no mortality at 6 years) or poor prognosis (node-positive, pS2-negative; 54% mortality at 6 years). Evaluation of pS2 expression in breast cancer at diagnosis may provide additional useful prognostic information to conventional staging.

0–65. Allelic imbalance at chromosome 17p13.3(YNZ22) and poor prognosis in breast cancer

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Molecular and immunohistochemical studies of genetic events on chromosome 17p were prospectively compared with conventional clinical and pathological parameters and disease behaviour at a minimum 72 months follow up. In a series of 91 patients with primary operable breast cancers, 37/91 (41%) patients had disease relapse and 23/91 (25%) had died during the follow up period. Allelic imbalance at the YNZ22 locus (17p13.3) examined by Southern blotting, demonstrated in 33/63 (52%) informative patients, was significantly associated with disease recurrence ($P < 0.01$, 2df, Cox analysis) and showed a trend towards impaired survival ($P = 0.08$, 2df, Cox analysis) after a mean follow-up of 84 months for survivors. By contrast, p53 mutation (in 10/60, 17% of cancers), p53 allelic imbalance (in 23/56, 41% informative patients), p53 mRNA expression (in 47/87, 54% patients), p53 mRNA overexpression (in 24/87, 28%) or p53 protein expression (detected in 25/76, 32%) were not associated with disease behaviour. There was no significant association between allelic imbalance at YNZ22 and any abnormality of p53 DNA, RNA or protein.

Allele imbalance at 17p13.3 (YNZ22) serves as a marker of poor prognosis in breast cancer. As yet unidentified genes on 17p13.3, distinct from p53, are therefore likely to be of clinical importance in breast cancer.

0–66. Applying the Nottingham Prognostic Index to a Swedish population

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To assess the applicability of the Nottingham Prognostic Index (NPI) in a Swedish population 641 patients consecutively diagnosed with primary operable breast cancer 1988–1991 were studied. Nodal status, tumour size, grade, steroid receptor-status and flow cytometric S-phase fraction were related to local and distant recurrence and breast cancer death within 7 years. A multivariate analysis was computed and compared to the original Cox analysis from which the NPI was calculated.

Grade and nodal status were the most significant predictors of distant recurrence and death in breast cancer. NPI with the original coefficients of relative importance were applicable. Grade predicted for local recurrence. Grade showed a successive regression with age. Women under the age of 40 presented with larger tumours and a higher proportion of grade 3 tumours than older women. Survival patterns were closely correlated to prognostic index scores in all age groups. The distribution of NPI values was similar to that seen in the Nottingham population. Our patients had a higher 7 year survival, possibly due to adjuvant systemic therapy being offered most of them.

If the grading protocol of Elston is strictly followed the NPI is highly reproducible. If the NPI was generally used a basic prognostic assessment could be made for all invasive breast cancers regardless of size. The results indicate that the worse prognosis associated with breast cancer in young women is related to their presenting with higher median NPI values.

0–67. Automated grading in a prognostic index

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The Nottingham prognostic index (NPI) for primary operable breast cancer (NPI = (0.2 × tumour size) + lymph-node stage + histological grade), validated with 15 year survival analysis, remains a powerful clinical tool which defines three subsets of patients with different chances of dying from breast cancer (good, moderate, and poor prognostic groups partitioned by NPI score: < 3.4, 3.4–5.4, > 5.4 respectively). Grade contributes significantly toward NPI scoring but is a semi-objective variable. Quantitative measurement of histological tumour grade derived from automated analysis offers less subjective assessment and potential substitution of conventional techniques. Putative substitutes for grade: MIB1 labelling, cell morphometry (CAS™ image analysis), and proliferative index (PI = %SPF+%G2M) (flow cytometry) were measured on tumour tissue from 102 patients with primary operable breast cancer (median follow-up, 144 months) who received no adjuvant therapy. Multivariate analysis generated a simple (3 level) grade substitute, SCORE = 0.02 (MIB1 + standard deviation of nuclear size + PI), weighted by NPI score frequency. A new prognostic index using automated grading, API = (0.4 × tumour size) + (0.6 × lymph-node stage) + SCORE, defined three subgroups whose survival curves superimposed the corresponding curves generated by the standard NPI. An automated score can substitute histological grade in an established prognostic index.

0–68. Fraction of normal remaining life: a new method of defining cure in early breast cancer

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The plotting of conventional survival curves for cancer, using the interval between diagnosis and date of last follow up or death to denote survival time, ignores the patient's expected life span had the patient been healthy. In human terms, the impact of a projected 10 year survival of a woman diagnosed to have breast cancer (for example) would be different for a 30 year old patient as opposed to a 70 year old. We believe that expressing outcome in terms of fraction of normal remaining life span may be more meaningful. We have recently described this method and we wish to present its application to the data available from the CRC clinical trials.

In the new method, each patient's age at diagnosis is subtracted from the average life expectancy for that age to obtain what we call her normal remaining life (NRL). At the time of survival analysis, the percentage of NRL that has actually been lived by the patient was calculated and used in place of survival time to plot actuarial survival curves which we call real life expectancy curves. For example, in UK, a healthy 40 year old woman has a normal life expectancy of 79 years and NRL of 39 years (79 minus 40). If at 40 she were diagnosed to have breast cancer, and she lived for 10 years, her survival is expressed as 26% of her NRL (10/39 × 100). If she were 60 at the time of diagnosis her survival would be 48% (10/21 × 100) of her NRL. To plot the Real Life Expectancy curves, these percentage figures were used instead of actual number of years. The mathematical and statistical procedures are exactly the same as conventional method. Using this method, we can say that a node –ve woman has a 68% chance of living her full NRL which is equivalent to 'cure'. Similarly, we can say that overall, tamoxifen increases the chance of 'cure' from 50% to 62%. The importance of the facility to express survival in terms of cure, especially for a disease such as cancer, is profound. We believe that by individualising survival estimates according to age and expressing survival in terms of 'cure' rates, the new method makes survival estimates more meaningful, relevant and human.