Magnetocardiography provides non-invasive three-dimensional electroanatomical imaging of cardiac electrophysiology

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ABSTRACT

Objective: More than two decades of research work have shown that magnetocardiographic mapping (MCG) is reliable for non-invasive three-dimensional electroanatomical imaging (3D-EAI) of arrhythmogenic substrates. Magnetocardiographic mapping is now become appealing to interventional electrophysiologists after recent evidence that MCG-based dynamic imaging of atrial arrhythmias could be useful to classify patients with atrial fibrillation (AF) before ablation and to plan the most appropriate therapeutic approach. This article will review some key-points of 3D-EAI and discuss what is still missing to favor clinical applicability of MCG-based 3D-EAI.

Methods: Magnetocardiographic mapping is performed with a 36-channel unshielded mapping system, based on DC-SQUID sensors coupled to second-order axial gradiometers (pick-up coil 19 mm and 55-70 mm baselines; sensitivity of 20 fT/√Hz in above 1 Hz), as part of the electrophysiologic investigation protocol, tailored to the diagnostic need of each arrhythmic patient. More than 500 arrhythmic patients have been investigated so far.

Results: The MCG-based 3D-EAI has proven useful to localize well-confined arrhythmogenic substrates, such as focal ventricular tachycardia or preexcitation, to understand some causes for ablation failure, to study atrial electrophysiology including spectral analysis and localization of dominant frequency components of AF. However, MCG is still missing software tools for automatic and/or interactive 3D imaging, and multimodal data fusion equivalent to those provided with systems for invasive 3D electroanatomical mapping.

Conclusion: Since there is an increasing trend to favor interventional treatment of arrhythmias, clinical application of MCG 3D-EAI is foreseen to improve preoperative selection of patients, to plan the appropriate interventional approach and to reduce ablation failure.
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Key words: magnetocardiography, body surface cardiac mapping, electroanatomical imaging, mathematical modeling, atrial fibrillation, catheter ablation

Introduction

Since cardiac electrophysiology (EP) procedures have become more complex, a better knowledge of heart chamber anatomy has been required to define cardiac structures, to optimize catheter navigation and to target arrhythmogenic substrates (1-3). New methods are increasingly developed to merge cardiac anatomy with electrophysiological information gathered with non-fluoroscopic three-dimensional (3D) imaging of catheter mapping of electric signal, by incorporation of pre-operative volumetric multidetector computer tomography (MDCT) or magnetic resonance (MR) data sets (4-9). This has allowed for more detailed maps of cardiac anatomy to be used intra-operatively; however, due to positional and physiological changes, the intra-operative cardiac anatomy can be different from that depicted in the pre-operative data. Therefore, methods are also under development to improve integration of 3D preoperative anatomic images with the interventional electroanatomical reconstruction (10, 11). A combination of preoperative and intraoperative data sets are then visualized and segmented intra-procedurally to provide anatomical data and surface models for intervention guidance. The 3D electroanatomical imaging (EAI) is increasingly used in the EP laboratory but, despite continuous developments to improve automatization of data fusion and to enhance accuracy during the intervention, there are still difficulties which might lead to interventional failure or complications (12, 13). This suggests that there can be still place and need for non-invasive tools to gather preoperative information, which can be relevant for selection of the most appropriate interventional approach data (14).

Indeed non-invasive imaging of cardiac electrogenesis with body surface potential mapping (BSPM) (15-18) and/or with magnetic field (MF) mapping (19, 20) has been proposed much earlier than first method for invasive 3D electroanatomical mapping (1). The proposal to use magnetocardiographic mapping to guide aimed electrophysiology and ablation of cardiac arrhythmias is more than 20 years old (21). Multiple modeling, experimental and clinical studies have assessed the accuracy of MCG and BSPM for non-invasive localization of arrhythmogenic substrates (15, 16, 22-25). Compared to BSPM, MCG has the advantages to be contactless, with fixed sensors position and less sensitive to the contribution of tissue conductivity, thus faster and theoretically more practical for routine clinical use (26). Recent clinical work

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has shown that MCG is a reliable tool for non-invasive 3D-EAI of well-defined arrhythmogenic substrates such as ventricular preexcitation or focal tachycardias (27-29), can also provide dynamic imaging of atrial tachyarrhythmias (30, 31), study the electrophysiological substrate of atrial fibrillation (AF) (32-34) and identify AF patients who will not respond to surgical AF ablation (35).

Indeed radiofrequency (RF) ablation of AF nowadays is one of the most advanced applications of catheter-based 3D-EAI (36), with the purpose to enhance accuracy in targeting and destroying the AF substrate (37). However, whereas it is definitely accepted that pulmonary vein premature beats are the most frequent AF triggers, the AF substrate is still only partially understood and may widely differ among patients (38-40). Thus, the present challenge is to find a reliable method of preoperative identification of which patients are candidates for successful ablation of AF and to localize their arrhythmogenic substrate. Recent work has shown that spectral analysis of atrial endocardial signals during AF can evidence a left-to-right frequency gradient of AF-waves, which is relevant to classify patients (41-43). Moreover, spectral analysis of atrial endocardial signals during sinus rhythm has evidenced distinct areas of anisotropic, out-of-phase myocardium, with shorter refractoriness, fewer intracellular connections, and multiple higher-frequency peaks defined "nests", which seems to be the real AF substrate and target for aimed ablation (44). Preoperative identification and 3D localization of "nests" with MCG could be useful to guide single-catheter ablation of such AF substrate. In a preliminary report Nakai et al (35) have shown that MCG can characterize 3D frequency distribution in patients with AF undergoing surgery for valvular heart diseases; however no additional data are available at the moment about the spatial resolution of MCG for the study of AF frequency distribution.

In this paper, we will summarize our experience in developing a clinical setup aimed to implement MCG-based 3D-EAI as a routine procedure in the diagnostic cascade of arrhythmic patients, candidates to ablation. We will also show preliminary examples of innovative signal processing of MCG of AF patients carried out in our unique unshielded laboratory for simultaneous MCG and interventional electrophysiology (45).

Methods

Different instrumentations for MCG have been developed along the last two decades. Comprehensive reviews with description of different technological and clinical approaches have been recently published (20, 46). Looking for a widespread use of MCG at patient's bedside, the most relevant technological feature among different systems for MCG is the capability to work reliable in any unshielded hospital environment (20, 46).

Instrumentation and patients

Our experience with clinical MCG accounts for 1439 MCG studies; more than 500 patients with cardiac arrhythmias have been studied so far, with different MCG instrumentations (45). In the present configuration our unshielded laboratory for interventional clinical electrophysiology is equipped with a 36-channel mapping system (CardioMag Imaging Inc, Schenectady, NY), based on DC-SQUID sensors coupled to second-order axial gradiometers (pick-up coil 19 mm and 55-70 mm baselines), with an intrinsic sensitivity of 20 fT/√Hz in the frequency range of clinical interest (47). With a single data acquisition of 90 seconds, the z-component (Bz) of local magnetic field at 36 positions in a plane (6 x 6 grid, covering an area of 20 x 20 cm) is recorded. Magnetocardiographic signals were digitally recorded in the DC-100 Hz bandwidth with a Windows-based acquisition system (24 bits A/D conversion, with automatic electronic noise rejection, at 1 kHz sampling rate) (Fig. 1).

Magnetocardiographic mapping can be acquired simultaneously with 12-lead electrocardiogram (ECG), esophageal and/or intracardiac electrograms, and monophasic action potentials, recorded with the CardioLab System (General Electric). One ECG lead (usually lead I) is used to connect the two recording systems and to trigger the averaging of magnetocardiographic and electrophysiologic signals (45).

Transesophageal and/or endocardial pacing are performed with a programmable cardiac stimulator (MEDICO TECS II, Padua, IT). A minimum of two orthogonal fluoroscopic cardiac images are digitally recorded with a mobile digital fluoroscopy system (Sias Spa, Bologna IT), at each MCG session.

Whenever required for catheter ablation, invasive 3D-EAI is performed with the CARTO, (Biosense Webster, USA) or Ensite NavX (St. Jude Medical, USA) systems, in another catheterization laboratory of our university. The 3D "rendering" of cardiac anatomy is obtained from MDCT/MR imaging (General Electric, USA) (27).

Multimodal integration of MCG imaging with cardiac anatomy and 3D invasive electroanatomical imaging

Magnetocardiographic signals are analyzed with the system software (27) and with the UNIX-based MCG software developed at the Helsinki University of Technology (Neuromag, Finland) (46). Contour maps of MF distribution are automatically constructed by interpolating, from MCG averaged signals, with a time resolution of 1 millisecond (ms). For dynamic imaging of electrophysiologic phenomena MCG data are analyzed as a movie of contour maps, of current-arrow maps and of 3D equivalent sources movement within 3D static models of the patient's heart or of 3D rendering of his cardiac MDCT/MR (20, 27). For AF signal imaging the analysis was performed with methods previously described (31, 33-35, 48).

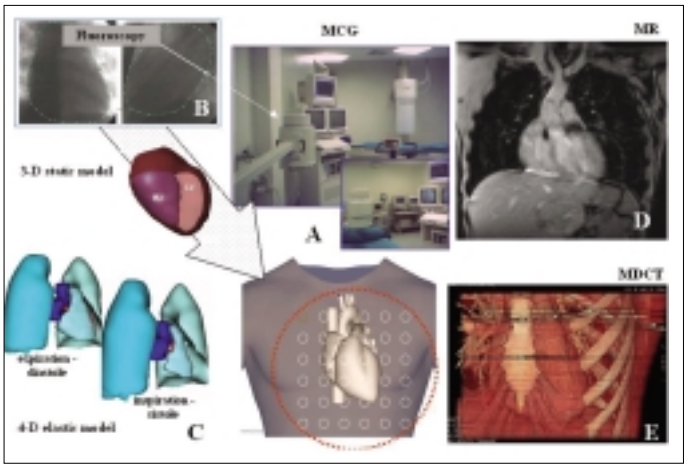

Figure 1. Overview of the unshielded Biomagnetic laboratory (A), where non-invasive, three-dimensional (3D) electro-anatomical imaging is obtained by integration of MCG electrophysiological information with 3D cardiac anatomy, obtained with cardiac modeling (B and C), or by integration of cardiac magnetic resonance (MR), or multidetector computer tomography (MDCT) images. (The large dotted circle represents the positioning of the MCG instrumentation in respect of the anterior chest wall. The small white circles indicate the position of the 36 recording channels).

MCG- magnetocardiographic mapping

Mathematical modeling is a key factor for MCG-based 3D-EAI (46). Cardiac source localization is based on the inverse solution from MCG data performed with different mathematical models of cardiac sources, such as the equivalent current dipole (ECD), the effective magnetic dipole (EMD), or current density imaging (46).

Different mathematical approaches have been tested to construct patient-tailored static cardiac models. Methods for numerical calculation of realistic torso and heart models from MR data of the patients and algorithms for 3D reconstructions of the patient's heart, by using two-dimensional fluoroscopic profiles have been also developed, or to scale an "elastic" standard model to the real dimensions of the patient's heart (49). Alternatively, the electrophysiological information can be nowadays directly merged into 3D images obtained with 3D rendering algorithms from MDCT or MR (27).

For multimodal imaging and fusion of images produced by different systems, it is necessary to use reference landmarks, which allow appropriate matching of the patient's heart position under different recording settings. The relative position of the patient's heart in respect of the MCG sensors is defined by projecting three laser beams from fixed points of the MCG cryostat onto the patient through a transparent acrylic grid, carrying 2 mm lead markers corresponding to the center of each MCG sensor. The lead markers are visible on simultaneously acquired frontal and lateral fluoroscopic cardiac images. The lead markers are placed on corresponding positions of the patient's chest, as landmarks during MDCT, to allow precise matching of the 3D heart reconstruction with respect to the MCG sensors (for MR the lead landmarks are substituted with nifedipine pills).

Results

For a more detailed description of our results using MCG for clinical study of patients with cardiac arrhythmias, the reader is referred to several recent papers (20, 27, 45); here we mainly focus on describing some difficulties which became evident using MCG routinely for non-invasive 3D-EAI and on discussing how to cope with them. We provide also some preliminary examples of different signal processing techniques, which are under investigation to analyze AF patients to be treated with catheter ablation.

Reliability of MCG-based 3D-EAI

Although clinical research has shown that MCG provided reproducible imaging and localization of arrhythmogenic substrates and mechanism(s) (19, 20, 27-35, 50), still MCG-based 3D-EAI is confined in only few clinical institutions and deserves a lot of interactive and manual work to obtain information that can be used clinically.

On one hand, it is evident that MCG 3D-EAI is useful to localize three-dimensionally well-defined arrhythmogenic structures, such Kent-type accessory pathway (27) or focal tachycardias (28, 29). On the other hand, there are technical limitations, which impede immediate and unbiased validation of such capability, by automatic matching of the results of MCG and invasive 3D-EAI (e.g. the lack of appropriate and user-friendly interface to manage the MCG imaging with the same approach used during invasive procedures to merge the automatically pre-interventional 3D imaging cardiac anatomy with interventional 3D electroanatomical mapping).

When multimodal imaging integration is attempted, possible sources of matching disagreement are the effects of biologic factors inherent to the patient (e.g. respiration (51), "twisting" movement of the heart during contraction, skin displacement, torso rotations), or external variable (e.g. different geometry of the imaging systems' bed, slight tilt of fluoroscopy or of the MCG systems). For example, we have found that the inaccuracy of 3D integration of dynamic fluoroscopic imaging of mapping catheters with pre-acquired static cardiac MDCT/MR images caused by respiration may be in the order of centimeters (See Figure 2 in reference 14). The 3D uncertainty can be even larger taking into account the cardiac twisting during the systolic phase, and the effects of respiration on the filling and distension of atria and pulmonary veins (52). Thus data acquisition should be gated with both respiratory and cardiac cycle phases to minimize the possibility of mismatch.

There can be also additional sources of error when multimodal integration is attempted among 2D and 3D images, acquired with different technologies and in separate sessions. In fact, even paying much attention in placing reference landmarks during data acquisition in different clinical settings (radiology, MCG laboratory, interventional electrophysiology), there is an unpredictable degree of displacement of the patient's heart in respect to the landmarks, which might significantly jeopardize accuracy. Without appropriate protocols and software tools for automatic data fusion, one has to figure out mentally and reconstruct manually the correlation between the information coming from different systems. This is impossible, especially in the daily reality of an interventional electrophysiology unit (14). Interestingly similar problems have been recently discussed on the basis of experience coming from AF ablation (10, 12).

An innovative way to improve accuracy of multimodal integration might be the implementation of more realistic anthropomorphic numerical models of dynamic anatomic structures for both non-invasive and interventional electroanatomical imaging. A four-dimensional (4D) model of the beating heart in a breathing thorax has been recently developed, from segmentation of dynamic functional MR images of a normal human male (53) (Fig. 1C). Obviously a single "standard" 4D model cannot be used to represent cardiac anatomy of all individual

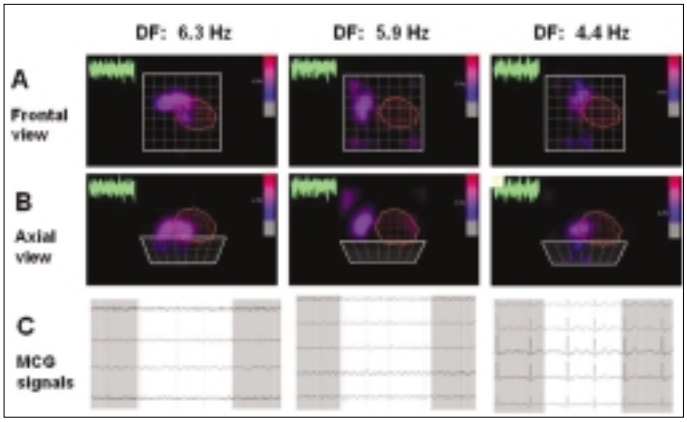

Figure 2. Example of 3D spectral analysis of AF activity, performed by Nakai K. (see ref. 31, 35) in a patient with chronic AF studied with our unshielded MCG system. The 3D (light-violet) cloud indicates where the Dominant Frequency (DF) is located, in respect of the recording grid (white square) and the ventricles outline (highlighted in red). Three different DFs where found and localized at different atrial sites. A) Frontal view. B) Axial view (slightly tilted). C) MCG tracings (the white area indicate the time interval used for spectral analysis).

MCG- magnetocardiographic mapping

patients, especially in the presence of major anatomical abnormalities (e.g. hypertrophy and/or dilatation). Therefore the next step should be to prepare a database of different standard models, grouped by gender and age decades, and to provide an interactive interface to tailor standard "elastic" 4D model to the individual patient's cardiac dimension on the basis of fluoroscopic imaging and echocardiographic measurements. To improve accuracy of multimodal data fusion the same kind of 4D models should be implemented for both MCG-based and interventional 3D-EAI.

MCG 3D-EAI of atrial fibrillation

Since invasive frequency mapping has proven reliable to identify atrial sites where the substrate potentially responsible for maintenance of AF is located, it has been suggested that spectral analysis of AF waves could be helpful to guide a more localized and targeted approach for less invasive substrate modification (41-44). A cooperative study with Japanese (31, 35) and Korean (33, 34) authors is ongoing, to evaluate if the signal resolution of MCG recordings carried out in our unshielded clinical laboratory might be adequate for spectral analysis and non-invasive frequency mapping in AF patients. A preliminary example of AF 3D spectral imaging, performed by Nakai using the data set of one of our AF patients, is shown in Figure 2. Three dominant frequencies were found in this patient, which were localized in three different atrial sites by 3D current density imaging using the space filtering technique (31, 35).

Another method to analyse MCG AF waves on a beat-to beat basis has been developed by Kim et al (33, 34). Also this method has been preliminary tested to analyse one of our AF patients (Fig. 3). The above are obviously only very preliminary data, which however demonstrate that beat-to-beat analysis of AF waves and spectral analysis of their dominant frequency component is possible even when MCG is recorded in an unshielded catheterization laboratory fully equipped for interventional electrophysiology.

Discussion

Magnetocardiography has been proposed as a method to localize three-dimensionally intracardiac sources since the early eighties (20, 46). A sort of 3D-EAI based on MCG localization results transferred into primitive drawings of the patient's cardiac anatomy, obtained by integrating fluoroscopic and echocardiographic imaging was published already in 1991 (19, 20). At that time the vision that MCG could be a useful non-invasive tool to guide aimed electrophysiology and ablation of cardiac arrhythmias (21) raised only scepticism, in spite of the clear-cut demonstration that MCG localizes intracardiac sources catheter with reasonable accuracy (24, 25). Instead, since the first invasive non-fluoroscopic electro-anatomical mapping system has become available (1), interventional cardiologists have adopted it to guide ablation relaying on its 3D localization accuracy in spite of very little knowledge and even less clinical validation of this approach (12). Only after more than ten years of clinical use, interventional electrophysiologists have reported some problems, becoming evident when clinical evaluation of the accuracy of 3D MDCT image integration using CartoMergeTM (Biosense Webster Inc., Diamond Bar, CA, USA) has been attempted (10). In the accompanying editorial (12), Ferguson has pointed-out that a combination of multiple variables might determine inaccuracy of 3D electroanatomical mapping resulting in improper delivery of adequate ablation lesions, error in catheters' display and manipulation, with consequent loss in presumed benefits of non-fluoroscopic 3D-EAI mapping. Indeed, those problems are well known since many years to researchers attempting non-invasive MCG-based 3D-EAI and have not been sufficiently solved yet (14, 19, 20). For example, one major limitation of 3D-EAI, as carried out at the moment, is that electrophysiological information is merged with static anatomical structures, whereas in the living patient the heart is beating in a breathing chest. This is surely a source of uncertainty for MCG-based pre-interventional localization of the arrhythmogenic substrate and causes mismatch between the real-time imaging of moving catheter and the static geometry of the cardiac chambers reconstructed with invasive 3D-EAI methods.

Respiration (51), heart rate and rhythm variations determine significant variability of cardiac volumes through the cardiac cycle, even the timing of ECG gating may significantly affect the 3D cardiac volume in the different recording settings (MCG, MDCT/MR, EP lab) (52). If we acknowledge the relevance of such limitations, it becomes evident that, in order to minimize problems during ablation, it is of critical importance to study the influence of the above variables non-invasively before the intervention. Thus, non-invasive 3D-EAI is fundamental, however the instrumentation and tools to merge EP information with cardiac anatomy should be designed in a way to enable a direct transfer of pre-interventional definition of arrhythmogenic targets and of a

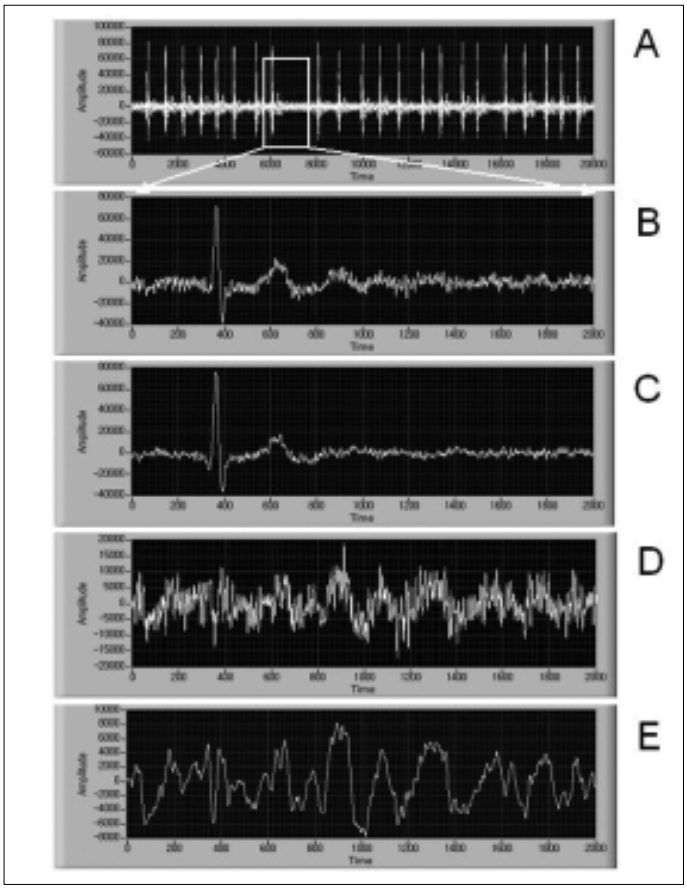

Figure 3. Example of signal processing of AF activity recorded with unshielded MCG (courtesy of Dr. K. Kim; see ref 33, 34). A) Raw data (one MCG channel). B) Selection of a long cardiac cycle with minimal overlapping of QRS on AF waves. C) QRST separation with ICA. D) Amplification of AF waves after QRS subtraction. E) Low-pass filtering (20Hz). The signal-to-noise ratio achieved is more than adequate for the beat-to-beat study of AF activity.

AF- atrial fibrillation, ICA- independent component analysis, MCG- magnetocardiographic mapping

pre-planned interventional strategy to the instrumentation for invasive 3D-EA mapping used in the catheterization laboratory. This could be particularly useful to study AF patients, candidates for ablation. In fact, although catheter ablation is a promising alternative for the management of AF (10, 12, 13, 37, 39, 40), there are still patients that are difficult to treat and relapse in AF (38). An accurate study of the same AF patients, before any invasive modification of their arrhythmogenic substrates and after unsuccessful ablation, can be a precious source of knowledge to understand reasons for failure and to find more appropriate selection criteria (13). Still the identification of AF substrate(s) is uncertain. Spectral analysis and invasive frequency mapping has been shown to identify atrial sites where the substrate potentially responsible for maintenance of AF is located (41-44). Nakai et al. (35) have given the first demonstration that MCG provide non-invasively pre-interventional knowledge of 3D localization of areas of dominant frequency with MCG. In this study, thanks to the collaboration of Nakai, we have preliminarily shown that his analytic method can be applied also to unshielded MCG data and that it differentiated three different dominant frequencies of AF localized at different atrial sites in the same AF patient (Fig. 2). Similarly high-resolution analysis of AF waves has proven possible using the signal processing developed by Kim et al (33, 34). Although such results have been obtained with custom research software tools, which are unavailable for immediate transition from research to patient's bedside, we foresee pre-interventional study of atrial electrophysiology of AF patients, as one of the most useful clinical applications of MCG-based non-invasive 3D-EAI.

Conclusions

Present knowledge suggest that MCG-based 3D-EAI is a robust and fast method for non-invasive localization of arrhythmogenic substrates, which can be useful to define the target(s) and to plan the most appropriate approach of arrhythmias ablation. However, the bottleneck at this moment is the lack of appropriate software tools for automatic multimodal integration with other instrumentations providing anatomical and functional imaging. One more advanced future application could be the development of complete 3D-EAI with MCG alone, e.g. without the need of other methods for anatomical imaging, using space filtering to visualize the 3D electric current density from Bz magnetic fields and to reconstruct from MCG the 3D outline of patient's endocardial boundaries (31, 35). Such unique capability could be used to automatically tailor a standard elastic 4D model (53) to the real patient's cardiac size, for preoperative planning of most appropriate ablation strategy and to program a robotic system for automatic computer-driven ablation catheters navigation on the basis of the MCG 3D coordinates of the target.

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References

1. Ben-Haim SA, Osadchy D, Schuster I, Gepstein L, Hayam G, Josephson ME. Nonfluoroscopic, in vivo navigation and mapping technology. Nat Med 1996; 2: 1393-5.
2. Smith G, Clark JM. Elimination of fluoroscopy use in a pediatric electrophysiology laboratory utilizing three-dimensional mapping. Pacing Clin Electrophysiol 2007; 30: 510-8.
3. De Ponti R, Salerno-Uriarte JA. Non-fluoroscopic mapping systems for electrophysiology: the 'tool or toy' dilemma after 10 years. Eur Heart J 2006; 27: 1134-6.
4. Verma A, Marrouche N, Natale A. Novel method to integrate three-dimensional computed tomographic images of the left atrium with real-time electroanatomic mapping. J Cardiovasc Electrophysiol 2004; 15: 968.
5. Tops LF, Bax JJ, Zeppenfeld K, Jongbloed MR, Lamb HJ, van der Wall EE, et al. Fusion of multislice computed tomography imaging with three-dimensional electroanatomic mapping to guide radiofrequency catheter ablation procedures. Heart Rhythm 2005; 2: 1076-81.
6. Dong J, Dickfeld T, Dalal D, Cheema A, Vasamreddy CR, Henrikson CA, et al. Initial experience in the use of integrated electroanatomic mapping with three-dimensional MR/CT images to guide catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol 2006; 17: 459-66.
7. Martinek M, Nesser HJ, Aichinger J, Boehm G, Purerfellner H. Accuracy of integration of multislice computed tomography imaging into three-dimensional electroanatomic mapping for real-time guided radiofrequency ablation of left atrial fibrillation-Influence of heart rhythm and radiofrequency lesions. J Interv Card Electrophysiol 2006; 17: 85-92.
8. Kistler PM, Rajappan K, Jahngir M, Earley MJ, Harris S, Abrams D, et al. The impact of CT image integration into an electroanatomic mapping system on clinical outcomes of catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol 2006; 17: 1093-101.
9. Malchano ZJ, Neuzil P, Cury RC, Holmvang G, Weichet J, Schmidt EJ, et al. Integration of cardiac CT/MR imaging with three-dimensional electroanatomical mapping to guide catheter manipulation in the left atrium: implications for catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol 2006; 17: 1221-9.
10. Fahmy TS, Mlcochova H, Wazni OM, Patel D, Cihak R, Kanj M, et al. Intracardiac echo-guided image integration: optimizing strategies for registration. J Cardiovasc Electrophysiol 2007; 18: 276-82.
11. Manzke R, Reddy VY, Dalal S, Hanekamp A, Rasche V, Chan RC. Intra-operative volume imaging of the left atrium and pulmonary veins with rotational X-ray angiography. Med Image Comput Comput Assist Interv Int Conf Med Image Comput Comput Assist Interv 2006; 9: 604-11.
12. Ferguson J. Optimizing catheter navigation for AF ablation: do not just follow the map! J Cardiovasc Electrophysiol 2007; 18: 283-5.
13. Bunch TJ, Day JD. Unravelling the mysteries of catheter ablation for atrial fibrillation: from clinical observations to mechanistic explorations. J Cardiovasc Electrophysiol 2007; 18: 266-8.
14. Fenici R, Brisinda D. Is there any place for magnetocardiographic imaging in the era of robotic ablation of cardiac arrhythmias? LNCS 2007; 4466: 230-9.
15. Taccardi B. Body surface mapping and cardiac electric sources. A historical survey. J Electrocardiol 1990; 23 Suppl: 150-4.
16. Hren R, Horacek BM. Value of simulated body surface potential maps as templates in localizing sites of ectopic activation for radiofrequency ablation. Physiol Meas 1997; 18: 373.
17. Burnes JE, Taccardi B, Rudy Y. A noninvasive imaging modality for cardiac arrhythmias. Circulation 2000; 102: 2152-8.
18. Berger T, Fischer G, Pfeifer B, Modre R, Hanser F, Trieb T, et al. Single-beat noninvasive imaging of cardiac electrophysiology of ventricular pre-excitation. J Am Coll Cardiol 2006; 48: 2045-52.
19. Fenici RR, Melillo G. Biomagnetic study of cardiac arrhythmias. Clin Phys Physiol Meas 1991; 12 (Suppl A): 5-10.

20. Fenici RR, Brisinda D, Meloni AM. Clinical application of magnetocardiography. Expert Rev Mol Diagn 2005; 5: 291-313.
21. Fenici RR & CNR, inventors. Biomagnetically localizable multipurpose catheter and method for magnetocardiographic guided intracardiac mapping, biopsy and ablation of cardiac arrhythmias. Unites States patent US 5056517. 1991 Oct 15. [filled July, 24, 1989].
22. Hren R, Stroink G, Horacek BM. Spatial resolution of body surface potential maps and magnetic field maps: a simulation study applied to the identification of ventricular pre-excitation sites. Med Biol Eng Comput 1998; 36: 145-57.
23. Hren R, Zhang X, Stroink G. Comparison between electrocardiographic and magnetocardiographic inverse solutions using the boundary element method. Med Biol Eng Comput 1996; 34: 110-4.
24. Fenici R, Pesola K, Mäkijärvi M, Nenonen J, Teener U, Fenici P, et al. Non-fluoroscopic localization of an magnetic catheter in a realistic torso phantom by magnetocardiographic and body surface potential mapping. Pacing Clin Electrophysiol 1998; 21: 2485-91.
25. Fenici R, Brisinda D, Nenonen J, Fenici P. Phantom validation of multichannel magnetocardiography source localization. Pacing Clin Electrophysiol 2003; 26: 426-30.
26. Koch H. Recent advances in magnetocardiography. J Electrocardiol 2004; 37 Suppl: 117-22.
27. Brisinda D, Fenici R. Non-invasive Classification and follow-up of WPW patients with unshielded magnetocardiography and transesophageal atrial pacing. Pacing Clin Electrophysiol 2007; 30 (Suppl 1): S151-5.
28. Yamada S, Yamaguchi I. Magnetocardiograms in clinical medicine: unique information on cardiac ischemia, arrhythmias, and fetal diagnosis. Intern Med 2005; 44: 1-19.
29. Agren PL, Goranson H, Jonsson H, Bergfeldt L. Magnetocardiographic and magnetic resonance imaging for noninvasive localization of ventricular arrhythmia origin in a model of nonischemic cardiomyopathy. Pacing Clin Electrophysiol 2002; 25: 161-6.
30. Yamada S, Tsukada K, Miyashita T, Kuga K, Yamaguchi I. Noninvasive, direct visualization of macro-reentrant circuits by using magnetocardiograms: initiation and persistence of atrial flutter. Europace 2003; 5: 343-50.
31. Nakai K, Kawazoe K, Izumoto H, Tsuboi J, Oshima Y, Oka T, et al. Construction of a three-dimensional outline of the heart and conduction pathway by means of a 64-channel magnetocardiogram in patients with atrial flutter and fibrillation. Int J Cardiovasc Imaging 2005; 21: 555-61.
32. Koskinen R, Lehto M, Vaananen H, Rantonen J, Voipio-Pulkki LM, Makijarvi M, et al. Measurement and reproducibility of magnetocardiographic filtered atrial signal in patients with paroxysmal lone atrial fibrillation and in healthy subjects. J Electrocardiol 2005; 38: 330-6.
33. Kim K, Lee YH, Kwon H, Kim JM, Bae JH. Independent component analysis for synthetic aperture magnetometry in magnetocardiography. Comput Biol Med 2006; 36: 253-61.
34. Kim K, Kim DS, Lee YH, Kwon H, Park YK, Lim SP. Visualization of the current source distribution for the atrial fibrillation by using a separative minimum variance beam former [abstract P-264]. In: Cheyne D, Ross B, Stroink G, Weinberg H, editors. Proceedings of 15th International Conference on Biomagnetism; 2006 Aug 20-26; Vancouver, Canada.
35. Nakai K, Fukuhiro Y, Fukushima A, Suwabe A, Ito M, Yoshizawa M. Three-dimensional frequency distribution of atrial fibrillation by magnetocardiogram is valuable for the restoration to sinus rhythm after pulmonary vein isolation [abstract P-275]. In Cheyne D, Ross B, Stroink G, Weinberg H, editors. Proceedings of 15th International Conference on Biomagnetism; 2006 Aug 20-26; Vancouver, Canada.
36. Rubenstein J, Kadish A. Three-dimensional image integration: a first experience with guidance of atrial fibrillation ablations. J Cardiovasc Electrophysiol 2006; 17: 467-8.
37. Cappato R. Towards more effective techniques for catheter ablation of atrial fibrillation: to aim for electrical disconnection of pulmonary veins or not? Eur Heart J 2005; 26: 627-30.
38. Lo LW, Tai CT, Lin YJ, Chang SL, Wongcharoen W, Chang SH, et al. Progressive remodeling of the atrial substrate--a novel finding from consecutive voltage mapping in patients with recurrence of atrial fibrillation after catheter ablation. J Cardiovasc Electrophysiol 2007; 18: 258-65.
39. Kanj MH, Wazni O, Fahmy T, Thal S, Patel D, Elay C, et al. Pulmonary vein antral isolation using an open irrigation ablation catheter for the treatment of atrial fibrillation: a randomized pilot study. J Am Coll Cardiol 2007; 49: 1634-41.
40. Takahashi Y, O'Neill MD, Hocini M, Reant P, Jonsson A, Jais P, et al. Effects of stepwise ablation of chronic atrial fibrillation on atrial electrical and mechanical properties. J Am Coll Cardiol 2007; 49: 1306-14.
41. Sanders P, Berenfeld O, Hocini M, Jais P, Vaidyanathan R, Hsu LF, et al. Spectral analysis identifies sites of high-frequency activity maintaining atrial fibrillation in humans. Circulation 2005; 112: 789-97.
42. Takahashi Y, Sanders P, Jais P, Hocini M, Dubois R, Rotter M, et al. Organization of frequency spectra of atrial fibrillation: relevance to radiofrequency catheter ablation. J Cardiovasc Electrophysiol 2006; 17: 382-8.
43. Lazar S, Dixit S, Callans DJ, Lin D, Marchlinski FE, Gerstenfeld EP. Effect of pulmonary vein isolation on the left-to-right atrial dominant frequency gradient in human atrial fibrillation. Heart Rhythm 2006; 3: 889-95.
44. Pachon M JC, Pachon M EI, Pachon M JC, Lobo TJ, Pachon MZ, Vargas RN, et al. A new treatment for atrial fibrillation based on spectral analysis to guide the catheter RF-ablation. Europace 2004; 6: 590-601.
45. Fenici R, Brisinda D. Bridging non-invasive and interventional electroanatomical imaging: role of magnetocardiography. J Electrocardiol 2007; 40 (Suppl 1) : S47-52.
46. Nenonen J. Magnetocardiography. In: Clark J, Braginski A, editors. SQUID Handbook. Berlin: Whiley-VCH; 2005.
47. Fenici R, Brisinda D, Meloni AM. Effects of filtering on computer-aided analysis for detection of chronic ischemic heart disease with unshielded rest magnetocardiographic mapping. Neurol Clin Neurophysiol 2004; 2004: 7.
48. Kim D, Kim K, Ahn H, Lee YH. Detection of atrial arrhythmia in superconducting quantum interference device magnetocardiography; preliminary result of a totally-noninvasive localization method for atrial current mapping. Interact. Cardiovasc Thorac Surg. In press 2007.
49. Veisterä H, Fenici R, Lötjönen J. Online heart model creation for magnetocardiographic measurements. In: Halgren E, Ahlfors S, Hämäläinen M, Cohen D, editors. Proceedings of the 14th International Conference on Biomagnetism; 2004 Aug 8-12; Boston, USA.
50. Fenici R, Brisinda D. From 3D to 4D imaging: is that useful for interventional cardiac electrophysiology? Conference Proceeding of the Annual International Conference of the IEEE Engineering in Medicine and Biology. IEEE Eng Med Biol. In press 2007.
51. Noseworthy PA, Malchano ZJ, Ahmed J, Holmvang G, Ruskin JN, Reddy VY. The impact of respiration on left atrial and pulmonary venous anatomy: implications for image-guided intervention. Heart Rhythm 2005; 2: 1173-8.
52. Hauser TH, McClennen S, Katsimaglis G, Josephson ME, Manning WJ, Yeon SB. Assessment of left atrial volume by contrast enhanced magnetic resonance angiography. J Cardiovasc Magn Reson 2004; 6: 491-7.
53. Haddad R. Un model numérique anthropomorphique et dynamique du thorax respirant et du cœur battant [dissertation]. Lyon, France: CREATIS-CNRS UMR 5220, Inserm U630: 2007.