Artificial Intelligence against Breast Cancer (A.N.N.E.S-B.C.-Project)

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INTRODUCTION: *Our preliminary study examined the development of an advanced innovative technology with the objectives of:*
– developing methodologies and algorithms for a Artificial Neural Network (ANN) system, improving mammography and ultra-sonography images interpretation;
– creating autonomous software as a diagnostic tool for the physicians, allowing the possibility for the advanced application of databases using Artificial Intelligence (Expert System).
MATERIALS AND METHODS: *Since 2004 550 F patients over 40 yrs old were divided in two groups:*
1) 310 pts underwent echo every 6 months and mammography every year by expert radiologists.
2) 240 pts had the same screening program and were also examined by our diagnosis software, developed with ANN-ES technology by the Engineering Aircraft Research Project team. The information was continually updated and returned to the Expert System, defining the principal rules of automatic diagnosis.
RESULTS:*In the second group we selected: Expert radiologist decision; ANN-ES decision; Expert radiologists with ANN-ES decision. The second group had significantly better diagnosis for cancer and better specificity for breast lesions risk as well as the highest percentage account when the radiologist's decision was helped by the ANN software. The ANN-ES group was able to select, by anamnestic, diagnostic and genetic means, 8 patients for prophylactic surgery, finding 4 cancers in a very early stage.*
DISCUSSION AND CONCLUSION: *Although it is only a preliminary study ,this innovative diagnostic tool seems to provide better positive and negative predictive value in cancer diagnosis as well as in breast risk lesion identification.*

KEY WORDS: Artificial Neural Network, Breast cancer, Breast risk lesion.

Introduction

Our preliminary study suggest the possibility of developing an advanced innovative technology applied to medical diagnosis in the sector of the Information Technology and a clinical software based on a Knowledge-Based System. The objectives of the project were:
– To develop methodologies and algorithms for a system that uses Artificial Neural Network (ANN) to improve the Mammography and Ultrasonography image interpretation;
– To create an autonomous software that serves as a diagnostic and prognostic tool for the physicians, opening new fields of investigation for genetic and bio-molecular researchers and leaving the possibility for the advanced application of databases informed by Artificial Intelligence (Expert System).

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The first application of neural network as an informatic tool in medicine began in the USSR and in Italy in the 70's [1-3], but we had to wait until 1995, when several studies demonstrated a wide range in the performance of mammogram-interpreting by physicians: sensibility 74%–96% of women with cancer and 11%–65% of women without cancer, and work-up rates of 47%–100% for women with cancer and 1%–64% for those without (Beam et al.) [4]. This was the reason for the development of Data Systems to support radiological diagnosis and one of the first to be approved by the American College of Radiology (A.C.R.) was the Breast Imaging Reporting and Data System (BI-RADS) in 1998 [5]. Clinical application of Neural Network diagnosis began before and since 1992 there was the first application improving specificity of ultrasonography [6] and in 1993, mammography sensibility [7] and then year by year in breast cancer diagnosis [8], hepatic masses identification [9], in differential diagnosis of solitary bone metastasis [10] by means of Artificial Intelligence or Neural Network. In 1994 there was the first patent of a Neural Network Software [11], followed by a lot of clinical studies evolving the original ANN project [12,13], until BI-RADS was developed, supported by the Baker and Floyd studies [14-16]. In 1997 we reported an interesting application to RMI-breast cancer diagnosis [17], and in 2000 there was the first international conference on Artificial Neural Networks in Medicine and Biology, ANNIMAB-1 which took place in Göteborg. Then finally in 2002, there was the first ANN Ultrasonic Signal Classification, followed by several studies on ANN application in radiological diagnosis.

Materials and methods

Since 2004, the 5th Division of General Surgery, Second University of Naples and the General Surgery Unit of St Johns Hospital of Frattaminore (Naples) selected 550 F patients, over 40ys old, 68.5 a.a. (range 40-89) for routine screening in the yearly prevention program. These were divided into two (double blind) groups:
1) 310 pts underwent echography every 6 months and mammography every year by expert radiologists (>10ys experience, >2000 procedure performed/year).
2) 240 pts had the same screening program, but were also integrated to our diagnosis software, developed with ANN technology by the Engineering Aircraft Research Project team [18-20].
In the second group we discriminate 3 subgroups:
– The radiologist first examining alone, in the same conditions as in the first group of pts.
– The same exam was than processed by ANN-ES
– The radiologist was than informed of the Artificial Intelligence decision and, if this was different, they were asked to correct the diagnosis by a new evaluation of the exam (radiologist + ANN-ES decision).

All the patients with mammary lesion at risk or positive for cancer, were enlisted for the specific surgical treatment or for the relative follow-up. The information was continually updated and returned back to the Expert System (teaching the System), that updated itself, and therefore started the learning phase and defining of the principal rules of automatic diagnosis.
A future objective of advanced computer applications, could also contemplate a meaningful reduction times in the performance through the possibility of automation in both the clinical and diagnostic imaging. The relationship with the subjects is initially with the general physician (Physician of General Medicine) that has the delicate decision to sensitize and inform the patients and to assist that they accept the diagnostic screening program. A suggestion would be to effect an out-patient specialist visit, inviting them to compile an information anamnesis card. The following step foresees a possible diagnostic integration for images (mammo-ultrasound). The mammograms and the echograms so acquired are inserted in a tool-software, based on the Artificial Neural Network (Fig. 1).
This last procedure analysis the acquired images, proposing a classification of the different mammary lesions. Then the information extrapolated by this software would inform the Expert System (Fig.2), planned on the acquired variables during the anamnestic and diagnostic iter. Such an expert system is able in time, thanks at the elaboration of these details, to furnish integrative and complementary information in addition to the opinion

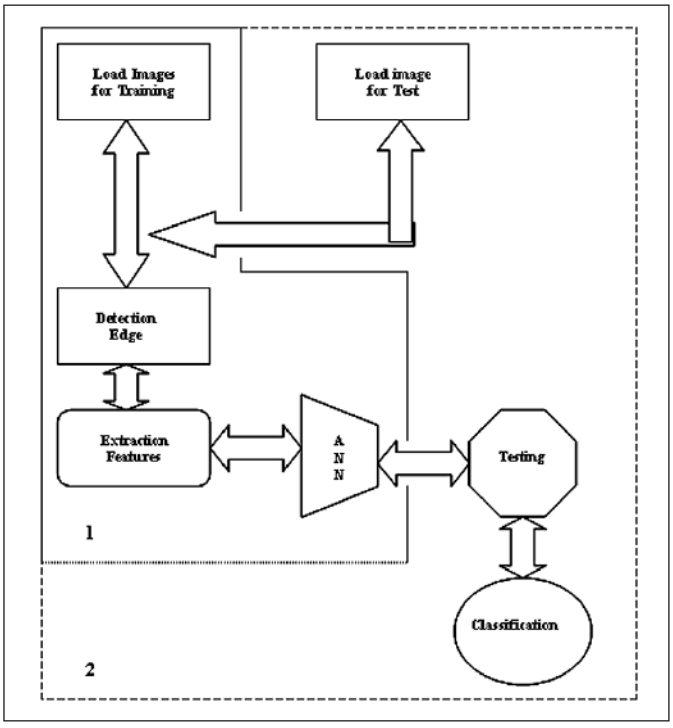

Fig. 1

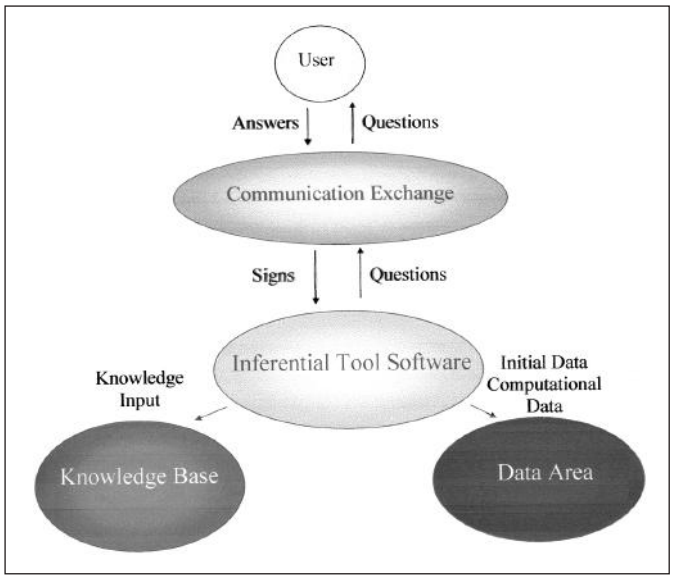

Fig. 2

of the physician and an automatic diagnostic information on the nature of the pathology. The following steps, give the possibility of integrating the system's information with bioptical or micro-histological examinations, thereby completing the phase of diagnostic acquisition. The patients divided in two groups were analyzed statistically, comparing for sensibility, specificity, positive and negative predictive value and accuracy for breast cancer and for breast risk lesion diagnosis.

Results

We report that in the first group an incidence of cancer of 12.5% (38/310) with a significative difference ($p<0.05$) and in the second group 14.5% (35/240), the difference between the incidence of breast risk lesions in first group 28.3% (88/310), compared with second group 38.3% (92/240) seems significant.
In the first group the sensibility for cancer - 73.6% is superimposable to the radiologist decision (a) of the second group - 74.2%, but significantly lower then ANN-ES sensibility (b) - 80%, and even lower then combined decision (c) – 88.5%. Much more clear are the differences between sensibility of the first group sensibility for breast risk lesion – 51.1%, and the radiologist decision for the second group (a) – 52.1%, but significantly lower than the ANN-ES (b) – 76%, compared to Radiologist + ANN-ES (c) – 70,6%. Regarding the specificity, this was quite different, with first group – 54%, a) group – 57.4%, b) group – 70.9%, c) group – 69.5%. In the first group we found only 23,6% of T1 cancers, compared to 42,8% of the 2nd group; from the first group we identified 3 pts, suggesting prophylactic and reconstructive surgery (anamnesis, diagnostic and BRCA1-2 selection): 2 accepted, only 1 was a ductal cancer (T1bN0M0); from the second group we recognize (same criteria, with Expert System analysis) 12 patients, suggesting the same procedure, 8 pts accepted, 6 were bilateral and 2 monolateral subcutaneous skin ad nipple sparing mastectomy with an immediate reconstructive submuscular breast expander implantation. We found 2 T1micN0M0, infiltrating ductal carcinoma, multifocal and multicentric and with contextual ductal in situ carcinomas bilaterally and 2 T1aN0M0, ductal infiltrating carcinoma of left UEQ. The 4 patients treated, fortunately, didn't have any major complication after surgery and histic exam was in any case positive for risk of breast lesions (Atypical Ductal and Lobular Hyperplasia, Intraductal Papillomatosis and Sclerosing Adenosis). 2 of the 4 cancers were not detected by clinicians but, fortunately, were detected by the Neural Network

Discussion and Conclusion

This innovative diagnostic tool seems to provide better positive and negative predictive value then the traditional screening in cancer diagnosis, where it is very important the Radiologist's sensitivity, a decision which when supported by ANN-ES, rises to 88.5%. It was notable that 5 radiologists changed decision after ANN-ES interpretation of the lesion. The diagnosis of early lesion is the main target in breast cancer treatment and breast risk lesions are very important findings, because they can represent an early stage of cancerogenesis [21-23] and togeth-

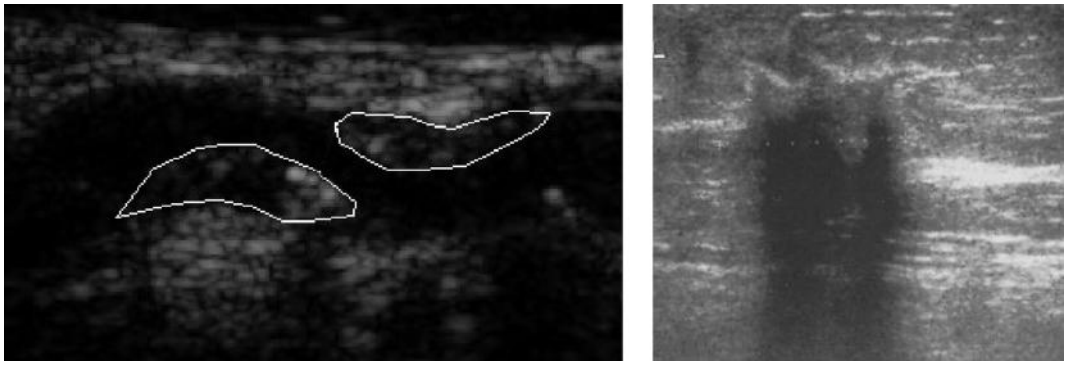

Fig. 3. An echographic image suspected by radiologists, ANN was correct in diagnosis: it was Granulomatous Mastitis.

er with anamnestic factors and/or genetics determination (BRCA1-2), can be a good reason to consider prophylactic surgery whenever an immediate reconstructive surgery can be offered. The second group had a significantly better prediction for risky lesions – from (b) - 76% to (c) – 70.6%, and significantly better specificity (b) – 70.9%, (c) – 69.5%, and importantly the finding in 8 prophylactic procedures of 4 cancers in a very early stage. This surgical aggressiveness paid back by faster treatments and with over-the odds percentage of customer satisfaction in both groups and with the consideration that in any case there were present a lot of risky lesions in the breasts of the over-treated patients. The international literature is rich in research regarding Artificial Neural Network [24-28] and their development for business, with a lot of commercial products available even on line (Medical Neural Engineering S.R.L.). Software are designed for aircraft structural control [29] and for every kind of medical research [30-32].

This is only a preliminary study, but probably the first to investigate the application of an Expert System, partially educated, in medical database and clinical multivariate analysis, including ANN diagnostic tools and biomolecular profiles (still under investigation). At the moment due to the poor casistic, it's not yet possible to make conclusions, but the objectives are:

– To produce an informed tool (Expert System), that integrated with our neural system, is able to identify and to classify a greater number of cancers in the initial stage in comparison at the normal diagnostic screening procedures, integrating the radiological evaluation and subsequently implementing the system, based on data processing; such tool represents a diagnostic clinical support, for all the operators involved in the different phases of the project;

– To determine in advance the presence of malignancy within a territorial screening for the prevention of the breast cancer;

– To determine diagnostic and histological classification of different types of mammary lesion, a characteristic evolutionary clinical behaviour. In advanced phase, the project will also individualize the biological profile of the cancer, choosing the type of surgical treatment and finding the oncologist protocol most suitable.

Riassunto

Il nostro studio preliminare ha esaminato lo sviluppo di una innovativa tecnologia con l'obiettivo di sviluppare nuovi algoritmi utilizzabili da un Artificial Neural Network per migliorare l'interpretazione delle immagini mammografiche ed ultrasonografiche e creare uno strumento diagnostico per gli specialisti. Dal 2004 abbiamo valutato 550 pazienti (età > 40 anni) sottoposte ad un programma di prevenzione annuale divise in due gruppi:

– 310 pazienti sono state sottoposte ad ecografia ogni 6 mesi e mammografia ogni anno da radiologi esperti;

– 240 pazienti sono state sottoposte allo stesso programma di screening ma sono state anche esaminate attraverso il software sviluppato con tecnologia ANN-ES dal team della Engineering Aircraft Research Project. Tutte le pazienti con fattori di rischio anamnestici, con lesioni mammarie a rischio o positive per cancro furono messe in lista per lo specifico trattamento o per il relativo follow-up.

Abbiamo comparato i risultati dei due gruppi. Nel secondo gruppo abbiamo selezionato: a) Diagnosi eseguite da radiologi esperti; b) Diagnosi eseguite da ANN-ES; c) Diagnosi eseguite da radiologi esperti con ANN-ES.

Nel secondo gruppo abbiamo riscontrato una diagnosi di cancro significativamente più precisa e una maggiore specificità per lesioni a rischio ,inoltre la più alta percentuale si raggiunge quando i radiologi sono aiutati dal software ANN. Questo innovativo strumento diagnostico sembra avere un miglior valor predittivo negativo e positivo per la diagnosi di cancro così come per la identificazione di lesioni a rischio;l'ANN-ES è stato infatti capace di selezionare attraverso parametri anamnestici,diagnostici e genetici 8 pazienti per un intervento profilattico, trovando 4 tumori in uno stadio molto precoce. Questo è solo uno studio iniziale basato su di una casistica limitata,però i dati preliminari sembrano suggerire interessanti applicazioni di ANN-ES nella prevenzione del cancro della mammella.

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