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PRIMARY BREAST CANCER IMAGING BY Tc-99m MDP SCINTIGRAPHY.
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Several radiopharmaceuticals are investigated to accurately diagnose and stage breast cancer. In this study we evaluated the uptake of Tc-99m MDP in breast glands in 200 patients with high suspicion of neoplastic disease and in 20 pts of the control group, during conventional bone scintigraphy . Repeated lateral views of both glands were acquired during the first 30-40 min after intravenous injection of 740 MBq of Tc-99m MDP. Scintigraphic results were compared with mammography (MM) and pathological findings.

Histology	N°	MDP scans		Mammography		
		Positive	(SENS)	Positive	Suspicious	Dubious
Cancer	**172**	**158**	**92%**	**120**	**27**	**25**
< 1 cm	30	20	66%	15	7	8
1-2 cm	70	66	94%	40	17	13
2-5 cm	40	40	100%	33	3	4
> 5 cm	15	15	100%	15	0	0
Infl. Cancer	17	17	100%	17	0	0
Benign Lesions	**28**	**2**	**----**	**0**	**0**	**28**

Focal tracer uptake occurred in visualized tumours and in 2 benign lesions, while involved lymphnodes, controlateral glands and those in the control group were not detectable. The overall specificity was 95%; the diagnostic accuracy was 93%; the PPV was 98% and the NPV was 76%. Thus, we suggest that this imaging procedure may be helpful in those cases were MM is not diagnostic and in patients younger than 50 years.

Key Words: Breast Neoplasms, Radionuclide Imaging, Phosphonates.

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INDOMETHACIN INHIBITS GROWTH OF A HIGHLY TUMORIGENIC BREAST CANCER CELL-LINE INDEPENDENTLY FROM PROSTAGLANDIN
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Most prostaglandins, acting through specific receptors (PG-R), cause accumulation of cyclic-AMP and inhibit cell growth. Indomethacin, a non-steroid anti-inflammatory agent, decreases prostaglandin production but, curiously, also inhibits cell-growth. In order to elucidate the mechanism of action of indomethacin, we compared its effects on a PGE2-sensitive, and a PGE2-resistant, cell-line. The first line, MCF7, derived from a pleural effusion of a breast adenocarcinoma. The second was a clone derived by transfection of the *Ha-ras* oncogene (MCF7-*ras*) and was more tumorigenic in *nude* mice. Indomethacin inhibited growth of both cell-lines in the same manner while PGE2 increased the cyclic-AMP level and inhibited growth of MCF7 only. The amount of PGE-R was lower in MCF7-*ras* than in the parental PGE2-sensitive line. These observations suggest that indomethacin has a specific prostaglandin-independent anti-proliferative effect and might be usefull in a systemic treatment of breast tumours.

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ABILITY OF TUMOR PROLIFERATIVE ACTIVITY TO PREDICT RESPONSE TO ADJUVANT CHEMOTHERAPY WITH PERIOPERATIVE CEF IN STAGE I-II BREAST CANCER
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Most patients (pts) with primary Breast Cancer (BC) receive postoperative adjuvant chemotherapy (ACT). ACT is able to reduce mortality from BC but most patients are treated without apparent benefit since either they are yet cured by surgery alone or recur and die from BC in spite of ACT. For this reason it is very important to individuate factors able to predict the impact of chemotherapy. The tumor proliferative activity evaluated by means of Thymidine Labelling Index (TLI) has been shown to correlate with the effectiveness of chemotherapy and with the dose intensity of CMF in studies carried out in Milan Tumor Institute.

In the present study we evaluated the ability of TLI to predict the effectiveness of the addition of perioperative chemotherapy to conventional treatment of primary BC. 600 pts entered a randomized protocol as follows: N- pts : 1 cycle of perioperative ACT versus no therapy; N+ pts : 1 cycle of perioperative ACT + 11 cycles of ACT at conventional times versus 12 cycles of ACT at conventional times. The perioperative ACT consisted of Cyclophosphamide, Epidoxorubicin and Fluorouracil. At a follow-up of three years Relapse Rate is similar in pts with low TLI independently from the treatment arm (6/36 versus 5/43). Patients with high TLI had less relapses if they were treated with perioperative ACT (3/40 versus 10/36).

In this study TLI predicted the effectiveness of perioperative ACT in reducing the relapse rate. Further studies are warranted in order to see whether the evaluation of tumor proliferative activity is able to find out the pts more likely to respond to chemotherapy or different types of chemotherapy (i.e. intensification).

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FACTORS AFFECTING OUTCOME OF PATIENTS WITH IMPALPABLE BREAST CANCERS
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A multivariate analysis (on a series of 152 patients with screen detected localised impalpable breast cancers undergoing needle guided wide excision) has been performed to determine factors influencing the completeness of excision and outcome (that is whether the patient was ultimately treated by breast conservation or mastectomy. Factors studied included experience of operator, nature of mammographic lesion, histology, nodal status and excision volume. Independent factors related to margin involvement were operator experience (p=0.0013 more experienced operators (>20 operations) having a higher rate of complete excision), size of lesion (p=.005), larger tumours having greater margin involvement and volume of excision (p=0.0037 larger volumes being less likely to have margin involvement). Independent factors related to surgical outcome were size (p=0.0001) and operator experience (p=0.0003).

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CAN BREAST RECONSTRUCTION WITH GEL-FILLED SILICONE IMPLANT INCREASE THE RISK OF DEATH AND SECOND PRIMARY CANCER IN PATIENTS TREATED BY MASTECTOMY FOR BREAST CANCER?
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An increased risk of cancer and auto-immune disease associated with polyurethane covered implants has been recently suggested, but the detrimental effect specifically associated with gel-filled silicone implants (GSI) has not been adequately studied in patients with breast cancer.

To evaluated the possible iatrogenic effect of GSI, we have studied 146 patients with breast cancer treated by mastectomy at IGR, between 1965 and 1983, and who received GSI for Immediate or Delayed Breast Reconstruction (BR) between 1976 and 1984. These patients were compared with 146 matched controls with breast cancer, treated at IGR by mastectomy without BR, matched for age at diagnosis (within 10 years), year of diagnosis (within 3 years), Stage (UICC), histologic type of the tumour, histological grade and nodal status. The relative risk of death, relapse, and second primary cancer was estimated by the Cox proportional hazards model, using stratification on age at diagnosis.

The risks of distant metastasis and death were significantly lower in the BR group than in the control group. The risks of local recurrence, second breast cancer, and second primary cancer in another site than the breast were not significantly different between the two groups of patients.

Our results do not support the hypothesis of a detrimental effect of GSI neither in the course of breast cancer, nor in the occurrence of other diseases. If there is a iatrogenic effect of GSI, it is low and the power of our study is insufficient to detect it.

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A MULTICENTRIC PHASE II STUDY WITH L-FOLINIC ACID (FA), FLUOROURACIL (F), ESCALATING DOSES OF EPIRUBICIN (E), CYCLOPHOSHAMIDE (C) PLUS G-CSF IN ADVANCED BREAST CANCER (ABC).

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From may 1992 to september 1993 in order to evaluate the efficacy and toxicity of a modified FEC regimen (F-FEC), including biochemical modulation of F with FA, untreated patients (pts) with advanced breast cancer were treated with the following combination: FA 100 mg/mq iv d1-3, F 375 mg/mq iv d1-3, E 90 mg/mq iv d1, C 600 mg/mq iv d1. G-CSF was administered as a daily 30 MU subcutaneous injection from day 5 to 15. Dose of E was increased of 10 mg/mq to a maximum of 120 mg/mq according to toxicity. The treatment was recycled every 3 weeks. Fifty-four pts are actually fully evaluable for response and toxicity. Patients' characteristics: median age 49 years, dominant site of disease: viscera 29 pts, bone 9 pts, soft tissue 9 pts, locally advanced disease (LAD) 4 pts, inflammatory breast cancer (IBC) 3 pts; multiple site of disease 38 pts. Results: 10 RC (19%), 31 PR (57%), 11 SD (20%), 2 PRO (4%), RR 76%. All pts with LAD and IBC achieved a response and underwent to the surgery. The median duration of response was 6+ months (3-18+). In 157/313 cycles (49%) the dose of E was increased while in 79 cycles (25%) interval between cycles was reduced. The treatment was generally well tolerated with few cases of grade III-IV toxicity (nausea/vomiting in 9 pts, stomatitis in 5 pts, anemia in 7 pts). Decrease in left ventricular ejection fraction up to 10% of basal value was seen in 5 pts. Conclusion: F-FEC regimen with G-CSF support allows a high response rate with an acceptable toxicity.