Selection and collection of multi parameter physiological data for cardiac rhythm diagnostic algorithm development

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Selection and collection of multi parameter physiological data for cardiac rhythm diagnostic algorithm development

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Abstract. Automated diagnostic algorithms are used in implantable cardioverter-defibrillators (ICD’s) to detect abnormal heart rhythms. Algorithms misdiagnose and improved specificity is needed to prevent inappropriate therapy. Knowledge engineering (KE) and artificial intelligence (AI) could improve this. A pilot study of KE was performed with artificial neural network (ANN) as AI system. A case note review analysed arrhythmic events stored in patients ICD memory. 13.2% patients received inappropriate therapy. The best ICD algorithm had sensitivity 1.00, specificity 0.69 (p<0.001 different to gold standard). A subset of data was used to train and test an ANN. A feed-forward, back-propagation network with 7 inputs, a 4 node hidden layer and 1 output had sensitivity 1.00, specificity 0.71 (p<0.001). A prospective study was performed using KE to list arrhythmias, factors and indicators for which measurable parameters were evaluated and results reviewed by a domain expert. Waveforms from electrodes in the heart and thoracic bio-impedance; temperature and motion data were collected from 65 patients during cardiac electrophysiological studies. 5 incomplete datasets were due to technical failures. We concluded that KE successfully guided selection of parameters and ANN produced a usable system and that complex data collection carries greater risk of technical failure, leading to data loss.

1. Background
Automated cardiac rhythm analysis is the most widely used computerised decision support in medicine [1]. It is incorporated in a variety of medical equipment, including implantable cardiac rhythm control devices, such as pacemakers and cardioverter-defibrillators (ICD’s).

ICD’s are implanted under the skin and connected to the heart by electrodes threaded through veins and lodged inside the heart chambers (figure 1). ICD’s sense electrical activity of the heart (intracardiac electrograms), apply a rhythm diagnostic algorithm and may deliver pacemaker pulses or electric shock therapies to the heart to correct rhythm abnormality (arrhythmia).

Current ICD algorithms over-prescribe, on the presumption that therapy delivery is preferable to it being withheld; therefore, “inappropriate” shock therapy may be received when not clinically indicated. Misdiagnosis is the commonest cause and inappropriate shocks are received by 15 to 20% of ICD recipients [3]. Current algorithms achieve sensitivities approaching 1 at the expense of lower specificities, varying from 0.6 to 0.99 [2]. Improvements to specificity are needed to reduce false-positive rates and inappropriate therapy.
2. Introduction
Manufacturers use signal processing techniques to improve ICD algorithm accuracy [4]; artificial intelligence (AI) shows promise [5] [6] but has not been incorporated, having poor physician acceptance, presumed due to mistrust of computer based decision making [7], as well as constraints of processing power and time-delays inherent in AI processes.

It has been suggested that additional physiological parameters could improve diagnostic accuracy [8]. ICD systems all incorporate an accelerometer to detect patient activity, some have bio-impedance measurement [9] [10] and some investigational devices have multi-parameter sensors [11].

Knowledge engineering (KE) involves processing knowledge in computers to solve problems that normally require a human expert [12] and is under-used in this field other than some research in ECG interpretation [14]. KE has three principal stages [13]: knowledge acquisition, knowledge representation and implementation. The aim of this study was to evaluate KE in selection and collection of physiological data, to generate datasets for use as training and test sets for cardiac rhythm diagnostic algorithm development using AI.

3. Methods
A pilot study was conducted using KE and AI to develop a prototype algorithm [15]. Evaluation of candidate AI techniques identified artificial neural network (ANN) as a good classifier, suited to diagnostic applications, so ANN was chosen as the AI methodology.

An ethically approved review of case notes of patients with an ICD implant at St. Thomas’ Hospital, London provided detail from arrhythmic events stored in ICD memory (figure 2).

Figure 1. A chest X-ray image showing an ICD in the upper left chest and an electrode with its tip in the right ventricle of the heart.

Figure 2. Detail of an arrhythmic event from an ICD, showing diagnosis of ventricular tachycardia (VT) followed by “burst” pacing therapy and termination of the arrhythmia (arrowed).
For each event, ICD algorithm output (diagnosis) was compared to “gold standard” validated domain expert diagnosis to assess accuracy. Statistical analysis used 2 x 2 contingency tables and chi-squared test at a 95% level of significance.

A subset of “unique” arrhythmic events was selected. Using KE, 7 parameters were selected as ANN inputs and the datasets manually re-analysed. The subset was encoded, without using formal language, using the following rules: numeric value (for time-series data, sequence was maintained) and parameters not easily measured or unchanging were allocated a binary (0 or 1 representing presence or absence) or integer value (scaled to represent degree of severity), as shown in table 1.

Table 1. Parameters Selected for ANN Inputs.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Ventricular interval change at onset of arrhythmia</td>
<td>(Value)%</td>
</tr>
<tr>
<td>Stability</td>
<td>Ventricular interval stability in arrhythmia</td>
<td>(Value)%</td>
</tr>
<tr>
<td>A:V</td>
<td>Atrial : ventricular electrogram ratio</td>
<td>(Value)</td>
</tr>
<tr>
<td>HR&gt;100</td>
<td>Heart rate during arrhythmia &gt;100 beats per minute</td>
<td>(0 or 1)</td>
</tr>
<tr>
<td>V First</td>
<td>Initial electrogram in arrhythmia was ventricular</td>
<td>(0 or 1)</td>
</tr>
<tr>
<td>Morph</td>
<td>Morphological difference normal vs. arrhythmia</td>
<td>(Value)</td>
</tr>
<tr>
<td>Width</td>
<td>Ventricular electrogram duration&gt;120msec during arrhythmia</td>
<td>(0 or 1)</td>
</tr>
</tbody>
</table>

Datasets were randomly assigned to training or test set and exported to text files. An ANN, with supervised learning, was designed using Numap v7.06a (Neural Decisions Lab LLC, Arlington, TX, USA) prototyping software. The training set was applied using an iterative approach to estimate the number of hidden units providing the lowest error and number of training cycles to achieve convergence. The trained network was stored and test set applied. ANN output accuracy was tested for significance as above.

A prospective study with improved data control was designed. Two methodologies were identified. Jenkins and Jenkins’ used a library of data acquired during electrophysiological studies to test algorithms [16], an alternative method used real-time intracardiac electrograms during invasive electrophysiological studies to test algorithms [2] [17]. As this study required reuse of data, Jenkins and Jenkins approach was adopted.

Knowledge acquisition was in two phases: elicitation of domain expert knowledge leading to a representation of knowledge of cardiac rhythm diagnosis and acquisition of parameters guided by the results. Parameters in current ICD algorithms were included as default, to allow comparison.

Consensus guidelines provide authoritative definitions and guidance on arrhythmia diagnosis, based on meta-analysis of study data and international expert consensus and endorsed by the American Heart Association and the European Society of Cardiology [18]. Systematic analysis of these guidelines and disease descriptions [19] generated a comprehensive list of arrhythmias and factors and indicators for each arrhythmia diagnosis. Literature searches for each were performed for evidence supporting their use in arrhythmia diagnosis. Parameters important to diagnosis of any arrhythmia were included. Measurable physiological parameters with equivalence or with potential as sensors were evaluated for utility. Consideration was made of practicalities of data collection. The results were reviewed by a domain expert consultant cardiac electrophysiologist and modifications made as required to final selection of parameters for the prospective study. The principles used for data encoding were as the pilot study for knowledge representation.

The study was approved by St. Thomas’ Hospital Research Ethics Committee. Waveforms were collected using an Ensite 3000 (St. Jude Medical, St. Paul, MN, USA) with 32 channel capability.
including up to 8 analogue inputs, a sampling frequency of 1200Hz with capability to export digitized waveform data to text file.

Intracardiac electrograms were obtained using conventional 5F Supreme JSN 401443 quadripolar electrophysiology electrode catheters (St. Jude Medical, St. Paul, MN, USA) with 5mm inter-electrode spacing. Electrodes were positioned in the heart under X-Ray control (figure 3) and connected to the Ensite system in parallel to the clinical electrophysiology system, using pin-tip jumpers.

**Figure 3.** X-ray image of four electrode catheters in the heart during an electrophysiological study.

Top left of image is the right atrial electrode; bottom right of image is the right ventricular electrode. (The remaining two electrodes in the centre, positioned at the bundle of His and the coronary sinus were not used in this study)

Impedance cardiography (ICG) (which measures the thoracic bio-impedance (Z) to estimate the haemodynamic performance of the heart [20]) was recorded using a Physio Flow model PF-05 Lab1 and v1.0.7 software (Manatec Biomedical, Paris, France), using the manufacturer’s recommended six-electrode placement. Analogue output of the Z waveform was recorded on the Ensite system. Body temperature was monitored using a TEMPerNTC USB thermometer (RDing Technology Ltd, Shenzhen, China) placed next to the skin in the patient’s axilla. No analogue output was available, and the manufacturer’s TEMPerNTC v3.2 data logging software was used at a sampling rate of 1Hz. Body motion was monitored using an Analog Devices ADXL202EB dual-axis accelerometer (Analog Devices Inc., Norwood, MA, USA) strapped to the patients upper arm. No analogue output was available and X-Analyze v2.02 software (Crossbow Technology Inc., San Jose, CA, USA) was used for data logging, with a sampling rate of 10Hz. A Windows XP SP3 desktop computer was used to run temperature and accelerometer software. The times of the system clock on Ensite and PC were noted to enable synchronisation to within one second, for later analysis.

Demographic and clinical history data were collected manually from the medical case notes at the time of the electrophysiology procedure.

4. Results

In the pilot study, from 105 patients 800 arrhythmic events were stored and 13 diagnostic algorithms used. The most accurate had sensitivity 1.00, specificity 0.69 with no significant difference to the gold standard (p<0.001). Inappropriate therapy was received by 13.2% patients.

75 datasets were selected for ANN inputs, 42 assigned to the training set and 33 to the test set. The training set produced a feed-forward, back-propagation network with 7 inputs, a single hidden layer with 4 nodes and a single output achieved the lowest error and convergence was reached over 25 iterations. The test set applied to the trained ANN showed sensitivity 1.00, specificity 0.71, and no significant difference to the gold standard (p<0.001).

For the prospective study, knowledge acquisition indicated signs, symptoms and measurements useful in cardiac rhythm diagnosis: electrocardiogram (ECG); physiologic stress; cardiac function; catecholamine level (adrenaline in the blood); clinical history; cardiac anatomic abnormalities; carotid sinus hypersensitivity; metabolic diseases; drug regime; thyroid function; lifestyle; pace termination of
arrhythmia. Data collection was planned based using equivalent measurable parameters: electrograms (intervals, relationship, morphology and vector); body temperature; body motion accelerometry; blood pressure and cardiogenic thoracic bio-impedance. Physiologic stress was estimated by heart rate (cardiac stress), body temperature (metabolic rate) and accelerometry.

65 patients undergoing invasive cardiac electrophysiological study were recruited, providing informed consent. 48% were male and 52% female. 60 complete datasets were obtained, an example of the waveforms is shown in figure 4.

Ensite data was not collected in 3 patients, ICG data in 1 and temperature data in 1 patient due to technical failures. Knowledge representation and implementation is incomplete as this is an initial report.

5. Discussion
The pilot study demonstrated that KE and use of an ANN was useful, producing a usable system. The results for incidence of inappropriate shock and accuracy measures for the production ICD algorithms were similar to previously published results, giving them credibility and encouraging further research.

The prospective study showed that KE could successfully guide the selection and collection of physiological and other parameters as part of the design process for cardiac rhythm diagnostic algorithms. The completed data acquisition phase demonstrates that complex physiological measurement data collection is possible but may be problematic, particularly where multiple acquisition systems are involved and that failure of a single system would result in incomplete data.

The pilot study was subject to selection bias as, although all patients were included, detection of arrhythmia depended on a minimum achieved heart rate, resulting in an unknown level of under-detection and errors in estimates of true negative and false negative rates. The accuracy measures assumed that all arrhythmias were detected. This was solved for the prospective study, where all arrhythmias will be analysed, without the need for these assumptions. The prospective study was affected by selection bias (patients pre-selected to have an electrophysiology study) and data loss due to technical failures in the multiple systems used.

In conclusion, knowledge engineering was successfully used in the design process to guide selection of parameters for collection of physiological data for training and test sets in automatic cardiac rhythm diagnostic algorithm development and that an artificial neural network produced a
usable system. The complex data collection approach used, using multiple systems was feasible, but subject to additional risks of technical failure, leading to data loss.

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