Guidelines for the management of Prostate Cancer

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Network Urology Lead Clinician

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Specialist MDT Lead Clinicians

Mr PA. Cornford
Mr N Parr
1. INTRODUCTION

This document sets out the guidelines for the management of patients with prostate cancer within the Merseyside and Cheshire Cancer Network (MCCN). Its scope is to aid all health practitioners involved in the patient from primary care and referral through treatment to follow up. However, these guidelines are endorsed by the network group and should only be used in conjunction with current evidence. They will be reviewed and updated on an annual basis as required.

These guidelines should be read in conjunction with: Improving Outcomes in Urological Cancer: the Manual, NICE, 2002 and should be used in combination with the EAU and NCCN Guidelines on Prostate Cancer and the National Institute for Clinical Excellence (NICE) document Prostate Cancer: diagnosis and treatment. These can be downloaded free of charge from the following websites:

www.nice.org.uk; http://uroweb.org/

Prostate cancer accounts for ~25% of new cancer diagnoses in the U.K., with 41,736 new cases diagnosed in 2011 constituting around 25% of new male cancer diagnoses. No systematic screening program exists but most cancers are diagnosed on the basis of opportunistic PSA screening.

2. REFERRAL OF SUSPECTED UROLOGICAL CANCER FROM PRIMARY CARE

All patients with suspected prostate cancer should be referred urgently to the local Urology Multi-disciplinary Team (MDT). Local MDTs are established in all 7 acute hospital trusts in MCCN. Specialist MDTs are based at the Royal Liverpool and Broadgreen University Hospitals NHS Trust and Wirral University Teaching Hospital NHS Foundation Trust. SMDT contacts are detailed in Appendix 1.

As defined in the Improving Outcomes Guidance, the following are indications for urgent referral under the ‘two-week wait’ system:

- Elevated age-specific PSA in men with at least a ten year life-expectancy
- High PSA (>20ng/ml) in a man with a clinically malignant prostate or bone pain.

3. DIAGNOSIS

Patients undergo full clinical assessment including a rectal examination and serum PSA, where this has not been measured prior to referral. T2 W and functional MRI scans prior to biopsy provide better diagnostic information. Histological confirmation is provided by transrectal ultrasound guided or transperitoneal template biopsy. For patients with metastatic disease and high serum PSA (>100ng/ml), consistent with carcinoma of the prostate, a limited (2-3 cores) TRUS biopsy, in frail patients, no biopsy is indicated.

In patients suitable for radical treatment, functional MRI of the prostate and pelvis and, for patients with serum PSA greater than 20ng/ml, poorly differentiated disease
(Gleason 8-10), or relevant symptoms, an isotope bone scan or whole body MRI is indicated to exclude metastatic disease.

All patients with biopsy proven prostate cancer should be discussed in a MDT. Those patients considered for curative treatments should be referred on to the Specialist MDT.

3.1 Histological Examination
Pathology specimens should be dissected and reported in accordance with the latest dataset for prostate cancer histopathology reports published by the Royal College of Pathologists. Standards and datasets can be found at http://www.rcpath.org/

3.2 Radiology Guidelines
Please refer to the Royal College of Radiologists guidelines attached http://www.rcr.ac.uk/. Network approved imaging protocols are detailed in Appendix 9.

4. SPECIALIST AND LOCAL MULTI-DISCIPLINARY TEAMS

The Royal Liverpool’s SMDT provides the IOG defined service for prostate cancer cases from the local MDTs for the Northern part of the Merseyside and Cheshire Cancer Network. Local MDTs are at Aintree University Hospital NHS Foundation Trust, Southport and Ormskirk Hospital NHS Trust and St Helen’s and Knowsley NHS Trust.

The Wirral Hospital’s SMDT provides a mirror service for the southern part of the network linked to local MDTs at Warrington and Halton Hospitals NHS Foundation Trust and Countess of Chester Hospital NHS Foundation Trust.

After each local MDT it is the responsibility of the MDT coordinator or the CNS to inform the SMDT coordinator of which patients need to be discussed at the SMDT and arrange for the completed form to be transferred for the SMDT meeting.

4.1 The MDT Co-ordinators

<table>
<thead>
<tr>
<th>Hospital</th>
<th>MDT Co-ordinator</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whiston</td>
<td>Gill Cauldwell</td>
<td>0151 430 2472</td>
</tr>
<tr>
<td>Aintree</td>
<td>Claire Phillips</td>
<td>015 529 8863</td>
</tr>
<tr>
<td>Southport</td>
<td>Heather Steele</td>
<td>01704 704 805</td>
</tr>
<tr>
<td>Royal Liverpool</td>
<td>Carmela Parisi</td>
<td>0151 600 1632</td>
</tr>
<tr>
<td>Warrington</td>
<td>Dawn Ingham</td>
<td>01925 665179</td>
</tr>
<tr>
<td>Countess of Chester</td>
<td>Karen Beckett</td>
<td>01244 365 268</td>
</tr>
<tr>
<td>Wirral</td>
<td>Graeme Totty</td>
<td>0151 678 5111 ext 2213</td>
</tr>
</tbody>
</table>

4.2 Referral to the SMDT
Any prostate cancer patient may be discussed at the SMDT at the request of one of the local teams but all of the cases outlined in table 1 must be referred. Referral
should be made on Wednesday pm to the SMDT co-ordinator by email on a SMDT proforma (Appendix 4). Patient x-ray file should be sent and loaded onto PACS by the MDT co-ordinator prior to the meeting. Pathology slides can be sent with referral to SMDT if a second opinion is necessary.

Table 1: Mandatory referrals to the Urological Oncology SMDT

<table>
<thead>
<tr>
<th>Organ</th>
<th>Refer to SMDT</th>
<th>Local Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>Patients with organ confined or locally advanced prostate cancer undergoing radical therapy in an attempt of cure</td>
<td>Patients not suitable for radical treatment (over 75 or significant co-morbidity)</td>
</tr>
<tr>
<td></td>
<td>Recurrent disease following failed radical therapy</td>
<td>Locally-advanced or metastatic disease suitable for hormone ablation</td>
</tr>
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</table>

4.3 The Specialist Urology Nurses are:

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Clinical Nurse Specialist (CNS)</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whiston</td>
<td>Nerys Williams, Nancy Chisholm, Eleri Philips, Jackie Williams,</td>
<td>0151 430 1898</td>
</tr>
<tr>
<td>Aintree</td>
<td>Claire Parker, Michelle Thomas</td>
<td>0151 529 3484</td>
</tr>
<tr>
<td>Southport</td>
<td>Sheila Coughlan, Ann Wearing</td>
<td>01704 704 301</td>
</tr>
<tr>
<td>Royal Liverpool</td>
<td>Clare Teaney, Salihu Samas</td>
<td>0151 600 1593</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0151 600 1595</td>
</tr>
<tr>
<td>Warrington</td>
<td>Mo Field, Jackie Thompson</td>
<td>01925 665208</td>
</tr>
<tr>
<td>Countess of Chester</td>
<td>Karen Hopkins</td>
<td>01244 365 457</td>
</tr>
<tr>
<td>Wirral</td>
<td>Beverley Rogers, Gill Riley</td>
<td>0151 604 7477</td>
</tr>
</tbody>
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4.4 MDT Documentation of Action Plans and Communication with GP

Patients should be referred using the SMDT proforma (Appendix 2). Each listed case will be discussed by the SMDT. The Chair will ensure that an action plan is formulated and recorded. It is the responsibility of the SMDT coordinator to transcribe the action plan to the electronic format and for this to be reviewed by the Chair. The MDT coordinator will distribute the completed proforma within 1 working day: the electronic copy to SMDT members, the faxed copy to GP and a copy for referral to other MDT’s.

The MDT action plan will include the name of the key worker who will be a core member of the MDT. The CNS from the local team will inform patients about the action plan. If appropriate, patients will be seen in joint clinics to discuss treatment...
options. If patients are referred back to the local MDT for further management, arrangements will be made for them to be seen by an appropriate core member of the local MDT. This process will be coordinated centrally by the Specialist Nurses. After the SMDT, the MDT coordinators liaise with the clinical nurse specialist (CNS) to ensure all clinical plans are carried out. Details of available trials that have been considered will also be included.

5. MANAGEMENT

5.1 Localised prostate cancer

Management of localised disease is controversial. Population based studies of men aged 65-75 indicate no loss of life expectancy for low risk prostate cancer treated expectantly but falls with increasing Gleason score. A randomised trial comparing radical prostatectomy with watchful waiting in early prostate cancer showed in men less than 65 years of age a 5% difference in overall survival after 10 years (number needed to treat 17) with a significant reduction in disease specific mortality and the incidence of metastatic disease. However 70% of subjects in the control arm showed no evidence of metastases after 10 years. This study was performed on patients diagnosed prior to the widespread PSA testing and MRI scanning and therefore probably over-estimates the effect of intervention in contemporary patients. The results of the PRORECT trial will provide an estimate of the benefit from radical surgery, radiotherapy or brachytherapy compared to observation. The Surveillance, Epidemiology and End Results Database suggest that radical prostatectomy and radical radiotherapy are associated with a 15-20% cancer specific survival improvement at 5 years in poorly differentiated tumours. Radical local treatment should therefore be considered for patients with intermediate and high risk disease less than 75 years and in good general health; it is less appropriate in older patients, those with low grade tumours.

Patients outside the criteria for radical treatment should be reviewed in the urology clinic with a clinical nurse specialist and followed up as appropriate. All patients following diagnosis of localised prostate cancer should be given written information about their diagnosis before referral to the combined uro-oncology clinic. Informed consent for radical treatment should be usually obtained following a combined consultation and with full knowledge of the alternative treatments.

Patients with newly diagnosed, organ-confined prostate cancer should be stratified into low, intermediate and high risk groups by the following criteria:

**Fig 1. Risk groups for localised prostate cancer**

<table>
<thead>
<tr>
<th>Risk</th>
<th>Serum PSA (ng/ml)</th>
<th>Gleason Score</th>
<th>Clinical Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>&lt;10</td>
<td>&amp; 6 or less &amp; T1-T2a</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>10-20</td>
<td>or 7</td>
<td>or T2b-2c</td>
</tr>
<tr>
<td>High</td>
<td>&gt;20</td>
<td>or 8-10</td>
<td>or T3-T4</td>
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</table>
Fig 2. Management of localised prostate cancer

<table>
<thead>
<tr>
<th>Low-risk</th>
<th>Intermediate risk</th>
<th>High-risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watchful waiting</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Active surveillance</td>
<td>✓</td>
<td>☐</td>
</tr>
<tr>
<td>Brachytherapy</td>
<td>LDR</td>
<td>LHR/HDR</td>
</tr>
<tr>
<td>Prostatectomy</td>
<td>☐</td>
<td>✓</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>☐</td>
<td>✓</td>
</tr>
<tr>
<td>Cryotherapy</td>
<td>X*</td>
<td>X*</td>
</tr>
<tr>
<td>HIFU</td>
<td>X*</td>
<td>X*</td>
</tr>
</tbody>
</table>

✓ Preferred treatment
☐ Treatment option
X Not recommended
X* Not recommended other than in the context of clinical trials

5.2 Active Surveillance
Active surveillance is a conservative option, suitable for men with low or intermediate risk prostate cancer, which aims to avoid or delay radical treatment. To minimise the risk of under staging or under grading, a repeated MRI scan and re-biopsy should be considered within the first two years. Evidence of disease progression (rising PSA, increased clinical stage or grade) should trigger a recommendation of radical treatment. The recommended protocol is described below:

• PSA should be tested 3-monthly for the first 2 years and then 6-monthly thereafter, yearly after year 5.

• Repeat MRI should be performed between 12 and 24 months after diagnosis to ensure there is no under-grading of the disease and repeat biopsies (trans-rectal or template) considered during the first 2 years.

• Radical treatment should be considered where: "PSA velocity exceeds 1ng/ml/yr" Grade migration occurs on repeat biopsy, MRI or DRE, The patient wishes to end surveillance

5.3 Radical Prostatectomy
Radical prostatectomy is a treatment option for patients with low and intermediate-risk prostate cancers and for those with high risk cancers where there is a realistic prospect of clear surgical margins or as part of multi-modality treatment. Given the lack of reliable comparative data between radical prostatectomy, radical conformal external beam radiotherapy and brachytherapy, all options should be discussed with the patient, who can choose the treatment most acceptable to them. Where
possible, a nerve-sparing radical prostatectomy technique should be used to minimise the likelihood of postoperative erectile dysfunction. Laparoscopic robotic prostatectomy is offered in both centres for suitable patients.

The surgeons performing radical prostatectomy in the MCCN are:

Arrow Park Hospital: Mr R Nambirajan Mr M Kumar
Royal Liverpool University Hospital: Mr PA Cornford Mr R Weston

5.4 Radical Radiotherapy
Radical radiotherapy is a treatment option for all patients with localised carcinoma of the prostate. Dose escalated intensity modulated radiotherapy and image guidance is offered at the Clatterbridge Cancer Centre (Wirral and Aintree). Targeting of the radiation to include the seminal vesicles and/or pelvic lymph nodes is varied according to stage and grade of tumour. Neo-adjuvant hormone ablation using either LHRH agonists or bicalutamide 150mg o.d. has been demonstrated to improve success rates after radiotherapy in patients with intermediate or high-risk disease. This is normally administered for at least 3 months prior to treatment and for a post-treatment period determined by the grade and stage of the cancer, up to 3 years.

5.5 Brachytherapy
Interstitial prostate brachytherapy is a third radical treatment option for low- or intermediate-risk organ-confined prostate cancer with good urinary function and no previous TURP. HDR brachytherapy is recommended for patients with high-risk prostate cancer, in conjunction with a 3 week external beam radiotherapy. Suitable patients counselled by the radiation oncologist locally and referred on to the Brachytherapy team at Clatterbridge.

5.6 Follow-up after radical treatment
Serum PSA should be checked 6 weeks after radical surgery and 3 months after brachytherapy. PSA should then be checked 6- monthly for 2 years and at least yearly thereafter. Stable patients can be discharged after 2 years to a nurse led clinic, telephone follow up clinic or primary care depending on local arrangements.

5.7 Management of complications of radical treatment
Radical prostatectomy routinely results in infertility and loss of ejaculation (to a lesser degree ejaculation volume is affected by radiotherapy); patients should be offered sperm storage where relevant. Erectile dysfunction after surgery or radiotherapy should be treated with phosphodiesterase 5 inhibition initially and referral to specialist ED services arranged if this is not successful. Patients with post-operative stress incontinence should be referred to the local incontinence team. They should be considered for insertion of an artificial urethral sphincter or male continence tape – intraurethral bulking agents are not recommended.

The risk of late complications should form part of the initial discussion of treatment options. A gastroenterologist with expertise in late radiotherapy bowel toxicity should investigate and manage symptomatic patients. Patients with symptoms of bladder overactivity should be referred to an urologist for assessment and treatment.
5.8 Management of relapse after radical treatment
Detection of relapse requires regular review as above and PSA testing. All patients considered for salvage therapy should be discussed at the specialist MDT.

There is no role for MRI or biopsy of the prostate bed after radical prostatectomy. Biochemical relapse after radical prostatectomy (any detectable PSA), with features suggestive of local recurrence (positive surgical margins, delayed recurrence and high PSA doubling-time) should be treated with radical radiotherapy to the prostate bed. Treatment should occur at an early stage (serum PSA <1ng/ml) to maximise the chance of cure. Such patients may be suitable for the RADICAL trial.

Biochemical relapse after radical radiotherapy is defined as 3 consecutive serum PSA rises and PSA >2+nadir ng/ml, at least 3 months apart (Phoenix). Biochemical recurrence precedes clinical recurrence by a number of years in virtually all cases; only fit patients with a PSA <10, no metastatic disease and PSA doubling time >12 months should be considered for salvage therapy. Patients require a positive biopsy before salvage therapy.

Hormone ablation is recommended where there is symptomatic disease, proven metastases or a serum PSA >20 and/or doubling time of less than 3 months.

5.9 Locally Advanced Disease
Definitions of locally advanced disease vary; for the purposes of these guidelines, the term can be taken to apply to bulky T3a, T3b and T4 cancers, or those with pelvic lymphadenopathy, but no evidence of metastases. This group overlaps with that described as ‘high-risk’ localised prostate cancer.

Radical treatment in the form of radical radiotherapy or radical prostatectomy (infrequently) may be appropriate for some patients depending on disease and patient factors. Radical radiotherapy is combined with neo-adjuvant and adjuvant hormone therapy, with possible lymph node treatment, HDR brachytherapy or dose painting) with neo- adjuvant/adjuvant LHRH analogues.

6. METASTATIC DISEASE
Metastatic prostate cancer can be effectively treated by hormone ablation. This may take the form of subcapsular bilateral orchidectomy, LHRH analogues (tumour flare should be prevented with bicalutamide 50mg o.d. or cyproterone acetate 50mg t.d.s. for 1-2 weeks pre-injection), LHRH antagonists or bicalutamide monotherapy (where patients wish to attempt to preserve potency). LHRH antagonists should be considered where there is a risk of impending cord compression. Intermittent hormone ablation is equivalent to continuous treatment (8 month LHRH analogues followed by a period of observation until the PSA >10 ng/ml).

6.1. Toxicity of long-term hormone therapy
- Osteoporosis: Screening (Bone mineral density measurement) and treatment (regular weight bearing exercise, calcium and vitamin D supplements and oral bisphosphonates) is recommended.
- Hot flushes: cyproterone 50mg o.d., Provera 10-20mg o.d., clonidine 0.1mg o.d. or b.d., bicalutamide 50mg o.d. or Prozac 10mg o.d. all can improve symptoms.
• Breast enlargement and/or discomfort are a common event with Bicalutamide monotherapy. A single dose of radiotherapy (8Gy) to the breast buds prior to treatment can prevent this; tamoxifen 10 mg daily to weekly helps with discomfort.

• Weight gain, metabolic syndrome: metformin, diet exercise

7. HORMONE-INDEPENDENT PROSTATE CANCER

Hormone-independence may be defined as 3 consecutive PSA rises despite castrate levels of testosterone. Many men benefit from newer treatment options (Fig 3) and should be referred to the SMDT to consider entry into clinical trials and involvement of oncologists and palliative care physicians. All patients with metastatic and hormone-independent prostate cancer should be aware of the symptoms of clinical progression and be encouraged to seek medical attention urgently, should these present.

7.1 Symptomatic metastases

Local field radiotherapy is very effective for controlling bone pain unresponsive to hormone therapy. Where there are multiple bones involved, radioactive isotope therapy with Ra223 can be considered.

7.2 Obstructive uropathy

Decompression of the upper urinary tract by percutaneous nephrostomy or intracorporeal stenting can restore renal function but should only be offered after an assessment of the patient’s wishes and quality of life.

9. PATIENT AND CARER INFORMATION

The Uro-Oncology team will discuss the diagnosis, MDT action plan and care pathway with patients and carers. All patients will be offered clear and comprehensive information in a format, which is suitable to their needs and stage of treatment in the cancer journey.

Patients with visual and hearing impairment will be offered aids to understand the patient information. Interpreter services are available for patients via the patient advisory liaison office. Many aspects of palliative care are also applicable earlier in the course of the illness in conjunction with anti-cancer or other treatment.

Following information should be provided:

• Nature of the disease
• Diagnostic procedures being undertaken
• Treatment options available
• Outcomes of treatment in terms of benefits, risks and side effects
• Management of side effects of treatment, and contact details for advice
• Details of future appointments/contacts
• The role and responsibilities of the clinical nurse specialist and MDT
• Contact details of clinical nurse specialist/key worker for urological cancers
• Contact details of clinical nurse specialist for other individual issues (stoma care/continence advice/sexual issues/body image issues) as appropriate
• Cancer information such as Prostate Cancer Charity Toolkit
• Contact details of the local Prostate Cancer Support Group.
• Appropriate patients should receive a copy of letters (surgeon/oncologist /GP

Fig 3. Management of metastatic prostate cancer

Newly diagnosed or relapsing
Biopsy not required if high PSA and positive bone scan

First line hormonal therapy
• LHRH analogues, LHRH antagonists or bilateral orchidectomy should be offered
  • Intermittent androgen withdrawal may be offered
  • Combined androgen blockade is not recommended

Hormone refractory disease
• Discuss at MDT and refer to oncology or palliative care if needed

Chemotherapy  
• Docetaxel
  • Up to 10 cycles
abiraterone  
• enzalutamide
Ra 223

Second line chemotherapy
Dexamethasone  
Bisphosphonate
local radiotherapy

10. PALLIATIVE CARE
Palliative Care is defined by the World Health Organisation (WHO 2002) as:
“...the active holistic care of patients with advanced progressive illness. Management of pain and other symptoms and provision of psychological, social and spiritual support is paramount. The goal of palliative care is achievement of the best quality of
life for patients and their families. Many aspects of palliative care are also applicable earlier in the course of the illness in conjunction with other treatments.”

Many patients with advanced incurable prostate cancer will not require referral to specialist palliative care, but will find that their supportive care can be managed by their GP and district nursing team. Patients felt to be in the last 6 – 12 months of life should be included on the GP practice’s Supportive Care Register (also known as a GSF register). This will ensure that the needs of both the patient and their carers are regularly assessed and will promote discussions about Advance Care Planning. A Holistic Needs Assessment should be undertaken to identify the patient’s needs and ensure the care plan meets those needs.

Patients with the following problems may benefit from referral to specialist palliative care services:

- Pain or other symptoms which are difficult to control
- Complex psychological or spiritual issues
- Complex family dynamics including the presence of young children in need of support
- Advice required for complex placement issues

Accessing Specialist Palliative Care Advice  Specialist Palliative Care Advice is available in each locality from the community and hospital specialist teams, and also from the local Specialist Inpatient Unit. Many inpatient units are able to give 24 hour telephone advice to healthcare professionals.

Useful resources  For patients - Macmillan support line: 0808 808 0000

For health care professionals – Holistic Needs Assessment for people with cancer:  

11. DATA COLLECTION

All newly presenting patients with a urological cancer are registered on BAUS. The minimum data set should be collected via the Somerset Cancer Register. Radiotherapy and chemotherapy information will be collected by the Oncology team. A complex operation data set should be completed for patients who have had:

- Radical prostatectomy
- Cystectomy
- Nephrectomy
- Nephroureterectomy
- Cryotherapy and HIFU