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SERUM LEVEL OF AMINOTERMINAL PROPEPTIDE OF TYPE III PROCAOLLAGEN (PIIINP) - NEW PROGNOSTIC FACTOR IN OPERABLE BREAST CANCER ?. PRELIMINARY REPORT.

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In breast cancer with bone metastases PIIINP levels were shown by Blomqvist et all. to have value as an indicator of response to teraphy.
In the group of 26 women with primary operable breast cancer,in 20 patients with non-malignant breast tumors and in 20 healthy controls serum levels of PIIINP just prior to surgery were estimated using RIA tests. In the 37 month follow-up period relapse occured as a distant metastases in liver and bones, in all 8 patients with operable breast cancer in whom elevated serum levels of PIIINP had been found.
Micro-metastases, undetectable by typical clinical examination may cause elevated levels of serum PIIINP. and therefore be of prognostic value in clinically operable breast cancer.

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LARGE CORE BREAST BIOPSY: A PRE-OPERATIVE TOOL IN BREAST CANCER PROGNOSIS

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Image-guided large core biopsy is a recently introduced method for pre-operative evaluation of breast lumps. Several studies reported a good agreement between needle-core and surgical diagnoses. In order to evaluate the usefulness of this technique as a pre-operative prognostic tool, we compared 41 cases of breast carcinomas diagnosed on core biopsies and corresponding surgically removed samples. There was a diagnostic agreement in 38 cases (92.6%). In addition, a significant correlation between core biopsy and definitive surgical sections was found with regard to immunohistochemical detection of estrogen receptors (r=0.78), progesterone receptors (r=0.80), p53 (r=0.86) and c-erbB2 (r=0.90). An agreement for histologic grading evaluation between the two techniques was obtained in 80 percent of cases (k=0.65) whereas in the disagreeing cases a lower grade was assigned by evaluating biopsy samples. Mitotic count was performed separately in the samples obtained by the two techniques and a good correlation was found (r=0.76). In conclusion, our data suggest that percutaneous core breast biopsy can be used as a tool for pre-operative prognostic evaluation of breast lesions. As a consequence, this technique can be performed to plan neoadjuvant regimes of treatment and to choose the correct line of treatment (i.e. extension of surgery).

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AXILLARY NODE SAMPLING IN BREAST CANCER: AN ASSESSMENT OF ITS EFFICACY

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Some surgeons have been unable to dissect out 4 separate nodes from the axilla. Reports have also indicated that as increasing numbers of nodes in the lower axilla are sampled, so the chance of identifying involved nodes increases. 392 patients undergoing consecutive axillary node sampling performed by all grades of surgeons have been studied. The number of nodes removed ranged from 0-12 and only 19 patients had less than 3 nodes in the specimen submitted for pathology (Table). The mean number of nodes sampled was 4.8 with a standard error (SE) of 0.16 and the mean was 4. The percentage of patients who were node positive did not increase significantly as the number of nodes increased (Table). Mean number of nodes sampled when axillary node negative was 4.6 (SE 0.10) and 4.89 (SE 0.24) when nodes were involved. These data show that it is possible to dissect out 4 axillary nodes consistently and the chances of identifying involved nodes does not increase significantly as the number of nodes sampled increases.

Nodes Found	0	1	2	3	4	5	6	7	8	9	>9
No Pts involved	2	9	8	50	148	101	33	10	8	8	15
Nodes (%)	0	33	38	28	21	22	18	30	13	38	47

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INDETERMINATE CYTOLOGY IN BREAST SCREENING : CORRELATION OF MAMMOGRAPHY WITH HISTOLOGY

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Purpose: A retrospective study was performed to evaluate the accuracy of radiological grading at assessment in predicting the final histology of a breast biopsy, when the fine needle aspiration cytology (FNAC) was indeterminate (C3). Interest was focused on the group with indeterminate radiology (R3) to construct a strategy for management of screen detected abnormalities judged as indeterminate in both modalities (R3/C3).

Material and methods: From 1st October 1988 to the end of October 1994, 45,379 women attended for breast screening through the Central and East London programme, St Bartholomew's Hospital. Of those attending for subsequent assessment, 125 women had indeterminate cytology, 45 of these undergoing excision biopsy. All 45 patients had mammograms reviewed without knowledge of histology and radiological grading was compared with final histology. Differences in initial grading at the time of assessment and subsequent more experienced review grading were also analyzed.

Results: Of the 45 patients with C3 cytology, 5 had invasive malignancy, 4 in-situ disease and 6 atypical epithelial hyperplasia. Of the 19 patients with both indeterminate radiology and cytology (R3/C3) 13 (68%) had microcalcification as the predominant mammographic feature. None of these was subsequently shown to have invasive malignancy, 2 had in-situ disease and 4 atypical epithelial hyperplasia. The two in-situ cases were regarded as R4 and R5 on later review and retrospectively showed doubtful accuracy of sampling. The consensus opinion was better than the original radiological grading. The opinion of the senior radiologist was better than the original and reviewing consensus. This has been tested applying a trinomial distribution, and the significance values will be presented.

Conclusion: In our experience, an R3/C3 screen detected abnormality has a low association with significant breast pathology and open biopsy can be avoided in most cases providing the experienced radiologist is satisfied as to the accuracy of cytological sampling. Although not generally suitable for women with screen detected abnormalities, this is one case where a short term recall may be suitably employed in order to avoid unnecessary benign biopsy. The results demonstrate the effects of the "learning curve" on the quality of radiological opinion, and underline the importance of an experienced multidisciplinary, specialist team.

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THE RELATIVE EXPRESSION OF EGFR AND p185c-*erb*B-2 DEFINES THE SPEED OF BREAST TUMOUR CELL PROLIFERATION

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Overexpression of either of these proteins has been associated with poor outcome in breast cancer. Since they form heterodimers their relative expression would seem important. We have developed a quantitative radio-immunohistochemical assay for both. Study of 81 tumours has shown a bimodal distibution of p185c-*erb*B-2 expression. Fluorescent in-situ hydribisation showed the second peak (21%) to comprise c-*erb*B-2 amplified tumours. In the first peak (79%) Epidermal Growth Factor Receptor (EGFR) expression correlated indirectly to that of p185c-*erb*B-2 (R^2=0.239, p<0.0005) but this relationship broke down in the presence of c-*erb*B-2 gene amplification (R^2<0.0005, p=0.951). 44 patients underwent in-vivo bromodeoxyuridine labelling allowing calculation of tumour potential doubling time (Tp). EGFR expression correlated indirectly to Tp (R^2=0.124, p=0.019), no such correlation was evident for p185c-*erb*B-2. To explore the possibility that the relative levels of protein expression were significant, tumours were split into EGFR neg. / c-*erb*B-2 neg., EGFR pos. / c-*erb*B-2 neg., EGFR neg. / c-*erb*B-2 pos., and EGFR pos. / c-*erb*B-2 pos. using the mean of protein expression in the first peak. Kruskall-Wallis analysis reveals a statistically significant shorter Tp in the pos. / pos. group (medians 18, 12, 19 and 4 days resp., p=0.029). An explanation of these results is that p185c-*erb*B-2 may not directly influence mitosis but can influence proliferation via EGFR.

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CHEMOPREVENTION OF BREAST CANCER: UPDATE OF THE ITALIAN TRIAL IN HYSTERECTOMISED WOMEN

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Three major studies are ongoing in the U.K., the U.S.A. and Italy in order to verify the efficacy of Tamoxifen to inhibit or reverse breast carcinogenesis and to evaluate the risk/benefit ratio of its use in healthy women. The 3 studies are similar: double blind, randomised trials with Tamoxifen (20 mg/day) versus placebo, in healthy women, aged 35 to 70. The main difference with the Italian Study is in the target population, which is hysterectomised women only. As of December 31, 1995 the Italian trial is run by 48 centers, under the coordination of the European Institute of Oncology in Milan, and the accrual has reached 4,320 subjects. Their median age is 51 and 18% of them have at least one first degree relative affected by breast cancer. Sixteen per cent of the enrolled women are using estrogen replacement therapy, which is not a cause of exclusion in our study. We had 63% of the participants with some side-effects, which have been mainly of moderate intensity and especially menopausal symptoms like hot flushes and vaginal dryness. Twentyeight cases of phlebitis were reported, of which 3 assessed as deep venous thrombophlebitis. The number of drop-outs, so far, is reasonably low (15.9%). Thirtyone cases of cancer have been reported, including fourteen breast cancers. The Italian study is showing the feasibility to run these chemoprevention trials in hysterectomised women, thus avoiding the risk of endometrial cancer, which seems to be the major side-effect of Tamoxifen.