Current perspective

Magnetocardiography: current status and perspectives. Part I: Physical principles and instrumentation

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Magnetocardiography (MCG) is a non-invasive and risk-free technique allowing body surface recording of the magnetic fields generated by the electrical activity of the heart. The MCG recording system allows spatially and temporally accurate measurements of the very weak magnetic fields produced by currents flowing within myocardial fibers during cardiac activity. MCG has now been around for over 30 years, but only recently has progress in instrumentation put the technique on the verge of clinical applicability. This review summarizes the physical principles, instrumentation, main clinical applications and perspectives for the clinical use of MCG. This first part is devoted to the description of the physical principles and instrumentation.

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Introduction

Magnetocardiography (MCG) is a non-invasive and risk-free technique allowing body surface recording of the magnetic fields generated by the electrical activity of the heart. The MCG recording system allows spatially and temporally accurate measurements of the very weak magnetic fields produced by currents flowing within myocardial fibers during cardiac activity. The electrical activity of the myocardium is commonly detected and recorded by electrocardiography (ECG), but biomagnetic data obtainable at MCG provide further information about heart function on top of what is retrievable from standard ECG or electrophysiological studies. The main clinical purpose of MCG is to obtain functional and clinical information about the heart, starting from the reconstruction of the cardiac magnetic field distribution.

In the last 40 years, cardiomagnetism has become a diagnostic tool available in several centers and applied to different diagnostic settings. MCG recording systems are however not commonly available in clinical practice, and the use of MCG is still currently regarded as an experimental technique. The aim of this review is to describe the state of the art of MCG, current applications and future perspectives. The first part will focus on physical principles and instrumentation.

History

The first magnetocardiogram was recorded by Baule and McFee[1] in 1963, at a time when the ECG had already been used as a clinical tool for more than half a century and was already recognized as a fast, inexpensive, simple, reproducible and non-invasive technique with a significant diagnostic value. MCG and ECG are generated by the same electrophysiological sources and, in fact, these techniques show several analogies. Cardiac contraction, triggered by the depolarization of myocardial cells, is associated with electrical phenomena within the heart and in the surrounding tissues, and with a very weak magnetic field detectable on the chest surface. The difficulty in the recording of a magnetocardiogram is, essentially, the weakness of the signal: in fact, the magnetic field generated by currents flowing in the heart is almost 1 million

times weaker than the earth's magnetic field, which is in the order of 10^{-5} Tesla (T). In the first recording of the human magnetocardiogram, Baule and McFee used two coils, each made of several million turns of thin copper wire around a ferromagnetic core, kept at room temperature. One coil was placed above the heart, the other coil parallel to the first but a few centimeters away. The coils were wound in series and in opposition to cancel the ambient magnetic field, which would have otherwise overridden the magnetic signal from the heart by several orders of magnitude. With this simple coil arrangement, termed a gradiometer, the first magnetocardiogram was recorded in a remote rural site, away from the urban electromagnetic noise. A few years later, in the early '70s, Baule and McFee[2] showed that MCG measurements could also be performed in a hospital environment, and that recordings obtained from patients were different from those obtained from normal subjects.

In the meantime, technological advances allowed the use of superconducting magnetometers. Cohen et al.[3] first used the superconducting quantum interference device (SQUID) magnetometer, in a magnetically shielded room, to record a magnetocardiogram with an improved spatial accuracy and a higher signal-to-noise ratio. The magnetically shielded room is very effective in reducing magnetic signals from metal objects or electrical instruments placed in the surroundings of the recording site. SQUID magnetometers are, at present, the only practical tools available for MCG recordings. The introduction of SQUIDs and of superconducting gradiometers has allowed the external detection of biomagnetic cardiac activity even in unshielded rooms or in moderately shielded environments, with a significant expansion in the number of MCG research groups in the mid '70s[4-7]. Early biomagnetometers, with a small number (from one to nine) of channels, covered only a small portion of the chest. Also, in order to obtain a sufficiently large map of the distribution of the cardiac magnetic field, the single sensor had to be sequentially repositioned over the chest at many points of a recording standard grid[8]. Therefore, the acquisition of a "single-shot" map for real-time recordings was not possible. Moreover, this procedure required a very long recording time and was thus associated with patient fatigue. For this reason, the routine clinical applicability of MCG was not feasible. In the '80s, rapid technological developments resulted in the introduction of multichannel systems, which greatly improved measurement conditions. An example has been the 37-channel Krenikon® system, introduced in 1990 by Siemens Medical Engineering (Erlangen, Germany), which allowed the simultaneous recording of a large field map, fully covering a great part of the chest without the need for repositioning of the sensors on the patient's chest[9]. In particular, in the early '90s at the University of Erlangen in Germany[10-12], but also by other research groups, the Krenikon® system has been one of the first commercial multichannel systems to be used for biomagnetic investigations.

An Italian development in clinical MCG was started at the Catholic University of Rome (Italy) in 1981, using a single-channel instrumentation in an unshielded hospital room[13]. Since the mid '80s, MCG mapping has been performed in patients with atrial and ventricular arrhythmias with the aim of localizing the arrhythmogenic foci within the heart[14,15]. The accuracy and reliability of MCG have been assessed by comparing them with those of invasive electrophysiological methods[16]. Between 1985 and 1998, efforts were also directed to the development of novel, specially designed amagnetic catheters for simultaneous MCG mapping, electrophysiological recording, and cardiac pacing. A refinement of this method led to the use of the multipurpose MCG-compatible amagnetic catheter for MCG-guided electrophysiological studies, myocardial biopsies, and arrhythmia catheter ablation[14,17-24].

Cardiac magnetic field mapping consists of iso-field lines, calculated on an ideal plane parallel to the patient's chest at instants of interest during the heart cycle. Magnetic field mapping has also been used in association with the ECG body surface potential mapping in order to combine, in the same subjects, the information from magnetic and electrical maps, thus improving knowledge about the patient's arrhythmia[25]. An MCG map has a better spatial resolution than body surface potential mapping, and is not hindered by false contacts at the skin surface. These conditions are particularly advantageous when complex sources are studied, such as those occurring in patients with ventricular tachycardia[26]. In the last 10 years, thanks to both technological developments and to improved conditions of measurements, MCG has become a useful instrument for the study of cardiac electrical activity in normal subjects, as well as in patients with different pathological conditions. These will be covered in the second part of this review. The main field of MCG application remains the study of cardiac arrhythmias in the adult, but the technique can also be applied to the evaluation of fetal cardiac activity with some advantages over standard fetal ECG[27]. Fetal MCG has been one of the first biomagnetic signal applications reported. The first successful measurement of the magnetic signals related to fetal cardiac activity was described in 1974[28]. Presently, in view of some advantages compared to electrical measurements, fetal MCG is regarded as one of the most promising applications of biomagnetism. Fetal ECG is indeed noisy, with a strong interference from the maternal signal and, especially in the critical period between the 25th and 36th weeks of gestation, is of very low amplitude due to the isolating action of the *vernix caseosa* around the fetus. Noise reduction in fetal MCG is crucial because of the small amplitude of fetal cardiac signals. Despite these limitations, spatial resolution in fetal MCG is better than in fetal ECG, and the signal is less influenced by the maternal beat and the *vernix caseosa*. For these reasons, starting from the 25th week of pregnancy fetal MCG is easy to record[27].

Physical principles of magnetocardiographic signals

MCG is essentially an electrophysiological study of the heart since it measures the magnetic field associated with the currents generated during cardiac activity. The magnetic field is a property of the space in which a moving charge undergoes a magnetic force. Some materials, called magnets, besides moving electrical charges in the vacuum or electrical currents flowing in a conductor, produce magnetic fields which can be represented by means of field lines. These lines have no beginning and no end, and always form closed loops, their shape being dependent on the magnetic field source (Fig. 1). MCG is able to measure and record the magnetic fields generated by volume currents in a volume conductor, e.g. the electrical current flowing within the heart conduction system. The main physical principle of MCG recording is magnetic induction. In 1819 Hans Christian Oersted observed that an electrical current flowing in a conducting wire exerted a force on a magnetic needle placed nearby. Later, in 1831, Michael Faraday showed that a relative change (in space or time) of a magnetic field around an electrical conductor induces an electrical current in the conductor (the phenomenon of magnetic induction). This induced current is always proportional to the magnetic induction (intensity of the magnetic field) and oriented in such a way as to delete its own cause (Lenz's law). This is the principle that permits the conversion of a magnetic field into an induced electrical signal. The magnetic field generated by an electrical current flowing in a conductor wire is characterized by circular and concentric field lines having their center on the wire and the orientation of a clockwise screw advancing in the same direction as the electrical current (Fig. 1). The commonly used measurement units of the magnetic field strength are the tesla, named after the inventor Nikola Tesla, and the gauss (G), named after Karl Friedrich Gauss. Ten thousand gauss equal 1 T (1 G = 10^{-4} T). The earth's magnetic field has been calculated to be 5×10^{-5} T, thus 1.0 T is 20 000 times stronger than the earth's magnetic field. The magnetic field generated by currents flowing within the heart is very weak, less than 10 picoTesla (pT), therefore around 10^{-11} T, and thus difficult to record without appropriate instrumentation.

In the human body, electrical currents flow in neurons and in muscular fibers. During heart contraction, activation currents produced by ions flowing through cell membranes span myocardial fibers. During electrical activation, each individual cell can be represented as a microscopic current dipole, too weak, however, to be detected externally. The resultant current, given by the sum of all current dipoles, is the electrical source for MCG measurements. In fact, since any electric current also generates a magnetic field, the heart becomes the source of a magnetic field. Currents in the heart, directly related to myocardial cell activity, are usually called "impressed currents". They determine an electrical potential distribution in the surrounding tissues as well as on the body surface, the latter being detectable as an ECG. As a consequence, passive currents, commonly called "volume currents", flow throughout the thorax. The same currents also contribute to the magnetic field measured close to the chest surface by an array of SQUID sensors covering a large portion of the thorax, and recorded as a magnetocardiogram. From such multiple ECG and MCG recordings, we can construct time sequences of the body surface potential maps or magnetic field maps, respectively. During a typical 1-s heart cycle, these maps can be acquired every 1 or 2 ms and used to determine cardiac function, to diagnose heart diseases and locate the sites of cardiac abnormalities[29]. Physically, both impressed and volume currents contribute to the magnetic field outside the thorax, but clinical and research interest concentrates, however, only on impressed currents. The different roles of impressed and volume currents can be taken into account when modeling the sources of the magnetic field and the volume conductor given by the surrounding conductive tissues. In a first approximation, volume currents are symmetrical around the electrical sources, thus giving a net contribution to the magnetic field which is close to zero. Since volume currents give a negligible contribution to the total external magnetic field, MCG essentially records the cardiac electromagnetic activity due to impressed currents.

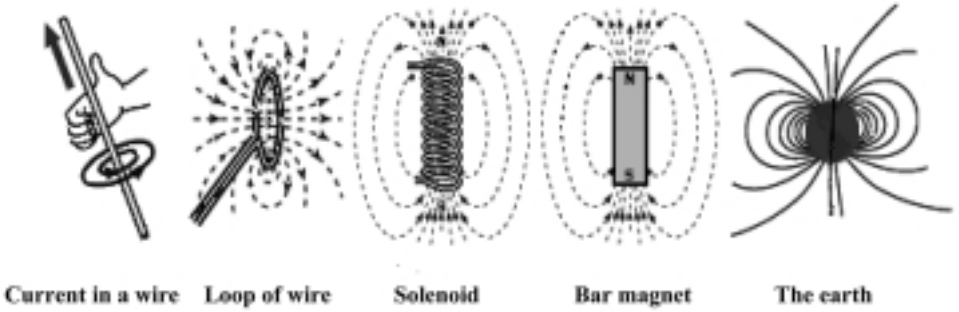


Figure 1. *Different magnetic field sources: current in a wire, loop of wire, solenoid, bar magnet and the earth, with relative magnetic field lines.*

The biomagnetic activity of the heart can be detected in the different phases of the cardiac cycle, and a typical MCG shows features similar to the ECG for having a P wave, a QRS complex and a T wave (Fig. 2).

MCG data are mainly used to localize and study cardiac electrical sources. The "forward problem" consists of the calculation, at the body surface, of the magnetic field distribution, when the electrical sources, the geometry of the chest and the conductivity of the different compartments and components of the chest are known. The main feature of the forward problem is that, for any given electrical source distribution, there is one, and only one, magnetic field distribution in the surrounding space. Forward solutions are essential to understand the relationship between the electrophysiological study and the magnetic maps acquired in the course of a MCG study. On the other hand, the "inverse problem" consists of the derivation of the maximum amount of information about the electrical sources associated with the measured magnetic field distribution, by analyzing the magnetic field recorded outside the body. It is important to realize that there is no unique solution of the inverse problem, i.e. for any given magnetic field distribution, as measured on a plane, there is more than one electrical current distribution in the space in which it might be generated. For this reason, the reconstruction of the electrophysiological information about the heart activity starting from the analysis of the body surface magnetic maps is far from being trivial. In order to achieve reliable results, two different boundary conditions have to be satisfied: 1) that a model is used to parameterize the space between the electrical source (volume conductor) and the measuring site, and 2) that a model is used to parameterize the source itself. The first requirement is often fulfilled by using a semi-infinite homogeneous half-space model for the torso. This can eventually be refined by means of realistic torso models or even subject-tailored models. The second requirement is satisfied by using the equivalent current dipole (ECD) model, which through the years has been shown to be the most adherent to a realistic physiological source, and the one yielding the best experimental results.

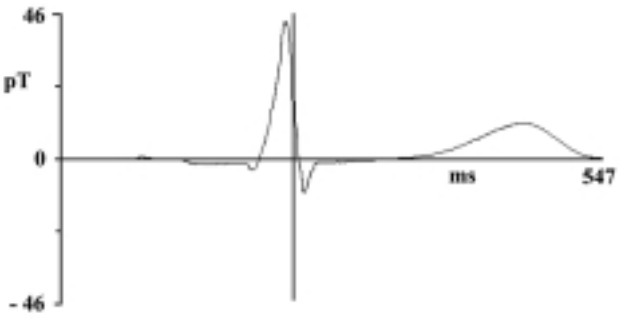


Figure 2. *Magnetocardiographic tracing recorded in one of the channels on the thorax. On the* x-axis*, time, measured in ms, on the* y-axis*, the intensity of the magnetic field, measured in picoTesla (pT). The* vertical line *soon after the R wave peak in the QRS complex marks the instant when the magnetic map (see Fig. 3) was calculated.*

According to this simple model, when the body is assumed to be a semi-infinite homogeneous volume conductor, all compartments have the same electrical conductivity. The relationship between the electrical source and the magnetic field thus becomes relatively simple. The different conductivity of the various compartments has however non-negligible effects on the magnetic field distribution, so that, in order to refine the localization of the source, these influences must be taken into account. The simplest source model taking these influences into account assumes that, at any particular moment during the heart cycle, the complex electrical sources can be concentrated into a single ECD.

The localization of the biomagnetic source and "torso" models

For the interpretation of biomagnetic data, several mathematical models are available. As discussed before, myocardial fibers can be represented as electrical current dipoles, but it is not possible to resolve the current distribution on such a small scale. We may only retrieve a macroscopic current distribution, where the current density at each point represents an average number of cells. The most frequently used electrical source model is a single ECD model, located in the center of the heart. More complex equivalent sources, such as multiple dipoles or a multipolar expansion can also be used[30]. The ECD model assumes that the human body can be represented as an infinite or semi-infinite homogeneous volume conductor. Being able to focus on restricted regions of the myocardium, such as arrhythmogenic areas or ventricular preexcitation pathways, the ECD model has been used to characterize and localize cardiac sources in patients with the Wolff-Parkinson-White syndrome[31]. When comparing MCG results with those obtained at cardiac surgery, electrophysiological studies and by ECG localization, a localization accuracy of 10-20 mm has been reported[32-34].

Analytical solutions for current dipole sources are available for different volume conductor geometries. When the human chest is assumed to be a homogeneous and semi-infinite medium[35], we are actually using an approximation that allows an easier mathematical approach for the interpretation of magnetic signals generated by the heart. The chest has, however, a complex shape and internal inhomogeneities (due to the presence of different structures such as the lungs, the myocardium, intracardiac blood masses and blood vessels), and these may reduce the accuracy of the biomagnetic localization sites obtained as described above[36,37]. Computerized numerical models, representing a realistically shaped volume conductor, have

thus been developed[38]. The shape of the torso, the internal body inhomogeneities, the presence of the lungs and of intracardiac blood masses, as well as myocardial anisotropy can all influence MCG measurements. In order to improve the accuracy of MCG recordings, more individualized torso models have been created, mainly using magnetic resonance imaging (MRI) data as an anatomic reference. In figure 3, realistic torso models with the relative magnetic distribution of cardiac electrical activity are represented. At present, MRI data are essential for the construction of individualized volume conductors which reflect the real body shape of the subject undergoing the MCG examination. This is useful to improve the spatial accuracy of any source reconstruction. Some of the most advanced models now include inhomogeneity and anisotropy. For each model, the corresponding method of mathematical solution for data elaboration has been developed. As previously stated, the homogeneous half-space model is a simple model for the volume conductor and consists of a medium bounded by a planar interface. This represents the anterior wall of the torso and is placed between a homogeneous conducting half-space and the remaining non-conducting half-space. Inhomogeneous models take the fact that the heart lies in the chest together with the lungs, blood vessels and mediastinal structures which have different electrical conductivities. Purcell et al.[37] strongly recommend the use of individualized and real-shaped torsos, including the lungs and heart boundaries – as derived from MRI data – to yield an accurate solution of the inverse problem for magnetic field mapping. Nenonen et al.[38] have studied the MCG functional localization using a current dipole in a realistic torso model. They reported a fast and numerically effective solution of the biomagnetic inverse problem, using a current dipole in a realistically shaped and homogeneous torso. Ten patients with the Wolff-Parkinson-White syndrome have been thus studied by MCG mapping and invasive catheter techniques. Using a standard-size torso model in all cases, the average three-dimensional distance between the MCG localizations and invasively obtained results had a mean value (± SD) of 2.8 ± 1.4 cm. When, in 5 cases, the torso was remodeled to better match the size of each patient, the three-dimensional average distance from the real localization was reduced to 2.2 ± 1.0 cm[38]. Tailored models consist of standard torso models of varying complexity that are built from an average patient and that are subsequently custom-adapted, on scale, to the particular patient undergoing examination. This procedure may be applied when MRI is not available or feasible, or when, as in some unstable patients, the length of the procedure would preclude that it be performed.

MCG electrical sources can be single or multiple, point-like (such as the ECD) or distributed (such as a depolarization wave). The latter source model has been successfully used for the MCG evaluation of ischemic areas and myocardial viability[39]. Because of its simplicity for mathematical treatment, the single ECD source is the most commonly used, and is associated with fairly good results in the real source localization.

Inaccuracies in MCG localization are often due to the poor approximation of the torso surface. This is particularly evident when the ECD model in a homogeneous half-space is used to study the Wolff-Parkinson-White syndrome or the localization of other ventricular preexcitation sites, especially if the preexcitation site is > 10 cm deep in the chest. The current dipole alone appears to be inaccurate in evaluating the depth of the source: for such cases, the introduction of current multipole models, despite the fact that they render mathe-

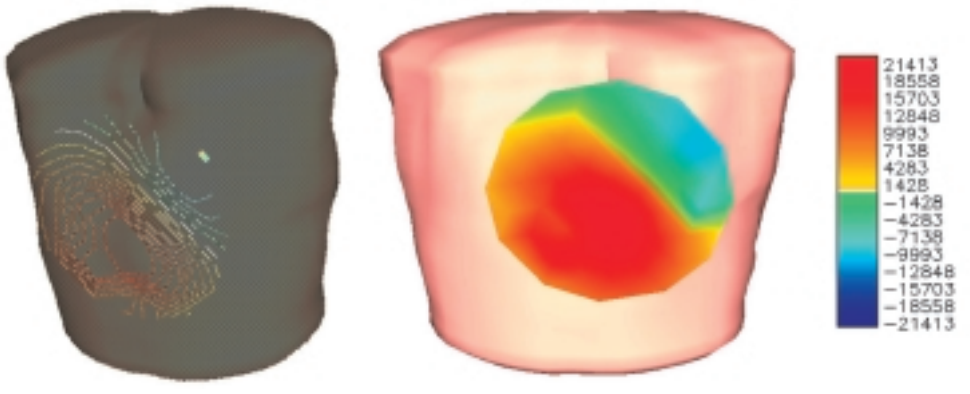


Figure 3. *Examples of magnetocardiographic maps.* A: *example of a magnetic map showing the localization of the equivalent current dipole. The map has been calculated by using the values of intensity of the magnetic field at the time instant t = 547 ms from the beginning of the cardiac cycle, recorded in all the 55 channels of the system. The* red *and* blue isofield lines *indicate the positive and negative values of the intensity of the magnetic field, respectively, the step being equal to 2 picoTesla. The map is reconstructed on a torso model.* B: *same magnetic map, calculated by using the values of the intensity of the magnetic field at time instant t = 547 ms from the beginning of the cardiac cycle for all the 55 channels of the recording system. The intensity of the magnetic field is calculated in femtoTesla (1 picoTesla = 1000 femtoTesla). The variations of the intensity of the magnetic field are shown as color gradations from* red *(maximum positive value) to* blue *(maximum negative value). The typical dipolar distribution of the magnetic field on the recording plane is evident. This map, similar to the previous one, is reconstructed on a torso model.*

matical elaboration more complicated, has considerably improved the results[30].

Artificial dipolar sources are often used inside thorax phantoms. The latter have the shape of the human chest and are filled with saline solution to experimentally study the accuracy obtainable with MCG recordings in the ECD localization. In a recent study, a phantom has been filled with saline solution, and a multichannel MCG system has been used to measure the magnetic field generated by different dipolar sources located at distances ranging from 25 to 145 mm below the phantom chest surface[40]. The average localization was found to be strongly related to the signal-to-noise ratio. In fact, with a signal-to-noise ratio ranging between 5 and 10, the average localization error was found to be 9 ± 8 mm (mean ± SD), while for a signal-to-noise ratio ranging between 30 and 40, the average error was reduced to 3.2 ± 0.3 mm.

Instruments for magnetocardiographic recording

The superconducting quantum interference device magnetometers. A single channel of a biomagnetic system schematically consists of two main parts: the SQUID and the detection coil or gradiometer. For an exhaustive description of such devices the reader is referred to more specific papers[41,42]. The low-T_C SQUID magnetometer (where T_C is the critical temperature below which a superconductor really behaves as such) is the most sensitive low-field sensor and the most common currently used device of this kind in MCG measurements. A SQUID is a highly efficient magnetic flux-electric voltage converter. It is based on flux quantitation and Josephson tunneling, two phenomena that are observed only in superconducting materials. The use of superconductors is due to the need of recording a very weak induced current, proportional to the very weak inducing magnetic field. A normal conductor would dissipate the electrical energy before any signal could be recorded. On the other hand, superconductors have the property of a null resistivity value, thus dissipating no energy and – consequently – "consuming" no signal. The main problem of such instruments is the presence of magnetic noise produced by external magnetic fields. These fields are generated by the earth's magnetic interference and by environmental magnetic objects (nearby electrical instruments, patient pacemakers or metallic prostheses). Developed in the early '70s, low-T_C magnetometers consist of a flux transformer and a SQUID amplifier which are immersed in a cooling medium (liquid helium) at the low critical temperature of -269°C (4.2 K) necessary to maintain the superconducting state. Containers for cryogenic liquid are called dewars or cryostats. The dewar is a vacuum-insulated container which reduces the thermal exchange with the environment. A dewar for MCG applications has to be made of non-magnetic materials, and has to generate a low noise in the electrically conducting parts. The pick-up coils, usually arranged in the dewar in a circular format, should be placed in such a way as to cover the largest possible area above the patient's chest and to be as close as possible to the biomagnetic source. We can briefly state that a sensing channel is the ensemble of a sensor assembly, a cryogenic probe, the readout electronics (preamplifier) and a remote control unit. The sensor assembly is associated with the detection coil (Fig. 4); the cryogenic probe is necessary because the superconducting coil is functional only at the temperature of liquid helium; the remote control unit, arranged in a console, monitors and controls the operating parameters for the SQUID far from the measuring site. The detection coil consists of one or more multiturn coils of a superconducting material having the property of null resistivity, thus dissipating no electrical signal. A variable magnetic field (associated with a variable impressed current in the body) induces a current $I \neq 0$ in the detection coil. A single multiturn coil, named magnetometer, responds to a variable magnetic field regardless of its distance from the source. While a magnetometer measures the magnetic field at a single point, a gradiometer measures the difference in magnetic field strength between two points, with configurations that can be obtained with various designs (Fig. 5).

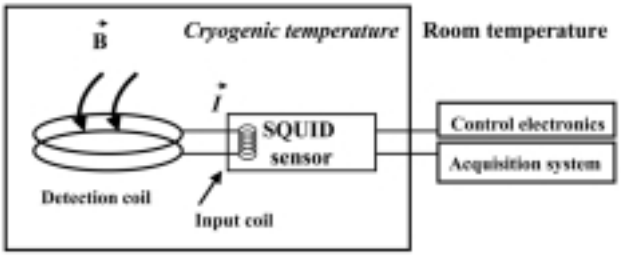


Figure 4. *Components of a superconducting quantum interference device (SQUID) magnetometer: the detection coil (sensing changes in the external magnetic field B and transforming them into an electrical current I), the input coil (transforming the induced current into a magnetic flux) and the SQUID sensor (kept at cryogenic temperature). The control electronics and the data acquisition system are placed at room temperature away from the SQUID.*

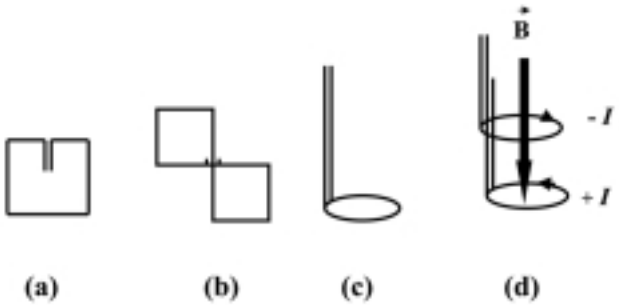


Figure 5. *Various coil designs: planar magnetometer* (a)*, planar gradiometer* (b)*, axial magnetometer* (c)*, and axial gradiometer* (d)*. In the case of an axial gradiometer, a varying magnetic field B induces currents (+I and -I) of opposite polarity, thus allowing the recording of variations of B_z along the Z-axis.*

Gradiometers are sensitive to sources placed near the pick-up coils, while they are not sensitive to uniform background fields. A first-order gradiometer (made up of two coils) measures the field gradient (the field difference between two coils), and is insensitive to uniform fields, whereas a second-order gradiometer (three coils), built by connecting two first-order gradiometers in series, is insensitive to both uniform fields and field gradients. Despite the loss of signal in the recordings, the use of second-order gradiometers is strongly recommended when performing MCG recordings without the use of magnetic shielding, since they only "see" the signal source under the coils[43]. Most MCG recording systems now actually use second-order gradiometers to reduce the environmental magnetic noise. Third-order software gradiometers have been proposed and constructed, but are mainly used in studies of neuromagnetism.

In the '80s, SQUID systems for MCG were single-channel devices used in unshielded environments. This implied sequential recordings on a grid of chest points[8] to reconstruct the magnetic maps, and therefore required a long-lasting measuring session. In the last decade, the number of sensors has increased up to 75, and biomagnetic studies have been carried out in magnetically shielded rooms. With a multichannel system, biomagnetic mapping has become faster. Including patient preparation, an MCG session now only takes about 30-40 min.

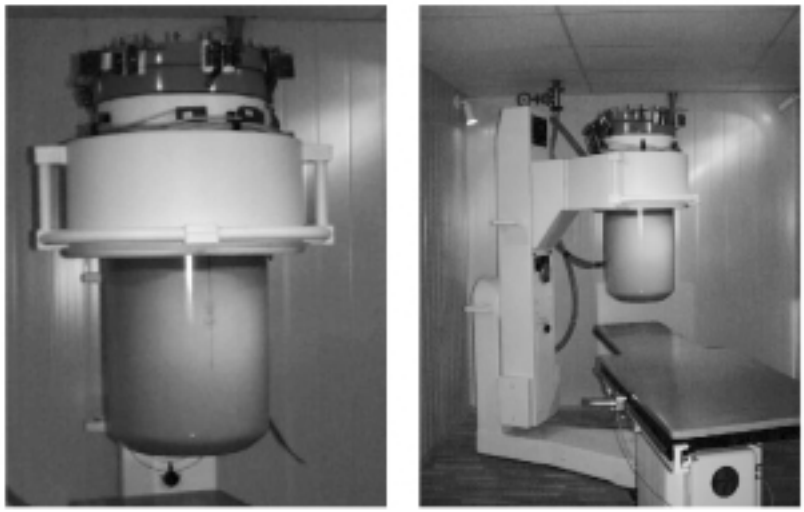
Multichannel magnetocardiographic recording systems. Many European centers, as summarized in table I, are now getting involved in biomagnetic research.

Within a joint project, the Institute of Advanced Biomedical Technologies at the University of Chieti (Italy) and the Central Institute for Biomedical Engineering at the University of Ulm (Germany) have both installed a 55 DC-SQUID system, specifically designed for MCG applications, and built by Advanced Technologies Biomagnetics (Fig. 6). This planar MCG system consists of a set of 55 measurement channels and a set of 19 reference channels. The reference sensors are used for the detection of magnetic field noise thus allowing subtraction from the signal recorded by the signal-sensing elements. The geometry of the sensors within the dewar follows a hexagonal pattern over a circular surface 23 cm in diam-

Table I. A list of the currently operative European biomagnetism centers, their instrumentation and fields of application.

Center	Instrumentation	Main applications	Shielding
Biomagnetism Center at the University of Erlangen-Nürnberg (Germany)	74-channel system (MAGNES II) installed by the Biomagnetic Technologies, Inc. (BTi) of San Diego, CA, USA	MCG, fMCG	Yes
BioMag Center at Helsinki University of Central Hospital (HUCT) (Finland)	99-channel - 33 measuring point system (Vectorview), by 4D-Neuroimaging, San Diego, CA, USA	MCG	Yes
Clinical Physiology-Biomagnetism Research Center at the Catholic University of Rome (Italy)	12-channel system with automatic electronic noise suppression	MCG	No
Central Institute for Biomedical Engineering at the University of Ulm (Germany)	55-channel system (Argos 55) installed by Advanced Technologies Biomagnetics Srl (ATB), Pescara, Italy	MCG	Yes
Biomagnetic Center at the Friedrich Schiller University of Jena (Germany)	50-channel system (Philips), Enthoven, The Netherlands	MCG, fMCG	Yes
Institute of Advanced Biomedical Technologies (ITAB) at the University of Chieti (Italy)	55-channel system (Argos 50) installed by Advanced Technologies Biomagnetics Srl (ATB), Pescara, Italy	MCG	Yes
Department of Biomagnetism of the Research and Development Center for Microtherapy in Bochum (Germany)	67-channel system (MAGNES 1300C) by 4D-Neuroimaging, San Diego, CA, USA	MCG, fMCG	Yes
University Clinic Benjamin Franklin of Berlin (Germany)	83-channel system, constructed by Physikalisch Technische Bundesanstalt (PTB), Berlin, Germany	MCG	Yes

fMCG = functional magnetocardiography; MCG = magnetocardiography.



A B

Figure 6. *Examples of magnetocardiographic equipment.* A: *the dewar in which liquid helium and the sensors of the 55-channel-SQUID system (Argos 50) installed at the University of Chieti (Italy) are contained.* B: *the 55-channel-SQUID system installed at the University of Ulm (Germany) showing the dewar, in which liquid helium and the sensors are contained, and the non-magnetic bed within the shielded room.*

eter. The distance between each sensor is approximately 3.2 cm (Fig. 7). The reference sensors, with features similar to those of the measurement sensors, are placed on a circular surface 9 cm above the sensing plane, and coaxial to it. This sensor structure is contained in a low-noise dewar with a flat bottom and with a distance of 1.8 cm between the sensing plane and the room environment. Both the measurement and the reference sensors are low-temperature DC-SQUID-integrated magnetometers[44].

A major limitation of conventional multichannel instrumentation has been the need of expensive and heavy magnetically shielded rooms, which prevent its use in unshielded laboratories used for clinical cardiac electrophysiology. The use in unshielded laboratories is an innovative approach pursued in parallel at the Catholic University of Rome, where a 12-channel MCG system (9 measuring and 3 reference channels for automatic electronic noise suppression) was successfully installed at the end of the year 2000 (Fig. 8). This is a "scout" system, developed to define the technical requirements for the construction of a 22-channel instrumentation (19 measuring and 3 reference channels for automatic electronic noise suppression), to be installed within the year 2002. With the 12-channel system, a sensitivity of about 20 femtoTesla/$Hz^{1/2}$ (Fig. 9), in the frequency range of interest for clinical MCG (1 to 100 Hz) even during rush hours, has been obtained, and routine clinical investigation of patients with cardiac arrhythmias has thus already started. With the 12-

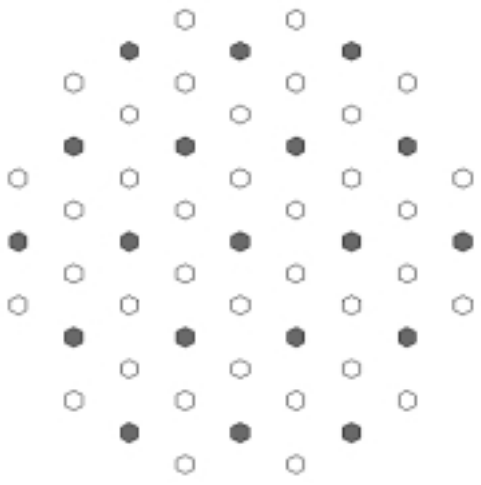


Figure 7. *Geometry of the distribution of the 55 magnetocardiographic channels contained in the dewar (total diameter approximately 23 cm) of the recording magnetocardiographic system operating at the University of Chieti (Italy). The* shaded coils *represent the positions of the 19 reference channels placed on a plane 9 cm distant from the sensing plane. The same positions are occupied, on the sensing plane, by measurement channels.*

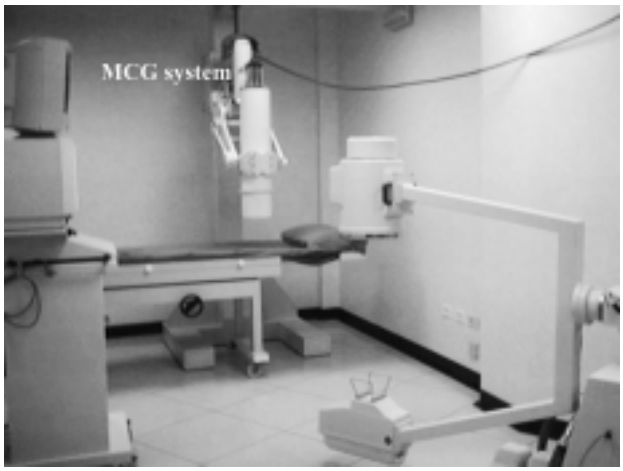
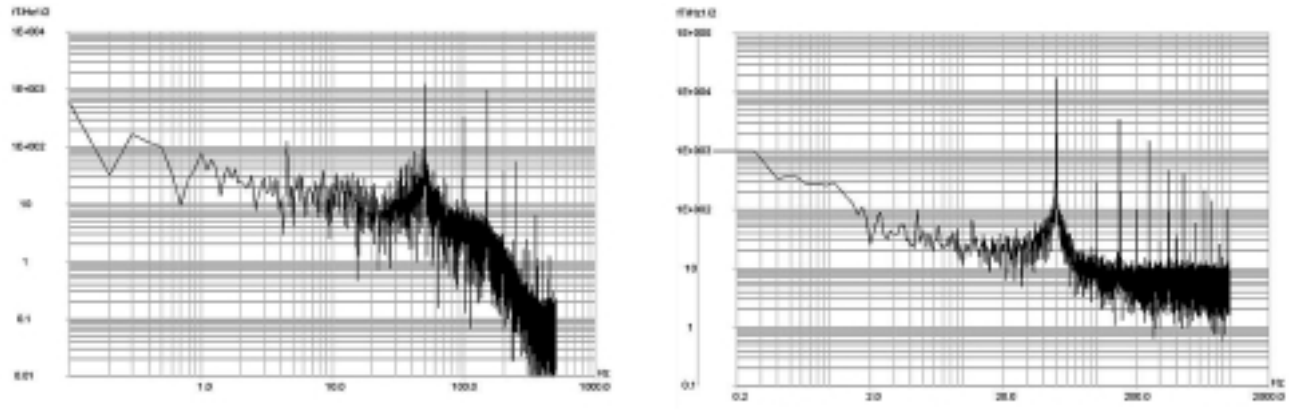


Figure 8. *Multichannel magnetocardiographic (MCG) system in the unshielded Clinical Electrophysiology Laboratory of the Clinical Physiology-Biomagnetism Research Center at the Catholic University of Rome (Italy).*



A B

Figure 9. *Typical noise spectrum of the multichannel magnetocardiographic system operating during rush hours in the unshielded Clinical Physiology-Biomagnetism Research Center at the Catholic University of Rome (Italy).* A: *recording bandwidth 0.05-100 Hz;* B: *recording bandwidth DC-1000 Hz (sampling frequencies 1 KHz and 2 KHz, respectively).*

channel system, the time required for a 36-position map is, at the moment, 4-6 min. Including digital filtering and averaging, the time required for the clinical MCG localization of arrhythmogenic foci or of the MCG-compatible amagnetic catheter tip is < 10 min[44].

The shielded room. Shielded rooms are designed to attenuate the external magnetic noise and to improve the signal quality during the recording. The first MCG recording in a shielded room was performed in 1970 by Cohen et al.[3], using a three-layer magnetic shielding. This room required considerable space for installation, and was very expensive. The most commonly used materials for shielding are aluminum and Mumetal, a ferromagnetic material with a high permeability. If the SQUID sensors are coupled to second-order gradiometers, a magnetocardiogram can be recorded without a shielded room in a magnetically silent location. However, because of the surrounding electrical equipment, it is rather difficult that these conditions be met in a hospital[45,46]. A limitation of shielded rooms is that they do not allow invasive electrophysiological evaluation. Thus, it is necessary to continuously move the patient to and from a room equipped with fluoroscopy.

Measurements and data analysis techniques

After accurate cleaning of the skin and demagnetization – with a common demagnetizer –, the subject lies supine on a non-magnetic bed. Small current-carrying coils are fixed to the chest and their magnetic field is recorded before and after the actual collection of cardiac data, in order to assess the position of the sensors during the recording session. Usually, a few ECG channels are recorded as well, and used to synchronize the magnetic signals for averaging. Non-magnetic electrodes must be used. Typically, three bipolar derivations in vectorial arrangement are recorded. In addition, a pressure sensor, consisting of a piezoelectric crystal, may be used to monitor the patient's breathing. Formerly, when only single-channel cardiomagnetic instruments were available, magnetic field maps were recorded by placing the sensors one by one over the chest at each of the 36 locations of a standard 6 × 6 grid scaled according to the subject's anatomy[8]. Data time courses were then synchronized using the ECG, which was mandatory in this case. In this way, only stationary signals could be recorded. The sampling frequency is typically 1 KHz, and the low-pass filter is set at 250 Hz. The field sensors of a multichannel biomagnetic system are located in the dewar (Fig. 6A) which can be adjusted vertically and tilted in two directions to gain access to any side of the patient. The superconducting pick-up coils are distributed over a flat, circular disk, placed above the chest. This large area allows recording from multiple sites, without sequential and time-consuming repositioning of the sensors over the patient's chest. Parameters normally acquired to establish their effect on the MCG localization accuracy include the environmental magnetic noise and the number of measurement points. The multichannel system allows the simultaneous recording of biomagnetic signals at different points over the chest surface, yielding a great deal of spatial and temporal information. Figure 10 shows the simultaneous acquisition of these signals from each channel using a 55-channel system. Biomagnetic data are acquired during the heart cycle at intervals of 1 or 2 ms. A large amount of information becomes therefore available and it may be difficult to display or analyze in a form useful and acceptable for clinical purposes. Therefore, at this point, it is necessary to present data in a comprehensive manner. This can be achieved through the display of a magnetic map, with iso-contour lines joining points where the magnetic field intensity is the same. The time course of magnetic field data can be displayed in real time for all channels on the console, and, if necessary magnetic field maps, interpolated from real data, can be shown as

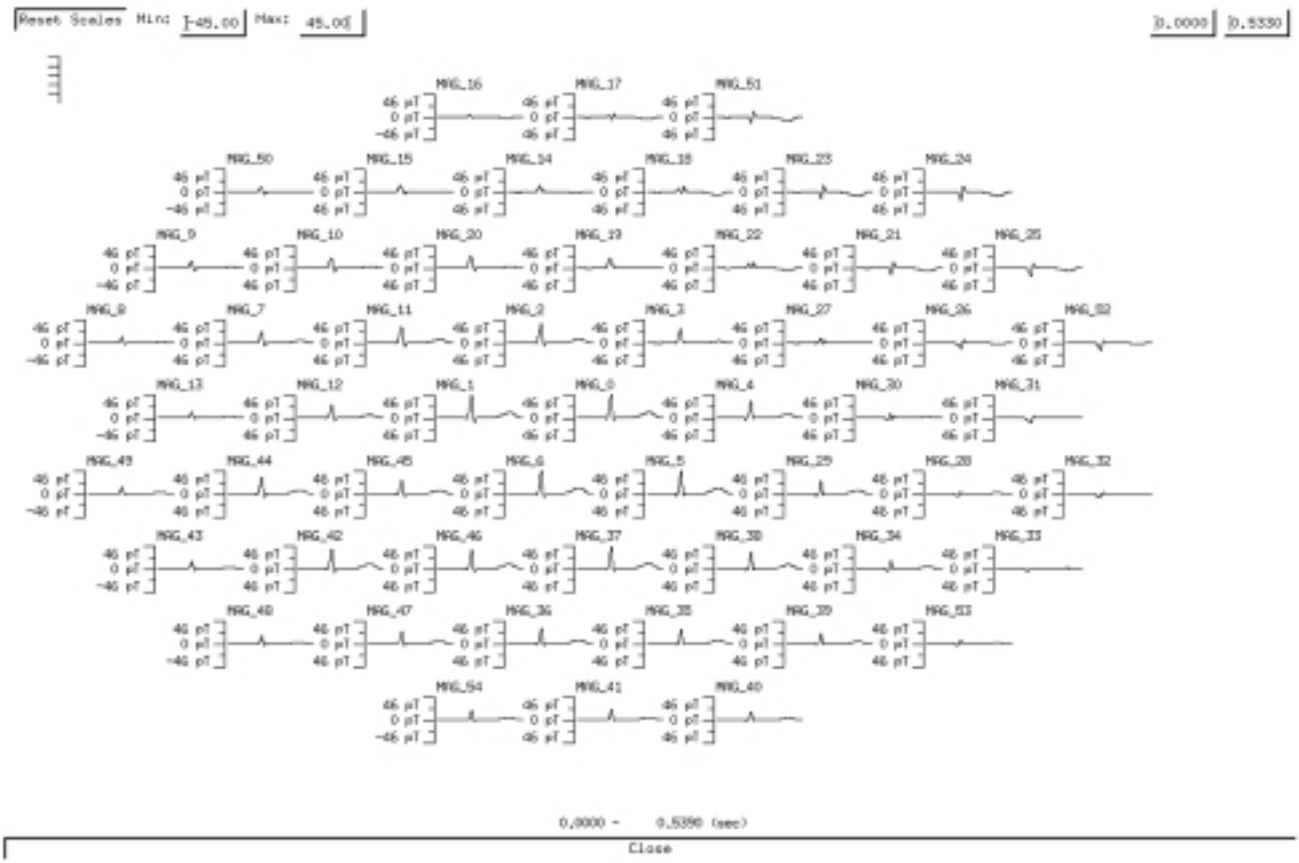


Figure 10. *Typical distribution of magnetocardiographic traces recorded on the thorax of a healthy subject. On the* x-axis*, the time measured in ms is reported; on the* y-axis*, the values of the intensity of the magnetic field, measured in picoTesla, are reported.*

well. Thus, a magnetic field map is available at each millisecond of the data acquisition time course. Time series analysis, usually performed on ECG data, can be performed on magnetic data such as beat analysis, RR or QT dispersion, spectral analysis, etc., and spatial analysis can be performed on magnetic field maps. The localization of myocardial sources is obtained using numerical models for the thorax and heart activation. Finally, these source localization sites can be displayed three-dimensionally by superimposing MCG data on previously obtained MRI images.

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