Uro-Oncology Clinic Handout

Hello and welcome to the Urological Oncology clinic! This handout is designed to optimise what you get out of your time in the clinic. Ideally, you will have a chance to have a glance through before seeing your first patient, and during down time. It includes information that will help you

- understand what goes on in the clinic,
- revise some relevant pathology knowledge and
- form expectations what to take away from your time here in the form of both learning objectives and a short quiz for self-assessment at the end.

We hope you find this useful and that you enjoy your time here.

Learning objectives

Ideally, in this clinic you will

- ☐ Take a history and present it under OSCE conditions. You will be scored and given formal feedback on your presentation skills.
- ☐ Do a physical examination (i.e. DRE) under supervision of your tutor.
- ☐ Learn 2 drugs for androgen deprivation therapy
- ☐ Know their side effects and relative importance
- ☐ Know their mode of action.

What happens in Uro-Oncology

Uro-oncology patients have bladder or prostate cancer. We will focus on prostate cancer in this handout.

Patients are usually referred from GPs via urology. The initial referral is often due to an elevated PSA. If prostate cancer is found, the patient is sent for oncological input. A vast majority of the caseload is patients with biopsy-confirmed prostate cancer for oncological input; many patients are here for review. Try and understand (i.e. ask the clinician) if the patient is a "new diagnosis" or for review, and if so, what stage in their journey they have reached – prototypical patient "careers" are in Figure 1 – to help you contextualise the consultation.

We encourage you to remind the clinicians to help you achieve these outcomes.

Box 1: PSA Screening

As of April 2014, there is **no** organised screening programme for prostate cancer in England. There is, however, an "**informed choice**" programme, where concerned patients are given an information pack at their GP and can then opt into being screened.

PSA screening is **controversially** discussed in the UK. The key datum in favour is that **mortality is reduced by 20 %** by screening, however, this comes at a significant cost of overtreatment: the **NNT is 48***, and the number needed to screen is 1,410 (which is similar to breast cancer). And, as no doubt you have picked up, this means significant side effects. This was deemed to violate Bradford criterion #9 – the chance of harm is less than the chance of benefit.

The reference range for PSA depends on age.

50-59	< 3.0 ng / ml
60-69	< 4.0 ng / ml
70+	< 5.0 ng / ml

*Cited data from the European Randomised Study of Screening for Prostate Cancer – the largest study on prostate cancer screening. A US study showed no benefits, but this study was smaller and had some issues.

Box 2: Jargon & Acronyms

AS: Active surveillance. Regular review with PSA measurement, usually 3-6 monthly, physical exam (DRE) every 6-12 months, plus MRI at enrolment and rebiopsy at the end of year 1.

ADT: Androgen deprivation therapy. Treatment with various drugs that reduce circulating androgen concentration, e.g. GnRH analogues

BOO: bladder outflow obstruction

Brachytherapy: radiotherapy administered via implantation of solid radioisotope. Derived from *brachys*, Greek for "short-distance"

DRE: Digital rectal examination

EBRT: External-beam radiotherapy

GnRH analogue: Gonadotrophin releasing hormone analogue. Lowers sex hormone levels.

GS: Gleason Score

IPSS: International prostate symptom score. 7 questions where patients score themselves on a 5-point scale for →LUTS.

LUTS: Lower Urinary Tract Symptoms.

MAB: Maximum androgen blockade – GnRH analogue plus other drugs.

PS: Performance status

PSA: Prostate-specific antigen

RP: radical prostatectomy

Teletherapy: Different term for →EBRT. From *tele*, greek for distant

TP biopsy: transperitoneal biopsy.

TRUS biopsy: trans-rectal ultrasound-guided biopsy.

TURP: Trans-urethral resection of the prostate

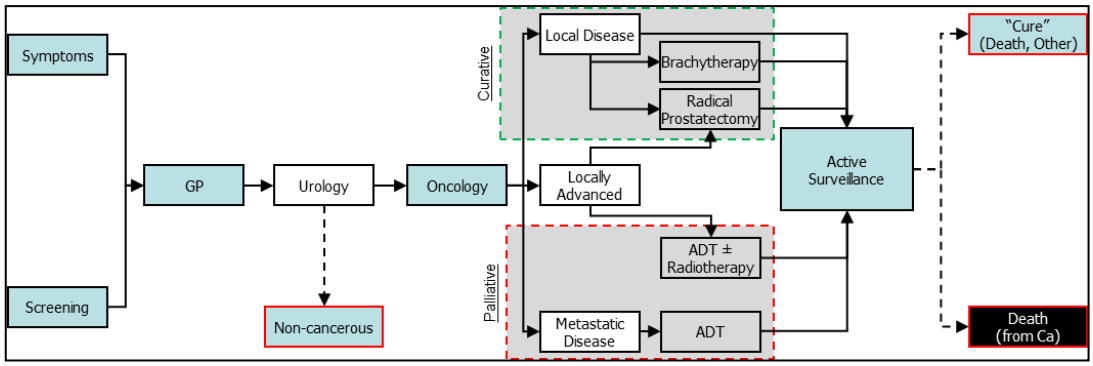

Figure 1: Typical pathways for patients with prostate cancer

Clerking a prostate patient (as an FY/ GP)

Patients can be picked up through screening – before noticing symptoms – or when presenting with symptoms. Prostate cancer being as common as it is, you stand a good chance of initiating investigations for prostate cancer either as an FY or in general practice; therefore knowing how to take a history and presenting it will be useful even if you are not planning on becoming an oncologist/urologist.

The key questions are about **LUTS** – **L**ower **U**rinary **T**ract **S**ymptoms – and about **systemic effects** of cancer. The L in LUTS is mostly redundant as you are *not* trying to differentiate it from any "upper" urinary tract symptoms. Within LUTS, differentiate **filling** (or **storage**) **symptoms** and **voiding symptoms**. Filling symptoms are treated with anti-cholinergics while voiding symptoms are treated with α1-adrenoceptor antagonists (e.g. **tamsulosin**).

Before you finish with your patient, you will want to know:
Do they have **LUTS**?

- **How often** do they urinate?
- Is there **nocturia**? If so, how often? (once is okay, more than that is suspicious)
- Are there **voiding symptoms?**
    - Is there hesitancy (difficulty starting) or dribbling (≈difficulty stopping)?
    - Do they have a weak stream? Do they have to strain to urinate?
- Are there **filling symptoms (a.k.a. storage symptoms)?**
    - Is there urgency or incontinence?
    - Do they feel that they fail to empty completely, or that they urinate only to feel they have to go again within a short space of time?
- Is there **haematuria**?

Do they have signs of **systemic disease** – weight loss, back pain?

Finally, do not forget to take the remainder of a thorough history – for your presentation the history of the presenting complaint is only a small part of the package!

Box 3: Androgen Deprivation Therapy (ADT)

Testosterone increases rates of growth in prostate cancer. In normal function, testosterone is controlled by the hypothalamo-pituitary axis.

GnRH secretion from the hypothalamus is pulsatile. Size and frequency of GnRH secretion control the amount of LH and FSH that is secreted. FSH stimulates testosterone production from testicular Leydig cells.

GnRH analogues (e.g. goserelin or Zoladex®) inhibit LH production due to desensitising the GnRH response, most likely as GnRH analogue concentration is non-pulsatile. These are usually given as depot injections. Immediately following administration, the cancer may "flare" as FSH and testosterone production increases before desensitising.

Anti-androgens (e.g. bicalutamide or Casodex®) are androgen receptor antagonists. They are taken orally and normally used to reduce the effect of the testosterone flare.

Side effects of ADT include hot flushes, weight gain, tiredness, loss of libido, sarcopenia (muscle bulk loss) and gynecomastia – hot flushes are usually the most bothersome to the patient.

PSA (ng / mL)	< 15	15 – 50	> 50
TNM Stage	T_{1-2}, no nodes	$T_{3/4}$, $N_{0\ or\ 1}$, **no** mets	M_1
Gleason score	< 8	8 -10	Essentially Irrelevant once mets +ve
Classification	Local disease	Locally advanced disease	Metastatic disease
Prognosis	Good	Intermediate	Poor
Treatment	**Curative (Radical treatment)** 1. Surgery 2. EBRT 3. Brachytherapy 4. Active surveillance (defer treatment until disease advances)	**Curative OR palliative** 1. Radical prostatectomy 2. Androgen-deprivation therapy 3. Androgen-deprivation therapy + radiotherapy	**Palliative** 1. Androgen-deprivation therapy

Table 1: A simple management algorithm for patients with prostate cancer

Managing a prostate cancer patient

Managing prostate cancer is a post-graduate specialty and you should not be expected to know more than the basics – these are summarised in Table 1.

The key investigation in prostate cancer is measuring plasma PSA which can help in screening as well as monitoring of disease progression during active surveillance. In newly diagnosed patients, biopsy and staging CT are usually required to confirm the diagnosis and decide on further management.
Note that conventional chemotherapy has a limited role in the treatment of prostate cancer as survival benefits are minimal (3 months approx.) while androgen deprivation therapy is essentially the baseline.

Box 4: Grading and staging

As you know, cancers are graded and staged – grading giving a rough indication how fast the cancer is expected to progress and stage giving an indication how far it has progressed already.

Grading is done on histology, therefore it requires a **biopsy**. Staging is done by spread and therefore it requires **soft-tissue imaging** (i.e. a CT or MRI).

Grading is done by **Gleason score**. It ranges from 2 to 10 and can be broken down into two numbers. These represent the commonest and second most common pattern seen by the pathologist. Higher numbers are worse, and 3 and upwards are cancerous. Therefore Gleason 3+3 is the lowest biopsy finding that would be declared malignant.

Staging is done by **TNM staging**. This system is in common use for most solid malignancies. We expect you know that it stands for **T**umour, **N**odes and **M**etastasis. Each component is assigned a score, higher numbers being higher stages.

Self-Assessment

There are two components to this self-assessment, some Single Best Answer questions in keeping with finals and a short scenario. The idea is that you can test yourself, the answers are provided to give you feedback. You will not be penalised for not using this tool.

Q1. Regarding prostate specific antigen testing…

A) PSA levels within the reference range exclude malignancy

B) Should be arranged after clinical examination on the same day to enhance convenience

C) PSA screening probably has no benefit

D) PSA levels less than 0.6 ng / mL predicts a risk of developing metastatic prostate cancer of less than 5% in the next 25 years of life.

E) PSA testing has no role in active surveillance

Q2. Which of these is the LEAST likely side effect of androgen deprivation therapy?

A) Loss of libido

B) Sarcopenia

C) Breast growth and tenderness

D) Hot flushes

E) Reduced insulin tolerance

Q3. Regarding prostate the histopathology of the prostate…

A) Transrectal ultrasound-guided fine-needle aspiration cytology is the gold-standard for prostate biopsy

B) The Gleason score is essential for management decisions in advanced disease

C) Small-cell prostate cancer does not increase plasma PSA

D) Most cancers of the prostate originate in the largest area of the prostate, the central zone

E) Immunostaining for the product of the expression of the oncogene ZIP1 is useful to identify cancerous cells

Q4. Which of these is the LEAST likely presentation of prostate cancer?

A) Faecal retention and tenesmus

B) Painful urination

C) Painful ejaculation

D) Nocturia

E) Fractured neck of femur

Q5. Regarding radiotherapy in prostate cancer…

A) Radiation colitis usually resolves within weeks in the majority of patients

B) Brachytherapy is an excellent palliative measure as it is more gentle than EBRT

C) Patients typically experience worsening urinary outflow symptoms immediately following EBRT as the tumour lyses and causes prostatic inflammation (prostatitis)

D) Radiotherapy is favoured in sexually active men over surgery as it nearly abolishes the chance of developing impotence

E) A high fibre diet helps manage the effects of long-term radiation colitis

For your foundation year you are assigned to a GP surgery in a small university city which shall go unnamed. Your second patient is an 73-year old retired university professor, accompanied by his 71-year old wife, a retired psychiatrist. He complains that it hurts to urinate — this has been going on for a week and it is getting worse—and mentions having to "get up constantly at night to go to the bathroom", but he thinks this is just age. After they leave, you write up the case and his wife pops back in—she mentions that he seems confused—he called her by the name of a PhD student of his from 30 years ago this morning!

Think about your differentials? What is your course of action?

You meet Professor Smith next week. His dysuria is gone but the nocturia remains and his PSA comes back as 9 ng / mL and you decide to refer him to the urology department. From your history from the week before you know that he has diabetes and hypertension but is otherwise well. He has had a left inguinal hernia repair 15 years ago and a right menisectomy; these procedures were uneventful. He is allergic to penicillin. He is an avid gardener, often spending days outside (and almost equally long talking about it in your clinic!) but has had to cut back to about 3 hours of gardening in the last 2 months as he gets tired. The DRE was unremarkable.

You want to dazzle your addressee with your brilliance and send them the best referral letter you can. Who would you refer to? What information do you need to include? Draft the letter out below.

Professor Smith is diagnosed with prostate cancer. He comes back to see you three days after seeing the clinical oncology team, again in the company of his wife. She tells you that they are somewhat confused about his management – he has prostate cancer, but they have not decided to operate! He went to the hospital alone and found the hospital experience baffling and would like you to talk them through why the hospital team. You have seen the clinic letter—his Gleason score is 7 (4+3) and a staging CT showed local invasion in the absence of nodal involvement or metastases. What do you tell Professor Smith and his wife about what you think is going on?

Self-Assessment Answers

Answers for the SBA-format questions:

Q1: The correct answer is D—we would expect you to work on the principle of exclusion here, but this finding is cited in the ERSPC white paper. A is false, certain prostate cancers do *not* raise PSA, esp. small-cell cancer. B is false— while scheduling the two on the same day would indeed be convenient, DRE increases PSA levels, as do ejaculation and strenuous exercise—all of these should be avoided *before* taking the blood sample. C is too simplistic—PSA screening does help early detection of cancers and can save lives, but can also cause harm. It would be fairer to say that a net benefit of PSA screening is doubtful. E is false—PSA is the mainstay of AS.

Q2. Reduced insulin tolerance does not occur in ADT. The others are all part of the side effect profile, even though some of these are rarely complained about (sarcopenia, gynecomastia)

Q3. The correct answer is indeed C. Small-cell prostate cancer does not tend to result in elevated PSA, but it only accounts for about 1 % of prostate cancers. A is false—transrectal ultrasound guidance is useful, but **core biopsy** is much better than aspiration cytology. Aspiration cytology has a limited role in diagnosing breast cancer, but it cannot provide histology, but only isolated cells—similar to the Pap smear. B is false since, once the cancer metastasises, Gleason score becomes essentially irrelevant for prognosis and management decisions. D is false—most cancers do indeed arise from the largest zone, but that is the peripheral zone (70% of volume, 80% of cancers). The central zone accounts for only about 25% of volume and 5 % of prostate cancer. E is false—ZIP1, the gene encoding the Zinc-transporter protein is not an oncogene but a tumour-suppressor gene. Zinc is not accumulated into malignant cells as part of their derangement of metabolism.

Q4. Faecal retention does not occur in prostate cancer—A is the correct answer.

Q5. The correct answer is A—the vast majority of radiation proctitis resolves rapidly, but in a small yet significant proportion it does not resolve and becomes chronic. In these patients, a high-fibre diet tends to make some of the symptoms (namely loose bowel movements) worse—hence E is false. B is false—brachytherapy is not used as a palliative measure. C is false—while brachytherapy can initially worsen outflow obstruction symptoms, EBRT can cause chronic obstruction, but this is not the result of tumour inflammation of the prostate but of a stricture of the urethra. D is false—radiation has a significant risk of causing chronic impotence (40-70 %).

Answers to the scenario:

These questions are somewhat open and the scope of clinical judgement allows for a variety of answers. We hope the following guides are helpful and reasonable guides to what sensible management may look like.

1. We would expect you to have taken a full history, you would probably want to examine him as well as arrange some tests, including a PSA—the PSA of course would have to be done before any examination (or 1 week later). Given his symptoms (and his apparent confusion) you may also be concerned about a possible UTI (which can coincide with urinary outflow obstruction as residual volume provides a good medium for bacterial growth) and may wish to dipstick his urine or send off cultures. You could empirically treat for UTI and reassess a week later and then decide whether to refer to urology/test PSA.
2. We would expect your letter to be polite and mention his presenting complaint with a short history of the presenting complaint as well as the status quo if different (i.e. if you treated for UTI, you would mention a failure of symptoms to resolve). Your PSA result should be included. Normally, a patient like Professor Smith would be referred to Urology first—as such you should ideally include a brief surgical history and an anaesthetic risk assessment. Including the patients performance status would be helpful. Keep the letter short—you should not need more than three sentences.
3. This is an explanation and planning scenario that is somewhat unfortunate—you have limited information and have to second-guess the experts. If you refuse to do so and say to him that you will write to the oncologists and get back to him, that would be a reasonable approach. For the purposes of this self-assessment, you could look back at Table 1 and recognise that he is an older patient with a lowered performance status who is mildly symptomatic and has local disease—not operating is reasonable in this setting, and we expect you to have been privy to several discussions about the risks and benefits of such management in the clinic. We would also point out that it is worth thinking about whether this patient is showing signs of dementia? He appears to have trouble understanding or at least remembering his consultation in the clinic and has called his wife by the wrong name. Onset of dementia can be insidious and it is worth screening for, especially for reversible causes such as benign intracranial hypertension.