologies were the fourth leading cause of admission in 2016.[106]

The unit carries out both TRUS guided biopsies and Trans-perineal prostate biopsies for the histological diagnosis of CaP. The hospital has expert histopathological services available. Furthermore MRI services are available in the hospital to assist with diagnosis and staging as well as 'GE Discovery 670' SPECT machine for bone scanning.

The brachytherapy team consists of Urologists, Radiation Oncologists and Physicists with support from Anaesthesiologists and Nursing Staff. The team uses the "Variseed Software" from Varian Medical Systems and imports the I-125 seeds for the procedure from the BARD Company, USA.

4.3 STUDY POPULATION

Patients who have been scheduled for brachytherapy for the treatment of prostate cancer at the Urology Unit of Korle Bu Teaching Hospital and have given their informed consent were enlisted into the study.

4.4 STUDY PERIOD

The study was being conducted to cover a period of 10 months. (June 2023 – March 2024)

4.5 INCLUSION CRITERIA

- Patients with localised prostate cancer who consented to participate in the study
- Patients who were fit for regional(spinal) or general anaesthesia

4.6 EXCLUSION CRITERIA

- Patients with neurological symptoms and signs such as paraplegia or paraparesis
- Patients who did not consent to the study

4.7 SAMPLE SIZE DETERMINATION

The primary outcome measure of this study will be IPSS score pre-implant and monthly IPSS scores post LDR brachytherapy up to 4months. In a study by Gutman et al.[95] , mean (SD) IPSS score pre-implant was found to be 6.0 (4.2) whilst mean IPSS score post brachytherapy at last follow up was 4.0 (4.0). Assuming these values for the current study at a standard deviation of 4.0 and 80% power, the sample size is determined as follows:

$$n = \frac{\sigma_d^2 (Z_\beta + Z_{\alpha/2})^2}{E^2}$$

n = sample size

σ_d^2 = standard deviation of the difference = 4.0

Z_β = corresponds to 80% power on standard normal distribution (80% power = 0.84)

$Z_{\alpha/2}$ = corresponds to two tailed significance level on the standard normal distribution (1.96 for α = 0.05)

E = mean difference (mean IPSS score before and after brachytherapy) = 2.0

$$n = \frac{4^2 (0.84 + 1.96)^2}{(6.0 - 4.0)^2}$$

$$n = 31.4 \approx 32$$

The minimum sample size will be thirty-two (32). Accounting for 10% attrition in case of incomplete data and drop out, the total sample size will be thirty-six (36).

4.8 STUDY PROCEDURE

Patients being prepared for prostate brachytherapy by the department were seen by the anaesthesiologists for clearance for general or regional anaesthesia. They were subsequently seen by the researcher (myself) and consecutively recruited into the study after giving their informed consent. The researcher estimated the prostate volume by TRUS in the Urology Unit. They were assisted to fill the questionnaire for the study with the assistance of the researcher. This included the basic demographic data, general medical data as well as data concerning prostate cancer management up to that point particularly the PSA. It also included assessment of urinary function with IPSS and Peak Flow Rate.

Patients were subsequently followed up using the department's routine protocol for prostate brachytherapy. They were admitted into the hospital a day before the surgery. They gave their signed consent for the procedure. Pre-operative counseling on what to expect was done. Phosphate enema was administered the night before surgery and at the dawn of the day of surgery.

Medications if any were taken before surgery as directed by the anaesthetist. The pre-operative medications were often related to management of co-morbidities such as hypertension or diabetes as the case may be.

The urology, radiation oncology teams and physicists of the hospital performed the procedure. The surgery was done under regional or general anaesthesia. IV Levofloxacin 500mg was administered 30min before the start of the procedure. The patient was placed in the lithotomy position thereafter and urethral catheter size 16 or 18Fr was passed and clamped. With the aid of TRUS, prostate was re-assessed, mapping and planning done and agreed on by the teams. Under aseptic conditions and guided by a template grid, perineal needles were inserted into prostate and I-125 seeds are loaded into prostate using the Mick's applicator. The following operative data were then captured: number of needles used, number of seeds implanted, and the radiation dose received by 90% of the target volume (D90) and by 30% of the urethra (u30).

Patients were discharged post-operative day 1. This was after catheter had been removed and patients have passed trial of micturition without a catheter. Patients were discharged on 2 months of tamsulosin 400mcg nocte, 7days of Diclofenac 75mg 12hourly and oral levofloxacin 500mg daily for 7days. Post-operative counseling was done and patients given counsel on what to expect, possible complications and how to take care of themselves. This included straining their urine and

recovering any seeds; such seeds were to be placed into the lead container given to the patient before discharge and returned to the unit. They were counseled to use condoms for sex, avoid prolonged close contact to pregnant women and children under 13years. They were given the phone number of the researcher in order to call for any clarification or assistance that they may need.

The first review was after 4weeks where implant quality was assessed by CT scan by the radiation oncologists. The IPSS was retaken by the researcher and any concerns of the patient are addressed. Monthly calls were done to assess voiding function up to 4months. Patients were to continue follow up care by the radiation oncologists. Urologists attended to complications especially those from urinary morbidity.

4.9 DATA HANDLING, ANALYSIS AND CONFIDENTIALITY

Patients who were part of the study were assigned an identification number that was recorded on the questionnaire. The data was entered and stored in Excel (on the researcher's secured personal computer where only the researcher had access). No third party had access to this except a statistician (Mr George Aryee) who assisted in data processing.

Continuous variables such as age, PSA levels and prostate size were summarized as means (standard deviation).

Analysis was done using Statistical Package for Social Sciences (SPSS) version 20.0.
Categorical data such as educational level, occupation, marital status, co-morbidities were summarized as percentages and graphs.

Repeated measure Analysis of Variance (RM-ANOVA) was used to compare the IPSS before and one month after surgery.

Pearson correlation coefficient, bivariate and multivariate regression were used to determine the correlation between various variables like prostate size, initial IPSS, prior use of tamsulosin and presence of co morbidities and extent of deterioration of IPSS. Chi-square test / Fisher's exact test was used to determine the association between categorical variables. All *p*-values less than or equal to 0.05 was considered statistically significant.

4.11 ETHICAL CONSIDERATIONS

Approval for the study was obtained from the Institutional Review Board of the Korle-Bu Teaching Hospital.

A written informed consent was obtained from all the participants in the study after adequate counselling, and only patients who willingly agreed to participate, and satisfy the inclusion criteria were included.

There was no differential treatment or special privileges as incentives for participants, and refusal to participate did not attract any punitive measure, denial, or alteration of the patient's management.

Voluntary participation was emphasized and any patient who chose to withdraw from the study at any stage did not face any penalty.

The study did not expose the participants to any additional risk or harm other than that expected for the procedure.

4.12 DISSEMINATION OF RESULTS

The completed study is being submitted to the Ghana College of Physicians and Surgeons. Relevant parts of the results will be made available to the Urology Unit of the Korle Bu Teaching Hospital.

It will also be submitted for publication in a peer-reviewed journal.

CHAPTER 5

RESULTS

5.1 Introduction

This chapter of the dissertation presents the analysis of the results from the data collected from the study participants to determine the burden of significant post brachytherapy voiding dysfunction. It also examines the factors that can predict the occurrence of this dysfunction.

5.2 Participants selection for the study

A total of 78 patients were seen for prostate brachytherapy during the study period. After accounting for those in the exclusion criteria, those unwilling to partake in the study and those lost to follow up, 71 persons were eventually recruited into the study. They all underwent prostate brachytherapy at the Korle bu Teaching Hospital.

5.3 Demographic characteristics of the study participants

5.3.1 Age distribution

The age range among study participants was from 47 to 79years. The overall mean age was 64.02years with standard deviation of 6.3. Only one participant was less than 50years with over 52% being between 60 and 69years. (Table 5.3.1)

5.3.2 Marital status distribution

53 out of the 71 participants were married as at the time of their procedure representing 74.3%.The rest were either widowed, divorced or single. This is shown in Table 5.3.1 as well.

5.3.3 Educational level distribution

The data gathered revealed that only 5 persons out the 71 had not had any form of tertiary education. This represents less than 10% of the study population. Please refer to Table 5.3.1

Table 5.3.1: Demography of study population.

Variable	n	Percentage (%)
Age		
40-49	1	1.4
50-59	19	26.8
60-69	37	52.1
≥70	14	19.7
Marital status		
Married	53	74.6
SDW	18	25.4
Level of education		
Secondary	5	7.0
Tertiary	66	93.0
Ethnicity		
Akan	47	66.2
Ga-Adangme	7	9.9
Ewe	13	18.3
Others	4	5.6

SDW- Single, Divorced or Widowed

5.3.4 Ethnicity

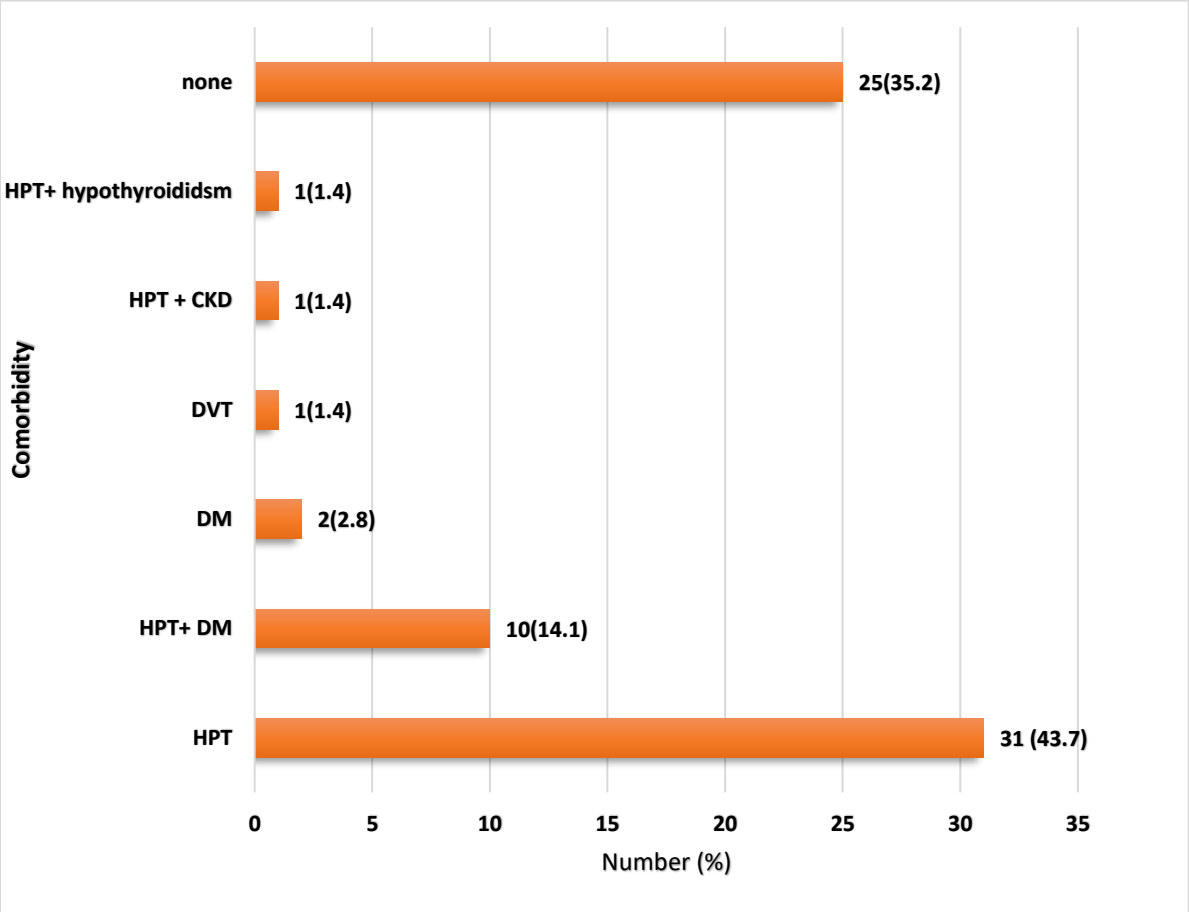
Two-thirds of the study participants belonged to the Akan Ethnic group. The other ethnic groups captured in the data set are Ga-Adangmes and Ewes making up 28.1%. (Table 5.3.1)

5.4 Clinical characteristics of study participants

5.4.1 Co-morbidities in the study population.

The most common co-morbidity accounting for 43.7 percent of the population was Hypertension. 14.1% of the patients had both hypertension and diabetes. 35.2% of the study population had no co-morbidity at all. (Figure 5.4.1)

Figure 5.4.1: Comorbidity.



HPT: hypertension, DVT: deep vein thrombosis, DM: diabetes mellitus, CKD: chronic kidney disease

5. 4 Significant Voiding dysfunction

At one month, 48 participants representing 67.6% had significant voiding dysfunction. This is captured in the table below. They include patients who had retention of urine, those requiring further medication as a result of worsening LUTS/QoL score and those whose IPSS has increased by 5 or more points after one month. (Table 5.4.1)

Table 5.4.1: Incidence of significant voiding dysfunction at 1 month

		Frequency	Percent
Valid	Those without significant voiding dysfunction	23	32.4
	Those with significant voiding dysfunction	48	67.6

5.4.2 Clinical data relating to prior use of tamsulosin.

Sixteen (22.5%) of the participants were taking tamsulosin for LUTS prior to the procedure. None of the study participants was on any other alpha blocker or 5 alpha reductase inhibitor for the same purpose. (Table 5.4.2)

Table 5.4.2: Participants on tamsulosin and hormonal therapy

Variable	n	Percentage (%)
Already on tamsulosin		
Yes	16	22.5
No	55	77.5
Pre-operative hormonal therapy		
Yes	32	45.1
No	39	54.9
Hormonal therapy type		
Gosirelin	28	87.5
Gosirelin and Stilbesterol	1	3.1
Bicalutamide	3	9.4

5.4.5 Clinical data relating to the use of Hormonal therapy.

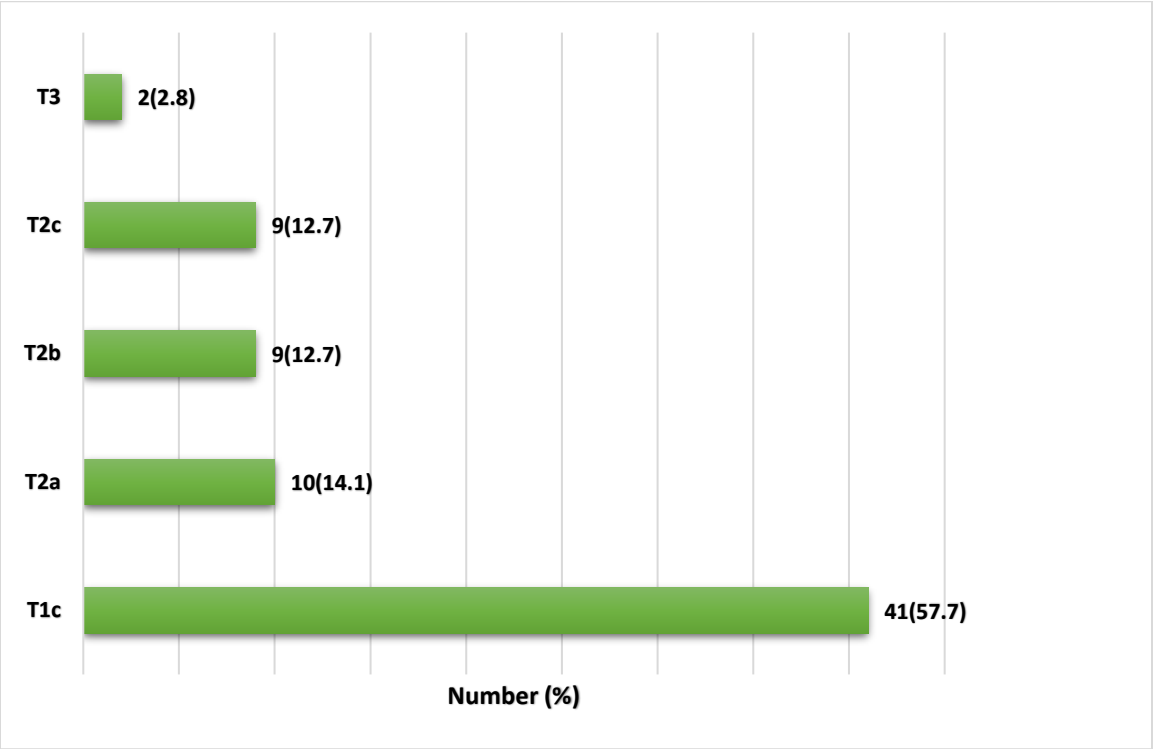
Some of the study participants were on hormonal therapy prior to the brachytherapy. This was either as part of the management of the prostate cancer or as a means to shrink the size of the prostate to facilitate the brachytherapy procedure. The results showed that 45.1 percent of them

had been on some form of hormonal therapy. Of this group 90.6% had used gosirelin. The other medications that had been used included stilbesterol and bicalutamide. (Table 5.4.2)

5.4.6 Clinical data on DRE findings.

Collation of the data showed that on DRE, majority of the participants had DRE findings of T1c. This group represented 57.7%. 14.1% of the study population had T2a whilst 12.7% of them had T2b or T2c at DRE. Only 2 participants had T3 findings on DRE. (Figure 5.4.2).

Figure 5.4.2: Distribution of DRE findings



5.4.7 Clinical findings on prostate volume.

The average prostate volume of the study participants was 45.2 with a standard deviation of 15.9. As many as 12 of them representing 16.9% had prostate volumes greater than 60g. One participant actually had a prostate volume of greater than 80g. (Table 5.4.4)

Table 5.4.4: Prostate volume and pre- biopsy PSA distribution

Variable	**n (%)**	**Descriptive**
Prostate volume(ml), mean(±SD)		45.2(±15.9)
10-20	1(1.4)	
21-30	16(22.5)	
31-40	11(15.5)	
41-50	21(29.6)	
51-60	10(14.1)	
61-70	4(5.6)	
71-80	7(9.9)	
81-90	1(1.4)	
Pre biopsy PSA(ng/ml), Median(IQR)		13.1(6.9─28.9)
0-10	29(40.8)	
10.1-20	19(26.8)	
>20	23(32.4)	

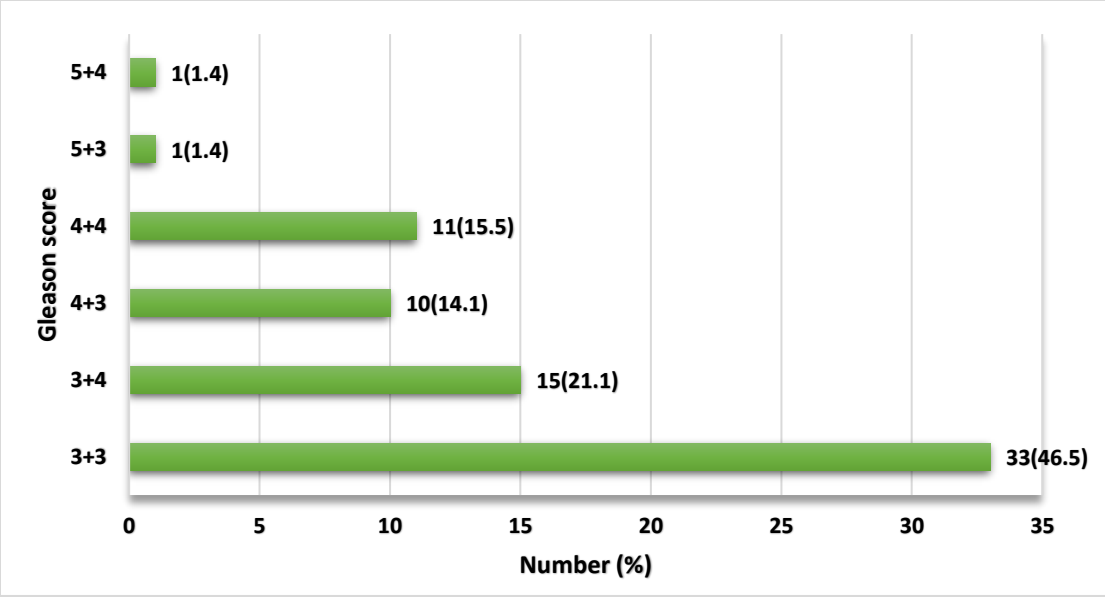
5.4.8 Clinical findings on the pre biopsy PSA

The clinical data showed that 40.8% of the participants had a PSA less than 10ng/ml. 32.4% had PSA's greater than 20ng/ml. The rest of them had PSAs between 10 and 20ng/ml. The median PSA was 13.1ng/ml. (Table 5.4.4)

5.4.8 Clinical data on Gleason Score Distribution

Gleason Grade Group 1 (3+3) was the most common grade amongst the study participants. It accounted for 46.5% of the Gleason Score results. Grade Group 5 was the least common with only one participant having this score. Figure 5.4.3 gives the distribution of the Gleason Scores.

Figure 5.4.3: Gleason Score distribution



5.5. Operative Data Results

5.5.1 Data on the number of seeds used

The average number of I-125 seeds implanted during each procedure was 53 with an interquartile range of 44-62 seeds. Six participants (8.4%) required more than 80 seeds implanted into the prostate. No participant required less than 20 seeds. Table 5.5.1

Table 5.5.1: Number of needles and I-125 seeds used

	n (%)	**Descriptive**
Total number of seeds, median (IQR)		53.0(44─62)
0-10	0(0.0)	
11-20	0(0.0)	
21-30	1(1.4)	
31-40	8(11.3)	
41-50	23(32.4)	
51-60	15(21.1)	
61-70	10(14.1)	
71-80	8(11.3)	
81-90	2(2.8)	
91-100	1(1.4)	
>100	3(4.2)	
Total number of needles, median (IQR)		19(16─21)
0-5	0(0.0)	
6-10	0(0.0)	
11-15	14(19.7)	
16-20	38(53.5)	
21-25	19(26.8)	

5.5.2 Data distribution on the number of needles used

No participant had less than 10 needles used for seed implantation with the median number of needles used being 19. Majority of the participants had between 16 and 20 needles inserted into the prostate (53.5%). 19 participants had between 21 and 25 needles implanted representing 26.8%. (Table 5.5.1)

5.5.3 Operative Data on D90

The median D90 for the study at surgery was 106.5% with an interquartile range of 103.7 to 110.1%. 23.9% of participants had a D90 in the uppermost range of between 111 and 115%. (Table 5.5.2)

Table 5.5.2: Data on U30 and D90

Variable	N (%)	Descriptive
D90,(%) median (IQR)		106.5(103.7─110.1)
90-95	0(0.0)	
96-100	2(2.8)	
101-105	22(31.0)	
106-110	30(42.3)	
111-115	17(23.9)	
U30, median (IQR)		118.2(112.5─126.8)
90-95	1(1.4)	
96-100	1(1.4)	
101-105	3(4.2)	
106-110	14(19.7)	
111-115	7(9.8)	
116-120	19(26.8)	
121-125	16(22.5)	
126-130	10(14.1)	

5.5.4 Operative Data on u30

The u30 data ranged from a lowest of 91.75% to a highest of 128.69%. The median value was 118.2%. As many as 26 participants (36.6%) had u30 values higher than 121%. (Table 5.5.2)

5.6 Post-Operative Data Analysis

5.6.1 Post-operative complaints and Retention of Urine occurring within one month of brachytherapy.

Two participants out of the 71 developed Retention of Urine representing 2.8%. One occurred on post-operative day 1 and the other on the second post-operative day. (Table 5.6.1)

Table 5.6.1: Post-operative ROU within 1month of procedure

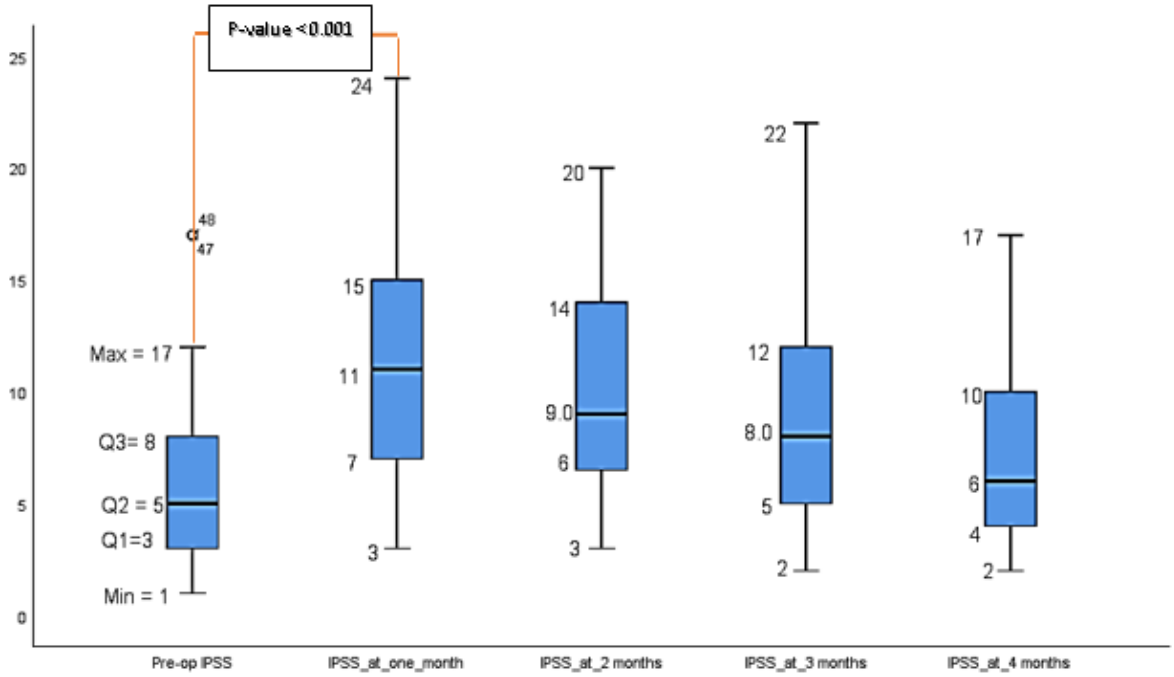
ROU within 1 month		
Yes	2(2.8)	
No	69(97.2)	
POD of ROU		
1 day	1(50.0)	
2 days	1(50.0)	

At one month post therapy the most common complaints were burning urethral pain occurring together with or without voiding. Also there were complaints of worsening LUTS particularly nocturia. At one month 24 out of the 71 participants complained of burning pain in the urethra representing 33.8%. Within the first month, only one patient had an episode of hematuria. At one month, only one patient had passed out an I-125 seed during urination. 21 participants (29.6%) complained of worsening LUTS at 1month. There were no urinary incontinence or gastro-intestinal related complaints at 1 month. 28 participants had no complaints at all one month after the procedure.

5.7 IPSS variations over the study period

The median pre-operative IPSS score was 5 with a range of 1 to 17. Pre-operatively no one had severe LUTS as judged by the IPSS score. At one month post brachytherapy the median IPSS score had increased from 5 to 11. This increase was statistically significant on bivariate regression analysis giving a p value < 0.001. (Table 5.6.1, figure 5.7.1). The IPSS range at one month had increased from 1 - 17 to 3 - 24. Further follow up beyond one month showed a gradual decline in the median IPSS to an average of 6 at 4 months. The box plot of Figure 5.7.1 illustrates these findings.

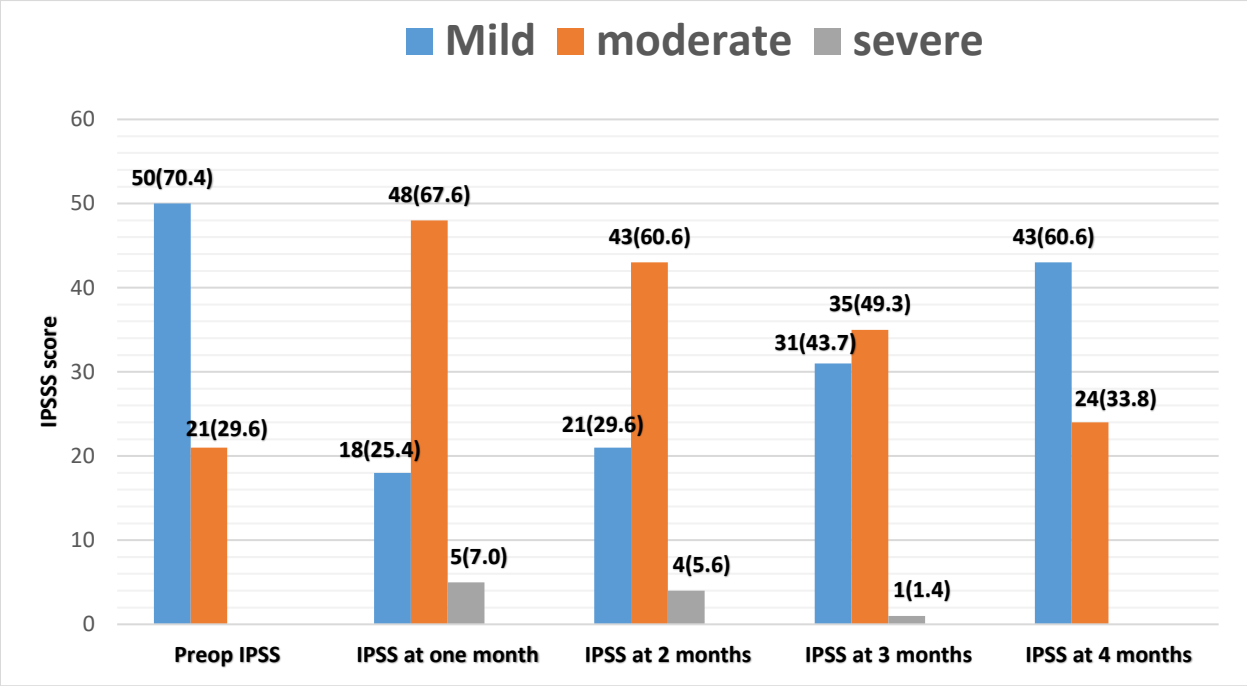
Figure 5.7.1: Average IPSS score over the study period.



Q2: Median, Q1: first quartile, Q3: 3rd quartile

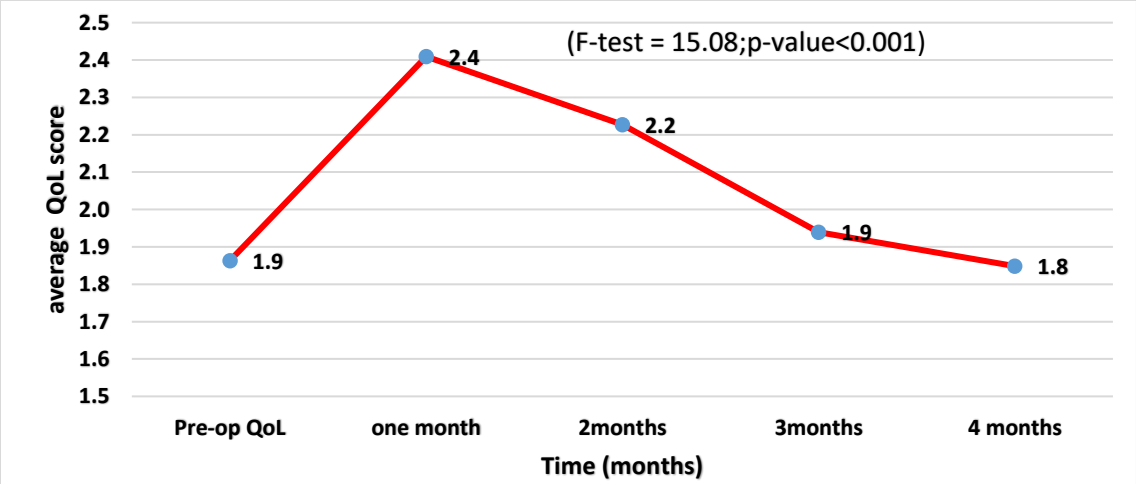
In terms of the severity of LUTS, at pre-operative period, 70.4% of the participants had mild symptoms with the remaining 29.6% having moderate symptoms. No one had severe symptoms. At one month post surgery those with moderate symptoms had increased from 29.6% to 67.6%. A further 7% now had severe symptoms. By 4 months those with moderate symptoms had decreased to 33.8% with no one having severe symptoms anymore. (Figure 5.7.2)

Figure 5.7.2: IPSS score distribution from Pre-op to 4 months post procedure.



The QoL score showed a similar pattern to the IPSS score. It peaked at 1 month rising from an average pre-operative QoL score of 1.9 to an average score of 2.4 atone month. The average QoL gradually decreased over the ensuing months. Fisher testing showed that the changes in the QoL were statistically significant (p <0.001)

Figure 5.7.3: Trend of QoL score over 4 months



5.6 Predictive factors for significant voiding dysfunction.

5.6.1 Association between Clinical variables and significant voiding dysfunction

From bivariate analysis of the data, the following variables had statistically no association with the occurrence of voiding dysfunction: DRE (p= 0.686), prostate volume (p=0.139), pre-biopsy PSA (p=0.949) and Gleason Score (p=0.779). (Please refer Table 5.6.2) Analysis of the prior use of tamsulosin showed a chi-square value of 6.45 and p= 0.011 showing statistical significance. Similarly the pre-operative IPSS ($p < 0.001$) and pre-operative nocturia $p < 0.001$ both showed strong correlation with incidence of voiding dysfunction.

Table 5.6.2: Association between listed variables and significant voiding dysfunction at 1 month.

	Significant voiding Dysfunction			
Variable	**Yes**	**No**	**Chi-square**	**p-value**
Already on tamsulosin			6.45	0.011*
Yes	15(93.8)	1(6.2)		
No	33(60.0)	22(40.0)		
DRE			2.25	0.686
T1c	28(68.3)	13(31.7)		
T2a	6(60.0)	4(40.0)		
T2b	7(77.8)	2(22.2)		
T2c	5(55.6)	4(44.4)		
T3	2(100)	0(0.0)		
Prostate size(g)			2.20	0.139
<60g	36(63.2)	21(36.8)		
≥60g	11(84.6)	2(15.4)		
Pre-biopsy PSA			0.10	0.949
0-10	19(65.5)	10(34.5)		
10.1-20	13(68.4)	6(31.6)		
>20	16(69.6)	7(30.4)		
Pre-op IPSS			2.39	<0.001*
Mild	27(54.0)	23(46.0)		
Moderate	21(100)	0(0.0)		
Severe	0(0.0)	0(0.0)		
Preoperative Nocturia			4.69	<0.001*
0-2	19(46.3)	22(53.7)		
3-5	28(96.6)	1(3.4)		
Gleason			2.48	0.779
3+3	21(63.6)	12(36.4)		
3+4	10(66.7)	5(33.3)		
4+3	6(60.0)	4(40.0)		
4+4	9(81.8)	2(18.2)		
5+3	1(100)	0(0.0)		
5+4	1(100)	0(0.0)		

When these 3 variables (prior use of tamsulosin, pre-operative IPSS and pre-operative nocturia) were analysed with multivariate regression only nocturia remained statistically significant with p=0.002. (Table 5.6.3)

Table 5.6.3: Multivariable analysis of factors associated with significant voiding function.

Variable	**OR(95% CI)**	**p-value**
Already on tamsulosin		
Yes	10.10(0.84−50.12)	0.069
No (reference)		
Pre-op IPSS		
Mild (reference)		
Moderate	1.85 (0.91−5.49)	0.635
Pre-op Nocturia		
0-2 (reference)		
3-5	4.53(1.35−10.59)	0.002*
D90	**1.32(1.02−1.71)**	**0.037***

*P<0.05(statistically significant)

Having a moderate score on IPSS gave an Odd's ratio of 1.85 over those with mild symptoms but this was not statistically significant. (p = 0.635) on the multivariate regression analysis. Nocturia score which is part of the IPSS score however gave statistical significance(p=0.002) on the multivariate regression analysis. A nocturia value of 3 to 5 versus 0 to 2 yielded an Odd's ratio of 4.53.

Association between u30, D90, number of seeds and number of needles with voiding dysfunction

Subjecting the data to bivariate regression analysis, u30 was not statistically associated with voiding dysfunction at one month yielding a p = 0.931. However, both bivariate and multivariate analysis showed that D90 was a good predictor of voiding dysfunction at one month. The P value after t- testing is 0.009, (Table 5.6.4). Table 5.6.3, which shows the results of the multivariate regression analysis, gives an Odd's ratio of 1.32 for D90(when comparing D90 values below 117.2% and those above it.) with p=0.037.

Table 5.6.4: Relationship between D90 and u30 and significant voiding dysfunction, t- test

	Significant voiding dysfunction		**t-test**	**p-value**
Variable	**Yes**	**No**		
D 90, mean(±SD)	107.8(±3.9)	105.1(±3.4)	2.69	0.009*
U30, mean(±SD)	117.2(±8.2)	117.1(±7.9)	0.07	0.931

The data showed that neither the total number of needles used nor the total number of seeds used was associated with significant voiding dysfunction. P was equal to 0.724 for the total number of seeds and p=0.465 for the total number of needles. Neither of these were significant. (Refer table 5.6.5)

Table 5.6.5: Relationship between total number of seeds/ number of needles used during the procedure and significant voiding dysfunction, chi- square analysis

	Significant voiding Dysfunction			
Variable	**Yes**	**No**	**Chi-square**	**p-value**
Total number of seeds				
0-10	0(0.0)	0(0.0)	5.31	0.724
11-20	0(0.0)	0(0.0)		
21-30	1(100)	0(0.0)		
31-40	6(75.0)	2(25.0)		
41-50	13(56.5)	5(33.3)		
51-60	10(66.7)	5(33.3)		
61-70	6(60.0)	4(40.0)		
71-80	6(75.0)	2(25.0)		
81-90	2(100)	0(0.0)		
91-100	1(100)	0(0.0)		
>100	3(100)	0(0.0)		
Total number of needles			1.53	0.465
0-5	0(0.0)	0(0.0)		
6-10	0(0.0)	0(0.0)		
11-15	9(64.3)	5(35.7)		
16-20	21(61.8)	13(38.2)		
21-25	15(78.9)	4(21.1)		

CHAPTER 6

6.1 DISCUSSION

Age and educational level

The average age of participants of the study, who all had localised CaP, was 64years with a range of 47 – 79years. This is consistent with a study in Ghana, by Mensah et al [109.] They reported the average age of patients undergoing prostate brachytherapy as 64years with a range of 46 - 78years. This is also akin to the report by Yeboah et al [108] in 2016. They also found the mean age of diagnosing prostate cancer in Accra to be 70years. However, Bernstein et al in 2018 stated that with the increasing usage of PSA screening, the mean age at diagnosis was 66 years.

Prostate cancer before 50years is generally rare accounting for about 1 in 350 cases worldwide.[107] This study had one participant out of the 71 with age less than 50years. This difference may be due to the higher incidence of CaP amongst blacks.

With regards to educational level of the participants, 90% of the cohort have had had tertiary education with the remaining population having had only secondary level education. A study in South Africa by Schreiber et al observed that brachytherapy was more likely to be used by those with higher socioeconomic status.[110] People with higher level education may be more likely to have access to PSA screening and also to brachytherapy services in the city of Accra. They may also have insurance packages that can cater for the cost of brachytherapy services.

Co-morbidities

Considering that prostate cancer occurs in the aging population it is not surprising to find that a large percentage have at least one co-morbidity. 64.8% of our cohort had at least one co-morbidity. Hypertension was the most common accounting for 43.7%. A study by Jefferson et al found that amongst prostate cancer patients, 51% had a comorbidity with hypertension accounting for 42%.[111] The differences here may be due to the different geographical settings of the studies.

Significant Voiding Dysfunction

Forty- eight (67.6%) of participants had significant voiding dysfunction at 1month. Many of these had an increase of 5 or more in their IPSS score (an IPSS flare). Those who required additional medication to aid in voiding were all part of this flare group. Cesaretti et al also

reported a peak in the IPSS post brachytherapy occurring at 1.3months post procedure.[88] Their flare rate was 35.5%.[88] Mensah et al in their study reported that 76.6% of their patients experienced worsening LUTS with symptoms of frequency, urgency and poor stream within the first 2 months.[109]

This study had an AROU rate of 2.8% representing 2 out of the 71 participants. This compares closely with the 4.4% reported by Mensah et al.[109] and a rate of 3.2% reported by Mabjeesh et al.[89] In this study both of these retentions occurred within the first 2 days of the procedure. Mabjeesh et al also did indicate that from their study the median time to developing AROU was 1 day post implantation.

IPSS score and voiding dysfunction at one- month.

The median IPSS score pre-operatively was 5 and at one month after surgery had increased to 11. This was the peak IPSS score within the period as the average IPSS score declined thereafter. In their study on urinary symptom-flare following I-125 prostate brachytherapy, Cesaretti et al had a mean baseline IPSS of 7.5 with a peak IPSS of 19.4 occurring at 1.3months post procedure. Kelly et al found that 97% of the study sample had worsening IPSS values at 1month. This peak of IPSS score started to decline by 3 months.[114]

From bivariate regression analysis this study showed pre – operative IPSS was statistically associated with incidence of significant voiding dysfunction yielding a chi- square value of 2.39 and a p-value of 0.001. Further logistic regression analysis showed that moderate IPSS symptom score was 1.85 times more likely to lead to significant voiding dysfunction (Odds ratio of 1.85) as compared to mild IPSS score. However, the multivariate regression did not prove statistical significance (p= 0.635). There were no participants with severe IPSS symptom score pre-operatively.

Interestingly this study found that the nocturia score at IPSS evaluation to be significant predictor of voiding dysfunction at one month. Bivariate analysis yielded a chi-square value of 4.69 and a p <0.001. Nocturia remained statistically significant on multivariate analysis. A nocturia value of 3-5 was 4.53 times more likely to result in significant voiding dysfunction than one between 0-2.

Mallick et al also found that an initial IPSS greater than eight was a significant predictive factors of urinary morbidity.[85] Keyes et al also reported urinary symptom flare to be related to higher

IPSS scores.[82] Cesaretti el al however found no such association between IPSS score and significant voiding dysfunction. [88]

The Quality of life (QoL) score generally tends to follow the IPSS pattern. It peaked after one month and gradually began to decline by the second month. Anecdotally, many participants said pre-operative counselling generally helped them cope better with worsening LUTS.

Use of tamsulosin for preexisting LUTS

Prostate cancer may co-exist with LUTS for which some patients may have been on alpha blockers. For this study the only alpha blocker patients used was tamsulosin. 22.5% of our study population were already taking tamsulosin even before the prostate brachytherapy for LUTS. Mallick et al had concluded from their study that prior use of alpha blockers before prostate brachytherapy predicted the incidence of acute voiding dysfunction, particularly urine retention.[85] Mallick et al position was further corroborated by Mendez et al.[112] In my study, of the 16 patients who were taking tamsulosin, 15 of them had significant voiding dysfunction at one month. (Table 9). The RM- ANOVA deduction gave us a $p < 0.011$ indicating statistical significance. Multivariate analysis of this yielded a $p = 0.069$. (which is not statistically significant). Hence from our data we cannot conclude convincingly that prior use of tamsulosin before brachytherapy would lead to significant voiding dysfunction at one month. Of the 2 patients who developed ROU only one of them was on tamsulosin prior to the brachytherapy.

DRE and pre-biopsy PSA.

The median PSA of this study of 13.1ng/ml with a range of 3.9 to 142ng/ml correlates almost exactly as that reported by Mensah et al.[97] They reported an average PSA of 13ng/ml (and a range of 2.1 to 133ng/ml) in their study of brachytherapy in Ghana.[97] There was also no statistical significance on bivariate analysis between PSA before the biopsy and significant voiding dysfunction. ($p = 0.686$). Cesaretti et al in their study on symptom flare after prostate brachytherapy came to same conclusion that DRE and pre-biopsy PSA did not influence the occurrence of symptom flare.[88]

The data from this study also shows no statistical correlation between findings at DRE and the incidence of significant voiding dysfunction at 1 month. The distribution of the DRE findings amongst our cohort T1 – 57.7%, T2- 39.9% and T3- 2.8% varies slightly from that reported by Mensah et al of T1 - 31.1%, T2 - 51.3%, and T3 -7.7%[97]

Prostate size.

Some studies have found prostate size to be strongly linked with significant voiding dysfunction after brachytherapy. In this study the only participant with a volume greater than 80g had an IPSS symptom flare. Of the 7 participants with prostate volume greater than 70g, 3 of them did not have an IPSS symptom flare. Bivariate analysis did not find a correlation between prostate size and occurrence of significant voiding dysfunction.

Mabjeesh et al and Guzman et al both however found prostate size to be strong predictor for urine retention. [89,116] Cesaretti et al however found no association between symptom flare and prostate volume.[88]

Number of needles used and number of seeds Implanted

The median number of needles used per case was 19 with an inter quartile range of 15-21. The number of needles used is affected by the prostate volume and the determined dosimetry. Hence it may vary from one center to another. In a United Kingdom based study the mean number of needles used was 23 and mean number of seeds were 72.[113] From my study the mean number of seeds used was 53.

Bivariate analysis of both number of needles used and number of seeds implanted did not show statistical significance with the occurrence of significant voiding dysfunction. Cesaretti et al in their study also found no correlation between number of needles or seeds and the occurrence of significant voiding dysfunction.[88] Contrarily, Eriguchi et al and also Lee et al found total number of needles used to be significantly be associated with significant voiding dysfunction.[98, 115]

D90 and u30

There was statistically no significant association between u30 value and the incidence of significant voiding dysfunction. However, the bivariate analysis showed a p- value of 0.009 for D90 indicating a strong association. This was further subjected to multivariate regression analysis and D90 remained statistically significant with p-value of 0.037.

Mallick et al had reported that both D90 and u30 were predictors of significant urinary morbidity.

6.2 CONCLUSION

The study has shown that prostate brachytherapy imposes significant voiding dysfunction in the acute setting on a large number of patients undergoing the procedure. It has shown a deterioration in the Quality of Life in this period but a general trend of improvement after the first month. The incidence of acute retention of urine at 1month following prostate brachytherapy remains small. The larger group of patients have worsening lower urinary tract symptoms. Other complications in the acute setting are infrequent.

The study found no statistically significant association between DRE, prostate volume, Gleason score, number of needles, number of seeds used, u30 and the incidence of significant voiding dysfunction at 1 month. The pre-operative IPSS score and prior use of tamsulosin are also not significant predictors of voiding dysfunction at one month.

There was statistically significant association between the pre-operative nocturia score and the D90 and the incidence of significant voiding dysfunction.

There was no report of enuresis during the study period.

6.3 LIMITATIONS

1. The study was limited by the small sample size as compared to what was done in reported studies
2. The different definitions of voiding dysfunction in different studies made comparing results with some other studies challenging.
3. The prior use of medications like tamsulosin for LUTS prior to the surgery makes the interpretation of voiding symptoms post procedure rather complex.

6.4 RECOMMENDATIONS

Adequate counselling should be given to patients as they make choices regarding treatment for localised prostate cancer. Patients with nocturia of 3 or more and those with high D90 values at the brachytherapy procedure should be followed up more closely in the immediate post-operative period.

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APPENDIX I: PATIENT INFORMATION SHEET

PROJECT TITLE: DETERMINANTS OF SIGNIFICANT VOIDING DYSFUNCTION AFTER IODINE-125 PROSTATE BRACHYTHERAPY FOR LOCALIZED CANCER OF THE PROSTATE AT THE KORLE BU TEACHING HOSPITAL ACCRA.

Investigator: Dr Jonathan C Lamptey

Carefully read this document before agreeing to partake in this study. It briefly explains the study to you. Please ask any questions where you require further details or clarity. Participation in this study or otherwise would not affect the care you would receive for your medical condition. Do remember also that you are at liberty to pull out of the study at any time and doing so would not affect your management. If you agree to be a study participant kindly, give consent by signing the form at the end of this document. This consent indicates that you have understood the nature of the study and voluntarily opt to participate in the study.

INTRODUCTION

The study would be done by Dr Jonathan C Lamptey, a senior resident with Urology Unit of the KBTH. The aim of the study is to assess the impact of the prostate brachytherapy you are scheduled to undergo on your voiding function

PURPOSE OF THE STUDY

The study seeks to assess the extent of urination problems patients undergoing prostate brachytherapy in KBTH would have. It also seek to find the factors that can predict these problems. This would greatly assist in counseling patients as they make choices on mode of treatment for localized prostate cancer.

PROCEDURE

After giving your consent, you would be guided to fill out your questionnaire by the investigator. This would include basic demographic and medical information as well as information related to the prostate cancer. Your voiding function would also be assessed before the surgery using a tool called IPSS. After the surgery, your voiding function and any other complaints would be captured again at one month and monthly up to 4 months. This would take place in-person where it is your scheduled OPD visit or by phone.

BENEFITS AND RISKS

This study might bring no benefit to you personally. It would also not expose you to any risks. You would receive the same care and medications as any other patient undergoing prostate brachytherapy would receive. Providing the needed information would take less than 15min per each session.

CONFIDENTIALITY

All reasonable efforts will be made to keep your information private and confidential. All the information collected will be assigned a unique study ID number instead of names. Any publication or dissemination of the findings will not have your name in it.

Any further questions or concerns should addressed by reaching out to the investigator

Dr Jonathan C Lamptey

Urology Unit

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Korle Bu Teaching Hospital

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APPENDIX II :CONSENT FORM

Declaration by Participant

I ……. have read the Participant

Information Sheet or it has been read to me in a language I understand.

I understand the purpose, nature and risks of the study being conducted.

I am satisfied with the answers given to my questions and concerns.

I willfully agree to participate in this study as described and understand that I can

withdraw from this study at any point without my healthcare being compromised.

Signature …….. Date ……..

APPENDIX 4

Data Collection Sheet

DETERMINANTS OF SIGNIFICANT VOIDING DYSFUNCTION AFTER IODINE-125 PROSTATE BRACHYTHERAPY FOR LOCALIZED CANCER OF THE PROSTATE AT THE KORLE BU TEACHING HOSPITAL ACCRA.

Date …….

Patient ID Number ……..

Contact phone Number …….

A. DEMOGRAPHIC INFORMATION

- AGE
- ETHNICITY
- EDUCATIONAL STATUS
- OCCUPATION
- MARITAL STATUS

B. CLINICAL INFORMATION

- CO-MORBIDITIES
    I. HYPERTENSION
    II. DIABETES MELLITUS
    III. OTHERS – SPECIFY
- MEDICATIONS
    I. TAMSULSOSIN
    II. FINASTERIDE
    III. TADALAFIL

IV. HORMONAL THERAPY FOR CAP

……. (STATE TYPE AND DURATION)

- DIGITAL RECTAL EXAMINATION FINDINGS
  I. T1
  II. T2a
  III. T2b
  IV. T2c
- PROSTATE VOLUME ……
- PRE-BIOPSY PSA ……

C. HISTOLOGY REPORT

- HISTOLOGY ……..
- PERCENTAGE OF SAMPLE INVOLVED WITH TUMOUR
- GLEASON SCORE…

D. OPERATIVE DATA

- DATE
- TOTAL NUMBER OF SEEDS USED
  I NUMBER OF PERIPHERAL SEEDS
  II. NUMBER OF CENTRAL SEEDS
- TOTAL NUMBER OF NEEDLES
  I NUMBER OF PERIPHERAL NEEDLES
  II. NUMBER OF CENTRAL NEEDLFES

- D90……
- U30 ……...

E. Occurrence of Inability to void Up to One Month requiring catheterization? ….

I. Yes II. No

F. Have you needed further medication to assist you to void due to worsening Lower Urinary Tract Symptoms? ….. I Yes II No

G. Any other complaints at 1 month …….

H. IPSS SCORE

PARAMETER	**PRE - OPERATIVE SCORE**	**1,2,3,4 MONTH POST OPERATIVE SCORE**
INCOMPLETE EMPTYING		
FREQUENCY		
INTERMITTENCY		
URGENCY		
WEAK STREAM		
STRAINING		
NOCTURIA		
TOTAL SCORE		
QoL SCORE.		