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Review

Diagnostic value of magnetocardiography in coronary artery disease and cardiac arrhythmias: A review of clinical data

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ABSTRACT

Despite the availability of several advanced non-invasive diagnostic tests such as echocardiography and magnetic resonance imaging, electrocardiography (ECG) remains as the most widely used diagnostic technique in clinical cardiology. ECG detects electrical potentials that are generated by cardiac electrical activity. In addition to electrical potentials, the same electrical activity of the heart also induces magnetic fields. These extremely weak cardiac magnetic signals are detected by a non-invasive, contactless technique called magnetocardiography (MCG), which has been evaluated in a number of clinical studies for its usefulness in diagnosing heart diseases. We reviewed the basic principles, history and clinical data on the diagnostic role of MCG in coronary artery disease and cardiac arrhythmias.

1. Introduction

Intra- and extracellular ionic activity in the myocardium generates electrical potentials on the body surface, which are detected by electrocardiography (ECG). Like all electrical activities, electrophysiological currents of the heart also generate magnetic fields. Magnetocardiography (MCG) is a technique that measures these cardiac magnetic fields, which at a magnitude of between 10^{-11} Tesla and 10^{-14} Tesla are extremely weak compared to the earth's natural magnetic field of approximately 10^{-4} Tesla (Fig. 1) [1]. This review summarizes the background and clinical applications of MCG in clinical cardiology, with a particular focus on its diagnostic yield in coronary artery disease (CAD) and cardiac arrhythmias.

2. Development of MCG

Much has evolved in the development of MCG system since the first reported experience by Baule and McFee, who measured magnetic fields in the human heart using a pair of copper induction coils around a ferromagnetic core at room temperature in an unshielded setting [2]. Although this was a major breakthrough in biomagnetism, the obtained magnetocardiogram was somewhat unsatisfactory compared to an equivalent electrocardiogram due to the weak nature of cardiac magnetic signals. Cohen et al. subsequently overcame this hurdle by introducing the superconducting quantum interference device (SQUID) magnetometers, with much improved spatial accuracy and signal-to-noise ratio [3]. The SQUID magnetometers are kept at −269 °C by liquid helium in an evacuated vacuum container called a dewar, and the procedure was conducted in a magnetically shielded room.

Most of the early-phase cardiomagnetometers are single-channel systems for which only a restricted portion of chest could be covered. The main limitation with single-channel MCG systems is the impracticality of sequential scanning of one position and then the next in order to obtain a large enough magnetocardiogram map. The patient would have to be available for a long time for the sensor to be repositioned over the entire chest area. Further research aimed to simplify the procedure and multichannel systems were subsequently developed to allow for simultaneous recording at multiple locations. The first commercially available multichannel SQUID MCG system was the 37-channel Krenikon® magnetometer, developed in the 1990s by Siemens [4]. Other systems such as the 64-channel MC-6400 by Hitachi and the 55-channel Argos 50 by AtB are also used in a shielded environment [4,5]. Further research efforts focused on using MCG in an unshielded setting, such as a hospital room, for convenience and cost-effectiveness [6,7]. Studies have proven the reproducibility of unshielded MCG, allowing the magnetometer to be set up in a conventional clinical environment without jeopardizing accuracy and reliability [8,9]. The 9-channel CMI-2409 by CardioMag Imaging is an unshielded SQUID MCG system approved by the U.S. Food and Drug Association (FDA) in 2004 for measuring and displaying cardiac magnetic signals [4]. Detailed description of the physical properties,

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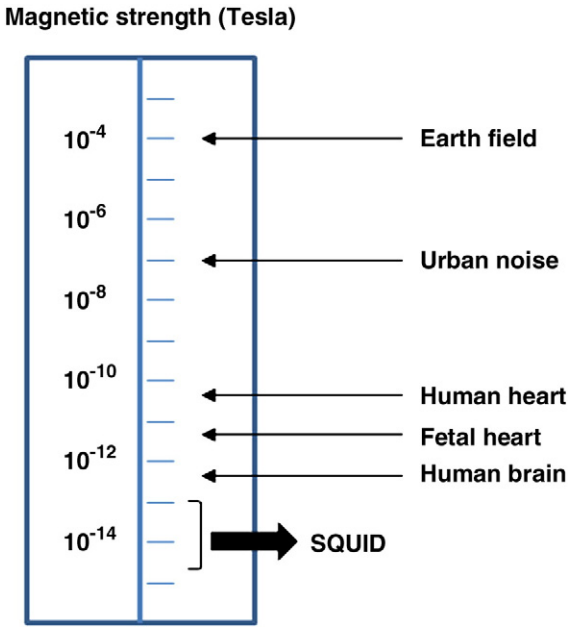

Fig. 1. Biomagnetism and the SQUID magnetometer.

instrumentation set-up and a list of SQUID MCG are available in relevant published literature [4,10,11].

Both ECG and MCG provide information about the same electrical activities of the heart and thus a magnetocardiogram can be viewed as the magnetic equivalent of an electrocardiogram. However, despite the fundamental similarities, there are numerous apparent advantages of MCG. Being a completely contactless technique, MCG does not require the use of electrode pads and allows for a relatively shorter preparation time prior to the procedure. Due to the lack of body contact, measuring magnetic fields is unaffected by conductivity of the human body, whereas electrical field detection by ECG is dependent upon body composition and electrode sensor positions [12]. The high sensitivity and the contactless, non-invasive procedural features have made MCG a popular tool in early diagnosis of heart diseases that are otherwise undetected by ECG. Fetal MCG is an exceptional example since ECG is literally prohibited in fetal heart development monitoring due to confinement of fetal electric currents by insulating tissue layers of the uterus [13].

3. Diagnosis of coronary artery disease

Coronary artery disease (CAD), including stable angina pectoris, unstable angina pectoris and myocardial infarction (MI), is associated with high mortality and morbidity. The challenge remains in effectively diagnosing CAD patients without obvious symptoms or electrocardiographic features [14]. The high sensitivity of MCG towards tangential and vortex currents, the latter of which are undetected by ECG, is extremely attractive in the diagnosis of *de novo* and recurrent CAD in symptomatic and asymptomatic patients [15]. Animal studies by Cohen et al. first demonstrated the role of MCG in diagnosing CAD by measuring the d-c injury current, which is undetected by ECG, and established a relationship between d-c and ST segment shift during myocardial ischemia [16,17]. A subsequent human study examined the ability of d-c MCG in identifying apparent ST segment shift accompanied by a baseline segment shift, which indicates acute ischemic injury and is not seen on an electrocardiogram [18]. D-c MCG was also able to illustrate ST-segment depression during exercise-induced stress test [19]. Further experiments revealed a number of MCG signal modalities that are sensitive to ischemic changes and are thus potential diagnostic markers of CAD, such as QT dispersion [20–22], QRS duration [23,24], ST segment and slope [25–27], ST-T integral [28], and T-wave [27–29]. It is also worth highlighting an interesting study by Chen et al., which reported a correlation of age or sex and significant variations in MCG parameters in 51 healthy subjects [30]. The authors found that, out of 29 MCG parameters there were significant differences in 19 parameters between females and males; for both sexes, 9 MCG parameters showed significant differences in a subgroup of older healthy subjects ($n = 33$, 58 ± 9 years) compared to the younger participants. The authors concluded that age and sex should be considered with the use of MCG although subsequent follow-up research is lacking to confirm their findings.

3.1. Rest versus stress MCG

Like ECG, MCG can be performed at rest and during stress. Various studies have investigated the ability of rest MCG as a non-invasive diagnostic method to distinguish patients with different types of CAD. Using the 37-channel Krenikon® magnetometer in a shielded room, Van Leeuwen et al. studied the magnetocardiograms of 43 CAD patients without prior MI and found that, compared to the healthy participants ($n = 50$), 67% of these CAD patients with no prior MI showed deviations in both magnetic field map orientation during QT interval; ECG at rest, however, revealed no changes in this group of patients [31]. Gapelyuk et al. employed a 7-channel magnetically shielded setting and discovered that, in addition to magnetic field map orientation, ST slope was also sensitive in differentiating CAD patients without prior MI ($n = 101$) and healthy controls ($n = 59$) [32]. Two separate studies by Lim et al. were conducted to evaluate differences in MCG parameters and magnetic field map orientations between CAD and healthy participants as well as distinguish between types of CAD using a 64-channel MCG system in a shielded setting [33,34]. One study enrolled 397 participants, of whom 110 had unstable angina pectoris and 83 with non-ST elevation MI (NSTEMI). All the 10 pre-defined MCG parameters were found to be significantly higher in patients with NSTEMI compared with healthy controls ($p < 0.001$) and 7 parameters were significantly higher in those with NSTEMI compared with patient with unstable angina ($p < 0.05$). Magnetic field maps also proved to be helpful, with abnormality observed more commonly in patients with worsened NSTEMI and unstable angina [33]. A second study using the same MCG setting recruited 105 participants presented with stable angina with no coronary artery stenosis ($n = 23$), unstable angina with severe stenosis ($n = 24$) and Q-wave MI with severe stenosis ($n = 20$), and reported similar trend in MCG parameters as those in the first study [34]. Rest MCG was also explored in an unshielded setting to diagnose CAD using a single-channel magnetometer and the study found that, in contrast to 12-lead ECG which revealed no changes, rest MCG illustrated clear differences between patients with stable angina without prior MI ($n = 55$) and the healthy subjects ($n = 55$) [35]. This particular study shone a light on the possibility of using unshielded MCG in a general clinical setting, which is a welcoming and attractive improvement to the expensive and sometimes impossible set-up of a magnetically shielded room.

Hänninen et al. performed stress MCG in 27 CAD patients and 17 healthy subjects during exercise using a 67-channel magnetometer in a shielded room, and found that MCG was able to distinguish the CAD group from the control group by the different orientation of magnetic field gradient during ST segment and at T-wave apex [36]. Another study by Kanzaki and co-workers used maximal QRS integral change as a diagnostic marker for exercise-induced ischemia and reported a higher diagnostic accuracy (sensitivity of 82% and specificity of 85%) with the 64-channel MC-6400 Hitachi magnetometer in the diagnosis of CAD patients compared to ECG (sensitivity 47% and specificity 85%) [37]. Interestingly, studies have found that MCG was not only useful in identifying the difference of current strength between rest and stress-induced phases but it could be performed