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# A Decision Support System for Aiding Heart Failure Management

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*Abstract*—**The purpose of this paper is to present an effective way to achieve a high-level integration of a Clinical Decision Support System in the general process of Heart Failure care and to discuss the advantages of such an approach.**
**In particular, the relevant and significant medical knowledge and experts' know-how have been modelled according to an ontological formalism extended with a base of rules for inferential reasoning. These have been also combined with advanced analytical tools for data processing. In particular, methods for the segmentation of echocardiographic image sequences and algorithms for ECG processing have been implemented and integrated into the system.**

## I. Introduction

The need for a more efficient, cost-effective and personalized care and for a more rational deployment of diagnostic resources is one of the reasons behind the strong demand and hence success of computerized applications developed to assist health care givers in their routine clinical workflows [1]. Actually, the provision of specialized care regimes depends on the optimization abilities of care professionals to apply the necessary medical knowledge by also integrating the interpretation of diagnostic test results, medication availability and responses to past treatments. This can be a particularly burdensome task and it may be now beyond the mental integration capabilities for unaided healthcare professionals to deliver patient care with the efficacy, consistency and safety that the full range of current knowledge could support. Nowadays, the development and increasing use of hospital or, even, cross-enterprise regional health information systems make possible the design of ambitious integrated platforms of services in order to guarantee the continuity of care across the various stakeholders. Clinical Decision Support Systems (CDSSs) are a natural ingredient of such integrated platforms, since they may foster adherence to guidelines, prevent omissions and mistakes, spread up-to-date specialistic knowledge to general practitioners and so on. A great value added to the efficacy and usefulness of a support application can be assured by the integration of advanced methods for diagnostic data processing. Actually, signal and imaging investigations are currently a basic step of the diagnostic, prognostic and follow-up processes of diseases.

Among chronic diseases, Heart Failure (HF) is a complex clinical syndrome, whose management requires –from the basic diagnostic workup– the intervention of several stakeholders and the exploitation of various diagnostic signal and imaging resources. Indeed, due to complexity and urgency of chronic HF patients' management, several attempts to cope with the problem have been made in different research projects and resulted in the development of dedicated IT solutions such as automated guidelines systems [2], decision support systems [3], or Machine Learning methods for automated HF diagnosis [4] or prognosis [5]. More recently, the European project HEARTFAID "A knowledge based platform of services for supporting medical-clinical management of the heart failure within the elderly population" [6] aims at defining efficient and effective health care delivery models for the optimal management of HF patients. The HEARTFAID platform 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 [7]. Specifically, the core of the platform is represented by a CDSS, which has been carefully designed by combining innovative *knowledge representation* formalisms, robust and reliable *reasoning* approaches, and innovative methods for diagnostic image and signal analysis.

In this paper, the CDSS design and development is discussed by focusing particularly on the knowledge formalization process and how signal and image processing results have been modelled in it.

## II. Background

### A. Clinical Background

HF is a progressive disorder caused by a decreased ability of the ventricle to fill with or eject blood and in which damage to the heart causes weakening of the cardiovascular system. HF progresses by underlying heart injury or inappropriate responses of the body to heart impairment. It is a progressive disorder that must be managed in regard to not only the state of the heart, but the condition of the circulation, lungs, neuroendocrine system and other organs as well. In its chronic form, HF is one of the most remarkable health problems for

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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.

The first, immediate and enlightening proof of HF complexity is represented by its diagnostic workup. Indeed, it can be considered as the first stage of HF patients' management which necessarily requires the acquisition and analysis of signals and images. Once assessed the presence of main signs and symptoms, physicians usually require diagnostic examinations such as ECG, chest X-ray and neuroendocrine evaluations (i.e. Brain Natriuretic Peptides) in order to check out the diagnosis, confirmed eventually by an echocardiography investigation. Supporting such a decision problem requires to encode the workflow into an opportune knowledge base that formalizes, for each step, the set of conditions evaluated by physicians.

### *B. Decision Support in Heart Failure*

Recent studies and experiences have demonstrated that accurate HF 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 [8], [9]. Actually, HF routine practice presents several aspects in which an automatic, computer-based support could have a favorable impact. A careful investigation about the needs of HF practitioners and the effective benefits assured by decision support was performed: four problems were identified as highly beneficial of CDSS point-of-care intervention [4]. 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 examinations
- early detection of patient's decompensation

The idea behind the development of a CDSS able to support this kind of problems was to provide clinicians with advices, suggestions and alerts in the different phases of chronic HF patients' management, without altering their normal activities.

In practice, the implementation of CDSS was mainly focused on the incorporation of high-quality, evidence-based medical knowledge, suitably formalized and employed in automated reasoning processes in order to obtain diagnostic, prognostic and therapeutic conclusions to be supplied to clinicians.

### *C. Significance of Signal and Image Processing Methods*

During the formalization of the main decisional problems in the heart failure domain and listing up all the pieces of knowledge, data and information relevant for decision making, the importance of considering and interpreting ECG signals and echocardiography images came forth. Indeed, HF diagnostic workup was a straightforward example of the importance of computer-aided data processing in HF decision making.

As it is well known, imaging techniques offer invaluable aid in the objective documentation of cardiac function, by supplying parameters relative to chamber dimensions, wall thickening and motion, systolic and diastolic function, regurgitations and pulmonary blood pressure. As previously mentioned, chest X-ray and echocardiography should be included in the HF initial diagnostic workup. Further, echocardiography will be regularly repeated to monitor in an objective way the changes in the clinical course of a HF patient. Thus, echocardiography and in particular 2-D TransThoracic Echocardiography (TTE) for its non-invasiveness and versatility is the key imaging technique for the practical management of HF. On the other side, ECG is recognized as the very basic examination performed in the evaluation and assessment of HF. According to [10], the negative predictive value of normal ECG to exclude left ventricular systolic dysfunction exceeds 90%. Summing up, ECG and TTE processing methods may allow for the automatic or semi-automatic computation of clinical parameters relevant in decisional problems in the HF domain, thus providing reproducible and reliable numerical values and reducing intra- and inter-observer variability.

## III. METHODS

### *A. The Clinical Decision Support System*

The CDSS was devised for processing patients' related information by exploiting the relevant medical knowledge opportunely elicited from medical experts, extracted from clinical guidelines, and suitably formalized for being used in reasoning processes. While encoding such knowledge, the integration of both signal and image processing methods was conceived in order to include parameters extracted from different data acquisition modalities into the more general process of health care management. In particular, the integration was focused on two main issues:

1) supplying relevant parameters to the inferential processes
2) personalizing the diagnostic investigations by suggesting which parameters should be evaluated.

An example can be used for better explaining the implications of these two issues: while processing patient's data for identifying the causes of her worsening, the CDSS may need a number of routine parameters not yet available. In such a case, a suggestion will be issued by the system asking the clinician to perform additional examinations, such as an ECG or a TTE, in order to obtain the missing parameters. On the other side, it can happen that such routine parameters are not able to completely explain patient's status and thus the system can require the extraction of other non standard features that can enlighten patient's peculiar conditions. In both cases, the reasoning process pauses, waiting for additional information. Reactivating the process requires data processing algorithms to be performed.

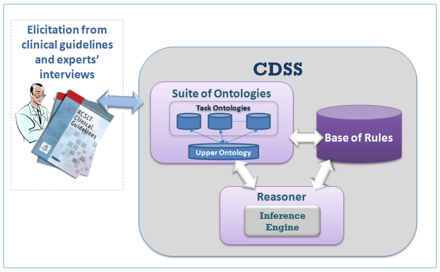


Fig. 1. The organization of the knowledge base and the reasoning component of the CDSS

A *symbolic* approach [11] was selected for formalizing the domain knowledge. In particular, among the several symbolic knowledge representation methods –most of which refers to logics in order for a formal semantics– a hybrid solution based on the use of *formal ontologies* and *rules* appeared the most promising.

Ontologies were selected as knowledge representation methods thanks to their main properties, such as *conceptuality* (i.e., an ontology corresponds to a conceptual model of a domain which can be easily understood and captured), *explicitness* (i.e., the relevant notions of the domain are explicitly included into the machine-interpretable conceptualization model), and easiness to *be shared* (i.e., an ontology is generally built after a certain agreement on the terminology to be used among a domain community). Another feature that appeared relevant in the choice was the spread of ontologies within the *Semantic Web* field and, thus, the availability of different up-to-date, open-source technologies developed by large communities. This was also considered important since the CDSS was conceived to be used in a web-based environment [7].

Although the various advantages, ontologies present some limits and lacks owed to their *description logics* foundations. This means that complex or derived relations cannot be induced from an ontological artefact. A *rule-based* formalism is generally employed for filling these lacks. Rules are used to reflect the notion of consequence; they come in the form of IF-THEN-constructs and allow expressing various kinds of complex statements. They are based on different kinds of logics and have, thus, a well definite semantics supported by assessed reasoning tools. Morevoer, rules are particularly suitable for encoding procedural knowledge, i.e., not only declarative information about the existence of domain concepts, but also action to be performed when specific conditions are met.

The medical-clinical knowledge was then formalized into a composite Knowledge Base (KB) that consisted in a suite of ontologies and a base of rules, as shown in Figure 1. Clinical guidelines [10] were used as knowledge source and experts' know-how was elicited through several interviews. Moreover, in order to maintain the focus on the actual routine activities of clinicians, some realistic scenarios were conceived in cooperation with the experts and followed during the knowledge representation process. This fostered the development of an effective supportive instrument able to integrate clinicians' routine workflows and provide correct suggestions when needed. A problem decomposition approach was adopted, by identifying the different CDSS interventions and the correspondent relevant pieces of knowledge which were then suitably structured.

In order to be more precise, examples of actual problems identified as requiring the CDSS help are the following:

*A patient, monitored at home, completes a periodic questionnaire (i.e. the Minnesota Questionnaire) which is transmitted for interpretation to the CDSS, which automatically detects any change in her symptoms*

*A patient undergoes a TTE examination and computed parameters are submitted to the CDSS which, once recomputed more objectively some of them by using the image processing tools, estimates additional information, such as the pulmonary pressure, and according to them suggests to the clinician a change in therapy*

A problem-specific point of view was maintained for building the KB. The ontology was hence structured so as to be functional to its use in the reasoning process, instead of being developed as a structured terminology.

A comprehensive conceptual model was firstly devised for capturing all the relevant information, concepts and relations. Figure 2 shows an excerpt of such a model, some aspects are worth of note: the class *"patient"* is central and links all the other classes; the class *"suggestion"* was used for modelling the responses of the CDSS to each possible query; the class *"currentStatus"* was included for modelling the dynamic situation of patients' conditions.

In order to optimize the reasoning process (i.e., to speed it up and make it easier), this model was organized into a suite of ontologies composed by a set of *sub-domain ontologies*, one for each of the identified sub-problems the CDSS had to provide suggestions for, i.e., *diagnosis*, *follow-up* and *therapy*, and these were further divided into *task ontologies*. An upper ontology was defined for linking all the information, more precisely the class *"patient"* is the main component of this upper ontology.

Particular attention were paid to the diagnostic procedures and, then, to the role signals and images have within the functioning of the CDSS. More precisely, the parameters that can be extracted from the different modalities were extensively analyzed and inserted into the conceptual model (see Figure 2). Actually, rules were formalized by using the concepts specified into the ontologies. Again, guidelines and experts' know-how were used as knowledge sources.

### B. Image Processing Methods

Since TTE is the key imaging modality for the management of heart failure patients, a careful analysis of the modality

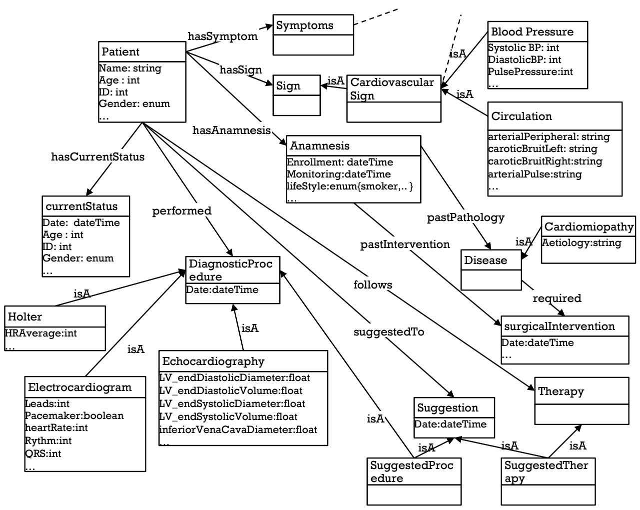


Fig. 2. An excerpt of the conceptual model used for building the ontology. Boxes represent classes and contain their simple datatype properties, while relations among classes are represented by the arcs (arrows between two boxes).

was carried out in cooperation with medical partners, from which it was concluded that the development of assisted segmentation methods, able to deal with echocardiographic image sequences, could represent a valid support to the physicians in the process of image report formation. Indeed, assisted segmentation methods may make more reproducible the most important measurement performed by TTE, which is Left Ventricle (LV) Ejection Fraction (EF). LV EF, which permits to distinguish patients with cardiac systolic dysfunction from patients with preserved systolic function, is given by the normalized (non-dimensional) difference between LV End-Diastolic Volume (EDV) and the End-Systolic volume (ESV). Among different models for the computation of such volumes, the American Society of Echocardiography [12] suggests the use of the so-called Simpson's rule, by which the LV is approximated by a stack of circular (or elliptical) disks whose centers lie on the major axis. The border of the LV cavity is needed for estimating its axis and the radii of the disks in the stack. For this reason, Simpson's method relies on the segmentation of the LV border. In the case of manual segmentation of TTE images, inter- and intra-observer variability is strong, since often the anatomical structures of interest are not easily distinguishable due to intrinsic limitations of the modality. Further, the error in the estimation of EDV and ESV greatly propagates to the value of LV EF; for these reasons manual contour tracing is unable to provide a satisfactory and reproducible measurement of LV EF. Image processing techniques may reduce variability of human interventions in border tracing, by providing automated or, at least, semi-automated methods for tracing contours of relevant structures found in an image. However, the segmentation problem for ultrasound images is by no means trivial, due mainly to low signal to noise ratio, low contrast, and image anisotropy and speckle noise [13]. From these considerations, it was judged important to develop a prototypical toolkit for the analysis of apical-view sequences and the estimation of LV EF.

### C. Signal Processing Methods

ECG signals play a crucial role in HF diagnosis and follow-up. After some interviews with the clinicians, a significant operative scenario was identified where a non-interpretive electrocardiograph acquires and transfers resting ECGs to the hospital gateway where the ECGs are processed in order to:

1) Detect the QRS complexes
2) Identify the dominant beats
3) Evaluate the averaged dominant beat

In fact, the averaged dominant beat is usually used by the cardiologists for the evaluation of the main measurements for the diagnosis or the follow-up of HF patients, like ST depression, QRS and QT durations, Sokolow-Lyon index, presence of left or right bundle branch block and presence of pathological Q waves. Thus, the algorithms developed for signal processing –together with a suitably designed graphical interface– may be used for the semi-automatic accurate estimation of such parameters, which, in turn, are used as input by other CDSS services.

The robust and scalable algorithms developed for ECG processing are briefly described below.

*1) QRS detection:* The selected approach for QRS detection [14] starts with a signal pre-filtering in order to reduce the baseline wandering and the high-frequency noise. Then, a QRS enhanced Signal (QeS) is built as the sum of the absolute derivatives of the pre-filtered channels. QRSs are detected using an adaptive threshold and special techniques are used in order to avoid indicating large-amplitude T-waves as other QRSs and to reject any QRS detection too closer to the previous one. In each channel, noise estimation for each QRS is performed and a number of consecutive noisy QRSs determine the presence of a noisy interval. In each noisy interval a procedure selects the results obtained by the QRS detection using QeS produced by channel combination with lowest noise.

*2) QRST morphological classification:* The QRST morphological classifier has been designed based on a two-phase decision tree [15] and starts with a pre-processing for the reduction of baseline wandering and high-frequency noise. In the first phase, each QRST complex is best aligned, using horizontal and vertical wiggling, with an estimated centroid in the point which minimizes the L1 distance. "Similarity" features like the L1 and L2 distances and the centroid-to-beat correlation coefficient are then evaluated and, using also the peak-to-peak value of the complex, it is determined with a decision tree whether the complex should be considered dominant or not. Then, the same algorithm is applied again to the remaining beats identifying all the other morphological classes. In the second phase, all non-dominant groups are reprocessed, after splitting the large groups into smaller ones. The centroid of each reformed group is compared to the dominant group centroid using the same features of the first phase and, if the new classification criteria are satisfied, its beats are put into the dominant class. For the last group of phase one, which is more a collection of leftover complexes than a group of similar complexes, each beat is separately compared to the centroids of all groups formed so far. In absence of a satisfactory likeness with any other class, a new group is formed with that beat. Noise is also estimated for each QRST in order to loosen the criteria for the beat assignment to the dominant class in the first phase and during the processing of the last group in the second phase.

*3) Evaluation of the averaged dominant beat:* A rough approach might be simply the average of all the beats classified as dominant, however:

- Beats with too much noise would corrupt the proper averaging.
- Incomplete beats (typically the first and the last of the recording) would corrupt the proper averaging.
- Beats not properly aligned to a proper reference point would provoke artifact in the averaged beat.

Thus, the set of the dominant beats -found during the classification process- is analyzed in order to exclude for each channel incomplete beats (usually the first and the last of the recording) and beats with high noise. Finally a subset of good dominant beats is identified for each channel and the averaging is performed on this subset based on the alignment values previously identified. The averaging is performed on the original signal band-pass filtered in the band 0.1-40 Hz in order to avoid non-linearities (mainly in the T-wave morphology) introduced by the median filters used in the classification pre-processing.

## IV. Results and Discussion

Results of the methods introduced are herein reported orderly.

**Clinical Decision Support.** 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: (i) accordance to standards, (ii) efficiency and (iii) robustness.

Several technologies were investigated, with particular attention to the Semantic Web field, since it offers various tools for building ontological models, knowledge bases and reasoning on them (plus, the CDSS was conceived to be integrated within a web-based application). For selecting the appropriate tools, the W3C recommendations were carefully analyzed and the performance, compatibility and maintenance of the different tools were considered. As to the knowledge representation formalism, the *Web Ontology Language* (OWL) [16] –and specifically the *OWL DL* sublanguage– was selected for defining the ontologies, since it can be considered as the actual de-facto standard semantic mark-up language for this task and offers all the power and expressivity of Description Logics. Standard medical ontologies such as UMLS [17], were taken into account for selecting a commonly recognized and agreed terminology.

For defining the rules, the *Semantic Web Rule Language* (SWRL), which combines OWL and *Rule Mark-up Language* [18], was selected as suggested by the W3C for extending the set of OWL axioms to include Horn-like rules. For the reasoning component, Jena [19] was preferred as a Java environment that includes OWL, a language for querying ontologies, i.e. [20], and a rule-based inference engine. In particular, for improving the reasoning capability of the rule-based inference engine, Bossam [21] and Pellet [22] were also used.

As discussed and illustrated in the previous section, the formalized KB contained a number of rules and conditions related to the signal and imaging procedures and processing methods. This means that the CDSS can issue suggestions regarding the necessity of performing an echocardiography examinations or can employ the parameters extracted from signals and images for issuing advices. An explicative illustration of the CDSS functioning in the latter case can be easily obtained considering a patient that performs a TTE. The acquired images and the parameters previously extracted from the echocardiographic device can be uploaded to the CDSS and submitted for further processing. The image analysis methods can be, then, launched for re-computing the left ventricle volumes and the LVEF. Once these values are available and transmitted to the CDSS, they are combined with other facts about the patient and used for obtaining further information and conclusions, such as the condition of the filling pattern, systolic pulmonary pressure and the type of heart failure.

For better showing and allowing to appreciate the results of this integration, it should be mentioned that the CDSS as well as the signal and image processing tools were developed to be integrated into the HEARTFAID platform of services, which also include a *Telemonitoring System* for acquiring and store patients' data at home, an electronic *Case Report Form* for managing patients' information, a web-based *User Interface*, and a *DICOM-compliant Image Archive*, also equipped with a web-based interface, for storing and browsing the results of imaging investigations. The platform was implemented as a web-based application according to a service oriented approach. Describing the platform and its implementation is beyond the purpose of this paper (see [6]), but it is worth mentioning that the CDSS was not developed to be invoked *explicitly* by clinicians; rather it was designed so as to assist them *contextually* during their work, offering suggestions at appropriate circumstances. For instance, when a clinicians is checking patient's status, the suggestion of performing an echocardiographic investigation may be automatically displayed. This type of integration is handled by the *Integration Middleware* component which is responsible for orchestrating all the platform services.

In particular, the situation described before was implemented by considering that the TTE images are uploaded into the Image Archive and the image analysis tool is launched so as to compute the mentioned parameters. Results of the segmentation are stored into the archive and displayed for being approved. If this is the case, the information is sent to

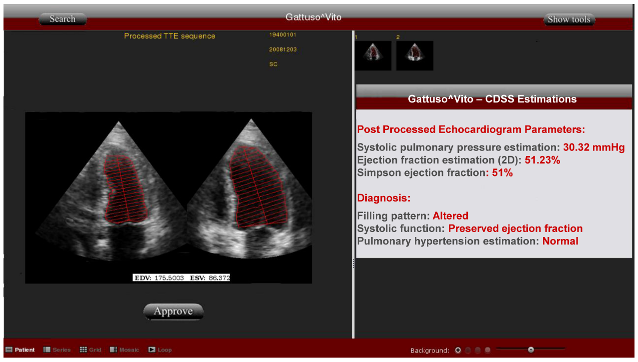


Fig. 3. Example of CDSS response after echo parameters are computed

the CDSS and results are displayed in a new page as shown in Figure 3. **Image Processing.** A toolkit –consisting of three modules– for the analysis of apical image sequences and the computation of LV EF has been designed and implemented. The first module (*Region Identification*), which takes in input an apical sequence of the heart, is able to identify the left ventricle cavity in every frame of the sequence by means of mimetic criteria, providing a rough segmentation of it. The second module (*Segmentation Refinement*), which takes in input an image and a rough segmentation of it, is able to refine the segmentation exploiting a variational formulation of level set methods, which achieves regularization of the boundary of the LV as well as better adherence to image edges. The third module (*Feature Extraction*) is able to extract significant features from a set of segmented left ventricles, the most important being EDV and ESV (both computed according to Simpson's rule) and, in turn, LV EF. The various procedures have been implemented in the Matlab environment, exploiting the Image Processing Toolbox (IPT), and have been tested on 2D image sequences, recorded from the apical window (2-chamber and 4-chamber views). The echocardiographic device was GE Vivid 7. The data consisted of image sequences acquired at the rate of 25 frames per second.

**Signal Processing.** The ECG processing algorithm were tested on the publicly available annotated MIT-BIH Arrhytmhmia Database [23]. For the QRS detection, a sensitivity of $99.76\%$ and a positive predictive value of $99.81\%$ have been obtained. Very satisfactory results were also obtained for dominant class discrimination on all the annotated beats of the same database with sensitivity $99.05\%$ and specificity $93.94\%$. A slight reduction of the performances was obtained on the detected beats obtained by the QRS detector described above, but the results were still very satisfactory with sensitivity $98.71\%$ and specificity $93.81\%$.

## V. Conclusions

In this paper we have presented a high-level integration of diagnostic signal and image processing into the wide-ranging services provided by a CDSS for the management of heart failure. In particular, we have motivated the choices made in designing suitably image and signal processing algorithms and we have shown how they can be deployed in decisional problems –and hence in the global process of care– by the CDSS. The CDSS was developed by integrating the knowledge elicited from clinical guidelines and experts' interviews into a hybrid KB consisting of a suite of ontologies and a base of rules. The feedbacks obtained so far by clinicians were encouraging.

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## References

[1] K. Doi, "Computer-aided diagnosis in medical imaging: Historical review, current status and future potential," *Comp. Med. Imaging and Graphics*, vol. 31, pp. 198–211, 2007.
[2] B. Purin, M. Rigo, S. Riccadonna, and S. Forti, "An interactive real-time visualization environment for patients with heart failure," in *AMIA Annual Symp Proc.*, 2005, p. 1088.
[3] S. Perlini, M. Piepoli, G. Marti, A. Rabino, and P. Rota, "Treatment of chronic heart failure: an expert system advisor for general practitioners," *Acta Cardiol.*, vol. 45, no. 5, pp. 365–378, 1990.
[4] W. J. Long, "Temporal reasoning for diagnosis in a causal probabilistic knowledge base," *Art. Int. in Med.*, vol. 8, pp. 193–215, 1996.
[5] F. Atienza, N. Martinez-Alzamora, J. D. Velasco, S. Dreiseitl, and L. Ohno-Machado, "Risk stratification in heart failure using artificial neural network," in *AMIA Annual Symp Proc.*, 2000, pp. 32–36.
[6] HEARTFAID, "A knowledge based platform of services for supporting medical-clinical management of the heart failure within the elderly population," Official Project Site, 2009, http://www.heartfaid.org/.
[7] S. Colantonio et al., "Decision support and image & signal analysis in heart failure. a comprehensive use case." in *HEALTHINF Proc.*, 2008, pp. 288 – 295.
[8] W. Tierney et al., "Effects of computerized guidelines for managing heart disease in primary care," *J. Gen Intern Med*, vol. 18, no. 12, pp. 967–976, 2003.
[9] J. Kim et al., "A novel data mining approach to the identification of effective drugs combinations for targeted endpoint," *Cardiovascular Drugs Ther.*, vol. 18, no. 6, pp. 483–489, 2004.
[10] K. Dickstein et al., "ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure," *European Heart Journal*, vol. 29, pp. 2388–2442, 2008.
[11] J. F. Sowa, *Knowledge Representation*. Pacific Grove, CA, USA: Brooks Cole Publishing, 2000.
[12] R.M. Lang et al., "Recommendation for Chamber Quantification," *J Am Soc Echocardiogr*, vol. 18, pp. 1440–1463, 2005.
[13] J. Noble and D. Boukerroui, "Ultrasound image segmentation: a survey," *IEEE Trans. Med. Imag.*, vol. 25, pp. 987–1010, 2006.
[14] F. Chiarugi, V. Sakkalis, D. Emmanouilidou, T. Krontiris, M. Varanini, and I. Tollis, "Adaptive threshold QRS detector with best channel selection based on a noise rating system," in *Proc. of Computers in Cardiology*, vol. 34, 2007, pp. 157–160.
[15] F. Chiarugi, D. Emmanouilidou, I. Tsamardinos and I. Tollis, "Morphological classification of heartbeats using similarity features and a two-phase decision tree," in *Proc. of Computers in Cardiology*, vol. 35, 2008, pp. 849–852.
[16] OWL, "http://www.w3.org/TR/owl-features/," , 2009.
[17] UMLS, "http://www.nlm.nih.gov/research/umls/," , 2009.
[18] SWRL, "http://www.w3.org/Submission/SWRL/," , 2009.
[19] B. MacBride, "Jena: Implementing the RDF model and syntax specification," in *WWW2001, Semantic Web Workshop*, 2001.
[20] SPARQL, "http://www.w3.org/TR/rdf-sparql-query/," , 2009.
[21] Bossam, "http://bossam.wordpress.com/," , 2009.
[22] Pellet, "http://pellet.owldl.com/," , 2009.
[23] MIT-BIH Arrhytmhmia Database, "http://www.physionet.org/physiobank/database/mitdb/," , 2009.