ORIGINAL ARTICLE

Variations in the processing of prostatic needle cores in the UK; what is safe?

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Aims: To determine the variation in the processing of prostatic needle cores in the UK and to compare the results with suggested guidelines.

Methods: A standard questionnaire was sent to 210 pathology departments enquiring about current practices.

Results: One hundred and thirty replies were received, which showed considerable variation in current methods. The number of cores received for each case ranged from three to 21, with the number of cores processed for each cassette varying from one to 10. Sixty per cent of centres used no special embedding techniques, and the number of sections cut for each case varied from two to 128, with a median of 12 sections for each case. Forty two per cent of laboratories did not take spare slides for immunochemistry.

Conclusions: There is great variation in the processing of prostatic cores in the UK. In particular, some laboratories process a large number of cores in each cassette and do not use special embedding techniques. At present there are no established guidelines for the processing of these specimens. Enhanced techniques may well increase the sensitivity of the test but would increase the workload and costs to the pathology department. In view of the increasing workload from these specimens, a consensus for their optimum processing is required.

Prostatic cores make up an important part of the workload of histopathology departments and are increasing in number. An aging population, the possibility of a screening programme in the future, together with the increase in prostate specific antigen testing mean that this workload will continue to increase. However, there are few published guidelines for the methods and adequacy of processing of these specimens and, in our experience, these methods varied between different laboratories. Therefore, we surveyed current UK practices in the handling of prostatic cores to determine whether any general guidelines could be formulated.

METHODS

A survey form was sent to departments of histopathology in the UK with a stamped addressed envelope to maximise the number of replies.

Questions asked were as follows:

- How many pots of prostate cores do you receive for each case?
- How many cores are included in each pot?
- How many cores do you process for each cassette?
- Do you use any special techniques to ensure the cores are flat in the cassettes and if so what?
- How many levels do you examine on each core?
- How many serial sections do you examine at each level?
- Do you take spares at each level for immunochemistry?
- What do you do with the spares when the case is reported?

Results were tabulated and when a numerical range was given the greatest number was included.

RESULTS

A total of 210 survey letters were sent out and 145 replies received, 15 of which were unusable in the survey because they were duplicates from centres that had amalgamated services. This gave a total number of usable questionnaires of

130 of 195, a 67% response rate. A wide variation in all areas of handling and processing of these specimens by the histopathology laboratory was observed.

The number of cores received for each case (fig 1A) ranged from three to 21, with a median of eight and a mean of 8.8. Seventy eight of the 130 (60%) laboratories received either six or eight cores for each case with a further 26 of 130 (20%) centres receiving 12 cores for each case, where two sextant cores had been taken and received in two separate pots. At the extremes of the range, two centres were receiving only three cores for each case and there were also two centres that were receiving 20 and 21 cores for each case.

No special techniques were used to embed the cores in 78 centres (60%). When special embedding techniques were used, 31 centres (24%) used sponges, with the next most common technique being paper aided embedding (6%). Other techniques in use included capsules or microcassettes (3%), prior staining with haematoxylin and eosin (H&E) (3%), gauze bag (2%), and finally flattening with a pad (2%).

Processing of the cores varied greatly (fig 1B), with 27 centres (21%) placing only one core in each cassette, whereas one centre was placing all 10 cores received in one cassette. Fifty nine centres (45%) were placing either three or four cores in each cassette.

The number of cassettes for each case (fig 1C) again showed considerable variation. Seventy two centres (56%) processed two cassettes for each case (usually six cores received, processed as three in each cassette). There was another trend evident where the number of cassettes for each case was either six (12% of centres) or eight (11% of centres). These tended to be the centres that were placing only one core in each cassette.

The number of sections cut for each case (fig 1D) showed considerable variation: from two to 128, with a median of 12

Abbreviations: H&E, haematoxylin and eosin; MISO, medical laboratory scientific officer

Figure 1 (A) Number of cores received for each case. (B) Number of cores processed in each cassette. (C) Number of cassettes processed for each case. (D) Number of sections cut for each case.

sections for each case. The figure was generated by multiplying the number of cassettes by the number of levels taken by the number of serial sections at each level. Eighty six centres (67%) were examining between six and 20 sections for each case. Four centres were found to be regularly examining over 60 sections for each case. One laboratory, which cut 128 sections for each case, was receiving eight cores for each case, placing one in each cassette, and examining eight serial sections at two levels. At the other extreme, 13 centres (10%) were looking at fewer than five sections in total for each case. Fifty five centres (42%) took no spare slides for immunohistochemistry. Of the 75 centres (58%) that did take spares, most (61%) kept the slides indefinitely and 33% kept the slides for a period of less than one year. The processing methods used by teaching hospitals were not significantly different to those used by district general hospitals.

DISCUSSION

The number of prostate needle biopsies performed each year continues to rise in the UK and the proposed commencement of screening programmes and an aging population will only serve to add to these figures. The workload impact of these specimens is already considerable. The variations in practice reported here emphasise the impact of prostatic cores on the workload of both medical laboratory scientific officers (MLSOs) and pathologists. To our knowledge, there are no data on current UK practice in the routine processing of prostatic cores and no recommended guidelines on what constitutes adequate sampling.

The number of cores taken for each case varied considerably in our survey, although 60% of centres performed six or eight biopsies for each case. This would seem to be in keeping with the standard practice for taking prostate biopsies.¹ The number of biopsies taken for each case has been shown to affect the diagnostic detection of tumours by Taylor *et al.*,² who suggest that the addition of lateral biopsies to the standard sextant protocol results in increased sensitivity of tumour detection.

Unlike breast needle core biopsies, which are generally targeted at well defined lesions accurately delineated by palpation, ultrasound, or mammography, most prostate needle core biopsies are taken "blindly" from different parts of the gland. Hence, it is more common for these biopsies to sample

only "the tip of an iceberg". Twenty five per cent of carcinomatous foci in prostate needle cores have been reported to comprise less than 5% of the core and measure less than 1 mm in length.³ The finding of limited cancer in the needle core is often clinically relevant. In one study, 82% of cases with minimal (< 1 mm) carcinoma in a sextant needle core biopsy were associated with pathologically relevant cancer in the corresponding radical prostatectomy.⁴ Hence, all parts of the needle core biopsy should be examined histologically. The contemporary 18 gauge needles yield thinner, more wavy cores than their 14 gauge predecessors, which are more difficult to embed flat, especially when multiple cores are embedded in a single cassette. If the core is not embedded flat in a single plane parallel to the plane of section of the microtome blade, part of the core may not be sampled in the sections examined or, worse still, be lost during "facing up" of the tissue. The optimum practice would be to have one core in each cassette, but this would have considerable workload implications and occurred in only 21% of the centres in our study. Special techniques may aid embedding of cores and would be particularly useful when multiple cores are submitted in each cassette. Such measures were used by 40% of the centres in our study, but we found no evidence that special techniques were more likely to be used at centres where more than four cores were placed in each cassette. When special techniques were used, sponges were by far the most popular, followed by paper embedding, a technique that has been recommended by Lane *et al.*⁵

Lane *et al* have also reviewed the effect of taking levels on the percentage of cross sectional area that is examined by the pathologist.⁵ They have shown that sampling the tissue at one level missed an average of 23.4% of the total core length. Sampling the tissue at three levels significantly improved this to 7%. In the study by Renshaw,³ 13% of atypical foci and 3% of carcinomatous foci were not present on the first level, and at least three levels were needed to detect all lesions in prostatic needle cores. Similarly, another study showed that reducing the number of levels from three to one results in a missed diagnosis of adenocarcinoma in 8% of cases and reducing the number of levels from three to two results in a 5% missed diagnosis rate.⁶ Most centres (81%) in our study routinely examine three levels, and almost 10% examine between three and six levels routinely. An expert panel recently recommended that prostatic cores should be routinely sampled at no

Take home messages

- The processing of prostatic cores in the UK varies greatly, although many centres practise thorough and rigorous techniques
- Some laboratories process a large number of cores in each cassette and do not use special embedding techniques
- Enhanced techniques may increase the sensitivity of the test but would increase the workload and costs to the pathology department
- Because there are no established guidelines for the processing of these specimens and in view of the increasing workload from these specimens, a consensus for their optimum processing is needed

fewer than two levels,⁷ and it has been reported that most USA pathologists (84% of 273) sample prostatic cores at three levels or more.⁸ Examination of further levels has been recommended in cases where the original levels revealed focal glandular atypia.⁹ Therefore, most UK centres appear to be taking adequate numbers of levels of prostate cores.

“Special techniques may aid embedding of cores and would be particularly useful when multiple cores are submitted in each cassette”

Wojno *et al* have highlighted the importance of retaining unstained sections from intervening levels on charged slides.¹⁰ In their study, high molecular weight cytokeratin immunostaining was not useful in 26% of cases, mostly because the suspect focus was not present in the deeper levels. It is particularly important to make every effort to establish a diagnosis of cancer in prostatic needle cores because repeat biopsies have been reported to be falsely negative in at least 20% of cases.¹¹ Seventy five UK laboratories (58%) routinely obtain spare slides for immunohistochemistry and in most of these centres these are kept indefinitely. However, given the progressive increase in the number of needle biopsies performed, retaining unstained spares indefinitely would have storage space implications, especially if the cores are submitted in separate cassettes. Another issue that has not been dealt with to date is the potential medicolegal implications of retaining unstained spares indefinitely, because these sections may contain atypical foci, high grade prostatic intraepithelial neoplasia, or even cancer that was not present in the original H&E stained sections. Performing immunohistochemistry on destained H&E sections would be an alternative option to retaining unstained spares.¹²

In summary, there is great variation in the processing of prostatic cores in the UK, although many centres practise thorough and rigorous techniques. Differences in how the cores are received, processed, and examined all have major effects on the workload for pathologists and MLSOs and the budgets of pathology departments. The increased costs of improved sensitivity need to be weighed against the impact on the patient of delayed diagnosis, in addition to the costs and morbidity of rebiopsy. Based on the current literature, an ideal practice would be flat embedding with one core for each cassette, examined at three levels with three serial sections at each level. Spares should be taken at each level. Further research is necessary to determine the costs of these changes and their impact on departmental workloads.

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REFERENCES

- 1 **Hodge KK**, McNeal JE, Terris MK, *et al*. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *J Urol* 1989;**142**:71–4.
- 2 **Taylor JA**, 3rd, Gancarczyk K, Fant GV, *et al*. Increasing the number of core samples taken at prostate needle biopsy enhances the detection of clinically significant prostate cancer. *Urology* 2002;**60**:841–5.
- 3 **Renshaw AA**. Adequate tissue sampling of prostate needle core biopsies. *Am J Clin Pathol* 1997;**107**:26–9.
- 4 **Thorson P**, Vollmer RT, Arcangeli C, *et al*. Minimal carcinoma in prostate needle biopsy specimens: diagnostic features and radical prostatectomy follow-up. *Mod Pathol* 1998;**11**:543–51.
- 5 **Lane RB**, Lane CG, Mangold KA, *et al*. Needle biopsies of the prostate: what constitutes adequate histologic sampling? *Arch Pathol Lab Med* 1998;**122**:833–5.
- 6 **Brat DJ**, Willis ML, Lecksell KL, *et al*. How often are diagnostic features missed with less extensive histological sampling of prostate needle biopsy specimens? *Am J Surg Pathol* 1999;**23**:257–62.
- 7 **Shaw EB**, Daniel BW, Wofford ED, *et al*. Prostate biopsies: optimized cancer detection and staging. *J S C Med Assoc* 1996;**92**:251–66.
- 8 **True LD**. Surgical pathology examination of the prostate gland: practice survey by the American Society of Clinical Pathologists. *Am J Clin Pathol* 1994;**102**:572–9.
- 9 **Reyes AO**, Humphrey PA. Diagnostic effect of complete histologic sampling of prostate needle core biopsy specimens. *Am J Clin Pathol* 1998;**109**:416–22.
- 10 **Wojno KJ**, Epstein JI. The utility of basal cell-specific anti-cytokeratin antibody (34 beta E12) in the diagnosis of prostate carcinoma. A review of 228 cases. *Am J Surg Pathol* 1995;**19**:251–60.
- 11 **Stroumbakis N**, Cookson MS, Reuter VE, *et al*. Clinical significance of repeat sextant biopsies in prostate cancer patients. *Urology* 1997;**49**(suppl 3A):113–18.
- 12 **Dardik M**, Epstein JI. Efficacy of re-staining prostate needle biopsies with high-molecular weight cytokeratin. *Hum Pathol* 2000;**31**:1009–10.