Prostate cancer: lessons to be learned from breast cancer

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There are a number of parallels between the management of breast cancer and prostate cancer. However, breast cancer has a much higher profile than prostate cancer and this has driven investment in research. Roger Kirby looks at what lessons can be learned from how breast cancer management has developed and what the future holds for prostate cancer.

Throughout the Western world, during the course of a lifetime, either prostate cancer or breast cancer will, in all probability, affect one in eight individuals, according to their sex. Because women have been much more proactive than men in lobbying government for investment, as well as having been more motivated to raise funds for research through charities, progress in the efficiency and effectiveness of diagnosis and management of breast cancer has been greater than that of prostate cancer.

It seems appropriate, therefore, to consider what lessons can be learned from the management of breast cancer that might be used to improve the diagnosis and treatment of prostate cancer.

SCREENING

Screening by mammography is central to the diagnosis of breast cancer, and women are routinely offered regular checks on the NHS. An abnormal mammogram is usually a trigger for a precisely targeted breast biopsy. The percentage of positive biopsies is an important quality control, as it is obviously important to avoid too many women having unnecessary biopsies of breast lesions that turn out to be benign. By contrast, there is currently no organised screening for prostate cancer, despite the evidence from Schroder that many lives could be saved. Instead, diagnosis has usually been based on case finding of individuals with abnormal values of prostate-specific antigen (PSA) in their bloodstream.

High-profile charity activity is just one area where prostate cancer can learn from breast cancer (photo courtesy of Against Breast Cancer – www.againstbreastcancer.org.uk)

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Only around 1 in 5 men with a PSA value between 4 and 10ng/ml will be found to harbour a prostate cancer if they undergo a biopsy.4 However, prostate biopsies performed via the transrectal route carry an approximate 2% risk of potentially severe infection.3 As a consequence, there has been a move by urologists to employ multiparametric magnetic resonance imaging (MpMRI) to detect and localise prostate cancer. Using the latest MRI technology, prostate cancers can be increasingly reliably distinguished from normal prostate tissue and benign prostatic hyperplasia (BPH). Unnecessary biopsies can thereby be avoided. Moreover, the total number of biopsies required can be reduced by targeting the biopsies towards the abnormal area detected on the MRI scan.4 In addition, the transperineal route is used increasingly for prostate biopsies to obviate the risk of biopsy-induced infection.

MOLECULAR SCRUTINY
In breast cancer, the biopsy specimen is not only examined under the microscope, but is also subjected to detailed molecular scrutiny, in particular to ascertain whether it is positive for oestrogen receptors (ER positive), human epidermal growth factor receptor 2 (HER2 positive) or both. An ER-negative and/or HER2-negative result indicates a poor prognosis, and is also predictive of a lack of response to hormonal and HER2-targeted therapy. The commercially available Oncotype DX analysis is based on analysis of the expression of a panel of genes capable of providing prognostic information, and this may influence treatment decisions. The MammaPrint test is another gene-based analysis, which is performed on frozen rather than paraffin-preserved sections.

Recently, the development of molecular genetic testing has refined the prognosis and prediction of the need for further therapy in men with prostate cancer.5 The Prolaris test analyses the expression of a number of so-called ‘cell cycle progression’ (CCP) genes. The result is expressed numerically; the greater the number, the more aggressive the behaviour of the cancer is likely to be if left untreated. The Oncotype DX molecular prognostic indicator for prostate cancer examines a different panel of genes, and similarly aims to predict the future behaviour of the tumour. Both tests can help refine treatment decisions. These and other tests are described more fully in the May/June 2015 issue of Trends.

PRECISION SURGERY AND RADIOTHERAPY
Breast cancer surgery has evolved from radical mastectomy and extensive lymphadenectomy to much less mutilating lumpectomy and sentinel node sampling. Similarly, prostate cancer surgery, which has been confirmed as more effective than watchful waiting in higher risk cases,5,7 has been transformed, firstly by the introduction of laparoscopic radical prostatectomy, and more recently by the use of robotically-assisted total prostate excision. These minimally invasive techniques have dramatically reduced blood loss, improved overall reliability and made the patient experience of radical prostate surgery far more acceptable. In higher risk cases, the lymph nodes in both obturator fossae can be sampled to confirm that the disease is localised. Although some interesting research into prostate-sparing techniques has been undertaken, including high intensity focused ultrasound and electroporation, these have not been confirmed as effective in the longer term, and are therefore still regarded as experimental. Lower risk cases are increasingly managed by active surveillance.8

As in breast cancer treatment, a variety of ways of delivering radiotherapy to the target organ have evolved. The majority of patients are still treated with a combination of seven weeks of external beam radiotherapy and prolonged androgen ablation. Robotically-controlled radiotherapy can be delivered over a shorter period by CyberKnife technology. Brachytherapy, which involves the implantation of radioactive seeds, remains popular in the USA, but less so in the UK. Proton beam therapy is not yet available in the UK, but plans are afoot to introduce this technology. The cost of proton beam delivery units has fallen from more than £100 million to around a third of that amount.

BEYOND HORMONAL THERAPY
Unlike the multimodality therapy used in high-risk breast cancer, patients with prostate cancer who present with metastatic disease have traditionally been managed by hormonal manipulation alone. This paradigm seems likely to change, however, following the recent presentation of the results of the STAMPEDE trial by Professor Nick James at the American Society of Clinical Oncology (ASCO). In this large study, patients with metastatic prostate cancer were randomised to standard androgen ablation, androgen ablation plus docetaxel chemotherapy, or androgen ablation plus docetaxel and the bisphosphonate zoledronic acid. The results reveal a statistically significant improvement in survival in the men treated with androgen ablation and docetaxel, but no additional advantage from the bisphosphonate. These data seem likely to be a game-changer. From now on, the
majority of men presenting with metastatic prostate cancer seem likely to be offered a course of docetaxel in addition to androgen ablation treatment.

Most hormone-dependent cancers eventually become resistant to treatment after one to three years and resume growth despite androgen ablation therapy. Previously considered ‘hormone-refractory prostate cancer’ or ‘androgen-independent prostate cancer’, the term ‘castration-resistant’ has replaced ‘hormone-refractory’, because while they are no longer responsive to castration treatment (reduction of available androgen/testosterone/DHT by chemical or surgical means), these cancers still show reliance on hormones for androgen receptor activation.

Before 2004, all treatments for castration-resistant prostate cancer (CRPC) were considered palliative and not shown to prolong survival. However, there are now several treatments available to treat CRPC that improve survival. Chemotherapy utilising the taxane antimitotic agent docetaxel has been used as treatment for CRPC, with a median survival benefit of 2 to 3 months. Cabazitaxel (Jevtana) is a second-line chemotherapeutic agent with a proven 5-month survival advantage over placebo.11 Enzalutamide (Xtandi) is another second-line hormonal agent with a proven 5-month survival advantage over placebo.11

PUBLIC AWARENESS AND CHARITY
Almost certainly, the most important lesson to be learned from breast cancer is how public awareness and charity action to support research can transform patient care and improve survival. There is little doubt that the work of Breast Cancer and Breast Care, as well as that of other charities including Cancer Research UK, have had a major impact on the way in which breast cancer is diagnosed and treated. For men, Prostate Cancer UK (PCUK) has established an impressive research programme focused on improving outcomes by developing better markers and prognostic indicators, and less invasive, less morbid therapies. In addition, The Urology Foundation (TUF) has also made an important contribution.

POSITIVE PROSPECTS
In conclusion, the prospects for the very many men who are currently diagnosed with localised or advanced prostate cancer are certainly better now than ever before. Although we still need a better marker than PSA, the use of multiparametric MRI to differentiate between those who do and those who do not require a biopsy seems capable of reducing unnecessary biopsies. In those individuals whose biopsies are positive and the disease is still localised, a watch-and-wait policy of ‘active surveillance’ is increasingly utilised for those with low-risk Gleason 3+3=6 cancer. Higher-risk cancers can be most reliably cured by surgery, but new radiotherapy options look very promising. The STAMPEDE trial looks likely to transform the situation in advanced disease through the use of docetaxel chemotherapy in conjunction with androgen ablation at the time of diagnosis. Eventually, when these men relapse, treatment with either abiraterone or enzalutamide has been shown to improve survival and quality of life.

Declaration of interests
Professor Roger Kirby has delivered lectures and chaired meetings on behalf of Pfizer, Astellas and Myriad Genetics.

REFERENCES