Predictive ECG-Gating for Cardiac MRI [1]

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1 Summary

Most Magnetic Resonance Imaging (MRI) techniques require to send and receive long electromagnetic pulse sequences. In order to scan regions of the body which do not remain static such as the heart, the pulse sequences have to be divided, and its parts sent during different heartbeats in order to capture the heart always at the desired phase of its cycle (this has recently been termed segmented cine MRI[1]). Therefore, a single image normally contains the averaged information of several heartbeats [2].

Electrically gated imaging techniques [3–5] employ electrocardiographic (ECG) signals in order to synchronise the data acquisition with a specific phase of the cardiac cycle. After detecting a peak in the electrical activity which corresponds to the QRS (or R) wave of the ECG, a constant time offset dictates the moment for collecting the data pulse in every heartbeat. In this way, the phase of the cycle to be imaged is selected by assigning a prefixed value to the offset. The longer the offset, the later the phase of the cardiac cycle.

These methods assume that the position of the heart within the cycle is uniquely determined by the time elapsed since the occurrence of the QRS wave in the electrocardiogram. However, this is only an approximation [6–8] and since data collected to form an image proceeds from somewhat different phases of the cardiac cycle, the obvious consequence is the degradation of the images, particularly those of the late (diastolic) phases.

Furthermore,in cases where images of the early systolic phase of the heart are required (in order to analyse, for instance, atrial contraction or supra-ventricular tachyarrhythmia [**?**]), standard (also known as *prospective*) ECG gating can not be used because it relies on the detection of the R-wave complex, and this takes place during ventricular contraction, after the early systolic phase. Methods such as *retrospective* gating continuously acquire MR data, which with the use of the ECG, can retrospectively be assigned to a phase of the cardiac cycle and hence used to form the corresponding image in the cycle. Although retrospective gating can be used to acquire images of the early systole, the quality of these images is inferior to mid-systolic images acquired with prospective gating. Another very important limitation is that retrospective gating cannot be used to produce tagged (SPAMM) imaging [**?**], probably the most reliable imaging technique used for the study of non-rigid motion of the heart [**?**,**?**,**?**,**?**].

In this work we propose a new imaging method where the time offset used for gating is not constant but changes from beat to beat. We will use the expected length of every cycle (basically the R-R intervals) to calculate an offset that can point more accurately towards the desired phase of the cardiac cycle, and which includes the early systolic phase that precedes the R-wave. For this purpose we need (1) to evaluate the existent formulas that relate R-R interval to the diastolic fraction [6–9], and then, during the time of imaging, (2) to predict the length of the next R-R interval using a priori knowledge of the dynamics of the heart and information of the data patterns obtained during the first minutes of the study.

Several time series analysis and forecasting techniques [10–12] have been proposed and used for the study of financial, biological and other naturally occurring time series [**?**,**?**,13–15]. In particular, there is widespread interest in the study of the cardiac rhythm, with specific applications for instance to defibrillators and pacemakers [16,17,**?**]. However, the present problem perhaps requires the development

[1] Project proposal for EPSRC *PredGate*, v0.31.

of a new or hybrid method in order to achieve the rapid and accurate forecast necessary to allow the computed time offset to be used for gating by the MR scanner [18], while at the same time exploiting the fact that there are virtually no limitations in terms of data storage space or computer size (which is not the case for pacemakers applications).

We intend to combine all possible subject-specific data, with general knowledge about heartbeat dynamics. Subject specific data will mostly be extracted from the relatively short data series acquired during the set up of the MR scan and accumulated through the study (studies using such short data sets of heartbeats have been shown to yield satisfactory results [16,17]), but will also incorporate any existing prior ECG studies of the subject. A hierarchical inference scheme for blending general heartbeat dynamics with the subject specific data will be developed.

To the best of our knowledge *Predictive Gating* is a completely novel and very promising technique that could also be used in other fields like nuclear imaging.

2 Previous Research and Track Record

Gerardo... Physics Institute (non-linear dynamical systems [15,14]), Imperial IP and MRI, Oxford 3Dechocardiography,Imperial EP, ...

Imperial College

EP project

3 Background

Motivation and main objectives OJO HERE MOVE / ADD more ?

- **Improve atrial and early-systolic ventricular imaging (without interpolation as in current techiniques)**,
- **Achieve tagged imaging of atrial and early-systolic ventricular contraction** ,
- **Improve general cardiac MR image quality– Produce MR images of arrhythmic heartbeat states – ... here ?**

3.1 Current Clinical Needs

Atrial Arrhythmias The heart's natural pacemaker, the sinoatrial (SA) node, is a specialized group of cells located high in the right side of the heart, where the electrical impulse that causes the heart to beat originates. The impulse travels down a pathway, first causing the atria to contract, followed by the ventricles. Arrhythmias are irregularities in the normal rhythm of the heartbeat that originate either in the atria (superventricular)or ventricles (ventricular). These alterations to the cardiac rhythm can be caused by a number of mechanisms and are a major cause of morbidity and mortality affecting all age groups.

In the most common abnormal cardiac rhythm, called **Atrial Fibrillation (AF)**, the impulses originate in a very fast and irregular manner and from various regions of the atria, not necessarily the SA node, causing the atria to quiver instead of beating. During AF, the upper chambers of the heart beat between 350 and 600 times per minute, instead of 60 and 80 times per minute of the normal heart rhythm. Recent investigation shows that if a patient has high blood pressure, heart valve problems, or cardiac muscle damage, AF can increase the risk of heart failure [**?**]. Because AF impairs the pumping function of the heart, the blood is not completely emptied from the heart's chambers, causing it to pool and sometimes clot. In about 5 percent of patients with AF, clotted blood dislodges from the atria and results in a stroke.

The American Heart Association estimates that in the U.S. alone, AF is responsible for over 70,000 strokes each year [**?**]. **Atrial flutter** is a more organized but still fast arrhythmia triggered when an impulse circles the heart's upper chambers instead of moving to the lower chambers. In atrial flutter the atria beats between 240 and 300 times per minute and usually only every other flutter wave reaches the ventricles.

Atrial and early-systolic ventricular imaging - state need for atrial imaging

- retrostpecive intepolted images..

We must mention that although alternative cardiac imaging modalities for atrial contraction exist, such as 3D echocardiographyand doppler ultrasound (which do not rely on ECG gating), the resolution and quality of the images is greatly inferior to that of cardiac MRI, and in particular the techinques are less suitable for tracking than tagged MR since they necesitate a number of, normally not present, naturally occurring landmarks [19,**?**,**?**].

- desirable to image arrhythmic heartbeat states.

Tachyarrhythmias and RF ablation Superventricular tachyarrhythmias are pathological fast beats often caused by an extra conducting pathway between the atria and ventricles. These pathways can allow retrograde conduction from the ventricles to the atria, and in combination with the normal pathway, form a conducting loop. The mechanism of tachyarrhythmia is propagation of current in the loop independent of the heart's natural pacemaker (atrioventricular re-entry tachycardia). A second and more difficult to treat form of tachyarrhythmia arises when the entire current loop lies within the atria (atrial re-entry tachycardias). In patients for whom antiarrhythmic drug treatment is ineffective, or leads to unacceptable side effects, and for patients with life threatening arrhythmias, radio-frequency(RF) ablation is the treatment of choice. The arrhythmia substrate is first assessed by an electrophysiological study, that is, using intravascular catheter electrodes placed in different position inside the heart to record intracardiac electrograms simultaneously with the surface electrocardiogram. This allows the electrophysiologist to mentally form an electrical map of the heart with which to identify the source and pathway of the arrhythmia. Treatment then follows by applying a RF current via an ablation electrode which induces local hyperthermia resulting in irreversible cellular destruction. Correctly choosing the ablation site is crucial as errors can damage the atrioventricular node and result in complete heart block and the need for a permanent pacemaker. Also, partial ablation is not only ineffective, but may even be proarrhythmic. The procedure is normally guided with x-rays (2D), and thus prone to errors in location and excessive radiation exposure.

Tagged MRI (SPAMM) of atrial and early-systolic ventricular phases - limitations: atrial/ arrhythmia / early systole

In previous work (funded by EPSRC grant **OJO EPSRC GRANT NUMBER**) we developed a method to provide pre- and intra-operative 3D MR guidance in XMR systems (combined X-ray and MRI room). In order to locate myocardial regions with abnormal electrical conduction pathways we aquired tagged MR sequences and tracked cardiac motion. We then related motion to electrical activation, solving the inverse electro-mechanical coupling problem and thus deriving activation isochrones to determine the locations of the abnormal conduction pathways [20,21,**?**]. A limitation found for this type of approach was the impossibility of acquiring tagged MR images of atrial and early-systolic contraction. Predictive gating overcomes this imaging limitation (see Section **??**) and provides a tool for the general study of atrial contraction.

We must mention that although alternative cardiac imaging modalities for atrial contraction exist, such as 3D echocardiographyand doppler ultrasound (which do not rely on ECG gating), the resolution and quality of the images is greatly inferior to that of cardiac MRI, and in particular the techinques are less suitable for tracking than tagged MR since they necesitate a number of, normally not present, natural landmarks [19, **?**,**?**].

3.2 Cardiac ECG Gating

One of the key challenges in cardiac imaging has long been the accurate and reliable synchronisation of the scan with the heartbeat. Because of the continuous movement of the heart, whenever data acquisition is too slow to occur during a short fraction of the cardiac cycle, synchronization is necessary to aquire data of a slice of the heart during a specific phase of the heartbeat. Image blurring due to cardiac-induced motion occurs for imaging times of above approximately 50 ms in systole, while for imaging during diastole the critical time is of the order of 200/300 ms. In cardiac ECG gated techinques, data acquisition is synchronised using the ECG signal recorded during image acquisition.

Prospectivegating with MRI consists of initiation of the radio-frequencypulses at a fixed time in the cardiac cycle determined by the ECG signal. Retrospective gating consists of continuous application of the radiofrequency pulses and simultaneous recording of the ECG signal. Later, the data acquired at specific phases of the cardiac cycle, as indicated by the recorded ECG signal, are reconstructed into images corresponding to specific intervals of the cycle.

Prospective ECG Gating These are techniques in which image acquisition is triggered by a start pulse derived from an ECG recorded from the patient while imaging. The ECG tracing is fed into a circuit which produces a trigger signal, to be used as a start signal for data acquisition of the imaging system. The imaging system then automatically acquires data for a time series of images or for a few images at different anatomical levels.

In MR imaging, the acquisition of a single image line (in k space) is well possible within the limit of 20/50 ms, however, the acquisition of an entire image in this time is only possible with using ultrafast MR imaging techniques.In simple cardiac gating, a single image line is acquired in each cardiac cycle. Lines for multiple images can then be acquired successively in consecutive gate intervals using the standard multiple slice imaging and a spin echo pulse sequence. Then, a number of slices at different anatomical levels is obtained. The MRI repetition time TR during a ECG-gated acquisition equals the RR interval, and the RR interval defines the minimum possible TR. If longer TRs are required, multiple integers of the RR interval can be selected. When using a gradient echo pulse sequence, either multiple slices at different anatomical levels, multiple phases of a single anatomical level or any combination of the two can be acquired over the cardiac cycle. Thereby up to 50 phases of a single anatomical slice can be obtained. When ultrafast imaging techniques are used, several image lines are acquired in the time intervals defined above. If these lines are recorded for a single rather than multiple images, imaging time can be shortened considerably maintaining an acceptable temporal resolution. As an example, the acquisition of 8 lines in each cardiac cycle for the same image reduces image acquisition of a 128-line image from 128 heartbeats by a factor of 8 to 16 heart beats, thus making image acquisition of multiple cardiac phases or anatomical slices possible in a breath-hold. These latter techniques are termed segmented data acquisition techniques and can be used in conjunction with all ultrafast MRI techniques. If multiple phases of the same anatomical slice have been obtained over the heart cycle, playback preset Tc are then rejected by the system or a retrospective gating is used. Obviously, gating methods yield suboptimal results whenever the patient has an irregular heartbeat such as in atrial fibrillation.

Retrospective Gating These are techniques used in nuclear and MR imaging, in which cardiac-gateddata is retrospectively assigned to a cardiac cycle phase and hence to the corresponding image in the cardiac cycle.

In nuclear imaging the RR interval is normally prospectively divided into the desired number N of subintervals in standard cardiac gating, and an image is assigned to each subinterval. With the collection of data, the exact event time after the ECG-QRS-complex is registered and with the advent of the next QRS-complex the actual length of the RR interval is measured. This length varies as each individual's heart rate is subject to normal RR interval variations; the so-called sinus arrhythmia. Alternatively, data are collected in the list mode, and the length of each subinterval for the actual RR interval is determined by

dividing it by N, and the data previously collected (for that RR interval) are retrospectively assigned to the N predefined image frames. The result is that all collected data are assigned to images, but that there is a small variation in the length of the subintervals, which is adjusted for each RR interval. The advantages of retrospective gating in nuclear imaging are subject to debate, because the sinus arrhythmia-induced variations of the RR interval predominantly produce changes in the length of diastole, whereas the timing of systolic events is much less strongly dependent on heart rate. Hence, retrospective gating introduces additional errors into the assignment of events during systole.

In MR imaging,one reasonto use retrospectivegatingis to avoid an undesiredsignal increase cine sequence than nomally appears when using standard (prospective) gating. This unwanted effect is due to the fact that for cine MR imaging the TR of the images are selected. Because of the sinus arrhythmia, however, the last subinterval before the next ventricular complex is variably prolonged. As a result, the radio-frequency pulses sent into the patient with the start of the next RR interval occur after a variable but somewhat longer TR compared to the other intervals. As longer TRs result in more signal (gradient echo pulse sequence), the first image of a prospectively gated MR cine loop is often noticeably brighter. In retrospective MR gating the repetition time TR is kept constant thereby avoiding this signal increase. The subinterval to which each image line belongs is then determined and the line is retrospectively assigned to the corresponding image data. When collecting data in this way, care has to be taken, that eventually the entire k space is filled, i.e. that all phase encoding steps are represented among the image lines assigned to each image. In cardiac gated spin-echo imaging, retrospective gating is not used, as the relative variation in TR resulting from the sinus arrhythmia (and thus the variation in image brightness) is much smaller than in its cine MR imaging.

Another reason for using retrospective gating is for early systolic or atrial imaging. The QRS complex of the ECG, which corresponds to ventricular contraction, appears after atrial contraction has already started, hence it cant be used as a trigger for starting data acquisition in real time. Also, because of the normal variations of the the R-R interval (called the sinus arrhythmia), a fix offset based on the current QRS can not be used to acquire data before the QRS complex of the next heart beat. For this reason retrospective gating is used

3.3 Non-ECG-based gating: self-gating

The closest state-of-the-art research by other groups trying to circumvent ECG gating is the so-called self-gating. This approach extracts gating information directly from the raw imaging data acquired, using interleaved radial k-space sampling, and has ben tried for cardiac [22] gating, in order to eliminate the need of ECG-gating, and more recently on for respiratory [1] gating, for aquiring free-breathing segmented cine MRI. Siemens Medical Solutions has released and recently patented [23] software based on this principle, although as they point out, “the information about this product is preliminary. The product is under development and is not commercially available in the U.S., and its future availability cannot be assured” [24], the approach could revolutionize the field.

However, because this method relies on detecting motion of the heart in order to identifing the desired cardiac phase, it seems unlikely that the method will work well for the very early stages of cardiac contraction such as atrial or early-systolic ventricular contraction, and there are no assertions on that respect [22,1,24]

Other limitiations of this approach are likely to be in the presence of arrhythmic heartbeat states, and ...

3.4 Heartbeat and Arrhythmia Detection and Forecast

Time Series Forecast and Cardiac Dynamics Approaches to cardiac arrhythmia analysis include various techniques such as spectral features [25,26], hidden Markov models [27], supervised learning algorithms [28], complexity measures [29], neural networks [30,31], least squares-based prony modeling algorithm

[32], autoregressive modeling for arrhythmia classification [33], and nonlinear dynamical modeling [34,35], among others.

Some of the main methods used for cardiac arrhythmia analysis and forecast include various techniques such as:

Frequency spectral features: Frequency-domain analyses of ECG (and R-R intervals) are widely used to detect, characterise and predict heart rate (HR) fluctuations and arrhythmia, using the distribution of frequency peaks in the power spectrum, and even achieving differentiation of general behaviour such as ventricular fibrillation-flutter, ventricular rhythms, imitative artifacts and predominant sinus rhythm [25, 26,36].

Hidden Markov models: Hidden Markov modeling (HMM) has been successfully used to model speech waveforms for automatic speech recognition. Classification of supra-ventricular arrhythmias, for instance, often requires detection of the P wave in addition to the QRS complex. The HMM approach [27] combines structural and statistical knowledge of the ECG signal in a single parametric model. Model parameters are estimated from training data using an iterative, maximum-likelihood re-estimation algorithm.

Machine learning algorithms: Machine learning algorithms for the diagnosis of cardiac arrhythmia from standard 12 lead ECG recordings use supervised and inductive learning algorithm for inducing classification knowledge from examples. The input training records contains clinical measurements from ECG signals and some other information such as gender, age, and weight, along with the decision of an expert cardiologist. The knowledge representation can be based on the projections of the training cases on each feature, and predictions seem to compare positively to other algorithms such as Naive Bayesian and Nearest Neighbor classifiers [28].

Complexity measures and nonlinear dynamical modeling: Sinus rhythm (SR), ventricular tachycardia (VT) and ventricular fibrillation (VF) are different nonlinear physiological processes with different complexity, and as such, can be detected and classified using non-linear dynamical systems and complexity measures, such as entropy, entropy rate, embedding dimension, frequent deterministic patterns and Lyapunov exponents [37,38,29,39,34,35,40].

Neural networks: Artificial neural network models have been proposed for the morphological classification of single and multichannelECG signals. These are adaptive classifiers with the capacity to dynamically self-organize its response to the characteristics of the input signals. Multilayer neural networks have also been used to classify arrhythmia QRS complexes, and for ischaemia detection, by differentiating between normal and abnormal ST segments using nonlinear principal component analysis feature extraction from ECG signals. [30,31,41,40]

Other common approaches include: **prony modeling** [32], **autoregressive modeling** [33], **principal component analysis** [41], **wavelet analysis** [42] and **fuzzy neural networks** [40] among others.

4 Methodology and Program

In order to overcome the above-mentioned limitations of prospective and retrospective cardiac imaging, in this work we propose the new predictive gating imaging techinique, where instead of waiting for the R-wave (QRS complex) to be detected in order to trigger image acquisition, the time of the start of the next heartbeat is forecasted using in-vivo and previously acquired ECG data. The time offset used for gating is calculated every heartbeat using both, the time of the R-wave of the current heartbeat, as time zero reference, and the predicted time when the next heartbeat will begin, that is, the length of the present heartbeat.

In this manner we can, on the one hand, acquire images of the very early systolic ventricular and atrial contraction, which precede the R-wave, and on the otherhand, point more accurately toward any desired phase of the cardiac cycle (including those systolic phases posterior to the R-wave, since in the worst case

scenario, the actual time of the the R-wave that is normally used as a trigger will become available as in standard prospective gating). Because we will have an estimate of the time of the initiation of the heartbeat, we will be able to produce tagged images preceeding the R-wave.

The **main benefits in terms of cardiac imaging** will be:

- improved image quality during the whole cardiac cycle
- create images of very early systole/atrial contraction
  - this is currently not possible with prospective gating
  - retrospective gating can but with interpolation and low image quality
    - predictive gating could be used without interpolation
    - predictive gating could also be used with interpolation, but improving the 'aiming' to the desired cardiac phase and hence with less image degradation than retrospective gating – create tagged images of very early systole/atrial contraction
  - currently there exists no cardiac imaging techinque capable of this. Given the importance of atrial related diseases (such as AF) and because tagged MR imaging is the best techinque currently available for monitoring cardiac motion [**?**], this objective could be an very important first step for cardiac disease monitoring and treatment.
- open the possiblity to produce MR images of the heart during arrhythmic heartbeat states such as AF.
- Predictive gating can applied to improve almost any other existing cardiac gating techinque.

In broad terms, the **main steps that we need to take in order to achieve our goals** are:

- To evaluate existent **ECG formulas** that relate R-R interval to the diastolic fraction, the P-wave (corresponding to atrial contraction), and to other relevant segments of the ECG that correspond to different phases of the cardiac cycle [6–9].
- To build a **model of the heartbeat dynamics** based both, on a priori knowledge of the general dynamics of the heart (or a population-specific behaviour), and on individual heart dynamical (or subjectspecific) information. The subject-specific information can be formed from (ECG) data obtained before the study, and (primarily) on real-time ECG data obtained durin the first minutes of the study and while the image acquistion takes place.
  - A **hierarchical inference model** for combining the above mentioned sources of information will be developed.
  - A system for the **classification of the current dynamic state** of the heartbeat will also be developed to differentiate between sinus rhythm, AF and other heatbeat modes.
- Design a **time series analysis and forecast** technique in order **to predict heartbeat intervals** in sinus rhythm and possibly in other arhythmic beating states, in real-time, but without some strong constraints typically present in other applications (such as limited storage and processing capabilities as in the case of implanted defibrillators [**?**,**?**]).
- Adapt currently existing standard anatomical and tagged **MR imaging sequences** to, during the time of imaging, receive one or several trigger pulses to synchronise data acquisition with the desired phase of the cardiac cycle. The timing of the trigger pulses will be computed in real-time from the predicted length of the R-R interval and the developed heartbeat dynamical model.

4.1 Objectives and original contributions

- Develop models for classifying the different dynamic states of the heartbeat.
- Develop a hierarchical inference system for fusing population- and patient-specific knowledge of cardiac dynamics.
- Model and predict heartbeat intervals, in sinus rhythm and some arrhythmic dynamic states.
- Implement a new ECG-gated MR sequence using heartbeat prediction.
- Acquire anatomical images of early-systole without interpolation.
- **Improve atrial and early-systolic ventricular imaging** ,

- **Acquire tagged MR images of atrial and early-systolic ventricular contraction** (currently not possible)
- **Improve image quality in real-time aqcusition**
- Open the possiblity to acquire MR images of the heart during arrhythmic heartbeat states such as AF.
- predictive gating can be used to improve almost any prospective and retrospective gating thechinques, because it introduces a better estimate of the actual times to send the pulses, instead of assuming a fix length for them, as the interpolation process of retrospecive gating does.

To the best of our knowledge *Predictive Gating* is a completely novel and very promising technique that could also be used in other fields like nuclear imaging.

4.2 ECG data acquisition

ECG data will be acquired and fed into the computer from the moment the subject lies down in the scanner. Normally a few navigation scans and standard (non-tagged) acquisitions are made giving between 15 and 25 minutes of ECG data. At least a thousand RR intervals can easily be acquired, which is a reasonable number of data points to start for methods based on short time series. As the scan progress, more data will be accumulated.

Another source of subject-specific data could be prior ECG recordings of the patient carried out either on the scanner, duringconsultation or duringany other study (for instance 24 hours Holter) with prior selection of the relevant dynamics at rest.

Generic data bases with the general pattern of cardiac heartbeats will also be incorporated.

4.3 Heartbeat and Arrhythmia Detection, Classification and Forecast

Several time series analysis and forecasting techniques [10–12] have been proposed and used for the study of financial, biological and other naturally occurring time series [**?**,**?**,13–15]. In particular, there is widespread interest in the study of the cardiac rhythm, with specific applications for instance to defibrillators and pacemakers [16,17,**?**]. However, the present problem perhaps requires the development of a new or hybrid method in order to achieve the rapid and accurate forecast necessary to allow the computed time offset to be used for gating by the MR scanner [18], while at the same time exploiting the fact that there are virtually no limitations in terms of data storage space or computer size (which is not the case for pacemakers applications).

We intend to combine all possible subject-specific data, with general knowledge about heartbeat dynamics. Subject specific data will mostly be extracted from the relatively short data series acquired during the set up of the MR scan and accumulated through the study (studies using such short data sets of heartbeats have been shown to yield satisfactory results [16,17]), but will also incorporate any existing prior ECG studies of the subject. A hierarchical inference scheme for blending general heartbeat dynamics with the subject specific data will be developed.

Parameters and approaches Some of the main parameters and approaches that we ought to consider in order to categorize and review the techniques to detect, classify and predict arrhythmia, are:

- **Continuous vs. Discrete ECG data**
  While our interest is mostly focused on exploiting the continuous ECG signal, a brief description of the most relevant discrete methods that only use the R-R intervals is included for comparison of advantages and performance [34,35,43]. Although many ventricular arrhythmias can be classified by R-R intervals, some others like supra-ventricular arrhythmias often require detection of the P wave or the ST segment in addition to the QRS complex [27,41].
- **Single vs. Multi-Channel ECG data**

Using several ECG lead signals (see configurations in Section **??**) can provide valuable information for the analysis and in particular for the classification of arrhythmia. The **principal features** exploited in **multi-lead analysis are the: relative size**, **morphology** and **timing** of the deflections in the individual leads [31,26].

– **Real-time vs.** *a posteriori* **analysis**
The aim for most applications is to perform real-time detection or forecast, for instance when using implantable devices such as the cardioverter-defibrillator. However slower algorithms that can analyse the data *a posteriori* and provide accurate detection, forecast or classification are also of valuable clinical importance [44,45].

– **Detection and Forecast**
While identification of the QRS complex remains an essential issue for arrhythmia detection [44,46], a wide variety of methods (using some of the "Discerning Features" listed below) have been developed for detecting and predicting all types of arrhythmia, either as a first step towards classification or independently of it, [16,18,42,46,31,47,40,48].

– **Discerning Features**
Several features can be extracted and used to detect, classify and predict arrhythmia, for instance:
- **Segment-based Values** (RR, QRS and ST, for instance) [41,30]
- **Heart Rate Variability** [48,17]
- **Frequency Spectral Features** [25,26]
- **Complexity Measures** [49,29,37–39]
- **Non-linearity Measures** (*e.g.*Fractality [40] and Lyapunov exponents [34]).

– **Classification**
Important to discern between life-threatening (for instance VT, VF) and other less lethal arrhythmias (such as APC, PVC, SVT) [33,31]. Extraction of QRS and ST segment features has been used to classify ischaemic cardiac beats [41]. Other approaches use the relative timing and morphology of multi-lead ECG signals, for instance, one can distinguish between the monomorphic re-entrant VT, in which depolarization is propagated by a simple single activation wavefront, and the polymorphic VT (such as PVT or VF), where the pattern of depolarization is more complex and sometimes propagated by multiple activation wavefronts [26].

RR intervals vs. full ECG dynamics forecast Some studies have pointed out the potentially chaotic nature of some beating patterns or attractors of the heart [**?**,**?**]. In order to characterise and model or forecast such attractors dynamical systems analysis methods can employ either the full trajectories on the phase space (position and velocities variables) [**?**,**?**,**?**], or use a discrete variable characteristic of the system such as a time series [**?**]. Although in the case of the ECG we have the time vs. potential recording,for every time during the recording, because of the distortion to which the ECG is subjected we will focus on analysing the R-R time intervals, that is the time elapsed between the R-waves of two consecutive heart beats. Besides being easy to record (for it's the highest potential and with sharper gradient), this time...

Analysis tools - recurrence plots

The use of Recurrence plots has been introduced for the analysis of non-stationary and rather short data series [37,50] and recently for the study of heart rate variability [17,51].

Applying these measures to the heart-rate-variability data, we are able to detect and quantify the laminar phases before a life-threateningcardiac arrhythmiaoccurs thereby facilitating a prediction of such an event. Our findings could be of importance for the therapy of malignant cardiac arrhythmias.

- k-nearest neighbours..

Cardiac Rhythms - sinus rhythm, arrhythmia, tachycardia, VT, VF

- [16] ”Ventricular tachycardia or fibrillation (VT-VF) as fatal cardiac arrhythmias are the main factors triggering sudden cardiac death. ... find early signs of sustained VT-VF in patients with an implanted cardioverter-defibrillator (ICD). These devices are able to safeguard patients by returning their hearts to a normal rhythm via strong defibrillatory shocks; additionally, they store the 1000 beat-to-beat intervals immediately before the onset of a life-threatening arrhythmia.We study these 1000 beat-to-beat intervals of 17 chronic heart failure ICD patients before the onset of a life-threatening arrhythmia and at a control time, i.e., without a VT-VF event. To characterize these rather short data sets, we calculate heart rate variability parameters from the time and frequency domain, from symbolic dynamics as well as the finite-time growth rates. We find that neither the time nor the frequency domain parameters show significant differences between the VT-VF and the control time series. However, two parameters from symbolic dynamics as well as the finite-time growth rates discriminate significantly both groups.These findings could be of importance in algorithms for next generation ICD’s to improve the diagnostics and therapy of VT-VF.” - define which state (type of attractor) is the heart beating in.

4.4 Hierarchical inference / Population and patient specific data

- The RR interval forecast will be based on three types of data.

Most importantly, *in-vivo* ECG data acquired and fed into the computer from the moment the subject lies down in the scanner. At least a thousand RR intervals can easily be acquired, which is a reasonable number of data points to start for methods based on short time series. As the scan progress, more data will be accumulated.

A secondary source of data could be, when available, prior ECG recordings of the subject.

Finally, a priori knowledge of the general cardiac dynamics will be incorporated in the form of a rule system and data bases with labeled cases of sinus rhythm, VT, VF and arrhythmia.

- The above knowledge will be fused using a hierarchical inference system...

Offset estimation - Determine current dynamical state of the heart (e.g. Sinus rhythm, VT..)

- Forecast RR interval

- Estimate length of the P-wave (using existent formulas, sufficient as a first approximation) in order to start acquisition at the beginning of atrial contraction.

4.5 MR Imaging

4.6 Computer processing and feedback to MRI scanner

The *in vivo* ECG signal can be taken out from the scanner and processed in a standard desktop or laptop computer in the control room, free of magnetic interference.

Two different approaches will be explored, one with homogeneous and one with non-homogeneous timesampling of the heart cycle. In the (standard) homogeneous case, the output of the computer algorithm will be a single trigger pulse, at the time when the cardiac cycle onset is predicted to take pleace, to initiate the image acquisition for that heartbeat.

In the second case in which we will investigate the improvement introduced by using the heartbeat model for non-homogeneous time-sampling of the heart cycle, a series of pulses will be passed to the scanner in order to better accomodate the RF pulse to the desired phase of the cardiac cycle.

Using the detected R-wave of the new heartbeat, the accuracy of the predicted length of the hertbeat can almost immdiately be assessed and corrected (at leats for the post R-wave part of the cycle).

Because the actual meassurement of the time of the R-wave provides immediate feedback, statistics of the accuracy achieved can be derived in real-time and in cases where performance might be poor after a few minutes, the sequence will be able to revert to a standard prospective (or retrospective) image acquistion. This mechanism bounds the worst case scenario performance to that of standard propsective sequence, making the approacha very low risk one in terms of image acquisition time.

The total time of image acquisition will only increase in cases where the hertbeat is very arrythmic and difficult to predict, because some heartbeats would have to be skipped. But given the success rate of time series forecast methods [**?**], and in particular for the heartbeat [**?**], we expect the time of acquisition to be reasonably similar to that of standard techinques.

4.7 MRI acquisition sequence

4.8 Validation

Hearbeatmodelling and classification We will test ourresults using some of the largeexisting databases[**?**,**?**,**?**] that contain pre-classified and annotated R-R intervals series (as well as digitised continuous ECG signals), for normal subjects and also for patients suffereningdifferenttypes of disorders (e.g. atrial fibrillation, atrial flutter, WPW syndrome and atrial and ventricular tachyarrhythmias).

RR intervals forecast Evaluation of the accuracy of the forecast is straight forward and will be carried out on several subjects and patients, verifying the percentage of error for each heartbeat (this can be done on a time series predicting the last time, for every time in the sequence after the minimum required to build the predictive system).

Compare results on healthy volunteers and patients. Existing databases will be used to test and validate our results [**?**,**?**,**?**,**?**,52]

MR image acquisition Image quality of anatomical (non-tagged) predictive gating will be tested against that of images produced with the equivalent prospective and retrospective gating techniques for systolic and diastolic phases posterior to the R-wave, and against retrospective gating for the whole cardiac cycle and with emphasis on the atrial and early-systolic phases preceeding the R-wave. Image quality will be assessed qualitatively with 'blind' visual(!) inspection of cardiac MRI imaging experts, and quantitatively by direct and indirect methods. Direct quantitative methods include measuring image properties like sinalto-noise noise ratio and contrast [53,**?**], while indirect methods would include automated and manual segmentation [54,19,**?**].

In the case of tagged images of atrial and early-systolic phases preceeding the R-wave, image quality cannot be compared against that of any other imaging techinques because currently there are no other ways to produce such images. Validation will be done on the one hand, against that of tagged images corresponding to a different phase of the cycle (those immediately after the R-wave), in terms of image quality like sinal-to-noise noise ratio, contrast [53,**?**], and sharpness and persistance of the taggs during the sequence [**?**,**?**], and on the other hand, by using the taggs to track atrial and early-systolic ventricular motion [55,**?**,**?**,**?**]. The accuracy of the later will be assessed by comparing against manually segmented anatomical images of atrial contraction, and perhaps also using a different cardiac imaging modality that does not rely on ECG gating, such as 3D echocardiography, despite the fact that tracking of the heart with ultrasound images is limited and not as precise as tracking carried out with tagged MRI [19,**?**,**?**].

For phases of the cardiac cycle posterior to the R-wave, the quality of tagged images produced with predictive gating will be evaluated by means similar to those described above for anatomical and early-systolic tagged images.

- compare image quality on healthy volunteers and patients.

Acquisition times and other factors will also be taken into consideration when assessing the performance of predicted gating.

- atrial motion tagged v. phase velocity ?

-

Potential problems

- are the innaccuracy of the methode to predict sinus and other rhythms...

- thin atrial wall for tagged MR

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References

[1] A. Arai G. A. Hirsch E. McVeigh D. Li O. P. Simonetti A. C. Larson, P. Kellman. Preliminary investigation of respiratory self-gating for free-breathing segmented cine mri. *Magn Reson Med*, 53:159–168, 2005.

[2] R. Underwood and D. Firmin. *Magnetic Resonance of the Cardiovascular System*. Blackwell Scientific Publications, 1991.

[3] D. Nelson S. Y. Kopiwoda M.E. Clampitt C.L. Schultz, R.J. Alfidi. The effect of motion in two- dimensional fourier transformation magnetic resonance images. *Radiology*, 152:117–121, 1984.

[4] L.E. Crooks C.B. Higgins, L. Kaufman. Magnetic resonance imaging of the cardiovascular system. *Am. Heart J.*, 109:136–52, 1985.

[5] Y. Taeymans D. Decramer P. Reygaert E. Nyssen P. Block M. Osteaux M. Bister, J. Cornelis. Cardiac ”nmr”: The ecg trigger. *Electrocardiology*, page 303, 1988.

[6] H. C. Bazett. An analysis of the time relation of electrocardiograms. *Heart*, 7:353–370, 1920.

[7] Ashman R. The normal duration of the qt interval. *Am. Heart J.*, 23:522–534, 1942.

[8] Boiselle E Soumis F Megelas M Coquette A. Davignon A, Rautaharju P. Normal ecg standards for infants and children. *Pedi. Card.*, 1:123–131, 1979/1980.

[9] Lewis RP Leier CV Weissler AM Boudoulas H, Rittgers SE. Changes in diastolic time with various pharmacologic agents: implication for myocardial perfusion. *Circulation*, 60(1):164–169, 1979.

[10] Sidorowich JJ. Farmer JD. Predicting chaotic time series. *Phys. Rev. Lett.*, 59(8):845, 1987.

[11] Linsay PS. An efficient method of forecasting chaotic time series using linear interpolation. *Phys. Lett. A*, 153(6,7):353, 1991.

[12] Ruggeri GJ Jimenez J, Moreno JA. Forecasting on chaotic time series: A local optimal linear- reconstruction method. *Phys. Rev. A*, 45(6):3553–3558, 1992.

[13] H. N. Nunez Yepez, A. L. Salas Brito, C. A. Vargas, and L. A. Vicente. Chaos in a dripping faucet . *European Journal of Physics*, 10:99–105, April 1989.

[14] G.I. Sanchez-Ortiz and A.L. Salas-Brito. Chaos in a Variable Mass Relaxation Oscillator Model for the Leaky Tap. *Physica D*, 89(1–2):151–168, 1995.

[15] G.I. Sanchez-Ortiz and A.L. Salas-Brito. Strange Attractors in a Relaxation Oscillator Model for the Dripping Water Faucet. *Physics Letters A*, 203(5-6):300–311, 1995.

[16] Wessel N., Ziehmann C., Kurths J., Meyerfeldt U., Schirdewan A., and Voss A. Short-term forecasting of life-threatening cardiac arrhythmias based on symbolic dynamics and finite-time growth rates. *Phys. Rev. E*, 61(12):733–739, 2000.

[17] Norbert Marwan, Niels Wessel, Udo Meyerfeldt, Alexander Schirdewan, and Jrgen Kurths. Recurrence-plotbased measures of complexity and their application to heart-rate-variability data. *Physical Review E*, 66:1–8, 2002. 026702.

[18] G.I. Sanchez-Ortiz and P. Burger. A Novel Gating Technique for Cardiac NMR Imaging using Heartbeat Time Intervals Forecast. In *International Workshop on Nonlinear Dynamics, Fractality and Self Organization of Complex Systems*, page D7, Wu¨rzburg, Germany, October 1994.

[19] G.I. Sanchez-Ortiz, G.J.T. Wright, N. Clarke, J. Declerck, and J.A. Noble. Automated 3-D Echocardiography Analysis Compared With Manual Delineations and SPECT MUGA. *IEEE Transactions on Medical Imaging*, 21(9):1069–1076, September 2002.

[20] K.S. Rhode, D.L.G. Hill, P.J. Edwards, J. Hipwell, D. Rueckert, G.I. Sanchez-Ortiz, S. Hegde, V. Rahunathan, and R. Razavi. Registration and tracking to integrate X-ray and MR images in an XMR facility. *IEEE Transactions on Medical Imaging*, 22(11):1369– 1378, 2003.

[21] G.I. Sanchez-Ortiz, M. Sermesant, K.S. Rhode, R. Chandrashekara, R.Razavi, D.L.G. Hill, and D.Rueckert. Detecting and comparing the onset of myocardial activation and regional motion changes in tagged MR for XMRguided RF ablation. In *Functional Imaging and Modeling of the Heart (FIMH'05)*, Lecture Notes in Computer Science, LNCS 3504, pages 348–358, Barcelona, Spain, Jun 2005.

[22] Laub G McVeigh ER Li D Simonetti OP Larson AC, White RD. Self-gated cardiac cine mri. *Magn Reson Med*, 51(1):93–102, 2004.

[23] Siemens receives patent for new cardiac mri. *Medical Imaging Magazine - online*, Feb. 2005.

[24] Siemens Press Release. Siemens receives u.s. patent for new cardiac magnetic resonance imaging technology. Oct. 2004.

[25] Alfonso VX and Tompkins WJ. Detecting ventricular fibrillation: Selecting the appropriate time-frequency analysis tool for the application. *IEEE Eng Med Biol Mag*, 14:152–159, 1995.

[26] R.H. Clayton, R.W.F. Campbell, and A. Murray. Characteristics of multichannel ECG recordings during human ventricular tachyarrhythmias. *IEEE Engineering in Medicine and Biology*, 17(1):39–44, 1998.

[27] DA Coast, RM Stren, GG Cano, and SA Briller. An approach to cardiac arrhythmia analysis using hidden markov models. *IEEE Trans Biomed Eng*, 37:826–836, 1990.

[28] HA Guvenir, B Acar, G Demiroz, and A Cekin. A supervised learning algorithm for arrhythmia analysis. *Computers in Cardiology*, 24:433–436, 1997.

[29] SZ Xu, SZ Yi, NV Thakor, and ZZ Wang. Detecting ventricular tachycardia and fibrillation by complexity measure. *IEEE Trans Biomed Eng*, 46:548–555, 1999.

[30] SL Melo, LP Caloba, and J Nadal. Arrhythmia analysis using artificial neural network and decimated electrocardiographic data. *Comp Cardiol*, 27:73–76, 2000.

[31] S. Barro, M. Fernandez-Delgado, J.A. Vila-Sobrino, C.V. Regueiro, and E. Sanchez. Classifying multichannel ECG patterns with an adaptive neural network. *Engineering in Medicine and Biology Magazine*, 17(1):45–55, 1998.

[32] SW Chen. Two-stage discrimination of cardiac arrhythmias using a total least squares-based prony modeling algorithm. *IEEE Trans Biomed Eng*, 47:1317–1326, 2000.

[33] Dingfei Ge, Narayanan Srinivasan, and Shankar Krishnan. Cardiac arrhythmia classification using autoregressive modeling. *BioMedical Engineering OnLine*, 1(1):5, 2002.

[34] Owis M.I., Abou-Zied A.H., Youssef A.B., and Kadah Y.M. Study of features based on nonlinear dynamical modeling in ECG arrhythmia detection and classification. *IEEE Transactions on Biomedical Engineering*, 49(7):733–736, Jul, 2002.

[35] A. Wolf, J.B. Swift, H.L. Swinney, and J.A. Vastano. Determining lyapunov exponents from a time series. *Physica D*, 16D:285–317, 1985.

[36] Barro S, Ruiz R, Cabello D, and Mira J. Algorithmic sequential decision-making in the frequency domain for life threatening ventricular arrhythmias and imitative artefacts: a diagnostic system. *Journal of Biomededical Engineering*, 11(4):320–328, 1989.

[37] M. Koebbe and G. Mayer-Kress. Nonlinear modeling and forecasting. In *Proceedings of SFI Studies in the Science of Complexity*, volume XXI, pages 361–378, Redwood City, CA, 1992. M. Casdagli and S. Eubank, Addison-Wesley.

[38] T. Sauer. Time-series prediction by using delay-coordinate embedding. In *Time Series Prediction: Forecasting the Future and Understanding the Past. Santa Fe Institute Studies in the Sciences of Complexity*, pages 175–193, Santa Fe, NM, USA, 1993. A. Weigend and N. Gershenfeld, eds., Addison Wesley.

[39] A. Porta, S. Guzzetti, N. Montano, R. Furlan, M. Pagani, A. Malliani, and S. Cerutti. Entropy, entropy rate, and pattern classification as tools to typify complexity in short heart period variability series. *IEEE Transactions on Biomedical Engineering*, 48(11):1282–1291, 2001.

[40] A Short-Time Multifractal Approach for Arrhythmia Detection Based on Fuzzy Neural Network. Yang wang and yi-sheng zhu and nitish v. thakor and yu-hong xu. *IEEE Transactions on Biomedical Engineering*, 48(9):989, 2001.

[41] N. Maglaveras T. Stamkopoulos, K. Diamantaras. ECG Analysis Using Nonlinear PCA Neural Networks for Ischemia Detection. *IEEE Transactions on Signal Processing*, 46(11), 1998.

[42] al-Nashash H Khadra L, al-Fahoum AS. Detection of life-threatening cardiac arrhythmias using the wavelet transformation. *Med Biol Eng Comput*, 35(6):626–632, 1997.

[43] Irena Jekova and Vessela Krasteva. Comparison of five algorithms for the detection of ventricular fibrillation from the surface ECG. *Physiol. Meas.*, 21:429–439, 2000.

[44] B.U. Koehler, C. Hennig, and R. Orglmeister. The principles of software QRS detection. *IEEE Engineering in Medicine and Biology*, 21:42–57, 2002.

[45] Domanski MJ, Sakseena S, Epstein AE, Hallstrom AP, Brodsky MA, Kim S, Lancaster S, and Schron E. Relative effectiveness of the implantable cardioverter-defibrillator and antiarrhythmic drugs in patients with varying degrees of left ventricular dysfunction who have survived malignant ventricular arrhythmias. *Journal of the American College of Cardiology*, 34(4):1090–1095, 1999.

[46] Ivan A Dotsinsky and Todor V Stoyanov. Ventricular beat detection in single channel electrocardiograms. *Biomededical Engineering Online*, 3(3), 2004.

[47] Irena Jekova and Vessela Krasteva. Real time detection of ventricular fibrillation and tachycardia. *Physiological Measurement*, 25:1167–1178, 2004.

[48] Fotiadis DI Tsipouras MG. Automatic arrhythmia detection based on time and time-frequency analysis of heart rate variability. *Comput Methods Programs Biomed*, 74(2):95–108, 2004.

[49] S. Pincus. Approximate entropy (apen) as a complexity measure. *Chaos*, 5(1):110–117, 1995.

[50] M. C. Casdagli. Recurrence plots revisited. *Physica D*, 108:206, 1997.

[51] R. S. Savit R. L. Gilmore S. Roper M. C. Casdagli, L. D. Iasemidis and J. C. Sackellares. Non-linearity in invasive eeg recordings from patients with temporal lobe epilepsy. *Electroencephalogr. Clin. Neurophysiol*, 102:98, 1997. [52] G. I. Sanchez-Ortiz and D. Rueckert. .

[53] G.I. Sanchez-Ortiz, D. Rueckert, and P. Burger. Knowledge-based tensor anisotropic diffusion of cardiac MR images. *Medical Image Analysis*, 3(1):77–101, 1999.

[54] M. Lorenzo-Valdes, G. I. Sanchez-Ortiz, R. Mohiaddin, and D. Rueckert. Segmentation of 4D cardiac MR images using a probabilistic atlas and the EM algorithm. In *Sixth Int. Conf. on Medical Image Computing and ComputerAssisted Intervention (MICCAI'03)*, Lecture Notes in Computer Science, pages 440–450, Montreal, Canada, Nov 2003.

[55] R. Chandrashekara, R. Mohiaddin, and D. Rueckert. Analysis of 3D myocardial motion in tagged MR images using nonrigid image registration. *IEEE Transactions on Medical Imaging*, 23(10):1245–1250, 2004.