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Original Article

Imaging for Prostate Cancer

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ABSTRACT:
The increased incidence and awareness of prostate cancer, together with developments in treatment, has generated a significant need for appropriate imaging to detect and stage the tumour initially, guide radiotherapy delivery and monitor disease on follow-up. Transrectal ultrasound is usually the first imaging investigation, and its role is primarily to guide prostate needle biopsy. It also has an established role in imaging-guided treatments, such as brachytherapy. Magnetic resonance imaging has developed considerably in recent years, and is now the principal staging investigation before treatment. Innovations in functional and biological imaging of the prostate will, in the future, contribute valuable information to support parallel developments in radiotherapy techniques for prostate cancer. The ultimate goal is a co-ordinated diagnostic and therapeutic approach to individualise and optimise the treatment plan for patients with prostate cancer. Carey, B. M. (2005). *Clinical Oncology* **17,** 553–559

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Introduction

The increased detection of prostate cancer has generated new challenges for diagnostic imaging and radiotherapy. Improvements in radiotherapy technique, and the desire to optimise the treatment for individual patients, have demanded more precise delineation of the location and extent of prostate cancer. Appropriate patient selection needs high quality and clinically relevant imaging that is best managed through multidisciplinary working, in which diagnostic radiologists can understand the clinical issues raised and radiotherapists can appreciate the indications and limitations of the imaging available to them.

Prostate imaging began with the introduction of transrectal ultrasound in the early 1970s [1], and has developed into a multimodality approach that has benefited considerably from technological developments in the past few decades. Our increased awareness of prostate cancer as a major cause of male cancer mortality has challenged the power of imaging to detect aggressive prostate cancers while still confined to the prostate gland. Traditional morphologically based prostate imaging is now being complemented by functional and molecular imaging techniques that yield information about the biology of prostate cancer. The ultimate goal is to identify the most appropriate treatment strategy for each patient while minimising treatment-associated morbidity.

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The introduction of serum prostate-specific antigen (PSA) has improved the earlier diagnosis and facilitated treatment monitoring of prostate cancer; however, the clinical dilemmas of how to institute active treatment for this disease remain. Clinical factors are paramount to the choice of treatment used, but imaging can contribute to this clinical decision by helping to identify more aggressive and potentially life-threatening cancers that might benefit from early intervention. PSA-based prostate cancer detection has led to a gradual downward stage migration at initial diagnosis, and nowadays most newly diagnosed cases have intermediate-grade, organ-confined prostate cancer [2]. The effect on diagnostic imaging has been significant, with increased emphasis on early diagnosis in response to elevation in the serum PSA. Clinicians can use nomograms, such as Partin's Tables [3], to counsel individual patients and make clinical decisions about management; however, currently, we have no reliable imaging method to distinguish prostate cancers that are biologically aggressive from those that may have a more indolent clinical course in life. This need to stratify prostate cancers by their life-threatening potential and tailor individual treatments accordingly is driving the development of molecular-based prostate cancer imaging, in particular. Our future understanding and delineation of the genetic factors underlying the pathogenesis of prostate cancer will become an integral part of the management of the patient and facilitate the integration of radiotherapy into the treatment plan.

Imaging-guided delivery of radiation therapy to the prostate is now a sophisticated process that uses three-dimensional reconstruction and targeting of tumour target volumes. Optimal integration of imaging data into the

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planning and delivery of radiation requires anatomical knowledge of the tumour target as well as technical expertise in volume-based treatment-planning techniques. The use of additional information from functional imaging and, ultimately, molecular imaging will require careful collaboration between radiologists and oncologists, closely supported by medical physics.

The purpose of this paper is to review the current status of diagnostic imaging in the diagnosis of prostate cancer, and the role of imaging in the treatment of prostate cancer.

Transrectal Ultrasound

Transrectal ultrasound is widely used as the initial investigation for prostate cancer, and has benefited from major technical advances since its introduction over 3 decades ago. In the early days of prostate ultrasound, before the advent of serum PSA testing, many cancers presented at a relatively advanced stage, and were typically visible as hypoechoic areas in the peripheral gland. Nowadays, with the earlier PSA-based detection of a larger proportion of T1c tumours, many cancers are not discernible even on modern high-resolution ultrasound. Central gland tumours cannot usually be distinguished from hyperplastic nodules. Furthermore, transrectal ultrasound has a high false-positive rate, as only about 20% of all hypoechoic nodules are actually malignant [4,5]. Despite advances in ultrasound technology, it became clear in the 1980s that ultrasound alone lacked both the sensitivity and specificity needed for early detection of prostate cancer. Currently, it has to be acknowledged that conventional transrectal ultrasound is neither sufficiently sensitive nor specific for the detection of prostate cancer, and it has limited use for staging purposes [6–8].

In clinical practice, the main use of ultrasound in diagnosis is to guide needle placement for prostate biopsy. Conventional transrectal ultrasound is not sufficiently sensitive for targeted biopsy alone, and systematic biopsy is advocated to maximise the yield from prostate biopsy. Ultrasound can demonstrate the peripheral zone of the gland reliably, where most cancers originate, and targeted biopsy of hypoechoic lesions can supplement systematic biopsy of the whole prostate gland. Consensus is lacking on the number or location of biopsy samples to be obtained, and efforts to improve the specificity of biopsy with refinements in ultrasound technique are countered by the trend at many institutions to simply increase the number of biopsies carried out on individual patients. The imaging data available from transrectal ultrasound is, therefore both subjective and variable, and reinforces the fact that transrectal ultrasound is operator-dependent, and prostate biopsy remains a sampling process.

Functional imaging is now possible with colour Doppler and contrast-enhanced prostate ultrasound [9,10]. As with other dynamic vascular-enhanced imaging, these ultrasound enhancements exploit the neovascularisation associated with prostate cancer (Fig. 1). Increased vessel density has been shown to be associated with pathological stage and cancer-specific survival [11–13]. The routine use of targeted biopsy purely on the basis of high-frequency colour or power Doppler imaging is not advocated, as these techniques will miss a substantial number of cancers. The sensitivity for cancer detection with contrast (microbubble)-enhanced ultrasound may be improved with the introduction of harmonic ultrasound imaging, but it remains to be established whether this will become a cost-effective and clinically relevant addition to diagnostic prostate cancer imaging.

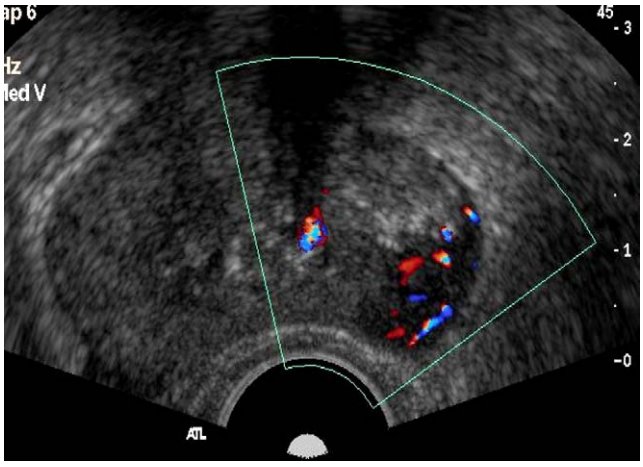

Fig. 1 – Transrectal ultrasound scan showing hypervascular tumour in left peripheral gland.

Transrectal ultrasound has probably reached a plateau for the present in its potential to detect prostate cancer and cancer staging. Further developments, such as three-dimensional prostate ultrasound, are unlikely to increase the diagnostic yield significantly, and adoption of more standardised biopsy protocols will be more clinically relevant. Ultrasound elastography is at an early stage of development, and its prospective role in prostate imaging is yet unknown. This new imaging technique examines the vibroelastic properties of tissue, and measures the relative stiffness of normal and pathological structures. Just as the palpating finger detects abnormal prostate, the hope is that this quantifiable technique will allow new, more sensitive, information about the nature of the prostate under study [14]. Prostate imaging with transrectal ultrasound does have a core role in imaging-guided radiotherapy, such as brachytherapy. Prostate brachytherapy is perhaps the ultimate conformal radiotherapy technique for the treatment of prostate cancer. It can be delivered with either permanent seed implants, typically Iodine-125 or removable implants using iridium. These radiotherapy techniques use transrectal ultrasound image guidance for transperineal source placement within the prostate, and maturing data now compare favourably with results from radical prostatectomy series [15,16]. Although, to date, the entire gland has been treated as a uniform target, developments in brachytherapy techniques may in future take advantage of newer functional and biological imaging methods that allow precise tumour localisation, and, therefore, potential radiation boosts within the prostate itself. The fusion of data from magnetic