



Overview

Focal Therapy for Prostate Cancer: Rationale and Treatment Opportunities



V. Kasivisvanathan^{*†}, M. Emberton^{*†‡}, H.U. Ahmed^{*†}

^{*}Division of Surgery and Interventional Sciences, University College London, UK

[†]Urology Department, Division of Surgery, University College London Hospitals Trust, London, UK

[‡]NIHR UCLH/UCL Comprehensive Biomedical Research Centre, London, UK

Received 17 February 2013; received in revised form 21 March 2013; accepted 8 May 2013

Abstract

Focal therapy is an emerging treatment modality for localised prostate cancer that aims to reduce the morbidity seen with radical therapy, while maintaining cancer control. Focal therapy treatment strategies minimise damage to non-cancerous tissue, with priority given to the sparing of key structures such as the neurovascular bundles, external sphincter, bladder neck and rectum. There are a number of ablative technologies that can deliver energy to destroy cancer cells as part of a focal therapy strategy. The most widely investigated are cryotherapy and high-intensity focussed ultrasound. Existing radical therapies, such as brachytherapy and external beam radiotherapy, also have the potential to be applied in a focal manner. The functional outcomes of focal therapy from several phase I and II trials have been encouraging, with low rates of urinary incontinence and erectile dysfunction. Robust medium- and long-term cancer control outcomes are currently lacking. Controversies in focal therapy remain, notably treatment paradigms based on the index lesion hypothesis, appropriate patient selection for focal therapy and how the efficacy of focal therapy should be assessed. This review articles discusses the current status of focal therapy, highlighting controversies and emerging strategies that can influence treatment outcomes for the future.

© 2013 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.

Key words: Focal ablation; focal therapy; future perspective; outcomes; prostate cancer; rationale

Statement of Search Strategies Used and Sources of Information

The MEDLINE database was searched using the PubMed Portal with the following search terms: '(focal and (therapy or radiotherapy or radiation or high-intensity focal ultrasound or laser or photodynamic or electroporation or ferromagnetic or cryotherapy or radiofrequency ablation or brachytherapy or microwave or proton or cyberknife)) and prostate cancer'. The search was expanded by looking through related articles and the references of included papers for further relevant papers.

Introduction

Focal therapy is an emerging treatment modality for localised prostate cancer that aims to reduce the morbidity

seen with radical therapy, while maintaining cancer control. This review summarises the rationale for focal therapy, its current status and future perspectives.

Rationale for Focal Therapy

Current options for men with localised prostate cancer include active surveillance and radical therapy. The ideal treatment would provide oncological cure with few side-effects. Although radical therapy offers treatment with curative intent there can be a high rate of associated functional complications, with erectile dysfunction seen in 24–90%, urinary incontinence in 2–72% and rectal toxicity in 2–15% [1–4]. These complications detrimentally affect quality of life [2,5].

In the era of prostate-specific antigen (PSA) screening, there has been an increase in the detection of prostate cancer [6]. Men are being diagnosed at an earlier stage and the proportion of men with low-risk disease is increasing [7,8]. The debate over population-based PSA screening continues, with differing findings from the European Randomised Study

Author for correspondence: V. Kasivisvanathan, Division of Surgery and Interventional Science, University College London, Charles Bell House, 67–73 Riding House Street, London W1W 7EJ, UK. Tel: +44-3447-9194; Fax: +44-3447-9303.

E-mail address: vk103@ic.ac.uk (V. Kasivisvanathan).

of Screening for Prostate Cancer (ERSPC) and the Prostate, Lung, Colorectal and Ovarian (PLCO) randomised controlled trials leading to the recent US Preventive Services Task Force recommendation against population-based PSA screening [9,10]. However, the high rates of contamination of the control arms in ERSPC Rotterdam Section (31%) and the PCLO trial (40–52%) [10,11] and the emerging patterns of PSA screening in other countries [12] show that physicians and men favour PSA screening. These men may be unnecessarily exposed to the harms of radical treatment. The Prostate cancer Intervention Versus Observation Trial (PIVOT) study, which randomised men diagnosed during the early PSA screening era between watchful waiting and radical surgery, suggests that men with low-risk localised prostate cancer have no benefit from treatment with regards to prostate cancer-specific mortality [13]. Other minimally invasive options for these men should be actively considered.

Active surveillance takes advantage of the slow progression of low-risk disease, allowing about two-thirds of men who enter an active surveillance programme to avoid radical treatment and its side-effects [14,15]. The mortality rates for patients on active surveillance is low at 0–1%, but due to the inherent errors of the diagnostic transrectal biopsy, it is unclear which cancers are intermediate- and high-risk at baseline and there are concerns that delaying radical therapy may lead to disease progression and missing the opportunity for curative treatment. Furthermore, the anxiety and burden of repeated hospital visits, PSA tests and biopsies to the individual and healthcare systems should not be underestimated [16–19]. This may explain why less than 8% of eligible patients in the USA and 39% of those eligible in the UK opt for active surveillance [7,20].

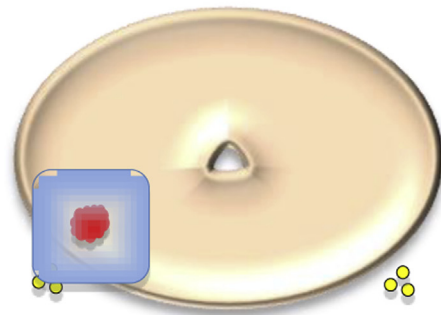
Focal therapy has been proposed as an alternative minimally invasive technique that aims to destroy the tumour itself or the region containing the tumour in order to preserve surrounding non-cancerous tissue. The goal is to maintain disease control at acceptable levels, while preserving erectile, urinary and rectal function by minimising damage to the neurovascular bundles, external sphincter, bladder neck and rectum. This approach has gained increasing attention over the last 5 years, with encouraging evidence accumulating on functional outcomes and short-term oncological outcomes [21–25].

Focal Therapy Treatment Strategies

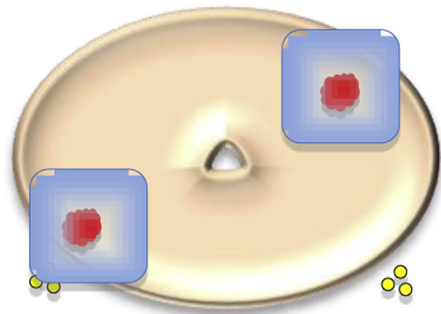
A number of focal therapy strategies have commonly been used (Figure 1). In general, they differ by whether they attempt to ablate specific cancer foci (lesion-targeted therapy) or whole regions containing cancer (region-targeted therapy).

Focal therapy is classically considered for men with a single discrete tumour or several foci in one half of the prostate. A recent systematic review showed that 13–67% of patients have unifocal or unilateral disease [26]. A further strategy, which extends the proportion of men eligible for focal therapy treatment, is the index lesion ablation strategy. This involves treating only the largest and highest-grade tumour (the index lesion), while sparing small foci

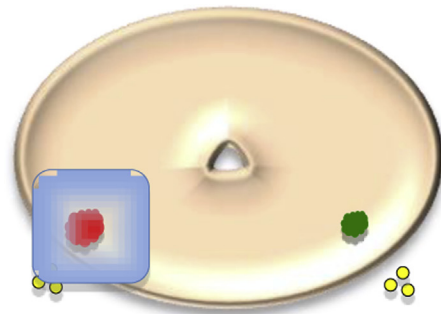
a Lesion-targeted unifocal ablation



b Lesion-targeted multifocal ablation



c Lesion-targeted index lesion ablation



d Region-targeted hemiablation

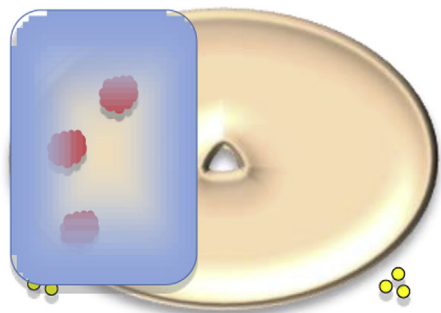


Fig 1. Diagrammatic representation of focal therapy strategies. The red lesion represents clinically significant prostate cancer and the green lesion represents clinically insignificant prostate cancer. The yellow circles represent the neurovascular bundles and the blue rectangle represents the ablation zone. Lesion-targeted therapy is represented by (a)–(c). In (a), unifocal ablation preserves the contralateral neurovascular bundle. In (b), although clinically significant cancer is present bilaterally, one neurovascular bundle is still spared. In (c), clinically insignificant cancer near the second neurovascular bundle is not treated. Only the index lesion is treated, allowing preservation of one neurovascular bundle. In (d), an example of region-targeted therapy, hemi-ablation, is presented.

Download English Version:

<https://daneshyari.com/en/article/5698635>

Download Persian Version:

<https://daneshyari.com/article/5698635>

[Daneshyari.com](https://daneshyari.com)