Estimating tumour volume in prostate cancer and the probability of detecting it with a needle biopsy.

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1.0 Introductory comments.

This note presents a simple model for estimating the tumour volume in a prostate and the probability of detecting it with a needle biopsy. It is concluded that for prostate cancer at a reasonably early stage (say, a PSA of 10 or less), the probability of randomly detecting a tumour with a needle biopsy is quite low with the present samples sizes (a sample of six is an oft quoted typical value) and that therefore bigger sample sizes need to be used along with any other techniques that might provide guidance on where to take samples.

2.0 The simple model.

The problem of sampling a volume is rather like the children's game of Battleships. For a prostate volume V in which there is a volume of cancerous material C, the probability p of striking the cancerous material from a single point random sample is simply

$$p = \frac{C}{V}$$

The volume of the prostate can be obtained from the ultrasound scans during the TRUS procedure or from a CT scan so that, to assess this probability, it is necessary to have an estimate of the volume of the cancerous tumour.

For a normal prostate, it seems that the PSA level in ng/ml released into the blood is about 0.1 times the prostate volume in cubic centimetres. In the case of cancerous cells, it seems that the PSA found in the blood stream is much greater than this and there have been a number of papers[1] published in which the factor by which it is increased has been related to Gleason score and the number of positive biopsy cores. However, the basis for the formula presented in these papers does not seem overwhelmingly convincing but typically the factor seems to be somewhere between ten and thirty times that of normal prostate cells. There is probably a considerable variability in this factor between patients with the same diagnostic parameters and so the simpler expedient will be adopted here of using ten and thirty as likely bounds on the factor. Let us assume that the PSA released by cancerous tissue is α times the cancer tumour volume in cubic centimetres – i.e α would have the value of 1ng/ml per cc for a factor of 10 and 3ng/ml per cc for a factor of thirty.

[1] Reference to these and the formulae can be found on the website www.prostate-cancer.org/tools/software/tumorvol.html. This website also contains an Excel spreadsheet for the calculation of tumour volume based on Gleason scores and the number of positive biopsy samples.

If we have a PSA value of P, we can expect that about 0.1V of this is due to normal prostate tissue and the rest is due to the tumour tissue. The volume of the tumour tissue is thus

$$C = \frac{P - 0.1V}{\alpha}$$

As a simple example, let us take a case of a prostate with a volume of 30ccs and a psa value of 7. The expected PSA value for a healthy gland would be about 3ng/ml so that the remaining 4ng/ml is being produced by the cancerous tissue. Taking values of α of 1 or 3 (i.e. ten or thirty times the normal tissue production rate), we find that the tumour volume would lie in the range from 4ccs to 1.33ccs. On this basis, the probability of hitting cancerous material with a random point sample would be between 13% and 4.5% respectively. Let us suppose that the probability of hitting cancerous tissue from a single sample is p then if we take N samples, the chances of hitting cancerous tissue can be shown to be

$$1 - (1 - p)^N \approx Np \text{ if } Np << 1$$

For our example, if 6 needle cores were taken then the probability of hitting a sample of cancerous tissue would lie between 58% (4cc tumour in a 30cc gland) and 24% (1.33cc tumour in a 30cc gland). If we increase the sample size to 12 then the corresponding figures become 82% and 42%.

Of course, it is known that the probability of finding cancerous tissue within the prostate gland is not uniform but is higher in the posterior lobe and so I understand that the sampling is weighted towards this region. Moreover, the sample is not a point sample but a sample of finite volume. Both of these factors will tend to increase the chance of hitting a tumour but nonetheless the crude calculations show that for small tumour volumes, the probability of hitting a tumour is not that high and that somewhere around a half of biopsies could fail to detect the presence of a small tumour.

3.0 Concluding comments.

By random sampling, it seems that the probability of finding a tumour for low or medium risk patients is not as high as one would wish for. In order to avoid repeat biopsies, it would be preferable to have a probability of hitting a tumour in the region of, say, 95% and this would require larger samples sizes than a patient could withstand and also sample sizes that would probably cause a high risk of post-biopsy complications. As has already been mentioned, this probability can be increased by knowledge of the where tumours are more commonly found but, as a technique, this has its drawbacks too because sampling in regions where tumours are less common needs to be undertaken on a weighted basis as well. Ideally, one would like more guidance from the ultrasound scans as to where to sample. In some of the literature, it is suggested that hyper-echoic areas may be more likely to be cancerous but I have heard the opinion that this is such weak evidence of cancerous tissue that it is not worth taking into account in the sampling. However, this misses the point that anything that can push the probabilities up is worth incorporating into the technique.

By using colour Doppler ultrasound, Frauscher et al claim to have enhanced the detection of cancerous tissue and this is something that might be comparatively easily incorporated into the biopsy technique. Furthermore, if the regions of significant Doppler signals from the blood flow can be compared to the hyper-echoic regions by a spatial correlation process, this might lead to a further improvement in the success rate of tumour detection.

From my experience of as a patient, it seems that the positions of the needle samples within the prostate gland are not recorded. For a single biopsy, this may not be very important but if a repeat biopsy is carried out then it is clear that the probability of finding a small tumour is reduced if a region already sampled is sampled again. Therefore, there may be a case for noting the sampling positions and, in any case, some interesting points might emerge over time from this procedure in terms of correlating the likelihood of tumours with position in the prostate. This data might form a useful adjunct to post-operative data obtained from radical prostatectomies.

The mathematical modelling of biological processes is notoriously difficult because of the wide spread of parameter values in the modelling – such as the present assumption that the PSA produced by healthy prostate tissue is 0.1 times the prostate volume. However, it is a council of despair to argue that such exercises are not worthwhile because even if modelling of this sort has a poor predictive value, it can highlight the influence of the various parameters involved in the model and so increase awareness about the relative importance or weighting that should be attached to such parameters.

References.

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