A methodology to approach the automatic monitoring and prognosis of diseases evolution is proposed. We define a multilevel system architecture capable to process multi-source biomedical data according to a coarse-to-fine paradigm. An application regarding neuro-signals and image categorization is also considered as a case study. The proposed methodology even preliminary has shown to be a possible approach to prognosis activity, mainly if suitably integrated into a hybrid system for medical decision support.

Keywords: Disease Monitoring, Disease Evolution Prognosis, Multilevel Architecture, Multi-source Signals and Images.

INTRODUCTION

The monitoring of chronic pathologies or disease with high risk of recurrence (e.g. cardiovascular diseases, cancer or stroke) has a fundamental role in supporting the assessment and improvement of patients’ therapeutic follow-up. The possibility of analyzing heterogeneous diagnostic data, acquirable by means of different modalities, allows more accurate diagnosis. Moreover, the richer information inherent to each case study improves the reliability of the prognosis on the expected long-term of the disease.

Monitoring models applied to the study of disease evolution are often based on diagnosis and prognosis approaches in which a cross comparison between a set of reference parameters and the information obtained from a set of diagnostic exams is performed. A set of rules integrated in these models can derive some type of prognosis for the health state evaluation of the patient (expert systems [1, 2]). Nevertheless, these models can be very rigid and do not easily adapt themselves to the evolution variability of diseases under different and aleatory conditions. Other diagnosis approaches need accurate domain models and require a fixed number of diagnoses classes (model-based [1]), decreasing the flexibility of the models themselves. In other cases, the expert’s knowledge is stored in a library of cases (case-based [1, 3]), even if the search for the best matching case can be computational expensive. Inductive learning, including decision trees, statistical classifiers or neural networks [1] has been also used with different performance.

The aim of this work is the design and development of a new methodology, belonging to the field of computational intelligence, able to assist automatic diseases monitoring by processing correlated multi-source biomedical data [4]. In particular, we propose a model for the realization of a valid diagnosis and prognosis methodology, which is also able to provide an evaluation of the course of the monitored disease, based on a multi-level system architecture.

1. MATERIALS AND METHODS

Multi-source information related to the diagnostic and/or therapeutic processes can be of different types and comes from several sources:
- images (e.g. CT, MRI, fMRI, etc.)
- signals (e.g. EEG, ECG, Evoked Potentials, pressure, etc.)
- historical and clinical data
- laboratory data (e.g. blood or specimen analysis, etc.)
Systems for disease evolution prognosis should be able to collect and process these different types of biomedical data, selecting the most important and relevant ones for the examined case, classifying them to identify the current state of the disease and, finally, suggesting a credible and reliable prognosis. The methodology we propose in this paper is based on this observation. For any given case under examination, a set of heterogeneous data is acquired accessing a centralized or distributed database and processed following three phases:

- **Pre-processing**, dedicated to input data filtering and validation
- **Diagnosis**, performed on the output of the previous phase to identify the actual state of the disease
- **Prognosis** to evaluate the course of the disease using the results of the previous phase together with patient’s historical and clinical data.

This multilevel architecture is shown in Figure.

Architecture of the model: The actual patient’s multi-source data are acquired and passed to the pre-processing phase. Then a classification phase is dedicated to the clustering of the pre-processed data, in order to evaluate the current patient’s state. The last phase gives a prognosis of the specific disease evolution.

Multi-source data from the patient are acquired through several diagnostic modalities and passed to the Pre-processing phase. Pre-processing is dedicated to the selection of data relevant for the specific disease under examination, with respect to a set of requirements (filtering). Then, the information useful for the diagnosis is derived through a feature extraction process, according to a set of constraints (validation).

Then, the pre-processed data are categorized, using a set of classifiers, in order to diagnose the patient’s current health state. Each classifier is specialized on the disease and a set of features extracted from the data of a specific diagnostic modality and can be set up adopting the machine learning technique which best fits the corresponding data type.
The final phase provides a sensible prognosis for disease evolution, elaborating the diagnosis information obtained from the previous level and historical and clinical data about the patient (e.g. patient identification, history of present illness, past medical history, current medications, social history, and family history).

The multilevel approach guarantees both specialization and adaptability, since the modular organization facilitates analysis of the Classifiers and the general operational hierarchy enables local optimization.

The described methodology has been applied to a real case study selected for its clinical interest and for the technical issues involved, regarding brain pathologies.

2. CASE STUDY AND RESULTS

In order to test the reliability and effectiveness of our system, we faced the problem of monitoring carotid and cerebrovascular diseases, and diagnosing cerebral anomalies, with the aim to provide a plausible prognosis for supporting the definition of treatment plan. To this end, a set of multi-source information was considered: (i) ultrasound signals obtained by means of Transcranial Doppler (TCD), for blood flow examination and microembolic signals (MES) detection, (ii) neuro-images obtained through Magnetic Resonance (MR) and (iii) other clinical data [5-7]. In particular, TCD examination allowed monitoring cerebral vessel perfusion, providing useful information about the degree of stenosis of the same vessels. Other important parameters derived from TCD were the number and typology (solid, gaseous) of microemboli, which were detected and displayed in dedicated high-resolution images. Processing MR images also highlighted ischemic regions.

About Pre-processing, we extracted features grouped into the following classes:

- **TCD signals:**
  - Time averaged velocity
  - Intracranial pressure
  - Systolic, Mean and End diastolic peak flow velocity
  - Pourcelot’s resistance index
  - Gosling’s pulsatility index

- **TCD MES images:** morphological and densitometric features extracted from the region of interest corresponding to the MES
  - Extension along x and y axis
  - Irregularity factor
  - Area
  - Orientation
  - Centroid
  - Mean intensity
  - Skewness
  - Sample volume length

- **MR images:** geometric and densitometric features extracted for each voxel of the 3D brain volume reconstructed from a dataset of parallel, equidistant slices
  - Position
  - Gray level
  - Local mean gray value, computed in a spherical neighborhood region
  - Difference between the local mean gray value and gray level
  - Gradient computed in the spherical neighborhood region

About Diagnosis, a specific classifier processed each class of features. In particular, for TCD signals, a Decision Tree [8] was used to recognize the degree of stenosis of the cerebral vessel under examination. Then, a MES categorization was performed using a structured neural architecture [5],
which supplied a gravity measure of the embolic phenomenon. Finally, a clustering algorithm based on the fuzzy $c$-means method was used to classify the 3D brain volume [9], in order to detect, localize and characterize regions relative to possible anomalies.

**Prognosis** was achieved by using a feed-forward neural network trained using the Error Back-Propagation [10]. Historical – clinical data, consisting in past medical diagnosis, current medications, and the patient’s family history, were combined with the diagnosis obtained from the previous computations and supplied as input to the network. The network results consisted of an estimation of a current scenario referred to an evolution state of the disease, within a known scale, useful to support the prognosis process of the physician.

In particular, 31 patients (21 men and 10 women), of which five affected by carotid stenosis, 18 with experienced Transient Ischemic Attack, and 8 with experienced stroke were considered. These patients were subjected to MRI and TCD examinations in at least 5 different time periods along their disease course, producing a total of 3180 MES images, 185 TCD recordings and MRI scans.

These data were used to define a knowledge base together with the aforementioned suitably coded historical – statistical information provided by the physicians and relative to confirmed prognosis. Moreover, data were also used to train the classifiers (Diagnosis) and the EBP network (Prognosis) according to the expert’s suggestions.

**CONCLUSION**

A research has been carried out finalized to the definition of a methodology useful to support the physician to assess the prognosis of a specific disease. We make use of multi-source biomedical data, which are suitably selected and correlated. The overall process is based on a system having multilevel architecture. A real case study, selected by experts, was faced using a hierarchical and modularly structured architecture to process the data, to derive a diagnosis and finally to achieve a prognosis for the specific disease considered for an actual patient. The obtained results have revealed interesting hints about effectiveness and reliability of the proposed methodology also suggesting to integrate our idea into a hybrid system for medical decision support.

**REFERENCES**