24. The Timing of Tests in Tumor Monitoring

H.	Tate
----	------

Stone House, Ickleton, Essex, UK

H. Tate, Stone House, 64 Frogge Street, Ickleton, Nr. Saffron Walden, Essex CB10 1SH (UK)

Presented April 1985

In general terms, this paper aims to make the best use of characterizations of tumor marker data. The specific problem addressed is that of deciding when to carry out a second tumor marker test given that a first test result suggests abnormality in a patient being monitored following apparently successful ablative treatment to the primary tumor. A single fairly high test result could indicate that the patient is normal and had, on that occasion, a particularly high level of the tumor marker, or that the patient is abnormal. When results fall into this 'gray area', a repeat test is often carried out a short time later. This paper examines the factors which are important in determining an optimum time interval between an initial and subsequent 'confirmatory' test. The work arises from a Medical Research Council study of carcinoembryonic antigen in the postsurgi-cal monitoring of colorectal carcinomas [1,2].

In the first part of the paper, statistical models are developed which describe the evolution of tumor marker values in normal and abnormal patients.

These models incorporate the factors responsible for variability between tumor marker readings, including differences between patients and random background variability due to, say, the laboratory procedure for assay. In addition, in the normal patient, there is assumed to be some degree of autocorrelation between readings taken on the same patient at different times; e.g. a high reading is unlikely to decrease dramatically overnight, but the level of autocorrelation between one reading and another will decrease as the time interval between the readings increases. In the abnormal patient, it is assumed that the underlying tumor marker level is increasing steadily over time, having started increasing from the baseline normal level at some unknown time [3]. This increasing value may be accentuated or masked by random variation.

The sensitivity of a test is the probability of detecting abnormality in the patient who is abnormal. The specificity of a test is the probability of declaring that a normal patient is normal. Ideally, a test should discriminate perfectly and have both a sensitivity and specificity of 100%. Using the statistical models described above, curves are gen-

180

Tate

erated for the sensitivity and specificity of the second test as a function of the time interval between tests. As this time interval increases, the test tends to be more reliable in terms of both sensitivity and specificity. The effect of altering the critical range is examined in terms of these curves. A repeat test carried out too early may be unreliable, but a delay may diminish the change of successful treatment, using decision theory, a trade-off between these can be resolved.

In the second part of the paper the concept of utility loss is used in a decision theoretic approach to choosing the best time interval. If a false positive error is made after the test, a normal patient is referred for further tests. If a false negative error is made, an abnormal patient is missed.

Utility loss weighs the relative importance of these two types of error [4, 5]. Utility loss also changes with time as delay reduces the chance of successful treatment to the abnormal patient.

Changing sensitivity, specificity and utility

loss are used to compute an overall index of utility loss with time. This reaches a minimum at the optimal time interval and is demonstrated using assumptions concerning how utility loss may change with time.

References

Tate H: Br J Cancer 1982;46:323–330.

Tate H: The Statistician 1984;33:273–281.

Staab HJ, Anderer FA, Stump FE, Fischer R: Am JSurg 1978;136:322–327.

Henschke UK, Flehinger BJ: Cancer 1969;20: 1819–1826.

Langlands AO, Gore SM, Kerr GM: Br Med J 1982;285:680–682.