Integrated Software Suite for Magnetocardiographic Data Analysis

A Proposal Based on an Interactive Programming Environment

S. Comani^{1,2}, D. Mantini³, B. Merlino⁴, M. Reale⁵, S. Di Luzio^{1,2}, G. L. Romani^{1,2}

¹Department of Clinical Sciences and Bio-imaging, Section of Physical Sciences, Chieti University, Italy

²Institute of Advanced Biomedical Technologies (ITAB) – University Foundation “G. D’Annunzio”, Chieti, Italy

³Department of Informatics and Automation Engineering, Marche Polytechnic University, Ancona, Italy

⁴Institute of Radiology, Catholic University, Rome, Italy

⁵Department of Oncology and Neuroscience, Chieti University, Italy

Summary

Objectives: This paper describes an integrated software suite (ISS) for the processing of magnetocardiographic (MCG) recordings obtained with super-conducting multi-channel systems having different characteristics. We aimed to develop a highly flexible suite including toolboxes for current MCG applications, organized consistently with an open architecture that allows function integrations and upgrades with minimal modifications; the suite was designed for the compliance not only of physicists and engineers but also of physicians, who have a different professional profile and are accustomed to retrieve information in different ways.

Methods: The MCG-ISS was designed to work with all common graphical user interface operative systems. MATLAB was chosen as the interactive programming environment (IPE), and the software was developed to achieve usability, interactivity, reliability, modularity, expansibility, interoperability, adaptability and graphics style tailoring. Three users, already experienced in MCG data analysis, have intensively tested MCG-ISS for six months. A great amount of MCG data on normal subjects and patients was used to assess software performances in terms of user compliance and confidence and total analysis time.

Results: The proposed suite is an all-in-one analysis tool that succeeded in speeding MCG data analysis up to about 55% with respect to standard reference routines; it consequently enhanced analysis performance and user compliance.

Conclusions: Those results, together with the MCG-ISS advantage of being independent on the acquisition system, suggest that software suites like the proposed one could uphold a wider diffusion of MCG as a diagnostic tool in the clinical setting.

Keywords

Integrated software suite (ISS), interactive programming environment (IPE), object-oriented programming, magnetocardiographic data analysis, user-machine interaction.

Methods Inf Med 2005; 44: 114–23

1. Introduction

Magnetocardiography (MCG) is a completely non-invasive technique that allows detecting the variations of the extremely weak magnetic fields associated with the electrical currents flowing through the myocardium during the cardiac cycle without any contact with the patient's body [1, 2]. Dedicated and sophisticated instrumentation using super-conducting technology can accurately quantify the magnetic field variations produced by the electrical activity of the heart, which, in the clinical practice, is monitored by means of electrocardiography (ECG) [1, 2]. Since the first magnetocardiographic measurements, dating back to 1967 [3], MCG has gained increasing attention due to its usefulness in many clinical applications, especially because the absence of electrodes contact, consequent minimization of artifacts from muscles and easy availability of mapping techniques are extremely valuable in cardiac assessment. Current and potential MCG applications are the evaluation of ischaemic cardiac disease [4–10], the localization of cardiac arrhythmic foci (pre-excitation syndromes, ventricular and atrial tachycardias) [11–16], the assessment of the effects of physiologically and/or pharmacologically induced cardiac stress [17–20], an early detection of ventricular hypertrophy [2, 5, 21, 22], prolonged QT syndrome [23–27], and support in the assessment of sudden cardiac death risk [9, 17, 28–30]. Finally, MCG has proven to be useful for monitoring and quantitatively assessing fetal cardiac activity, mainly during advancing gestation when ECG techniques become inadequate [31–40].

The actual MCG evolving role from an experimental to a clinical tool has been boosted by a lot of basic research but also by the progressive improvement of cryogenic and super-conductors technology leading to the development of multi-channel MCG systems, composed of up to 151 channels, located in shielded rooms and able to record high temporal and spatial resolution signals [1].

The major drawback in the use of multi-channel MCG systems has been the significant increase of the amount of data gathered during each recording session; it largely depends on both the system characteristics and the recording procedure [1], but in any case it implies heavy processing of the original raw data with the consequent need for computational units highly-performing and supplied with dedicated software.

During the last decade MCG analysis has been changing from a simple visualization of few recorded traces to more complex techniques allowing the simultaneous drawing of multiple signals, the calculation of cardiac intervals variability, the automatic computation of field maps and/or indices for the assessment of cardiac function.

Moreover, the changing scenarios of MCG applications from basic research to clinical environment have seen different users approaching the analysis of MCG recordings, not only physicists and engineers but also cardiologists and gynecologists, each with a specific background and peculiar interests, aiming at retrieving information in different ways. That situation has led to the development of multiple software modules for MCG visualization and analysis, driven by specific needs but with-

out integration nor interoperability and standardization.

A comprehensive tool for MCG data processing would be highly desirable, due to the recent evolution of the technique and in the effort of supporting its use in the clinical setting. Particularly important would be the availability of a MCG-dedicated software suitable to:

- 1) read and manage MCG data independently on the number of traces, format, size or characteristics of the acquisition system;
- 2) provide a “one-stop-shop” solution for all common processing procedures and be sufficiently open to easily include future developments and implementations;
- 3) provide display and printing of detailed reports from MCG analysis;
- 4) include tools finalized to the extraction of parameters and/or data according to the professional profile of the single user (basic researcher, physician).

We propose an integrated software suite for MCG data analysis (MCG-ISS), built with the specific purpose of using data with different formats, highly flexible and programmable, including several toolboxes for most current MCG applications, organized according to an open architecture and designed for the accomplishment of a pleasant and user-friendly interface for both researchers and physicians [41-43].

2. Materials and Methods

2.1 MCG Signals

Nowadays MCG signals are generally recorded by means of several channels (up to 151) with a sampling frequency that can be up to 10 kHz. Our software suite validation has been performed on data acquired with a multi-channel MCG system located inside a shielded room to reduce the influence of environmental magnetic fields; a standard MCG data set consisted in 55 recordings obtained with 55 low-temperature dc-Superconducting Quantum Interference Device (dc-SQUID) integrated magnetometers kept at liquid helium temperature inside a

cylindrical cryostat, homogeneously distributed on a circular surface (sensing plane) at few centimeters from the cryostat bottom. Raw data were sampled at 1 kHz and digitally band-pass filtered from 0.016 Hz to 250.0 Hz. MCG signal intensity could vary from hundreds of fT to some tens of pT [44]. Three reference electrical traces were generally recorded during each MCG session. Depending on the acquisition parameters, a recording of five minutes produced a data set ranging from 50 to 150 MB, on which post-processing took place after acquisition.

2.2 MCG Analysis

Four different classes of MCG analysis and correspondent software modules have been considered on the basis of both current experience and accepted modalities for MCG processing according to the cited literature. The following analysis groups have been identified: a) *qualitative analysis*, including modules dedicated to MCG visualization in various arrangements; b) *quantitative analysis*, comprising tools for time-domain and frequency-domain analysis, different scrolling options, measurements, scaling, zooming, etc.; c) *raw data basic processing*, comprising averaging, filtering, etc.; d) *modeling*, including isofield mapping, source localization through inverse problem solution, parameterization for MR-MCG matching, etc.

Specific modules dedicated to clinically-oriented analysis, such as arrhythmias detection, cardiac hypertrophy and sudden cardiac death risk assessment, heart rate variability analysis, fetal MCG analysis and so on, have been developed and implemented by including one or more functions of the above listed classes. Data display and printing have been arranged according to notations and modalities currently used in clinical ECG practice, for better compliance and acceptance by clinicians (cardiologists, gynecologists). However, scientific notation and symbolism have alternatively been assured, in order to provide cross-usability.

2.3 Software Design and Programming

MATLAB software (MathWorks, USA) has been chosen as the interactive programming environment (IPE). At the beginning release 5.0.0 was used, with a progressive implementation up to version 6.5.1. MATLAB was preferred for its features of integrating mathematical computing, visualization tools and powerful programming language, as well as for its open architecture.

A flowchart diagram describing the architecture framework of the proposed MCG-ISS is given in Figure 1.

Software implementation has been focused on the following key requirements:

- *usability*: full control of the processing steps through easy-to-use commands and control panels;
- *interactivity*: great flexibility in the configuration of parameters, although some default values are suggested by the program;
- *reliability*: before being linked to the software suite, tools have been previously validated according to the literature; tools for clinical analysis were implemented according to the suggestions and expectations of the clinicians involved in our laboratory research;
- *modularity*: the principal interface was in charge of loading, visualizing and saving data, but all processing was entrusted in external toolboxes;
- *expansibility*: new toolboxes could be added without restrictions;
- *interoperability*: data could be exchanged among toolboxes, allowing the development of more complex assignments in an integrated environment;
- *adaptability*: MCG data acquired with other systems or pre-processed with other software could be loaded and processed, due to the flexible configuration of parameters;
- *graphics style tailoring*: default parameters were preset, but fonts, colors and labels could be changed.

Reference literature has been largely used for the development of each module [17-22, 34-38], with some integration based on the experience of our group, especially regard-

Fig. 1 Overview of the MCG-ISS architecture. Software suite applications are divided into two layers: 1) a general tools layer, providing wide-ranging data processing and elaboration tools, and 2) the clinical tools layer, which uses data gathered from other layers and embeds specific modules dedicated to clinical applications. Both layers communicate with a user interface, which, by means of a visualization tool and a data manager, provides the end users with access to all applications. A tool generator is devoted to addition of new modules to the general and clinical tools layers; it allows accessing common routines and software settings so that a programmer can create new applications by defining modules with either dedicated or shared routines. SCDRA: sudden cardiac death risk assessment; TD: time domain; FD: frequency domain.

ing recently published or in publication contribution on fetal MCG [39, 40, 45].

Three users (one cardiologist, one technical assistant and one programmer), each with at least six months experience in MCG data analysis, performed intensive testing following software implementation and programming. The test period lasted for six months, and a total of 136 MCG recordings from control subjects and 143 MCG recordings from patients, covering an age range from 18 to 65 years, were processed using both the standard set of routines developed during the last eight years and already used in our laboratory and the MCG-ISS. An average learning time of three to six hours was applied to each user before starting the assessment phase, depending on his/her professional profile. The experimental setup regarded the basic research and clinical trials carried on in our laboratory. Parameters used for software assessment were semi-quantitative (user compliance and confidence, classified according to the fol-

lowing grading scale: 1 – poor, 2 – sufficient, 3 – good, 4 – very good) and quantitative (overall time of analysis).

The software suite was developed and tested for internal use, but it will be distributed under the General Public License (GPL) to other research groups, so as to perform a more comprehensive test and to have their feedback contributions to further improve MCG-ISS.

3. Results

The final software release includes modules allowing complete analysis of MCG traces from different multi-channel systems, commonly used procedures in MCG evaluation and new analysis packages developed by our group or elsewhere.

MCG signals acquired with different multi-channel systems, each with a specific data format and channel spatial distribution, can be analyzed. Before being loaded in our

software suite, all formats are converted to a .RAW format used to identify data stored as they have been recorded before any processing. By averaging .RAW files, new data files are produced and stored in .AVE format. The averaging process is based on the automatic categorization of QRS complexes. The instants corresponding to selected R peaks act as trigger points used to set the time window for beats alignment and averaging [46, 47]. The *Control Panel* is integrated in the main interface; at present it allows entering five modules to perform various processing functions:

- 1) MCG visualization;
- 2) time domain and frequency domain analysis;
- 3) raw data processing (averaging, filtering, smoothing, ...);
- 4) modeling (dipole direction, integral maps, ...);
- 5) clinically-oriented modules (sudden cardiac death risk assessment – SCDRA, cardiac hypertrophy assessment, fetal MCG analysis, ...).

The main menu of the MCG-ISS is shown in Figure 2. Data type can be chosen from a menu in the *Control Panel* and MCG data can be loaded in the shared memory and visualized. Raw data processing functions are available through menu selections. When .RAW files are selected, only a few beats can be displayed on the screen, whereas .AVE files can be shown entirely. In this window the MCG signals are displayed in the corresponding sensor positions, and labeled with the same ID (Fig. 2). At the left bottom side of this window, the average electrical signals from the three leads recorded during MCG acquisition are also displayed.

Several actions, included in the qualitative and quantitative analysis groups, can be performed on loaded data:

- time and intensity intervals can be modified with buttons placed on the right bottom corner of the window;
- each trace can be enlarged and/or displayed with the adjacent channels by clicking on the right mouse button;
- loaded .RAW files or .AVE files can be scrolled to check recordings reliability before data processing;

- traces that look unreliable can be excluded from the analysis (excluded traces are highlighted to be immediately identifiable);
- signals can also be arranged in vertical order (modality “expanded”) or gathered together (modality “collapsed”) (useful to check the timing of simultaneous cardiac events throughout recordings);
- time and signal intensity scales can be changed, traces can be amplified, and a signal value pop-up window is available by clicking on the right mouse button (function available in a frame on the right bottom side of the window).

Modeling functions include several tools for 2D or 3D management of MCG data. The *Maps Correlation* module has two major features: isofield map reconstructions and estimation of correlation coefficients between subsequent field distributions along the average cardiac cycles at preset time intervals. These functions are particularly useful for the assessment of ventricular repolarization abnormalities – not revealed with conventional ECG – are expressed as uneven changes of the field distribution throughout the ST segment [22, 48, 49]. An automated module devoted to evaluate the stability of ventricular repolarization can be based on the computation of subsequent field maps calculated during the interval corresponding to the ST segment, which can be marked on a reference MCG trace displayed in the frame on the right bottom side of the window. Isofield maps are produced using the field intensity in all averaged magnetic signals at a given time instant, and can be calculated every millisecond as a consequence of the acquisition sampling frequency. A source code listing of the isofield mapping function is shown in Figure 3.

Furthermore, the average value of 2-D correlation coefficients calculated between subsequent isofield maps during ventricular repolarization can be used to quantify the degree of those abnormalities [22, 48, 49]. The total number of utilized field maps can be chosen on the basis of both ST duration and time interval between subsequent maps (10 ms, 20 ms or 25 ms). The result is an index, normalized to the total number of

Fig. 2 Example layout of MCG-ISS *Main Interface* with two average data sets recorded with different acquisition systems: the upper panel refers to MCG recordings performed with the 55-channel system installed at our Institute, whereas the lower panel refers to MCG recordings performed with a 36-channel system installed at the Biomagnetism Research Center of the Catholic University of the Sacred Heart in Rome, Italy. Averaged magnetocardiograms are arranged following the sensing magnetometers distribution inside the cryostat; each trace is labeled with the identification number of the corresponding acquisition channel. In case an acquisition channel was not working properly, such as channel MAG_2 in the upper panel, the corresponding signal would be disregarded in all subsequent processing. The *Control Panel*, from which data can be loaded and processing tools started, is on the right upper side of the window; ECG traces acquired during the MCG session are shown in the left lower corner.

maps, which can range from -1 to 1. Based on previously published work [22, 48, 49] and on our experience, values greater than 0.90 indicate a high correlation level among all maps, which means a good stability level during ventricular repolarization. The ma-

trix of correlation coefficients among all maps can be visualized in a pop-up window (Fig. 4).

Another important routine relates to the estimate of the equivalent source for MCG fields (*Dipole Modeling*). This toolbox aims

Fig. 3 Pseudo-code representation of the source code used in MCG-ISS to compute the isofield maps. The model used to represent the source of cardiac electrical activation is the Equivalent Current Dipole (ECD). Comment lines are written in italics.

Fig. 4 Layout of *Maps Correlation* module. The isofield map shown in the main frame corresponds to the instant chosen as starting point for the calculation of the 2-D correlation coefficients: all instants for which maps are calculated are marked on the average beat in the frame at the lower right hand corner. The number of maps used, selected time interval and normalized correlation coefficient are shown in the *Correlation* frame at the upper right hand corner. By pushing the "matrix correlation" button a pop-up window is activated where details on the maps correlation coefficients, modules and variances are given.

at estimating the effectiveness of the Equivalent Current Dipole (ECD) model to represent the electrical cardiac source generating the field distribution recorded at a given instant during the average heartbeat. This procedure can be useful when arrhythmogenic foci or accessory pathways have to be local-

ized for clinical purposes [50-52]. A source code listing of this module is shown in Figure 5. The magnetic field map produced with .AVE files is compared with the field map generated by a current dipole according to the ECD model, based on infinite homogeneous half-space. The sensor posi-

tions are shown on the map, and excluded channels are marked with an "x". The instant at which the field map is calculated is selected using a frame on the bottom right of the window where one or more average beats are displayed upon selection. By pressing the button "Suggest" in the frame on the upper right side of the window, the ECD parameters that best fit the experimental map are calculated. Once the ECD position (x, y, z), direction and intensity are given, the correlation between experimental and theoretical maps is estimated: high correlation values ($r > 0.90$) indicate that the model is suitable to represent the electrical cardiac activation (Fig. 6). In addition, MCG functional localizations of the equivalent source of cardiac activation are suited to be integrated with anatomical MR cardiac volume reconstructions [48]. This coupling can be performed using a portable reference system positioned on the patient's chest and permitting coordinate conversion between MCG and MRI measurements.

Useful for the assessment of cardiac hypertrophy is the calculation of the Electrical Cardiac Axis (ECA) direction: it can be assessed for a chosen instant of the average beat. The window is arranged similarly to that for Dipole Modeling (Fig. 7): the lower right frame shows the average beats from which the time instant can be selected. The calculation of the angular deflection of ECA is performed when activating the option "Deflection angle" of the top right panel; the ECA orientation is then shown on the magnetic field distribution. Moreover, by clicking on the map the user can activate a pop-up window that gives the ECA direction in the clinical and physical notations (clockwise and counterclockwise degrees from the positive x-axis respectively). In both cases deflections are grouped in four quadrants that are named according to the clinical and physical standards (Fig. 7).

In order to integrate map analysis for cardiac hypertrophy assessment, a module allowing the computation of *Integral Maps* for different cardiac intervals (QRS, T wave etc.) is available; several *Integral indices* are calculated from the power integrals of the averaged signals during selected intervals for all channels according to previously published algorithms [21, 22] (Fig. 8). The

intervals of interest can be selected directly on the average traces displayed in the main frame of the window; tags can be moved, cancelled, loaded and saved. A normalization procedure is automatically loaded before the calculation of integral maps. This procedure is based on the ECD model, the parameters of which are visualized in the upper right window. By pushing on the “view indexes” button, the integral maps for the selected intervals are calculated and summarized in a pop-up window (Fig. 8).

As an example of a clinically oriented module, the *Fetal MCG analysis* routine is described. This toolbox is dedicated to the study of fetal MCG traces and uses .RAW files that are fetal MCG recordings containing a mixture of maternal and fetal signals. Before being processed, fetal MCG recordings are visualized and scrolled to eventually exclude from analysis those intervals during which too large or too rapid drifts occurred because of uncontrolled fetal movements. Several recordings can be loaded and used for fetal trace reconstruction and processing. The separation of maternal and fetal signals is accomplished by loading one of the two available procedures through a pop-up window that appears when the toolbox is loaded. Both separation procedures work in the time domain; one technique is based on the adaptive maternal beat subtraction (AMBS) and is a deterministic method triggered with a maternal ECG, whereas the other method is based upon Independent Component Analysis (ICA) and uses statistical assumptions and neural networks [45]. Since both procedures take a few minutes to reconstruct the fetal signal, a time slide bar appears in the meantime. The reconstructed fetal traces are displayed in a new window similar to that for *Channel Scrolling*. Signals can be scaled in time and amplitude with control buttons placed on the right bottom side of the window. A trace smoothing option is provided to reduce residual noise and to ease the identification of cardiac phases (P, Q, R, S, T waves). The source code for fetal MCG smoothing is given in Figure 9. Interval analysis can be performed after labeling the onset and offset of each cardiac wave with tags on all beats of the entire traces using the scrolling option; the corresponding time instants can be moved

Equivalent Current Dipole Pseudo-code Representation

```
function [dipole,angle,intensity,Bz_max_out] = suggest_dipole(method)

hnd = get(gcf,'Userdata');
time = str2num(get(hnd,'t_edit','String'));
active_squids = find(mag(0:54,'active')==1)-1;
position_squid_mm = mag(active_squids,'position_mm');
Bz = mag(active_squids,time);

asx = -120:2:120;
[XI,YI] = meshgrid(asx,asx);
Bz_map =
griddata(position_squid_mm(:,1),position_squid_mm(:,2),Bz,XI,YI,'cubic');

[Bz_min.x, Bz_min.y, Bz_min.val] = minZ(XI,YI,Bz_map);
[Bz_max.x, Bz_max.y, Bz_max.val] = maxZ(XI,YI,Bz_map);
Bz_max_out = Bz_max.val;

min_max_vector = [Bz_max.x Bz_max.y] - [ Bz_min.x Bz_min.y ] ;

dipole = [round((Bz_min.x+Bz_max.x)/2),...
round((Bz_min.y+Bz_max.y)/2),...
round(-norm(min_max_vector)/sqrt(2)) ];

alfa = 180/pi * ( atan2( min_max_vector(2) , min_max_vector(1) ) );
if alfa < 0
    alfa=alfa+360;
end
angle = round(alfa) + 90;

intensity = mean([Bz_max.val -Bz_min.val])*dipole(3)^2;
```

Fig. 5 Pseudo-code representation of the source code used in MCG-ISS to calculate the position, orientation and intensity of the Equivalent Current Dipole (ECD). Comment lines are written in *italics*.

Fig. 6 Layout of the *Dipole Modeling* function. The magnetic isofield map shown in the main frame corresponds to the instant indicated with a circle on the average beat in the frame at the lower right hand corner. The Equivalent Current Dipole position (x, y, z), direction and intensity, displayed in the *Dipole frame* at the upper right hand corner, are calculated after pushing the “Suggest” button. The correlation coefficient between the experimental and theoretical maps is estimated and shown in the same frame.

by dragging the right mouse button above the trace, saved for further analysis, loaded and cancelled. At the end of this procedure the duration and variability of all tagged in-

tervals are calculated and displayed in a pop-up window (Fig. 10).

This module includes other applicative functions, such as the Heart Rate Variability

analysis that allows calculating a series of parameters in the time and frequency domains following the European Guidelines [53]. The used architecture allows for all modules to be open: new functions can be added without restrictions to improve or expand analysis potentialities.

The results from the testing by all users are summarized in Table 1. In all cases the testing variables have provided better figures for the MCG-ISS than for the separated routines traditionally used in laboratory. Compliance, confidence and overall time of analysis were better with MCG-ISS for all users at the selected significance level ($p < 0.001$). Particularly remarkable is the reduction of analysis time, which underwent an average decrease greater than 50% also for the clinician.

4. Discussion

Diagnostic techniques naturally evolve from the first experimental stages, when data analysis procedures are proposed and developed in research laboratories with the implementation of new routines dedicated to specific tasks, to the final step of technique assessment in the clinical environment. The latter phase requires that the standardization process has been completed, the analysis procedures have been set up, dedicated software (suitable for data acquired with different systems) has been developed and end-users (clinicians and/or specialized technicians) have become confident in handling MCG data.

Although relatively old, MCG is still in the middle of this evolution; it is becoming more and more trusted and widespread in the clinical environment, but still it is somehow linked to research laboratories and specific acquisition systems, hence lacking complete standardization.

Our work aimed specifically at developing an application providing full integration of well-established MCG analysis procedures, still remaining open to new toolbox additions, speeding up the data processing and improving their clinical presentation. Our final target was to overcome the most common problems that limit a widespread

Fig. 7 Example of the calculation of the Electrical Cardiac Axis (ECA) direction. The picture refers to a control volunteer. The isofield magnetic map and corresponding ECA orientation are calculated at the instant indicated by the vertical line drawn on the overlapped average beats in the frame at the lower right hand corner; ECA parameters are shown in the "Direction" frame at the upper right hand corner. ECA orientation is drawn on the main frame, but also provided in a pop-up window where both physical and clinical notations are used to indicate the deflection angles and quadrants.

Fig. 8 Layout of the module for the computation of *Integral Maps*. An example of intervals tagging is shown in the main frame where average magnetic traces are drawn in *butterfly* modality. By pushing the "view indexes" button at the lower right hand corner a pop-up window is activated where the calculated *Integral indices* are shown.

acceptance of MCG in a hospital setting, especially when MCG is compared to other competitive techniques, such as ECG, already familiar to cardiologists.

The development of an integrated software suite for all needs in MCG is a basic requirement and corresponds to what is commonly available for other diagnostic techniques. Our experience showed that this basic condition for MCG data processing has now become feasible through the implementation of the proposed MCG-ISS with a significant improvement in MCG analysis independently on the professional profile of the end-user, as summarized in Table 1. The advantages have been described and are mainly intuitive.

When compared to other commercial software for MCG data analysis, MCG-ISS has a number of different characteristics. It certainly has similar tools for basic signal treatment and clinical diagnosis support, such as signal averaging and display. Nonetheless, commercial software packages are usually sold together with an acquisition system; hence, they cannot be customized in terms of data format and/or sensor configuration. The more efficient C language is generally used to optimize memory and computation times, but different versions have to be used depending on the adopted Operating System (OS). Commercial software packages are closed, preventing the user from accessing the source code, and consequently hampering the implementation of new processing tools on the same platform.

On the other hand, MCG-ISS was not developed as a fixed, static architecture, but, MCG still being investigational, we aimed at developing an open, scalable, modular environment able to integrate several signal processing functions, some belonging to the state-of-the-art, others newly developed, such as the use of Independent Component Analysis (ICA) for fetal signals reconstruction [45, 47]. MCG-ISS was sufficiently stable for all described modules and it could be customized in terms of data formats and channel numbers and positions (see Fig. 2). MCG-ISS was also open to integrations and upgrades with minimal adjustments in the original architecture, still ensuring a substantially homogeneous framework for easy user-compliance.

Fetal MCG Smoothing Pseudo-code Representation

```
function [smoothed_trace_out]=smoothing(t_in,peaks,start_qrs,stop_qrs)

for i=1:length(peaks)
    beg=start_qrs(i);           position of i-th Q tag
    fin=stop_qrs(i);           position of i-th S tag
    values = [beg:fin];         i-th QRS complex interval
    aux = [beg fin];            i-th QRS complex boundaries
    aux_val = interp1(aux,t_in(aux),values,'linear');    linear interpolation
    trace_no_qrs(values)=aux_val;    QRS complexes elimination in the trace
end

smoothed_no_qrs=smooth_trace(trace_no_qrs,'kaiser',50,3);    full trace smoothing
en_in=std(trace_no_qrs);
en_smoothed=std(smoothed_no_qrs);
smoothed_trace=smoothed_no_qrs*(en_in/en_smoothed);    amplitude scale correction

for i=1:length(peaks)           QRS complexes restoring
    smoothed_trace(start_qrs(i):stop_qrs(i))=t_in(start_qrs(i):stop_qrs(i));
end
```

Fig. 9 Pseudo-code representation of the source code used in MCG-ISS to smooth raw fetal signals reconstructed from fMCG recordings either with AMBS or with ICA. Comment lines are written in italics.

Fig. 10 Layout of the *Fetal MCG analysis* routine. Only selected fetal traces are shown in the main frame: in this example there are two reconstructed fetal signals (MAG_36 and MAG_38), and corresponding smoothed traces (MAG_35 and MAG_34), on which time intervals have been tagged for variability analysis. Data refer to a healthy fetus at 36-week gestation. Time intervals variability analysis is performed by pushing on the "Beat Variability" button at the right of the window; results are listed in a pop-up window.

MATLAB was used as the programming environment because it is dedicated to scientific programming and suitable for integration within research groups, but also because of the large number of available libraries. Of course MATLAB is not a programming language, but a collection of rou-

ties; it is therefore affected by a relatively slower performance and is not suited for the implementation of a commercial application, but our goal was rather to create and test an integrated solution for MCG data management, deferring the efforts for a commercial software solution after the vali-

Table 1 Performance of the MCG-ISS in comparison to standard reference routines as assessed by different users. Parameters are semi-quantitative (Compliance and Confidence) and quantitative (Analysis Overall Time). Standard deviations are given in parenthesis. Percent performance variations of MCG-ISS with respect to standard reference routines are also given. Statistical significance was set for $p < 0.001$. All figures were significant at the chosen level. Tc and Pr performed their testing on the control group (136 subjects), whereas Ph on the patient group (143 patients).

	Compliance*			Confidence*			Analysis Time**		
	Tc	Pr	Ph	Tc	Pr	Ph	Tc	Pr	Ph
Reference routines (StDev)	2.13 (1.01)	2.34 (1.08)	1.60 (0.76)	2.25 (0.99)	3.10 (0.86)	2.12 (0.95)	125.95 (31.81)	107.20 (25.35)	136.83 (32.16)
MCG-ISS (StDev)	3.20 (0.93)	3.19 (0.91)	3.34 (0.71)	3.28 (0.87)	3.32 (0.82)	3.45 (0.58)	55.65 (14.33)	52.43 (13.76)	62.15 (19.12)
MCG-ISS performance variation (%) with respect to Reference routines	50.2	36.3	108.8	45.8	7.1	62.7	-55.8	-51.1	-54.6
Statistics used	WT	WT	WT	WT	WT	WT	PTT	PTT	PTT

* defined as: 1 – poor; 2 – sufficient; 3 – good; 4 – very good;
 ** time expressed in minutes.
 Tc: technician; Pr: programmer; Ph: physician (cardiologist); WT: Wilcoxon Test; PTT: Paired T Test.

dation phase of the software suite had been properly completed.

We estimated that MATLAB was probably the best available solution to achieve our target, and in fact the cited drawbacks have been largely compensated by the wide availability of libraries and the high flexibility provided. We can therefore state that MATLAB has substantially satisfied the initial requirements, giving the software the expected support.

The fulfillment of the needs of both non-physicians (programmers, physicists, engineers) and physicians (cardiologists, gynecologists) within a single integrated software suite is one of the most important achievements of the proposed MCG-ISS.

In our experience, traditional single software packages for MCG data treatment were inadequate for clinical use also because of unpleasant user interfaces and data handling; in fact, they have limited the use of MCG in a hospital setting for a long time, especially when other techniques, well-established and easier to understand, could be used as an alternative (ECG).

Our major effort was to provide an instrument comfortable for cardiologists and other clinicians willing to use MCG; the achievement of this target represents one of the most valuable advantages of this software suite, and it should be considered as a starting point for further development and integration with other research groups' requirements. Particularly significant is the reduction of the overall analysis time, which

was extremely high also for the clinical user (see Table 1), who had less confidence with software tools and in the meantime had the more difficult task of analyzing MCG data in the perspective of a clinical application. In the light of the above considerations, the proposed MCG-ISS is reasonably expected to uphold the use of MCG in a clinical context, where the time factor is much more critical than in a research laboratory.

5. Conclusions

The community of MCG users, both researchers and clinicians, is increasing worldwide. They ask for reliable, easy-to-use and fast systems to record and process MCG data. The true challenge of MCG is nowadays to demonstrate its usefulness and competitiveness in a clinical setting. Many efforts are presently being made to develop new acquisition systems working in unshielded environments and therefore suitable for bedside recordings in a hospital environment. Although the availability of user-friendly interfaces for data handling is not the only limiting factor for a regular clinical use of MCG, software suites like the one presented in this paper might give a contribution to abridge the gap between the use of MCG for research purposes only and its routine employment as a diagnostic tool.

References

1. Tavarozzi I, Comani S, Del Gratta C, et al. Magnetocardiography: current status and perspectives. Part I: Physical principles and instrumentation. *Ital Heart J* 2002; 3: 75-85.
2. Tavarozzi I, Comani S, Del Gratta C, et al. Magnetocardiography: current status and perspectives. Part II: Clinical applications. *Ital Heart J* 2002; 3: 151-65.
3. Tumanovskii M, Safonov I, Provotorov V. Certain aspects of the clinical application of magnetocardiography. *Kardiologiya* 1967; 7: 70-5.
4. Pesola K, Hanninen H, Lauerma K. Current density estimation on left ventricular epicardium: a potential method for ischemia localization. *Biomed Tech* 1999; 44: 143-6.
5. Comani S, Merlino B, Di Luzio S et al. Magnetic map analysis during ventricular repolarization to differentiate between normal subject and patients affected by cardiac hypertrophy. *Phys Med* 2001; 17: 9-15.
6. Shiono J, Horigome H, Matsui A, et al. Evaluation of myocardial ischemia in Kawasaki disease using an isointegral map on magnetocardiogram. *Pacing Clin Electrophysiol*. 2002; 25: 915-21.
7. Hanninen H, Takala P, Korhonen P, et al. Features of ST segment and T-wave in exercise-induced myocardial ischemia evaluated with multichannel magnetocardiography. *Ann Med* 2002; 34: 120-29.
8. Hailer B, Chaikovsky I, Auth-Eisernitz S, Schafer H, Steinberg F, Gronemeyer DH. Magnetocardiography in coronary artery disease with a new system in an unshielded setting. *Clin Cardiol* 2003; 26: 465-71.
9. Van Leeuwen P, Hailer B, Lange S, Gronemeyer D. Spatial distribution of repolarization times in patients with coronary artery disease. *Pacing Clin Electrophysiol*. 2003; 26: 1706-14.
10. Kanzaki H, Nakatani S, Kandori A, Tsukada K, Miyatake K. A new screening method to diagnose coronary artery disease using multichannel magnetocardiogram and simple exercise. *Basic Res Cardiol* 2003; 98: 124-32.

11. Fenici R, Melillo M. Biomagnetic study of cardiac arrhythmias. *Clin Phys Physiol Meas* 1991; 12: A5-A10.
12. Weissmuller P, Abraham-Fuchs K, Schneider S, Richter P, Kochs M, Hombach V. Magnetocardiographic non invasive localizations of accessory pathways in the Wolf-Parkinson-White syndrome by a multichannel system. *Eur Heart J* 1992; 13: 616-22.
13. Oeff M, Burghoff M. Magnetocardiographic localization of the origin of ventricular ectopic beats. *Pacing Clin Electrophysiol* 1994; 17: 517-22.
14. Korhonen P, Montonen J, Makijarvi M, Katila T, Nieminen MS, Toivonen L. Late fields of the magnetocardiographic QRS complex as indicator of propensity to sustained ventricular tachycardia after myocardial infarction. *J Cardiovasc Electrophysiol* 2000; 11: 413-20.
15. Korhonen P, Pesola K, Jarvinen A, Makijarvi M, Katila T, Toivonen L. Relation of magnetocardiographic arrhythmia risk parameters to delayed ventricular conduction in postinfarction ventricular tachycardia. *Pacing Clin Electrophysiol* 2002; 25: 1339-45.
16. Fenici R, Brisinda D, Nenonen J, Fenici P. Non-invasive study of ventricular preexcitation using multichannel magnetocardiography. *Pacing Clin Electrophysiol* 2003; 26: 431-5.
17. Brockmeier MD, Comani S, Ern SN, Di Luzio S, Pasquarelli A, Romani GL. Magnetocardiography and exercise test. *J Electrophysiol* 1994; 27: 137-42.
18. Brockmeier K, Schmitz L, Bobadilla Chavez JDJ, et al. Magnetocardiography and 32-lead potential mapping: repolarization in normal subjects during pharmacologically induced stress. *J Cardiovasc Electrophysiol* 1997; 8: 615-26.
19. Takala P, Hanninen H, Montone J, et al. Magnetocardiographic and electrocardiographic exercise mapping in healthy subjects. *Ann Biomed Eng* 2001; 29: 501-9.
20. Hanninen H, Takala P, Korhonen P, et al. Features of ST segment and T-wave in exercise-induced myocardial ischemia evaluated with multichannel magnetocardiography. *Ann Med* 2002; 34: 120-9.
21. Karvonen M, Oikarinen L, Takala P, et al. Magnetocardiographic indices of left ventricular hypertrophy. *J Hypertens* 2002; 20: 2285-92.
22. Comani S, Gallina S, Lagatta A, et al. Concentric remodeling detection by magnetocardiography in patients with recent-onset arterial hypertension. *Pacing Clin Electrophysiol* 2004; 27: 709-18.
23. Schwartz PJ, Wolf S. QT interval prolongation as a predictor of sudden death in patients with myocardial infarction. *Circulation* 1978; 57: 1074-7.
24. Oikarinen L, Paavola M, Montonen J, et al. Magnetocardiographic QT interval dispersion in post-myocardial infarction patients with sustained ventricular tachycardia: validation of automated QT measurements. *Pacing Clin Electrophysiol* 1998; 21: 1934-42.
25. Giesler T, Pohle K, Flug M, et al. Detecting the spatial distribution of QT dispersion in bipolar magnetocardiography with various myocardial infarct sites. *Biomed Tech* 1998; 43: 230-1.
26. Menendez T, Achenbach S, Beinder E, et al. Prenatal diagnosis of QT prolongation by magnetocardiography. *Pacing Clin Electrophysiol* 2000; 23: 1305-7.
27. Shabalina A, Tret'jakova T, Kuznetsov A, Motorin S, Golyshev N. Comparative analysis of parameters of corrected and uncorrected QT-interval dispersion of magnetoelectrocardiography and isomagnetic maps in patients with ischemic heart disease. *Kardiologiia* 2002; 42: 20-3.
28. Comani S, Brockmeier K, Del Gratta C, et al. Magnetocardiography in healthy subjects: validation of "risk analysis". In: Hoke M et al. (eds). *Biomagnetism: Clinical aspects*. Amsterdam. Excerpta Medica 1992; pp 531-4.
29. Comani S, Merlino B, Brockmeier K et al. Role of magnetocardiography in sudden cardiac death risk evaluation: significance of RS score in a normal population. In: Baumgartner C et al. (eds). *Biomagnetism: Fundamental Research and Clinical Applications*. Amsterdam. IOS 1995; pp 612-4.
30. Korhonen P, Tierala I, Simelius K, et al. Late QRS activity in signal-averaged magnetocardiography, body surface potential mapping, and orthogonal ECG in postinfarction ventricular tachycardia patients. *Ann Noninvasive Electrocardiol* 2002; 7: 389-98.
31. Menendez T, Achenbach S, Moshage W, et al. Prenatal recording of fetal heart action with magnetocardiography. *Z Kardiol* 1998; 87: 111-8.
32. Van Leeuwen P, Hailer B, Bader W et al. Magnetocardiography in the diagnosis of fetal arrhythmia. *Br J Obstet Gynaecol* 1999; 106: 1200-8.
33. Horigome H, Takahashi MI, Asaka M, Shigemitsu S, Kandori A, Tsukada K. Magnetocardiographic determination of the developmental changes in PQ, QRS and QT intervals in the fetus. *Acta Paediatr* 2000; 89: 64-7.
34. Peters M, Crowe J, Piri JF et al. Monitoring the fetal heart non-invasively: a review of methods. *J Perinat Med* 2001; 29: 408-16.
35. Stinstra J, Golbach E, Van Leeuwen P, et al. Multicentre study of fetal cardiac time intervals using magnetocardiography. *Br J Obstet Gynaecol* 2002; 109: 1235-43.
36. Wakai RT, Strasburger JF, Li Z, Deal BJ, Gotteiner NL. Magnetocardiographic rhythm patterns at initiation and termination of fetal supraventricular tachycardia. *Circulation* 2003; 107: 307-12.
37. Grimm B, Kaehler C, Schleussner E, Schneider U, Haueisen J, Seewald HJ. Influence of intrauterine growth restriction on cardiac time intervals evaluated by fetal magnetocardiography. *Early Hum Dev* 2003; 74: 1-11.
38. Lowery CL, Campbell JQ, Wilson JD, et al. Non-invasive antepartum recording of fetal S-T segment with a newly developed 151-channel magnetic sensor system. *Am J Obstet Gynecol* 2003; 188: 1491-7.
39. Comani S, Liberati M, Gabriele E, Lagatta A, Di Luzio S, Romani GL. Detection of fetal arrhythmias by means of magnetocardiography: a case report. *Biomed Tech* 2004; 48 (2): 156-8.
40. Comani S, Liberati M, Gabriele E, et al. Fetal Intra-cardiac Intervals for Different Gestational Epochs as Evaluated from Fetal Magnetocardiograms. *Biomed Tech* 2004; 48(2): 150-2.
41. Claus K. Synergy and Subsidiarity: The Systematic Determination of Software, User, and Operating Instructions. *IJHCI*, 2000; 12: 415-30.
42. Bellotti V, Edwards K. Intelligibility and Accountability: Human Considerations in Context Aware Systems. *IJHCI* 2001; 16: 193-212.
43. Corritore CL, Wiedenbeck S. An Exploratory Study of Program Comprehension Strategies of Procedural and Object-Oriented Programmers. *IJHCS*, Academic Press 2001; 54: 1-23.
44. Della Penna S, Del Gratta C, Granata C et al. Biomagnetic systems for clinical use. *Philosoph Magaz B* 2000; 80: 937-48.
45. Comani S, Mantini D, Pennesi P, Lagatta A, Cancellieri G. Independent component analysis: fetal signal reconstruction from magnetocardiographic recordings. *Comput Meth Prog Biomed* 2004; 75/2: 163-77.
46. Abraham-Fuchs K, Hrer W, Schneider S, Stefan H. Pattern recognition in biomagnetic signals by spatio-temporal correlation and application to the localization of propagating neuronal activity. *Med Biol Eng Comput* 1990; 28: 398-406.
47. Comani S, Mantini D, Lagatta A, Esposito F, Di Luzio S, Romani GL. Time course reconstruction of fetal cardiac signals from fMCG: Independent Component Analysis vs. Adaptive Maternal Beat Subtraction. *Physiol Meas* 2004; 25: 1305-1321.
48. Ern SN, Fenici R, Hahlbohm HD, Jaszczuk W, Lehmann HP, Masselli M. High resolution iso-field mapping in Magnetocardiography. *Il Nuovo Cimento* 1983; 2D: 291-300.
49. Comani S, Merlino B, Di Luzio S, Ern SN, Romani GL. Magnetic map analysis during ventricular repolarization to differentiate between normal subjects and patients affected by cardiac hypertrophy. *Phys Med* 2001; 17(1): 9-15.
50. Fenici R, Brisinda D, Nenonen J, Fenici P. Phantom validation of multichannel magnetocardiography source localization. *Pacing Clin Electrophysiol* 2003; 26: 426-30.
51. Fenici R, Brisinda D, Nenonen J, Fenici P. Non-invasive study of ventricular preexcitation using multichannel magnetocardiography. *Pacing Clin Electrophysiol* 2003; 26: 431-5.
52. Comani S, Tartaro A, Lagatta A, Morana G, Di Luzio S, Romani GL. Magnetocardiographic functional imaging and integration with 3D MRI reconstruction of the heart: preliminary results for source localization during myocardium activation. *Physica Medica* 2003; 19: 119-30.
53. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. *Eur Heart J* 1996; 17: 354-81.

Correspondence to:

Dr. Silvia Comani
Dipartimento di Scienze Cliniche e Bioimmagini
Universit "G. D'Annunzio"
Via dei Vestini 33
66013 Chieti, Italy
E-mail: comani@itab.unich.it