Magnetic Quantities: Healthcare Sector Measuring Demands and International Infrastructure for providing Metrological Traceability

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Abstract:

Innovations in the healthcare sector along the last half-century have created a growing demand for metrological traceability of measurement results regarding magnetic quantities. This work discusses these challenging requests for traceability, from the lowest to the highest values of magnetic flux densities associated with the recently developed biomedical technologies as well as other relevant health demands. The worldwide availability of quality metrological infrastructure for providing measurement standards appropriate to the demanding quantity range is analyzed based on the information of the BIPM key comparison database (KCDB) appendices. Results indicate that the demands for metrologically traceable measurement results regarding power frequency magnetic field exposure have demonstrated to be a notable driver toward the establishing of metrological infrastructure by National Metrology Institutes. Although limitations of available measurement standards for magnetic quantities produce significant impacts on the possibility of meeting medical innovations' demands, the recent fast expansion of comprehensiveness of declared CMC capabilities for ensuring metrological traceability of magnetic quantities points toward the possibility of meeting the demanding values from healthcare sector in the near future.

Keywords: healthcare technologies, magnetic quantities, metrological traceability

1. Introduction

Reliability of measurement results, as well as its worldwide comparability, is assured with the possibility to obtain metrological traceability to the International System of Units (SI). Traceable calibrations are required to ensure appropriate function of measuring instruments used in production and testing processes of a wide variety of industries; safety and performance of equipment used in healthcare; environmental safety; and Research & Development sector. In 1927, driven by the expansion of the range of scientific domains demanding the International Committee for Weights and Measures (CIPM) attention under the Meter Convention, signed on May 20, 1875, the first CIPM Consultative Committee was created, the Consultative Committee for Electricity (CCE). However, it was only seventy years later, in 1997, that the full denomination of the committee was given as Consultative Committee for Electricity and Magnetism (CCEM). The custodians of the national measurement standards necessary to support the metrological traceability chain to SI system in a country are the National Metrology Institutes (NMIs). By June 2018, Calibration and Measurement Capabilities (CMC) declarations for magnetic quantities, namely magnetic fields at frequencies below 50 kHz, were included in Appendix C of the BIPM key comparison database (KCDB) by 18 NMIs, being most of the measurands related to low-frequency magnetic flux density measurements. In turn, the demands for traceable calibration chain between magnetic measurements and the SI is growing all over the world and so is the number of countries with CMC declared for these measurands. Among the challenging demands to be met by standardization associated with magnetic quantities are those arisen from the high rate of innovation of the healthcare sector. However, it is particularly recent, in 1999, when the 21st General Conference on Weights and Measures (CGPM) explicitly considered, in its resolutions, the demands for metrological traceability of measurement results derived from biomedical sectors (Costa Monteiro, 2007; Costa Monteiro and Leon, 2015; Costa Monteiro, 2017). The Consultative Committee for Amount of Substance: Metrology in Chemistry (CCQM), which was created in 1993, took on the task of promoting the development of infrastructure to provide metrological traceability in the health sector, but naturally restricted efforts toward biochemical, biomolecular, and biotechnological aspects (Costa Monteiro, 2007; Costa Monteiro & Leon, 2015; Costa Monteiro 2017). Along the last half-century, several innovations using physical principles based on magnetic quantities and aimed at providing non-invasive diagnosis and treatment are being introduced in the clinical environment. These recently available biomedical tools create new demands for metrological traceability of measurement results. In the present work, these emerging magnetic measuring requests for traceability to SI originating from the health sector are described and discussed along with the possibility of being attended by measurement standards provided by the available worldwide quality infrastructure.

2. Health technologies based on magnetic quantities demanding metrological traceability

In the context of the recent progress in the healthcare sector of the last decades, the early seventies have witnessed the birth of biomedical technologies providing innovations in the non-invasive diagnosis and treatment. These new developments making use of operating principles & based on magnetic quantities generated a growing request for metrological traceability of magnetic measurement results for a variety of intensity and frequency ranges. This section presents some examples of these demands emerging from medical environment.

2.1 Biomagnetic field sensors

Since 1970, with the development of highly sensitive magnetometers based on superconductivity, the Superconducting Quantum Interference Device (SQUID), scientific studies of the ultra-weak biomagnetic signal were introduced (Zimmerman et al., 1970). The magnetic flux densities generated by biomagnetic sources comprise values between femtotesla and nanotesla, and their frequencies are in the range of DC to 1 kHz (Andrä &Nowak, 2007).

Biomagnetic fields are generated by the bioelectrical activity of excitable tissues or by magnetic particles placed in the organism. The non-invasive, contactless, and harmless detection of the biomagnetic field allows to obtain information about the temporal and spatial distribution of the field sources, making it possible to identify the location and propagation of bioelectrical activity in excitable tissues, the so-called primary current sources, without being disturbed by the non-homogeneity of the torso volume conductor (Costa Monteiro et al, 1987; Andrä & Nowak, 2007). This information cannot be reached by the conventional measurement of the electric potential difference using surface electrodes, as in Electrocardiography (ECG), Electroencephalography (EEG), Electromyography (EMG), among others, which, being based on the currents generated in the volume conductor, the secondary currents, these measurements are strongly influenced by the non-homogeneity of conductivities of body tissues (Costa Monteiro et al, 1987; Costa Monteiro et al, 2001a). The biomagnetic field measurement allows, for instance, a non-invasive access to the propagation of bioelectric activity in cardiac tissue, which consists of primary current, being undetectable by surface ECG, unless biopotential electrodes are placed directly on the heart muscle (Costa Monteiro et al, 2001a; Costa Monteiro et al, 2001b; Yamada & Yamaguchi 2005) and precise localization of foreign bodies for surgical removal, significantly reducing the procedure time, the exposure to radiation during intervention, and odds of failure, ensuring successful treatment outcomes (Costa Monteiro et al, 2000).

Considering the SQUID drawbacks of needing cryogenic cooling, its high cost of fabrication, installation and operation, alternative sensors have been studied as a new possibility for measuring the ultra-weak biomagnetic fields, based on Giant Magnetoimpedance (GMI) (Cavalcanti et al, 2008; Silva et al, 2011) showing the most promising results. Recent studies indicate that transducers based on the impedance phase characteristics of GMI sensing elements are considerably more sensitive than the usualy applied magnitude-based GMI magnetic transducers (Silva et al, 2014; Benavides et al, 2018). The development of this high sensitivity phase-based GMI sensor allows the measurement of ultra-weak biomagnetic fields to be pursued by using a low-cost device, which would facilitate the application and dissemination of this non-invasive and innocuous diagnostic tool in clinical environments.

2.2 Magnetic resonance imaging

Magnetic resonance imaging (MRI) uses the physics principle of nuclear magnetic resonance (NMR). The technique allows obtaining chemical and physical information about molecules in multiple planes, enabling clinicians to identify abnormalities in various regions of the organism, with the distinct advantage of better image contrast of the soft tissue in body structures (Andrä & Nowak 2007).

The first scan on a human using nuclear magnetic resonance (NMR), performed in 1971, indicated its potential to detect diseases. Subsequently, clinical Investigations with magnetic resonance imaging (MRI) equipment continuously grew up, introducing, in 1980, the first commercial MRI scanner. In 1992, the functional magnetic resonance imaging (fMRI) expanded the clinical use, allowing identifying brain regions and their functions (Andrä & Nowak, 2007; Roth et al, 2018).

Magnetic resonance operates using the interaction between an external magnetic field, radio frequency energy and nuclei possessing spin. Superconductive magnet immersed in liquid helium (-269 ºC) creates magnetic fields from 0.5 to 3.0 T. Protons generate a nuclear magnetic resonance frequency of 42.577 MHz in a magnetic flux density of 1 T. With the aid of an RF field in the MHz range, and a variable static magnetic field along the longitudinal axis, the sharp resonance absorption of magnetic nuclei in biological tissue is used to obtain the spatial distribution of the nuclear magnetization. In particular, hydrogen atoms, which occur naturally in large numbers, allow medically meaningful images to be produced (Webster, 2010). Future perspectives on improving clinical diagnostic applications, even more, preview the implementation of ultra-high-field MR systems, emitting magnetic flux density intensities up to seven teslas (Roth et al, 2018).

2.3 Transcranial Magnetic Stimulation

The first TMS procedures were introduced over the latter half of the 1980s. The technique consists of applying intense pulses, with magnetic flux densities of the order of two to three teslas and short duration (few kHz). The rapidly changing magnetic field generated by an external coil induces electrical currents sufficient to stimulate bioelectrical activities located in different levels of the brain structure, useful in the treatment of neurological and psychiatric disorders. The induced electric field in the conducting brain tissue is associated with the geometry of the stimulating coil employed. TMS equipment has been continuously evolving by developing several coil configurations suitable for direct stimulation of brain regions with different sizes and depths. Currently, there are several TMS coil designs available: ring coil, the figure-of-eight coil, angulated figure-of-eight coil, double cone, Halo (H) coil, and Halo-circular assembly (HCA) coil. With the advantage of inducing currents in brain regions without stimulating the skin, and therefore being painless, TMS has been used in the treatment of several neuropsychiatric disorders, being useful in treating drug-resistant conditions (Bersani et al, 2013; Palatnik de Souza & Costa Monteiro, 2015; Lu & Ueno, 2017; Palatnik de Souza et al, 2018).

2.4 Instrumentation for monitoring levels of environment exposure to magnetic fields

Considering the risks of electromagnetic fields to health, World Health Organization carried out initiatives towards limiting human exposures since 1989 (Tourab & Babouri, 2015). Founded in 1992, the International Commission on Non-Ionizing Radiation Protection (ICNIRP) develops scientific research and publishes guidelines regarding adverse effects of non-ionizing radiation in human health and the environment, including static magnetic fields and electromagnetic fields. As for 1998, ICNIRP publishes guidelines for limiting exposure to electric, magnetic and electromagnetic fields, defining acceptable reference levels. In the same year, the International Electrotechnical Commission issued the IEC 61786, with requirements for instruments and guidance for measurements of low-frequency magnetic and electric fields concerning exposure of human beings. Subsequently, ICNIRP and IEC publications of guidelines and technical standards, respectively, introduced a significant demand for calibrated instruments for measuring magnetic quantities. For example, regarding the power frequency magnetic field exposure (50/60 Hz), according to the ICNIRP's guideline published in 2010, the magnetic flux density of 200 mT is reference level for general public exposure.

3. NMI measurement capabilities for magnetic quantities compared to health technologies demands

With the advent of the mutual recognition arrangement (CIPM MRA) the equivalence of national measurement standards is established through BIPM intercomparisons. Information on CIPM and RMO key and supplementary comparisons, available in Appendix B of KCDB, by June 2018, indicates a total of 235 intercomparisons carried out by the CCEM, being only twelve of them associated with magnetic quantities (Table 1), namely magnetic fields at frequencies below 50 kHz. More than half of CCEM comparisons consisted of key comparisons (128), being, however, only two of them directed to magnetic quantities. Both the magnetic key comparisons already accomplished were performed to low-frequency magnetic flux density, being concluded in 2000 and 2003, with eight and ten participating NMIs, respectively (Table 1).

Table 1 – Intercomparisons regarding magnetic quantities conducted up to june 2018.

year	RMO/CCEM INTERCOMPARISONS	Magnetic Quantity	Participating NMIs
1998	EUROMET.EM- S1	Comparison of measurements on electrical sheet steels	2
1998 - 2000	EUROMET.EM.M- K1	Comparison of low frequency magnetic flux density	8
1998 - 2001	EUROMET.EM- S13	Comparison of measurements on electric sheet steels	3
2001 - 2002	EUROMET.EM.M- S1	S1 Measurement of magnetic flux	5
2001 -2003	CCEM.M- K1	Comparison of low frequency magnetic flux density	10
2009	COOMET.EM- S9	Comparison of measurements on electrical sheets	4
2010	APMP.EM- S9	Comparison of magnetic flux density standards	2
2011	COOMET.EM- S12	Magnetic losses in isotropic and anisotropic electrical steel	3
2012	APMP.EM- S13	DC magnetic flux density	2
2013 - 2014	APMP.EM- S14	Earth-level DC magnetic flux density	6
2013 - 2015	COOMET.EM- S16	Pulsed electric and magnetic fields	2
2014 - 2015	EURAMET.EM.M- S2	Polarization and specific total power loss in soft magnetic materials	5

In June 2018, among the 103 institutes signatories of CIPM MRA, there were eighteen with internationally recognized CMC for Magnetic fields at frequencies below 50 kHz. Regarding magnetic flux density and applied magnetic field strength, a particularly relevant magnetic quantity for health technologies. Seventeen NMIs had their quality infrastructure declared for DC values, and 13 NMIs for AC values associated with magnetic flux density and applied magnetic field strength. Since 2013, metrological traceability for higher levels of magnetic flux densities is offered. Two NMIs approved their declarations up to 1 or 1.2 T in 2013. Along the following years, other eleven NMIs declared capabilities higher than 1 T. It is worth mentioning that a level of 2.5 T was provided by KRISS (Korea Research Institute of Standards and Science), in 2014, and the highest value achieved, 3.5 T, was declared in 2017, by the Czech Metrology Institute. However, a single CMC declaration, from the Russian Federation NMI, comprises AC magnetic flux densities up to 1 T, within the frequency range of 20 Hz to 200 Hz.

Approved in 2013, magnetic flux density of 0.01 μT is the lowest value for which metrological traceability is being provided. Levels of μT have been declared, since then, by five NMIs for static fields, being three of them approved in 2016 and the fifth one, in 2017; and for AC fields by 13 national institutes.

Comparing the capabilities published in the KCDB for magnetic quantities with the health demands highlighted in section two, it can be noticed a progressive improvement of comprehensiveness of quantities' ranges being provided toward meeting the demanding values of the health sector. The high levels of DC magnetic flux densities up to 3.5 T, recently published in Appendix C evolve to complying with MRI needs. Although achieving magnitudes that could be appropriate to TMS demands, the current CMC does not meet the necessary frequency range, since the equipment emits pulses with around 3 kHz.

Metrological traceability for biomagnetic measurements, in turn, cannot be provided by any of the CMC published, once the demands regarding intensities are lower than nanotesla while the lowermost value declared is 0.01 μT.

Regarding the needs originating from the exposure limits established by ICNIRP guideline for magnetic flux density of 200 mT at power frequency (50/60 Hz), a worldwide concern, the entire group of 13 NMIs with AC magnetic flux density CMC, has declared capabilities complying with the frequency and intensities to provide metrological traceability in the necessary range. The Swedish CMC, however, is restricted to 50 Hz, which does not meet power frequency typically used in the American Continent and parts of Asia; and covers 0.1 μT to 300 μT, which is a narrow range around the ICNIRP limit.

Human safety regarding exposure limits for magnetic flux densities has been widely addressed by international technical standards and national regulatory documents, resulting in a triggering factor for the NMIs introduction of infrastructure to provide traceability of magnetic quantities. The IEC 61786 series, published since 1998 by IEC TC 108, deals with the measurement of low-frequency magnetic and electric fields concerning human exposure. Later, additional documents were produced such as the IEC 62311:2007 for assessment of electronic and electrical equipment related to exposure restrictions, as well as, the IEC 62110:2009 addressing measurement procedures with regard to public exposure for electric and magnetic field levels generated by AC power systems. The regulatory effect can be exemplified with the Brazilian NMI, the eighteenth among the set of 18 institutes to declare CMC for magnetic quantities, with approval received on 27 March 2017. Following the publication, in 2009, of a Federal Law 11.934 setting maximum limits for human exposure, the Brazilian Electrical Energy Regulatory Agency (ANEEL) issued normative resolutions establishing the requirements of the Federal Law, with restrictions for time-varying electric and magnetic fields with frequencies of 60 Hz, the power frequency in Brazil (França et al. 2012, Mendonça 2013), according to the limits established by ICNIRP guidelines, in 2010. The regulatory document required using measuring instruments calibrated by accredited laboratories, providing the appropriate evidence of metrological traceability. As a consequence, the Brazilian NMI invested efforts to implement the infrastructure for ensuring national traceability for measurements within the requested range and, since March 2017, it declared CMC for low-frequency magnetic flux density from 1.1 μT to 700 μT, 50/60 Hz; accrediting, on May 2017, the first calibration laboratory for magnetic quantities.

Discussion and Conclusion

Along the last five decades, important innovations in the non-invasive diagnosis and treatment have generated a growing demand for metrological traceability of measurement results regarding magnetic quantities. Research and development of biomedical technologies created requests from ultra-low magnetic flux densities from femtotesla to nanotesla levels (DC to kHz) for magnetic measurements allowing the non-invasive, contactless, and innocuous assess of biomagnetic sources; up to ultra-high values of few teslas, associated with technologies for transcranial magnetic stimulation and magnetic resonance imaging. Emphasized by WHO since 1989, followed by the publication of several ICNIRP guidelines with exposure limits, a series of IEC international technical standards and national regulatory documents; a worldwide concern regarding the risks of human exposure to magnetic fields has been, in turn, a decisive demand for the introduction of infrastructure to provide traceability of magnetic quantities.

High levels of DC magnetic flux densities, up to 3.5 T, of recent declarations published in the Appendix B of KCDB shows that only 5 % of CCEM key and supplementary comparisons are associated with magnetic fields at frequencies below 50 kHz as well as, Appendix C indicates that only 17 % of the institutes signatories of CIPM MRA (18 NMIs) possess internationally recognized CMC for these magnetic quantities. Appendix C of KCDB, drifts toward complying with MRI needs. Although achieving magnitudes that could be appropriate to TMS demands, the current CMC does not meet the necessary frequency range, since the equipment emits pulses with around 3 kHz.

While appropriate measurement standards for demands associated with the mentioned biomedical technologies of high clinical relevance are not fully available, the need of metrologically traceable measurement results regarding power frequency magnetic field exposure (50/60 Hz) has been the primary driver toward the establishing of metrological infrastructure, being provided by the whole set of NMIs with CMC for AC magnetic flux densities.

Although the highlighted limitations, the recent improvement of the international infrastructure for ensuring metrological traceability of magnetic quantities, with the expanding comprehensiveness of the declared quantity's ranges, points toward the possibility of reaching the requested values of healthcare sector demands in the near future.

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