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ULTRASOUND-GUIDED BREAST SURGERY: A NOVEL TECHNIQUE FOR SCREEN DETECTED IMPALPABLE LESIONS.

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Impalpable breast lesions are frequently found in mammographic screening. Accurate surgical removal depends on localisation before operation using sophisticated needle placement techniques. These can be difficult, lengthy and potentially distressing. We have developed an alternative technique by means of ultrasound scan imaging in conjunction with skin marking. 111 patients with mammographically identified impalpable breast abnormalities were localised preoperatively by this technique. Surgical resection was accurate in 110 cases, confirmed by specimen radiography. The mean size of excised lesions was 10.2 mms and malignant tumours were removed in 73 (66.4%). We consider that this novel technique is preferable to needle localisation. It is non-invasive and is recommended whenever an impalpable lesion can be identified by ultrasound scan imaging.

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HIGH RISK BREAST CANCER PATIENTS: AN INTENSIVE ADJUVANT REGIMEN ADMINISTERED WITH OR WITHOUT G-CSF

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From January 1991 to October 1992, 13 operable breast cancer patients (pts) with 10 or more metastatic axillary nodes have been treated according to the Abeloff scheme (Abeloff et al. J Natl Cancer Inst. 82:570-574, 1990). Myelosupression was the predominant cause of dose reduction and treatment delay resulting in a decrease of the Actual Dose Intensity (ADI) of each drug. In an attempt to investigate if short courses of G-CSF (300 ug s.c. total dose) may allow the delivering of the planned dose intensity we modified the original Abeloff regimen as follows: CTX600 mg/sqm iv day 1, EpiADR 60 mg/sqm iv day 1, VCR 1 mg iv day 1, MTX 100 mg/sqm, L-leucovorin 10 mg/sqm p. os q 6 hr six times, 5-FU 600 mg/sqm day 2, 5-FU 600 mg/sqm iv day 9. 19 pts entered the study: 5 pts received no G-CSF (35 evaluable courses); 6 pts (level 1) G-CSF days 10 to 14 (38 courses), 6 pts (level 2) G-CSF days 4 to 7 (35 courses) and 2 pts (level 3) G-CSF days 4 to 7 and 10 to 14 (4 courses). The following grade III/IV (WHO) toxicities were observed:

	Control		Level 1		Level 2	
gr III/IV	day 1	day 9	day 1	day 9	day 1	day 9
Neutropenia	57	8.5	36.8	42	57	8.5
Mucositis	/	2.8	2.7	5.4	8.5	8.5
Anemia	/	/	5.4	5.4	2.8	2.8

5 episodes of febrile neutropenia were reported in the control group, 9 and 3 episodes in level 1 and 2 respectively. The ADI of each drug is similar in the 3 groups except for the ADI of 5-FU on day 9 in level 1 which is significantly lower (53% vs 80%) in comparison to the others. In this schedule the addition of G-CSF seems not to produce any significant increase in ADI. The study is still open and we are evaluating the toxicity and the ADI in level 3.

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SYNERGISTIC EFFECT OF TAMOXIFEN PLUS THE PINEAL HORMONE MELATONIN(MLT)IN INHIBITING INSULIN-LIKE GROWTH FACTOR-I(IGF-I)SECRETION IN BREAST CANCER:A BIOLOGICAL STUDY.

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Recent studies have shown that IGF-I is one of the most important growth factors for breast cancer.IGF-I levels are often increased in breast cancer and they would play a promoting role on tumor development.Therefore,the inhibition of IGF-I secretion could constitute a new endocrine approach in the treatment of breast cancer.The antiestrogen tamoxifen(TAM)has been proven to decrease IGF-I levels in breast cancer,irrespectively of estrogen receptor(ER)status.The pineal hormone MLT,in addition to its capacity of stimulating ER expression,may exert a lowering activity on IGF-I.On this basis,we have performed a study to evaluate IGF-I levels in metastatic breast cancer treated with TAM(20 mg/day)or TAM plus MLT(20 mg/day orally in the evening).IGF-I levels decreased in both groups.However,mean decrease in IGF-I was significantly higher in TAM/MLT group than in TAM alone.

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THE TRIP CONCEPT : A NEW SYNCHRONIZED AND POTENTIATED NEO-ADJUVANT CHEMOTHERAPY BY TRIPTORELIN (DECAPEPTYL) + INSULIN AND *LOW DOSE* CMF IN BREAST CANCER. CHROMOSOME 8P IS USEFULL.

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•The rational of the "TRIP" concept and the clinical application to 24 Breast Cancer patients is the result of experimental observations as: a)LHRH analog are requiered because of pituitary (chemical castration) and extra pituitary effects as:-Synchronization in Go/G1-S phase of the cell cycle, - Target directly to nucleus inducing apoptosis and regulation of transcription factors.(c-fos) ,-LHRH gene is located on 8p12. b)Why Insulin create an ideal climate to pharmacokinetics and seems a good carrier to potentiate drug therapy ?-Role of chronology action and binding of insulin to insulin receptor , IGF-I/II and homology to EGF-R.,-Role on Glucose transport and transmembrane permeability (enhancement of Methotrexate transport and uptake) , -Miming estrogen effects on cell cycle by recruitment in S-phase and augment the pharmacological sensitivity to MTX (specificity to S-Phase drug) c) Role of related loci on chr 8p and deletions (LOH) in this band 8p12(On poster) was correlated to clinical breast cancer specimen and used as a marker

•During this regimen , several parameters with informative biomolecules an FCM were evaluated. In order to synchronize physiologically human breast cancer before chemotherapy induction , we have initiated a protocol (24 patients) with prior sensitization of breast cancer by LHRH analog (Decapeptyl 0.1 mg sub cut/days=28) and weekly (3 months) Insulin (0.3 U/kg IV at hypoglycemia) immediatly followed in a preset IV line hypertonic glucose bottle containing low dose CMF (Methotrexate= 5mg/m^2, 5FU= 50mg/m^2, Cyclophosphamide= 75mg/m^2) . On non chemotherapy days patients are taken per os Methotrexate:2.5mg and Cyclophosphamide 50mg . From Day28 Decapeptyl is administrated by 3.75 mg LP intramuscular injection every month. According to this response (CI Stratification of responders) , patients were treated after 3 months of TRIP/low-CMF by surgery (7 pts) +/- radiotherapy (5 pts) and chemotherapy CAF protocol for good responders (12 pts) and maintenance of Decapeptyl LP injection for all patients . 16/24 pts have a CR at 5 years+ . Hypoglycemia was fully recovered in all cases and patients + team well informed.

No major hematology or other toxicity. Safety protocol because of lower total doses/potentiated administrated .Excellent cosmetic results and well preparation by this regimen TRIP to neo-adjuvant strategies.

Key Words:LHRH, Insulin ,Methotrexate. Full bibliography by written request

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LYMPH NODE METASTASES PREDICT SHORT-TERM DISTANT RECURRENCE IN LOCALLY ADVANCED BREAST CANCER (LABC) TREATED BY PREOPERATIVE CHEMOTHERAPY.

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From March 1990 to December 1992, 56 consecutive T2>4 cm and T3-4, N0-1, M0 breast cancer patients were treated by induction chemotherapy (FEC+/- C-GSF, EC). To evaluate this strategy we determined the prognostic importance of the number of axillary lymph node metastases relative to other patient and tumor variables. At a median follow-up of 24 months overall metastases free-survival (MFS) was 67%. Univariate analysis revealed that the number of metastatic lymph nodes, clinical tumor stage at presentation, nipple involvement, clinical and pathological response were significant variables associated with MFS, while drug regimen, tumor site, menopausal status, ER status and type of resection were not. Multivariate analysis (log-logistic model) showed that only the number of metastatic lymph nodes was of independent prognostic value for the rates of distant metastases (p=0.002). These results confirm that axillary dissection is an important component of this multimodality protocol because of its capability to identify subgroups of patients that may benefit from different treatments.

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MARGIN STATUS EVALUATION IN BREAST CARCINOMA TREATED WITH PRIMARY CHEMOTHERAPY AND CONSERVATIVE SURGERY.

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From January 1991 to December 1993, 46 patients with T2>4 cm and T3-4, N0-1, M0 breast carcinoma were analyzed after three cycles of preoperative chemotherapy of 5-fluorouracil, epidoxorubicin and cyclophosphamide. Twenty-eight (61%) were potential breast conservation (quadrantectomy) candidates based on criteria of breast to tumor volume ratio consistent with acceptable cosmesis rather than of absolute size of the tumor. Of these, 15 (54%) had microscopically positive surgical margins. All but three re-excisions showed persistent margin involvement (+ → +) that precluded breast conservative surgery.

The distribution according to histologic type of tumor and the residual tumor in the second-procedure specimen is as follows:

Infiltrating ductal	**9/6 (67%)**
Infiltrating ductal with extensive intraductal component	**3/3 (100%)**
Infiltrating lobular	**3/3 (100%)**

These results indicate that to perform oncologically safe breast conservative surgery following primary chemotherapy a careful pathologic evaluation of surgical margin status is mandatory.