

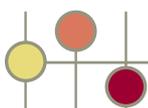
# Prostate Cancer

## Biopsy Schemes

### A systematic review of prostate cancer biopsy schemes

- Prostate cancer is the second leading cause of male cancer death in Europe and North America.
- Generally, men with raised PSA levels or abnormal rectal digital examination undergo ultrasound guided transrectal needle biopsy to obtain samples of prostate for diagnosis.
- The sextant biopsy scheme has been standard for many years, however a number of more extended prostate biopsy schemes are now being used in practice.
- The sextant scheme showed a significantly lower cancer yield than most of the more extensive biopsy schemes.
- The addition of laterally directed cores from the lateral peripheral zone to the mid lobe peripheral zone increases the yield significantly.
- As the number of cores increases, the yield improves for most of the schemes.

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## Background

Prostate cancer is the second leading cause of male cancer death in Europe and North America.<sup>1</sup> The disease is uncommon in younger men, with incidence increasing with age. There is considerable uncertainty about the natural history of prostate cancer. Post mortem studies show that 30% of men over 50, who had no symptoms of prostate cancer whilst alive, had histological evidence of prostate cancer at the time of death.<sup>2</sup> This percentage rises to 60-70% in men over 80 years of age. In other words, most men with prostate cancer die with, rather than from, the disease.<sup>2</sup> As a result, the prostate specific antigen (PSA) test is used not only in men presenting with prostate related symptoms, but also for those presenting opportunistically and in formalised screening programmes, to detect latent cancer stages.<sup>3</sup>

Generally, patients with raised PSA levels or abnormal rectal digital examination undergo ultrasound guided transrectal needle biopsy (TRNB) to gain specimens of the prostate for a histopathological diagnosis. The variety of routes for men to receive PSA testing means referrals for biopsy come from a range of healthcare settings and there is a wide age range in those referred. Some patients will undergo repeat biopsies after a negative first biopsy. As a result the use of TRNB has considerable public health implications.<sup>4</sup>

## Nature of the evidence

This short report is based on a systematic review commissioned by the NHS Cancer Screening Programmes.<sup>4</sup> The review compared the diagnostic value and possible adverse effects of different systematic prostate biopsy schemes. Full methodological details are given in the CRD report.<sup>5</sup>

## Biopsy techniques

There are a number of prostate biopsy schemes and strategies established in routine practice, which use systematic, rather than lesion directed, biopsy patterns. The ways in which they vary relate to their two main features:

- the number of biopsy cores to be taken
- the anatomical areas within the prostate gland from which the cores are taken

The systematic sextant biopsy protocol, a fixed pattern with six cores from the mid-lobar peripheral zone (see Table 1), has been the standard procedure used for many years.<sup>6</sup> However, recent studies with more extended

Table 1: Anatomical regions for needle biopsies of the prostate

Region of tissue sample	Region (see Fig 1)
LPZ - lateral peripheral zone	1 and 5
MPZ - mid-lobar peripheral zone (the area of the standard sextant pattern)	2 and 4
TZ - transition zone and possibly of the MLiPZ - mid line peripheral zone	3

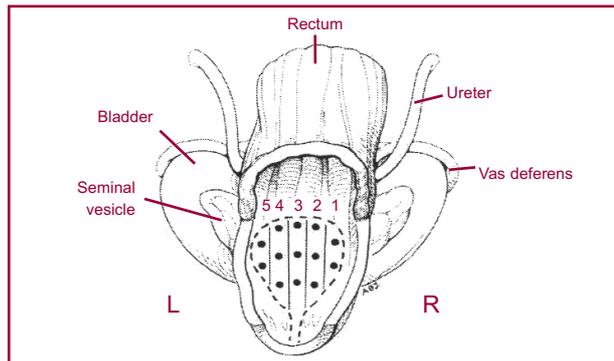


Figure 1: '5-region anatomic model' of the prostate in longitudinal plane.<sup>9</sup>

schemes have shown that the sextant protocol fails to detect between 10% and 30% of cancers.<sup>7,8</sup> Consequently many new biopsy protocols have been proposed.

In this review, the '5-region anatomic model' (Figure 1) was used to describe the different biopsy patterns currently used in practice so they could be grouped for comparison with the standard sextant scheme.

**Biopsy patterns:** Most of the studies included in the systematic review evaluated schemes from the:

- Mid-lobar peripheral zone and the lateral peripheral zone
- Mid-lobar peripheral zone and the transition zone
- Mid-lobar peripheral zone, lateral peripheral zone, and the transition zone

The number of cores taken ranged from 4 to 22. Most of the studies referred to the standard sextant method as the reference test.

The sextant scheme showed a significantly lower cancer yield than most of the more extensive biopsy schemes.

Biopsy schemes of the 5-region pattern had the highest cancer yield depending on the number of cores taken. Schemes with 18 to 22 cores in this pattern showed the highest cancer yield,

### Box 1: Relative Positivity Rate (RPR)

The RPR indicates the relative diagnostic value of the index test in comparison to a reference test. It is the ratio of the cancer detection rate of the index test to the cancer detection rate of the reference test.

Example: New extended biopsy pattern detects 40 cancers in a sample of 100 patients, the standard sextant pattern detects 30. The index test finds a 40% cancer rate, the reference test a 30% rate, therefore the RPR of the index test =  $40\%/30\% = 1.33$

however this was only based on three studies (RPR: 1.48; 95%-CI: 1.32-1.66). (See Box 1)

Sixteen studies analysed the biopsy scheme mid-lobar peripheral zone plus lateral peripheral zone with 12 cores. These produced an RPR of 1.31 (95%-CI: 1.25-1.37). This means that if the standard sextant scheme detected 30 cancers in a sample of 100 men, this 12 core scheme would detect an additional 9 cancers.

Thirteen studies analysed the same pattern but with 10 cores, resulting in an RPR of 1.25 (95%-CI: 1.19-1.33). In a sample of 100 men, if 30 cancers were detected by the sextant test, the mid-lobar peripheral zone plus lateral peripheral zone pattern with 10 cores would detect an additional 8 cancers.

Cancer yields from mid-lobar peripheral zone plus transition zone were in general lower than in the two previous patterns (RPR ranged from 1.04 to 1.23). Likewise, where cores were taken from the lateral peripheral zone only, cancer yield was also lower than in the two previous patterns (RPR varied from 0.86 to 1.15).

#### Number of cores and anatomic regions:

The number of cores taken was significantly associated with the cancer yield. A regression analysis showed that the addition of laterally directed lateral peripheral zone cores to a mid-lobar peripheral zone pattern enhanced the cancer yield significantly. If transition zone biopsies were added to get a 5-region biopsy (mid-lobar peripheral zone plus lateral peripheral zone and transition zone) the additional cancer yield was not statistically significant.

**Combined effect:** Analysing the combined effect of the biopsy pattern and the number of cores showed that the cluster of studies with the highest RPR (18-22 cores from the 5-region pattern) had a significantly higher yield than most of the clusters. However, there was no statistically significant difference between this scheme and taking 12 cores from the mid-lobar peripheral zone plus the lateral peripheral zone

pattern or taking 10 cores from the 5-region pattern.

**Adverse events:** Half the included studies mentioned adverse events but only 36/87 studies provided data for adverse events. Minor adverse events like pain/discomfort, minor haematuria, minor haematospermia or minor rectal bleeding were common. Major complications were less frequent: major infections (e.g. bacteraemia, urosepsis, or abscess) from 0.0% to 1.8%, and major bleeding from 0.0% to 0.6%. Studies with more extended schemes sometimes used more invasive strategies to achieve patient tolerance or avoid adverse events (e.g. extended antibiotic regimens; urinary catheter).

Adverse events for schemes with 10 to 12 cores were similar to those of the standard sextant scheme. There was some evidence for higher rates of minor rectal bleeding with 10 to 12 core schemes. Reporting of adverse events for more extended schemes was poor.

**Methodological considerations:** The quality of reporting in the primary studies was often poor with a lack of important information for patient variables and for adverse events. As a result judgements about applicability in other settings are difficult.

The chosen anatomic model with five biopsy regions may have some limitations. Core length and angle of the needle can sometimes be modifying factors. However, the anatomic model seems to be a reasonable compromise of accuracy and practicability.

## Summary

The standard sextant scheme showed a significantly lower cancer yield than most of the more extensive biopsy schemes. As the number of cores increases, the yield improves for most of the schemes. The addition of laterally directed cores from the lateral peripheral zone to the mid-lobar peripheral zone increases the yield significantly. Biopsy schemes with 18-22 cores from the 5-region pattern showed the highest RPR and had a significantly higher cancer yield than most of the compared schemes. However, the cancer yield of 12 cores from the mid-lobar peripheral zone plus lateral peripheral zone pattern and 10 cores from the 5-region pattern was not significantly lower.

Adverse events for schemes up to 12 cores were similar to those of the sextant pattern. Reporting of adverse events for more extended schemes was poor.



## Implications for practice

More extensive schemes that apply additional laterally directed cores should be encouraged.

Applying a more complex biopsy procedure will need special training for less experienced examiners and measures for quality control. Patient tolerance, which can be improved by appropriate local anaesthesia, must also be considered for extended schemes in clinical practice.<sup>10</sup>

In clinical practice obtaining the highest possible cancer yield has to be balanced against efficiency of cancer detection, taking the rate of adverse events into account. If the highest possible cancer yield is the first aim, the 5-region biopsy schemes with 18 and more cores are an option. However, data on adverse events are scarce and cost issues and patient tolerance have to be considered as well.

If a maximum of 12 cores are taken the pattern mid-lobar peripheral zone plus lateral peripheral zone may be appropriate. If a maximum of 10 cores is aimed at, either 10 cores from the pattern mid-lobar peripheral zone plus lateral peripheral zone or alternatively 10 cores from the 5-region pattern may be appropriate.

The European Randomised Study of Screening for Prostate Cancer (ERSPC), a large-scale multinational study evaluating the efficacy of prostate cancer screening, decided in their initial protocol to apply sextant biopsies.<sup>11</sup> However, in many of the centres involved in the study it has become common practice to take 10 to 12 cores. In addition, in the British ProtecT-study the biopsy protocol has been recently modified to a 10-core pattern.<sup>12</sup>

## Implications for future research

Studies should use a standardised nomenclature of anatomical prostate regions, provide detailed patient characteristics and

consider restriction to prognostically homogeneous subgroups. A standardised reporting of patient preparation, biopsy procedure, adverse events and the method of histological work-up will enable a better comparison of the diagnostic performance.

It still has to be demonstrated that more extensive biopsy schemes with a higher cancer yield do lead to reduced cancer mortality due to early detection of prostate cancer.<sup>13</sup>

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This summary article is based on a systematic review commissioned by the NHS Cancer Screening Programmes and conducted by CRD and the Horton Centre, Switzerland. The objective of the review was to compare the diagnostic value and possible adverse effects of different systematic prostate biopsy schemes used in the diagnostic work up of men suspected of having prostate cancer. The systematic review is published in full in CRD report 29. This can be downloaded free of charge from the CRD website at: <http://www.crd-pub@york.ac.uk> or the NHS Cancer Screening Programmes website at: <http://www.cancerscreening.nhs.uk/prostate/publications.html>. For more information about obtaining copies of the full report contact the CRD publications office ([crdpub@york.ac.uk](mailto:crdpub@york.ac.uk)) or the Department of Health publication orderline: 08701 555 455, ([doh@prolog.uk.com](mailto:doh@prolog.uk.com)).



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