DECISION SUPPORT AND IMAGE & SIGNAL ANALYSIS IN HEART FAILURE

A Comprehensive Use Case

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Abstract: The European STREP project HEARTFAID aims at defining an innovative platform of services able to intelligently support clinical operators in the daily management of heart failure patients. The core of the platform intelligence is a Clinical Decision Support System, developed by integrating innovative knowledge representation techniques and hybrid reasoning methods, and including advanced tools for the analysis of diagnostic data, i.e. signals and images. Aiming at showing how all these issues are combined in the HEARTFAID platform, we present a comprehensive use case, centred on echocardiography workflow and covering the clinical course leading from visit scheduling to therapeutic choices, highlighting the intervention and the value added by the CDSS.

1 INTRODUCTION

Heart Failure (HF) is a complex clinical syndrome resulting from any structural or functional cardiac disorder and which impairs the ability of the ventricle to fill with or eject blood. In its chronic form, HF is one of the most remarkable health problems for prevalence and morbidity, especially in the developed western countries, with a strong impact in terms of social and economic effects. All these aspects are typically emphasized within the elderly population, with very frequent hospital admissions and a significant increase of medical costs. Recent studies and experiences have demonstrated that accurate heart failure management programs, based on a suitable integration of inpatient and outpatient clinical procedures, might prevent and reduce hospital admissions, improving clinical status and reducing costs.

The European STREP project HEARTFAID ("A knowledge based platform of services for supporting medical-clinical management of the heart failure within the elderly population"' — IST-2005-027107) aims at defining efficient and effective health care delivery organization and management models for the "optimal" management of the care in the field of cardiovascular diseases.

The HEARTFAID platform (HFP) has been conceived as an integrated and interoperable system, able to guarantee an umbrella of services that range from the acquisition and management of raw data to the provision of effective decisional support to clinicians. All the functionalities and services supplied by the entire HFP can be further grouped into *data*, *decision* and *end-users contexts* three macro "contexts". The former is devoted to the collection and management of continuous flows of information, which consists of biomedical data, acquired from biomedical devices and structured/unstructured information such clinical reports during patient hospitalisation and outpatient visits, from analysis laboratories, and within a homecare program by *telemonitoring* patients' conditions. The decision context includes a *knowledge-based Clinical Decision Support System* (CDSS) whose main goal is supporting the HF health care operators, by making more effective and efficient all the processes related to diagnosis, prognosis, therapy and health care personalization of the HF patients. The latter context provides the doorway to a multitude of end-user utilities and services, such as accessing an electronic health record, querying the CDSS, applying advanced models and methods for the extraction of new knowledge, and so forth.

The CDSS represents the core of HFP and has been carefully designed by combining innovative knowledge representation formalisms, robust and reliable *reasoning* approaches, based on *Machine Learning* and inference methodologies, and innovative methods for diagnostic images and biomedical signals processing and analysis (VV.AA., 2007).

This paper aims at showing how all these issues are combined within a comprehensive use case, centred on an echocardiography workflow and covering the clinical course leading from visit scheduling to therapeutic choices, highlighting the intervention and the value added by the CDSS.

In the following sections, we will briefly review the related literature, then introduce the HEARTFAID CDSS and its main functionalities, and, finally, describe the use case and CDSS interventions.

2 DECISION SUPPORT AND DATA PROCESSING IN HEARTFAID

The development of computerized applications for supporting health care givers is an old but still alive quest, started more than 45 years ago, in the early 1960s, and with ascending and descending periods of interest and growth (Greenes, 2007).

A plethora of CDSS has already evolved with different platforms and architectures, encompassing a variety of services, from information retrieval and reporting, scheduling and communications, to cost-effectiveness, error prevention, safety, and improvement of health care quality. The most common realizations include electronic medical/patient records (Poissant et al., 2005), computerized alerts and reminders, clinical guidelines formalizations (GEM, 2003), provider order entries (Park et al., 2005), diagnostic support, clinical result interpretation, adverse event monitoring, shared patient-doctor decision-making (Wirtz et al., 2006).

The primary task for developing effective CDSS is to select the corpus of *pertinent* knowledge and/or collect and process data to create pertinent knowledge which is relevant for bringing the health care to effect. Knowledge representation just concerns understanding, designing, and implementing ways of formally coding the knowledge necessary for deriving other knowledge, planning future activities, solving problems that normally require human expertise. Representing knowledge requires the selection of a suitable *language* or *formalism* and the definition of a *Knowledge Base* (KB) built by formalizing clinical experts' know-how and guidelines. Usually, the formalism is *symbolic* and the KB contains *statements* or *expressions* of one of the following formalisms: (i) rule based; (ii) frame based; (iii) network based; and (iv) logic based (Helbig, 2006). Workflow based representation is also becoming well-known, especially for modelling guidelines (Boxwala *et al.*, 2004). Moreover, in recent years ontologies are emerging as a powerful knowledge representation formalism which is conceptually equivalent to the frame based and to first order logic approach (Bayegan et al., 2002).

The KB is exploited by a *reasoning engine* which processes available information for formulating new conclusions and answering questions. *Inferential* reasoning is employed for inferring new knowledge from the KB by deduction, induction or abduction.

In some cases, making a decision requires an investigation on the hidden, complex, often non-linear correlations among data, together with high-level analytical processing functions. In such cases, the knowledge needed for the solution should be acquired directly from data (*inductive knowledge*) and stored in a model (e.g. *Artificial Neural Networks*, *Support Vectors Machines*), able to induce *sub-symbolic* knowledge by data-driven processing. Computational models are also useful for representing uncertain knowledge, as *Bayesian Networks* and *Fuzzy theory*.

HF routine practice presents several aspects in which an automatic, computer-based support could have a favourable impact. Some attempts to support HF clinical operators have been presented, such as an Electronic Patient Record (Bosmans et al., 2000) or computerized guidelines (Dassen et al., 2003). More complex decision support systems have been developed for suggesting the most appropriate therapy (e.g. Perlini et al., 1990).

Within HEARTFAID, a careful investigation about the needs of HF practitioners and the effective benefits assured by decision support was performed: four problems have been identified as highly beneficial of HEARTFAID CDSS point-of-care intervention. They can be referred as *macro domain problems* and listed up as: (i) HF diagnosis, (ii) prognosis, (iii) therapy planning, and (iv) follow-up. Further detailed decision problems were identified for specifying these macro domains, focusing as much as possible on the medical users' needs; explicative examples are:

- severity evaluation of heart failure;
- identification of suitable pathways
- planning of adequate, patient's specific therapy;
- analysis of diagnostic exams
- early detection of patient's decompensation.

An accurate analysis highlighted that the needed corpus of knowledge mainly consisted of domain know-how. Nevertheless, the solution of some of these problems seemed still debated in the medical community, due to the lack of validated and assessed evidences. In such cases, computational models appeared the best solution for modelling the decision making extracting knowledge directly form available data. Moreover, specific processing algorithms were designed for analyzing diagnostic examinations. In this perspective, HEARTFAID CDSS was designed for combining different models of reasoning, as will be described in the next sections.

2.1 Significance of signal acquisition and analysis in HF

Electrocardiography (ECG) is one of the very basic examinations performed in the evaluation and assessment of HF. According to ESC (2005) guidelines, the negative predictive value of normal ECG to exclude left ventricular systolic dysfunction exceeds 90%.

The most common ECG examinations are the "Resting ECG" and the "Holter ECG". While the latter is more commonly used for the discovery of rhythm abnormalities and the computation of the Heart Rate Variability (HRV), the former is more commonly used for the evaluation of morphological abnormalities in the PQRST shape.

In both examinations, the first step to be performed is the QRS detection with the identification of the time occurrences of each heart beat. This series of data allows for the evaluation of the heart rate and is preparatory to the beat classification for the discrimination between normal and abnormal beats. This task is usually performed in the "Holter ECG" reading stations as a starting point for the arrhythmias' classification and for the evaluation of the NN series (time intervals between consecutive normal beats) that is the input for the HRV evaluation. In case of "Resting ECG" examination (typical duration is 10 seconds), the evaluation of the normal beats allows the normal beat averaging with the construction of a more noise-free reference beat that can be used for a better evaluation of wave durations and amplitudes.

Wave durations and amplitudes are paramount in the evaluation of the "Resting ECG" (usually with 12 leads) parameters of high significance for the HF patients like ST depression, QRS and QT durations, Sokolow-Lyon index for left ventricular hypertrophy, presence of left or right branch bundle block and presence of pathological Q waves.

2.2 Significance of imaging techniques and image processing in HF

Imaging techniques offer invaluable aid in the objective documentation of cardiac function, allowing for the computation of parameters relative to chamber dimensions, wall thickness, systolic and diastolic function, regurgitations and pulmonary blood pressure.

According to ESC (2005), chest X-ray and echocardiography should be included in the HF initial diagnostic work-up. Further, echocardiography will be regularly repeated to monitor in an objective way the changes in the clinical course of a HF patient. Additional techniques, like nuclear imaging and cardiac magnetic resonance, may be also considered for particular patients, since they have not been shown to be superior to echocardiography in the management of most HF population.

Thus, echocardiography —and in particular 2-D TransThoracic Echocardiography (TTE) for its portability and versatility— is the key imaging technique for the practical management of HF.

The most important measurement performed by TTE is Left Ventricle Ejection Fraction (LVEF), which permits to distinguish patients with cardiac systolic dysfunction from patients with preserved systolic function. LVEF is given by the normalized (non-dimensional) difference between left ventricle End-Diastolic Volume (EDV) and the End-Systolic volume (ESV). Among different models for the computation of such volumes, the American Society of Echocardiography (Lang et al., 2005) suggests the use of the so-called Simpson's rule, by which the left ventricle is approximated by a stack of circular (or elliptical) disks whose centres lie in the major axis. Simpson's method, therefore, relies on left ventricle border tracing. It is well-known that manual border tracing, besides being time-consuming, is prone to inter- and intra- observer variability, and thus is unable to provide a satisfactory and reproducible measurement of LVEF.

Image processing techniques may relieve this problem, by providing automated or, at least, semi-automated methods for tracing contours of relevant structures found in an image, an issue called *image segmentation* in the specific literature. However, the segmentation problem for ultrasound images is by no means trivial, due mainly to low signal to noise ratio, low contrast, image anisotropy and speckle noise (Noble and Boukerroui, 2006).

3 A SIGNIFICANT SCENARIO

HEARTFAID CDSS was designed after a careful analysis of the problems to be faced and the expectations of the medical users.

A complete use case was defined for guiding the development activity of CDSS by considering many of the integrated services of the platform.

More in detail, we are considering a 65 years old patient, already enrolled in the HFP, former smoker, suffering from hypertension from several years. The patient was enrolled in the HFP six months ago and, in particular, the telemonitoring services offered by the platform were activated. At the baseline visit, the patient referred a slight limitation of physical activity, since he felt comfortable at rest but ordinary activity resulted in fatigue and dyspnoea. For these reasons, the patient was assigned to NYHA class II. Anamnesis data were also collected, from which it is known that the patient had an acute myocardial infarction five years before and that he underwent to aorto-coronary bypass. The patient had a post ischaemic dilated cardiomyopathy, with associated systolic dysfunction.

The TTE test (performed at baseline evaluation) showed an LVEF equal to 40%, ESV and EDV being respectively 114 ml and 190 ml. The LV end-diastolic diameter was 6.0 cm. The pharmacological treatment consisted in ACE-inhibitor, beta-blockers, spironolactone, aspirin and statin. Neither pulmonary nor systemic congestion signs were present. Blood examinations of renal function and electrolytes were normal. During these six months, the patient has been telemonitored. In particular, the pharmacological therapy has been followed with care and no relevant changes have been identified by the platform.

Suddenly, the patient observes a worsening of his symptoms, with a marked limitation of physical activity. After he fills in a periodic questionnaire suggested by the platform based on Minnesota questionnaire, the changes in the symptoms are automatically detected and considered relevant. A medical visit is suggested by the CDSS, accepted by the referent physician and immediately scheduled.

At the visit, the NYHA class changes from II to III. No variations in the signs are observed by the cardiologist, apart from a slight worsening of blood pressure (150/90 mmHg) and an increase of 10 beats/min in the heart rate. An ECG is performed to confirm such an increase in heart rate.

The cardiologist, supported by the CDSS, decides however to evaluate other parameters by echocardiography. During TTE examination, the sonographer acquires images and images sequences according to a protocol specified by the platform. Finally the images and the parameters manually evaluated by the sonographer are stored in the platform image archive. The reviewing cardiologist visualizes the echocardiographic images and the estimated parameters. Left ventricle volume and ejection fractions are computed again by automatic methods, exploiting the available image sequences. These values are compared with the historical data of the patient. EDV increases to 210 ml, ESV increases to 145 ml, EF decreased from 40% to 30%.

Mild tricuspidal insufficiency is Doppler-detected by its regurgitation. By tricuspidal regurgitation extent, the pressure gradient (mmHg) between right ventricle and right atrium is measured. Pulmonary pressure is then estimated. With this aim, the subcostal view is taken into account, so as to determine Inferior Vena Cava (IVC) diameter and its collapsibility index. The pulmonary pressure is estimated to be 40 mmHg, by using a lookup table with entries consisting in the tricuspidal gradient, IVC diameter and collapsibility index. Since this value indicates a slight pulmonary congestion, the

CDSS suggests the physician to integrate the pharmacological therapy with diuretics, for example loop diuretics or thiazides. Further, since there are no up-to-date information about the renal function and electrolytes, the CDSS suggests to start with a safe diuretic dosage and to perform blood examinations, which are scheduled for few days later. The physician opts for a loop diuretics therapy, for quicker beneficial effects.

Back to his home, the patient is monitored in the subsequent days. In particular control of weight, urine output, blood pressure, symptoms are scheduled daily. Blood examinations are scheduled seven days after the beginning of the new treatment. The results of such blood examinations are uploaded to the platform.

An up-titration table for the diuretics is compiled by the CDSS, considering in particular symptoms and electrolytes balance, creatinine clearance, blood pressure, weight slope and urine output. The CDSS also suggests to control weight and urine output daily and to schedule blood examinations weekly. A visit is also suggested in one month, to appreciate the response to the therapy. The physician reviews this program and decides to approve it. After approval, the up-titration table for diuretics is automatically sent to the patient.

One week after, telemonitoring evidences persistence of symptoms; the patient is thus required to continue the up-titration program for diuretics. During the subsequent weeks symptoms get better until the visit. At that visit, the patient refers that symptoms are relieved. NYHA class is moved back to II. However, the CDSS suggests to the physician to explore the possible origins of the change in the symptoms reported in the previous visit (i.e. the probable cause of heart failure decompensation). In particular, with the aim of controlling the ischemic disease, a stress test is scheduled.

3.1 Methods

The CDSS was defined for an overall support of HF management, facing the main decisional problems of diagnosis, prognosis, therapy and follow-up, by using patients' heterogeneous information (e.g., actual status, anamnesis, clinical history, diagnostic parameters, and clinicians' evaluation).

Ontologies combined with rules were chosen as representation formalism, because of the more suitable and up-to-date methodology for formalizing the declarative and procedural knowledge derived from the guidelines and the experts' know-how. Actually, ontologies constitute a logic-based representation which also assures easy re-use and sharing of knowledge. Moreover, the rule based approach appeared the more appropriate both to complete possible representation lacks of ontological model and to involve the experts in the elicitation process. An inference engine was then devised for the corresponding inferential reasoning processes, by induction and deduction on the formalized knowledge for assessing patients' status, formulating diagnosis and prognosis, assisting therapy planning, and patients' monitoring.

Computational reasoning models were included for those difficult HF decision problems, such as prognosis assessment and early detection of patient's decompensation.

The HEARTFAID CDSS architecture was designed according to a multilevel conceptualization scheme for distinguishing among

- the *knowledge level*, corresponding to all the information needed by the system for performing tasks, e.g. data, domain knowledge, computational decision models;
- the *processing level*, consisting of the system components that are responsible for tasks accomplishment by using the knowledge level;
- the *end-user application level*, including the system components whose functionalities are specifically defined for interacting with the user.

More in detail, the CDSS architecture consists of the following components (Figure 1):

- *Domain Knowledge Base*, consisting of the domain knowledge, formalized from the guidelines and of the clinicians' know-how;
- *Model Base*, containing the computational decision models, signals and images processing methods and pattern searching procedures;
- *Meta Knowledge Base,* composed by the strategy knowledge, i.e. about the organization of CDSS tasks.
- *Brain*, the system component endowed with the reasoning capability, which is divided into the meta and object level;
- *Explanation Facility*, providing a means to explain conclusions taken.

The Brain was modelled by functionally separating a *meta level*, devoted to task accomplishment and organisation, and an *object level*, responsible for actually performing tasks, by reasoning on the computational and domain knowledge. A *Strategy Controller* was inserted for performing the meta level functionalities, by orchestrating the two components of the object level, i.e. the *Inference Engine* and the *Model Manager*.

Moving from the design to the development activity, the use case is being used as a real scenario for implementing the above architecture.

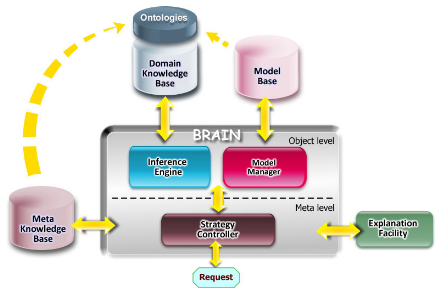

Figure 1: The general view of the HEARTFAID CDSS architecture – dashed arrows correspond to reference to the ontologies, while the others denote a direct communication.

The required CDSS interventions consist in the following services, listed in order of occurrence in the workflow:

- interpretation of telemonitored data and assessment of patient's status;
- visit scheduling;
- suggestion of new diagnostic examinations;
- analysis of imaging examinations;
- interpretation of diagnostic findings;
- suggestion of therapy changes.

The necessary pieces of knowledge have been identified as mainly symbolic and an elicitation process has been performed for their formalization in the Domain KB. Specific algorithms for extracting a number of useful parameters from the echo images have been developed and inserted into the Model Base.

In particular, the use case highlights the interventions of other components of HFP which hold important roles in assuring the effectiveness of the support services, e.g. the agenda for scheduling new visits or examinations. Actually, HFP was conceived for consciously distributing the work load among the various components. A sketch of the platform with the components that interact with the CDSS is shown in Figure 2.

An EHR module was inserted for suitably organizing, visualizing and managing patients' data, stored into the platform *Repository*. In particular, a dedicated *Repository* for storing examination images was conceived in accordance to the DICOM standard. An *Agenda* module was included for managing patients' care planning, e.g., scheduling new visits, prescribing new examinations and so forth. The *User Interface* was designed as a fundamental component, responsible for all the interactions and communications with the users.

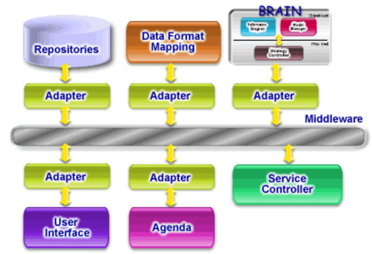

Figure 2: A sketch of HFP with the components that interact with the CDSS.

The different components of the platform were seen as *resources*, by *virtualizing* the operations required for their management. When involved, the different components are dynamically integrated for supplying sophisticated but much flexible applications. The responsible for guaranteeing integration and interoperability among all the HFP components was defined as the platform *Middleware*, which includes all the adapters necessary for the virtualization. For simplifying the provision of different services, a *Service Controller* (SC) was comprised for managing platform events and invoking the other components.

In this perspective, the CDSS component was designed as a resource able to offer a number of functionalities and to interact with the other resources for performing its tasks. Each decision-making problem has to be translated into a *request* or a *class of requests* committed to the CDSS, which is then activated *on-demand*. The system handles every request according to a specific policy encoded in the Meta KB, interacting, when necessary, with the other platform components.

A brief (and partial), discursive description of how the scenario has been mapped onto a workflow of HFP services is useful for understanding its implementation.

Description of the mapping into the HFP

The patient answers a questionnaire through his web-based user interface and sends the information to the HFP that checks eventual missing values. Then the Service Controller stores this information into the repository, gets historical data and opportunely invokes the specific CDSS service responsible for handling the request.

The CDSS analyzes data and answers supplying the current patient's status, i.e. worsening of symptoms, and a set of suggested actions the clinician should undertake, i.e. schedule a new visit, change the NYHA class, change the therapy and so forth. Then the SC stores CDSS results into the repository.

When the doctor on duty logs in the HFP, the list of patients is displayed ordered by their severity status and the timestamp of the last related event. Then he chooses to analyze the patient's situation and the change in his status is shown along with the list of suggested actions, for instance as a list of operations that can be selected. He then approves the schedule of the visit and the SC forwards the request to the Agenda component that opportunely records it and informs the patient. During the visit, the physician inserts his observations into the patient's record and decides to approve the change of the NYHA class: he selects the corresponding action within the list and the SC takes care of registering the change in the patient's record. An ECG is then performed for further investigations. Once the information obtained by the ECG have been inputted, a request for its interpretation is sent by the SC to the CDSS, which suggests performing an echocardiography as displayed in the recommended actions list.

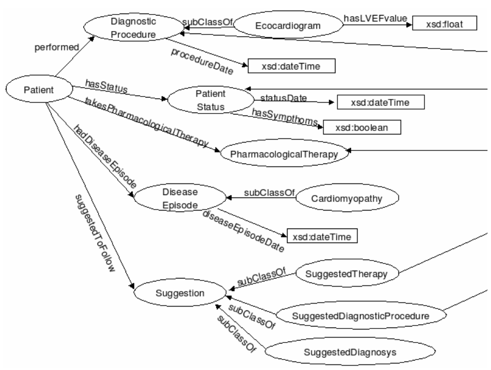

Figure 3: Some relevant classes and properties of the ontology.

Inference on patients' data

In order to include information derived from the use case, starting from a preliminary ontology mainly corresponding to a structured terminology of the domain, we began to develop a new ontology by inserting relevant properties, classes and relations for a coherent and comprehensive formalization, also in accordance to standard medical ontologies, such as the Unified Medical Language System (UMLS, 2007). An excerpt of this new ontology is shown in Figure 3. A careful elicitation activity was performed for formalizing a set of rules, founded on the developed ontology and to be encoded in the KB. An elicited rule which is used for therapy suggestion is: "*If a patient has Left Ventricle Ejection Fraction <= 40% and he is asymptomatic and is assuming ACE Inhibitors or ARB) and he had a myocardial infarction then a suggestion for the doctor is to give the patient Betablockers*".

Echocardiography images analysis

A prototype module for the computation of LVEF has been developed (Barcaro et al., 2007). The module is able to process an apical-view sequence of the heart (the so-called two- and four-chamber views) in order to identify the left ventricle cavity in every frame of the sequence. This segmentation stage is accomplished augmenting a variational formulation of level set methods with *mimetic criteria* for contour initialization (see Figure 4).

After segmentation, the left ventricle volume is computed as a function of time by applying monoplane Simpson's method. Then ESV and EDV are regarded as the minimum and maximum respectively of the volume time-course. Finally LVEF is obtained by the simple formula: $\mathrm{LVEF} = \dfrac{\mathrm{EDV} - \mathrm{ESV}}{\mathrm{EDV}}$.

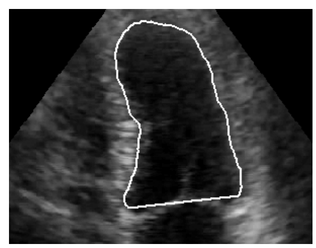

Figure 4: Segmented left ventricle cavity at end-systole.

4 RESULTS AND CONCLUSIONS

A number of tools and instruments are available for developing the CDSS according to the design specifications. The key factors that were taken into account for defining an up-to-date system were accordance to standards, efficiency and robustness.

We investigated several technologies, with particular attention to the Semantic Web field, since it offers various tools for building ontological models, knowledge bases and reasoning on them. Moreover, the platform was conceived for web applications developed in Java. For selecting the appropriate tools, we carefully analyzed the W3C recommendations along with the performance, compatibility and maintenance of the same tools.

As to the knowledge representation formalism, we selected the Web Ontology Language (OWL, 2007) for defining the ontologies, since it is the actual de-facto standard semantic markup language for this task.

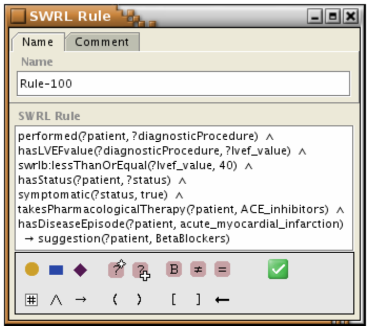

Figure 5: A rule developed in SWRL.

The ontology is being built using the two editors Protégé and Swoop. For defining the rules of the KB, we chose SWRL (2007), the Semantic Web Rule Language combining OWL and Rule Mark-up Language, which is a submission to W3C that extends the set of OWL axioms to include Horn-like rules. For realizing the reasoning component, Jena (McBride, 2001) was selected as a Java programmatic environment that includes OWL, a language for querying ontologies, SPARQL (2007), and a rule-based inference engines. In particular, for improving the reasoning capability of the latter, we also used Bossam (2007) and Pellet (2007). An example of the rules we are developing in SWRL is shown in Figure 5 as it has been defined in Protégé. A prototypical methods for processing the echo images were realized implementing the various procedures in Matlab.

Future activities consist in finalizing the platform implementation by concluding the realization of the Domain KB, the algorithms contained in the Model Base and the Brain, in particular of its meta level for integrating all the object models and the interface.

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REFERENCES

Barcaro, U., Moroni, D., Salvetti, O. (2007) Left ventricle segmentation in ultrasound sequences for the automatic computation of ejection fraction. In *OGRW07 Open Gern Russ Work on Pat Rec & Im An.*

Bayegan, E. Nytro, O. Grimsmo, A. (2002). Ontologies for knowledge representation in a computer-based patient record. In *ICTAI 2002, 14th IEEE Int. Conf. on Tools with Artificial*. IEEE.

Bosmans, J.E., Dassen, W.R.M., van der Velde, E.T., Dijk, W.A., Spruijt, H.J., Baljon M.H. (2000). Towards ICT Support for Treatment of Congestive Heart Failure. *Computers in Cardiology*, 27, 641-644.

Bossam (2007) http://bossam.wordpress.com/

Boxwala, A.A., Peleg, M., Tu, S. et al. (2004) GLIF3: a representation format for sharable computer-interpretable clinical practice guidelines. *J. Biomed Inform.*, 37(3), 147-161.

Dassen, W.R.M., Gorgels, A.P.M., Berendsen, A., Dijk, W.A., de Clercq, P.A., Hasman, A., Baljon M.H. (2003). Guideline Assessment and Implementation in Congestive Heart Failure. *Computers in Cardiology*, 30, 331-334.

ESC (2005) Swedberg, K. et al., "Guidelines for the diagnosis and treatment of Chronic Heart Failure: full text (update 2005)", *European Heart J*, 45 pages.

GEM (2003) *E2210-02 Standard Specification for Guideline Elements Model (GEM)* Book of Standards Volume: 14.01. ASTM International.

Greenes, D. (2007). *Clinical Decision Support: The Road Ahead*. Academic Press.

Helbig, H. (2006) *Knowledge Representation and the Semantics of Natural Language*, Springer, Berlin, Heidelberg, New York.

Lang, R.M. et al., (2005). Recommendation for Chamber Quantification.. *J Am Soc Echocardiogr*, 18, 1440-1463.

McBride, B. (2001) Jena: Implementing the RDF Model and Syntax Specification. In *WWW2001, Semantic Web Workshop*.

Noble, J.A., & Boukerroui, D. (2006). Ultrasound image segmentation: a survey. In *IEEE Trans. Med. Imag.*, 25, 987-1010.

OWL (2007) http://www.w3.org/TR/owl-features/

Park, R.W., Shin, S.S., Choi, Y.I., Ahn, J.O., Hwang, S.C. (2005). Computerized physician order entry and electronic medical record systems in Korean teaching and general hospitals: results of a 2004 survey. *J Am Med Inform Assoc.* 12(6):642-7.

Pellet (2007) http://pellet.owldl.com/

Perlini, S. *et al.* (1990) Treatment of chronic heart failure: an expert system advisor for general practitioners. *Acta Cardiol.*, 45(5), 365-78.

Poissant, L., Pereira, J., Tamblyn, R. Kawasumi, Y. (2005). The impact of electronic health records on time efficiency of physicians and nurses: a systematic review. *J Am Med Inform Assoc.* 12 (5), 505-16.

SPARQL (2007) http://www.w3.org/TR/rdf-sparql-query/

UMLS (2007). http://www.nlm.nih.gov/research/umls/

SWRL (2007) http://www.w3.org/Submission/SWRL/

VV.AA. (2007). Functional Specifications of Data Processing and Decision Support Services. Deliverable D15, HEARTFAID IST-2005-027107.

Wirtz, V., Cribb, A., Barber, N. (2006). Patient–doctor decision-making about treatment within the consultation—A critical analysis of models. *Social Science & Medicine.* 62, 1, 116-124.