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MEDICI: Inpatient/Outpatient Monitoring for Diagnosis and Medical Research in Ischaemic Cardiopathy TIC2003-09400-C04

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Abstract

The aim of this project (MEDICI: Inpatient/Outpatient Monitoring for Diagnosis and Medical Research in Ischaemic Cardiopathy: Tools for Acquisition, Visualization, Integration and Knowledge Discovery) is the design, development and implementation of a set of tools for inpatient and outpatient monitoring of patient suffering Ischaemic Cardiopathy. These tools will provide support for both medical care and clinical research tasks. The work is organized around three development lines: a) Subsystems for data collection in different scenarios, including clinical history data, monitored electric and hemodynamic signals and data related to remotely monitored signals outside the hospital. b) Techniques for integrating the collected information and presenting it as a unique virtual clinical history associated to the patient; and c) tools for the extraction and validation of medical knowledge.

Keywords: Temporal Data Mining, Electronic Patient Record, Semantic Web Based Clinical Information Integration, Acquisition and Processing of Biomedical Signals, Telemedicine.

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1 Project Goals

1.1 Introduction

MEDICI (Inpatient/Outpatient Monitoring for Diagnosis and Medical Research in Ischaemic Cardiopathy: Tools for Acquisition, Visualization, Integration and Knowledge Discovery) is an interdisciplinary project organized in four subprojects (**http://perseo.dif.um.es/~medici/**):

- **MEDICI-TDM:** Temporal Data Mining Techniques for Medical Research (University of Murcia).
- **MEDICI-MRF:** Phonocardiogram Remote Monitoring by means of an Intelligent Signal Interpretation System (Technical University of Cartagena).
- **MEDICI-ISI:** Information System Integration (University of Sevilla).
- **MEDICI-SICAU:** Cardiology Information System with Automatic Extraction and Acquisition of Medical Knowledge and Ubiquitous Access (University of Santiago de Compostela).

There are different hospitals involved in the project: Hospital Clínico Universitario of Elche, Hospital General Universitario Reina Sofía of Murcia y Hospital Virgen de la Macarena of Sevilla. Moreover, due to the project, collaborations are being carried at different levels with other hospitals, which will be cited in section 3.

Table 1 summarizes the human resources allocated in MEDICI project. Three predoctoral student has to be added to the total final count which corresponds to the three grant associated to the University of Murcia Subproject.

	UMU	UPCT	US	USC	TOTAL
EDP	6.5	8.5	3	6	24
Doctorate Researchers	5	8	1	7	21
Total Researchers	9	12	4	11	25

Table 1: Human resources involved in MEDICI

1.2 Project Goals

The **aim** of this project is the design, development and implementation of a set of tools for inpatient and outpatient monitoring of patient suffering from Ischaemic Cardiopathy. These tools will provide support for both medical care and clinical research tasks.

The developed tools cover two **application domains**, both focused on Ischaemic Cardiopathy:

- Patients who have been admitted at an Intensive Care Unit (ICU) suffering an Acute Myocardial Infarction (AMI), with or without associated complications. Two local scenarios are considered: a) Intensive Care Unit (ICU) and b) home remote monitoring after his or her discharge from hospital
- Renal patients with risk of Ischaemic Cardiopathy and subjected to dialysis. The working scenarios are: a) Peripheral Dialysis Center b) External Consultations and c) Hospital Admission

The work is organized around three development lines: a) Subsystems for data collection in different scenarios, including clinical history data, monitored electric and hemodynamic signals and data related to remotely monitored signals; b) Tools for the extraction and validation of medical knowledge; and c)

Techniques for integrating the collected information and for presenting it as an unique virtual clinical history associated to the patient.

The **first line** provide our hospitals with a technological infrastructure that may improve asistential tasks and, at the same time, may enable the application of Data Mining techniques to provide support to medical research. This infrastructure is also expanded to the outpatient sceneries in order to follow-up patients for a longer time.

The **second line** provides models, algorithms and tools for Temporal Data Mining. The main idea is to discover patterns described by temporal association of clinical history data and/or signal event and episodes.

The **third line** is composed of a set of models and tools to integrate the whole infrastructure around a general information system based on a multiagent architecture, which will provide access to data and visualization capabilities to the different data bases in the project. This philosophy is in the line of other emerging proposals in the field of VHCR (Virtual Healthcare Record). Furthermore, and in order to facilitate the technology transfer process of the project outcomes, an especial emphasis will be paid to interoperability issues related to the integration of projects results into conventional hospital information systems.

The two first lines are being applied to the first of the two applications domains (Acute Myocardial Infarction in ICU). The second domain (Ischaemic Cardiopathy in Nephrology) is used as a testbed for the VHCR developments and database interoperability through web services. These techniques will be applied to the first domain in the final stages of the project.

The **specific goals** of this project are:

1. Design, development and implementation of tools oriented to the follow-up of patients with Ischaemic Cardiopathy (inside and outside the hospital), that have been admitted in an ICU after suffering an Acute Myocardial Infarction.

2. Integration of the developed tools around a virtual information system, by means of ontology servers, VHCR techniques, standards for representation and sharing of clinical data, and semantic web techniques.

3. To provide tools for ubiquitous monitoring of biomedical signals, based on PDA-like devices, and in the bidirectional transmission of information through mobile telephony resources (GPRS), so that the patient follow-up from his or her stay in the ICU and the weeks following his or her discharge from hospital.

4. Phonocardiographical signal processing focused on the detection and tracking of heart murmurs patients suffering in heart valve related pathologies. This signal is included in the set of signals to be remotely monitored at home.

5. Research and development of temporal data mining techniques to intensively analyze the collected data, with the goal of detecting and discovering temporal patterns with possible clinical interest.

6. Clinical validation and evaluation of the developed modules.

1.3 Project Schedule

Until the elaboration of this document, the execution of the project fulfils the working plan (Figure 1). The incidences have had minimal importance and have not affected the achievement of the objectives. At the moment of writing this report, the project is located in the middle point of its development (18 months).

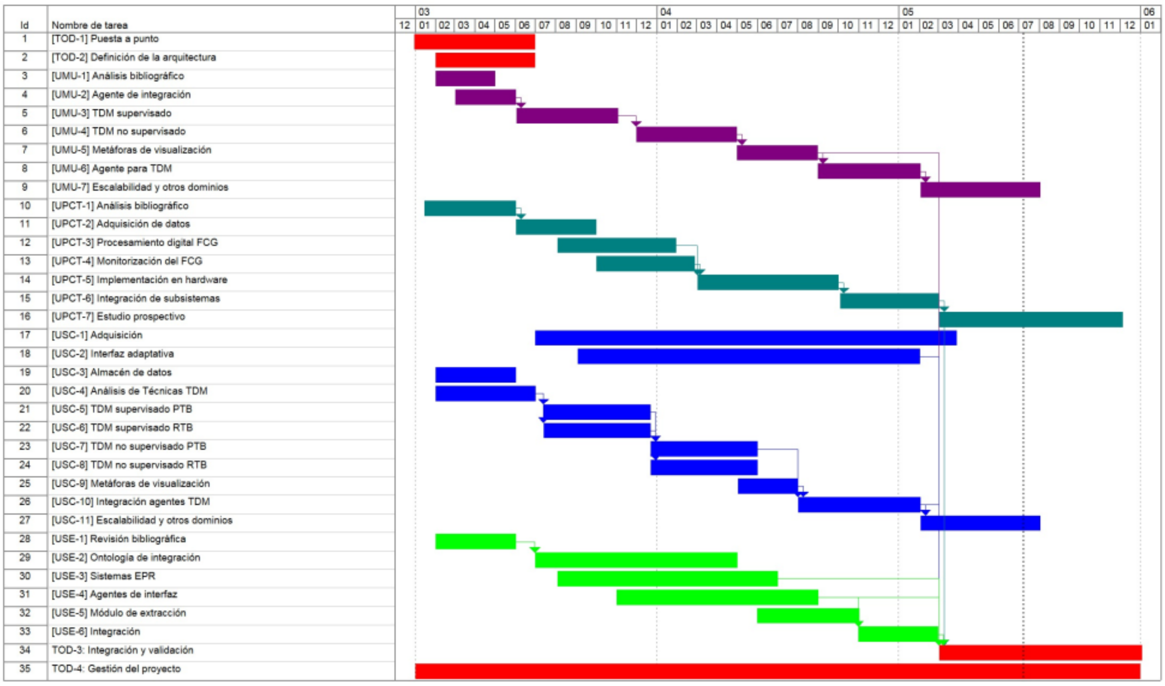

Figure 1: Project Tasks and Scheduling.

2 Level of success reached in the project

Next, we will describe the technical and scientific results achieved during the project, structured in the three development lines described in section 1.2.

2.1 Information Collection Tools Level

2.1.1 Inpatient infrastructure

- **CH4:** Information System for the management of Patient Clinical Histories that allows: the registry of all possible incidents during the stay of the patient at ICU, the automatic generation of all reports and documents legally required by the hospital administration, as well as management procedures and remote query (taking into account security measures). The validation of CH4 has been done at the ICU of the Hospital General Universitario of Elche. Furthermore, there is an agreement for the implantation of CH4 at the ICU of the Hospital Universitario of Getafe.
- **Nursing Sheets Management Tool:** Developed for nursery staff, this tool allows the collection of physiological and hemodynamical parameters, clinical analysis information, treatment, and feeding. Other facilities, such as remote access via PDA, have also been developed.

2.1.2 Outpatient Infrastructure

- **Home Outpatient Monitoring Prototype based on PDA and mobile phone:** [17]. We have developed the data acquisition drivers and the algorithms required for real time monitoring of different physiological signals, basically ECG and oxygen saturation. It is worthy to mention here the detection and morphological classification of heart beats, the detection of the main pathological arrhythmia, and the extraction of several parameters from the ECG signal, such as cardiac frequency, width and height of the different waves that conforms the cardiac cycle. Furthermore, all this information has been integrated together with the data from the oxygen saturation sensor. An encoding algorithm has been implemented as well as the data-transmission algorithm through mobile phone connected to a PDA via Bluetooth. The validation of the system has been done at The ICU)of the Hospital General Universitario of Elche.

2.1.3 Tools to objectivate auscultation findings: e-PCG

- **Tools for the acquisition and management of phonocardiographic and echocardiographic information:** A graphical environment (running on PC and PDA) has been implemented to acquire all the information related with the auscultation process, in order to objectivate and assist decisions involving the phonocardiographic signal (PCG). Then, it is necessary not only to acquire PCG and auxiliary (peripheral pulse) signals, but also to register additional information (physiological data of the patient, auscultation area, maneuvers, etc.), which have great influence in the analysis of PCG. These tools include a multimedia database for storing, querying and visualization of annotated PCG signals, which uses visual metaphors to represent the cardiac cycle. Methods for guaranteeing security and confidentiality of patients have been implemented. Also, a web service enables the remote access to the patient data and the associated signals[7]. Besides, a tool for the analysis of echocardiographic images has been implemented on a high-performance DSP (*Digital Signal Processors*) platform[25, 26, 27]. This tool uses algorithms to remove the speckle noise and to track the endocardium through active contour model.
- **ASEPTIC: Processing algorithms for the PCG signal:** The analysis of PCG signal has been implemented using a hierarchical structure based on four abstraction levels (Envelopes, Events, Sounds, and Diagnosis), and several tasks specialists in each level. The modularity of this structure allows a high degree of independence in the implementation of the processing blocks, and it establishes a growing up abstraction level as we climb through the hierarchy. This approach tries to mimic the interpretation process of the cardiac auscultation carried out by the physician, which uses also a hierarchical approach to search and characterize the cardiac events [14]. The advantage of this method is that it allows to refine the search of events, even inside other events, following a knowledge-based progressive depth approach.
- **Continuous monitoring techniques for PCG:** Due to slow evolution characteristics of this signal, it is enough to perform a periodical analysis of PCG segments rather than a continuous monitoring, which makes easier the implementation of specific purpose modules on reconfigurable hardware circuits. An efficient method for the compression of PCG based on the discrete wavelet transform (DWT) [12, 13] has also been developed. This method improves the storage and transmission of PCG, and it has achieved higher compression rates than the main audio compression methods used nowadays, for a given quality level.
- **Prototype of an FPGA-based intelligent stethoscope:** The general architecture of the prototype of intelligent stethoscope has been defined, and many of the time-consuming tasks has been implemented on high performance FPGAs (*Field Programmable Gate Array*). The processing blocks implemented on FPGA are the following ones: digital filters, using a technique that improves commercial tools, and whose size and operating frequency are independent of the number of coefficients of the filter [4, 10]; the computation of the instantaneous frequency [3]; the FFT (*Fast Fourier Transform*); the envelope computation (using digital filters); and the DWT (*Discrete Wavelet Transform*).

Systems related to the processing of PCG are being used at the cardiology service of the Hospital Universitario Reina Sofía of Murcia.

2.2 Knowledge Discovery Level

- **Temporal Abstraction Agent:** It can be considered the first step for the information treatment in order to feed the TDM process. Its goal is to reduce the event set granularity and to allow a higher level of the abstraction. Moreover, this agent provides a summary of the patient evolution (CH4 tool incorporates this feature) and allows to discover hypotheses at different levels of abstraction. It is based on a Fuzzy Temporal Constraint Network model (FTCN), and it is domain independent. This agent takes into account different contexts, that could change the result of the abstraction, and enables the composition of mechanism of temporal abstraction.
- **Algorithms and tools for Sequences and Temporal Episodes mining:**
  - A theoretical model of Fuzzy Temporal Diagnostic Patterns (FTDP)[5, 6, 8, 16] has been adapted as representational framework for supervised temporal episode mining. The mined hypotheses, that could not be completely specified, are introduced by the user using $CATEKAT-2$[15], an adapted version of a previous tool for causal and temporal medical knowledge acquisition.
  - We have also developed and implemented two algorithms for temporal sequences mining: $TSET$ and $TSET^{MAX}$. The first one is an Apriori-like algorithm that uses a single data structure (set-enumeration tree) to store the detected sequences. The second algorithm, $TSET^{MAX}$, improves the computational efficiency of $TSET$, by means of using a lookahead technique. This algorithm implements a model based on Dempster-Shafer Theory to generalize frequent sequences into temporal episodes, in order to describe, in a compact way, all the possible temporal orders in which frequent events may appear. This latter can be applied as a post-processing algorithm for the sequences discovered by $TSET$ and $TSET^{MAX}$. The evaluation proves that both algorithms are scalable -concerning to the data-base size.
  - Finally, a model for temporal episode mining has been proposed, using a FTCN as representational framework. This model allows the use of metric temporal constraints, and not only qualitative ones. To this end, an Apriori-like method -based on brute force- has been designed. This method mines the temporal relations instead the events. This algorithm has been partially implemented and some theoretical problems, concerning the consistency of detected episode constraints, will be solved in the next step of the project.
- **Algorithms and tools for mining Multivariable Fuzzy Temporal Profiles (MFTP):**
  - **TRACE:** [19] This is a new version of a previous tool for the acquisition and recognition of signal profiles. It is based on Multivariable Fuzzy Temporal Profiles (MFTP)[18, 20] and is oriented to the representation of hypotheses using signal finding patterns. The TRACE tool also allows the definition of signal morphology patterns based on generic templates and refine them using the occurrence detected by the recognition algorithms. Furthermore, it is possible to select signal fragments that can be relevant for the physician, disposing a graphical representation of a pattern that generalizes the morphology of the given fragment. The TRACE Tool has proved to be useful at the ICU of the Hospital General Universitario of Elche for discovering several patterns related to carotid sinus sensitivity from the electrocardiographic records. A more detailed clinical evaluation of this system, that eventually could permit a novel research line on migraine, is ongoing. Visual methaphors has also been integrated using profiles highlighting and a predefined

color coding scheme. This system facilitates the understanding and the labelling task of the recorded and processed signals, as well as the result of the mining techniques used in this project.

- **Algorithms for Mining Fuzzy Temporal Rules (FTR):** The starting point of this line has been the application to biomedical signal of a FTR model already validated in control and landmark identification in mobile robotic [1]. A FTR defines conditions on signal values, their occurrence times (instants and intervals), and the relations between different occurrence times. Currently, we are testing supervised and non supervised learning algorithms. The algorithm output is a FTR set, which may point out relevant clinical situations that could be missed otherwise. In the biomedical signal field, the goal of the FTR is also to provide some diagnosis (totally or partially), to verify a previously established diagnosis, or too detect possible failures or complications.

2.3 Clinical history integration and presentation level

- **Integration Ontologies.**. Despite several stable versions of different ontologies for the integration of the information within the clinical history are available, it must be taken into account that the clinical information system knowledge model (ontology) cannot be considered completed because the concepts can be changed and extended. This model is based on the separation of concepts related to the system engineer (reference model) from those concepts closer to clinical staff (archetypes). The advantage of this paradigm is to permit that clinical staff could define new concepts without knowing in depth the information system, and to have a flexible and interchangeable representation of concepts, avoiding semantic conflicts. To this end, the following ontologies have been developed:
  - **Reference Model Ontology:** A federated ontology based on the openEHR reference model. These reference models have been constrained to those aspects related to the representation of archetypes. Besides, mechanisms for extending the reference model and archetype specification have been defined. The work developed in this line can be extrapolated to any health system architecture. OWL, which is a normalized language, has been used as specification language.
  - **Demographic Model Ontology.** As practical case of higher level concept specification (archetypes), we have paid special attention to demographic information, as the first agents implemented have been those related to the identification and retrieval of patient's personal data. To this end, we have implemented a federated ontology based on the GPICs of CEN and the reference model of openEHR. Furthermore, other local ontologies about demographic concepts have been developed in order to perform integration tests of different domains with different semantics.
- **Agent Based Integration Platform based** Since designing a system as open as possible is one of the main goals of this line, we have considered the use of the CEN guidelines, in particular its HISA (Healthcare Information System Architecture) norm which describe the use of the ODP for systems development. Taken into account the main goals of the system, the design of the basic architecture of services is based on the service decomposition of the health environment as described in: CORBAmed, HISA[4] and PICNIC. In parallel, the typical clinical sessions of each scenario of MEDICI project has been analyzed; this analysis will allow the establishment of protocolized workflows that show the interaction between the agent implied in each session [24]. In current version of the architecture the following agents can be found: clinical observation access agent [9], laboratory access agent [21], security Agent [22], identification and integration of demographic data agent [24], and integration mapping and ontology mapping agents[23].

- **Clinical Case Visualization Tool** This tool allows to visualize temporal and atemporal data, using time line diagrams (Gantt Diagrams), graphs for causal relation description and conventional visualization techniques. Thanks to the use of techniques of weight and selection of the importance of different data, together with the selection of keywords in free text data, this tool allows to select the very relevant parts of the clinical case that could be lately used to apply mining algorithms. The current version of this tool is adapted to the particular case of an Intensive Care Unit.
- **Prototype of data warehouse for monitoring** In the project there is a prototype of datawarehouse for store all information related to generated signal monitoring, in such a way that it can be queried from both user interfaces and mining tool applications. Associated to the data warehouse, an adaptive interface has been implemented to query patient monitoring information, as well as other data generated by different data mining tools. This interface has a secure communication with the datawarehouse, and allows the access to the information depending on the user profile. Moreover, a user management tool has been implemented for registering new users and devices in the system.

3 Achievement indicators

3.1 Publications

Table 2 shows the number of publications related to the project. Because of the space limitation, only the most significant ones are cited in the References section. A full relation can be found at the project website (**http://perseo.dif.um.es/∽medici/**).

International Journals	5
International Book Chapters	3
National Journals	1
National Book Chapters	2
International Conferences	34
National Conferences	9
Published Manuals	1
Degree Projects	23

Table 2: Project publications

3.2 Training accomplishments

Currently, there are 3 people under research training, all of them associated to the subproject in Murcia: a contract, a FPI grant, and a FPU grant. One more person, coming from the Udine University (Italy), will enroll next October, as he has obtained a Juan de la Cierva spanish MEC grant.

3.3 PhD Theses in progress

Table 3 summarizes ongoing PhD theses associated to the project. A more detailed description can be found in the project web page (**http://perseo.dif.um.es/∽medici/**).

Universidad de Murcia	3
Universidad Politécnica de Cartagena	3
Universidad de Sevilla	1
Universidad de Santiago de Compostela	3

Table 3: Ongoing Doctoral Theses Associated to the Project

3.4 Collaborations with International and National Groups

Several groups, hospitals and services have been contacted during the development of the project. The goals and the current state of these collaborations follow briefly:

- Servicio de Anestesia, Reanimación y Unidad del Dolor del Hospital Universitario Morales Meseguer of Murcia. As a first goal, we have proposed the development of a tool for detecting patient profiles in anaesthesia. Possibly, a few residents in the service, currently developing doctoral theses, will be enrolled in this collaboration. We will also ask for contracting a programmer, and we are now looking for research funding.
- Servicio de Aparato Digestivo at Hospital Universitario Morales Meseguer of Murcia. The contacts with this service, besides technology transfer, are focused on the elaboration of joint projects oriented to the development of applications for clinical research and decision support systems.
- Departamento de Neumología at Complejo Hospitalario Universitario of Santiago de Compostela (Dr. Carlos Zamarrón Sanz). As a result of this collaboration, the group of the University of Santiago de Compostela has applied for and obtained fund support from the Xunta de Galicia for the development of a research project related to the topics of this project, but applied to data from patients who suffer from Síndrome de Apnea del Sueño (SAS). This project has been entitled "Minería de datos en polisomnografías de pacientes con alteraciones cardiopulmonares del sueño" (PGIDIT04SIN206003PR).
- Grupo de Investigación Bioimagen y Modelos de Visión del Instituto de Óptica "Daza de Valdés", which belongs to the CSIC (Spanish National Research Council). With this group we have recently started a collaboration for the application of disorder measures developed in that group to time-frequency representations of the phonocardiographical signal. This collaboration will be fixed in short time by means of an agreement between the Technical University of Cartagena and the CSIC Institute.
- Department of Medical Informatics of the Amsterdam University (Dr. Ameen Abu-Hanna). D. Manuel Campos Martínez, member of the University of Murcia group, spent four months visiting that department, working on Temporal Data Mining. Dr. Abu-Hanna currently coordinates a research project which has some goals in common with MEDICI. Dr. Abu-Hanna has also visited University of Murcia, taking part in a doctoral programme with ANECA Quality Mention.
- Departamento de Informatica de la Universidad del Piamonte Oriental Amadeo Avogrado, Italia (Dr. Luigi Portinale). From august to December 2005, D. José Manuel Juárez Herrero (University of Murcia), will carry out a stay in that department to work in the field of the temporal Case-Based Reasoning applied to medicine. Dr. Portinale will be invited to take part in the doctoral programme given next year by the University of Murcia group.
- In the field of models for the clinical history, the University of Sevilla group has collaborated with the openEHR workgroup. They have shown the interest in the development of archetypes using the OWL language. In this moment a CR (Change Request) is being elaborated in order to modify the demographic reference model of openEHR and make it closer to the CEN standards.

As a profit from this relation, in May 2005 the Sevilla group invited the responsible of the group, Dr. Thomas Beale, with whom possible collaboration lines were defined.

- Fraunhofer Institute for Integrated Circuits IIS. It is one of the most well-known institutions in Europe for the microelectronic design. The Technical University of Cartagena group has started contacts with it, and there is an agreement for collaborating in the development and implementation of efficient low-consumption architectures for analog-digital converters, for the integration of the signal acquisition in a future mixed-signal ASIC.

3.5 Patents and Technology Transfers

- CH4 has been registered in the Registro Territorial de la Propiedad Intelectual (register number: 08/2005/347, with date 2005.05.24 and title CH4-UCI)
- Successful contacts: We have reached an agreement to computerize the ICU Service of the Hospital Universitario of Getafe, adapting the CH4 environment to the service. Currently an agreement has been elaborated, pending from approval at the University of Murcia.
- Contacts in progress: We have contacted with ASISA and Virgen de la Vega private hospital in Murcia through the OTRI of the University of Murcia, and we are trying to reach an agreement to develop a project centered around the tools to objectivate auscultation findings (e-PCG).

3.6 Other difussion activities

- Some informative brochures related to the technological offer of the group have been edited (some of them are available at http://perseo.dif.um.es/∽aike/htm/resultado.htm), which were sent to the OTRI (Oficina de Transferencia de Resultados de Investigación) of the University of Murcia). These brochures allowed us to contact ASISA (Asistencia Sanitaria Interprovincial de Seguros, S.A.).
- Organization of an invited session at IWINAC-2005 ("Advances on Intelligent Methods and Applications for Health-related Processes"). Project results were presented and discussed with others researchers working on similar research lines (16th Jun 2005), as for example Dr. Abu-Hanna.
- Courses related to the project are given in two Phd Studies programs with Quality Mention of ANECA (Murcia and Santiago)
- High Mountain expedition UMU8000 to Broad Peak (K3) in Pakistan. Sponsored by the University of Murcia, one of the scientifical goals are related to telemedicine experience oriented to telemonitoring PCG signals in high altitude conditions. Data transmission is done via satellite telecommunication technology. The records are evaluated at the Servicio de Cardiologia of the Hospital Universitario Reina Sofia of Murcia. This study aims to study high altitude heart adaptation. One member of the project team (Dr. Félix C. Gómez de León Hijes) is in the climbing team. He keeps a blog (http://www.um.es/broadpeak/) from the base camp, at 5,900 m.

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