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# Ovarian Function Suppression Plus Fulvestrant in Premenopausal Women with Metastatic Breast Cancer

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**Background:** Endocrine therapy is the preferred treatment for hormone-receptor (HR) positive metastatic breast cancer. In premenopausal patients eligible for endocrine treatment, ovarian function suppression combined with tamoxifen is superior to ovarian function suppression alone. Luteinising hormone releasing hormone (LHRH) agonists plus anastrozole yielded promising results in phase II studies. Fulvestrant, a pure antioestrogen, yields high rates of disease stabilization in postmenopausal women. Therefore, we investigated the feasibility and safety of fulvestrant plus goserelin in premenopausal women with HR-positive metastatic breast cancer.

**Methods:** Pretreated premenopausal patients with metastatic breast cancer eligible for ongoing endocrine treatment received fulvestrant 250 mg and goserelin 3.6 mg every four weeks as first- to fourth-line therapy. Clinical benefit rate (CBR; response rate plus disease stabilization  $\geq 6$  months) was defined as primary study endpoint; secondary endpoints were response rate (RR; CR + PR), time to disease progression (TTP), overall survival (OS), and toxicity.

Based upon previous data, a CBR of 50% was considered to indicate meaningful clinical activity; a CBR  $< 25\%$  was considered unacceptable. If  $\geq 11$  patients had clinical benefit, a sample size of 26 evaluable patients provides statistical power of 80% to reject the null hypothesis that CBR is  $< 25\%$  with an  $\alpha$  of 0.05.

**Results:** Twenty-six patients received treatment as scheduled. 81% were pre-treated with tamoxifen and 69% had received prior aromatase inhibitors in combination with goserelin. The majority of patients (69%) presented with visceral metastases.

Complete response was observed in a single patient, partial response in three and disease stabilization  $\geq 6$  months in eleven patients, resulting in a CBR of 58%. Median TTP was six months (95% CI, 2.4–9.6) and OS 32 months (95% CI, 14.28–49.72), respectively.

Treatment with fulvestrant and goserelin was well tolerated and none of the patients discontinued therapy due to toxicity. No case of grade 4 toxicity was recorded; grade 3 toxicities consisted of one case of pulmonary embolism (3.9%) and one case of grade 3 anorexia (3.9%), respectively.

**Conclusions:** Results suggest that the combination of fulvestrant and goserelin offers meaningful activity in premenopausal patients with HR-positive metastatic breast cancer and further investigation is warranted.

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# A United Kingdom National Survey of Breast Surgeons o Primary Endocrine Therapy of Early Operable Breast Cancer

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**Background:** A large number of elderly breast cancer patients in the UK and Europe are treated with primary endocrine therapy (PET), where patients receive an endocrine agent as the only treatment for their breast cancer. Despite this, PET remains one of the poorly studied areas in breast cancer therapy and very little is known about the practice of PET in Europe.

**Materials and Methods:** We sent a questionnaire comprising of 14 questions to 489 breast surgeons who were members of the Association of Breast Surgery, UK.

**Results:** 228 (47%) were returned; 220 from consultants and 8 from associate specialists. 93.4% of those responded use PET in elderly patients with early operable breast cancer. Among those 40% said 10% of their elderly patients were treated with PET while 2% said 70% received PET. The main indications for PET were unfit for surgery under GA or patient preference but 7.4% of surgeons would recommend PET even to a fit elderly patient. Letrozole is the drug of choice for 76% and tamoxifen in 10%. Follow-up varied widely but the majority of surgeons see PET patients 3 monthly and 34% use no imaging during follow up. 77% of surgeons have not formally audited their patients treated with PET. If the first drug used failed to control the tumour, 51% try another endocrine agent, 18% consider surgery and 2.3% use radiotherapy. When asked to guess the survival of a woman aged 80 living in the UK, over 70% of surgeons underestimated the expected survival.

**Conclusions:** This survey, for the first time, sheds some light on the practice of PET in a European country. Over 93% of UK breast surgeons use PET in elderly with surgically resectable breast cancer. Most use an

aromatase inhibitor. While most consider it in unfit, frail ladies, a minority would treat even fit elderly women with PET. Most have not formally audited the outcome of their patients treated with PET and underestimate the expected survival of elderly patients.

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# Triple Negative Breast Cancer – Experience of a Single Tertiary Center

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**Background:** Triple negative breast cancer (TNBC) accounts for approximately 15% of breast cancers in Western populations and is generally associated with poor prognosis. Racial differences in the incidence of triple negative breast tumors have been observed in Western populations; however, there are limited data regarding TNBC in Arab women.

**Material and Methods:** We analyzed pathological and clinical data from 519 women diagnosed with breast cancer at the American University of Beirut Medical Center between 1990 and 2001. Among these, 138 (26.6%) patients were identified as having TNBC and 381 (73.4%) patients had non-TNBC (HER2 positive, ER/PR negative 63 patients (12.1 %), ER positive, HER2 negative: 238 patients (45.8 %), ER positive, HER2 positive: 80 patients (15.4 %).

**Results:** The median age at diagnosis of the patients with TNBC was 50 years (range 26–81), for those with Luminal A: 52(27–83), for Luminal B patients 50(27–84) years and for HER2-overexpressive breast cancer was 42(32–78) years. The mean and the 5-year survival for TNBC was 7.9 and 74.5%, 9.2 years and 96.8% for Luminal A, 9.1 years and 91.1% for Luminal B, 7.6 and 84.9% for Her2+.(p = 0.001).

**Conclusions:** Compared to Western populations, women in our region present with all types of breast cancer at a younger median age with a higher proportion having the triple negative phenotype.

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# Introduction of a Novel Computerized Quantitative MR-based Breast Density Measurement System Using the Dixon Sequence

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**Purpose:** Breast density is one of the strongest predictor of breast cancer risk. To-date estimation of breast density is performed qualitatively using ACR-BIRADS and based on mammography (MG), a 2D-method using radiation and compression. To overcome the limitations of MG-based breast density measurement the aim of this study is to develop an accurate computerized observer-independent 3D breast density measurement system with MRI using the Dixon sequence.

**Material and Methods:** 35 women (mean 44 years) undergoing routine screening mammography with full-field digital mammography were included in this IRB approved prospective study and breast density and breast density was measured with MRI using the Dixon sequence at 3T Tesla (TR/TE 6 ms/ 2.45 ms/2.67 ms, 192 slices, matrix 352 x 352, 1 mm isotropic, TA 3:38 min), which acquired two datasets, one representing fatty and one fibroglandular tissue. The computerized MRI breast density measurement system calculated the percentage of fatty and fibroglandular tissue (%) and the total volume of the breast (cm<sup>3</sup>).

**Results:** Computerized quantitative breast density measurement using the Dixon sequence was successfully performed in 33 patients. In 2 patients the MRI dataset was severely hampered by motion artifacts and therefore no sufficient segmentation and breast density calculation was possible. MR measurements of fibroglandular tissue translating into breast density ranged from 3.5% to 60% (mean 22.3%). MR breast volume measurements ranged from 580.3 cm<sup>3</sup> to 3832.2 cm<sup>3</sup> (mean 2386.7 cm<sup>3</sup>).

**Conclusion:** MRI breast density measurement using the Dixon sequence is feasible and reliably allows assessment of breast density, a strong predictor of breast cancer risk.

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# Breast Cancer in Patients 40 Years Old or Younger Treated at the Department of Radiation Oncology of CHU Oran

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**Background:** The objective of this retrospective study was to discuss the clinical feature, the therapeutic results and the prognostic factors of breast cancer in younger women, in the Algerian west.

**Patients and Methods:** Data were collected from 83 patients  $\leq 40$  years diagnosed with BC and treated at our department from January to December 1998. Survival rates were estimated using the Kaplan-Meier method. Univariate and multivariate analyses were performed using the Cox proportional hazards regression models.

**Results:** The mean age was  $34.8 \pm 0.8$  years (Range 19–40). We have found: 12 T1 (14%), 29 T2 (35%), 17 T3 (21%), 16 T4 (19%), 8 Tx (10%) and 1 Tis (1%); 48 N0 (58%), 19 N1 (23%), 7 N2 (8%), 1 N3 (1%) and 8 Nx (10%). It was a CCI in 93% of the cases and a CLI in 5% of the cases. 3 cases (4%) were SBR grade I, 42 (52%) grade II and 30 (37%) grade III. 7 patients (8%) received a conservative surgery and 76 (92%) a radical surgery (Patey). The median histological tumour size was  $37.5 \pm 5.2$  mm (range 10–95). 23 patients (28%) were lymph node negative (pN0). 24 patients (29%) were classified: pN1, 27 (33%); pN2, 7 (8%); pN3 and 2 (2%); pNx. 27% were presented with RH+. 98% received chemotherapy (neoadjuvant and/or adjuvant) and 36% hormone therapy. All the patients received adjuvant radiotherapy, delivered by cobalt therapy. The median follow-up was 66 months (range 9 to 116). 48 patients (58%) developed recurrences (locoregional, distant and secondary breast cancer).

9-year locoregional relapse-free, disease-free (DFS) and overall survival (OS) were respectively: 86.2% ( $\pm 4.1\%$ ), 37.3% ( $\pm 6.6\%$ ) and 58.4% ( $\pm 11.6\%$ ). In univariate analysis,  $pN + > 3$  seems to have an influence for the locoregional recurrences ( $p = 0.127$ ; HR 5.2).  $pN1$  ( $p = 0.058$ ; HR 2.381) and extra capsular extension ( $p = 0.061$ ; HR 1.757) had an influence within the limit of the significance for the DFS. The factors influencing the occurrence of recurrences was: T3-T4 and  $pN + > 3$  in univariate ( $p = 0.01$ ; HR 2.181 –  $p = 0.002$ ; HR 3.935) and multivariate analysis ( $p = 0.019$ ; HR 2.065 –  $p = 0.012$ ; HR 3.037).

**Conclusion:** The breast cancer in young woman in the Algerian west is diagnosed at an advanced stage. On the therapeutic level, we observe the prevalence of the radical surgery. With a high rate of recurrences (loco-regional, distant and secondary breast cancer), the prognostic is unfavourable specially in cases classified tumours T3-T4 and  $N + > 3$ , where the necessity of an intensification therapeutic.

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#### Long Term Results and Prognostic Factors in Patients with Unicentric and Multicentric Breast Cancer

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**Background:** Among many oncologists the opinion exists, that multicentric breast cancer (MBC) shows greater metastatic dynamics and has worse prognosis comparing to unicentric breast cancer (UBC) in the same TNM. Some researchers think that proper evaluation of pT in MBC should be based on combined diameters not on the largest diameter of tumor.

The aim of the work is estimation of the treatment results with regard of multicentricity in breast cancer.

**Material and Methods:** The retrospective analysis included 954 consecutive women with breast cancer in stage IA-IIIC after radical mastectomy treated between 1995–1998 at the Cancer Center in Warsaw. Adjuvant chemo- or hormone therapy received 449–47% and 262–27% of patients respectively. Two hundred forty three (26%) of patients had not been given systemic treatment. Postsurgical irradiation was performed only in 135–14% of patients. (20/104–19% vs 115/850–13%,  $p = 0.08$ ), ale różnica nieistotna statystycznie. Cox's regression model was used to analyse the prognostic factors having influence on disease-free survival (DFS) and overall survival (OS). Median of follow-up was 134 months.

**Results:** MBC was diagnosed after mastectomy in 104–10.9% of patients. There were no significant differences in characteristics between UBC and MBC groups according to age, stage, pT, pN, type and grade of histology and methods of adjuvant treatment. The 10-year actuarial DFS and OS for patients with UBC and MBC were 51%, 62% and 58%, 72% respectively (Log Rank  $p > 0.05$ ). Locoregional recurrence rates were higher in UBC than in MBC: 78/850–9.2% vs 7/104–6.7% of patients  $p = 0.03$ . There were no statistical significant differences in frequencies of lymph nodes metastases among groups with UBC and MBC according to pT- measured as greatest diameter. In multivariate logistic regression analyses the following classical prognostic factors had independent influence on DFS and OS: pN, pT, G, and vascular invasion –  $p < 0.01$ . Multicentricity of breast cancer did not appeared significant prognostic factor neither for DFS and OS –  $p > 0.1$ .

**Conclusions:** From present retrospective analysis results that MBC does not deteriorate of prognosis compare to UBC and the largest rather than combined diameters of multicentric lesions should be used

to establish pT what is recommended and concordant with TNM system. However, multicentricity breast cancer should be considered at postsurgical radiotherapy planning because it can have influence on improvement of locoregional control.

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#### Very Young Women (<35 Years) with Primary Breast Cancer. a Single Institution Retrospective Analysis (2005–2009)

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**Background:** Breast cancer at a very young age has been reported to have a more aggressive biological behavior and to be associated with a relatively poor prognosis compared to older patients. The objective of this study was to evaluate the clinicopathological trends and therapeutic strategies in a very young breast cancer population.

**Materials and Methods:** During 2005–2009, 460 invasive breast cancer patients were referred to our department. 28 of them (6.1%) were <35 years of age, with the youngest patient aged 20 years old. The medical records and final pathological reports were reviewed retrospectively.

**Results:** The median age was  $31.82 \pm 3.2$  (range 20–35). The prevailing clinical symptom was a mass in all cases, while there were palpable axillary lymph nodes in 15 patients (53.5%). 16 patients (57.1%) had a right-sided breast cancer, there was a family history of breast cancer in 12 cases (42.9%), but only 4 patients had germ-line BRCA1 mutations (14.2%). 19 patients underwent breast-conserving surgery and axillary node dissection, 9 had modified radical mastectomy, while 3 patients followed neoadjuvant chemotherapy. The tumor size was  $< 2$  cm in 9 patients,  $> 2$  cm and  $< 5$  cm in 16 patients,  $> 5$  cm in 3 patients. All cancers in our series were invasive ductal carcinomas, most of them poorly differentiated. 10 patients expressed a triple-negative pattern on immunohistochemistry, whereas 19 were node negative. 25 patients received radiotherapy and 26 (92.8%) chemotherapy. The median observation time was  $42.4 \pm 18.43$  months at the follow-up cut-off date (range 18–76 months). 5 patients (17.8%) experienced early distant metastasis, whereas 2 (7.1%) patients died because of cancer-related reasons.

**Conclusions:** Breast cancer arising in young women, although uncommon, represents an aggressive phenotype and should be considered as a distinct form of breast cancer. Very young female patients have a greater tendency of having an endocrine unresponsive tumor, usually present with a higher tumor grade and there is an increased rate of local recurrence. Long life expectancy, fertility and risk of premature menopause resulting from chemotherapy should be specifically addressed in preoperative counseling of these women.

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#### Surgery Treatment Improves Breast Specific Survival in Elderly Patients with Early Stage of Breast Cancer

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**Introduction:** Increase in survival of the general population has been associated with an increase incidence of breast cancer in advanced ages. However, there is controversy regarding the management of breast cancer in elderly patients. The objective of this study was to assess different treatment strategies in elderly breast cancer patients ( $\geq 80$  years old) and the impact of surgery on survival.

**Patients and Methods:** All patients with breast cancer  $\geq 80$  years of age who were treated at our institution between 1995 and 2009 were reviewed. Data were collected from the patients' medical records, and patient characteristics and treatment modalities were analyzed. Patients were divided into those presenting with early stages (I, IIA, and IIB) and those presenting with locally advanced stages (IIIA, IIIB, and IIIC). Breast cancer-specific survival (BCSS) was assessed in both groups according to whether or not patients have undergone surgical treatment.

**Results:** A total of 306 patients were included in the study, of this 196 (64%) underwent surgery as part of their treatment (surgical group) and 108 (36%) did not undergo surgery (non-surgical group). The median follow-up was 49 months (95% CI 45–53). Mean ages of these groups were 83.8 and 85.2 years, respectively. Both groups were homogeneous regarding type and histological grade of tumor, hormone receptor status, and lymphovascular invasion. There were no statistically significant differences in oncological treatment received (hormone therapy, chemotherapy and radiation therapy). In 189 patients with Stage I, IIA and IIB, 150 (79.4%) had surgery and 39 (20%) did not. In 71 patients with locally advanced tumors, 46 (64.8%) patients underwent surgery and 25 (35%) did not. Among patients with early stage breast cancer, BCSS was 109 months