THE NEW ERA OF BREAST ULTRASONOGRAPHY: HIGH FREQUENCY

This special issue discusses topics related to new technologies in order to help dedicated breast radiologist in the detection and diagnosis of breast and malignant diseases.

In the first section, a new experimental high frequency probe is presented, especially for superficial breast lesions and cutaneous involvement of breast disease (The new era of breast ultrasonography: high frequency).

A focus on the breast radiologist training (Breast Ultrasonography: Who makes the best diagnosis?) can emphasize the central role of the imaging in the diagnostic-therapeutical course of breast disease with attention to the primary role of the confidence between the physician and the patient (Trusted physician in breast cancer exams).

Breast diseases, indeed, present not only physical involvement but also very significant psychological consequence that can influence personality and temperamental traits (Personality disorder and temperamental traits in patients with breast disease: a pictorial essay) of the patient with different facets in young (Level and conditioning of knowledge in benign breast disease in very young patients) or old women (Awareness of breast cancer in old women: psychopathological features) and in men, especially in presence of genetic syndromes (Breast cancer in an old male with Klinefelter syndrome: awareness and knowledge).

This special issue focused not only to the breast physician or patient, but also to the ill caregiver (Metastatic breast cancer caregiver: needs and quality of life evaluation), with the intent to optimize the quality of life, also in presence of advance disease.

Authored by experts in the field, we believe these articles would serve as a very important resource on breast disease.
Edit by

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THE NEW ERA OF BREAST DISEASE: AWARENESS AND PSYCHOPATHOLOGICAL FEATURES

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Abstract
High-Frequency Ultrasonography is a recent advance in Ultrasonography. It allows improving spatial resolution reducing penetration of ultrasound beam. This facility allows studying more accurately cutaneous diseases, blood vessels wall and eyes anatomy. However it could be useful also to evaluate breast superficial lesion, cutaneous involvement in breast cancer and several cutaneous diseases of nipple and breast.

In our experience, HFU allows optimal definition of cutaneous layers of pre-mammary zone, when compared to conventional ultrasonography, offering an optimal tool for better assessing superficial layers diseases of breast and pathologies involving pre-mammary zone.

Key words: high frequency ultrasonography, breast cancer
Introduction
In last years, advances in diagnostic imaging were made possible by developing new technologies first applied on animal models only in preclinical settings [1,2]; indeed small animals investigations allowed the development of more powerful systems, such as ultra-high-frequency ultrasonography (HFU).

The availability of ultra high-frequency US probes equipped with Color-Doppler permits an easy, advanced and non invasive evaluation of a variety of superficial targets within the first centimeter of the skin surface; HFU has improved spatial resolution although the reduced depth of penetration. Primary application of this new technology is in the evaluation of cutaneous diseases, blood vessel wall and eye [3]. However, an amazing HFU’s utility are the study of superficial breast diseases with skin or first order ductal involvement [4], of breast lesions with subcutaneous involvement, the analysis of very superficial structures [5], such as the nipple-areolar complex and very small lesions. So, actually, HFU represents a valid completion of a conventional breast ultrasonography, conducted by an experienced breast radiologist [6], leading to a decrease in errors number during conventional ultrasound examinations. In this way, it could reduce the numbers of invasive procedures like biopsies and fine needle aspirations [7], resulting in lower costs and less anxiety for patients [8].

Moreover, ultra-high-frequency US could be useful as guide to biopsy superficial lesions of the breast [9]. Potential indications of this technique are the measurement of thickness, invasion depth, evaluation of breast and/or skin tumors borders and post-surgery follow-up, skin thickening or retraction assessment, inflammatory carcinoma, papillary lesions, Paget disease or dermatologic diseases of the breast. It could be also useful in monitoring of topical and systemic drugs effects also in hereditary syndromes with breast involvement, such as gynecomastia in Peutz-Jeghers syndrome [10; 11]. In our institution, we conducted experimental studies with the first ultra-high-frequency US system available today for clinical routine (Vevo MD; FUJIFILM VisualSonics, Amsterdam, the Netherlands; with a 48–70-MHz linear-array transducer). Our experience underlined the HFU capability in improving spatial resolution as fine as 30 μm. We analyzed and compare ability of conventional US with respect to HFU in imaging normal ultrasonography anatomy of the breast skin, the axilla, the nipple-areola complex and retroareolar ducts.

HFU allows to highlights the different layers of the skin. Cutaneous and subcutaneous structures are represented by a succession of hypo and hyperechoic bands. Epidermis is a hypoechoic line, the dermis, indeed, a hyperechoic band, less shiny than epidermis and subcutaneous tissue a hyperechoic outer interrupted by hyperechoic longitudinal structures corresponding to fibrous septa. In the axilla, there are also hyperechoic structures arranged obliquely, corresponding to hair follicles; depending on the stage of the hair cycle, these structures might be in the dermis or subcutaneous tissue. The nipple skin is similar to the areola, but without sebaceous glands and subcutaneous tissue. It has 10 to 20 pores corresponding to the output of the main ducts [12; 13; 14]. It appears as a hyperechoic structure at skin surface that occasionally produces an intense acoustic shadow due to the connective tissue; the areolar muscle fibers have two directions: radial (muscle of Meyerholz) and circular (muscle of Sappey) [4]. HFU provides more detailed information concerning the anatomy of the pre-mammary zone (skin and overlying breast fat, in particular breast skin thickness and absence of hair follicles in the areola skin) and of the sub-areolar region [14]. For these reasons, we believe that the use of high-frequency transducers should increase for women with nipple discharge. In addition, ultrasonography showed the superficial layer of superficial fascia in the subcutaneous adipose tissue, and its thick turning point, key structures of the periareolar area.

Some authors believe, indeed, that it is important to suture the SLF securely, and that the suture should include the thick turning point to reduce scar widening and hypertrophy at the periareolar incision [15]. In conclusion, HFU promises for addressing important biomedical applications offering unique advantages over the existing non-invasive imaging modalities such us in other districts [16, 17]; it can be use in the evaluation of benign and malignant neoplasms, inflammatory diseases and infectious diseases [18]. Future goals for US trials need to include further validation studies, studies of diagnostic and therapeutic impact and longer-term outcomes from clinical and therapeutic decisions based on the US examinations.

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TRUSTED PHYSICIAN IN BREAST CANCER EXAMS

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Abstract
The breast radiologist is in the ‘voice of reason’ in the breast cancer diagnosis; he should to be careful neither to be conservative, nor too alarmist, in interpreting the initial breast cancer screening results because of there is a subtle balance between over and underdiagnosis. Radiologists’ interpretations of screening mammograms improve during their first few years of practice and continue to improve throughout much of their careers. Additional residency training and targeted continuing medical education may help reduce the number of work-ups of benign lesions while maintaining high cancer detection rates.

Keyword: breast cancer, radiologist, training
Introduction
If early diagnosed early, breast cancer now represents a highly curable disease, often small and node negative; women not only survive, but to also keep their female integrity [1]. Therefore, the breast radiologist is “THE” physician, often the first that encounters a breast cancer, the one that cares for patient and takes on their own responsibilities; he is the physician that goes with the patient along many years during breast clinical-instrumental evaluation. The breast radiologist is the first physician that discuss with the patient about breast abnormalities or suspicious, sometimes in disagreement with the patient that tries to find a justification to a breast lesion [2]. The breast radiologist has to ‘self-tune’ in terms of image findings and in terms of decision whether biopsy is needed or not [3]. The radiologist should be an experienced in communicating to a patient and her family that breast cancer is present, and knows how to respond to sorrow and anxieties [4].

Breast radiologists use imaging in its entire bandwidth. They need to be familiar with mammography, ultrasound [5] and with dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) [6] and with interventional radiology. Sometimes, breast diseases are also related to congenital or inherited syndromes and a genetic counseling could be useful to diagnose the primary disease which can manifest with breast symptoms [7,8]. The breast radiologist is in some ways the ‘voice of reason’ in the breast cancer treatment chain, and he needs to be careful neither to be conservative, nor too alarmist, in interpreting the initial breast cancer screening results because of there is a subtle balance between over and underdiagnosis. Radiologists’ interpretations of screening mammograms improve during their first few years of practice and continue to improve throughout much of their careers. Additional residency training and targeted continuing medical education may help reduce the number of work-ups of benign lesions while maintaining high cancer detection rates [9]. Residency breast imaging training, dedicated post-residency courses, continuing medical education, annual interpretive volume could improve the radiologist learning curve and accuracy of breast exams with an earlier stage breast cancer detection with low rate of unnecessary biopsies that result in both patient anxiety and increased medical costs [10,11].

The most common reasons given for not considering a fellowship or interpretation of mammograms were that breast imaging was not an interesting field, that they feared lawsuits, and that it was too stressful [12]. Radiologists’ performance continued to improve, though to a lesser extent, through 20 years of practice. The standardization of the procedure performed by a radiology resident or a radiographer as happens in the U.S., can cause many mistakes including an undiagnosed cancer. Therefore, the opportunity to make the instrumental analysis mechanical and schematic, is a useful investigative tool but only if made by an experienced radiologist. Considering as a whole medical investigations, experience is required for a correct diagnosis, as its automation leads to inevitable misdiagnosis, unless it is made by an expert.

The Computer Aided Detection (CAD) systems for breast cancers operate with a simple ‘artificial intelligence’ which compares measured parameters of the scanned breast tumor to a database of known diagnostic results for previously scanned tumors. Generally speaking, the computer aided detection system has proven to be useful as a ‘second-opinion’ or a training test, but is not suitable to provide the interpretation of the breast X-ray or other image. CAD systems are really not that much help to an experienced breast cancer radiologist, but can be quite beneficial for inexperienced radiologists, or perhaps in more remote settings where breast cancer may not be the primary area of expertise for the attending senologist.

Using computer aided detection systems has tended to result in a higher ‘recall’ rate for screening patients. Computer-suggested interpretations can often ‘psych-out’ a less experienced radiologist, resulting in many more biopsies than are really necessary. Incidentally, the rate of accurate radiologically detected breast cancer is usually around 91% or higher [13]. In conclusion, only an expert radiologist with a dedicated breast imaging training [14] can be accurate in breast cancer detection with benefit for women and for the health care system, with a reduction of unnecessary work-up and biopsies that result in both patient anxiety and increased medical costs [9]. Because the population grows, the average life is elongated, especially for women, and the number of prevention exam will increase in future decades, we need qualified radiologists to interpret breast exams and to perform diagnostic work-ups. The training of a number of residents to interpret mammograms and to do breast ultrasonography will be a good challenge for radiologist and a precious opportunity for patients, minimizing extra-costs for biopsy or in-depth analysis.
References
BREAST ULTRASONOGRAPHY:
WHO MAKES THE BEST DIAGNOSIS?

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Abstract
To evaluate the most efficient between breast and general radiologists and any significant or clinically relevant differences in breast ultrasound diagnosis. Four hundred consecutive patients attending for breast ultrasound were included. Each patient was examined by a breast radiologist and subsequently by general radiologist. Both operators noted their findings and wrote a concluding report without conferring. Reports were compared, with histological and biological analysis. 400 patients with 384 females and 16 males, with age range 16-86 y.o. and mean age about 48 y.o., are examined. The breast radiologist results most accurate in comparison the general radiologist in breast ultrasound (p-value = 0.0625) with a significance level of 10%. The breast radiologist is more accuracy in comparison to general radiologist in the evaluation of breast pathology in the US diagnoses.

Key words: ultrasonography, breast cancer, radiologist
Introduction

Breast ultrasonography is a quick, cheap, noninvasive and safe diagnostic method; it is the first choice in underforty women and a complementary examination for overforty women also to evaluate palpable abnormalities and characterize masses detected at mammography and magnetic resonance imaging (MRI) [1]. It was primarily used to distinguish cystic from solid masses. Solid masses with spiculation, taller-than-wide orientation, angular margins, microcalcifications, and posterior acoustic shadowing are to be consider malignant or suspicious; instead, if a mass presents two or three lobulations, ellipsoid shape, a thin capsule and a homogeneously echogenic echotexture, could be consider benign [2]. But often breast lesions form an extremely heterogeneous group consisting of benign lesions mimicking carcinoma [3,4] with a poor interobserver agreement in US BI-RADS classification [5]; therefore, sonography is also currently used to guide for interventional breast procedures, such as US-guided fine needle citology or biopsies [6]. Fine-needle aspiration plays an important role also in characterization, in tumor grading and in immunocytochemical identifying specific tumor markers, even if biopsies allow precise and accurate diagnosis avoiding repeated examinations causing the patient anxiety and unnecessary surgical procedures [7].

However, the main limitation of breast ultrasonography are operator dependent nature and its low specificity, leading to a high rate of false positive results [8]. Several methods are developed to improve the performance of US and cost/effectiveness ratio, such as higher resolution transducers, Doppler imaging, harmonic imaging, spatial and frequency elastosonography, contrast US, 3D US and automated breast ultrasonography. Although these advanced technology, interobserver agreement between radiologists in breast ultrasonography is poor and only a fellowship training in breast imaging could improve the accuracy of image interpretation [1, 9]. Purpose of our study is to analyse the accuracy of general radiologists in breast disease diagnosis and to assess the quality of their work. In particular we wanted to know whether there was agreement between the findings of the breast radiologists and those of general radiologists.

Methods

This research is a prospective study on accuracy between general radiologist and breast radiologist. This study included 400 patients in the period between 01 December 2010 and 01 December 2012. The patients sample was composed from 96 % females and 4 % males with ages into range 16-86 and with mean ages about 48 and standard deviation about 15. Inclusion criteria were: breast and ovarian familiarity, BRCA 1 and/or 2 mutation, history of breast surgery, history of ≥2 years hormone replacement therapy and recurrent cyclical mastodynia. Exclusion criteria were: proliferative benign breast diseases, breast implants. To start by our sample data (400 patients), we have considered four random subgroups of 100 patients. Each subgroup was examined by a breast radiologist with 25 years of experience of breast diseases (that have read at least 480 screening mammograms or breast exams (ultrasonography, MRI) per year or 960 exams every two years, according to Mammography Quality Standards Act) [10] and subsequently by general radiologist, with 25 years of experience who did not work exclusively in breast diagnostic field. Each breast radiologist and general radiologist had examined one subgroup only. In the diagnostic phase, there was no communication between the general and breast radiologist. For each group both the breast radiologist and general radiologist separately has recorded the number of images taken, the number of images saved, their confidence in their diagnostic findings and conclusions. The examinations in the study were limited to the breast. US was performed using a Logiq S6 scanner (GE Healthcare, Waukesha, WI, USA) with a multifrequency matrix-array linear transducer (7-14 MHz). Colour Doppler US was also performed to study intraloesional vascularity.

For each exam, radiologists defined the age intervals (≤40, 40-70, ≥70 y.o.), the number of the lesions detected (1, 2 or 3), the lesion size (<5 or ≥5mm), breast pattern (fibroglandular or no fibroglandular), the localization (UOQ, LIQ, LOQ, UIQ, RA) and placed lesions in two categories: not suspicious (negative exams, cysts or fibroadenoma) or suspicious lesions (cancer). The effective diagnosis was performed with 2 years follow-up (152 patients), cytological diagnosis (66 patients) after US-guided fine needle aspiration, histopatological diagnosis (32 patients) after US-guided biopsies or surgical excision. US-guided biopsies were performed with 14-gauge needles. Two to seven samples were obtained (mean two to three). Histological examination was performed by an experienced pathologist.

The effective diagnosis was performed with 2 years follow-up (US examination every six months) for lesions included in BI-RADS 1 and 2 category,
US-guided cytology or biopsies for lesions included in BI-RADS 3, 4 and 5 categories.

**Statistical analysis**

The statistical analysis were performed by Matlab statistic toolbox ver. 2008 for Windows at 32 bit. The chi-square test [11] were performed to define if the subgroups were statistically equal, instead the McNemar’s exact test [12] was performed to evaluate the diagnostic accuracy between breast radiologists and general radiologists in breast ultrasound examination. Finally Sensitivity and specificity with confidence intervals [13] were computed on the all results obtained by breast radiologists and general radiologists.

**Results**

Our goal was to evaluate the most efficiency between breast and general radiologist in the evaluation of breast pathology with US diagnosis [14]. In table 1 we have described the characteristics and the diagnostic responses to the breast ultrasound for each subgroup. The subgroup 1 had a major patients number with ages into range 40-70 (56%), one lesion (40%), lesion size 5 mm (32%), breast pattern NO FG (52%), 9% of multicentric benign pathologies and 3 % of the multifocal cancers. The subgroup 2 had a major numbers of patients with ages into range 40-70 (52%), one lesion (46%), lesion size 5 mm (32%), breast pattern NO FG (60%), 6% of multicentric benign pathologies and 4 % of multifocal cancers. The subgroup 3 had a major numbers of patients with ages into range 40 (44%), one lesion (44%), lesion size 5 mm (36%), breast pattern FG (52%), 5% of multicentric benign pathologies and 3 % of the multifocal cancers. Finally the subgroup 4 had a major patients number with ages into range both 40 and 40-70 (44%), one lesion (48%), lesion size 5 mm (40%), breast pattern NO FG (52%), 5% of multicentric benign pathologies and 3 % of the multifocal cancers. In table 2 we had reported the diagnosis responses for each breast and general radiologists. We observe by Table 2 that both the breast radiologist 1 and 4 were perfect in all diagnoses; the breast radiologist 2, had not identified one cyst evaluating the patient negative; the breast radiologist 3 had not identified one fibroadenoma, evaluating the patient negative. The general radiologist 1, had not identified one fibroadenoma evaluating the patient negative; the general radiologist 2, had not identified two fibroadenomas, evaluating one negative case and one cyst, while one cancer was evaluated like cyst; the general radiologist 3 had not identified two fibroadenomas and one cyst, evaluating the three patients negative to the diagnosis; finally the general radiologist 4, had not identified one cyst evaluating the patient negative. In table 3 and in figure 1, we have showed the results on total group of 400 patients, for the breast and general radiologists. Particularly in table 3 we have expressed in parentheses the total number of errors, considering both false positive and false negative. We observe by Table 3, that the breast radiologists had a total error in breast diagnosis of 0.5% (they hadn’t correctly identified one fibroadenoma and one cyst), 46.50% of negative responses with 0.5% of error (two false negative cases: one fibroadenoma and one cyst), 13.75% of fibroadenoma responses with 0.25% of error (one fibroadenoma was not correctly identified), 8.00% of cancer responses with 0.00% of error and finally 31.75% of cyst responses with 0.25% of error (one cyst was not correctly identified). Indeed the general radiologists had a total error in breast diagnosis of 2.00% (they hadn’t correctly identified five fibroadenomas, one cancer and two cysts), 47.50% of negative responses with 1.50% of error (six false negative cases: five fibroadenomas and one cyst), 12.75% of fibroadenoma responses with 1.25% of error (five fibroadenomas were not correctly identified), 7.75% of cancer responses with 0.25% of error (one cancer was not correctly identified) and finally 32.00% of cyst responses with 1.00% of error (two false positive cases: one Fibroadenoma and one cancer; and two cysts were not correctly identified). In Figure 1 we had shown graphically the results of Table 3. To start Table 2, we had compared the proportion of correct diagnoses between breast and general radiologists. One tail McNemar’s exact test was performed with a significance level 10%. The result was that the breast radiologists had a proportion of correct diagnoses (53.5 %) statistically major in comparison to the proportion of correct diagnoses of general radiologists (52.5 %), p-value = 0.0625 (Table 3).

In conclusion, we had compared the accuracy between breast radiologist and general radiologist in terms of Sensitivity (Se) and specificity (Sp)[14] and computed the confidence intervals with score method with continuity correction. The results on total sample were for the breast radiologists, Se = 0.99 with confidence interval (0.973, 0.998) and Sp = 0.989 with confidence interval (0.971, 0.997), while for the general radiologists, Se = 0.972 with confidence interval (0.949, 0.986) and Sp = 1 with confidence interval (0.988, 1.00), i.e. with a significance level of 5%, there were no significant...
differences in the evaluations both true-positive and true-negative between breast radiologists and general radiologists (Table 4).

Discussion
By this study we have observed that the breast radiologists identifies all cases of breast cancers (32/32), 55/56 fibroadenomas, 127/128 cysts and 186/184 negative cases, with global error of 0.5% (2/400). Instead, the general radiologist reported 190/184 negative cases, 31/32 cancers, 128/128 cases of breast cysts (but with four errors) and 51/56 fibroadenomas, with global error of 2% (8/400). Two false negative cases reported by breast radiologists were one cyst and one fibroadenoma, both with a diameter <5mm. Instead, 6 false negative cases were evaluated by general radiologists and were four fibroadenomas (with diameters < 5mm) and two cysts (one with diameters < 5mm and one with diameter 5mm); one fibroadenoma was evaluated like a cyst (with diameter < 5mm) and one cancer was evaluated like a cyst (with diameter <5mm).

We had that the subgroups were not statistically different about patients number responses (p-value = 0.69, with \( \chi^2 \) test. We don’t had significant differences among the breast radiologists diagnoses p-value = 0.368 (\( \chi^2 \) test) and among the general radiologists diagnoses, p-value = 0.836 (\( \chi^2 \) test) in comparison to effective diagnosis (Table 2). In each group the patients underwent the standard breast examination by a breast radiologist and subsequent in the same day, by a general radiologist. These tests and procedures, imply that on our results there could be a very low probability of statistical bias. By Table 2, we had compared the proportion of correct diagnoses between breast radiologists (53.5 %) and general radiologists (52.5 %), with one tail McNemar’s exact test. The results were, with a significance level 10%, that the breast radiologists had a proportion of correct breast diagnoses statistically major in comparison to the proportion of correct diagnoses of general radiologists, p-value = 0.0625 (Table 3). Finally, we had compared the performances both breast and general radiologists in terms of Sensitivity (Se) and specificity (Sp) and computed the confidence intervals with score method with continuity correction. On total group the breast radiologists had Se = 0.99 with confidence interval (0.973, 0.998) and Sp = 0.989 with confidence interval (0.971, 0.997), instead the general radiologists had Se = 0.972 with confidence interval (0.949, 0.986) and Sp = 1 with confidence interval (0.988, 1.00), i.e. with a significance level of 5%, on total sample there were not significant differences in the evaluations both true-positive and true-negative between breast radiologists and general radiologists (Table 4). In comparison with cytological, histological and/or 2 years follow-up diagnosis performed on all patients, breast radiologists are more accurate in comparison to general radiologists in the evaluation of breast pathologies with US methodology with a probability of 90 %. Our study complies with other studies proving that a higher volume of procedures among individual physicians are associated with better outcomes across a variety of conditions [15,16]; despite United States requires interpretation of only 960 breast exams over a 2 years period, European Commission guidelines recommend a minimum volume of 5000 mammograms per year for interpreting radiologist [17-19]. Thèberge in 2014 affirms that only if a interpretive volume is consistently less than this requirement, radiologist accuracy may be compromised and that accuracy improves with increases in volume of up to approximately 3000 breast exams interpreted annually [20,21].

Some studies did not find evidence that great volume or experience at interpreting breast exams is associated with better performance [21] probably because these radiologists may not receive feedback on the outcome of all women. Disagreement is probably related also to the absence of learning curves in radiology [22], because it has been demonstrated that radiologists with more years of experience in interpreting mammograms have low false-positive rates, without significatively effects on sensitivity [23, 24]. The irreplaceable breast training demostre also that automated breast volume scanning cannot be preferred to a manual US examination [25,26]. Residency breast imaging training, dedicated post-residency courses, continuing medical education, annual interpretive volume could improve the radiologist learning curve and accuracy of breast exams with an earlier stage breast cancer detection with low rate of unnecessary biopsies that result in both patient anxiety and increased medical costs. [1,27]. Even if this study was monocentric and analyzed only one technique, the main advantages were a big sample and a prospective study; furthermore, we examined breast US accuracy within individual radiologists, comparing with cytological, histological and/or 2 years follow-up diagnosis; we compared the results obtained by breast and general radiologists in four different subgroups of 100 patients to minimize a possible statistic bias and to obtain statistically significant
results. and we used only two categories for breast lesions, avoiding any specific breast classification, such as BI-RADS classification.

In conclusion, a multicentric prospective study in future could confirm the more accuracy of breast radiologist in comparison to general radiologist in the evaluation of breast pathology in the US diagnoses.
Table 1. Subgroups description (in parenthesis the patients number with multifocal cancer)

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<td>LIQ-RA</td>
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<td></td>
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<tr>
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<td>12.00</td>
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<tr>
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<td>16.00</td>
<td>12.00</td>
<td>16.00</td>
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<tr>
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<td>32.00</td>
<td>32.00</td>
</tr>
<tr>
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<td>48.00</td>
<td>44.00</td>
<td>48.00</td>
<td>44.00</td>
</tr>
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</table>
**Table 2.** US response for each subgroup of Breast Radiologist and General Radiologist, and effective diagnosis.

<table>
<thead>
<tr>
<th>US response</th>
<th>% Total error</th>
<th>% Negative</th>
<th>% Cyst</th>
<th>% Fibroadenoma</th>
<th>% Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Radiologist 1</td>
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<td>48.00 (0.00)</td>
<td>36.00 (0.00)</td>
<td>12.00 (0.00)</td>
<td>4.00 (0.00)</td>
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<tr>
<td>Breast Radiologist 2</td>
<td>1.00</td>
<td>45.00 (+1.00)</td>
<td>27.00 (-1.00)</td>
<td>16.00 (0.00)</td>
<td>12.00 (0.00)</td>
</tr>
<tr>
<td>Breast Radiologist 3</td>
<td>1.00</td>
<td>49.00 (+1.00)</td>
<td>32.00 (0.00)</td>
<td>11.00 (-1.00)</td>
<td>8.00 (0.00)</td>
</tr>
<tr>
<td>Breast Radiologist 4</td>
<td>0.00</td>
<td>44.00 (0.00)</td>
<td>32.00 (0.00)</td>
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<td>8.00 (0.00)</td>
</tr>
<tr>
<td>General Radiologist 1</td>
<td>1.00</td>
<td>49.00 (+1.00)</td>
<td>36.00 (0.00)</td>
<td>11.00 (-1.00)</td>
<td>4.00 (0.00)</td>
</tr>
<tr>
<td>General Radiologist 2</td>
<td>3.00</td>
<td>45.00 (+1.00)</td>
<td>30.00 (+2.00)</td>
<td>14.00 (-2.00)</td>
<td>11.00 (-1.00)</td>
</tr>
<tr>
<td>General Radiologist 3</td>
<td>3.00</td>
<td>51.00 (+3.00)</td>
<td>31.00 (-1.00)</td>
<td>10.00 (-2.00)</td>
<td>8.00 (0.00)</td>
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<tr>
<td>General Radiologist 4</td>
<td>1.00</td>
<td>45.00 (+1.00)</td>
<td>31.00 (-1.00)</td>
<td>16.00 (0.00)</td>
<td>8.00 (0.00)</td>
</tr>
<tr>
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<td>36.00</td>
<td>12.00</td>
<td>4.00</td>
</tr>
<tr>
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<td>44.00</td>
<td>28.00</td>
<td>16.00</td>
<td>12.00</td>
</tr>
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<td>44.00</td>
<td>32.00</td>
<td>16.00</td>
<td>8.00</td>
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</table>

**Table 3.** US response for breast radiologists, general radiologists and effective diagnosis for total group

<table>
<thead>
<tr>
<th>US response</th>
<th>% Total error</th>
<th>NOT SUSPICIOUS</th>
<th>SUSPICIOUS</th>
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<tr>
<td></td>
<td>% Negative</td>
<td>% Cyst</td>
<td>% Fibroadenoma</td>
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<tr>
<td>Breast Radiologists</td>
<td>0.50</td>
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<td>31.75 (0.25)</td>
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<td>47.50 (1.50)</td>
<td>32.00 (1.00)</td>
</tr>
<tr>
<td>Effective diagnosis</td>
<td>46.00</td>
<td>32.00</td>
<td>14.00</td>
</tr>
</tbody>
</table>
Figure 1. US response for breast radiologists, general radiologists and effective diagnosis, for total group

Table 3. One tail McNemar’s exact test in the evaluation the accuracy between breast and general radiologists.

<table>
<thead>
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<th>Test : McNemar’s exact test</th>
<th>significant test</th>
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<tr>
<td>$H_0 : \text{general radiologist} \geq \text{breast radiologist}$</td>
<td>False</td>
</tr>
<tr>
<td>$H_1 : \text{general radiologist} &lt; \text{breast radiologist}$</td>
<td>True</td>
</tr>
<tr>
<td>p-value one-tail (&lt; $\alpha$)</td>
<td>0.0625</td>
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<td>$\alpha$ (significance level)</td>
<td>0.1</td>
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</table>

Proportion of correct diagnosis

| Breast Radiologist | 53.5 % |
| General Radiologist | 52.5 % |

Table 4. Sensitivity and Specificity with confidence intervals, for breast and general radiologists in the breast pathologies diagnoses with US ultrasound.

<table>
<thead>
<tr>
<th>Breast pathologies diagnoses</th>
<th>Sensitivity ($Se$)</th>
<th>Confidence interval at 95% for $Se$</th>
<th>Specificity ($Sp$)</th>
<th>Confidence interval at 95% for $Sp$</th>
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<tbody>
<tr>
<td>Breast Radiologists</td>
<td>0.990</td>
<td>(0.973, 0.998)</td>
<td>0.989</td>
<td>(0.971, 0.997)</td>
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<tr>
<td>General radiologists</td>
<td>0.972</td>
<td>(0.949, 0.986)</td>
<td>1.000</td>
<td>(0.988, 1.000)</td>
</tr>
</tbody>
</table>
PERSONALITY DISORDER AND TEMPERAMENTAL TRAITS
IN PATIENTS WITH BREAST DISEASE:
A PICTORIAL ESSAY

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Abstract
Personality disorders and temperamental traits could influence patient’s perception of breast disease, impairing patient compliance and treatment effectiveness. Preexisting psychopathological condition increases risk for developing anxiety disorders and major depression in patients with breast cancer. This evidence underlines the importance of improving knowledge of psychiatric background for oncologists radiologists and pathologists involved in management of female receiving this kind of diagnosis.
Psychiatric assessment of personality disorders and temperamental traits is useful in breast unit to reach a better management and an optimal compliance to treatment.

Key Words: Personality disorders; breast cancer; temperamental traits; pictorial essay
Introduction
Many women fear breast cancer and this is the main reason that induce them to prevention exams, with the purpose of early detection and diagnosis, that could guarantee better therapeutic results, prognosis and living conditions. However, in these women, many breast diseases are diagnosed and, regardless of the type of the physical condition (benign or malignant) [1] and such as pelvic diseases [2-4], psychological distress may accompany the patient for a long period [5]. Personality disorders and temperamental traits can influence the patient’s perception of the disease, treatment and its effects, reflecting knowledge, experiences, individual and collective values that concern different times and places in history with effect also on daily activities [5]. Increasing evidence indicates that the presence of specific traits or dimensions of the personality may have an important predictive value in terms of therapeutic response in patients with breast disease diagnosis and in the development of other diseases related to the psychopathological condition, not last secondary osteoporosis [6] and temporomandibular disorders [7]. The role of a psychopathological condition in predisposing to breast cancer or in correlating to severity of the disease has been a long-running controversy; psychosocial factors may also influence cancer risk and cancer progression [8]. Moreover, personality disorders, but not cancer severity or treatment type, are risk factors for later generalized anxiety disorder and major depressive disorder in non metastatic breast cancer patients [9]. Patients with breast disease should be screened for personality disorders because specific interventions for these patients could prevent psychiatric disorders. Whereas in young women (≤ 39 yo), benign or malignant disease can occur, over 40 y.o., a primary breast cancer should be rule out in any kind of breast abnormality. Breast benign disease are more frequent than malignant ones [10]; the evolution of senologic diagnosis, thanks to ultrasonography, mammography, magnetic resonance with contrast media [11] associated with interventional procedures (fine needle aspiration and biopsies) and the availability of dedicated radiologists can avoid useless surgery in majority of patients affected by benign diseases, term that includes a heterogeneous group of lesions that may be detected as incidental findings [12]. It is relevant for radiologists, pathologists and oncologists to diagnose benign lesions, both to distinguish them from in situ and invasive breast cancer and to assess a patient’s risk of developing breast cancer, so that the most appropriate treatment modality for each case can be established [1;13], either in female or in male patients[14;15]. The strength of the study assessment of personality is the standardized and widely accepted SCID II interview that captures the most important dimensions of personality differences between individuals [5] In literature there is no associations between personality traits with cancer and no correlation with the severity of breast disease. In the Miyagi cohort of Japanese participants this individual-participant meta-analysis based on the full Five Factor Model assessment of personality provides strong evidence to suggest that people's personality dispositions do not influence their risk of developing cancer [16]. All patients presented a different personality disorders and the prevalent personalities are characterized by extraversion, irritability, neurocitsm and sometimes aggression, typical aspects of these personality disorders [17]. The association between neuroticism and cancer may be a common feature but negative predictor of disease and the personality scores may have been influenced by the cancer treatment; smoking or alcohol consumption are associated with extraversion or other personality characteristics as well as cancer out [18].
Cancer patients should not think that their personality traits may have affected their cancer or cancer prognosis. To date, there are no enough data on temperament and participation in cancer screenings to estimate the plausibility of this scenario. With respect to the four temperament, it is particularly notable that there was association between depressive type and malignant breast cancer . Multivariate analysis in chinese study demonstrated that breast cancer as a dependent risk factor accounted for 6.3% and 7.4% of the variance of depressive disposition in oncologic patients [19]. The role of definite personality traits has been considered in the assessment of temperament and character as a predictor of a certain psychopathological state in patients with breast disease diagnosis. Based on these considerations, it could be useful a psychiatric counselling in breast units in the diagnostic cluster detection.

References
LEVEL AND CONDITIONING OF KNOWLEDGE IN BENIGN BREAST DISEASE IN VERY YOUNG PATIENTS

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⁎ teresaiannaccone84@libero.it

Abstract
Purpose of the study was to identify individual psychopathological features in young patients suffering from benign breast disease. Participants were interviewed using a structured clinical test (SCID-II, version 2.0) disorders, and the Italian version of Akiskal’s semi-structured clinical interview for temperamental profiles (TEMPS-I) after clinical breast exams and ultrasonography. All patients presented different personality disorders and heterogeneity in temperamental profiles. Of 19 patients recruited, four patients with negative breast exam had istrionic-narcisistic personality; nine patients suffering from fibroadenoma, three patients with breast asymmetry had mainly B group disorders with high prevalence of avoidance and obsessive-compulsive personality. Patients suffering from hematoma and gynecmastia had the C group antisocial disorder. In fibroadenoma, hematoma and gynecomastia cases the temperamental trait is mainly depressive. In breast asymmetry cases and in patients without breast disease, temperamental trait is cyclothymic and irritable. The study demonstrate the significance of psychiatric counselling also for young patients in breast units. Future purpose is to extend the sample and to add a follow-up evaluation.

Key word: personality, temperament, breast disease, young patients, gynecomastia, fibroadenoma
Introduction
Many young patients fear breast cancer and this is the main reason that induce them to consult a specialist with the purpose of early detection and diagnosis in case of palpable mass [1,2]. Breast asymmetry, fibroadenoma [3,4], hematoma and gynecomastia [5] are the most frequent breast palpable mass in young patients ≤ 20 years old. Even if breast cancer is rare at this age, a careful history, physical examination and ultrasonography should be performed to obtain a diagnosis. Mammography, fine needle aspiration and Magnetic Resonance are indicated in selected cases [6]. Surgical intervention usually is contraindicated in prepubertal patients and recommended only in few cases in postpubertal patients [7]. However, in these patients, benign breast diseases are diagnosed and psychological distress may accompany the patient for a long period [8,9]. Personality disorders and temperamental traits can influence the patient’s perception of the disease, reflecting knowledge, experiences, individual and collective values that concern different times and places in history. The role of specific personality traits has been considered in the assessment of temperament and character as a predictor of a certain psychopathological state in patients with breast disease diagnosis. Patients with breast disease should be screened for personality disorders because specific interventions for these patients could prevent psychiatric disorders. Breast benign disease are more frequent than malignant ones [10]. Objective of the study was to investigate individual characteristics in young patients with breast palpable mass.

Material and Methods

Population
This prospective observational study included 19 patients in the period between 1st January and and 31th March 2015. Informed consent was obtained from all individual participants included in the study in over 18yo patients; in the others, parents gave informed consent for their sons (Table 1). Senologic inclusion criteria: ≤ than 20 years old; first breast examination. Senologic exclusion criteria: breast implants; previous breast or gynecological surgery. Psychiatric inclusion criteria: medium-high socio-cultural background; no previous visits with a psychiatrist or therapy with psychotropic drugs. Psychiatric exclusion criteria: familiarity for mental illnesses.

Breast exams
All patients underwent clinical breast exam and breast ultrasonography; US was performed using a Logiq S6 scanner (GE Healthcare, Waukesha, WI, USA) with a multifrequency matrix-array linear transducer (7-14 MHz); a lower frequency transducer was used for the larger attenuative breasts, inflammatory masses and the axilla. The use of a stand off was required for nipple, superficial/or skin lesions. Colour Doppler US was also performed to study intralesional vascularity. In one case of giant fibroadenoma, US-guided fine needle aspiration was performed, as presurgical planning.

Psychiatric evaluation
Patients with a breast disease diagnosis underwent a psychiatric visit within three days after senological exams. To all patient, after informed consent, diagnosis was established with the aid of a structured clinical interview for DSM-IV Axis II (SCID-II, ver 2.0) disorders [11]. Each patient furnished relevant anamnestic data regarding personal, physiological and clinical history through ad hoc interviews. Participants were also interviewed using the Italian version of Akiskal’s Semi-structured Clinical Interview for Temperament (TEPSS-I) [12]. This interview consists of 32 items and distinguishes 4 basic affective temperaments: depressive, cyclothymic, hyperthymic and irritable. These profiles don’t corresponding to the DSM-IV nosological categories.

Statistical analysis
The statistical analyses were performed by Matlab statistical toolbox version 2008 (MathWorks, Natick, MA, USA) for Windows at 32 bit. The statistical tests performed: Student T-test [2] and Z-test [2], were considered significant with p-value < 0.05. The Pearson’s linear correlation coefficient R, where the correspondent p-values were computed with T-Student test, under null hypothesis of Pearson’s linear correlation coefficient R = 0. In addition the qualitative variables were changed in qualitative numeric variables: study grade (university student = 1, school student = 0), personality disorders (avoidant = 1, dependent = 2, obsessive-compulsive = 3, istrionic = 4, narcissistic = 5, borderline = 6, antisocial = 7), temperament (depressive = 1, irritable =2, cyclothymic = 3), breast diagnosis (negative = 0, positive: breast asymmetry = 1, FAD = 2, hematoma = 3, gynecomastia = 4), sex (female = 1, male = 0) and relative affected by breast cancer (present = 1, absent = 0) [13-15].
Results
The patients sample was composed from 84.21% females (16/19) and 15.79% males (3/19); with age into range 15-20, mean age about 17 y.o. and standard deviation about 2 y.o. In addition this group was composed by 7 university students and 12 school students (Table 1). At breast exams, 15 patients (78.95%) had benign diagnosis, 4 patients (21.05%) breast examination were negative. Of the 15 positive patients, 13 were female, 2 were male. Of the 13 female patients, nine had diagnosis of fibroadenoma, three of breast asymmetry, one of hematoma; in the two male patients gynaecomastia was diagnosed (Table 2). Four patients had relatives affected by breast cancer; in one of these patients, fibroadenoma was diagnosed, one had a post-traumatic hematoma; in two patients breast examination was negative. In correlation analysis both univariate and multivariate were performed among variables. The significant results were obtained both in univariate and multivariate analysis only between personality disorders II and personality disorders I. For radiologist variable: breast diagnosis was a significantly negative correlation with age (R= -0.465, p-value = 0.0446) according our classification, and in multivariate analysis study grade, age and relative affected by breast cancer were a significant predictors for dependence variable breast diagnosis. All patients presented different personality disorders and heterogeneity in temperamental profiles, as shown in SCID II and TEMPS-I results. Of 9 patients with FAD presented 5/9 avoidant disorder and 3/9 antisocial and 1/9 obsessive-compulsive disorders. Of 3 patients with benign breast asymmetry, 2/3 presented avoidant and obsessive compulsive disorders. Of 2 patient with gynaecomastia presented avoidant and antisocial disorders. One patient with hematoma presented antisocial and dependant disorders. Of 4 patient with no breast mass presented 2/4 istrionic and narcissistic disorders and 2/4 dependent. In addition the temperamental analysis:

- Of 9 patients with FAD presented 6/9 a depressive and 3 a cyclothymic temperamental traits;
- Of 3 patients with benign breast asymmetry presented 2/3 cyclothimic and 1 an irritable temperament;
- Of 2 patient with gynaecomastia presented a depressive temperament;
- One patient with hematoma presented a depressive temperament;
- Of 4 patient with no breast mass presented 3/4 an irritable and 1/4 a cyclothymic temperaments (Table 3).

Discussion
The evolution of senologic diagnosis, thanks to ultrasonography and interventional procedures, such as fine needle aspiration and biopsies can avoid useless surgery in majority of patients affected by benign diseases, term that includes a heterogeneous group of lesions that may be detected as incidental findings [16]. Breast asymmetry, fibroadenoma, hematoma are the most frequent lesion detected in female young patients; gynaecomastia is a common finding in male adolescents.

Breast asymmetry can be differentiate in three classes in relation to shape (due to tubular breast and Poland Syndrome, position (in patients suffering from scoliosis), and volume (macromastia and hypoplasia). The diagnosis can be carry out with clinical examination and the therapy consists in surgical intervention [17].

Fibroadenoma is the most common benign breast disease in young women; the lesion is a hormone-dependent neoplasm that develop from the special stroma of the lobule, that can arise since 15 yo. The management of this lesion depends on growth and diameter; only lesions with a diameter >2.5/3 cm or growing lesions should be undergone surgical excision; other lesions can be monitored with ultrasound follow-up [3].

Hematoma can occur in case of a major trauma (road accident) or minor (assaults or falls); the lesion can be followed by central necrosis and liquefaction of the adjacent fat. Unless a massive blood extravagation, requiring surgical drainage, occurs, this can lead to the development of a fibrotic or cystic tissues that will almost entirely calcify within 2 or 3 years [18].

Gynaecomastia is characterized by the presence of palpable breast tissue in boys without other signs of sexual maturation; it is a rare condition, and some cases have been associated with excessive estrogen production by adrenal or testicular tumors, congenital adrenal hyperplasia, rare syndromes, such as Peuts-Jeghers’ or can be related to the use of drugs that affect androgen and estrogen production and metabolism; surgical approach can be the treatment of choice in this disease [19].

The strengths of our study is the standardized and widely accepted SCID II interview that captures the most important dimensions of personality differences in young population. Our assessment of personality was free from such distortions, because the test were drawn up within.
three days from breast examination. In our experience, all patients presented a different personality disorders. Of 19 patients enrolled, four had no breast disease and present istrionic-narcissistic personality, nine suffered from fibroadenoma and three cases of breast asymmetry present B group disorders with prevalence of avoidant and obsessive compulsive personality. In patients suffering from hematomata and gynecomastia C group antisocial disorder overbears. The prevalent personality disorder (cluster b avoidant type) is characterized by social isolation, relationship anxiety, low esteem and altered perception of body image due to breast disease. Assertive training in a cognitive behavioral therapy can improve patients' esteem. Generally, psychotherapy can reduce the emotional distress and allows to cut down the unsuitableness in social life due to breast disease [20]. The body image is a multifactorial concept, widely used in scientific literature, that roots in biological and psychological bases and that can change during the life. Inter alia, neurobiological, somatic and psychological factors contribute to body image, that represents a key element of sexual identity, especially in adolescents that live in natural conflictuality [21,22]. Breast appearance and beauty are the most important elements because of the influence on femininity, esteem, self confidence and the belonging to own gender [23]. Sexual identity and relationship are physically and emotionally influenced by changes due to breast disease in a young patient. Emotional and unconscious perception of own body is the main factor of “private body consciousness”; in these cases there is the loss of social adaptation with an attitude of closure also with own physician [24]. Besides personality disorders, temperament was analyzed; of 9 patients with FAD presented 6/9 avoidant a depressive and 3 cyclothymic temperamental traits; of 3 patients with benign breast asymmetry presented 2/3 cyclothymic and 1 an irritable temperaments; of 2 patient with gynecomastia presented a depressive temperament; one patient with hematomata presented a depressive temperament; of 4 patient with no breast mass presented 3/4 an irritable and 1/4 a cyclothymic temperament. Depressive temperament overbears in case of fibroadenoma, hematomata and gynecomastia; in case of breast asymmetry and in patients without breast disease cyclothymic and irritable temperament predominates. There are some factors that can cause a reactive - depressive behavior in these patients. Psychosocial factors such as a restless youth, pessimism, social inadequacy, stressful events, can predict depressive symptoms in this population [25]. Physical factors such as pain, physicc disability and other symptoms are associated to depression, but there is no association with the stage of the disease, the treatment and the doctor-patient relationship that can cause maladaptive response. Our results, according to literature, suggest that a depressive trait in these patients is influenced by personality more than temperamental profile that can be modified by the clinical course [26].

**Conclusion**

In young patients with breast palpable mass, personality disorders do not influence the clinical course, but can modify the quality of life in relation to interpersonal relationship because they tend to social-labor insulation due to anxiety and low esteem (B group personality). Furthermore, our study investigate also temperamental traits; a depressive temperamental can characterize some diseases, such as fibroadenoma and gynecomastia; in these cases a reactive-irritable behavior can influence the compliance in the medical approach and in the therapy decision. Limitations of our study include: the small sample of patients, the duration of the study and the therapy response. Data obtained from our study suggest a psychiatric consulence for young patients in breast units. Future purpose is to extend the patient sample, add a follow-up evaluation that can validate psychoterapeutic approach associated to the standard treatment for these diseases.

**References**

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### Table 1 – study population

<table>
<thead>
<tr>
<th>P.</th>
<th>SEX</th>
<th>AGE</th>
<th>STUDY GRADE</th>
<th>PERSONALITY DISORDERS I</th>
<th>PERSONALITY DISORDERS II</th>
<th>TEMPERAMENT</th>
<th>BREAST DIAGNOSIS</th>
<th>RELATIVE AFFECTED BY BREAST CANCER</th>
</tr>
</thead>
<tbody>
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<td>irritable</td>
<td>breast Asymmetry</td>
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<td>depressive</td>
<td>Fibroadenoma</td>
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<tr>
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<td>M</td>
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<td>depressive</td>
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<td>F</td>
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<td>istrionic</td>
<td>narcissistic</td>
<td>irritable</td>
<td>Negative</td>
<td>grandmother</td>
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### Table 2 - Sample patients composition

<table>
<thead>
<tr>
<th>Patients</th>
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<th>Negative</th>
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<tr>
<td>16 F</td>
<td>9 FAD</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>3 BREAST ASIMMETRY</td>
<td>1 HEMATOMA</td>
</tr>
<tr>
<td>3 M</td>
<td>2 GYNECOMASTIA</td>
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**Table 3.** Univariate and Multivariate linear correlation analysis among: personality disorders, temperament, breast diagnosis, age, study title and relative affected by breast cancer.

In table were indicated the Pearson's linear correlation coefficient and in parentheses the correspondence p-value in column univariate analysis and in multivariate analysis. The partial correlation coefficient \( R_{\text{partial}} \) was the coefficient of correlation of the variable with the dependent variable, adjusted for the effect of the other variables in the linear model. In bold the significant tests.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Univariate analysis</th>
<th>Multiple linear correlation analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>( R (p\text{-value}) )</td>
</tr>
<tr>
<td><strong>Personality disorders I / Temperament</strong></td>
<td>0.309 (0.198)</td>
<td>0.404; p-value = 0.884</td>
</tr>
<tr>
<td><strong>Personality disorders I / Breast diagnosis</strong></td>
<td>0.175 (0.475)</td>
<td>0.476; p-value = 0.085</td>
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<tr>
<td><strong>Personality disorders I / Study grade</strong></td>
<td>0.042 (0.863)</td>
<td>0.356; p-value = 0.212</td>
</tr>
<tr>
<td><strong>Personality disorders I / Age</strong></td>
<td>0.0301 (0.903)</td>
<td>0.395; p-value = 0.162</td>
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<tr>
<td><strong>Personality disorders I / Sex</strong></td>
<td>0.281 (0.244)</td>
<td>0.489; p-value = 0.076</td>
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<tr>
<td><strong>Personality disorders I / Relative affected by breast cancer</strong></td>
<td>0.133 (0.588)</td>
<td>0.432; p-value = 0.123</td>
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<tr>
<td><strong>Personality disorders II / Personality disorders I</strong></td>
<td>-0.0552 (0.0142)</td>
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<td>0.143 (0.558)</td>
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<td><strong>Personality disorders II / Study grade</strong></td>
<td>-0.152 (0.535)</td>
<td>-0.135; p-value = 0.660</td>
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<td><strong>Personality disorders II / Sex</strong></td>
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<td>0.097; p-value = 0.752</td>
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<td>0.137; p-value = 0.655</td>
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<td><strong>Breast diagnosis / Study grade</strong></td>
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<td><strong>Breast diagnosis / Age</strong></td>
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<td><strong>Breast diagnosis / Sex</strong></td>
<td>-0.363 (0.127)</td>
<td>-0.395; p-value = 0.130</td>
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<tr>
<td><strong>Breast diagnosis / Relative affected by breast cancer</strong></td>
<td>-0.191 (0.433)</td>
<td>0.576; p-value = 0.0196</td>
</tr>
</tbody>
</table>
AWARENESS OF BREAST CANCER IN OLD WOMEN:
PSYCHOPATOLOGICAL FEATURES

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Abstract
Although breast cancer in elderly has favorable biological features, low aggressiveness, the mortality is high due to the comorbidity and to the low rate of prevention, also in symptomatic patient. To this, must be added a general psychopathology than mere anxiety and depressive symptoms related to organic comorbidities and at the elder's frailty; women belonging to the middle-high educational level group were shown to have significantly lower state and trait anxiety scores, which might be explained by a combination of the above alongside a more stoic approach to illness.

Key words: breast cancer, elderly, STAI, MADR-S
Introduction

Even if breast cancer is more frequent in over 70 yo women, it is often less aggressive if compared with premenopausal women with a superimposable life expectancy of women without this diagnosis. For these reasons, women should conduct prevention exams even in the range of over 70 years; some authors propose biannually clinical instrumental evaluation in absence of comorbidity [1].

Sing demonstrates that there is no significant difference of tumor size between women under 70 and elderly women [2] with a low grade and high positivity for estrogen and progesterone receptors [3]. However, despite the favorable biological features of the elderly breast carcinoma, the mortality is high [4], due to the comorbidity, the undertreatment and especially due to the low sensitivity to the prevention in these women [5], like Africans women [6]. However, the prevention of breast cancer, conducted by dedicate physicians [7] can reduce mortality even in the presence of comorbidities [8], even in absence of survival improvement in ≥ 80 yo women [9]. Numerous studies have investigated psychiatric morbidity in breast cancer elderly women, in particular depression and/or anxiety and personality disorders linked to psychological factors underlying the no cure breast disease [10,11]. For the assessment general psychopathology features, are usually used some psychometric instruments such as: the Spielberger's State-Trait Anxiety Inventory (STAI), a 40-statement self-report inventory designed for the assessment of state (S-Anxiety) and trait (T-Anxiety) anxiety in adults, which has been extensively used in research and clinical practice. It evaluates how the respondent feels “right now, at this moment”, as well as how he feels “generally”. Each STAI item is given a weighted score of 1 to 4 [12]; the Montgomery-Asberg Depression Rating Scale (MADRS), a clinician-rated 10-item scale designed to measure the severity of depressive symptoms. Because there is little emphasis on somatic symptoms, it can also be used for the assessment of depression in people with physical illness. It measures the severity (on a scale from 0 to 6) of a number of symptoms, including mood and sadness, tension, sleep, appetite, energy, concentration, suicidal ideation and restlessness [13]; the Symptom Checklist-90-R (SCL-90-R), a self-rated 90-item checklist objectively evaluating a broad range of symptoms of psychopathology. It measures nine symptom dimensions and is designed to provide an overview of a patient’s psychological symptoms and their intensity at a given time point. The symptom scales measured are: somatization, interpersonal sensitivity, obsessive-compulsive symptoms, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychotism. The SCL-90-R has a high reliability and validity, and has been widely used [14]. The scale were adjusted for age, education level, employment status, family status, number of children, smoking, alcohol consumption, age at menarche, psychiatric treatment and the presence of thyroid, cardiac or gynecological diseases. Elderly women suffering from breast cancer had significantly higher general symptoms of psychopathology. It is noteworthy that all measures of psychopathology, as assessed by the SCL-90, were increased. This indicates that disease activates complex mechanisms giving rise to a more general psychopathology than mere anxiety and depressive symptoms related to organic comorbidities and at the elderly frailty despite these women are well educated, they have a good income and a family present. This is important because this is one of the few existing studies which directly focuses on the evaluation the life stress event life events related to the history of these women who have had a trauma of various kinds which modified the temperament eliminating the physical health perception [15]. The trait anxiety was found to be higher in these patients which probably indicates that personality features may become more prominent if exposed to stress; similarly, symptoms of depression as measured by the MADRS were significantly which is consistent with the high depression scores measured with different instruments. Sometimes underestimation of physical pathology also seen in such circumstances, which comprises a component of denial through which individuals may attempt to minimize the severity of their condition [16] that often requires a pharmacological approach, not without aftermath [17]. Besides the aforementioned psychological reactions to a life-threatening disease, biological components associated with the disease could be responsible for psychiatric symptoms often observed in cancer patients. Thus, hormonal changes (e.g. abrupt changes in steroid levels) occurring for various reasons appear to be associated with symptoms of mood disorders in a subgroup of these women, such as in some other pathological conditions [18,19]. Of interest is also the observation that several chronic diseases, including different types of cancer in elderly frail people [20]. Anger/aggressiveness were found to be significantly increased in the breast cancer group. The association between breast cancer and aggression/hostility is unclear and relatively little researched. However,
there is evidence that there might be a link between the two and specifically with the suppression of these feelings. Furthermore, psychological responses to breast cancer such as “helplessness/hopelessness” have been postulated to be factors influencing survival, although the causal mechanisms are unclear. Helplessness and repression seem to be two key factors closely associated and interrelated with anger/aggressiveness, as repressed hostility, negative emotions and a feeling of loss of control often described by breast cancer patients are likely to contribute through a vicious circle to unfavorable prognosis, while denial/minimizing have been reported to be associated with a more favorable prognosis [21]. In this line of thought, the increased psychotism and obsessionality observed in the SCL-90 subscales, may reflect the emotional restriction, suppression of negative feelings, and wish of control. This particular association has not been previously reported and its significance needs to be further clarified. So far, no psychological factor has been convincingly demonstrated to influence cancer development; however, some factors putatively play a role. The so-called “cancer-prone personality”, whose core characteristics are those of emotional suppression and emotional control (i.e. suppressing negative emotions of anger and hostility, abrogating one’s needs in favor of the needs of the others and an attitude of helplessness or hopelessness), has been suggested to actually predispose some individuals to developing cancer or to prompt disease progression. Nevertheless, the findings remain controversial [22]. Several known risk factors were considered, including age at menarche, other coexisting medical conditions, previous psychiatric history and treatment, and various socio-demographic variables. Age at menarche, which is considered to be important for women and is known to be a strong and established factor associated with breast cancer, was found to positively correlate with depression and psychotism. Women who had undergone psychiatric treatment were found to have high somatization, phobic anxiety, depression, and general psychopathology scores on the SCL-90. This is in agreement with existing studies showing that previous psychological treatment was associated with depression and/or anxiety around diagnosis, with some studies suggesting that the risk factors for these conditions are related to the patient itself rather than to disease or treatment [23].

Regarding the role of various socio-demographic variables, including educational level, employment status, and family status, for the development of psychopathology in the two studied groups, it was observed that divorced/widowed women with breast cancer scored higher on obsessionality and depression, which indicates a higher vulnerability associated with such life events [24]. Anger/aggressiveness scores were found to be lower in women with middle or high educational level, which possibly suggests that these women have a more developed and sophisticated coping system and more access to information compared to women with a lower educational level. Similarly, women belonging to the middle-high educational level group were shown to have significantly lower state and trait anxiety scores, which might be explained by a combination of the above alongside a more stoic approach to illness [25].

References
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Abstract
We describe a case of an old man affected by Klinefelter Syndrome (47, XXY) in which has been diagnosed a breast cancer with metastatic axillary and supraclavicular lymph nodes. The case analyzed the role of bilateral gynecomastia and of pharmacological replace therapy in the evaluation of breast cancer risk in these patients. The usefulness of breast cancer screening could be evaluated in a retrospective cohort study.

Key words: Klinefelter Syndrome, gynecomastia, male breast cancer
Introduction
A 70-year-old man, D.C., with a diagnosis of Klinefelter syndrome 25 years before by genetic testing (47XXY), came to our Hospital for breast palpable mass on left side. The patient underwent clinical breast exam and breast ultrasonography; US was performed using a Logiq S6 scanner (GE Healthcare, Waukesha, WI, USA) with a multifrequency matrix-array linear transducer (7-14 MHz); Colour Doppler US was also performed to study intralobular vascularity. The patient received a medical report at the end of the examination. The exam showed bilateral gynecomastia and, in the site of the palpable mass, a hypoechoic lesion with smooth margins and inhomogeneous internal echopatter (14 mm diameter) associated to round, hypoechoic lymph node in left axilla and supraclavicular region (mm 11 max diameter) (Figure 1). The patient underwent us-guided fine needle aspiration citology that confirm the malignancy of the lesion (CS) [1].
The patient underwent also Chest CT that revealed cylindrical bronchiectasis on lower segments; lymph nodes enlargement in supraclavicular region, abdominal ultrasonography that showed hepatic steatosis; prostatic hyperplasia; abdominal aorta calcifications. The result of thyroid ultrasonography was a diffuse inhomogeneity without focal lesions; reactive lymphoadenomegaly, of testes ultrasound was low testicular volume and absence of focal lesions. Echocardiography and ecocolordoppler was within normal limits.

Discussion
Klinefelter syndrome is one of the most common congenital chromosome disorders associated to hypogonadism and infertility; the incidence is 1 to 2 per 1000 neonates (47, XXY karyotype) and the life expectancy is 11.5 years less than general population. The most frequent disorders are small testes, cognitive impairment and hypergonadotrophic hypogonadism with risk of metabolic syndrome, type 2 diabetes and cardiovascular disease (varicose veins, thrombosis, embolism), gynecomastia (38% of patients), osteoporosis and epilepsy; may occur also with other syndrome, such as the rare Job’s Syndrome. However, the diagnosis of Klinefelter Syndrome is carried out only in 25% of patients and at an adult age (mid-30s yo). A Klinefelter Syndrome associated to male breast cancer was first suggested by Bauer and Erickson in 1955 [2,3]; even if breast cancer and extragonadal germ cell tumors are more frequent in patients with Klinefelter Syndrome, such as in other hereditary syndromes [4,5], cancer risk is generally stackable to general population. The base condition is gynecomastia, a benign situation characterized by enlargement of the male breast due to proliferation of glandular tissue; it is common in normal males during the neonatal period, at early puberty, and with increasing age, but can be pathological in some hereditary/iatrogenic conditions. The rarity of old patients suffering from Klinefelter Syndrome justify this case of a breast cancer in an old man (47 XXX). During puberty, Klinefelter Syndrome patients is exposed to elevated levels of gonadotrophins and decreased levels of testosterone, that determine the characteristic body proportions and gynecomastia; during adulthood, low testosterone in relation to estradiol levels result in increased estrogen-to-androgen ratios [6] that can explain the relationship between bone fractures and an increased risk of male breast cancer. Indeed, both hormones are involved in bone maintenance and osteoporosis among men and androgens decrease during aging with the consequent predilection for bone loss and fractures; conversely the androgen replace therapy can increase male breast cancer as a iatrogenic effect of exogenous hormones [7]. It has been demonstrated the transition from atypical proliferative ductal epithelium in gynecomastia to carcinoma in Klinefelter Syndrome patients, supporting the notion of abnormal hormonal stimulation of cell proliferation in the mammary ductal epithelium [8]; perhaps XXX males may inherit the same predisposition to breast cancer as XX females [9]. However, the risk, although elevated, is still considerably lower than that of women in the general population [10]; therefore, the level of risk does not justify prophylactic mastectomy, also for psychological effects [11], but could be useful patient education with breast self-examination ever 30 days and periodical clinical and ultrasound examination conducted by a breast radiologist [12] and/or mammography [13], also to avoid incorrect clinical-anamnestic association [14]. In future, to evaluate the risk of breast cancer in Klinefelter Syndrome patients, could be useful a retrospective cohort study, in which a cohort of patients with Klinefelter Syndrome is enrolled from historical records that can allow the subsequent assessment of cancer development. Psychiatric examination disclosed paranoid ideation, delusional convictions of influence and broadcasting , ideas of reference, associative thinking and preoccupations with religious themes. There was a marked lack of insight. Mood was slightly euphoric and effect was inappropriate.
Psychomotor behaviour was somewhat agitated and mild pressure of speech was noticed. Hallucinatory experiences of any kind were not present. Extensive neuropsychological assessment disclosed low average to average intelligence (Kaufman adolescent and adult intelligence test - KAIT - total intelligent quotient (IQ): 86; Crystallised IQ: 90; Fluid IQ: 84; National Adult Reading Test - NART - IQ: 88) [15,16]. Cognition was characterised by dysfunctions in attention such as distractibility, executive dysfunctions and impulsivity. In addition, memory problems and fragmented perception were found, partially related to attentional deficits. His personality showed marked traits of extraversion combined with eccentricity. Based on the findings obtained in psychiatric and neuropsychological examination, a final diagnose of schizotypal personality disorder (diagnostic and statistical manual of mental disorders-IV: 301.22; international classification of diseases-10: F21) was made with eccentric behaviour, anomalies of thinking and affect, paranoid ideas and circumstantial speech as most prominent symptoms. In this report, the psychiatric disorder of the patient was characterised by quasi-psychotic episodes with intense illusions, circumstantial thinking and speech, delusion-like ideas occurring without external provocation and odd eccentric behaviours. The symptom profile matched a schizotypal personality [17,18].

References
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Figure 1. Male, 70 yo – ultrasonography shows a) the ovalar hypoechoic lesion in upper medial right breast, associated to suspected lymph nodes in axillary (b, c) and sovraclavicular regioe (d,e).
Abstract
Objectives of the study were: a) to analyze the quality of life in metastatic breast cancer caregiver and to monitor the trend during and after the support; b) to divide caregivers in different profiles and risk categories; c) to analyze the predictor elements of major or minor physical, psychological and social well-being. 15 subjects were enrolled in this study (mean age 52 yo; DS ± 11); they underwent two questionnaires for the evaluation of caregiver’s needs CNAT-C: Comprehensive Needs Assessment Tool for cancer Caregivers) and fot the analysis of the quality of life (CQOLC: Caregiver Quality of Life Index-Cancer). Female caregivers have more needs if compared to men in physical and psychological health, to information and to the care staff. There is a statistically significativity correlation between the two scales. Data consent to personalize intervention and resources in patient-caregiver couple; the caregiver can be included in the metastatic breast cancer caregiver with the aim of optimize the quality of life.

Key words: breast cancer, caregiver, quality of life, needs, help
Introduction
In most cases, caregiver and relatives are the first essential resource in patients suffering from metastatic breast cancer, in whom quality of treatment and the achievement of positive results depends on the ability of the caregiver [1]. However, the caregiver is exposed to physical, psychological, social, spiritual and practice issues that can influence the quality of life of the patient and of his family [2]. Caregiver can sick with cognitive impairment, anxiety, depression and other psychiatric disorders [3,4]. This person can also have difficulties in the workplace, due to the psychological impact of the disease not only in the patient, but also on his relatives that often suffering from a mental distress; it has been demonstrated a similar distress level in patients, caregiver and/or relatives in case of an oncological disease [5].

A caregiver can present relational difficulties due to the patient’s cynism and to the therapeutical objectives [6]. A prospective cohort study highlighted the increased mortality risk of 63% in five years due to the psychopathological symptoms [7]. Purpose of the study were to a) analyze the quality of life of the caregiver and to follow up during and after the attendance; b) to divide caregivers in different profiles and risk categories and c) to analyze the predictor elements of major or minor physic, psychological and social well-being, in order to insert the caregiver role in a breast metastatic patients care.

Methods
Population
In this study were enrolled 15 subjects (6 M, 9 F9), mean age 52 yo, DS ±11; all included subjects gave written informed consent to partecipate to the study and to personal data processing.
Inclusion criteria: relative of an oncologic patients with the role of main caregiver. Exclusion criteria: age < 21 yo; history of personal oncologic or psychiatric disease.

Evaluation instruments
Enrolled subjects underwent two questionnaires.
- CNAT-C (Comprehensive Needs Assessment Tool for cancer Caregivers), developed for a complete evaluation of caregiver needs of oncological patient caregivers. It is composed of 41 items divided in 7 groups: physical and psychological health (6 items); social/familiar support (5 items); health personnel (8 items); information (8 item); social and religious/spiritual support (2 items); health facilities (6 items); practical support (6 items). Subjects may indicate their needs splitting them into “little, medium and very” [8]
- CQOLC (Caregiver Quality of Life Index-Cancer), an instrument used to evaluate the quality of life in relatives of oncologic patients. The scale includes four quality of life domains: physic, emotional, familiar and social functioning. CQOLC consists of 35 items with a score of 5 points (Likert scale): 10 items relating to the charge, 7 to disruptiveness, 7 to positive adaptation, 3 to financial concern and 8 items to additional factors (sleep disorders, satisfaction of sexual behaviour, mental fatigue, illness information, patient preservation and patient pain management [9].

Results
The analysis of the questionnaire CNAT-C shows that the most frequent needs are related to physical and psychological health, to information and to personal care. In the area of physical and psychological needs, the most frequent are the worries about the patient (72%), anxiety (53%) and anger (52%). In the area of social and/or familiar support, caregivers need an “help to relax and for their personal lives” (56%) and an “help because of the excessive addiction of the patient” (49%). In the area of personal care (physician and nurses), caregiver need to easily and quickly meet the physician if necessary” (54%).

Regarding to the needs of information, caregiver indicated “information on the patient care” (64%), on “alternatives and/or complementary treatment” (64%), on “the stress management due to the patient care” (57%) and “information about the disease and the progression” (56%).

Regarding to services and health facilities, the most frequent request were “an operator reference, that can support the caregiver during the assistance”, that can be the landmark for the whole process of assistance (65%), a domiciliary nursing service (62%), instructions on facilities and hospitals” (57%) and “assistance and help for caregiver, like psychological counselling (55%). In the area of practical support, caregivers need “treatment near home” (44%), transport services (40%) and assisted treatment in a hospital or at home (39%). Women are more needs if compared with men in physical and psychological problems (p < 0,01), social and familiar support (p<0.05) and spiritual support (p<0.05). The CQOL-C allows an evaluation on the quality of life to analyze the well-being of the caregiver; there is a linear correlation between the CQOL-C and the CNAT-C questionnaire, expecially in the filed of physical and psychological health (r di Pearson = .566; p < 0.01)
and of the disruptiveness, especially in the filed of physical and psychological health, in the social, familiar and spiritual support and practical needs (r di Pearson: from 0,251 to 0,465). The global quality of life scale correlates positively with the scale of needs in CNAT-C (r di Pearson comprise tra ,211 e ,476). Women represent the 63% of the total sample; there were some differences between male and female on the well-being in the caregiving. Women had a worsen quality of life if compared with men in the assistance (p<0.01), in the disruptiveness, and the their own quality of life (p<0.05). Regarding to the items of the quality of life questionnaire, there are some differences in the sleeping (p<0.05), mental fatigue (p <0.01) and the pain management (p<0.01).

Discussion

Breast cancer represent the most frequent neoplastic disease in women; in absence of a valid and efficacy primary prevention, is essential the early diagnosis of asymptomatic woman [10], with a correct detection and differential diagnosis between benign and malignant disease [11,12] not only in women, but also in men [13,14], thanks to dedicated breast radiologists [15]. A late diagnosis often is associated to nodal involvement and metastatization [16] with a life expectancy reduction, recidive or the presence of almost all organs (lungs, liver, bone, skin and central nervous system). A valid support and a dedicated assistance could be a useful help in the disease progression. Questionnaires related to needs were administered to plan a psychological personalized help to the caregiver [17] and to define a caregiver-patient couple [18]. These information can facilitate and guide the assistance with time savings and improving the quality of the treatment.

The quality of life monitoring can provide information on well-being and on the disease progression, in order to have a true overview of the caregiver and can be used as a clinical indicator [19]; in some cases, a psychological support could be useful also if not required because of the low awareness of the psychological well-being and the needs of the caregiver [20] with a risk for himself and for the patient [21]. The monitoring of these conditions allows the evaluation of the caregiver status in terms of improvement or worsening in order to avoid depression status or mental distress [22] that can condition negatively on health condition of the patient [23]. Indeed, the evaluation of the needs and the quality of life not only in a breast metastatic patient [24-26], but also in the caregiver, allows to define a couple to whom direct personalized intervention to optimize the outcome and to meet the needs oft the patient and of the caregiver.

References


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