



## Decision support in heart failure through processing of electro- and echocardiograms

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### ABSTRACT

**Objective:** Signal and imaging investigations are currently key components in the diagnosis, prognosis and follow up of heart diseases. Nowadays, the need for more efficient, cost-effective and personalised care has led to a renaissance of clinical decision support systems (CDSSs). The purpose of this paper is to present an effective way of achieving a high-level integration of signal and image processing methods in the general process of care, by means of a clinical decision support system, and to discuss the advantages of such an approach. From the wide range of heart diseases, heart failure, whose complexity best highlights the benefits of this integration, has been selected.

**Methods:** After an analysis of users' needs and expectations, significant and suitably designed image and signal processing algorithms are introduced to objectively and reliably evaluate important features involved in decisional problems in the heart failure domain. Then, a CDSS is conceived so as to combine the domain knowledge with advanced analytical tools for data processing. In particular, the relevant and significant medical knowledge and experts' knowhow are formalised according to an ontological formalism, suitably augmented with a base of rules for inferential reasoning.

**Results:** The proposed methods were tested and evaluated in the daily practice of the physicians operating at the Department of Cardiology, University Magna Graecia, Catanzaro, Italy, on a population of 79 patients. Different scenarios, involving decisional problems based on the analysis of biomedical signals and images, were considered. In these scenarios, after some training and 3 months of use, the CDSS was able to provide important and useful suggestions in routine workflows, by integrating the clinical parameters computed through the developed methods for echocardiographic image segmentation and the algorithms for electrocardiography processing.

**Conclusions:** The CDSS allows the integration of signal and image processing algorithms into the general process of care. Feedback from end-users has been positive.

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### 1. Introduction

Signal and imaging investigations are currently a basic component of the diagnostic, prognostic and follow-up processes. Current advances in diagnostic examination technologies and enhancement of the different modalities have made it possible to obtain high-resolution images and signals that are able to provide more and more precise information regarding body structure and function. These extraordinary accomplishments have provided clinicians

with the possibility to make more accurate and efficient diagnoses, often in a non-invasive way. It is no coincidence that, during the last decades, the development of automatic or semi-automatic processing methods has attracted a great deal of interest and effort in the areas of medical imaging, diagnostic radiology and electrocardiography [1], in some cases reaching the level of a practical clinical approach. The main aim is to provide a *second opinion* or a *second reader* that can assist clinicians by improving the accuracy and consistency of signal and image based diagnoses [2].

In practice, the clinical interpretation of diagnostic data largely depends on the reader's subjective point of view, knowledge and experience. If computer-aided methods are able to make this interpretation reproducible and consistent, they could be fundamental in diagnosis, reducing subjectivity while increasing accuracy. The presence of structure noise, or the vast amount of data generated by some devices, can make the detection of

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potential diseases a burdensome task and can limit the reader's ability in data interpretation. For these reasons, computerised data processing methods are likely to become an essential component of applications designed to support physicians' decision making in their clinical workflow.

Diagnostic data interpretation can be considered as one of the fundamental steps in the routine procedures followed by clinical professionals when providing personalised medical regimens. The quantity and complexity of data and information to be analysed and managed for this task is one of the reasons behind the renaissance of *clinical decision support systems* (CDSSs), whose development, although a long-standing quest (started more than 45 years ago in the early 1960s), is experiencing a period of rapid expansion in knowledge [3]. CDSSs can cope with the increasing bulk of clinical data by providing an integrated approach to analysis; in addition, they may foster adherence to guidelines, prevent omissions and disseminate up-to-date specialist knowledge to general practitioners.

This being the general setting, the purpose of this paper is to address the integration of signal and imaging investigations with the wide-ranging services provided by CDSS. Signal and image processing methods may be understood and embedded as a part of a *model base* of the CDSS. In such a way, it is possible to achieve an effective high-level integration of signal and image processing methods into the general process of care.

With the aim of avoiding unnecessary generality, this paper addresses the specific, yet complex and paradigmatic example of image and signal processing for decision support in *heart failure* (HF). HF is a clinical syndrome, whose management requires – from the basic diagnostic workup – the involvement of several stakeholders and the exploitation of various imaging and non-imaging diagnostic resources. Indeed, given the complexity of the management of chronic HF patients, several attempts to address the problem have been made in various research projects and have resulted in the development of dedicated information technology solutions, such as automated guidelines systems [4], decision support systems [5], or machine learning methods for automated HF diagnosis [6] or prognosis [7]. More recently, the European project “A knowledge based platform of services for supporting medical-clinical management of the heart failure within the elderly population” (HEARTFAID) [8] aims at defining efficient and effective health care delivery organisation and management models for the optimal management of care in the chronic HF

domain. The HEARTFAID platform has been conceived as an integrated and interoperable system, able to guarantee an umbrella of services ranging from the acquisition and management of raw data to the provision of effective decisional support to clinicians [9,10]. 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, innovative methods for diagnostic image analysis, and robust and high-performance algorithms for signal processing.

## 2. Background

### 2.1. 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 [11]. It usually manifests itself via fluid congestion or inadequate blood flow to tissues and progresses to underlying heart injury or inappropriate responses of the body to heart impairment. Unfortunately, HF is a progressive disorder that must be managed with regard, not only to the state of the heart, but also to 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 in terms of prevalence and morbidity, especially in the developed western countries [12], with a strong impact in terms of social and economic effects. All these aspects are typically emphasised within the elderly population, with very frequent hospital admissions and a significant increase of medical costs [13].

The first, immediate and enlightening proof of the relevance of biomedical image and signal investigations in HF is represented by its *diagnostic workup*, which can be considered as the first stage of management of HF patients. Fig. 1 shows the sequence of steps that composes the HF diagnostic workflow [11]: after having assessed the presence of main signs and symptoms, physicians usually require diagnostic examinations such as *electrocardiogram* (ECG), chest X-ray and neuroendocrine evaluations (i.e. *brain natriuretic peptides* (BNP)), in order to arrive at the diagnosis, which is eventually confirmed by an echocardiographic investigation. Supporting such a decision process requires encoding the workflow into an appropriate *knowledge base* (KB), which formalises, for

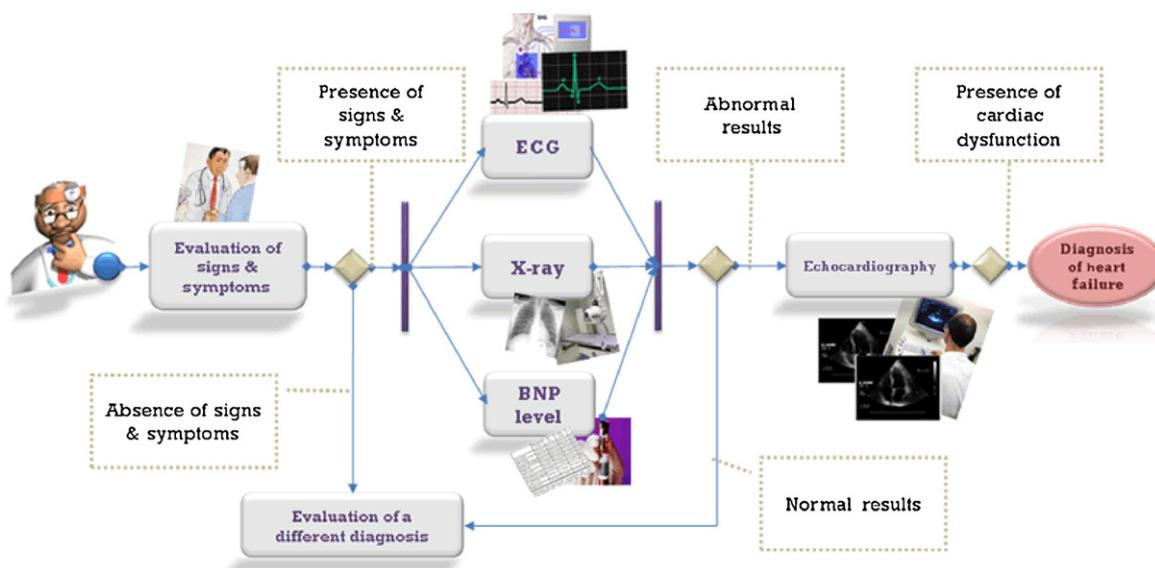


Fig. 1. HF diagnostic workflow.

each step, the set of conditions evaluated by physicians. The first step concerns the presence and severity of signs and symptoms such as breathlessness, swelling, fatigue, hepatomegaly and elevated jugular venous pressure. Then, ECG signals are acquired for investigating the presence of anterior Q waves and left bundle branch block, signs of left atrial overload or left ventricular hypertrophy, atrial fibrillation or flutter, and ventricular arrhythmia. If ECG abnormalities are present, a tentative diagnosis of HF diagnosis is made [14] and is further investigated by analysis of the chest X-ray.

The latter examination is useful for detecting the presence of cardiac enlargement and pulmonary congestion [15]. In the meantime, a laboratory analysis of neuroendocrine function is performed to test for high levels of BNP, which would suggest the presence of cardiac disease [16]. Whether or not all these examinations confirm the presence of abnormalities, an echocardiographic investigation is performed for the documentation of any cardiac dysfunction. The most important parameter to be evaluated from such a diagnostic modality is the *left ventricular (LV) ejection fraction (EF)*, together with other relevant data regarding chamber dimensions, wall thickening and motion, systolic and diastolic function, valvular regurgitation, and pulmonary blood pressure [17]. The diagnosis of HF is finally confirmed if symptoms and signs and ECG/X-ray/BNP level/echocardiographic abnormalities are all present.

## 2.2. Significance of signal and image processing methods

Imaging techniques offer invaluable aid in the objective documentation of cardiac function and, as mentioned in Section 2.1, chest X-ray and echocardiography have to be included in the HF initial diagnostic workup. Further, echocardiography is regularly repeated to monitor the changes in the clinical course of an HF patient in an objective way. Additional techniques, such as nuclear imaging and cardiac magnetic resonance, may also be considered for specific patients, since they have not been shown to be superior to echocardiography in the management of most of the HF population [11]. Thus, echocardiography – and in particular 2D *transthoracic echocardiography* (TTE) for its non-invasiveness and versatility – is the key imaging technique for the practical management of HF.

On the other hand, the ECG is recognised as the most fundamental examination performed in the evaluation and assessment of several heart abnormalities, including HF. A typical ECG tracing of a cardiac cycle consists of a P wave, a QRS complex (*structure on the ECG that corresponds to the depolarisation of the ventricle and is composed of the Q, R and S waves*) and a T wave. According to [18], the negative predictive value of a normal ECG in excluding 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 heart rate variability, the former is more commonly used for the evaluation of morphological abnormalities in the heartbeat.

In the context of this paper, TTE and ECG processing methods may allow for the automatic or semi-automatic computation of clinical parameters relevant to decisional problems in the HF domain, thus providing reproducible and reliable numerical values and reducing intra- and inter-observer variability. Other significant and advanced image and signal processing applications that may aid physicians in facing critical cases or critical problems can be envisaged, including (i) the support of physicians' case-based reasoning processes and (ii) the discovery of novel pertinent knowledge. In fact, not only are the parameters derived from TTE and ECG examinations significant to physicians in formulating a response, but also the data themselves can be useful in giving a

general overview of a patient's condition. This means that allowing clinicians to explore data could ensure the availability of many other items of information hidden in the same data. Moreover, when dealing with a difficult case, comparing the one at hand with assessed responses for other patients' situations can be extremely helpful. This entails maintaining and making available a database of cases with annotated images and signals that can be retrieved by similarity based on a set of computed features. Difficult diagnoses and, most of all, prognosis assessment are examples of these situations. For such critical problems, data processing facilities can have further relevance for the discovery of novel knowledge by granting the computation of a wide range of parameters that can be explored and correlated in order to find out new relevant patterns.

Finally, opportune knowledge formalisation may be helpful in personalising diagnostic imaging and non-imaging investigations. This means that adequate conditions could be encoded within the CDSS in order to suggest which kind of parameters could be more usefully evaluated for a given patient during, for instance, a TTE or an ECG session.

## 2.3. Decision support in HF

Recent studies and experience 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 [19,20]. Routine practice in HF cases presents several aspects on which automatic, computer-based support could have a favourable impact. A careful investigation of the needs of HF practitioners and the effective benefits assured by decision support was performed, and four problems were identified as highly beneficial for CDSS point-of-care intervention [10]. They can be described as macro-domain problems and listed as: (i) HF diagnosis, (ii) prognosis, (iii) therapy planning, and (iv) follow up. Further detailed decision problems have been identified for specifying these macro-domains, focusing as much as possible on the medical users' needs; indicative examples are:

- Evaluation of HF severity;
- Identification of suitable pathways;
- Planning of adequate, patient-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 problem has been to provide clinicians with advice, suggestions and alerts in the different phases of management of chronic HF patients, without altering their normal activities. One imperative requirement was to tailor the process to the routine workflow of medical professionals. This means that the CDSS must be designed to be appropriately active and accessible, so as to require neither too much learning nor significant changes in clinicians' routine activities, while meeting their needs as far as possible. A strong cooperation with medical practitioners has been profitable for understanding their expectations as to how the CDSS could support their activities. In practice, the implementation of the CDSS has been mainly focused on the incorporation of high-quality, evidence-based medical knowledge, suitably formalised and incorporated in automated reasoning processes in order to obtain diagnostic, prognostic and therapeutic conclusions that can be supplied to clinicians. A symbolic approach has been selected as the knowledge representation method, and – among the different solutions available (most of which refer to logic for a formal semantics [21]) – a hybrid solution based on the use of *formal ontologies* and *rules* has appeared to be the most promising. Indeed, ontologies appeared in artificial intelligence as computational

artefacts used for building conceptual models of a domain of discourse [22]. They can come in different forms with increasing levels of complexity, ranging from simple catalogues of terms, to thesauri, to complex models with logical constraints that allow automated reasoning. In the latter case, an ontological model is developed according to the *description logics* theory [23] and hence consists of concepts, individuals and their properties and relations. Despite their advantages, ontologies present some limits and deficiencies, owing to their foundation in descriptive logics (e.g. complex or derived relations cannot be induced from an ontological artefact). A *rule-based* formalism has been employed for filling these gaps, and for encoding procedural knowledge, i.e. not only declarative information about the existence of domain concepts but also actions to be performed when specific conditions are met.

### 3. Methods

The provision of decision support in heart failure through processing of electro- and echocardiograms is necessarily based on the confluence of several areas of expertise to solve a common goal. For the purposes of this paper, however, the focus is more on the overall decision systems, thus avoiding too technical a treatment of signal and image processing issues. To this end, the methods developed for the segmentation of echocardiographic image sequences and algorithms for electrocardiogram processing (including heartbeat detection and morphological classification, and dominant beat averaging) will be described only briefly, with emphasis on their importance in decisional problems in HF. Then, the methodologies used for the design and realisation of the clinical decision support system will be discussed.

#### 3.1. Methods for image processing

Since TTE is the key imaging modality for the management of HF patients, a careful analysis of this modality was carried out in cooperation with medical partners. It was concluded that the development of assisted segmentation methods, able to deal with echocardiographic image sequences, could represent a valid form of support to the physicians in the process of image report formation. Indeed, assisted segmentation methods may render the estimation of LV EF more reproducible. LV EF, the most important measurement performed by TTE, permits patients with cardiac systolic dysfunction to be distinguished from those with preserved systolic function. It is defined as the normalised (non-dimensional) difference between LV *end-diastolic volume* (EDV) and *end-systolic volume* (ESV):

$$LVEF = \frac{EDV - ESV}{EDV} \quad (1)$$

Among different models for the computation of such volumes, the “*American Society of Echocardiography*” [24] suggests the use of the so-called Simpson’s rule, in which the LV is approximated by a stack of circular (or elliptical) disks whose centres lie on the major axis. The border of the LV cavity is needed in order to estimate 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 high, since the anatomical structures of interest may often not be easily distinguishable as a result of intrinsic limitations of the modality. Further, any error in the estimation of EDV and ESV is propagated in the calculation of the value of LV EF by formula 1; for these reasons manual contour tracing is unable to provide a satisfactory and reproducible measurement of LV EF. Image processing techniques may reduce the variability of human interventions in border tracing by

providing automated or, at least, semi-automated methods for tracing contours of the relevant structures found in an image. However, the segmentation problem for ultrasound images is by no means trivial, given the low signal-to-noise ratio, low contrast, image anisotropy and speckle noise [25]. From these considerations, it was judged important to develop a prototypical toolkit – composed of three main modules – for the analysis of apical-view sequences and the estimation of LV EF.

The first module (*region identification*), which takes in input an apical sequence of the heart, is able to identify the left ventricular 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 as input an image and a rough segmentation of it, is able to refine the segmentation by exploiting the variational formulation described in [26] of level set methods [27,28], which achieves regularisation 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 toolkit is flexible enough to support different operational scenarios, offering a variable level of automaticity. The following operational scenarios may be envisaged:

- Manual selection of the end-diastolic and end-systolic frames and rough manual contour tracing. In this case, the toolkit provides a refinement of the manually traced left ventricle contour in the manually selected frames. Instead of using the common freehand selection, the user may just quickly select a polygonal region approximating the LV cavity. The *segmentation refinement* module is then triggered. In brief, the manually drawn contour is used for the initialisation of the level set method. Finally, the third module is used for feature extraction.
- Manual selection of the end-diastolic and end-systolic frames and automatic contour tracing. In this case, the toolkit traces the contour of the LV automatically in the manually selected frames. The *region identification* module is used to find an approximate LV contour. Then the contour is refined by the level set segmentation step as in (a).
- Automatic selection of the end-diastolic and end-systolic frames and automatic contour tracing. This is the most automatic way to use the developed algorithms; the workflow is schematically represented in Fig. 2. The toolkit takes the entire image sequence as input and applies the *region identification* module to every frame in order to obtain a rough segmentation of the LV. Then the volume of the cavity is computed on this rough segmentation by using the *feature extraction* module. The indices of the frames corresponding to the extreme values (i.e. maximum and minimum) of the volume are found and stored. Then, the *segmentation refinement* is applied to the contours in the frames which are near to those with extreme values. Computing volumes on the basis of the refined contours by the *feature extraction* module again leads to the identification of the end-systolic and end-diastolic frames and to the computation of related clinical parameters.

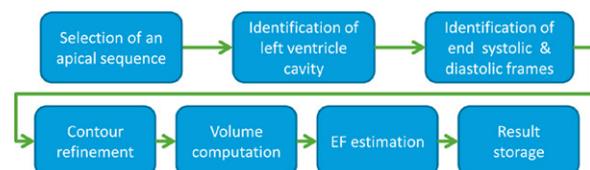


Fig. 2. Sketch of the workflow in the operational scenario (c) of Section 3.1.

Each of the image processing modules developed was tested on 2D image sequences recorded from the apical window (2-chamber and 4-chamber views). The echocardiographic device was *General Electric Vivid 7*. The dataset, provided by the *Department of Cardiology, University Magna Graecia, Catanzaro, Italy*, consisted of image sequences acquired at the rate of 25 frames per second. Three full cardiac cycles were imaged for each patient. Given the interactive nature of the methods provided, validation of the segmentation quality was performed by expert users using visual inspection. In the limited number of cases in which fully automatic segmentation, as described in case (c) above, was not satisfactory, optimal segmentation was achieved with minimal interaction using the two assisted procedures described in (a) and (b).

### 3.2. Signal processing methods

Considering the crucial role of ECG signals and the various related examinations, it was clearly important to design and implement some *basic, robust* and *scalable* algorithms for ECG processing that could be applied to raw data acquired by devices for different ECG examinations, with different numbers of leads and acquisition durations. After some interviews with the clinicians, a standard procedure was devised, involving a non-interpretive electrocardiograph that acquires the resting ECG and transfers it to the hospital gateway, where the ECG is processed in order to perform:

- QRS detection;
- Morphological classification of heartbeats;
- Evaluation of the averaged dominant beat.

In fact, in the very large majority of cases, the averaged dominant beat can be used by the cardiologists for the evaluation of all the measurements of interest relating to the diagnosis or the follow up of HF patients, such as ST (*the segment connecting the QRS complex with the T wave*) depression, QRS and QT (*interval from the beginning of the QRS complex to the end of the T wave*) durations, Sokolow-Lyon index for left ventricular hypertrophy, presence of left or right bundle branch block and presence of pathological Q waves. Observe that, since the average dominant beat has less noise than the original signal, performing measurements on this average beat leads to more accurate results, thus reducing inter- and intra-observer variability. The algorithms developed for ECG processing are briefly described below.

#### 3.2.1. QRS detection

The selected approach for QRS detection belongs to the time-domain techniques [29]. The first step consists in a signal pre-filtering using a moving-average linear filter in order to reduce the baseline wandering and the high-frequency noise and to select the typical frequencies contained in the QRS complexes. Then, a *QRS enhanced signal (QES)* is built as the sum of the absolute derivatives of each pre-filtered channel. The filter for the generation of the derivatives was chosen so as to reduce the effect of the residual noise. In practice a pass-band filter with a derivative behaviour in the band of interest was used. The beginning of a QRS is detected when the QES exceeds a suitable defined adaptive threshold and the QRS end is obtained when the QES becomes lower than the adaptive threshold for a defined number of consecutive samples. To avoid marking large-amplitude T-waves as other QRSs, the QRS detection threshold is artificially increased after a QRS peak is detected. Furthermore, a dead-time zone of 200 ms is set up in order to reject any QRS detection too close to the previous one. Using only the above algorithm, the QRS detection results are quite good, especially in recordings with low or medium noise content. However, when the noise in one or both channels is high, the performance of the detector is significantly reduced.

Therefore, a further technique was introduced in order to improve the detection performances when noise is present only in one channel. In particular, a *noise index (NI)* is associated with every detected QRS on the basis of the average power in the estimated T–P interval (*interval from the end of the T wave to the beginning of the P wave of the next heartbeat*) divided by the QRS average power. The NI can be used as an indicator of the noise in the two different channels and of the presence of noisy QRSs. The appearance of a number of consecutive noisy QRSs determines the beginning of a noisy interval, which ends once a few consecutive non-noisy QRSs appear. For each noisy interval the detection algorithm is also executed with the QES obtained using only one channel and a procedure for best channel selection can be obtained, leading to significant improvement of the overall detection performance.

#### 3.2.2. Morphological classification of heartbeats

A prerequisite for the construction of the average dominant beat is the morphological classification of each detected QRST (*the QRS complex with the following T wave*). In fact, it is necessary to avoid the introduction of extrasystoles or non-dominant beats in the averaging process, since they would alter the quality of the averaged beat. Normally, the evaluation of the heartbeat type is performed by considering its morphology and its occurrence compared to the previous and following beats (rhythm), but in this case the requirement is not to obtain a complete rhythm evaluation, but only to identify the morphologically dominant beat. For this reason, in the classification algorithm only the basic morphological parameters are taken into account, in an attempt to limit the complexity of such a system as far as possible.

The algorithm for the morphological classification of heartbeats is based on a two-phase decision tree [30]. In the first phase, a possible classification of all beats is performed, while in the second phase the classes created are re-estimated and, if necessary, redefined. In particular, the clusters containing a large number of non-dominant beats (according to the first stage) are split into smaller ones and reconsidered as having possibly been misclassified as non-dominant.

#### 3.2.3. Evaluation of the averaged dominant beat

For a proper averaging, some further processing is necessary in order to avoid distortions in the averaged beat. In fact, all the beats classified as dominant could be averaged in order to identify the centroid; however, beats with too much noise could corrupt the proper averaging and beats that are not properly aligned could cause artefacts in the averaged beat.

The list of dominant beats is analysed in order to exclude from each channel any incomplete beats (usually the first and the last of the recording) and beats with high noise immediately after or before the QRS occurrence. Finally, a set of good dominant beats is identified for each channel and the averaging is performed on this set.

The ECG processing algorithms have been tested on the publicly available annotated “MIT-BIH Arrhythmia Database” [31]. For QRS detection, a sensitivity of 99.76% and a positive predictive value of 99.81% have been obtained. Very satisfactory results have also been achieved for dominant class discrimination on all the annotated beats of the same database, with sensitivity 99.05% and specificity 93.94%. There was a slight reduction in performance for the detected beats obtained by the QRS detector described above, but the results are still very satisfactory, with sensitivity 98.71% and specificity 93.81%.

The algorithms were easily extended to the 12-lead resting ECG, producing even better results on a testing set provided by the *Department of Cardiology, University Magna Graecia, Catanzaro, Italy*, and consisting of 63 short-term 12-lead ECG files sampled at 500 Hz and acquired from HF patients.

**Table 1**  
A few of the elicited rules expressed in natural language.

|           | Rules in natural language   |
|-----------|---|
| Diagnosis | <i>If patient has systolic blood pressure &lt;85 mmHg or has systolic blood pressure &gt;140 mmHg or has fatigue and left ventricular ejection fraction &lt;45% then suggest diagnosis systolic heart failure</i><br><i>If patient's symptoms worsened and physical examination has no relevant results and blood pressure increased and heart rate increased then suggest an echocardiographic examination</i> |
| Follow-up | <i>If heart rate differs by 10% from the previous measurement then issue an alert</i><br><i>If left ventricular diastolic diameter decreased or stroke volume decreased or left ventricle ejection fraction decreased then patient's status worsens</i>   |
| Therapy   | <i>If patient has left ventricular ejection fraction ≤ 40% and is asymptomatic and is taking angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and had a myocardial infarction then suggest prescribing beta-blockers</i><br><i>If symptoms are worse and there is (pulmonary congestion or peripheral oedema) then suggest prescribing diuretics</i>                                   |

### 3.3. CDSS design

The CDSS was devised for processing information by exploiting the relevant medical knowledge elicited from medical experts, extracted from clinical guidelines, and suitably formalised for exploitation in reasoning processes.

During the encoding of this knowledge, particular emphasis was given to the diagnostic modalities in order to integrate the extracted parameters into the more general process of health care management.

The integration of signal and image processing methods into the management of care delivery contributed to identifying CDSS functionalities and modelling its architecture.

As shown in Table 1, the processing of electro- and echocardiograms functions in such a way as to provide suggestions: parameters extracted from diagnostic procedures, such as QRS and QT durations on the ECG or LV EF in echocardiography, are important for understanding if the patient's condition is deteriorating, and, at the same time, also form the basis of a proper therapy assignment.

This integration focused on two main issues:

1. Supplying relevant parameters to reasoning processes;
2. Personalising the diagnostic investigations by suggesting which parameters should be extracted.

The implications of these two issues can be best explained by the following example: while a patient's information is being processed with the goal of identifying causes of deterioration, the CDSS may need a number of routine parameters that are 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. On the other hand, it can happen that such routine parameters are not able to completely explain the patient's status; thus, the system can request other data that may shed light on the specific patient's condition.

The medico-clinical knowledge was formalised into a composite KB that consists of a suite of ontologies and a base of rules. Clinical guidelines [11] were used as a knowledge source and experts' know-how was elicited through several interviews. Fig. 3 shows the main structure of the CDSS, where a reasoner is capable of inferring from the ontologies and the base of rules.

The KB was structured modularly, in order to provide suggestions and to assist clinicians with classes of problems. To this end, a number of core ontologies, such as *Patient* and *Disease*, were introduced in order to organise minimal domain concepts. These were combined into upper ontologies, such as *TherapyAssignment* and *EchoFindingsInterpretation*, which are devoted to solving specific problems. In this way, the entire KB can be understood as a graph, with core and upper ontologies as vertices and their relationships as edges. Each problem is solved by reasoning on a specific sub-graph. The therapy assignment is the most complex problem, correspond-

ing to an upper ontology that includes almost all the other ontologies. All the core ontologies are light compositions of taxonomies of concepts (i.e. *dyspnoea*, *irregular\_heart\_rhythm*), sets of relationships among these (i.e. *hasSymptom*), and constraints (i.e. cardinality of severity class). In addition, the designed sets of ontologies are also associated with sets of forward chaining rules (see Table 1).

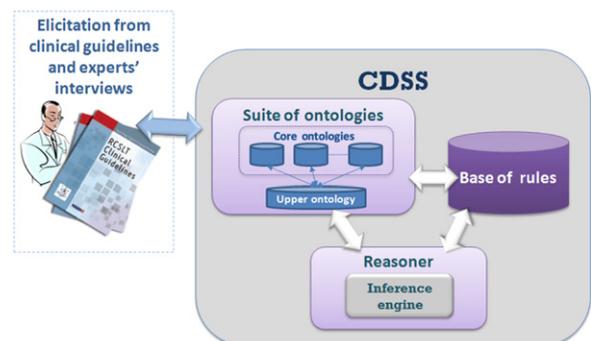
This approach was chosen because of its similarity to the one followed by clinicians in their daily practice, and also because the domain tends to be dynamic and the use of a modular approach makes it easier to handle changes. Moreover, in the attempt to obtain maximum flexibility, especially during the validation, inferences were performed on values not hard-coded in the ontologies. The main advantages of this design choice were that, since clinical guidelines may vary, it is simpler to change rules than it is to remodel a huge ontology without forward chaining rules and only based on constraints, and it is also easier to manage and maintain such "lighter" ontologies that can also be more easily combined into upper ontologies.

In order to maintain the focus on the actual routine activities of clinicians, a problem decomposition approach was then adopted, identifying the different CDSS interventions and the corresponding relevant fragments of knowledge, which were then structured appropriately. Some examples of actual problems identified as requiring CDSS assistance are the following:

*The CDSS detects the presence of signs and symptoms of a patient monitored at home, and suggests performing a diagnostic examination for checking out the causes.*

*A patient undergoes a TTE examination and the computed parameters are submitted to the CDSS, which estimates additional information, such as the pulmonary pressure, and accordingly suggests a change in therapy to the clinician.*

A comprehensive conceptual model was firstly devised for capturing all the relevant information, concepts and relations.



**Fig. 3.** The organisation of the knowledge base and the reasoning component of the CDSS.

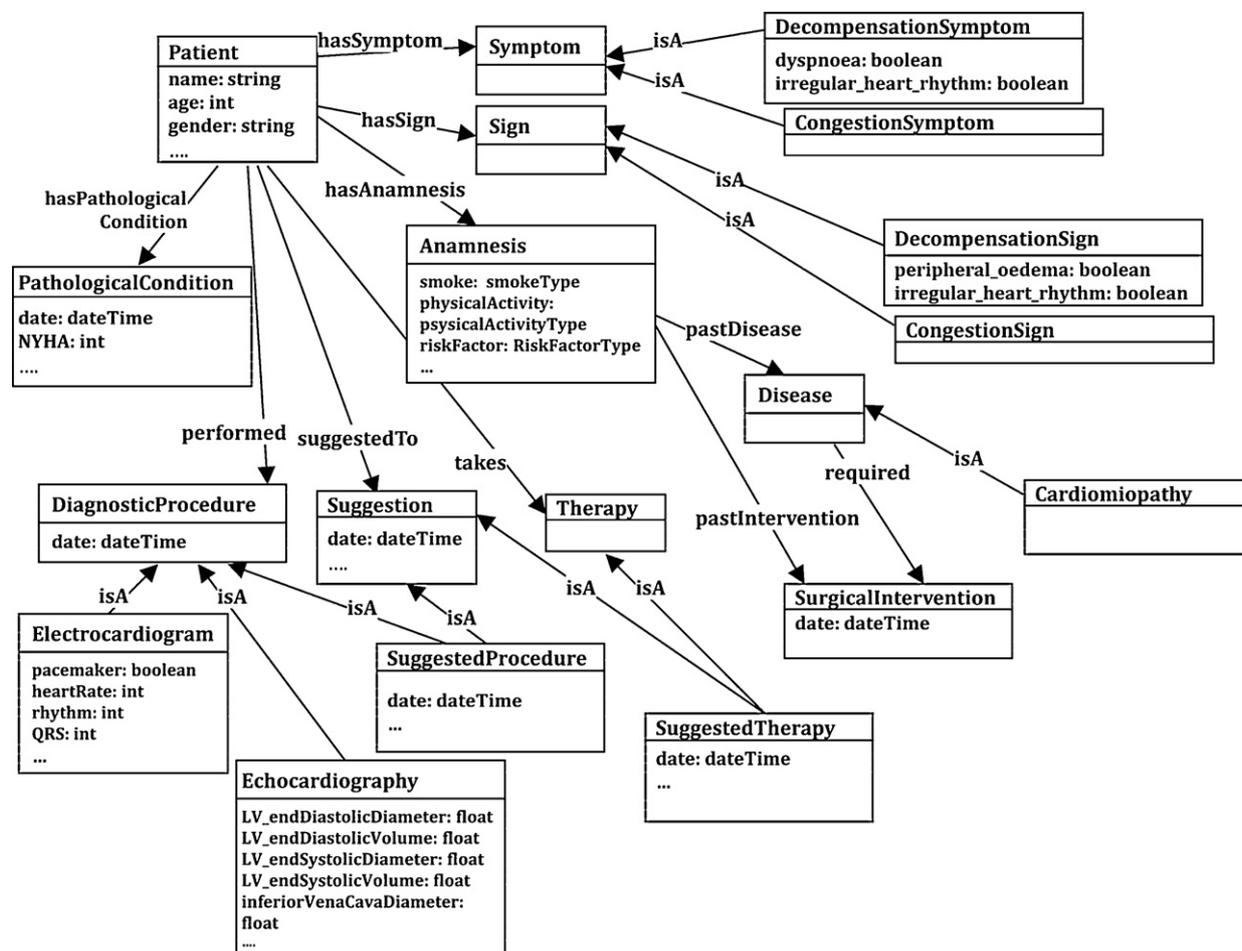


Fig. 4. An excerpt from the conceptual model used for building the ontology: boxes represent classes and contain their datatype properties, while relations among classes are represented by the arcs (arrows between two boxes).

Fig. 4 shows an excerpt from such a model. Some aspects are worthy of note: the class “*Suggestion*” was used for modelling the responses of the CDSS; the class “*PathologicalCondition*” was included for modelling the dynamic features of a patients’ condition (i.e. the New York Heart Association severity class).

Particular attention was paid to the diagnostic procedures and to the role signals and images have within the functioning of the CDSS. More precisely, all the parameters computed from the different modalities were extensively analysed and inserted into the conceptual model. They were modelled as *datatype properties* of each diagnostic procedure sub-class: some examples are *leftVentricle\_endSystolicVolume*, *systolicPulmonaryPressure\_estimated* and *leftVentricle\_ejectionFraction\_estimated* taking *float* values, or *leftVentricle\_ejectionFraction\_method* which takes values from the set {Teicholz, Simpson2CH, Simpson4CH, SimpsonBi-plane}. This choice is motivated by the foreseen use of these parameters in the rule base: some of the rules are structured for drawing conclusions according to particular values such parameters may take. Examples are given in Section 4.

Rules were formalised utilising the concepts specified in the ontologies. Again, guidelines and experts’ knowhow were used as knowledge sources.

#### 4. Results

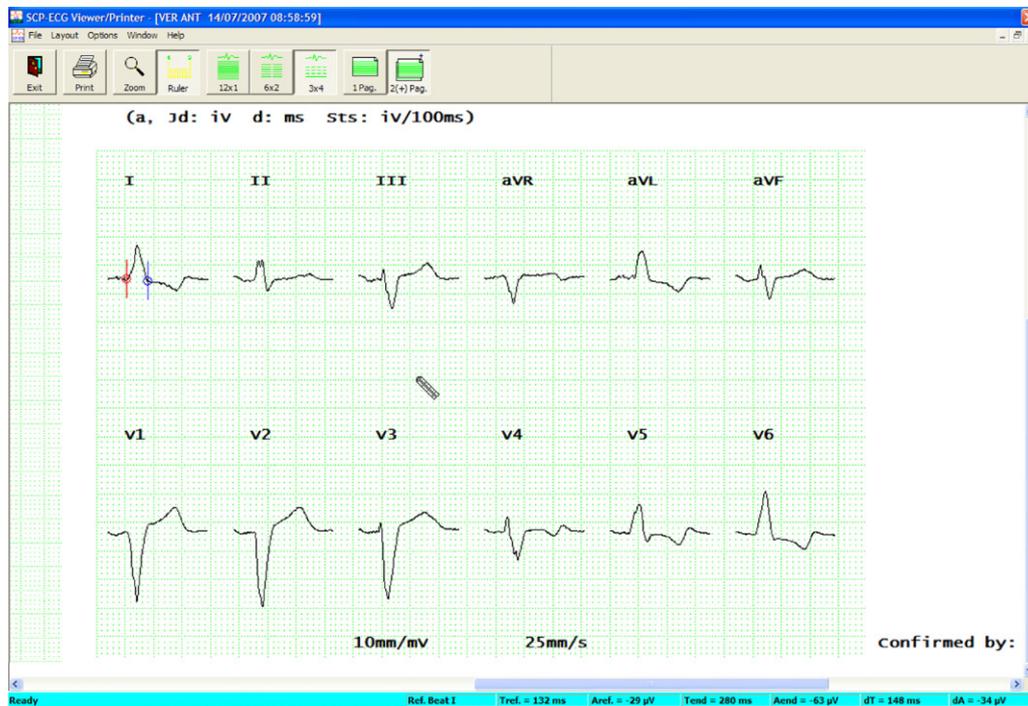
For the implementation of the CDSS, several tools were selected, also taking into account the *World Wide Web Consortium* (W3C) recommendations.

In particular, regarding the knowledge representation formalism, the *Web Ontology Language* (OWL) [32] – and specifically the *OWL Description Logic* (OWL DL) sublanguage – was selected for defining the ontologies, since it can be considered as the de facto standard semantic mark-up language for this task and it offers all the power and expressivity of *description logics*. Standard medical ontologies, such as *Unified Medical Language System* (UMLS) [33], were taken into account for selecting a commonly recognised and agreed terminology.

For realising the reasoning component, Jena [34] was preferred as a Java programming environment that includes OWL, a language for querying ontologies, i.e. [35], and a rule-based inference engine. In particular, for improving the reasoning capability of the latter, Pellet [36] was also used. For defining the rules, the *Semantic Web Rule Language* (SWRL) [37], combining OWL and rule mark-up language, was selected as suggested by the W3C for extending the set of OWL axioms to include Horn-like rules.

The implemented system was evaluated at the Department of Cardiology, University Magna Graecia, Catanzaro, Italy. Since heart failure in the elderly was the primary concern, participants in the study were 79 persons over 60 years old (age  $74.01 \pm 6.66$ ). In particular, 63 males (age  $71.74 \pm 5.33$  years) and 16 females (age  $82.93 \pm 2.59$  years) were included.

The system was tested in the daily practice of the physicians operating in the hospital, taking into account different scenarios in which decisional problems based on the analysis of biomedical signals and images were involved. One of these scenarios involved the HF diagnostic workup, which is discussed below in order to



**Fig. 5.** A screen of the ECG viewer displaying (in zoom mode) the automatically computed averaged dominant beat: the calliper (ruler) is active and is being used to measure the QRS duration.

describe the functional features of the developed system and to show the results achieved (a 70-year-old male patient is considered for illustrative purposes).

In this scenario, a clinician performs a clinical assessment when the patient visits the hospital and verifies the presence of signs and symptoms. The clinician then fills in a form on the web site and, on the basis of the presence or the worsening of signs or symptoms, an ECG is suggested by the CDSS: in this example, dyspnoea, peripheral oedema and heart rate are worsened; the CDSS then suggests that an ECG should be recorded.

The clinician can decide whether to perform an ECG or not. Supposing he decides to perform an ECG, the physician may use the tools provided for ECG processing. In particular, once the recorded data have been provided to the CDSS, the average dominant beat is automatically computed and, using a graphical interface, the clinician may perform measurements on this beat, which is cleaner and less affected by noise. On the basis of the computed values, entered in a suitable format, the system may propose a list of further investigations. Specifically, for example, if the value of the QRS complex duration is greater than or equal to 120 ms, then there is a bundle branch block and the CDSS suggests performing other checks. For example, the same suggestion is also given when the *interval between the onset of the P wave (atrial depolarisation) and the QRS complex (ventricular depolarisation)* (P–R interval) is greater than 200 ms (presence of a first degree atrioventricular block) and when parameters are increased with respect to their previous borderline or abnormal values. The list of further investigations includes laboratory analysis and, in particular, the evaluation of BNP levels, which may be performed by commercially available assays. Indeed, BNP assessment works extremely well in ruling out the presence of HF [11], since its negative predictive accuracy is 97%.

After the results of lab analysis are ready, the system checks the value of BNP based on the adaptive thresholds, depending on age and gender [38], that have been suitably encoded in the KB. If the BNP level is low, the diagnosis of HF should be carefully revised.

Otherwise, the CDSS, integrating the evidence gathered by the ECG examination and the lab analysis, suggests performing an echocardiographic examination.

In the particular case, where the ECG reported a QRS of 150 ms (as shown in Fig. 5), the CDSS suggested performing an echocardiography.

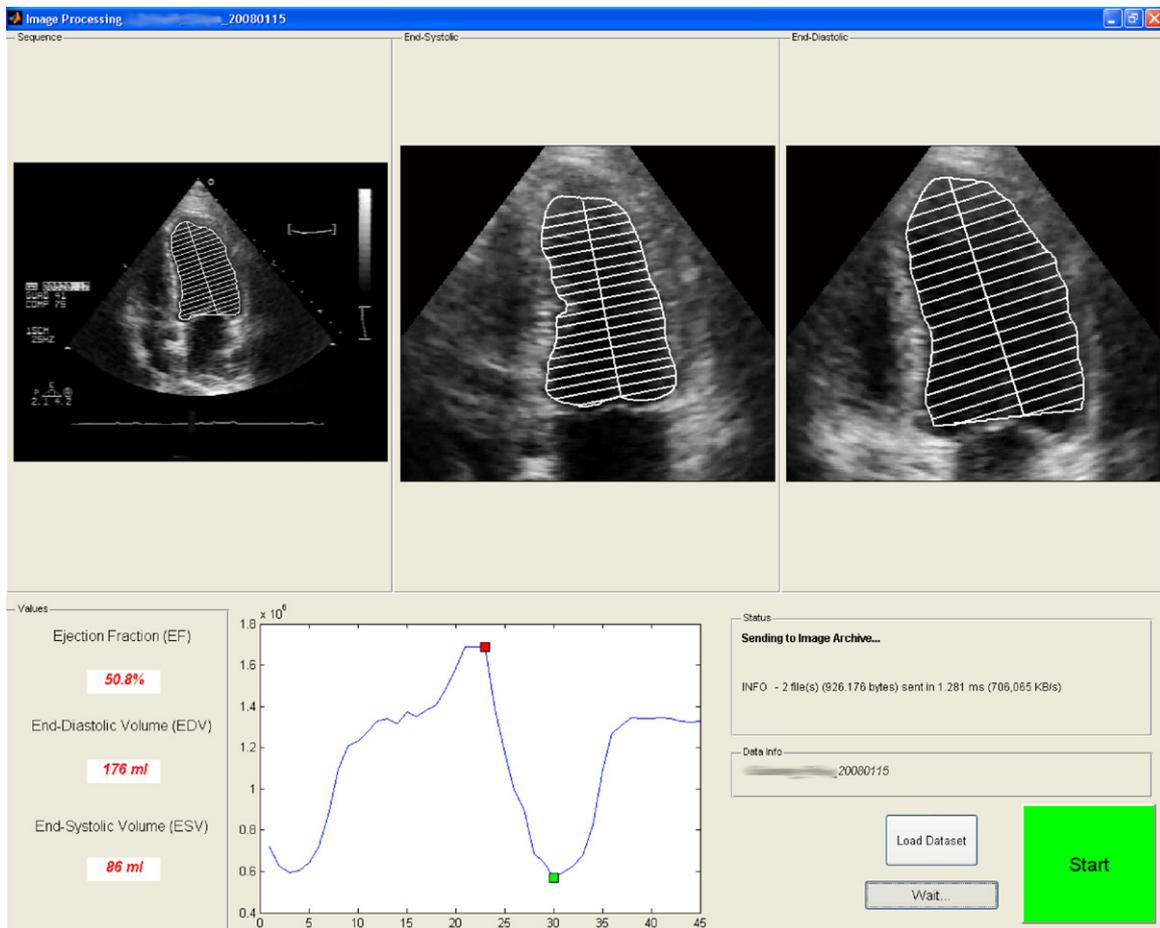
If the clinician decides to follow the suggestion, he orders an echocardiographic examination for his patient using a dedicated web form. On the specified date, a sonographer performs the echocardiography and data, images and extracted parameters are stored in dedicated archives. The over-reading clinician may then review the acquired images and image sequences and he may trigger the algorithms for image processing, using a graphical interface (see Fig. 6). Once having computed the LV volumes and the LV EF and having approved the results, the clinician sends the parameters to the CDSS. By integrating all the relevant data about the patient, the CDSS determines whether there is heart failure and, if so, whether it is systolic or diastolic.

Specifically, these are some examples of the rules the CDSS takes into account. First, some rules evaluate the filling pattern on the base of allowable parameters. Among these, some parameters need to be extracted from echocardiography, such as the ratio of early to late diastolic filling velocities. Other rules evaluate if there is presence of HF or not and, in the positive case, classify it as systolic or diastolic HF. Examples, in natural language, of implemented rules are:

*If patient has signs or symptoms and has an altered filling pattern and has not pulmonary pathologies and has a left ventricular ejection fraction greater than 40, then he has diastolic heart failure.*

*If patient has a left ventricular ejection fraction less than or equal to 40 and has signs or symptoms then he has systolic heart failure.*

In the particular case, the CDSS provided quantitative post-processed parameters, namely the systolic pulmonary pressure, Teicholz EF and Simpson's EF estimations. Moreover, it suggested a



**Fig. 6.** The graphical user interface for the analysis of echocardiographic sequences, running in the mode described in the operational scenario (c) of Section 3.1 (in the upper left panel the results of the *region identification* module are shown, while in the upper middle and right panels the results of the *segmentation refinement* module are presented in the end-systole and end-diastole frames, respectively).

diagnosis of an altered filling pattern, a preserved EF, and a normal estimation of pulmonary hypertension.

At any moment during this process, the clinician can see all the information concerning a patient; moreover, all the suggestions of the CDSS are also shown contextually. In order to improve the situation of the patient at the end of the clinical assessment, the clinician in general assigns the patient to a new or revised therapy.

## 5. Discussion

Besides the correctness of the suggestions provided, the impact of the clinical decision support system on routine workflows was carefully taken into account, since this factor is deemed to be essential for the success of the system. This preliminary evaluation was carried out at the Department of Cardiology, University Magna Graecia, Catanzaro, Italy in the framework of a clinical study, supported by the system, using a significant number of heart failure patients (79 persons over 60 years old). During this study several interviews were performed with the clinical partners at different times (shortly after the introduction of the system and after 3 months) in order to evaluate the performance of the CDSS and its impact on the routine workflow.

The system was perceived as non-invasive from its introduction, although some training was necessary to let the medical personnel become acquainted with the web interfaces provided. Suggestions were judged to be correct from the beginning, but only after 3 months of use, during which they prevented omissions and assignment of suboptimal therapy, were they considered useful.

The substantially positive results of this preliminary evaluation were very encouraging and showed that, at least in the real setting of the selected validation site, the system contributed to a better delivery of care, thus suggesting the CDSS is ready for a more extensive phase of qualitative and quantitative evaluation before its definite release to be used by clinicians in their daily routine.

## 6. Conclusions

In this paper a CDSS for the management of HF has been presented. The wide range of services provided by the CDSS is enabled by a high-level integration of diagnostic signal and image processing. In particular, the choices made in designing suitable image and signal processing algorithms have been analysed and it has been shown how the algorithm results can be deployed by the CDSS in decisional problems and hence in the global process of care.

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. A modular organisation of the KB was maintained in order to ensure its flexibility, efficiency and upgradability.

The functioning of the CDSS and the effectiveness of its responses, as well as the efficiency of the signal and image processing methods, were analysed and evaluated by clinical experts during the development activities. The feedback obtained so far from clinicians has been encouraging. However, while building the KB, some

considerations about possible improvements emerged, such as the possibility of managing uncertainty and fuzzy conclusions.

Moreover, in the future, the methods developed for ECG and TTE processing will be extended so as to permit the computation of a richer set of clinical parameters (e.g. relative to heart chamber motion and synchronisation). Introduction of *computational reasoning* methods (as opposed to the *inferential reasoning* considered in this paper) will be taken into account to compensate for the lack of established rules for exploiting such richer parameter sets.

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