NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of transperineal template biopsy and mapping of the prostate

The prostate is a small gland near a man's bladder. A test to collect a sample of tissue may be needed when there are concerns about possible prostate cancer.

Transperineal template biopsy involves the insertion of many fine needles though the skin between the scrotum and the anus in order to obtain tissue samples from the prostate for testing. The procedure is carried out with the patient under local or general anaesthesia.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in December 2009.

Procedure name

- Transperineal template biopsy and mapping of the prostate

Specialty societies

- The British Association of Urological Surgeons

Description

Indications and current treatment

Prostate biopsy in patients with suspected prostate cancer is usually carried out by a transrectal needle biopsy. Transperineal template biopsy is intended primarily for patients with suspected prostate cancer who have had a negative or inconclusive transrectal biopsy.

The use of transperineal template biopsy of the prostate has also been proposed for other indications including mapping to determine the location and extent of prostate cancer as a guide to focal treatment (such as ablation); as part of active surveillance of low-risk localised prostate cancer through repeated biopsies; and as a reference test for evaluation of new methods of imaging the prostate.

One pathology specimen grading system commonly used with prostate biopsy sample is the Gleason score. This gives a total score of 2 (most normal looking) to 10 points (the most abnormal looking).

What the procedure involves

The proposed advantages of this procedure are that it can obtain a relatively large number of tissue samples from across the prostate, in three dimensions, in order to help detect small lesions. This may improve the detection of small cancers compared with other biopsy methods. The transperineal approach also aims to lower risks of infection complications compared with transrectal biopsy.

A template guided biopsy is carried out with the patient under local or general anaesthesia and under intravenous prophylactic antibiotic coverage. The procedure is done under transrectal ultrasound guidance. A grid template (similar to that used for insertion of brachytherapy implants) with multiple holes approximately 5 mm apart is placed on the perineum. Biopsies are taken throughout the prostate gland using sampling needles inserted to a range of distances into the gland. The catheter is removed before the patient is discharged.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to transperineal template biopsy of the prostate. Searches were conducted of the following databases, covering the period from their commencement to 1 December 2009 and updated to 28 May 2010: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published

studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with suspected prostate cancer.
Intervention/test	Transperineal template biopsy of the prostate.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on approximately 2602 patients from one randomised controlled trial[1], one non-randomised controlled study[2], and six case series[3,4,5,6,7,8].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on transperineal template biopsy and mapping of the prostate

Abbreviations used: TRUS, transrectal ultrasound; PSA, prostate specific antigen

Study details	Key efficacy findings	Key safety findings	Comments
Hara R (2008)[1] Study type: **Randomised controlled trial** Country: Japan Recruitment period: 2003 to 2005 Study population: Patients with PSA level 4 to 20 ng/ml n = **246 (126 transperineal vs 120 transrectal)** Age: 71 years (mean) Sex: 100% male Patient selection criteria: **No previous biopsy**, no history of prostate cancer, and no prostatitis Technique: under spinal anaesthesia or caudal block and with TRUS specimens sampled with a 18G 'tru-cut' needle 8 from the peripheral zone and 4 from the transition zone (no template system described) with a transperineal vs transrectal approach. **Follow-up: 1 to 2 weeks** Conflict of interest/source of funding: not reported.	Number of patients analysed: **246 (126 transperineal vs 120 transrectal)** **Procedure characteristics** Number of specimens obtained per patient not reported. **Pathology scoring** 12 core transperineal (8 from the peripheral and 4 from the transition zone) vs Transrectal Cancer detection rate: 42.1% (53/126) vs 48.3% (58/120), p = 0.323 Subgroup PSA level 4.0 to 10.0 ng/ml: 36.2% (34/94) vs 42.7% (38/89), p = 0.366 Subgroup PSA level 10.1 to 20.0 ng/ml: 59.4% (19/32) vs 64.5% (20/31), p = 0.674	**Complications** Major (requiring treatment): 12 core transperineal vs Transrectal, p = Sepsis/mortality: 0% (0/126) vs 0% (0/120), Not reported Fever > 38.5C: 0% (0/126) vs 1.7% (2/120), 0.136 Rectal bleeding: 0% (0/126) vs 0% (0/120), Not reported Urinary retention: 1.6% (2/126) vs 2.5% (3/120), 0.612 Length of follow up period not reported Minor: 12 core template transperineal vs Transrectal, p= Haematuria >1 day: 10.3% (13/126) vs 9.2% (11/120), 0.761 haematospermia: 1.6% (2/126) vs 0% (0/120), 0.166 Vasovagal event: 0.8% (1/126) vs 1.7% (2/120), 0.533 .	**Follow-up issues**: Loss to follow-up not reported. **Study design issues**: Randomisation stratified on PSA level and age. **Study population issues**: No significant difference between groups in clinical or demographic characteristics. **Other issues**: Comparison hard to comprehend as it is not clear how much under diagnosis has occurred in each group. It is possible that the two groups had different true rates of cancer. Postdural puncture headache was reported in 5 patients in the perineal group but thought to relate to spinal anesthesia rather than the procedure itself

Abbreviations used: TRUS, transrectal ultrasound; PSA, prostate specific antigen			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**

Abbreviations used: TRUS, transrectal ultrasound; PSA, prostate specific antigen

Study details	Key efficacy findings	Key safety findings	Comments
Emiliozzi P (2004)[2] Study type: **Non-randomised controlled study** Country: Italy Recruitment period: 2001 to 2003 Study population: patients undergoing laparoscopic radical prostatectomy. **Previous biopsy not reported** n = **135 (46 transperineal 12 core vs 89 transrectal 6 cores)** Age: 63 years (mean) Sex: 100% male Patient selection criteria: Not reported Technique: 12 core transperineal biopsy under TRUS guidance (no template system) vs 'standard' transrectal biopsy with 18G needle (6 to 8 cores). Follow-up: **Not reported** Conflict of interest/source of funding: Not reported.	**Number of patients analysed: 135 (46 vs 89)** **Procedure characteristics** Number of specimens obtained per patient not reported. **Pathology scoring** 12 core transperineal vs 6 core transrectal: Final post prostatectomy pathology T2: 76.1% (35/46) vs 70.8% (63/89); p = Not reported Final post prostatectomy pathology T3: 23.9 % (11/46) vs 29.2% (26/89); p = Not reported Agreement between core biopsy and final post prostatectomy pathology (Gleason score): 69.6% (32/46) vs 49.4% (44/89); p = 0.013 Final Gleason score higher: 23.9% (11/46) vs 39.3% (35/89); p = 0.037 Final Gleason score lower: 6.5% (3/46) vs 11.2% (10/89); p = 0.189 Agreement ± 1 point between core biopsy and final pathology (Gleason score): 97.8% (45/46) vs 85.4% (76/89); p = 0.012	Safety outcomes were not reported on.	**Follow-up issues**: Retrospective study comparing needle biopsy score with final pathology following prostatectomy. Case accrual method not described. Patients not requiring prostatectomy but initially sampled by core biopsy not included in analysis **Study design issues**: Pathologist studying sample from prostatectomy was unblended to the number of cores sampled at previous biopsy (6 or 12). **Study population issues**: No significant difference in PSA levels between groups at baseline. **Other issues**: Not clear if method of pathological assay was the same for both core biopsy sample methods.

Abbreviations used: TRUS, transrectal ultrasound; PSA, prostate specific antigen

Study details	Key efficacy findings	Key safety findings	Comments
Moran B J (2009)[3] Study type: **Case series** Country: USA Recruitment period: 2004 to 2008 Study population: Previously untreated patients with rising PSA levels (not described). Median prostate volume 46.1 cm^3 **Previous biopsy not reported** **n = 747** Age: 61 years (median) Sex: 100% male. Patient selection criteria: Not reported Technique: General anaesthesia, TRUS guided biopsy using a perineal brachytherapy template with 5 to 10mm spacing. 2cm long tissue cores obtained. Follow-up: **Not reported** Conflict of interest/source of funding: not reported.	Number of patients analysed: **747** **Procedure characteristics** A median of 40 specimens were obtained per patient (range 13 to 117). Estimated blood loss < 5 ml in all patients **Pathology scoring** Adenocarcinoma identified in 39.0% (291/747) of patients. Gleason Score ranged from 6 to 10. 20% of patients were found to have adenocarcinoma in 6 to 8 of octants of the prostate. Malignancy was detected significantly more often in apical than basal regions of the prostate ($p < 0.001$) and more often in anterior than posterior regions ($p = 0.036$)(absolute numbers not reported).	**Complications** Pain level was reported to be minimal in the recovery room. Urinary retention requiring catheter on discharge (95% removed < 3 days). 10.3 % (77/747) Recatheterisation 0% (0/747) Infection (not otherwise described) at 4 weeks follow up. <1% (1/747) Period of follow up not reported	**Follow-up issues**: Consecutive patient accrual. Loss to follow-up not reported. **Study design issues**: Method used for pathological analysis not described. **Study population issues**: PSA level for inclusion in study not described. **Other issues**: None.

Abbreviations used: TRUS, transrectal ultrasound; PSA, prostate specific antigen

Study details	Key efficacy findings	Key safety findings	Comments
Demura T (2005)[4] Study type: **Case series** Country: Japan Recruitment period: 2000 to 2004 Study population: Patients undergoing **first biopsy (digital rectal examination positive or negative), or repeat biopsy** after previous negative transrectal sextant biopsy. n = **371** Age: 67 years (mean) Sex: 100% male. Patient selection criteria: Not reported. Technique: Spinal anaesthesia, Foley catheter inserted. Under TRUS guidance sampling with a 18G 'Tru-Cut' needle through a 5mm diameter grid. Follow-up: **Not reported** Conflict of interest/source of funding: not reported.	**Number of patients analysed: 371** **Procedure characteristics** A mean of 20.1 cores were obtained per patient (range 9 to 38). **Prostate carcinoma identification rates** All patients 48.5% (180/371). Patients with first biopsy and negative digital rectal examination 47.0% (111/236). Patients with first biopsy patients with positive digital rectal examination 63.2% (48/76) Patients having repeat biopsy 35.6% (21/59) In the digital rectal examination negative group (n = 4806 cores) malignancy was not detected more often in anterior than posterior regions (p = 0.964). In the digital rectal examination positive group (n = 1428 cores) malignancy was detected significantly more often in the posterior than the anterior region (p < 0.0001). In the repeat biopsy group (n = 1224 cores) malignancy was detected significantly more often in the anterior than the posterior region (p = 0.0008). There was no significant difference in the carcinoma core rates between the left and right lobe in all groups.	**Complications** Event — Rate Haematuria and Urinary retention requiring overnight catheterisation — 1.6% (6/371) Haematospermia (> 1 month) — <1% (1/371) Continuous haematuria and anal pain. — <1% (1/371) Length of follow up not reported. No patients reported fever, and all cases of haematuria were treated conservatively.	**Follow-up issues**: Method of follow-up not reported. Patient accrual method not described. **Study design issues**: Method of pathological assay not described. **Study population issues**: Includes a wide range of indications in terms of suspicion of cancer. Authors state that population were Japanese men who may have a higher proportion of prostate cancer developing in the transition zone. **Other issues**: None.

Abbreviations used: TRUS, transrectal ultrasound; PSA, prostate specific antigen

Study details	Key efficacy findings	Key safety findings	Comments
Taira A V (2010)[8] Study type: **Case series** Country: USA Recruitment period: 2005 to 2008 Study population: Patients undergoing biopsy, mean PSA 8.3 ng/ml, **Some with Previous negative biopsy, some as 1st biobsy.** n = **373** Age: 64 years (mean) Sex: 100% male. Patient selection criteria: Nto reported. Technique: Under general anaesthesia, and TRUS guidance biopsy using a 18G needle through a brachytherapy template within 24 regions (1 to 3 cores from each region). Follow-up: **Not reported** Conflict of interest/source of funding: none	Number of patients analysed: **303** **Procedure characteristics** A mean of 54.0 biopsy cores were obtained per patient **Cancer detection** Number of previous biopsies — Rate 0 — 75.9% (60/79) 1 — 55.5% (81/146) 2 — 41.7% (35/84) 3 or more — 34.4% (22/64) For all repeat biopsies cancer detection was 51.6% (112/217) in patients with elevated PSA, 37.3% (22/59) in patients previously diagnosed with atypical acinar proliferation, and 22.2% (4/18) in patients with prostatic intraepithelial neoplasia.	Safety outcomes were not reported on	**Follow-up issues**: Prospetive follow up. Loss to follow up not reported **Study design issues**: All biopsies undertaken by same operator,a dn all samples evaluated by the same experienced pathologist. Only patients with Gleason score 6 or above were included as having been diagnosed with prostate cancer. **Study population issues**: Both biopsy naïve and patients with previous biopsy (of whatever sort / technique) are included. Patients undergoing repeat biopsy had larger prostates and higher baseline PSA than those undergoing their 1st biopsy. **Other issues**: None..

Abbreviations used: TRUS, transrectal ultrasound; PSA, prostate specific antigen

Study details	Key efficacy findings	Key safety findings	Comments
Li H (2007)[5] Study type: **Case series** Country: China Recruitment period: 2003 to 2005 Study population: Patients undergoing biopsy, median PSA 13.7 ng/ml, prostate volume 55 cm^3. **Previous biopsy not reported.** n = **303** Age: 70 years (mean) Sex: 100% male. Patient selection criteria: PSA level > 4.0 ng/ml, or abnormal digital rectal examination, or suspicion on imaging study. No history of prostate cancer of androgen ablative treatment. Technique: Under general (n = 13) or local (n = 290) anaesthesia, and TRUS guidance biopsy using a biopsy gun and 18G needle through a 5mm brachytherapy template within 11 regions (1 to 4 cores from each region). Follow-up: **Not reported** Conflict of interest/source of funding: not reported.	Number of patients analysed: **303** **Procedure characteristics** A mean of 23.7 cores were obtained per patient (range 11 to 44). **Pathology scoring** Diagnosis — Rate Prostate cancer — 37.6% (114/303) Intraepithelial neoplasia — 2.6% (8/303) 'Atypia' not otherwise defined — 4.6% (14/303) Prostatitis — 2.6% (8/303) Normal prostate — 52.5% (159/303) Breakdown of rate of prostate cancer by baseline PSA level PSA level — Rate 0 to 4.0 ng/ml — 22.2% (4/18) 4.1 to 10.0 ng/ml — 8.2% (6/73) 10.1 to 20.0 ng/ml — 21.6% (22/102) 20.1 to 30.0 ng/ml — 48.4% (15/31) 30.1 to 70.0 ng/ml — 68.4% (26/38) > 70 ng/ml — 100% (41/41) Of 114 patients diagnosed with prostate cancer Gleason score was available for 110. Score 5 = 10.9% (12/110), score 6 = 22.7% (25/110), score 7 = 38.2% (42/110), score 8 = 16.4% (18/110), score 9 = 10.9% (12/110), score 10 = 0.9% (1/110) There was no significant difference in the cancer rate between the different regions sampled (p = 0.749).	**Complications** Event — Rate Urinary retention — 2.3% (7/303) Haematuria (mild/transient < 7 days, not requiring hospitalisation) — 35.3% (107/303) Length of follow up not reported. No patient developed fever, chills, or rectal bleeding.	**Follow-up issues**: Prospective study, loss to follow-up not reported. **Study design issues**: Specimens examined by two experienced uropathologists. **Study population issues**: Despite 4.0 ng/ml PSA level inclusion criteria 18 patients analysed had level less than this. **Other issues**: Regions designated within the prostate not similar to those used in other studies.

Abbreviations used: TRUS, transrectal ultrasound; PSA, prostate specific antigen			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Bittner N (2009)[6] Study type: **Case series** Country: USA Recruitment period: 2005 to 2007 Study population: Patients with elevated PSA and **negative TRUS guided biopsy** (method and time since initial biopsy not otherwise described), median PSA 7.0 ng/ml, median 1.8 previous biopsies. prostate volume 73.0 cm^3. **n = 217** Age: 64 years (median) Sex: 100% male. Patient selection Criteria: negative biopsy with continued PSA elevation and or diagnosis of atypical small acinar proliferation. Technique: Under general anaesthesia, and TRUS guidance biopsy using a Maxcore 18G biopsy needle through a template (not described) within 24 regions (1 to 3 cores from each region). **Follow-up: Not reported** Conflict of interest/source of funding: Not reported.	**Number of patients analysed: 217** **Procedure characteristics** A mean of 53.8 cores were obtained per patient **Pathology scoring** Prostate adenocarcinoma identified in 44.7% (97/217) of patients. A premalignant condition (atypical small acinar proliferation o r high grade prostatic intraepithelial neoplasia) identified in 11.5% (25/217) of patients. PSA velocity (change in PSA level in 12 months prior to biopsy) was not associated with a biopsy outcome of cancer on univariate analysis (p = 0.239). Among the 97 patients with a positive biopsy, 82.6% had a Gleason score of 6 to 7, and 14.4% had a score of 8 to 9 (absolute figures not reported). And 88.7% had a positive specimen in ≤ 33% of cores sampled. .	Safety outcomes were not reported on.	**Follow-up issues**: Consecutive patients treated. Loss to follow-up not described. **Study design issues**: Patients subgrouped based on changes to PSA level in previous 12 months. Reason for categorical grouping used not described. Experience of clinicians performing biopsy not described. PSA levels at baseline and in the previous 12 years were not performed to a standard protocol. **Study population issues**: Patients undergoing rebiopsy. **Other issues**: None.

Abbreviations used: TRUS, transrectal ultrasound; PSA, prostate specific antigen

Study details	Key efficacy findings	Key safety findings	Comments
Pinkstaff D M (2005)[7] Study type: **Case series** Country: USA Recruitment period: 1999 to 2003 Study population: Patients with elevated PSA and **negative previous biopsy**, mean PSA 13.6 ng/ml. **n = 210** Age: 66 years (mean). Sex: 100% male. Patient selection criteria: PSA elevation > 10 ng/ml or PSA velocity > 0.75 ng/ml/year, or prostatic intraepithelial neoplasia/atypical small acinar proliferation on previous biopsy. Technique: under general anaesthesia, and TRUS guidance biopsy using a 'Biopty gun' and 18G needle through a template (not otherwise described). Follow-up: **Not reported** Conflict of interest/source of funding: not reported.	**Number of patients analysed: 210** **Procedure characteristics** A mean of 21.2 (range 12 to 41) cores were obtained per patient. **Pathology scoring** Prostate adenocarcinoma identified in 37.1% (78/210) of patients (95% CI 31% to 44%). Only age and prostate volume were associated with a biopsy outcome of cancer on univariate analysis (p = 0.002, and p = 0.027 respectively). Among the 78 patients with a positive biopsy 76.9% (60/78) had adenocarcinoma identified in a core within the transition zone. Gleason score (sum) — Rate (n=78 positive biopsy) 2 to 4 — 1.3 % (1/78) 5 — 3.8 % (3/78) 6 — 50.0 % (39/78) 7 — 28.2. % (22/78) 8 — 14.1 % (11/78) 9 — 2.6 % (2/78) 10 — 0% (0/78) Of the 78 patients with positive biopsy 30 underwent radical prostatectomy. 90% (27/30) of these patients had stage pT2 (organ confined) disease on final pathology.	**Complications** Event — Rate Urinary retention — 11.4% (24/210) The mean prostatic volume in patients that developed urinary retention was significantly greater (74.5 cm^3) than in those who didn't develop urinary retention (61.6 cm^3) (p = 0.014). Similarly a greater number of cores were obtained in patients that developed urinary retention (22.7) than in those that did not (21.0) (p = 0.018). Foley catheter was inserted for haematuria or prostatomegaly or both in 5.2% (11/210) of patients. This was removed on the first postoperative day in all patients. No other complications were reported	**Follow-up issues**: Prospective study. Loss to follow up not reported. Only 70.0% (210/300) of patients who underwent transperineal template biopsy were eligible for analysis based on the selection criteria. **Study design issues**: None. **Study population issues**: Patients undergoing rebiopsy. **Other issues**: Authors state that additional comparative studies of this and other saturation biopsy techniques are required to determine the optimal method to maximise cancer detection in high-risk patients.

Efficacy

Interpretation of the evidence is challenging because of different study populations and outcomes reported for different patient subgroups (e.g. patients having 'first biopsy' or re-biopsy after a negative previous transrectal biopsy); and because of different techniques in relation to number of biopsy samples obtained.

A randomised controlled trial of 246 patients reported no significant difference in cancer detection rate following 12-core transperineal biopsy 42% (53/126) than following 12-core transrectal biopsy 48% (58/120) ($p = 0.323$). There was also no significant difference in cancer detection between the two biopsy approaches within subgroups based on prostate specific antigen (PSA) levels[1]. A non-randomised controlled study of 135 patients reported significantly greater agreement in Gleason score between final pathology (from radical prostatectomy sample) and 12-core transperineal biopsy, 70% (32/46), than 6-core transrectal biopsy 49% (44/89) ($p = 0.013$)[2].

A case series of 747 patients undergoing transrectal ultrasound guided transperineal template biopsy reported that adenocarcinoma was identified in 39% (291/747) of patients[3]. Malignancy was detected significantly more frequently in apical rather than basal regions of the prostate ($p < 0.0001$), and in anterior rather than posterior regions ($p = 0.036$) (absolute numbers not reported). A case series of 371 patients reported that overall carcinoma was identified in 49% (180/371) of patients. In patients with a negative digital rectal examination 47% (11/230) of patients were found to have prostate carcinoma, and in patients undergoing a re-biopsy 36% (21/59) had a positive biopsy[4].

A case series of 373 patients reported that cancer was detected in 76% (60/79) of patients who were having their first prostate biopsy, and in 34% (22/64) of men who had 3 or more previous negative biopsies[8].

A case report of 303 patients with raised PSA levels undergoing transperineal template mapping biopsy reported that 38% (114/303) of patients had prostate cancer, and 3% (8/303) had intraepithelial neoplasia[5]. Of patients with PSA level 30.1 to 70 ng/ml 69% (26/38) had a positive biopsy, and of those with PSA >70 ng/ml 100% (41/41) had prostate cancer. A case series of 217 patients reported that prostate adenocarcinoma was identified in 45% of patients. Of these 89% had a positive specimen in ≤ 33% of all cores sampled[6].

A case series of 210 patients reported that prostate adenocarcinoma was identified in 37% (78/210) of patients. Of these 78 patients, 30 underwent radical prostatectomy and 90% (27/30) were found to have stage pT2 disease on final pathology (follow-up period not reported)[7].

Safety

A randomised controlled trial of 246 patients reported haematospermia in 2% (2/126) of patients in the transperineal group and in 0% (0/120) of patients in the transrectal group (p = 0.166)1. In the same study there were no incidents of sepsis/mortality or rectal bleeding in either the 12-core transperineal biopsy or the 12-core transrectal biopsy groups

Infection (not otherwise described) was reported in <1% (1/747) of patients in a case series of 747 patients (length of follow-up not reported)[3].

In a randomised controlled study of 246 patients, fever > 38.5°C occurred in 0% (0/126) of the transperineal biopsy group and 2% (2/120) of the transrectal group (p = 0.136)[1]. Urinary retention requiring treatment occurred in 2% (2/126) of patients in the transperineal group and 3% (3/120) of the transrectal biopsy group.

Urinary retention requiring a catheter on discharge was reported in 10% (77/747) of patients in a case series of 747 patients[3]. A case series of 371 patients reported haematuria and urinary retention requiring overnight catheterisation in 2% (6/371) of patients[4]. A case series of 303 patients reported urinary retention (not otherwise described) in 2% (7/303) of patients[5]. A case series of 210 patients undergoing prostate biopsy with a transperineal approach with ultrasound guidance and template mapping reported urinary retention in 11% (24/210) of patients. Those developing urinary retention had significantly larger mean prostate volume (p = 0.014) and larger mean number of cores sampled during biopsy (p = 0.018)[7].

Validity and generalisability of the studies

- Considerable variation between studies in terms of technique and equipment used as template.
- Some studies limit inclusion to only first biopsy while others include rebiopsy or a mixed cohort. Differences in patient risk factors make comparisons between studies difficult.
- Most studies do not report follow-up; where stated this can be assumed to be the date when biopsy results are available. In a small number of studies a minimum period of follow-up for safety outcomes is stated.
- None of the studies reported sensitivity and specificity versus what can be considered the gold standard (i.e. post prostatectomy pathology).

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Clinical guidelines

- Prostate cancer: diagnosis and treatment. NICE clinical guideline 58 (2008). Available from www.nice.org.uk/CG58

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr D Greene (British Association of Urological Surgeons), Prof. S Langley (British Association of Urological Surgeons)

- Both Specialist Advisers commented that the status of this procedure is established and no longer new.
- No reported or anecdotal safety concerns were noted.
- Theoretical adverse events may include septicemia, bleeding, urinary retention, urinary tract infection and haematuria.
- The safety profile of this procedure is very similar to standard saturation biopsy, and the advisers did not believe there were any safety concerns.
- The main comparator procedure would be saturation biopsy of the prostate under general anesthetic, or transrectal prostate biopsy.
- The key efficacy outcomes for this procedure are detection rate of prostate cancer (particularly apical tumours) and better localisation of tumour(s) within the gland.
- There is currently no agreement on the best technique.
- Transrectal ultrasound equipment is required to undertake this procedure.

- This procedure should ideally only be limited to cancer centres with sufficient expertise and specialist pathology services.
- Only patients with ongoing suspicion after initial biopsy or in future those considering focal therapy will need such biopsies.
- Patient should be offered this technique if they have a normal transrectal biopsy and a rising PSA level.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to obtain patient commentary for this procedure.

Issues for consideration by IPAC

- Non English studies were excluded from this overview.
- There is some lack of clarity within the literature as to what represents template mapping biopsy, some studies describe multiple core sampling with transrectal ultrasound guidance but without a physical grid template being used.

References

1 Hara R, Jo Y, Fujii T et al. (2008) Optimal approach for prostate cancer detection as initial biopsy: prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy. Urology 71: 191–5

2 Emiliozzi P, Maymone S, Paterno A et al. (2004) Increased accuracy of biopsy Gleason score obtained by extended needle biopsy. Journal of Urology 172: 2224–6

3 Moran BJ, Braccioforte MH (2009) Stereotactic transperineal prostate biopsy. Urology 73: 386–8

4 Demura T, Hioka T, Furuno T et al. (2005) Differences in tumor core distribution between palpable and nonpalpable prostate tumors in patients diagnosed using extensive transperineal ultrasound-guided template prostate biopsy. Cancer 103: 1826–32

5 Li H, Yan W, Zhou Y et al. (2007) Transperineal ultrasound-guided saturation biopsies using 11-region template of prostate: report of 303 cases. Urology 70: 1157–61

6 Bittner N, Merrick GS, Andreini H et al. (2009) Prebiopsy PSA velocity not reliable predictor of prostate cancer diagnosis, Gleason score, tumor location, or cancer volume after TTMB. Urology 74: 171–6

7 Pinkstaff DM, Igel TC, Petrou SP et al. (2005) Systematic transperineal ultrasound-guided template biopsy of the prostate: three-year experience. Urology 65: 735–9

8 Taira AV, Merrick GS, Galbreath RW et al (2010) Performance of the template-guided mappign biopsy in detecting prostate cancer in the intial and repeat biobsy setting. Prostate Cancer and Prostatic Diseases 13: 71-77

Appendix A: Additional papers on transperineal template biopsy and mapping of the prostate

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Bigliocchi M, Marini M, Nofroni I, et al. (2007) Prostate cancer detection rate of transrectal ultrasonography, digital rectal examination, and prostate-specific antigen: results of a five-year study of 6- versus 12-core transperineal prostate biopsy. Minerva Urologica e Nefrologica 59 (4) 395–402	n = 1151 (836 – 6 core, 315–12 core) Follow-up: not reported	In prostate biopsy, a higher number of cores seems to definitely improve its diagnostic value by dramatically decreasing the number of negative findings.	No template used
Bott SR, Henderson A, Halls J E et al. (2006) Extensive transperineal template biopsies of prostate: modified technique and results. Urology 68 (5) 1037–41	n = 60 Follow-up: not reported	In men with a clinical suspicion of prostate cancer, but benign or equivocal prostate biopsies, extensive transperineal template biopsy of the prostate is a useful diagnostic tool. It allows sampling of the whole prostate in a systematic and safe fashion.	Larger studies are included in table 2
Buskirk SJ, Pinkstaff DM, Petrou SP et al. (2004) Acute urinary retention after transperineal template-guided prostate biopsy. International Journal of Radiation Oncology, Biology, Physics 59 (5) 1360–66.	n = 157 Follow-up: not reported	Needle trauma alone may cause urinary retention in men undergoing transperineal procedures. The number of needle incursions and prostate size are predictors of postprocedure urinary retention.	Larger studies are included in table 2. Safety outcome reported elsewhere
Emiliozzi P, Scarpone P, DePaula F et al. (2004) The incidence of prostate cancer in men with prostate specific antigen greater than 4.0 ng/ml: a randomized study of 6 versus 12 core transperineal prostate biopsy. Journal of Urology 171 (1) 197–9	n = 214 (107–6 core, 107–12 core) Follow-up: not reported	The 12 core transperineal prostate biopsy is superior to 6 core biopsy. The technique provides optimal prostate cancer diagnosis. About half of the patients with PSA greater than 4.0 ng/ml and a slightly lower percent with PSA between 4.1 and 10 ng/ml have prostate cancer.	No template used
Emiliozzi P, Longhi S, Scarpone P et al. (2001) The value of a single biopsy with 12 transperineal cores for detecting prostate cancer in patients with elevated prostate specific antigen. Journal of Urology 166 (3) 845–50	n = 141 Follow-up: not reported	A high cancer detection rate is achieved by 12-core transperineal prostate biopsy. Most tumors represent clinically significant cancer. Further randomised trials are required to confirm these data.	No template used Possibly same patients as Emiliozzi (2004)
Fergany AF, Angermeier KW (2000) A technique of transrectal ultrasound guided transperineal random prostate biopsy in patients with ulcerative colitis and an ileal pouch. Journal of Urology 163 (1) 205–6	n = 1 Follow-up: 2 days	Random transperineal biopsy of the prostate was accurately performed under transrectal ultrasound guidance. With the increasing availability of brachytherapy equipment we believe that this method may be used for prostate biopsy in patients with rectal disease.	Larger studies are included in table 2.
Ficarra V, Martignoni G, Novella G (2006) Needle core length is a quality indicator of systematic transperineal prostate biopsy.	n = 509 Follow-up: not reported	The length of the needle cores sampled during transperineal prostate biopsy fulfils the parameters of quality required by pathologists for an	No template used

European Urology 50 (2) 266–71		appropriate evaluation of the biopsy specimen.	
Ficarra V, Novella G, Novara G et al. (2005) The potential impact of prostate volume in the planning of optimal number of cores in the systematic transperineal prostate biopsy. European Urology 48 (6) 932–7	n = 480 Follow-up: not reported	Transperineal prostate biopsy is a safe procedure with a very low complication rate and high cancer-detection rate.	No template used Possibly the same patients as Ficarra (2006)
Furuno T, Demura T, Kaneta T et al. (2004) Difference of cancer core distribution between first and repeat biopsy: In patients diagnosed by extensive transperineal ultrasound guided template prostate biopsy. Prostate 58 (1) 76-81	n=113 Follow-up: not reported	These results suggest that transrectal sextant biopsies miss more cancers in the anterior region than in the posterior. We believe the template technique has an advantage in being able to detect cancer equally in the anterior and posterior regions.	Larger studies are included in table 2
Merrick GS, Taubenslag W, Andreini H et al. (2008) The morbidity of transperineal template-guided prostate mapping biopsy. BJU International 101 (12) 1524–9	n = 129 Follow-up: 30 days	Morbidity differs from that of standard TRUS biopsy primarily in the incidence of temporary urinary retention, and is comparable in terms of urinary, bowel and erectile function.	Larger studies are included in table 2
Merrick GS, Gutman S, Andreini H, et al. (2007) Prostate cancer distribution in patients diagnosed by transperineal template-guided saturation biopsy.[see comment]. European Urology 52 (3) 715–23	n = 102 Follow-up: maximum 12 days	Transperineal template guided saturation biopsy diagnosed prostate cancer in 42.2% of patients. Considerable anatomic variability in prostate cancer distribution was documented.	Larger studies are included in table 2 Probably the same patients as Merrick (2008)
Moran BJ, Braccioforte MH, and Conterato DJ (2006) Re-biopsy of the prostate using a stereotactic transperineal technique. Journal of Urology 176 (4:Pt 1) t-81	n = 180 Follow-up: not reported	Stereotactic transperineal prostate biopsy is extremely well tolerated and useful for diagnosis of nonpalpable isoechoic occult prostate malignancy.	Larger studies are included in table 2
Miller J, Perumalla C, and Heap G (2005) Complications of transrectal versus transperineal prostate biopsy. ANZ Journal of Surgery 75 (1-2) 48–50	n = 178 (75 transperineal, 103 transrectal) Follow-up: not reported	Although the present study was limited by retrospective design and size, it suggests that both techniques are equally safe.	No template used
Nomura T, Mimata H, Hata S, et al. (2005) Recto-peritoneal fistula following transperineal prostate biopsy. International Journal of Urology 12 (3) 322–4	n = 1 Follow-up: 3 months	We report herein on a peritonitis arising from a recto-peritoneal fistula 5 days after undergoing prostate biopsy.	No template used
Onik G, Miessau M, Bostwick D G (2009) Three dimensional prostate mapping biopsy has a potentially significant impact on prostate cancer management. Journal fo Clinical Oncology. 27: 4321 - 4326	N=180 Follow-up: not reported	3D prostate mapping biopsy is a transperineal biopsy that can be safely used to accurately stage prostate cancer patients.	Larger studies are included in table 2
Pepe P, and Aragona F (2005) Prostate needle biopsy: 12 vs. 18 cores – is it necessary?	n = 372 (256–12 core, 116–18 core)	Extended schemes of prostate needle biopsy of 18 or more cores increases the prostace	No template used

Urologia Internationalis 74 (1) 19–22	Follow-up: not reported	carcinoma diagnosis in the early stage, and should be adopted for young patients with a PSA < 10 ng/ml, negative digital rectal examination and in case of rebiopsies.	
Satoh, T., Matsumoto, K., Fujita, T (2005) Cancer core distribution in patients diagnosed by extended transperineal prostate biopsy. Urology 66 (1) 114–8.	n = 128 Follow-up: not reported	The results of our study have shown that transperineal approaches are appropriate for sampling from the anterior half of the prostate gland. In patients whom the diagnosis of prostate cancer is suspected, we believe that systemic 22-core transperineal ultrasound-guided template prostate biopsy might be the next optional diagnostic step after an initial negative prostate biopsy.	Larger studies are included in table 2
Yamamoto S, Kin U, Nakamura K, Hamano M, et al. (2005) Transperineal ultrasound-guided 12-core systematic biopsy of the prostate for patients with a prostate-specific antigen level of 2.5-20 ng/ml in Japan. International Journal of Clinical Oncology 10 (2) 117–21	n = 300 Follow-up: not reported	We demonstrated a high prostate cancer detection rate by the transperineal ultrasound-guided 12-core systematic biopsy method in patients with PSA levels of 2.5 to 20 ng/ml.	No template used
Yokomizo Y, Miyoshi Y, Nakaigawa N et al. (2009) Free PSA/total PSA ratio increases the detection rate of prostate cancer in twelve-core biopsy. Urologia Internationalis 82 (3) 280–5	n = 419 (235 – 8 core, 184 – 12 core) Follow-up: not reported	12-core biopsy can achieve a higher detection rate of prostate cancer than 8-core biopsy using free/total PSA ratio.	No template used

Appendix B: Related NICE guidance for transperineal template biopsy and mapping of the prostate

Guidance	Recommendations
Clinical guidelines	**Prostate cancer: diagnosis and treatment NICE clinical guideline 58 (2008)** 1.2.1 To help men decide whether to have a prostate biopsy, healthcare professionals should discuss with them their prostate specific antigen (PSA) level, digital rectal examination (DRE) findings (including an estimate of prostate size) and comorbidities, together with their risk factors (including increasing age and black African and black Caribbean ethnicity) and any history of a previous negative prostate biopsy. The serum PSA level alone should not automatically lead to a prostate biopsy. 1.2.2 Men and their partners or carers should be given information, support and adequate time to decide whether or not they wish to undergo prostate biopsy. The information should include an explanation of the risks (including the increased chance of having to live with the diagnosis of clinically insignificant prostate cancer) and benefits of prostate biopsy. 1.2.4 Healthcare professionals should carry out prostate biopsy following the procedure recommended in 'Undertaking a transrectal ultrasound guided biopsy of the prostate' (PCRMP 2006).

Appendix C: Literature search for transperineal template biopsy and mapping of the prostate

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	02/04/2009	Issue 4, 2009
Database of Abstracts of Reviews of Effects – DARE (CRD website)	02/04/2009	-
HTA database (CRD website)	02/04/2009	-
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	02/04/2009	Issue 4, 2009
MEDLINE (Ovid)	01/12/2009	1950 to November Week 3 2009
MEDLINE In-Process (Ovid)	01/04/2009	December 1 2009
EMBASE (Ovid)	02/04/2009	1980 to 2009 Week 48
CINAHL (NLH Search 2.0/EBSCOhost)	02/04/2009	1981-present
BLIC (Dialog DataStar)	30/11/2009	-

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Prostatic Neoplasms/
2	(Prostat* adj3 (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan*)).tw.
3	1 or 2
4	Biopsy, Fine-Needle/
5	biopsy, needle/
6	((needle* or probe* or saturation or periton*) adj3 biops*).tw.
7	or/4-6
8	TTMB.tw.
9	((transperineal* or transperitoneal*) adj7 (template* or mapping)).tw.
10	(prostat* adj7 (template* or mapping or transperitoneal or transperineal)).tw
11	or/8-10

12	3 and 7 and 11
13	from 12 keep 1-120
14	Animals/ not Humans/
15	13 not 14
16	from 15 keep 1-119