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European Association of Urology

Prostate Cancer

Focal Therapy: Patients, Interventions, and Outcomes—A Report from a Consensus Meeting

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Article info

Article history:
Accepted September 11, 2014

Keywords:
Prostatic neoplasms
Consensus development conference
Organ-sparing treatments

Abstract

Background: Focal therapy as a treatment option for localized prostate cancer (PCa) is an increasingly popular and rapidly evolving field.
Objective: To gather expert opinion on patient selection, interventions, and meaningful outcome measures for focal therapy in clinical practice and trial design.
Design, setting, and participants: Fifteen experts in focal therapy followed a modified two-stage RAND/University of California, Los Angeles (UCLA) Appropriateness Methodology process. All participants independently scored 246 statements prior to rescoring at a face-to-face meeting. The meeting occurred in June 2013 at the Royal Society of Medicine, London, supported by the Wellcome Trust and the UK Department of Health.
Outcome measurements and statistical analysis: Agreement, disagreement, or uncertainty were calculated as the median panel score. Consensus was derived from the interpercentile range adjusted for symmetry level.
Results and limitations: Of 246 statements, 154 (63%) reached consensus. Items of agreement included the following: patients with intermediate risk and patients with unifocal and multifocal PCa are eligible for focal treatment; magnetic resonance imaging–targeted or template-mapping biopsy should be used to plan treatment; planned treatment margins should be 5 mm from the known tumor; prostate volume or age should not be a primary determinant of eligibility; foci of indolent cancer can be left untreated when treating the dominant index lesion; histologic outcomes should be defined by targeted biopsy at 1 yr; residual disease in the treated area of $\leq$3 mm of Gleason 3 + 3 did not need further treatment; and focal retreatment rates of $\leq$20% should be considered clinically acceptable but subsequent whole-gland therapy deemed

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http://dx.doi.org/10.1016/j.eururo.2014.09.018

a failure of focal therapy. All statements are expert opinion and therefore constitute level 5 evidence and may not reflect wider clinical consensus.
Conclusions: The landscape of PCa treatment is rapidly evolving with new treatment technologies. This consensus meeting provides guidance to clinicians on current expert thinking in the field of focal therapy.
Patient summary: In this report we present expert opinion on patient selection, interventions, and meaningful outcomes for clinicians working in focal therapy for prostate cancer.

1. Introduction

Focal therapy is gaining interest as a potential treatment for localized prostate cancer (PCa) [1]. In this rapidly evolving field, there is a need for robust trial designs to evaluate tissue-preserving strategies so that clinically meaningful outcomes can be presented to physicians and their patients. However, there has been much debate with respect to the ideal patient group, the type of intervention, and acceptable outcomes [2].

Researchers have been involved in a phased evaluation of focal therapy over the last 5 yr, culminating in a number of published studies summarized in a recent systematic review [1]. One of the next phases will involve greater targeting precision through the possible incorporation of accurate preoperative imaging—such as multiparametric magnetic resonance imaging (mp-MRI) to define the desired boundaries of ablation—at the time of the operative intervention.

An international consensus meeting of experts was convened to provide guidance on patient eligibility, interventions, and meaningful outcome measures for focal therapy in clinical practice and to assist in the development of a new focal therapy trial that will incorporate image fusion in the delivery of the ablative process. A number of consensus groups and panels reporting on focal therapy have used informal or formal consensus methodology [3–5]. Our current report used the formal RAND/University of California, Los Angeles (UCLA) Appropriateness Methodology as a two-stage consensus process.

2. Methods

The consensus panel consisted of 15 voting members, 1 independent chairperson with expertise in consensus methodology (J.vdM.), and 4 nonvoting observers (I.A.D., L.S., N.M., and S.W.). Members were selected for their expertise in focal therapy and clinical trials. Their background and experience are outlined in Table 1. The meeting was supported by a grant from the Wellcome Trust and the UK Department of Health to fund the evaluation of an MRI/ultrasound fusion device for targeted biopsy and focal therapy. Available funding limited the total number of participants.

The consensus process used the RAND/UCLA Appropriateness Methodology format [6]. The 237 items on which to derive consensus were formulated in two initial small-group rounds comprising I.A.D., C.M.M., J.vdM., S.W., A.M., and H.U.A., informed by current literature. Prior to a face-to-face meeting, all participants were asked to independently score these statements on a scale ranging from 1 (strongly disagree) to 9 (strongly agree).

At the face-to-face meeting, the premeeting scores were displayed graphically (Fig. 1). After discussion, each panel member independently rescored all questions. Rewording and addition of statements were allowed if the original text was considered by the group to be ambiguous or not fully comprehensive.

After the meeting, agreement levels (disagree, uncertain, agree) for each statement were calculated as the median panel score. A median of 1–3 indicated disagreement with the statement; 4–6, uncertainty; and 7–9, agreement. The level of consensus (interpanel score variation) for each statement was calculated by the interpercentile range adjusted for symmetry (IPRAS) method [6]. An IPRAS score >0 indicates consensus among the group, with higher scores indicating a stronger consensus level. Only statements reaching agreement or disagreement can be included in these recommendations.

The results presented in this paper are expert opinion and therefore constitute level 5 evidence.

3. Results

All participants returned questionnaires prior to the meeting, and all attended the full day. From the 237 original statements, 17 additional statements were added, 46 were reworded, and 8 were removed during the panel discussion. The removed questions were considered to be unnecessary or outside the scope of this meeting.

As a result, 246 final statements were rescored at the face-to-face meeting. Consensus was reached for 154 statements (63%), indicating agreement for 85 and disagreement for 69. The full consensus document with final statements, agreement level, and IPRAS levels is included in Supplementary Table 1.

3.1. Definition of focal therapy

Various minimally invasive tissue ablation strategies exist for the treatment of localized PCa [1]. In clinical trials, ablation strategies have included hemi-ablation, so-called hockey-stick ablation (extended hemi-ablation), and quadrant ablation [2]. The panel agreed that focal therapy should be defined as ablation of the dominant or index lesion only. There was agreement that quadrant ablation is a possible focal therapy strategy, but with a lower level of consensus than lesion-only ablation.

Given that the ablative pattern of brachytherapy or cryotherapy differs from that of electroporation and high-intensity focused ultrasound, it was agreed that the morphology of the disease should guide the selection of the energy source to be used. If only one source of ablation is available, there was agreement that this situation would limit the type of focal therapy that could be delivered.