Preface

Electromagnetic interference (EMI) is the disruption of operation of an electronic device when it is in the vicinity of an electromagnetic field that is caused by another electronic device.

The section "Electromagnetic Interference with Medical Devices" of this issue of the Annali dell'Istituto Superiore di Sanità *features original investigations and reviews of the proper functioning of medical devices in the presence of external sources of electromagnetic fields.*

Research groups, manufacturers, and governmentall/non-governmental agencies have reported EMI-related incidents with medical devices. Some of them had life-threatening consequences, others could have had, others can be considered just a nuisance. Over the past 15 years, the US Food and Drug Administration has had more than 500 incident reports suspected to be attributable to EMI affecting medical device in hospitals. These reports prompted the need for an increased attention to medical device electromagnetic compatibility by users, manufactures, and standard organizations.

The large number of different medical devices, the peculiarity of some of them (e.g., implantable vs non-implantable or diagnostic vs therapeutic), and the gravity of the potential consequences of EMI render it difficult to treat this matter with a unique approach. The wide number of potential sources of interference and related mechanisms (e.g., conducted vs radiated) make the problem even more complex. The fast-changing area of telecommunications and the increasingly complex technology of medical devices call for the continuous updating of the knowledge on EMI with medical devices.

The safety aspects regarding the functioning and use of medical devices are extremely interesting for the Istituto Superiore di Sanità. The Institute is, indeed, committed to focusing on individual health, but at the same time it considers the collective dimension of public health. Electromagnetic compatibility of, and electromagnetic interference with, medical devices are part of the general problem of medical device safety.

This special section is devoted to reviews and innovative works in the following areas: electromagnetic interference with non-implantable medical devices; electromagnetic interference with active implantable devices; technical standards and regulations.

Given the dimension and the complexity of the EMI problem, this special section deals with topics which are expected to emerge in the near future: new experimental data and methodological approaches to address the impact of innovative services – e.g., TETRA mobile phones (to be adopted in many European countries by police, firemen and ambulance staff) and WiFi networks (installed in many hospitals worldwide) – as well as a global approach to the EMI environment management of an entire hospital; the state of the art of knowledge on low- and high-frequency EMI (power lines, magnetic resonance scanners and mobile phones) with the most widespread implantable devices (pacemakers and cochlear implants); a comprehensive review of the technical standards and norms concerning both medical devices and human exposure, including those guidelines which will constitute the basis for risk assessment in hospitals.

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Electromagnetic interference from GSM and TETRA phones with life-support medical devices

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Summary. Disturbances in hospital devices caused by cellular telephone signals were investigated. The interference sources were GSM900, GSM1800, and TETRA380 phones. The number of medical appliances tested was 23. Most measurements were taken in a semi-anechoic laboratory. To simulate the worst situation, the phones were adjusted to emit at their maximum power levels. No interference was observed if the distance from GSM1800 phone was over 5 cm. Corresponding safety distance for GSM900 phone was 70 cm, and for TETRA phones over 3 m. Hence, the use of GSM1800 type mobile phones can be considered safe, whereas GSM 900 and TETRA phones may cause considerable interference in hospital devices, which can result in life-endangering situations.

Key words: electromagnetic fields, equipment and supplies, hospital, cellular phone.

Riassunto *(Interferenze elettromagnetiche da telefoni GSM e TETRA su dispositivi medici di supporto vitale)*. In questo lavoro vengono studiati i disturbi su dispositivi medici in ospedale causati da telefoni cellulari. Le sorgenti di interferenza erano telefoni GSM a 900 MHz, a 1800 MHz e TETRA 380. Il numero di dispositivi medici testati era 23. La maggior parte delle misure sono state raccolte in camera semianecoica. Per simulare le condizioni di caso peggiore, i telefoni sono stati regolati per trasmettere alla loro massima potenza. Nessuna interferenza è stata osservata con i telefoni GSM1800 per distanze superiori a 5 cm. La corrispondente distanza di sicurezza per i GSM900 è risultata 70 cm, per i TETRA oltre 3 m. Quindi l'uso di telefoni GSM1800 può essere considerato sicuro, mentre i GSM900 e i TETRA possono creare interferenze che possono dare luogo a situazioni pericolose.

Parole chiave: campi elettromagnetici, apparecchiature e forniture ospedaliere, telefono cellulare.

INTRODUCTION

Safety of patients and acute medical treatments in hospitals require fast and constant attainability of the staff. Traditionally, the hospitals use a paging system that can usually show only phone number of the caller. The person answers the call by using a special number code in the nearest telephone. The limitation of the paging system is that it functions only in the hospital area. The best technical solution for the staff would be the use of mobile telephones. They are, however, forbidden in most hospitals, indicated by warning labels outside the front door of a hospital as shown in *Figure 1*. This prohibition is based on the suspicion that mobile phones cause disturbances in medical equipment, hence endangering safety of the patients.

This study aimed to test interference by cellular telephones in the hospital environment, and to find areas where the use of mobile phones is safe. The objective was, therefore, to clarify whether the traditional paging system could be replaced by cellular phones.

Requirements for electromagnetic compatibility of medical equipment have been defined generally in the IEC standard 601-1-2 [1, 2]. Concerning radiofrequency (RF) fields emitted by cellular phones, the immunity of medical devices is defined by the electromagnetic compatibility requirement which is 10 V/m for life-support equipment in the frequency range of 26 to 2500 MHz.

MATERIALS AND METHODS

Mobile phones used as the interference source during the immunity tests were GSM900 MHz and GSM1800 MHz-phones (global system for mobile communication), and TETRA380 MHz (terrestrial trunked radio) functioning in the TETRA network and restricted for the authorised use, such as police, firemen and ambulance staff. In the normal use the base stations adjust the transmission power of the phones according to the traffic. In order to simulate the worst possible situation, the emitted power of the test phones was set at the maximum level using a specific service program.

GSM phones transmit pulsed signals, which consist of short carrier wave bursts of 580 μs of dura-

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Fig. 1 | *Label indicating that use of cellular phones is forbidden inside a hospital.*

tion, at repetition frequency of 217 Hz. The duration of a pulse is only 12.5% of the duration of the whole transmission period, and the average power of a GSM signal is 1/8 of its peak power. The pulse power was set to 2 W for the GSM900 phone and to 1 W for the GSM1800 phone during the tests. TETRA-phones transmit digital 380 MHz signals with a pulse frequency of 17 Hz. During the immunity tests the transmission power was set to 3 W.

The testing focused particularly on the equipment that could endanger patients' safety because of electromagnetic disturbance *(Table 1)*.

During the immunity tests all equipment were measured using the same measurement methods. The general principal was to arrange effective interference conditions in order to disturb the appliances as strongly as possible. Most of the measurements were made in the semi-anechoic, electronically isolated laboratory where the only sources of interference were the active mobile telephones. The possible disturbances in the function of the tested equipment were thus caused by RF fields transmitted by the mobile phone.

The medical appliances tested were connected to a patient simulator aimed to test the operations of the appliance. If there was no simulation equipment available, the appliance to be tested was connected to electric circuitry mimicking the function of the simulation equipment or to an assisting test person. Some of the tested appliances were so complicated that they could only be partly simulated.

The functions of the tested appliance were disturbed with the mobile phones by approaching the appliance from various directions. The antenna of phone was held both in vertical and horizontal position during the testing in order to assess the effect of the field polarization. The wiring, couplers and other similar components were set to stay straight for approximately one meter's distance and the possible metal objects that could cause reflections were removed from the vicinity of the equipment.

Measurement errors caused by a fault in a simulator were eliminated by following measures:

- simulation equipment was placed outside the testing room or as far as possible from the source of interference;
- electromagnetic immunity of the simulator was tested before the actual testing of the hospital equipment;
- some of the appliances were tested several times with different types of measurement circuits.

Some of the appliances were tested in the premises of a hospital due to transportation problems. Although the repeatability of these tests was not so effective as in the semi-anechoic laboratory, the testing in real surroundings corresponded to the normal hospital conditions and hence added validity of the research. In hospital conditions, the tested appliance was measured either by connecting the appliance to a patient-simulator or to a test subject. The measuring coupling used in the laboratory tests was not always possible to use in the hospital. Also the test phone, the tested appliance and the simulator were often close to one another due to the lack of space. When using a simulator, the possible interference was tested separately.

RESULTS

The results of the project indicate that the phone GSM1800 disturbs the tested appliances the least.

Table 1 | *The hospital equipment tested*

Equipment type	Name and model
Anaesthesia machine	Engström EAS 9010
Dialyzer	Fresenius 4008B DrakeWillock SYS1000
Defibrillator	HP 43120A Cardiolife TEC 7200H
Diathermy device	Martin ME 401 Radiotom 704
ECG Monitor	Cardiocap II CH-2S Cardiocap II CH-S-25-01 AS/3 F-C4B5
Endoflator	Endoflator 257
Sphygmo-manometer	Dinamap 8100 Dinamap 1846
Insufflator	Laparof Electronic 3509
Pulseoxymeter	Criticare 503 Datex OSP 200 Biochem BCI 3303
Respirator	Bird 6400 Evita 2 Dura 8413930
Ultrasound device	Aloka SSD-830 Aloka SSD-1400

Table 2 | *Distance (cm) of interference caused by the TETRA phone*

Device in test	Interference on the screen	Function interrupted	Faulty action	Interference sound	Device reported error
Fresenius 4008B	-	-	-	-	5
DrakeWillock SYS	5	-	5	-	5
HP 43120A	60	-	60	-	-
Cardiolife TEC	-	-	100	-	40
Biochem BCI 3303	30	-	-	30	-
Bird 6400	-	10	150	-	150
Evita 2 Dura	90	-	50	-	50
Cardiocap II CH-2S	60	-	300	-	-
Cardiocap II CH-S-25-01	-	-	50	-	-
AS/3 F-C4B5	10	-	10	-	-
Aloka, SSD-830	80	-	15	-	-
Aloka, SSD-1400	300	-	-	300	-
Dinamap 1846	50	50	-	-	50

No interference was observed when the distance of the phone to the device in test was more than 5 cm. None of the tested hospital equipment was disturbed to the extent the interference would have caused danger to a patient during the treatment.

Similarly, none of the equipment was disturbed when the distance from GSM900 phone was over 70 cm, with the exception of an interference sound in the ultrasound appliance when the distance was still 2,5 meters.

The hospital equipment tested was disturbed most by the TETRA380 network phones which caused interference as far as at a distance of 3 m *(Table 2)*.

DISCUSSION

In this study, the interference sensitivity of various hospital appliances to RF fields emitted by cellular telephones was tested. The functions of some of the appliances were so complicated that their simulation, and testing could only be carried out partially.

The results showed that GSM1800 phones did not cause significant disturbances and they can therefore normally be considered safe to use in the hospital environment. GSM900 phones, on the other hand, are recommended to be used only in the limited area where there are no interference-sensitive appliances. It must also be reminded that GSM1800 phones used presently are so called dual band-phones, which transmit randomly either 1800MHz or 900 MHz frequency unless the phone has been supplied only by a 1800 MHz card. Therefore, the security instructions given for GSM900 phones must also be applied to the dual-band phones if there is no certainty of the transmission frequency.

Cellular phones of the TETRA380 network caused the most serious disturbances in the tests. Their use should thus be allowed only in strictly limited areas. In certain circumstances, such as in urgent transportation of patients, in fire and rescue service and in police work, the use of TETRA phones in the hospital area cannot be avoided. Particularly the use of TETRA phones inside an ambulance should be minimized.

The disturbances caused by the phone in transmission mode to the equipment critical for patient's vital functions, such as defibrillator or respirator, could cause life-endangering situations.

CONCLUSIONS

In conclusion, the use of GSM1800 type mobile phones can be considered safe provided that the users are aware of the possibility of disturbance. Also, the staff which is allowed to use these phones should observe the functions of medical equipment and report all the suspected interference. GSM900 phone types can, on the other hand, have considerable interference effects, and their use should be assessed separately in each place. When defining safe areas, one should take into consideration the background field strength in the area, which depends on the base station's distance and settings. Normally the transmission power of a cellular phone and hence the interference risk of the equipment are the smaller the nearer from the hospital the base station is located.

The use of mobile phones by the patients and visitors should be allowed, if a hospital has specific rooms reserved for this purpose, where medical equipment is not being used ("cellular phone safe - wards"). Permitting the use of mobile phones freely in the hospital environment would require testing of a considerably larger variety of equipment and hospital-specific risk assessments.

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The electromagnetic environment of hospitals: how it is affected by the strength of electromagnetic fields generated both inside and outside the hospital

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Summary. Most problems with the electromagnetic environment of medical institutions have been related to radiated electromagnetic fields and have been constructed from reports about electromagnetic interference (EMI) with electronic medical equipment by the radio waves emitted from mobile telephone handsets. However, radiated electromagnetic fields are just one of the elements. For example, little attention has been placed on problems with the electric power source. Apparatus for clinical treatment and diagnosis that use electric power sources have come into wide use in hospitals. Hospitals must pay careful attention to all elements of the electromagnetic environment. Herein, I will show examples of measurements and measuring methods for radiated electromagnetic fields, static magnetic fields, and power-source noise, common components of the medical electromagnetic environment.

Key words: electromagnetic fields, electric power supplies, equipment and supplies, hospital.

Riassunto *(L'ambiente elettromagnetico negli ospedali: come è influenzato dalla potenza dei campi elettromagnetici generati all'interno e all'esterno dell'ospedale)*. La maggior parte dei problemi con l'ambiente elettromagnetico all'interno di istituzioni mediche, sono stati sino ad ora messi in relazione ai campi elettromagnetici radiati, come risulta da molti lavori riportati in letteratura circa l'interferenza elettromagnetica prodotta dalle onde radio emesse da telefoni cellulari su dispositivi medici elettronici. Tuttavia i campi elettromagnetici radiati sono soltanto uno degli elementi. Ad esempio poca attenzione è stata finora posta sulla problematica dell'interferenza con una sorgente di energia elettrica. Poiché i dispositivi medici, per la terapia e la diagnosi del paziente, che utilizzano una sorgente di energia elettrica, sono sempre più utilizzati negli ospedali, quest'ultimi debbono porre particolare attenzione a tutti gli elementi dell'ambiente elettromagnetico. In questo lavoro vengono riportati esempi di misure e metodi di misura delle componenti elettromagnetiche più comuni che si possono trovare in un ambiente medico: campi elettromagnetici radiati, campi magnetici statici e noise dovuto a sorgenti di energia elettrica.

Parole chiave: campi elettromagnetici, fonti di energia elettrica, apparecchiature e forniture ospedaliere.

INTRODUCTION

Most problems with the electromagnetic environment of medical institutions have been related to radiated electromagnetic fields and have been constructed from reports about electromagnetic interference (EMI) with electronic medical equipment by the radio waves emitted from mobile telephone handsets [1-6]. Regulations for use and hospital guidelines for mobile telephone handsets have been issued in many countries.

In Japan, over 95 million sets of cellular phones were in use as of the end of March, 2006 (75% diffusion rate) [7]. The increase in use has raised attention to the issue of radiated electromagnetic fields. The Ministry of Internal Affairs and Communications of Japan has done studies almost every year since 1996 to respond to this issue and has released many reports concerning the influence of EMI by cellular phones, wireless LANs, RF-ID tags (electronic tag), etc. on medical equipment. However, the electromagnetic environment does not consist solely of radiated fields. The electromagnetic environment in a clinical setting has many components such as:

- electromagnetic field;
- electric power supply;
- grounding;
- surge (thunder, static electricity);
- static magnetic field

with radiated electromagnetic fields just one of the elements.

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Although hospitals must pay attention to each component of the electromagnetic environment, the level of attention that needs to be devoted to each component differs. For example, the attention necessary to deal with problems with the electric power source is low, because the power sources currently available are more stable than earlier sources. Apparatus for clinical treatment and diagnosis that use electric power sources have come into wide use in hospitals. When misused, the possibility of stoppages increases. The environment in which medical treatment is given at home is similar, but when a patient or family member operates medical equipment, their knowledge of electric installation is far inferior to the knowledge of hospital professionals, and thus problems that might occur in this environment must be addressed.

Herein, I will show examples of measurements and measuring methods for radiated electromagnetic fields, static magnetic fields, and power-source noise, common components of the medical electromagnetic environment.

RADIATED RADIO FREQUENCY ELECTROMAGNETIC FIELDS

Introduction

The possibility of EMI with electronic medical equipment caused by radio waves coming from outside the hospital has been reported [8]. We also reported the poor shielding capacity of a concrete wall [9]. Because communication and broadcasts using radio waves are expected to increase, radio wave intrusion from outside will increase. In this section, we reported an experience to determine the radio wave frequency environment surrounding a modern urban hospital, published in [10]. Incoming radio waves were recorded at various positions in a hospital under construction, and these results will be also shown.

Methods

When evaluating the electromagnetic environment if there is no information about surrounding electromagnetic fields, three measurements should be done to determine the origin of irradiation and its possible effect on medical equipment. An accurate measurement method using an actual example is given.

The electric field intensity induced by radio waves coming from outside the hospital was measured in Fukuoka, an urban area with a population of 1.3 million. The hospital building is 56 m high and has 11 above ground floors and one basement floor. Because it is only 3.2 km from Fukuoka International Airport, the height of the building is regulated by aviation law, and there are no buildings exceeding 56 m around the hospital. The equipment used for the three measurements consisted of a biconical antenna (BBA9106, Shuwartz-Becke), a log-periodic antenna (KBA601A, Kyoritsu Electronic), a double-ridged guide antenna (3115, EMCO) and a spectrum analyzer (8566B, Hewlett-Packard).

The frequency distribution of the electric field intensity was measured at six points on the 1st, 4th, and 11th floors. The measured frequencies ranged from 30 MHz to 3 GHz. Electric field intensity was measured at vertical and horizontal polarizations over 360 degrees with slow antenna rotation, and the strongest electric field intensity was recorded.Measurement was performed on a Sunday, and the weather was fine.

In order to confirm the reproducibility of the measured values, we again measured electric field intensity after a 6-week interval. This measurement was done at the point on the 11th floor where the strongest field was recorded in the first measurement. Because no strong electric field intensity was observed at frequencies lower than 300 MHz in the first measurement, the measured frequency range was set from 300 MHz to 3 GHz. Measurement was performed on a Sunday, and the weather was fine.

Measurement was also done to determinate the source of incoming radio waves in areas where especially strong electric field intensity was observed, with the intensity measured every 45 degrees. Because no wave at the frequency of the strongest intensity we had previously noted was found in the area near the subject hospital, we continued our search for the antenna on foot and by map.

Even though the main radio wave transmitting station was identified by use of the second measurement, in order to investigate in detail the distribution of the electric field intensity, measurements were done with horizontal and vertical polarization at three points on the southeast side of the building. Because of the prefecture government office building between the measurement points and the radio wave transmitter, angles and visibility differed at every measurement point. Electric field intensity tended to be stronger as the measurement point was moved higher, with the highest intensity found in the ward on the highest floor. For all measurement points, when the intensity was 3 V/m or higher in either polarization, measurement was also done one floor lower. Otherwise, if the intensity of both polarizations was under 3 V/m, measurement on the floor below was not done. The threshold value was the electromagnetic compatibility marginal value of the general electronic medical equipment specified in IEC 60601-1-2 [11]. Because the frequency of the radio waves that induced the strongest electric field intensity was known by the measurement results, the frequency range for measurement was set from 2.5 GHz to 3.2 GHz. The measurement was performed on a Sunday, and the weather was cloudy.

Results

The number of radio waves coming into the hospital at electric field intensities higher than 0.1 V/m (100 dBμV/m) increased as the measurement point location became higher (12 radio waves at 1st floor, 19 at 4th floor and 28 at 11th floor, as reported in table 2 of [10]). Electric field intensity exceeding 3 V/m, the compatibility marginal value of general elec-

tronic medical equipment in a radiated electromagnetic field, was observed on the 11th floor.

After six weeks, we found that the maximum value was almost the same as that of the first measurement, indicating that the observed radio wave was not temporary, but was regularly coming into the hospital building. From the 45 degree measurements, the source of the transmission was determined to be from the southeast. The maximum intensity was 5.01 V/m (134 dBμV/m). Investigation of all strong radio wave transmitting sites in a southeasterly direction from the hospital found the airport surveillance radar (ASR) at Fukuoka International Airport to be the probable source.

The measurements done to investigate in detail the distribution of the electric field intensity, gave a maximum value of 199.53 V/m (166 dBμV/m) in a position on the 10th floor which is not covered by the prefecture government office building. In the same position on 6th floor, the electric field intensity decreased to below 3 V/m as well as on 10th floor in a position covered by the prefecture government office building.

Discussion of irradiated radio waves

The frequency distribution of incoming radio waves changes with height, position of measurement, and the direction of the receiving antenna. There are 14 cellular phone base stations (the minimum distance is approximately 200 m) within 2 km of the hospital. Since none of the measuring crew used cellular phone handsets, the 800 MHz and 1.5 GHz band radio waves were thought to be from cellular phone system base stations. The maximum radio wave from a cellular phone system base station was observed on the 4th floor. UHF television signals (500 MHz to 600 MHz) were also observed on all floors.

A strong electric field intensity was observed periodically at frequencies of 2.79 GHz and 2.87 GHz. The source was thought to be the ASR antenna at Fukuoka International Airport, the only ASR antenna transmitting strong electric waves within 5 km to the southeast of the hospital. The ASR antenna, which transmits radio waves at a 500 kW power output using 2.79 GHz and 2.87 GHz radio waves, is located at the Fukuoka International Airport [12]. ASR transmits and receives by rotating a parabolic antenna. The electric field intensities of 2.79 GHz and 2.87 GHz observed on the 11th floor [10] were almost 20 times the immunity standard of life support equipment set by IEC 60601-1-2. Without modification of the building, EMI with electronic medical equipment could have been a serious problem.

Over 95 million mobile telephone handsets were in use in Japan at the end of March 2006 [7]. Therefore, many cellular phone base stations are installed at short distances. The base stations are, in many cases, installed on the roofs of buildings or on towers at a height of 30 m to 50 m, the height of the 6th to 10th floors of the hospital. The direction of signals emitted from base station antennas is slightly downward. The 4th floor, therefore, had the strongest electric field intensity by radio waves from cellular phone base stations (800 MHz band and 1.5 GHz band).

The electric field intensity of a radiated electromagnetic field can be calculated by the following formula (1).

$$E = \frac{K\sqrt{G \cdot Pin}}{r} \quad (1)$$

where *Pin* is input electric power, *G* is antenna gain, *K* is constant, and *r* is the distance from the transmission source

Therefore, although the observed values were under 3 V/m in this measurement, because the distance between the measurement point and the nearest base station was 200 m, if the base station were nearer, the electric field intensity would be over the standard.

The ASR antenna at Fukuoka International Airport (radar) can be seen from measurement point on the 9th, 10th and 11th floors, even though it is located 3.2 km distant. From the 8th floor down, the prefecture government office building shades the ASR antenna. If the measurement points are located within the perpendicular transmission angle of the ASR antenna and the antenna can be seen from these points with no obstacles around them, the measurement points would be in the Fresnel Zone, where reflective waves amplify the intensity. This would be the cause of the particularly strong electric field intensity measured on the 10th floor compared with the other measurement points. Even on the 8th floor, where the radar antenna cannot be seen, strong electric field intensity was observed. Diffraction and reflection of radio waves are factors in electric wave observation from transmission sources that are not visible. The prefecture government office building located between the measurement points and the transmission source was thought to be shielding the waves.

This study showed various radio waves entering a hospital building at strong electric field intensity. Radio waves from cellular phone base stations and an ASR induced strong electric field intensity. All hospitals, especially those in urban areas, should take protective measures against EMI by incoming radio waves.

ALTERNATIVE MAGNETIC FIELDS

Introduction

As an international standard, the immunity test method for a magnetic field of commercial frequency is defined in IEC61000-4-8. EMC (electromagnetic compatibility) standard for medical electric equipment IEC60601-1-2 states that life-sustaining equipment, such as infusion pumps, should work normally in a magnetic field of 400 A/m and other medical equipment should work normally at 3 A/m.

Although electromagnetic fields have the properties of both electric and magnetic fields, they are enlarged by the property of the magnetic field in the power

supply frequency. Generating a magnetic field around an electric wire through which current is flowing, the magnitude is proportional to the amount of current.

In a large hospital, the number of pieces of medical equipment driven by electric power sources is rapidly increasing, as is the number of computers. Therefore, the demand for electricity is growing, and the amount of contract demand has increased in response to this demand. Because voltage is fixed at 100 V in Japan, an increase in electricity use means an increase in the amount of current, which makes it a factor in increasing the magnetic field strength inside a hospital. Here, I show an investigation of the possibility of EMI by the magnetic field of a power supply.

Methods

We measured the magnetic environment of two rooms in a 25 year old university hospital building. One was a nurse station in a ward above the electricity transformation facility (hereafter "room A"), and the other was right above a telephone exchange room (hereafter "room B").

A gauss meter (HM-320, MTI) and a 3 axis probe (attached to HM-320, MTI) were used for measurement. This apparatus can measure the magnetic flux density of each axis of the probe, x, y, and z, a maximum range of 2 G (= 200 μT), and with an accuracy of 1 mG. At each point, after measuring the magnetic field of each axis, the actual value was computed according to the formula (2).

$$Fe = \sqrt{Fx^2 + Fy^2 + Fz^2} \qquad (2)$$

where, *Fx*, *Fy*, and *Fz* are the magnetic flux densities obtained by the Gauss meter for the three directions.

The measurement points defined were fixed at intervals of 1m in the subject rooms. At each point, magnetic flux density (magnetic field intensity) was measured at 10 cm and 1 m in height from the floor.

Result

A maximum intensity exceeding 290 mG (= 29 μT ≒ 23.09 A/m) at 10 cm from the floor above room A was recorded. The maximum magnetic field detected above room B was 185 mG. This value can make a CRT (cathode-ray tube) screen swing.

To determine the source of the magnetic field found in the nurse station, we checked the position of the wiring in room A. The source was found to be an electric wire with a maximum current of 900 A.

Discussion

In the nurse station, a magnetic field exceeding 20 μT at maximum was measured. In this environment, malfunctions could occur with some medical electric devices. However, since a magnetic field is in inverse proportion to the square of the distance from the source, only a small area of the nurse station was danger. As for the human environment, the reference level for magnetic field exposure to the whole body was set at 0.33 A/m at 60 Hz by ICNRP (International Commission on Non-Ionizing Radiation Protection) in 1998 [13]. In the nurse station, the measured maximum magnetic field at 1 m above the floor was 100 mG (= 10 μT ≒ 7.97 A/m). Therefore, this nurse station needed to be protected from this magnetic field.

The source of the measured magnetic field was wiring with a current of several hundred amperes in rooms A and B. The amount of current had increased from 200 A to 900 A over 20 years due to increases in electricity demand. In Japan, there are no standards or criteria, other than the criteria for the electric wiring in a common building, concerning the amount of current flowing through wiring. The standards and criteria for magnetic field exposure to the human body are defined only at frequencies of 10 kHz or higher.

STATIC MAGNETIC FIELDS

Introduction

Another type of magnetic field with a possibility of EMI with electronic medical equipment is static magnetic fields. EMI with an artificial heart pacemaker by a static magnetic field was reported [14]. European standard EN 45502-2-1 was formulated to insure that an implanted heart pacemaker would run normally in a 1 G or less static magnet field.

The following is an investigation of EMI by static magnetic fields in which the residual magnetization at electric welds, a possible source of static magnetic fields in a steel structured hospital building, was measured.

Methods

A ward at a university hospital was the subject of this test. At the time of the investigation, the steel framing had been completed, and the interior finish work was being done. We measured magnetic flux density in the emergency treatment room, intensive care unit, coronary care unit, and recovery rooms; all rooms in which a number of pieces of electronic medical equipment would be installed. Magnetic flux density measurement was done 10 cm and 1 m above the floor at each corner of a 1 m grid drawn on the floor of each room measured. Measurement was done on a holiday when there was no construction activity. The weather was cloudy.

The same Gauss meter and 3-axis probe as used in the measurement of the alternative magnetic field were used. Also, the same equation for magnetic flux density calculation at each point as used in the measurement of alternative magnetic fields was used.

Result

Two examples of measurement results are shown in *Figure 1*. Values on the X and Y axes show the distance of the measurement point from the wall, and the value on the Z axis shows the magnetic flux density. Magnetic flux density changes greatly with slight differences in probe location. Especially strong magnetic

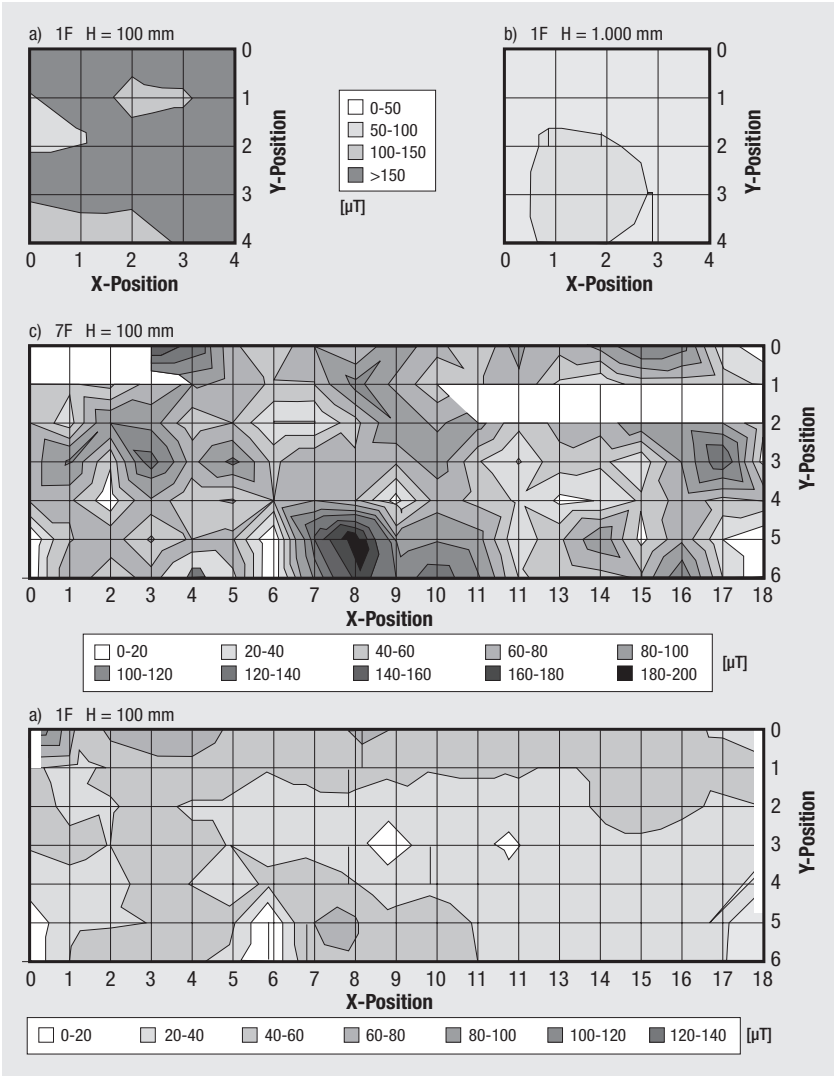

Fig. 1 | *Magnetic flux density distribution: a) 100 mm above the floor in the emergency treatment room (1F); b) 1000 mm above the floor in the emergency treatment room (1F); c) 100 mm above the floor in the Neurosurgery ICU (7F); d) 1000 mm above the floor in the Neurosurgery ICU (7F). Reproduced with kind permission from [21]. ©IEEE, 2001.*

flux density was observed at the welds of deck plates, the piping holes of metal deck plates, and the welds of metallic ornaments hanging from the deck plates. Strong magnetic flux density was also observed close to the following points; aluminum sash frame to metallic wall structure welds, the welds of steel girders to each other, and welds of the metal frames in partition walls.

The maximum magnetic flux density observed at each measurement point is shown in *Table 1*. Strong magnetic flux density was observed on every floor. The magnetic flux density exceeded the range of the Gauss meter at 10 cm above the first and seventh floors. The magnetic flux density 10 cm above the floor was higher than at 1 m above the floor at most

Table 1 | *Maximum magnetic flux density at each observation point*

Rooms	Floor	Magnetic flux density (μT) (H = 100 mm)	(H = 1000 mm)
Emergency treatment room	1F	214.5	77.8
ICU, CCU	3F	-	86.8
Surgical operation room	3F	-	138.6
Common patient bedroom	5F	65.9	83.8
Neurosurgical ICU	7F	210.6	110.6
Recovery room	11F	130.5	112.1

ICU: intensive care unit; CCU: coronary care unit

of the measurement points. For example, the maximum magnetic flux density measured in the recovery room on the seventh floor was 210.6 μT at 10 cm above the floor and 110.6 μT at 1 m above the floor.

Discussion

In the case of static magnetic fields, magnetic flux density is in inverse proportion to the square of the distance from a magnetized point. Therefore, it is possible to prevent EMI by keeping electronic medical equipment away from magnetized welds. When equipment cannot be placed far enough from a weld, de-magnetization [15, 16] or shielding may be necessary. De-magnetization can negate the magnetic energy by emitting the same volume of magnetic energy in a reverse direction to every magnetized point, after investigation of magnetic energy and its direction. Magnetic shielding, such as highly permeable materials, can be used to protect electronic medical equipment from magnetism. However, highly permeable materials are expensive. One standard for safe performance in cases where magnetic flux density is over 80 μT (0.8 G), the standard for CRT [17], is placement from 10 cm to 30 cm above the floor. This is considered the lowest safe installation height for general electronic medical equipment.

In this section, we confirmed that the residual magnetization of welds in a hospital should not be overlooked. Near the electric welds of steel frames and deck plates, strong residual magnetic flux density, which could produce EMI with electronic medical equipment, was found. Therefore, it would be beneficial for hospitals to do residual magnetic-field measurement and to place electronic medical equipment away from strongly magnetized points when strong magnetic fields are found. De-magnetization or magnetic shielding would be helpful for the prevention of EMI.

NOISE SUPERIMPOSED ON POWER LINES

Introduction

The use of mobile medical electronic equipment has increased rapidly in recent years, with many types of medical electronic equipment now including electronic circuits that are driven at low electric power outputs. Because electronic circuits can be damaged by momentary changes in voltage, some types of medical electronic equipment also have rechargeable batteries as a power source. In hospitals, a safe environment for using equipment should be provided. However, other than introducing laws and standards concerning the installation of power supply apparatus, such as emergency power generators, uninterruptible power supply (UPS), voltage and frequency stabilization equipment (CVCF, constant voltage and constant frequency), and grounding, the quality of electric power has hardly been considered.

Changes of voltage and noise superimposed on the power supply are possible obstacles to the efficient operation of medical electronic equipment [18]. Therefore, we observed the quality of the power supply of electronic medical equipment used in a modern hospital. Because strong installation standards have already been set for large-size medical equipment, only mobile medical electronic equipment, such as infusion and syringe pumps, will be discussed.

Methods

The quality of the electric power supply was observed by recording and comparing voltage waveforms in a new university hospital building. The same five wall sockets were used for all tests, as shown in *Table 2*.

Immediately after completing the building and before patients were admitted, a recording device, Hioki Memory hi-coder/ Model 8807, was connected to each of the wall sockets and the voltage waveform was recorded before any equipment was connected. After the building was opened to patients, the same recording device was connected to the wall sockets, and the voltage waveforms were again recorded. Before and after opening, recordings were done in an operating room, in a nurse station and at bedside in an intensive care unit (ICU), and a critical care patient room for neurosurgery patients on the 7th floor and in a standard patient room on the 9th floor.

When distortion in voltage waveforms was found, we analyzed the distortion by connecting a hi-frequency power distortion analyzer, the Dranetz Power Platform / Model 3400.

Results

The recorded voltage waveforms immediately after completion of the building and after patients were admitted are shown in *Figure 2*. Although distortion can already be seen in some of the voltage waveforms immediately after completion of the building, distortion increased after various pieces of mobile medical

Table 2 | *Locations of the subject wall sockets*

Room/area (floor)	The tested socket
Operating room (3F)	A wall socket connected to UPS
ICU; a single room (3F)	A bedside socket connected to UPS
ICU; a nursing station (3F)	A socket connected only to the general power supply
A critical care patient room for neurosurgery patients (7F)	A bedside socket connected to UPS
A standard patient room (9F)	A bedside socket connected to UPS

UPS: uninterruptible power unit; ICU: intensive care unit.

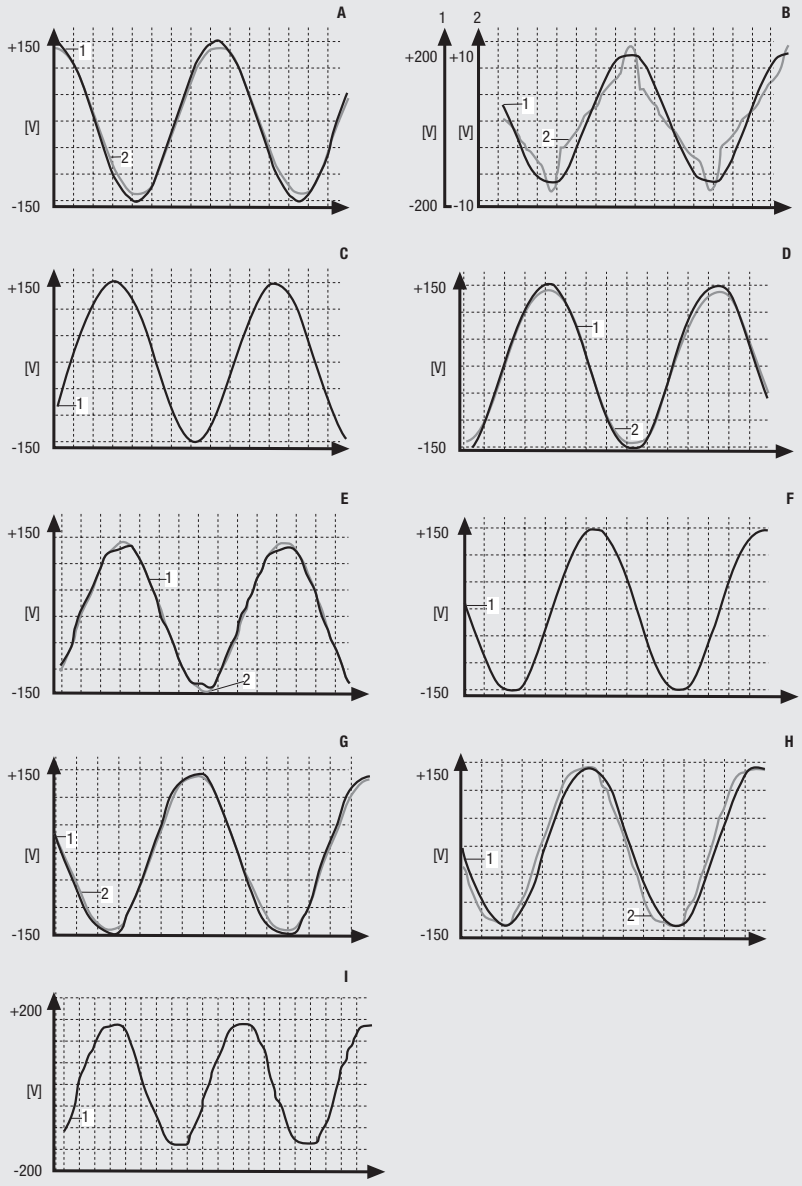

Fig. 2 | *Panels a) and b): Power supply waveforms at a wall socket in a surgical operating room. a) After completion of the new hospital but before opening; 1(bold): Observed voltage, 2(thin): Reference sine wave. b) During a surgical operation (operation for a patient with a hernia); 1: Voltage, 2: Current. Panels c and d): Power supply waveforms at a bedside wall socket in an ICU single room. c) Immediately after completion of the new hospital, but before opening. d) After opening the hospital; 1 (bold): Observed voltage, 2 (thin): Reference sine wave. Panel e) Power supply waveforms at a wall socket in an ICU nursing station. Several PCs were connected and in operation; 1 (bold): Observed voltage, 2 (thin): Reference sine wave.; Panels f) and g): Power supply waveforms at a bedside wall socket in a seventh floor, critical care patient room. f) Immediately after completion of the new hospital, but before opening; g) After opening the hospital; 1 (thin): Reference sine wave, 2 (bold): Observed voltage. Panel h): Power supply waveforms at a wall socket in a standard patient room on the ninth floor, 1 (bold): Observed voltage, 2 (thin): Reference sine wave. Panel i) An example of distortion of the power supply waveform with 10 sets of syringe pumps connected to the same wall socket.*

equipment were connected. The largest distortion was observed in a nursing station in the ICU (*Figure 2*, *panel e*). The minimum voltage was 96 V.

Discussion

Causes of voltage waveform distortion

Fluctuation and unusual outputs of generated voltage and current may be caused not only by supply side sources (primary side), but also at the terminal side (secondary side). In many cases, medical electronic equipment includes motors, discharge tubes, and electronic circuits. When these types of equipment are connected to a wall socket, they may cause voltage distortion that would be transmitted toward the primary side. Hereafter, we refer to this type of electromagnetic noise as "reflective noise."

Because reflective noise is transmitted over power supply lines, there is little decrease in the noise and it seldom disappears completely. However, when circuit breakers are placed in the wiring or transformers or relay switches are inserted, little noise is transmitted to the primary side. Therefore, even if reflective noise is caused by electronic equipment, voltage distortion will only influence wall sockets branched from the same circuit breaker.

In this observation, several desktop-type personal computers (PC) were used in the nursing station in the ICU. These PC would seem to have been the main cause of the distortion increase. As a result of analysis of the distortion, high frequency noise was found on the voltage waveform. This type of power supply distortion is called "high frequency distortion" or "harmonics" [19]. "High frequency distortion" of the power supply has increased with the spread of

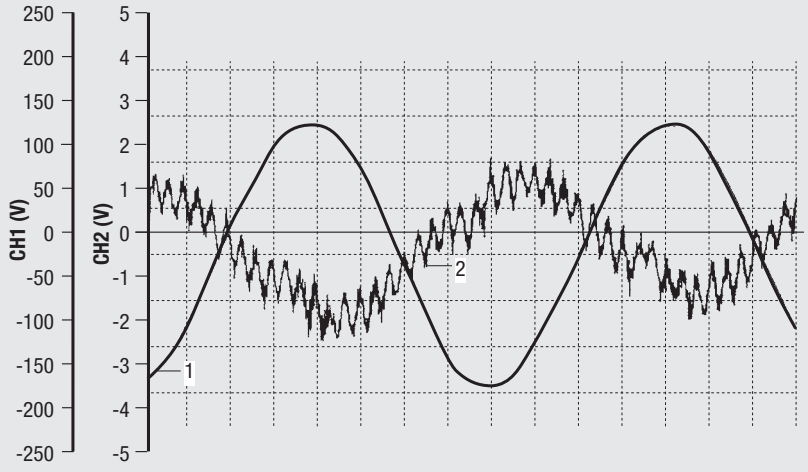

Fig. 3 | *An example of distortion of the voltage waveform by induction by a power line. 1: Observed voltage. 2: Subtraction of observed voltage from reference sine wave .*

electronic devices and computers in recent years. An example measured in another hospital is shown in *Figure 2*, *panel i*. This example is of a voltage waveform taken from a wall socket from which ten sets of syringe pumps, all in operation at the same time, received their electric power supply. In this case, 5% or more voltage change was observed. The cause of this distortion was high frequency voltage emission by the electronic parts in the pumps, such as inverters or by components that change the alternating current into direct current.

Other factors of power supply distortion

Besides the voltage changes observed above, the following is an example of a known factor in voltage/current distortion. If distortion is caused by two or more overlapping factors, the distortion rate becomes larger.

1) Electromagnetic induction by high current power lines ("Induction"). *Figure 3* is an example of the voltage waveform distortion of a commercial power supply caused by power supply lines used for elevators. In this example, two power supply lines are branched from different circuit breakers. However, because the power lines were very close, electromagnetic induction occurred and the voltage waveform of the general power supply was distorted. Distortion at almost the same frequency as the power supply frequency is a typical feature of voltage change caused by power lines, lines for motors, and air compressors.
2) Noise derived from phase differences ("transient"). The noise derived from phase differences is referred to as "transient" [18]. Other than voltage noise including surges or sags, the phase of power supply waveforms has been barely been considered in Japan. As for hospitals in Japan, extraordinary power supply installation requirements are imposed by standards in some areas *(Table 3)*: Japan Industrial Standards (JIS) (T1001 [19] and T1022 [20]). When the electric power supply from an electric power company is cut, hospitals with private electric generation capability change to their private generator. If the phase of the sine waves differs, the voltage may drop to a low level at the time of change. Moreover, the electric power company may sometimes change the equipment in a power transmission route or a substation, and a phase difference may arise from these changes. However, low voltage when continued for a few

Table 3 | *Installation requirements for emergency power supply equipment in Japanese hospitals*

Room (purpose of use)	Installation of general/special extraordinary power supply	Installation of instant special extraordinary power supply
Operating rooms	Required	Required
ICU, CCU, NICU, LDR, cardiac catheterization rooms, recovery rooms, rooms for hemodialysis, rooms for first-aid	Required	Depend on needs
Sterile, patient rooms; delivery room	Required	Depend on needs
Rooms other than above	Depend on needs	Depend on needs

• Japanese hospitals are required to install one or both types of extraordinary power supply according to the medical electronic equipment to be used. ICU: intensive care unit; CCU: coronary care unit;NICU: neonatal intensive care unit;LDR: room for labor, delivery and recovery.

cycles (about 0.1 seconds) is sufficient to be detected by the voltage sensor of medical electronic equipment. Any voltage loss may cause equipment stoppage.

Important considerations in investigations of power supply

- Directors of hospitals whose buildings have been newly built or repaired should not only check to see that the power supply system meets the requirements for power supply waveforms, but also insure that wall sockets are safe before starting use. Data taken before the hospital is put in operation can be useful when problems occur. The initial recorded voltage/current waveforms can be used for later reference.
- Recording devices with a short time interval (high frequency sampling) should be used in waveform investigations or high frequency noise will not be detectable. An example is shown in *Figure 4*. The same power source waveform was recorded using two recording instruments: a) a waveform recorded by equipment with 3 kHz sampling, and b) a waveform recorded with 50 kHz sampling.
- If voltage decreases, overload and superimposed noise should be distinguished, as they are derived from different causes.

In this section, I mainly investigated the changes in the power supply voltage. Using medical electronic equipment in a carefully controlled environment improves the safety and quality of clinical medicine. All who operate or manage medical electronic equipment, such as doctors, nurses, clinical engineers, and administrative staff, should carefully monitor the electrical environment. When performing delicate measurements, such as brain-wave measurement, we must be careful of not only electromagnetic waves superimposed on cables etc., but also of other aspects of the power supply.

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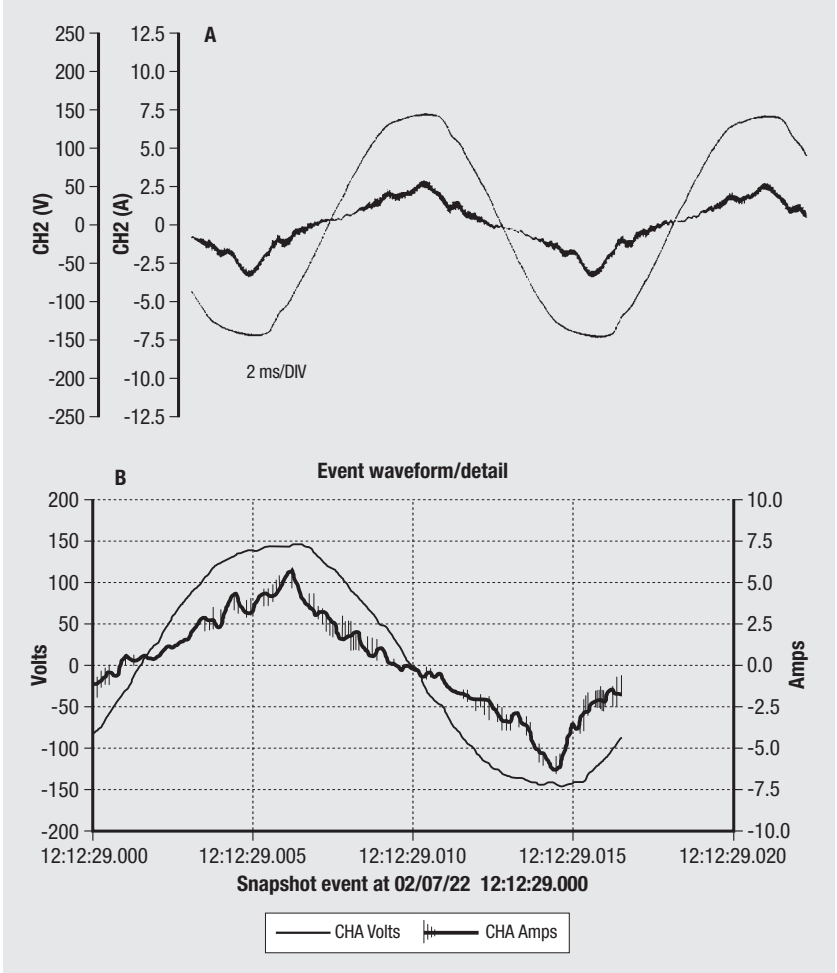

Fig. 4 | *An example of recorded voltage and current distortion as measured by two pieces of recording equipment. Waveforms recorded at 50 kHz sampling. A: Voltage. B: Current. Waveforms recorded at 3 kHz sampling.*

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Electromagnetic compatibility management of wireless transceivers in electromagnetic interference sensitive medical environments

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Summary. The diffusion of wireless technology has caused concerns about interference in the hospital environment. Most hospitals have banned the use of cell phones on their premises although wireless technology can help in delivering time critical help to patients. We discuss some factors of radio frequency (RF) near field interference. These phenomena do not lend themselves easily to theoretical evaluation. It is possible to avert medical equipment interference by performing *ad hoc* tests. The method requires measurements of electromagnetic fields and the observation of interference events with increasing distance between equipment and RF transmitters. The results are applicable only to the specific testing environment. The *ad hoc* proposed method can be found in the draft document C63.18 of the American National Standard Institute.

Key words: medical equipment, interference management, equipment and supplies.

Riassunto *(Gestione della compatibilità elettromagnetica di dispositivi* wireless *in ambienti medici sensibili ad interferenze elettromagnetiche)*. La diffusione della tecnologia *wireless* ha generato preoccupazione su possibili interferenze in ambiente ospedaliero. Molti ospedali hanno proibito l'uso di telefoni cellulari nei propri locali sebbene la tecnologia *wireless* può aiutare nel fornire aiuto ai pazienti in tempo utile. Nel lavoro sono discussi alcuni aspetti dell'interferenza a radio frequenza (RF) in campo vicino. Questi fenomeni non si prestano facilmente ad una trattazione teorica. È possibile evitare interferenza verso i dispositivi medici effettuando delle prove *ad hoc*. Questo metodo richiede la misura di campi elettromagnetici e l'osservazione di eventi di interferenza all'aumentare della distanza tra il dispositivo medico e il trasmettitore a RF. I risultati sono applicabili solo a quello specifico ambiente di prova. Il metodo *ad hoc* proposto può essere trovato nel documento *draft* C63.18 dell'American National Standard Institute.

Parole chiave: equipaggiamenti medici, gestione delle interferenze, apparecchiature e forniture.

INTRODUCTION

The immunity of medical devices is by convention determined in the far field using a fixed source (*e.g.*, log periodic antenna) emitting a defined (AM modulated 80% sine wave) signal swept across a wide (80-2500 MHz) band in an anechoic or semi-anechoic chamber [1-3]. Immunity levels for life critical devices are currently set at 10 V/m. Although corollary directives in Europe enforce this level, it is only recommended in the USA. In contrast, some of the most abundant and potentially problematic sources for electromagnetic interference (EMI) take the form of mobile radio frequency (RF) transmitting handsets (*e.g.*, mobile phones, PDAs, laptop computers). These RF sources can be brought within the immediate proximity to medical devices. At such close distances from resonant antennas, the RF energy distribution has a near field character with steep gradients, and can result in significantly elevated field strengths (*e.g.*, over 100 V/m at 5 cm from a 900 MHz dipole radiating 1 W power, as shown below), due to stored reactive energy in the space near the antenna. Moreover, the well known relationship between electric and magnetic energy in the far field of RF sources is not valid in the near field, so EMI pathways and mechanisms may be different from those established in conventional far-field exposure settings.

The implicit assumption in current testing procedures that predictable electric (E) and magnetic (H) field components will be maintained within the incident electromagnetic wave from a RF source (transmitter) as it illuminates the victim medical device (receiver), therefore, may not always be accurate.

For implantable medical devices such as cardiac pacemakers and defibrillators, immunity levels are defined differently by placing the device in a container with a saline solution and exposing it over a series of defined frequency bands with dipole antennas at

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2.5 cm away [4] from the surface of the solution. The most recent revisions of this test procedure include higher immunity requirements and addition of test frequencies corresponding to common licensed and unlicensed communication devices. These modifications largely arose from well-documented studies reporting that EMI could be caused by mobile phone transmitters [5, 6]. In these studies, modulated RF signals (*e.g.*, GSM), close proximity, and older pacemaker models seemed to collectively contribute to vulnerability, although subsequent studies and surveys have indicated that significant EMI events in actual pacemakers are not common.

Several global regulatory agencies including the US FDA [7], UK MHRA [8], Health Protection Branch of Health Canada [9], and Australian Department of Therapeutic Devices [10], have suggested separation distances between implantable cardiac devices and mobile phones as well as other measures to avoid interaction, but admit these are precautionary and not a result of a verified risk in practice.

Several synergistic factors, including the proliferation of mobile RF communication and computing devices, the rapid diffusion of new electronic and wirelessly enabled medical devices, and the growing age of the population in need of healthcare monitoring increase the probability that mobile RF transmitters (sources) may be brought in close proximity to medical devices (victims). Anecdotal reports regarding medical device EMI from mobile phones initially caused concern and led to numerous bans of wireless communication devices from many hospitals during the 1990s. In recent years, however, increasing dependence upon mobile communication and computing within the medical community [11, 12] as well as a better understanding and qualification of EMI-related risks has led to the development of international standards outlining strategies for managed use of mobile phones and other RF transmitters in healthcare facilities (ISO Technical Report 21730; AAMI TIR n. 18). However, increased testing and evaluation of potential EMI effects can further improve management strategies.

The process currently adopted in evaluating interference events in medical devices close to wireless communication equipment is empirical and has consisted of observing the fall off of interference with distance from the RF source. In this paper, we show that this approach is the most appropriate, as an analytical methodology is faced with an array of variables that make the mathematical modeling unrealistic. In addition to the complex array of leads, internal wires and circuits, and apertures associated with the medical device itself, other variables such as the placement in relationship with other medical instruments, the environment and potential reflecting/shielding structures, personnel monitoring activity of the medical devices, power level, signal modulation and position of the source transmitter all do affect greatly the potential for interference.

COMPLEXITY OF THE EMI PHENOMENA IN MEDICAL DEVICES NEAR RF SOURCES

Complexity of the near field structure of antennas

EMI phenomena of import need the efficient transfer of the electromagnetic energy of the incident fields to a particular circuit within a medical monitor. This event is facilitated if the electric and magnetic energy content of the incident fields matches the dipole moment, electric and magnetic, of the affected circuit with all its metal, capacitive and inductive coupling connections. These extensions of a circuit enhance its ability to capture EM energy from incident waves essentially by turning it in an efficient receive antenna.

In the far field of RF sources the EM waves carry equal amounts of electric and magnetic energy. Metal leads, straight wires and runners on PC boards normally couple efficiently with the electric energy (E-field) of an incoming wave, so EMI measurements are appropriately performed with a linearly polarized antenna for different positions of the devices under test.

In the reactive and radiative near field of an antenna the balance between the electric and magnetic energy and the polarization of the electric and magnetic field vectors can change radically within a quarter wavelength of the operating frequency. For this reason, the pathways to EMI are much more complex and multifarious in the near field than in the far field of antennas. Circuits with a weak magnetic dipole moment can sustain EMI phenomena if the local magnetic field is very high (*e.g.*, near a strong RF current); conversely a weak electric dipole moment of a circuit can be strongly excited by the intense E-fields near the tips of a helical antenna [13]. *Figure 1* and *Figure 2* show the electric

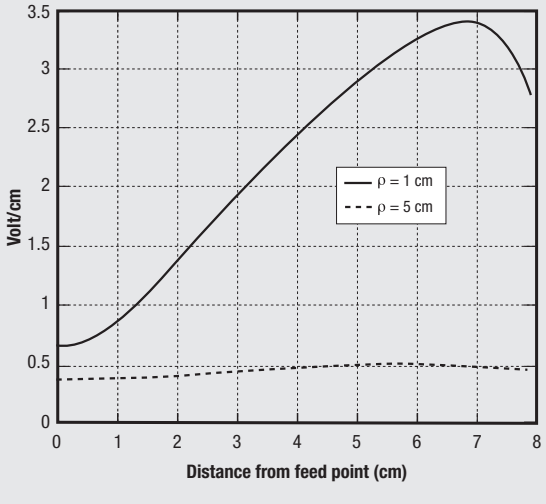

Fig. 1 | *Modulus of the near electric field of a resonant dipole 15.8 cm long radiating 0.25 W at 900 MHz. Note the rapid drop of the field over only 4 cm distance.*

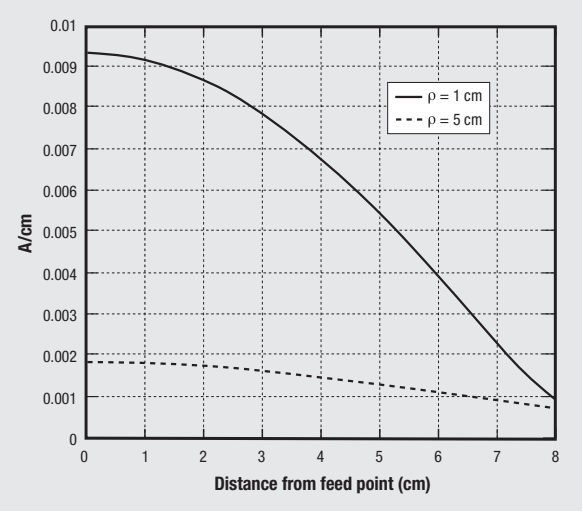

Fig. 2 | *Modulus of the near magnetic field of the resonant dipole of Figure 1. Note that near the center of the antenna the H-field decreases by the magnetostatic law of Biot-Savart. Near the tip there is minimal attenuation vs distance.*

and magnetic field intensities at two distances ($\rho = 1$ cm and $\rho = 5$ cm) from the axis of one branch of a resonant cylindrical dipole at 900 MHz (wavelength $\lambda = 33.33$ cm) radiating 0.25 W. The dipole is 15.8 cm long and has a radius of 0.1 cm.

Twenty harmonics have been used to compute the current on the antenna [14], so the field amplitudes are quite accurate. By denoting $\eta = 377\Omega$ the impedance of free space, one can see that for $\rho = 1$ cm the EM energy is predominantly magnetic near the center of the radiator ($H >> E/\eta$) and predominantly electric near its tips ($E/\eta >> H$). Very different EMI mechanisms are triggered in these two regions of the near field. The authors in [5] reported that some cardiac pacemakers were suffering EMI events near the feed point of antennas, but not near the tips of a dipole where the E-field is the strongest.

It is worth noticing that the field intensity distribution changes radically in only 4 cm (about 0.12λ). At 5 cm distance from the axis of the antenna the intensity of the electric and the magnetic field is approximately uniform along a path parallel to the axis of the radiating element. This distance is approximately equal to $\lambda/2\pi$ and conventionally marks the end of the reactive near field of the antenna.

Complexity of the EMI susceptibility of sensitive medical monitoring devices

In general, medical monitoring devices employ high gain electronic amplifiers to detect and measure low voltage signals. As discussed above, the electromagnetic susceptibility of these circuits depends on the geometrical, physical and circuital factors of the monitoring apparatus. We shall describe these factors as the incident electromagnetic waves encounter them.

First, the size, shape, material, grounding of the metal enclosure and the presence of slots are parameters of importance in determining the susceptibility of the device. The power chord length and its shape (coiled or extended) also can cause EMI phenomena at certain frequencies by acting as an RF antenna and injecting RF currents into the electronics within the metal enclosure, particularly common mode currents featuring in-phase amplitudes on both power chord conductors. Metal leads attached to a patient or simply dangling from a monitor can become effective EMI antennas at certain RF frequencies depending on their length and terminations. Even metal studs or metal walls can reflect or couple RF EM fields into a medical device; *e.g.*, if a monitor is at the proper distance from two joined metal walls, these can act as a corner reflector focusing EM energy on the device, which becomes a receive antenna.

Metal enclosures with air venting slits can be EM shields at certain low frequencies, but can become resonant cavities well coupled to the near fields of an antenna at higher frequency bands. A parallelepiped enclosure example can vividly demonstrate this phenomenon. *Figure 3* shows a metal enclosure with a slot on one side. The enclosure could contain the electronics of a medium size medical monitor; the slot is for cooling and ventilation. *Figure 4* gives the amplitude of the E-field inside the enclosure at 5 cm from the slot *vs* frequency. A plane wave polarized in the z direction *(Figure 3)* is incident on the slit side of the box. One can see the selectivity with which the E-fields penetrate into the enclosure. At most frequencies, the enclosure acts as a good electromagnetic shield, but in selected narrow bands the shielding is lost. The computations of *Figure 4* have been performed using the software package CST MICROWAVE STUDIO® [15].

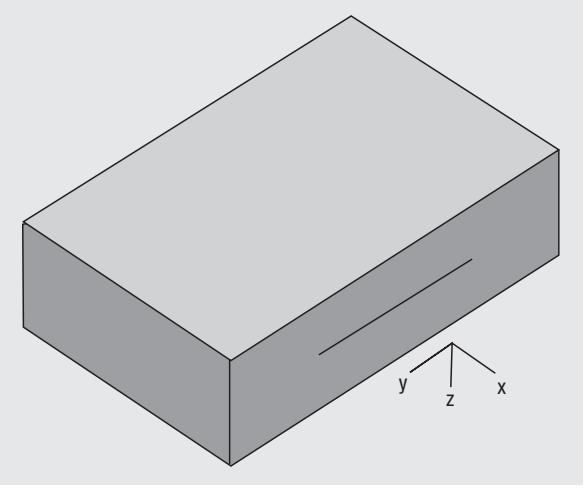

Fig. 3 | *Metal box representing the enclosure of a medium-size medical instrument. The metal box size is 190×300×90 mm³. The box has a slit representing an air cooling intake. Slot length: 140 mm, slot width: 2 mm.*

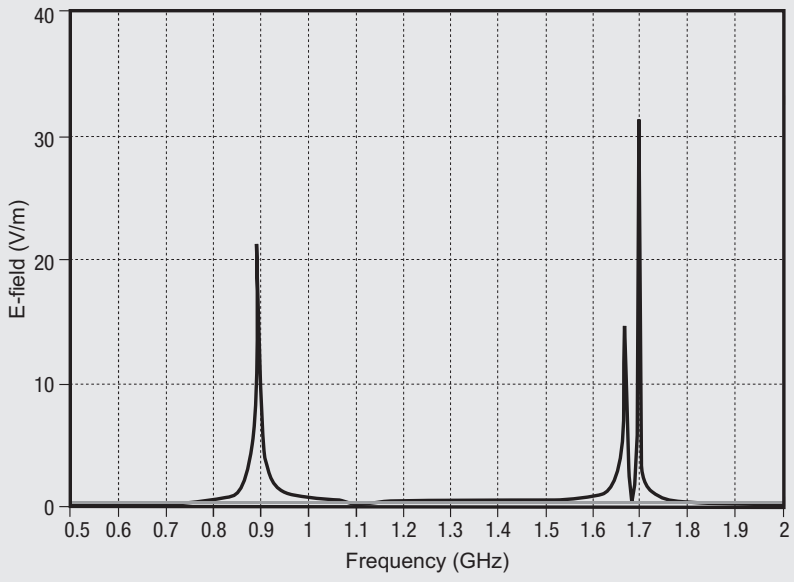

Fig. 4 | *Electric field intensity* vs *frequency at 5 cm inside the metal enclosure of* Figure 3. *The metal enclosure has selective electromagnetic energy absorption* vs *frequency. Interference phenomena inside the box depend strongly on the wavelength of the external incident fields.*

The loss of shielding function by the same metal enclosure is shown more clearly in *Figure 5*, which plots the computed E-fields from a resonant dipole antenna radiating 1W placed at 5 cm distance from the center of the slot. The computations were performed using the FEKO software package [16]. There are two radically different coupling situations between a dipole antenna and the metal enclosure with a single slot. The solid line in *Figure 5* plots the E_z *(*see *Figure 3)* field component from the antenna along a line from the center of the dipole to the center of the slot; the axis of the antenna is perpendicular to the slot. For reference, the same component of the antenna in free space is also shown in *Figure 5*. While the free space field intensity decays with the inverse distance law (a straight line in log scale) past the first 5 cm of the reactive near field, the E_z inside the box does not. There is a substantial field enhancement in the immediate vicinity of the slot, followed by a region of near constant E_z. The field decreases past the position x = -205 mm and goes to zero at the back wall of the enclosure (x = -240 mm). The important point depicted by the solid line in *Figure 5* is that there is a substantial amount of RF energy in a large area of the cavity in the plane of the slot.

The computed E_y *(*see *Figure 3)* component values with the same antenna parallel to the slot are shown as a broken line in *Figure 5*. The results show that the energy coupled inside the enclosure is minimal and hangs

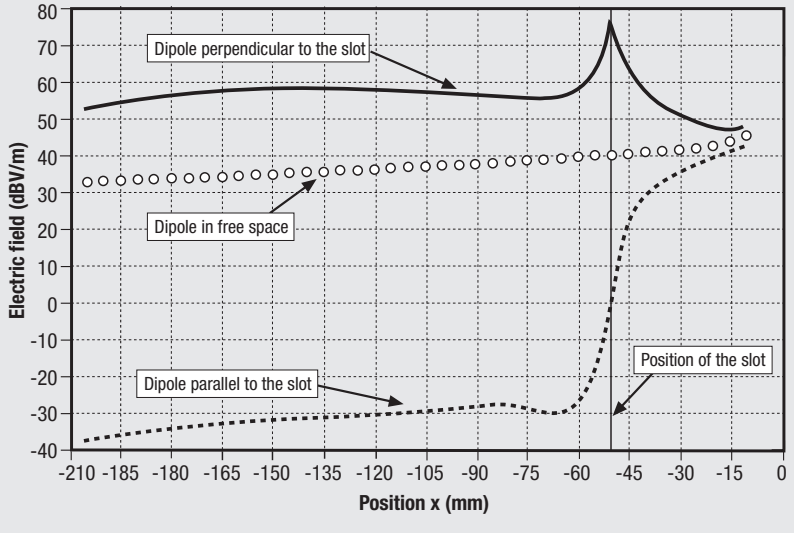

Fig. 5 | *Electric field attenuation inside the box of* Figure 3 *for two polarizations of an external resonant dipole. Note the minimal electromagnetic energy penetration with the antenna is parallel to the slot. The metal box offers no shielding (attenuation lower than in free space) with the antenna orthogonal to the slot.*

around the place of entry, *i.e.* the shield is preventing the penetration of the RF energy inside the medical monitor. The ratio of the field energies coupled into the metal enclosure by the slot for the two orientations of the same antenna is about 80 dB.

The situation of the solid line in *Figure 5* must be conceived along with the presence of an electronic device with substantial dipole moments (electric, magnetic or both) located at or near the peak of the EM field intensity. Such device could be exposed to RF electric and magnetic fields far above (*e.g.*, 40-80 dB) design specifications. A nonlinear component could be saturated and become non functional.

Inside a medical monitor there are printed circuit boards (PCB), which are grounded and there may be inter or intra board electrical connections (*e.g.*, signal traces or ribbon cables). The interconnect paths can act as high frequency antennas; grounding contacts designed for the low frequency operation (few KHz) of medical devices may fail to maintain a constant potential at higher frequencies, if RF energy leaks or is conducted inside the metal enclosure.

The PCB metal runners (traces) are poor or good RF antennas depending on their geometry and proximity to the ground layer. Traces can become good antennas at certain frequencies also depending on the components they connect. Capacitors and inductors can tune a particular runner to be an efficient receive antenna over a certain frequency band.

The layout of traces, capacitors and inductors can cause mutual coupling between different parts of a board or between boards, thus increasing the chance of creating a resonant structure at some high frequency band. If the RF energy penetrates the shield, it can well be sucked in a particularly sensitive electronic circuit whose performance is severely impaired by saturation, rectification or other nonlinear events.

Even with the most sophisticated PC board layout and electromagnetic analysis tools available today [16, 17], engineers are not able yet to simulate the complex electromagnetic environment of thickly populated boards inside a resonant metallic enclosure coupled through air venting slots to the near field of an antenna.

A PRACTICAL METHOD FOR CHARACTERIZING EMI IN MEDICAL DEVICES FROM WIRELESS TRANSMITTERS

From the previous discussion it is clear that EMI phenomena in the near field of wireless transmitters are very difficult to predict or simulate by analysis. Only well-tested and reliable experimental procedures can establish, with some confidence, the minimum safe distance between a RF transmitter and a medical device in the hospital environment. By "safe distance" is meant the distance where there is no detectable EMI phenomenon that impairs the function of the medical apparatus. *Ad hoc* procedures are well-accepted methods for system-level EMI testing [18].

The ANSI draft document C63.18 [19] has captured and systematized the procedures used by several engineers and hospital personnel [20-23] in trying to establish a minimum safe distance between medical devices and RF transmitters.

The draft document gives detailed suggestions on the procedures for each phase of an EMI test program. It starts with a section on preparation for *ad hoc* testing which includes recommendations on the selection of the medical devices to be tested, of the RF transmitters to be used as test sources, and of the test areas. This section also gives the minimum specifications for the RF field strength meter to be used during the tests.

The next section offers careful considerations on transmitter use during the test and specifies how to determine the recommended minimum test distance for each transmitter. If testing is performed closer than the recommended minimum test distance, damage to the medical device under test could result. A table relates the minimum test distance with the RF transmitter output power. Devices with RF power higher than 8 W should not be tested in a hospital environment. The recommended operation of RF transmitters during *ad hoc* tests is presented in detail. These include:

- hand-held transceivers;
- cellular and PCS telephones;
- table-top RF transmitters;
- medical telemetry transmitters;
- wireless information technology transmitters (*e.g.*, wireless LAN).

The test method section suggests the procedures for the evaluation of the performance of a medical device under test, which consists of increasing the distance between the transmitter and the medical device, starting from a pre-established minimum distance with the transmitter set at maximum power output.

During the *ad hoc* RF immunity test, the responses of the medical device must be recorded as a function of the RF transmitter distance, orientation, and frequency.

In noting the response of the medical device to the RF transmitter, it is also important to distinguish between effects that would and effects that would not impact patient or operator safety or the diagnosis, monitoring, and/or treatment of patients.

If the transmitter does not affect the medical device, or if there are effects but they are determined to be acceptable, then the minimum recommended separation distance between that transmitter and that medical device is the minimum recommended test distance.

The compilation of the measured data and observations constitute the test results. These should be used to determine a minimum separation distance between each tested transmitter and medical device (including cables, sensors, and electrical accessories). When assessing the test results, it is essential

that they be interpreted bearing in mind the caveats and limitations of an *ad hoc* test procedure. The test results apply only to that specific, individual medical device. Other units of the same model may behave differently. The test results also apply only to the frequency, modulation, and field strength characteristics of the RF transmitter used. The medical device may be either susceptible or immune to other frequencies, modulations, and/or field strengths. In addition, the tests are affected by the structure of the facility, in which the tests are performed, as well as by furniture and nearby objects. Results may be different in another location. Multiple reflections of RF fields in the actual use location can sum in such a way that interference can occur at distances greater than the minimum separation distance determined from the *ad hoc* procedure.

The healthcare organization should determine whether the effect or performance degradations observed during the tests are acceptable or not. The advice of clinical staff is helpful in determining the clinical acceptability of any observed performance degradations. Results of the test should be considered in the development of policies and procedures for mitigation of EMI with respect to each medical device and RF transmitter used in the test program.

SHORT SUMMARY OF THE RESULTS TO DATE

Minimum safe distance data and detected EMI phenomena are presented for some common medical devices. The information has been collected by visiting four US hospitals (St. Luke Mayo Clinic, Sunnybrook NY, Stanford CA and University of Chicago, IL) and EMI testing the analog and digital signals of the US wireless networks, following the procedure outlined in the previous section. In *Table 1* we report only the extreme cases of EMI for the various devices tested.

In general, but not always, signals with high pulse amplitude and low (less than 100 Hz) repetition rate caused the extreme cases of interference in terms of disruption vs distance. In addition, if a device shows high EMI susceptibility for one type of RF signal, it is also most likely susceptible to others. Good electromagnetic compatibility (EMC) design of a product protects the device from the interference of any RF signal, while poor EMC design leaves it open to interference from a wide variety of modulated electromagnetic fields.

From the data presented above, it is clear that keeping cell phones and other low power transceivers (less than 0.5 W) at 0.75 meter or greater distance from medical equipment, there is a small probability of EMI events that trigger the malfunction of the devices. One should keep in mind that the data were collected with the transmitters set at maximum operating power (0.25-0.5 W), and several options exist to provide infrastructure to a hospital facility to keep handheld units transmitting at minimal output power (3-6 mW). There are exceptions to the simple rule given above, so compatibility tests should be performed for the specific equipment of a hospital. Finally, if a device is found to be particularly susceptible to EMI, it can be clearly marked for minimum safe distance and properly isolated or just replaced. This decision can be made by the hospital administration in concert with the medical personnel.

Table 1 | *Detected extreme cases of electromagnetic interference (EMI)*

Medical device	Detected EMI effect / distance
Blood warmers	No effect at 0.25 m
Gas analyzers	Some speaker distortion at 0.25 m
Ventilators/monitors	Shut down at 5 cm, substantial change of respiratory volume at 1 m
Infusion pumps	Stopped pumping at 0.75 m
ECG readers	Unacceptable noise in ECG waves at 0.5 m
Defibrillators	Unacceptable noise in ECG waves at 1.25 m
Multipurpose ECG Monitors/ Pulse oxymeter/ Arterial pressure	Unacceptable ECG wave distortion at 0.25 m
Infant incubators	Temperature alarm at 0.25 m
EEG	Unacceptable noise on waves at 0.25 m from the monitor. No noise at 5 cm from patient leads
Dialysis machines	Screen wobble, decrease in arterial and venous pressure readings, pump slowed at 0.5 m
Sonogram machines	No effects at 5 cm
Mobile ECG units	Disrupted transmission at 10 cm
Pulse oxymeters	Unacceptable audio distortion at 0.25 m

CONCLUSIONS

This paper has attempted to explore the mechanisms of EMI phenomena in medical devices exposed to the near field of wireless transmitters. The complexity of these events has inspired experimental *ad hoc* procedures, rather than analytical approaches to resolve EMI issues for medical equipment in the hospital setting. All the data collected so far point out that with careful planning, coupled with an *ad hoc* evaluation of the potential EMI phenomena in the hospital, it is possible to resolve the issues of compatibility between medical equipment and low power RF portable transceivers.

In the future, if a large enough set of measurements is made on the same medical devices in various hospital environments it will be possible to give a statistical range to the limits of variability of the measurements obtained using the *ad hoc* method described in this paper.

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Electromagnetic immunity of infusion pumps to GSM mobile phones: a systematic review

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Summary. Electromagnetic interference with life-sustaining medical care devices has been reported by various groups. Previous studies have demonstrated that volumetric and syringe pumps are susceptible to false alarm buzzing and blocking, when exposed to various electromagnetic sources. The risk of electromagnetic interference depends on several factors such as the phone-emitted power, distance and carrier frequency, phone model and antenna type. The main recommendations and the relevant harmonized standard are also reported and discussed. From the data available in literature emerges that, for distances lower than 1 m there is a non negligible risk of electromagnetic interferences, although significant differences exists in the reported minimum distances. Interference effects clinically relevant for the patients are rare. No permanent damage to the pumps has been ever reported, although in several cases intervention of personnel is required to resume normal operation.

Key words: electromagnetic interference, infusion pumps, cellular phone, risk reduction behaviour.

Riassunto *(Immunità elettromagnetica di pompe ad infusione a telefoni cellulari GSM: un'analisi sistematica della letteratura)*. Interferenze elettromagnetiche su dispositivi medici sono state descritte da vari gruppi. Studi pubblicati hanno dimostrato che le pompe a infusione e le pompe siringa sono suscettibili a falsi allarmi e interruzioni dell'erogazione, se esposte a varie sorgenti di campi elettromagnetici. Questo studio è quello di analizzare i dati pubblicati in letteratura relativamente al rischio di interferenze elettromagnetiche dovute a telefoni cellulari GSM su pompe ad infusione e pompe siringa. Le principali raccomandazioni per limitare i rischi associati e la normativa internazionale di riferimento sono inoltre riportate e discusse. Dall'analisi della letteratura disponibile emerge un rischio non trascurabile di interferenze elettromagnetiche, quando le pompe ad infusione sono esposte a telefoni GSM a distanze inferiori al metro, anche se significative differenze esistono relativamente alle distanze minime osservate. Non esistono dati relativamente a danni permanenti alle pompe, anche se in molti casi dopo interferenza è necessario un intervento manuale sulla pompa per ripristinarne il corretto funzionamento.

Parole chiave: interferenze elettromagnetiche, pompe ad infusione, telefono cellulare, comportamento di riduzione del rischio.

INTRODUCTION

Problems with electromagnetic compatibility (EMC) of medical devices have been known for some time in hospitals. Research groups, manufacturers, and governmental and non-governmental agencies have reported incidents related to electromagnetic interference (EMI) to medical devices. Some of them had life-threatening consequences, others could have had, others can be considered just a nuisance. From 1979 to 1993 the Food and Drug Administration (FDA) received more than one hundred reports related to EMI. These reports prompted the need for an increased attention to medical device electromagnetic compatibility by users, manufactures, and standard organizations. There are several motivations behind the increasing researches and efforts in this field: deaths and severe injuries have occurred due to EMI on life-supporting medical devices; the ambient electromagnetic environment continues to intensify (*e.g.*, mobile phones, wireless local area networks, paging system); use of higher carrier frequencies the medical devices have not been tested for; increase in electronic sensors, actuators, and microprocessors based medical devices (*e.g.*, ventilators and infusion pumps); increased number of patients with electrical active implanted devices (pacemaker and cardioverter/defibrillator); widespread of new EM sources such as anti-theft systems and metal detectors, due to the increased need for security in public areas and buildings.

Interestingly, most of the reported incidents before 1993 involved EMI originated from other sources (*e.g.*, electrosurgical units, other medical devices, power line interferences). In the report of Silberberg, 3% of the reports involved mobile phones and 6% hand-held transceivers. It should be observed that

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in 1993 the usage of mobile phones was much less prevalent than today. The large number of different medical devices, the peculiarity of some of them (*e.g.*, implantable *vs* non-implantable or diagnostic *vs* therapeutic), and the gravity of the potential consequences in case of EMI make difficult to treat this matter in a unique way. The wide number of potential sources of interference and their associated mechanism (*e.g.*, conducted *vs* radiated) make the problem even more complex. These differences are also reflected in the international standard on EMC for medical devices. According to these standards, three groups of devices may be considered: electrical active implantable devices (*e.g.*, pacemakers, implanted defibrillators, nerve stimulators); life-support devices (*e.g.*, ventilators, external defibrillators, electrosurgical units, infusion pumps, monitors); non life-support devices (*e.g.*, ECG, EEG, ultrasound scanner, MRI, CT-SCAN).

Since the early studies of FDA, various groups have reported problems attributed to EMI from mobile phones with medical devices such as ventilators, external defibrillators, wheelchairs, monitors and infusion pumps [1-8]. Prompted by these reports, recommendations to restrict the use of mobile phones in critical areas of hospitals have been issued. These recommendations include either the definition of a separation distance or the total banning of mobile phones from intensive care areas and surgical theatres, if not from the entire hospital. In view of the lack of evidence reported in other studies [2, 4], the above mentioned restrictions have been criticized [9, 10]. Since most of the reported EMI with medical devices occur only under worst-case conditions (*i.e.* maximum emitted power and/or very short distances), and because in several cases the clinical consequence might be not significant, the debate whether mobile phones pose a real risk is still open [12].

In this review we addressed the EMI problem of infusion pumps. The reason for focusing on this type of devices are various. First, as mentioned before, a large number of parameters are involved in the EMI problems with medical devices., making a unique approach difficult; volumetric pumps and syringe pumps are commonly used in hospitals both in non-critical (wards) and critical areas (*e.g.*, intensive care, surgical theatres, first aid departments). Recently, their use at patient's home has gain popularity; in some cases, a malfunction of such devices may pose a significant risk for the patient.

Evidence of cellphone EMI with infusion pumps were observed and documented by [1, 6, 8, 11] while no effects were observed by Turcotte and Witters [2]. According to Klein and Djaiani [13], infusion pumps are particularly prone to EMI. In 2005, Hahm *et al.*, documented the case of an acute Epinephrine poisoning due to cellular phone interference with an infusion pump [14]. In a previous study our group carried out an experimental investigations on EMI to infusion and syringe pumps exposed to 900 Mhz and 1800 Mhz GSM phones [15]. A systematic review, focused on mobile phones and technologies used in Australia can be found in [16].

METHODS

The major databases were searched (Medline and Science Citation Index) using the key words "mobile phones", "cellular phones" and "equipment" or "medical devices". From a first list of papers, the research was then refined searching for cited authors and papers.

Studies were considered eligible if published in peer-reviewed journal in English and if included testing of infusion and syringe pumps against electromagnetic interference from mobile phones.

In the published studies, several differences in the methodology used to investigate the EMI problem do exist, and it makes difficult a perform a meta-analysis of the published data. In addition, the different standards of mobile phones adopted worldwide likely contribute to the heterogeneity of the studies and of the reported effects. Thus, we did not attempt to draw conclusions, but reported the conclusions of each author.

RESULTS

Table 1 summarizes the main findings of our review. We found 6 studies which included GSM mobile phones and infusion pumps among the devices investigated. The percentage of devices susceptible to various kind of EMI ranged from 0% to 58%. Some of the studies investigated a very limited number of pumps, thus an underestimation of the rate of susceptibility may be occurred. In all the studies the maximum distances between the mobile phones and the devices were always relatively short (< 0.5 m). There were only two cases of documented changes in the delivery rates [1, 14]. In all the other cases the effect of the EMI consisted in buzzing, alarm sound, changes in the displayed information and pump stopping.

DISCUSSION AND CONCLUSIONS

Several studies have investigated the susceptibility of medical devices to EMI from mobile phones. As far as infusion pumps are concerned, the percentage of devices susceptible to various kind of EMI ranged from 0% to 58%, indicating real significant differences in the findings of the various groups. Differences exist among the papers, especially regarding the testing protocol, the mobile phones technology, the handset model and the number of pump tested.

Two main international standards are currently applied for evaluating EM compatibility of medical devices [17, 18]. The IEC-EN-60601-1-2:2003 establishes the minimum immunity levels, as well as the methods for conformity assessment. This standard is mainly intended for manufactures and notify bodies, as it requires specialized facilities (*e.g.*, anechoic chambers, radio frequency - RF - signal generators, power meters) and trained personnel. In

Table 1 | *Papers investigating the electromagnetic interference (EMI) of GSM phones with infusion pumps*

First author Year	Number of model tested	Incidence of EMI	Maximum distance (cm)	Notes	Author's conclusions
Medical Device Agency 1997 [1]	59	32 (54%)	100	EMI source included: analog and digital phones, 2-ways radios, and LAN	Mobile communication equipment does present a real risk for medical devices Restrict use of mobile phones in critical areas.
Irnich 1999 [3]	66	28 (42%)	n.a.	Results obtained grouping drop-controlled, volume-controlled and syringe pumps	Medical device must be made resistant to mobile phones 1 m minimum distance recommended Replace of device with more than 50 cm interference distance
Robinson 1997 [11]	1	0 (0%)	-	Immunity up to 40V/m	Suggested safe distance of 1.2 m
Hanada 2000 [6]	6	0 0%	-	EMI source: PHS phones (max 80 mW power)	No interference with PHS phones (the power is ten times lower than GSM)
Morissey 2002 [8]	9	2 (22%)	25	Infusion, perfusion and feeding pumps	To mitigate EMI, reduce the emitted power by providing good coverage in the hospitals. Identify most sensitive devices.
Calcagnini 2006 [15]	12	7 (58%)	30 (900 MHz) 30 (1800 MHz)	EMI probability as a function of emitted power also calculated	Limit the emitted power of GSM using in-building repeaters

n.a.: information not available.

addition, infusion and syringe pumps must comply with the particular harmonized standard EN 60601-2-24:1998 [19], which requires an immunity level of 10 V/m, in the frequency range 80-2500 MHz.

The ANSI C63.18 is a technical guide developed to aid clinical and biomedical engineers in assessing the immunity of medical devices to radiated electromagnetic fields from portable RF transmitters. According to this guideline, medical devices can be tested in the hospital, and RF transmitters can be selected among commercial equipment used in the health facilities. Recently, the ANSI C63.18 has gained diffusion also in papers investigating EMI in hospitals. Indeed, the use of commercial handsets makes it difficult to compare and reproduce results from previous studies: since most of the EMI phenomena occur in the near field regions, the antenna patterns of commercial devices play a rule [15].

Since systematic analysis of the clinical relevance of the observed effects have not been carried out in most of the study, it is difficult to obtain the probability of clinically significant EMI. According to Irnich and Tobish [3], there is no realistic danger for drop controlled, infusion and syringe pumps. The most serious effects reported so far included a reversal in the motor drive of an IVAC 960 exposed to a GSM phone [1], and an acute epinephrine poisoning probably due to resetting of the pump to the maximum delivery rate (999 mL per hour) [14]. All the other potentially dangerous effects consisted in shutdown of the pump, or in displaying various error modes and alarms, most of the time requiring an external intervention to be restarted.

The recommendations issued to mitigate the EMI risk include either the definition of a separation distance or the total banning of mobile phones from intensive care areas and surgical theatres, if not from the entire hospital. The various proposed recommendations are mostly based on the precaution principle to the risk minimization, rather than on the results of the published study. The "1-m rule" or the "arm's length rule", as well as the total ban from intensive care and surgical rooms are the most suggested recommendations. Education and sensibilitazion of medical and nurse staff has been also suggested.

If the GSM phone emitted power is reduced, the risk of EMI significantly decreases, as we demonstrated in a previous work [15]. If an adequate base station signal is present, GSM phones are designed to automatically reduce the emitted power to battery saving. Morissey [20] investigated the feasibility of an improved signal coverage as a mean for reducing the emitted power of GSM phones. He compared the power level fluctuations of a GSM phone while walking through a facility with poor and moderate-good coverage. In the presence of an adequate base station signal, the average power barely exceeded 0.01 W. This level corresponds to 0.08 W peak-power. Although we found that a limitation of the mobiles to peak power levels as low as 0.05 W for 900 MHz and 0.0025 W for 1800 MHz is required for the total immunity of the pumps tested, values lower than 0.08 W would significantly reduce the probability of EMI (< 20%). The limitation of the mobile power may be thus obtained increasing the field coverage by install-

ing in the hospital in-building repeaters amplifiers or dedicated mini base-stations.

The problem of infusion pump in the domestic environment has so far received poor attention. The fast developing of information technology and telecommunication infrastructures in the hospitals makes even harder to develop effective guidelines for EMI mitigation. The harmonized international standard on EMC of medical devices (IEC-EN 60601-1-2:2003) has been recently revised to cover the frequency band up to 2.5 GHz, and it has also increased the minimum immunity requirements for life supporting devices from 3 V/m to 10 V/m.

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Magnetic resonance induced heating of implantable leads

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Summary. In this study a methodological approach for measuring temperature and local absorption rate (SAR) on thin metallic structures, such as pacemaker (PM) leads, is provided. First preliminary experiments were performed to evaluate the error in temperature and SAR measurements made by fluoroptic® temperature probes when the temperature probe is in different contact configuration with the PM lead tip. Our results show how the position of temperature probes affects the temperature and SAR value measured at the lead tip. The transversal contact between the thermal sensor and the lead tip is the configuration which leads to the highest values for temperature and SAR. In the second part of this paper we describe two physical models of a human trunk and an experimental set-up to investigate the influence of the implant geometry and of the lead path on the heating and the local SAR deposition. Experiments reveled that the implant location and configuration are crucial elements for the heat generation at the lead tip.

Key words: magnetic resonance imaging, pacemaker, artificial, heating, electromagnetic energy, fluorescent probes.

Riassunto *(Riscaldamento prodotto su cateteri metallici impiantati durante risonanza magnetica)*. Nel presente contributo viene in primo luogo proposto un metodo di misura per temperatura e potenza depositata (*specific absorption rate*, SAR) su strutture metalliche sottili, quali un elettrocatetere di un pacemaker, utilizzando sonde a fluorescenza in fibra ottica. A tal fine, un primo gruppo di prove sperimentali è stato dedicato alla valutazione dell'errore che si compie sulle misure di temperatura e SAR in funzione della posizione che le sonde a fibra ottica occupano nell'intorno dalla punta dell'elettrocatetere. I risultati ottenuti mostrano come il posizionamento delle sonde influenzi in significativamente il valore di temperatura misurato: il contatto trasversale tra il sensore termico e l'elettrodo di stimolazione è la configurazione che permette di misurare il più alto valore di temperatura e SAR. Nella seconda parte del lavoro sono descritti due modelli fisici di simulatori di tronco assieme ad un *set-up* sperimentale utilizzato per studiare il contributo dato al riscaldamento dalla geometria e dal percorso compito dall'elettrocatetere. Le prove condotte dimostrano come il posizionamento e la configurazione dell'impianto siano elementi discriminati per il riscaldamento prodotto sulla punta dell'elettrocatetere.

Parole chiave: imaging a risonanza magnetica, pacemaker artificiale, riscaldamento, energia elettromagnetica, sonde a fluorescenza.

INTRODUCTION

Magnetic resonance imaging (MRI) is a widely accepted tool for the diagnosis of a variety of disease states. However, the presence of a metallic implant, such as a cardiac pacemaker, or the use of conductive structures in interventional therapy, such as guide wires or catheters, are currently considered a strong contraindication to MRI [1-4]. Potential effects of MRI on pacemakers (PM), implantable cardioverter defibrillators (ICD) and other active implantable medical devices (AIMD) include: force and torque effects on the pacemaker [5, 6]; undefined reed-switch state within the static magnetic field [7]; potential risk of heart stimulation and inappropriate pacing [8, 9] and heating effects at the lead tip [10-12]. In particular, most of the publications dealing with novel MR techniques on patients with implanted linear conductive structures [13-17] point out that the presence of these structures may produce an increase in power deposition around the wire or the catheter. Unfortunately, this increased local absorption rate (SAR) is potentially harmful to the patient due to possible excessive temperature increase which can bring living tissues to necrosis. The amount of heating has been investigated by several groups and temperature elevations observed spread from not significant values up to tens of degrees. For example, Achenbach *et al.* [10] reported a temperature increase of 63.1 °C for a PM lead; Rezai *et al.* [18], observed 25.3 °C at the end of a

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deep brain stimulation electrode; Roguin *et al.* [19] reported a maximum increase of 5.7 °C at 3.54 W kg^{-1} whole body specific absorption rate (WB-SAR). Sommers *et al.* [11] with a WB-SAR of 1.3 W kg^{-1} obtained temperature increase ranging from 0.1 to 23.5 °C, depending on the electrode type. Also some numerical approaches have been attempted: Irnich *et al.* [20] calculated the electric field distribution around a lead tip as function of the distance from the electrode surface and assessed that the sharp decrease of the power density could not cause any significant histological damage on living tissue, even with pretty high electrode temperature rise.

To date, as many as 10 deaths have been attributed to MRI procedures in patients with PM [21]. However, during clinical investigations and physician-supervised MRI procedures, some studies report no adverse events, suggesting that the presence of a permanent PM may no longer represent a strict contraindication to MRI [22].

Several factors influence the degree of heating: 1) the WB-SAR has been shown to correlate to the temperature increase [17], 2) the cooling effect of the blood around the leads is often not quantified, 3) the length and the geometric structure of the lead and 4) the implant location as well as the lead path. In addition, since thin linear structures such as PM leads may generate temperature gradients which can not be neglected with respect to the physical dimension of temperature probes, also the relative positioning of the temperature probe and the lead tip may significantly affect the measurement and can explain, at least partially, the inconsistency of the results in literature.

This paper describes two physical models of a human trunk and an experimental set-up to investigate the role of the implant geometry to the heating and the local SAR deposition. An estimation of the temperature and SAR measurement error made by using Fluoroptic® temperature probes is also provided. In addition, for a given whole body SAR, we compared the temperature increases induced by a real MRI scanner to those obtained in a MR coil simulator, in order to understand whether the whole body averaged SAR calculated by a clinical MRI system can be used as a reliable metric for radiofrequency (RF) induced heating or not.

MATERIALS AND METHODS

We used three different experimental set-ups: in the first one, we performed temperature measurements on the tip of a PM lead inside a rectangular box phantom, using different types of contact positions between the probe and the lead tip. In this preliminary configuration, the heating was obtained by injecting into the lead a RF current which flowed through the lossy-gelled material the phantom was filled with. Then, we placed inside the same rectangular box a PM can with its leads and measured the temperature increase inside a MR birdcage coil *(Figure 1a)*. The third experimental set-up was a human-shaped phantom implanted with a PM and its leads, placed inside a real clinical MRI scanner *(Figure 1d)*.

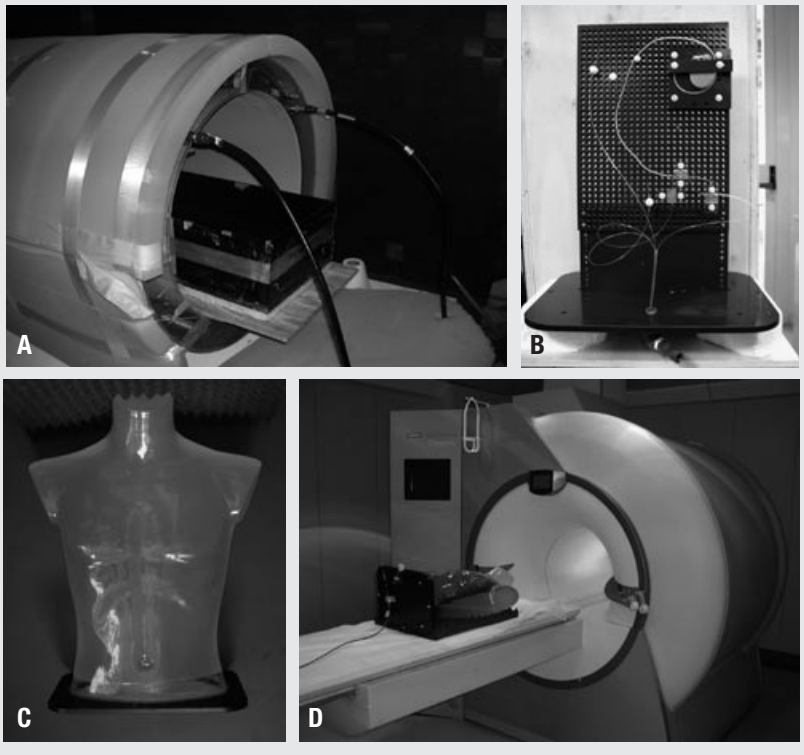
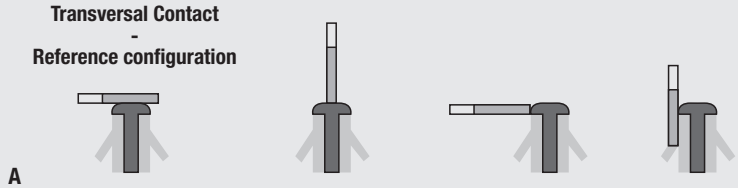


Fig. 1 | *Pictures of the MRI birdcage coil used for the rectangular box phantom (a); the PVC grid which supports the pacemaker implant and the Fluoroptic® temperature probes (b); the human-shaped phantom (c) filled with the HEC gel and used in a clinical MRI scanner (d).*



A

Contact configuration	Tip-to-side	Tip-to-tip	Side-to-side
25 MHz	-39%	-35%	-34%
64 MHz	-36%	-32%	-28%
128 MHz	-7%	-6%	-4%

B

Contact configuration	Tip-to-side	Tip-to-tip	Side-to-side
25 MHz	-72%	-75%	-68%
64 MHz	-65%	-65%	-48%
128 MHz	-30%	-20%	-15%

Fig. 2 | *Comparison among measurements obtained with the electrode of the pacemaker lead in transversal contact with the pigmented part of the Fluoroptic® probe (reference) and underestimation obtained with other contact configurations: temperature (a) and SAR (b) comparison. A schematic representation of each contact configuration we tested is also reported in the upper panel of the figure.*

In our experiments, we used a dual chambers PM (Elect D, Sorin Biomedica CRM, Italy) and a biventricular PM (three chambers, NewLiving CHF, Sorin Biomedica CRM, Italy), with both unipolar and bipolar leads (mod. S80T and S80TB, Sorin Biomedica CRM, Italy). Lead length was 62 cm, tip area 6 mm^2, and ring area 36 mm^2. Both the rectangular box and the human shaped phantom were filled with 2% hydroxy-ethyl-cellulose (HEC), 0.36% sodium chloride and the rest water: a gel saline solution with 0.59 Sm^{-1} conductivity and 79 permittivity at 64 MHz, and 4178.3 J $kg^{-1}K^{-1}$ heat capacity [23].

Because of the well-known limitations of conventional thermometry methods in radio frequency (RF) energy environments [24, 25], we used a Fluoroptic® thermometry (Luxtron, Model 3100, USA – SMM probes), with resolution of 0.1 °C, operating at 8 samples per second. This method has become the "state-of-the-art" and the industry standard in temperature and SAR evaluation inside MRI system and has been used to examine radiofrequency energy-induced heating of tissues, *in vitro* and *in vivo* [25-29]. In such probes, the temperature sensor is a half-sphere of approximately a 0.3 mm diameter encapsulated inside a cylindrical pigmented jacket and located at the terminal portion of a flexible fiber optic cable. The pigmented jacket (approx. 3 mm length, 0.8 mm diameter) has to prevent ambient light from interfering with the sensor, as well as acts as a reference for the probe positioning.

With the experimental data obtained from the Fluoroptic® probes we estimated the local SAR by calculating the slope (dT/dt) of the initial temperature increase. This slope was estimated by minimizing the least square error over about 40 samples; the estimation was assumed valid when the Pearson coefficient r^2 was greater than 0.98 [30].

Probe positioning

Our first experiment was aimed to identify the optimal contact configuration between the temperature probe and the lead tip, in order to minimize the underestimation related to temperature measurements. To investigate how the position of the pigmented region of the probe affects the temperature measured on a PM lead tip, we used a PVC box (a 28 × 20 × 26 cm box) filled with the gel described above. A 26 × 18 cm grid was submerged in the gel to support the pacemaker and its lead and maintained a consistent separation distance between the implant, phantom gel surface and the temperature probes. The grid was adjusted so that the top of the implant was positioned below the phantom surface. SAR and temperature were measured on the tip a unipolar lead. A RF signal was injected into the lead using a coaxial cable connected to the lead. The outer conductor (signal ground) was connected to a 1 × 20 × 10 mm silver plate located on one side of the PVC box. The current through the gel went from the lead tip to the silver plate. The lead was placed in the gel 5 cm below the phantom top surface, simulating an implant in the human body. The distance between the silver plate and the lead tip was 7 cm. Three sinusoidal excitations were studied: 25, 64 and 128 MHz, which approximately correspond to the RF field used in 0.5, 1.5, and 3 T MRI systems. The signals were generated by a RF generator (Rhode & Schwartz – SMT 06), and then amplified (RFPA – RF 06100-6, France); a power meter (Rhode & Schwartz – NRT Z14) connected to the output of the amplifier measured the average net-input power to the lead.

The preliminary measurements investigated various contact configurations between the terminal part of the temperature probes and the pacing electrode at the lead tip. Aim was to identify the temperature probe position which results in the maximum temperature result and to assess the relative underestimations associated with other configurations.

We studied the following possibilities *(Figure 2)*:

a) transversal contact between the side of the temperature probe and the circular surface of the lead tip;

b) transversal contact between the tip of the temperature probe and the side surface of the electrode;
c) axial contact between the tip of the temperature probe and the circular surface of the lead tip;
d) axial contact between the tip of the temperature probe and the side surface of the electrode.

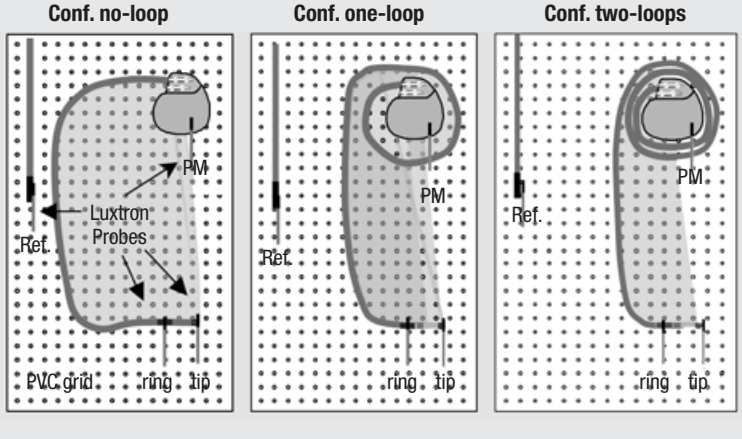
The underestimation was expressed as the percentage difference of the temperature increase measured with the particular temperature probe position in respect to the position leading to the maximum temperature measurement.

Rectangular phantom

Once we identified the temperature probe position which results in the maximum heating, we used it to perform several measures on a PM can and PM lead tip, inside a MR birdcage coil *(Figure 1a)*. These measurements were performed at the Center for Device and Radiological Health (CDRH), Food and Drug Administration (FDA) in Rockville, MD, USA. The birdcage coil was housed in an anechoic chamber and fed in quadrature sinusoidal excitation by a signal generator (HP8647A, USA) connected to a 150 W 64 MHz RF amplifier. The output power was continuously monitored by a directional coupler and a power meter (HP436A, USA). In this configuration, we used the same rectangular box phantom described in the previous section, and the RF energy (~100 W) delivered to the box corresponded to a WB-SAR of about 1.0 W kg^{-1}. Also the position of the grid did not change. The PM (dual chambers and biventricular) was mounted on the grid and programmed either in sensing or pacing mode. We tested both unipolar and bipolar leads and no more than two leads were tested simultaneously.

First goal of these measurements was to evaluate the contribution to the lead tip heating from the area covered by the implant. In our experiments, the total area of the implant was varied by wrapping the exceeding lead near the PM body or by changing the lead geometry. An example of varying the lead geometry is shown in *Figure 3a*, when the lead is placed in loops around the PM can. Different areas of the implant were also obtained by keeping the position of the PM can and the lead tip constant and varying the lead path. For each configuration we computed the total area of the implant, defined as the region delimited by the lead itself, the PM can and the line connecting from lead tip to the center of PM can (*Figure 3a*, shaded areas). In this series of experiments, the PM was always positioned as a

a



b

Implant area (cm^2)	PM Configuration	Temperature increase (°C)	SAR (W kg^{-1})
280	No loop	7.3	2100
270	No loop	11.9	3000
225	No loop	10.5	2565
150	No loop	2.0	500
210	One loop	5.8	1500
180	One loop	4.0	1250
150	One loop	2.1	600
120	One loop	1.8	480
115	Two loops	0.4	60
90	Two loops	0.2	40
70	Two loops	0.5	80
65	Two loops	0.9	180

Fig. 3 | *Examples of implant configurations tested in the MRI simulator: no loop, one loop and two loops configurations (a). The position of the optical probes and of the wire used as reference is also illustrated. (b) Values of temperature increase and SAR measured during the experiments with the rectangular box simulator, reported in function of the implant area and configuration. Different implant areas were obtained either by wrapping the lead around the PM body and by changing the lead path.*

Table 1 | *Main parameters of the MRI clinical sequences used during the human-shaped phantom experiments. In the last columns of the table the two time length used for each type of sequence are reported*

Sequence type	Siemens sequence name	TR (ms)	TE (ms)	Flip angle	Length of long sequences (s)	Length of short sequences (s)
Single shot (turbo fast) spin echo	HASTE	1190	83	150	402	42
Steady state free process	TrueFISP	3.78	1.89	54	379	38
Spoiled gradient echo	FLASH	960	40	20	417	53

left sided implant and the main vertical segment of the lead was always to stay in the central portion of the rectangular phantom.

We then focused on the position of the implant inside the gelled material: different lead geometries were tested, with the main straight segment in one experiment close to the edge, whereas in the other centered in the phantom. The dual chambers PM allowed investigating two different lead geometries at the same time. Great care was taken to maintain a consistent separation distance between the tips to avoid interactions between the two lead tips. Temperature was measured by Fluoroptic® probes at the lead tips and at the PM can. In case of bipolar lead, a probe was positioned in transversal contact with the ring at the lead. Moreover, the temperature increase was also measured at the terminal part of an insulated metallic wire, which was placed always in the same position on the grid, far from the PM and its leads. This value was used as a reference for data acquired in different experiments.

Each experiment consisted in a base measurement of about 60 seconds, followed by an exposure to RF lasting 200 seconds. Also the cooling phase after RF exposure was recorded for a period of 200 seconds.

The acquisition system was made of an analog-digital converter connected to the output of the Fluoroptic® thermometer and to a 16-bit acquisition card (DAQCard-AI-16XE-50 – National Instruments) boarded on a personal computer, where the temperature changes were displayed in real time.

Human-shaped phantom

In order to simulate physiological implant configuration and realistic MRI procedures, further experiments were performed in real MRI scanning system using a human-shaped torso simulator developed at the Department of Technology and Health of the National Institute of Health (Istituto Superiore di Sanità, ISS) in Rome *(Figure 1c)*. The simulator consists of a torso-shaped transparent PVC phantom of the size of a 70 kg male. Internal volume of the torso is 32 liters [23]. A PVC grid is mounted inside the torso to support a dual chambers PM connected to two bipolar leads, and the temperature probes. The torso was filled with the same gel as described above.

The actual lead geometry and PM placement can vary from patient to patient. The PM can be located in the left or right pectoral region. Since the length of the lead may not fit the patient's anatomy and size, the exceeded length is usually wrapped near or around the PM can. Our experiments were performed on a siemens magnetom sonata maestro class scanner (1.5 Tesla) *(Figure 1d)*. Three different RF sequences commonly used in clinical MRI procedures with two different sequence lengths each were tested. The main parameters of the sequences are summarized in *Table 1*. The MRI parameters (TR, TE and Flip Angle) were adjusted to reach a WB-SAR of 2 W kg^{-1}, as estimated by the scanner. The geometry of the implant reproduced left and right PM placements. For each implant, three lead paths were tested: without lead looped around the PM (no-loop configuration) and with the lead forming one or two loops around the PM (1-loop configuration and 2-loops configuration, respectively). For each lead path, the length and the position of the linear section of the lead as well as the lead tip position were kept constant. Only the PM was moved from the left to the right pectoral location.

Temperature was recorded during the time when the RF excitation was on and in the following cooling period, for about 60 s. The Fluoroptic® probes were positioned at the lead tips, on the PM can and in the gel, far from metallic structure, as reference.

RESULTS

Probe positioning

In *Figure 2* we reported the differences in temperature and SAR measurements at the peacemaker lead tip due to different contact configurations with the Fluoroptic® probes. At the three frequencies we tested (25 MHz, 64 MHz and 128 MHz) we used an average net power of 0.7 W, 1.36 W and 2.04 W, respectively. These power levels were chosen to obtain heating comparable to those reported in the literature [1, 3, 13, 14]. We found that the position of the temperature probe significantly affects the measurement: transversal contact between the side of the temperature probe and the circular surface of the lead tip is the configuration which leads to the highest measured temperature. We define the temperature measured with other positions than the one leading to the maximum value as an underestimation *(Figure 2)*.

The highest temperature underestimation occurred at 25 MHz and it decreases as the frequency increases, regardless of the temperature probe contact. The configurations "tip-to-side" and "tip-to-tip" result-

ed in temperature underestimations ranging from 28% to 39%. The underestimation associated with the side-to-side contact was significantly lower (4% - 7%).

The underestimation associated with the measurement of local SAR at the lead tip showed a similar behavior: transversal contact between the side of the temperature probe and the circular surface of the lead tip is the configuration measuring the highest SAR (1444 W kg^{-1}). The underestimation associated with other temperature probe configurations is reported in *figure 2b*. In the worst case, the SAR underestimation can be up to 75%. The effect of the frequency on SAR underestimation was similar to that observed for the temperature.

More details about the error associate to temperature and SAR measures using Fluoroptic® probes in contact with thin metallic structures can be found in [31].

Rectangular phantom

The major increase of temperature was always observed at the lead tip. No significant increase of temperature was observed at the PM can and no differences were observed between the two PM models (dual chambers and biventricular). The ring electrode of bipolar leads showed much lower temperature increase than the tip. We did not observe any significant difference in the tip temperature between unipolar and bipolar leads, as well as changing the programming of the PM from unipolar to bipolar sensing/pacing. When the PM was connected to multiple leads simultaneously, we did not observe significant changes in the amount of heating of each tip, if consistently separated, respect to the single lead configuration.

Figure 3b shows the temperature increase at the lead tip, for various implant areas. In *Figure 3c*, SAR values at the lead tip, for the same experiments, are plotted as a function of the implant area. As the area increases, we observed a temperature increase and a local SAR increase. Note that the different areas were obtained either by wrapping the exceeded lead near the PM body or by changing the lead path.

The increase of temperature and SAR at the lead tip seems to be directly related to the implant area. The lead around the PM body or the number of loops does not seem to play a significant role. Configuration with no-loop and one-loop, but approximately sharing the same areas, produced simi-

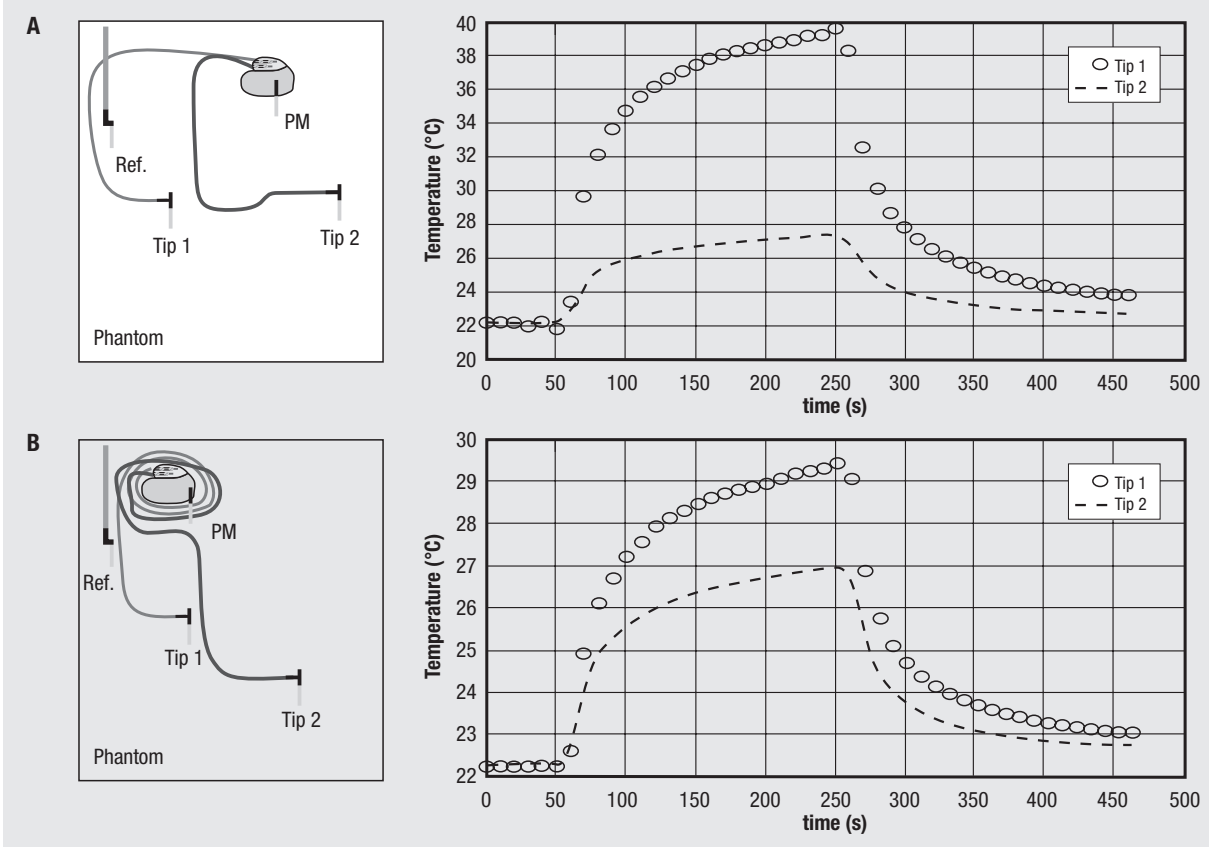


Fig. 4 | *Examples of temperature increases measured in the rectangular box phantom: comparison between two configurations with the same implant area but different position inside the box (a); comparison between an implant with a larger area but in the centre of the phantom and an implant with a smaller area but placed close to the edge of the box (b). The position of the optical probes and of the wire used as reference is also illustrated.*

Table 2 | *Temperature increase (°C) and lead tip SAR (W kg-1) of human-shaped phantom experiments. Average whole body SAR calculated by the scanner is also reported. The data refer to long MRI sequences*

Sequence	Left pectoral implant			SAR* (W kg^{-1})	Right pectoral implant			SAR* (W kg^{-1})
	No loop	*1-loop*	*2-loops*		No loop	1-loop	2-loops	
HASTE	6.3 (1362)	0.9 (-)	0.7 (-)	1.70	11.9 (2345)	2.68 (641)	1.0 (-)	1.72
TruFISP	6.2 (1255)	1.0 (-)	0.6 (-)	1.70	12.3 (2375)	2.5 (536)	1.0 (-)	1.70
FLASH	0.1 (-)	< 0.1 (-)	< 0.1 (-)	0.02	< 0.1 (-)	< 0.1 (-)	< 0.1 (-)	0.02

**SAR: average whole body specific absorption rate computed by the scanner; (-): SAR not estimable, due to low temperature increase..*

lar temperature increase local and SAR. Two experiments showed temperature increase (and SAR values) significantly higher then what expected from their implant area. A retrospective analysis of these configurations showed that the lead had a relatively long straight path (approximately 20 cm).

The position of the implant inside the phantom seemed to be even more important than the implant area. *Figure 4a* shows the temperature increase for two leads with a pretty similar geometry but with their main vertical segment in different regions inside the phantom: the lead along the edge of the box produced a significant higher heating at its tip than the one placed in the central region. Even when the implant in the middle of the phantom covered a larger area that the one close to the edge of the box (1-loop *vs* 2-loop configuration), the temperature increase is higher if the lead is aligned along the edge of the box *(Figure 4b)*.

In all our experiments, the temperature measured by the probe not in contact with the wire used as reference did not change significantly. It gives good consistency and reproducibility to the measures.

Human-shaped phantom

The temperature increase and local SAR values for the experiments using a real MRI scanner are reported in *Table 2*. As for the clinical sequences, the gradient echo (Flash) did not induce detectable temperature increase (below the Luxtron probe sensitivity, 0.1 °C) in all the configurations tested. Scanning sequences with as relatively high whole body SAR, led to a temperature increase up to 12.3 °C. For left pectoral PMs the lead area appears to be the major factor relevant for the heating. A high implant area (no loop) showed always a higher temperature increase than the 1-loop and 2-loops configurations.

Surprisingly, when the PM is right pectoral implanted, the lead position seems to play the major role: the vertical segment of the leads did not change for the two implant configurations, whereas the initial horizontal parts were placed on opposite sides on the grid *(Figure 5)*. No-loop configurations showed always a temperature increases significantly greater then the 1- and 2-loops configurations. In addition, the temperature increase observed were even greater then those of the left implants. In both configurations (left and right) the temperature increase and local SAR were proportional to the whole body SAR reported by the scanner.

The data reported in *Table 2* refer to long sequences; the comparison between short and long sequences showed that, as observed during continuous wave exposition in the rectangular box simulator, the major temperature increase occurred within the first minute. Experiments were repeated changing MRI parameters such as the center of view (chest, abdomen and pelvis) and the field of view (200, 300 and 400 mm) without significant changes in the heating.

In all experiments no significant temperature increase was observed in the gel, far from the PM and its leads, for all the sequences we tested.

DISCUSSIONS

Previous studies investigating MRI induced PM lead heating reported a large variability in the induced heating. All investigations showed that the maximum RF-induced heating occurs at the electrode tip. However, the reported temperature increase at the lead tip varied between 0.1 °C [11] and 63.1 °C [10]. This variability comes from several factors, such as the type and positioning of the temperature probes next to the lead tip, the whole body SAR used, the cooling effect of the blood flow, and the lead geometry and placement.

The aim of this paper was first to identify a positioning of temperature probes next to PM lead tips to measure the maximum lead tip heating. Then we investigated the effect of the geometric structure of the PM leads (lead geometry) and the placement of the pacemaker on the PM can heating and PM lead tip heating, induced by MRI.

Using temperature measurements on a physical model of a pacemaker lead we found that the positioning of the temperature probes strongly affects the temperature and SAR results. Due to the comparable dimension of the temperature probes with

the pacing electrode and due to the large spatial temperature gradient around the lead tip, temperature probes tend systematically to underestimate the real value of local temperature and SAR. In particular, using the SMM Luxtron fluoroptic® probes, we found that a transversal contact of the temperature probe with the lead tip always gives the highest temperature and SAR values. Such a result points out that the active sensor is likely to occupy the central region of the pigmented jacket of the temperature probe. Assuming this configuration as reference, the underestimation by other configurations may be as high as 39% for temperature and 75% for SAR. Furthermore, we found less underestimation as the frequency increases. We can speculate that the heating pattern at higher frequencies is more spread and thus the effect of probe size and positioning is less marked. A deeper analysis of this issue was beyond

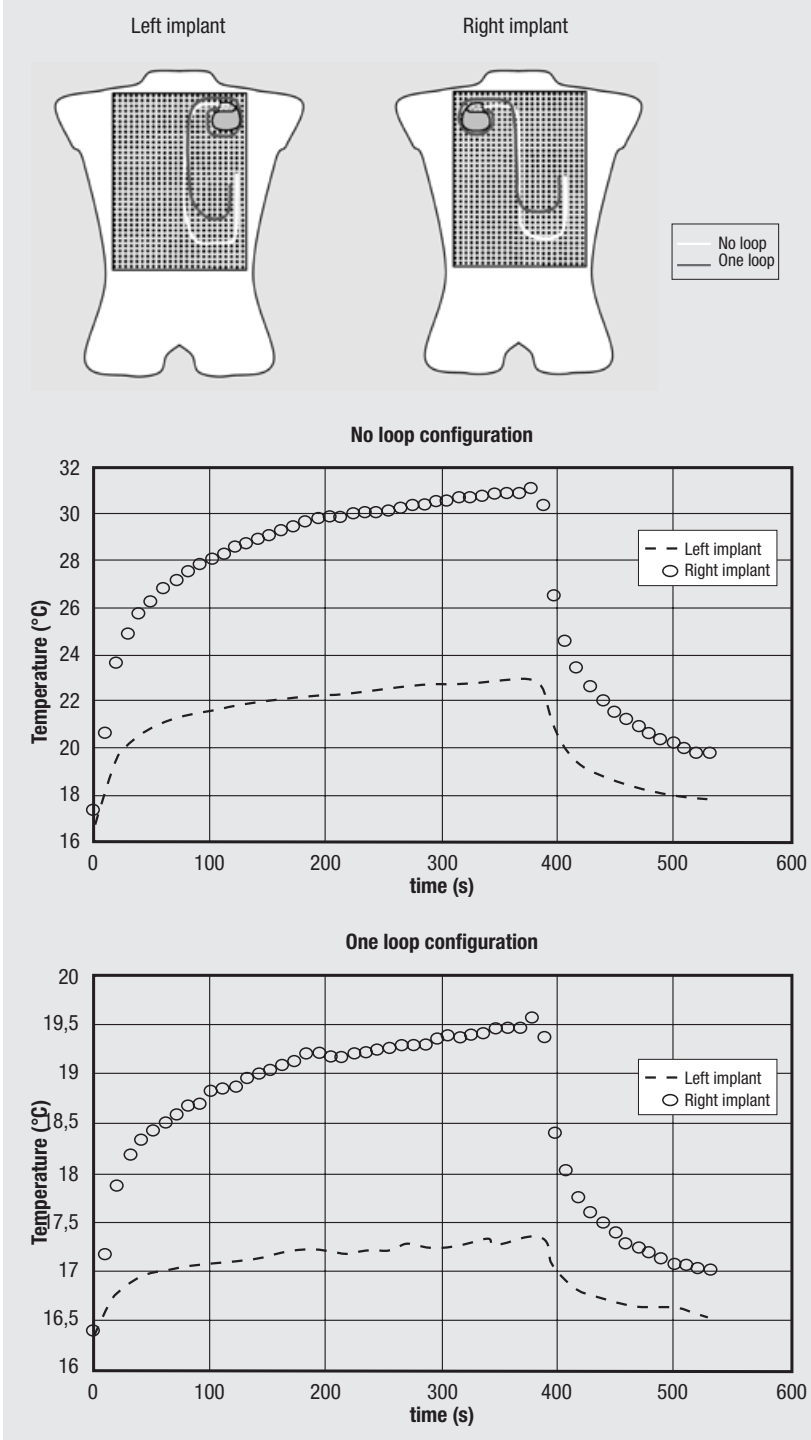


Fig. 5 | *Sketches of the two implant configurations tested in a real MRI scanner using the human-shaped phantom and graphs of the temperature increase measured at the lead tip: no loop and one loop configurations for both left and right pectoral implants.*

the aim of this study. The investigation of the temperature and SAR errors from other Fluoroptic® probe types, such as surface and remote style probes, was also beyond the aim of this study. Additional experiments are needed to evaluate the usability of surface and remote style probes for MRI implant heating evaluations. The SMM probes were chosen because they can guarantee a reliable contact even with very thin wires. In addition, since heating is generated at the interface between the metallic structure and the gel, surface contact probes would not be located in the actual hot spot area.

Experiments in the rectangular box phantom revealed two major factors on the lead tip heating: the length of the straight segment of the lead and their position inside the phantom. At first we correlated the heating induced by a MRI exposure to the area covered by the implant: several papers in the literature [11, 19] chose a configuration of the pacemaker lead in the coronal plane to achieve a maximal magnetic induction area, in order to maximize the heating at the lead tip. Our data clearly shows that the temperature increase is proportional to the implant area. Interestingly, in some cases, similar areas gave different temperature increase. It suggests that the lead tip heating is more affected by the length of the straight lead segment than the area. Generally a larger area implies a longer straight lead segment, as it happens for the no-loop, 1-loop and 2-loops configurations.

Resonance phenomena in various kinds of linear metallic leads and wires (*e.g.*, catheters used in interventional radiology) have been hypothesized by various groups [32, 33]. From a theoretical point of view, the maximum electrical coupling occurs when the length of a linear wire is half the wavelength of the RF field. At 64 MHz, the critical length of a straight lead implanted in the human body is around 26 cm [33]. This value is close to the length of the linear section of the lead in the experiments where the highest temperature increase and SAR values were observed.

The position of the implant inside the phantom seems to play a major role in the heat generation process. When the lead is placed close to the edge of the phantom, the temperature increase at the tip is significantly higher than for implants of the same area, or even larger, but positioned in the central region of the box. The electric field generated by the MR coil is higher at the phantom's edges, which represent a discontinuity between air and a lossy material, such as the HEC gel. The electric field sharply decreases towards the centre of the phantom. The inducted currents generated inside the simulator by the magnetic field are as well confined along the border of the box. In conclusion, we can define an implant configuration with long straight lead segments close to edge of the phantom to maximize the lead tip heating.

In our experiments using the rectangular box phantom, we kept the position of the PM can constant, simulating a left implant configuration. That is the most common situation for a real pacemaker. The results obtained for a left implanted PM inside the human shaped phantom were consistent with those obtained by the rectangular box: the longer the vertical segment of the lead, the higher the temperature increase. The importance of the position of the lead inside the phantom rather than the area of the implant is once again highlighted by the results from the right-implant configurations: they showed smaller lead areas than left pectoral implanted PMs, but the temperature increase observed were higher. In the two implant configurations, the vertical segment of the lead did not change, whereas only the PM can and the initial horizontal parts of the lead were placed on opposite sides on the grid. This suggests that the magnetically induced voltage could either add to or subtract from the voltage generated by coupling with the electrical component of the RF field to the linear part of lead [18]. The higher temperature increase for right-pectoral implants may also come from an asymmetric distribution of the electromagnetic field inside the phantom, with a "hot spot" area in the upper-right region of the torso simulator.

For approximately 1 W kg^{-1} WB-SAR we observed, in worst case, 12 °C lead tip heating and local SAR up to 2300 W kg^{-1}. The *in vitro* test methods used here are not intended to simulate the dynamics of blood and body fluid, but rather simulate the nearly instantaneous energy deposition. Thus, in a patient the temperature elevation may be reduced by the surrounding tissue heat absorption. Moreover, the power density at the lead tip decreases very sharply as the distance from the electrode increases: Irnich *et al.* [20] developed a numerical model for the evaluation of the electric field distribution around the lead tip and they found that a temperature increase of 80 °C was necessary to achieve a 5 °C degree heating 1 mm away from the electrode's surface. This could be true if the SAR were the only determinant for the thermodynamic equilibrium, neglecting any conductive processes from the hot spot to the surroundings tissues. Actually, our results suggest that the lead tip heating caused due to MRI exposure may damage, in particular configurations, biological tissue or at least may cause an alteration of the contact impedance at the tip, compromising the pacing capability.

The major impact of the implant positioning inside the phantom implies the need to perform temperature and SAR measurements inside a realistic human shaped trunk simulator, so to reproduce a realistic and worst case distribution of the inducted current inside the phantom.

Both the rectangular box and the human-shaped phantom measurements showed that wrapping the exceeding lead near the PM can does not contribute to the heating. We either observed that unipolar and bipolar leads produced similar heating and that no significant temperature increase was measured on the PM can. For bipolar leads we measured the temperature also at the ring electrode and found

little temperature increase (less than 2 °C). Similar results were found by other groups, even with different types of heating sources [34]. Due to the larger surface area of the ring electrode compared to the lead tip, the current density, and therefore the temperature increase, is much lower than at the tip.

We also explored if other PM settings influence the lead tip heating. We found that the lead tip heating is independent of the PM programming (*e.g.*, unipolar/bipolar sensing and pacing). Particularly we found no significant difference between bipolar to unipolar leads. The simultaneous use of two or three leads does not change systematically the heating of each tip, even when the tips are close to each other. However, a certain temperature increase with respect to the single lead configuration may happen.

The measurements inside the real MRI scanner showed that also the RF excitation sequence is a discriminating factor for the lead tip heating: in particular, the gradient echo sequences did not cause a significant temperature increase any of the implant configurations we tested.

Baker *et al.* [17] demonstrated that the whole body averaged SAR calculated by different MRI systems is not a reliable metric for RF induced heating. They found that in one system a WB-SAR of 0.07 W kg^{-1} induced temperature increase of 8.4 °C, while the same implant had a temperature increase of 1.2 °C with a WB-SAR of 0.88 in a different MRI system from the same manufacturer. We found similar differences when we tried to compare, for a given WB-SAR, the heating found in the rectangular torso simulator with a real MRI system. Using the rectangular box phantom (WB-SAR 1.0 W kg^{-1}) we obtained for a given lead configuration a temperature increase of about 12 °C. The same configuration gave in a real MRI system a temperature increase of about 6 °C for a SAR of 1.70 W kg^{-1}. We assume that this difference is due to an overestimation of the WB-SAR by the real MRI system. In this case the real MRI system overestimates the WB-SAR by a factor of 3.4. Such a WB-SAR overestimation leads to the same factor of underestimation for the implant heating because most testing of implant heating relates the temperature increase to the whole WB-SAR given by the MR system (M-WB-SAR). This may be due to the use of different assumptions and algorithms by the MR systems and due to the fact that the estimation by the scanner might not be valid for phantoms. In phantoms the M-WB-SAR estimation (M-WB-SAR-P) can be verified using calorimetry (C-WB-SAR-P) whereas in humans the M-WB-SAR estimation (M-WB-SAR-H) can only be verified using computational methods and high resolution anatomical models or the power per pulse method (C-WB-SAR-H). For implant heating evaluations the question comes up what relation between M-WB-SAR-H, C-WB-SAR-H, M-WB-SAR-P, and C-WB-SAR-P gives a conservative and therefore safe estimation of the actual implant heating in a patient. For implant heating evaluations an ideal relation between the WB-SAR values for humans and phantoms would be:

$$\text{M-WB-SAR-H} = \text{C-WB-SAR-H} \quad (1)$$

$$\text{M-WB-SAR-P} = \text{C-WB-SAR-P} \quad (2)$$

However, for patient safety the M-WB-SAR-H value is usually a conservative estimation of the C-WB-SAR-H:

$$\text{M-WB-SAR-H} \geq \text{C-WB-SAR-H} \quad (3)$$

Manufacturers of MR systems indicate that the WB-SAR estimation of the machine is not valid for phantoms. An M-WB-SAR-P overestimation leads to an underestimation of the same factor for the reported implant heating. This does not necessarily pose a problem for implant heating evaluations if the overestimation for M-WB-SAR-H is the same as for M-WB-SAR-P:

$$\frac{\text{M-WB-SAR-H}}{\text{C-WB-SAR-H}} = \frac{\text{M-WB-SAR-P}}{\text{C-WB-SAR-P}} \quad (4)$$

the actual implant heating occurring in the patient at a certain M-WB-SAR-H level would be correctly predicted. Also, as long as the overestimation of the WB-SAR for humans (M-WB-SAR-H) is greater than the overestimation for the phantom the implant heating evaluation can be considered as conservative:

$$\frac{\text{M-WB-SAR-H}}{\text{C-WB-SAR-H}} \geq \frac{\text{M-WB-SAR-P}}{\text{C-WB-SAR-P}} \quad (5)$$

Inequality (5) must be true for all humans to ensure patient safety. For safety considerations a conservative approach is desirable which has to assume that the C-WB-SAR-H can reach the M-WB-SAR-H in a worst case patient:

$$\frac{\text{WB-SAR-H}}{\text{WB-SAR-H}} = 1 \quad (6)$$

Assuming (6) as the worst case for implant heating it can be followed:

$$\text{M-WB-SAR-P} \leq \text{C-WB-SAR-P} \quad (7)$$

Inequality (7) states that for conservative implant heating evaluations the M-WB-SAR-P must be an underestimation of the real SAR in the phantom (C-WB-SAR-P). Unfortunately this seems not to be the case. Our results indicate the M-WB-SAR-P is

also an overestimation of the true WB-SAR in the phantom (C-WB-SAR-P). Further research, comparisons and re-evaluations of WB-SAR estimation of real MR systems for humans and phantoms is urgently needed to resolve this problem.

CONCLUSIONS

Our experiments showed the sensitivity of temperature and SAR measurements on Fuoroptic® probe contact positioning. The transversal contact of the pigmented portion of the temperature probe and the lead tip minimized the underestimation for temperature and SAR and gave therefore always the highest values for this type of pacemaker lead. Other contact configurations may cause a temperature underestimation of up to 39% and a SAR underestimation of up to 75%. For all MRI heating evaluations with temperature probes, a contact position leading to the lowest maximum error should be used, and the error should be specified. Scientific sound MRI heating evaluations need to be accompanied by a thorough uncertainty budget. Therefore, other uncertainty factors should also be evaluated when specifying temperature and SAR values on implants based on measurements with Fluoroptic® temperature probes.

The results from the rectangular box and the human torso simulator showed that the lead tip heating during MRI exposure strongly depends on the implant geometry and its position inside the phantom. The maximum heating at the lead tip was found for a PM lead path with long straight segments close to the border of the phantom: in such a configuration, the temperature increase measured inside the MR birdcage coil for a WB-SAR of 1 W kg^{-1} was as high as 18 °C, with a local SAR of 4300 W kg^{-1}. In the human shaped phantom, more realistic implant configurations were reproduced: the maximum temperature increase was found for right implant configurations suggests that the magnetic-induced voltage could either add to, or subtract from the voltage generated by coupling of the electrical component of the RF field to the linear part of lead.

In conclusion, implant geometry and positioning inside the phantom has to be taken into account to understand the large variability of lead tip heating reported in the literature: lead paths with long straights segments close to the edge of the phantom have to be chosen to maximize the induced currents and the tip heating. In addition, the WB-SAR calculated by commercial MRI scanner is somehow correlated to the local heating, although it is not yet a reliable tool to estimate the hating and the local SAR at the lead tip.

Disclaimer

The opinions and conclusions stated in this paper are those of the authors and do not represent the official position of the Department of Health and Human Services. The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by the Department of Health and Human Services.

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Electromagnetic interference and cochlear implants

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Summary. This paper reviews the most common sources of electromagnetic interference (EMI) with cochlear implants (CI). Particular attention will be given to the description of the mechanisms of electromagnetic interaction with CI; main disturbances caused to CI; relevant scientific investigations; and existing requirements and tests for electromagnetic compatibility (EMC) immunity applicable to CI.

Key words: cochlear implants, electromagnetic interference, electromagnetic compliance, magnetic resonance imaging, non-ionizing radiation.

Riassunto *(Interferenze elettromagnetiche e impianti cocleari)*. Questo articolo ha l'obiettivo di fornire una rassegna esaustiva delle principali sorgenti di interazione elettromagnetica con gli impianti cocleari. In particolare, per ogni tipologia di sorgente verranno riportati: i meccanismi di interazione con gli impianti cocleari; gli effetti che tali interazioni hanno sugli impianti; i principali studi scientifici pubblicati sull'argomento; le vigenti prescrizioni e prove di compatibilità elettromagnetica degli standard europei ed internazionali applicabili agli impianti cocleari.

Parole chiave: impianti cocleari, interferenza elettromagnetica, compatibilità elettromagnetica, imaging a risonanza magnetica, radiazioni non-ionizzanti.

INTRODUCTION

A cochlear implant (CI) is an active prosthetic device implanted into the inner ear, *i.e.*, the cochlea, and it is used to stimulate, through electrical impulses, the neural tissue of the spiral ganglion (*i.e.*, the inferior root of the acoustic nerve). The neural discharges resulting from the electrical stimulation induce auditory sensations at the level of the brain cortex area, which can restore partial hearing to severe to profound deaf people [1]. Most of the people with cochlear implants can communicate without lip-reading or signing, and some can even communicate over the telephone. Several cochlear implants have been designed over recent years, with slightly different specific characteristics, but all the devices share the common features described in the following. An ear level microphone picks up, amplifies, and converts the speech sound into an electrical signal. The electrical signal is transmitted, through appropriate cabling, to the speech processor. The speech processor analyzes and converts the speech into appropriate digital information about the pattern of the electrical stimulation that has to be delivered to the cochlea through the implanted electrode array. The speech processor delivers the digital information to the external transmitting coil, which is located on the head of the patient over the implant site. The external transmitting coil, in turn, transmits both power and digital information through a radio frequency (RF) link to the receiver/stimulator of the implant, which is implanted in a depression of the skull bone, behind the mastoid. The external coil is held in place over the internal receiver/stimulator package (which contains the internal coil) with a pair of external and internal magnets. The receiver/stimulator decodes the digital information coming from the speech processor through the radiofrequency link and delivers the electric stimulation pulses to the electrode array (consisting of multiple electrodes) which is implanted in the inner ear. The electrodes implanted into the cochlea stimulate the ear nervous terminals by means of a series of bipolar current pulses, whose amplitude, width and frequency are controlled by the speech processor [2-5].

Adults and children can get a CI, even very young children and babies. In 1990, the United States Food and Drug Administration (FDA) lowered the approved age for implantation to 2 years, then 18 months in 1998, and finally 12 months in 2002, and special approval has been given for babies as young as 6 months in the United States and 4 months internationally. According to 2005 data reported by the United States National Institute

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on Deafness and Other Communication Disorders, nearly 100 000 people worldwide have received a CI. Currently (as of 2006), the main three CI devices are manufactured by Advanced Bionics (United States) (a subsidiary from 2004 of Boston Scientific Corporation, United States), Cochlear Corporation (Australia), and MED-EL (Austria).

Sources of electromagnetic interference (EMI) with cochlear implants can be found not only in particular circumstances due to specific medical treatments, such as magnetic resonant imaging (MRI), therapeutic ionizing radiation, electrosurgery, diathermy, neurostimulation, and electroconvulsive therapy, but also and very often even in the everyday life of a CI patient. Examples of frequent sources of EMI are mobile phones, electronic article surveillance (EAS) systems, and metal detection systems, which may interfere with the operation of the CI speech processor and cause distortion of the sounds processed by the CI. Last but not least, electrostatic discharge such that generated by removing clothes over the head or by playing on plastic slides may damage CI components or corrupt the program in the CI speech processor.

In the European Union, EMI or, more specifically, electromagnetic compatibility (EMC) in active implantable medical devices (such as CI) is regulated under the Council Directive 90/385/EEC [6] and its harmonized standard [7], as part of a family of safety standards in which EMC is viewed in terms of safety and clinical function of the device. In particular, the harmonized standard [7] is the primary standard containing general requirements applicable to all types of active implantable devices. As of December 2006, there is no product-specific standard for CI with the exception of the draft European standard [8] which is not yet active and is currently submitted to European Committe for Standardization (CEN) and European Committee for Electrotechnical Standardization (CENELEC) members for enquiry. This draft European standard has been prepared under a mandate given to CEN and CENELEC by the European Commission and will cover (when approved) essential requirements of Directive 90/385/EEC [6]. In absence of a CI-specific standard, usually most of CI devices are tested to be compliant with the international standard IEC 60601-1-2 [9] which is related to requirements and tests for EMC in medical electrical equipment. The text of the international standard IEC 60601-1-2 was approved without any modification by CENELEC as the European standard EN 60601-1-2:2001.

Despite the widespread diffusion of CI and the large number of interference sources, a relatively few studies were published on the topic of EMI and CI. Objective of this paper is to review the most important sources of EMI with CI, giving particular attention to: mechanisms of interaction with CI; main disturbances caused to CI; relevant scientific investigations; and existing requirements and tests for EMC immunity applicable to CI.

SOURCES OF EMI WITH CI

Magnetic resonance imaging

To ensure in CI a good transmission quality and exact alignment between the external transmitter and the internal receiver coil, usually a pair of magnets, one integrated into the transmitter coil of the external headset and the other integrated into the internal coil are applied. Although this is a very good solution for with regard to the quality of the transmitted message between external and internal coils, the presence of the two magnets creates serious problems with MRI. The electromagnetic fields produced during MRI (static, RF pulsed, and pulsed gradient magnetic fields) may interfere with the implant in several ways [10, 11]: eddy currents could arise in the conductive part of the implant and cause heating and damage of the surrounding tissues; magnetic field gradient could exert force and torque on ferromagnetic parts of the CI and dislodge the implant, thus damaging the device and surrounding tissues; electric field induced in conductive loops by RF magnetic field could seriously damage the electrodes and the stimulator of the implant; the CI internal magnet could be demagnetized thus reducing transmission functionality and, finally, could give raise to artifacts in MR images.

MRI is thus always contraindicated for patients with a CI except under specific circumstances, *i.e.*, when the implant is specifically designed for MRI compatibility and safety. Two different approaches are typically implemented to achieve MRI compatibility. In the first approach, CI internal magnet is enabled to be surgically removed before MRI. Examples of CI with removable magnets are the Nucleus 24 cochlear implant (Cochlear Corporation, Australia) and the HiResolution Bionic Ear System's HiRes 90K (Advanced Bionics, United States), which were approved by FDA to be safe for MRI up to 1.5 T [12] and at 0.3 and 1.5 T [13], respectively. In the second approach, the internal magnet is MRI safe and there is no need for removal before MRI. Example of this type of CI is the MED-EL Combi 40+ (MED-EL, Austria) in which the internal magnet is put in a robust ceramic case. This implant was approved in 2003 by FDA to be safe for MRI at 0.2 T [14].

However, up to date, there is no standard procedure to assess MRI compliance and safety. Published scientific investigations are not homogeneous and differ greatly as to experimental setup (patients, cadaver specimens, and phantom models), tested MRI levels and protocols, and parameters measured to assess MRI safety. For example, Baumgartner *et al*. [15, 16] performed a retrospective study over patients with CI who underwent MRI at 1.0 T. No adverse effects were reported by the patients, and no damage nor malfunctioning was observed for all the implants. Also, all MR images were of diagnostic value (*i.e.*, image artifacts caused by the presence of the CI were small). Similar results were obtained by Youssefzadeh *et al*. [17] in patients who underwent MRI at 1.0 T: in particular there was no detectable movement of the electrode and receiver coil nor any

temperature change near the electrode. In the study by Weber *et al*. [18], a magnetless implant (*i.e.*, an implant where the receiver coil was held in place without a magnet) was tested for MRI safety at 0.3 and 1.5 T in 11 patients. Results revealed that the tested magnetless implant was MRI compatible. Gubbels *et al*. [19] evaluated the effect of MRI at 1.5 T on the Nucleus 24 cochlear implant without removing the internal magnet before MRI. A compression dressing was used to prevent magnet displacement. CI were implanted in four cadaver heads and exposed to MRI. In no case displacement occurred if the compression dressing was applied and no decrease in the strength of the magnet was observed after MRI. The authors concluded that surgical removal of the internal magnet may not be necessary before scanning at 1.5 T. Wackym *et al*. [20] measured the demagnetization of the internal magnet of the MED-EL Combi 40+ implant in two fresh cadaver heads exposed to MRI at 0.2 and 1.5 T and in three patients who underwent MRI at 0.2 T. In all cases, the magnet was not removed from the implant before MRI. In cadavers, sagittal T1-weighted, axial T1-weighted, and axial T2-weighted sequences were performed at different head orientations. No significant demagnetization of the internal magnet was observed in CI implanted in cadaver heads both at 0.2 and 1.5 T. The same result was obtained in the patients after a 0.2-Tesla-MRI. More extensive studies on MRI were done using cochlear phantoms. In the studies of Teissl *et al*. [21, 22] phantoms were used to measure demagnetization, movement, force and torque on the magnet, temperature increase, induced voltage due to switched gradients or RF pulse, artifacts and geometric distortion area of MR images at 0.2 and 1.5 T MRI. The tests were done with the MED-EL Combi 40+ implant. Except for the torque at 1.5 T, the measured electromagnetic interferences between the CI and the 0.2 and 1.5 T scanners remained within acceptable limits. The authors concluded that MRI at 0.2 should be safe; at 1.5 T MRI examination should only be performed if there is a strong medical indication. As a final example of published investigation on MRI safety with CI, the documentation accompanying the FDA Premarket Approval (PMA) [12] of the Nucleus 24 cochlear implant reported the results of the tests done by the manufacturer with a MRI scanner having 1.5 T static field, 64 MHz pulsed field, and pulsed gradient fields up to 20 T/s. Pulsed gradient fields did not produced any stimulus output from the implant; temperature rise in the neighbourhood of the implant was non significant (< 0.1 °C); under the worst case scan parameters, MR image could be distorted in the area around the implant (approximately 2 cm medial and 6 cm inferior). With MRI static field, the force exerted on the implant was small (less than the normal weight of the implant) and not harmful.

The various models of CI currently available are quite different and therefore no general conclusion can be drawn about MRI compliance. To this purpose, CEN and CENELEC are currently working on the standardization of the procedures to be used to assess MRI compliance and to the definition of the main hazards (such as force, heat generation, unintentional output, etc.) of a subject implanted with a CI [8].

Mobile phones

Successful use of a telephone, at least with a familiar speaker, has been frequently reported in adults [23-29] and also in children [30] implanted with CI. Survey by Sorry *et al*. [26] showed that 27/61 respondents of Finnish postlingually deafened adult implantees used a cellular phone, a digital one in the vast majority of cases. However, in a subgroup (n. = 9) of the respondents using a body-worn processor, EMI problems turned out to be common. Another report [28] also mentioned problems of CI users with sound quality over the ordinary telephone and/or cellular phone. EMI problems are caused by both electrical and magnetic components of electromagnetic fields in the audio and ultrahigh frequencies, with the magnetic components predominating at the audio frequencies [31].

As CI enable telephone communication, and as EMI problems are evident and common, new solutions are needed to provide CI users with the possibility of benefiting from modern mobile communication. Up till now, only few laboratory works have been conducted to address interference, listening comfort, and speech recognition [26-32]. According to Sorry *et al*. [26] some body-worn processors are highly susceptible to EMI problems. Because of their small size and their well performing signal processing features, behind the ear signal processors have become ever more popular, but body-worn processors are still in wide use all over the world. Some cochlear implant users themselves have tried to solve listening problems with cellular phones with custom-made adapter cords and jacks [28].

Qian *et al*. [32] proposed a wireless phone adapter that could be used to route the audio signal directly to the hearing aid or cochlear implant processor. This adapter was based on Bluetooth technology. The authors stated that the favourable features of this wireless technology made the adapter superior to traditional assistive listening devices. Three cochlear implant users were tested with the proposed phone-adapter and reported good speech quality. Sorri *et al*. [26] studied three new assistive listening device prototypes that eliminate or diminish EMC problems. Ten experienced CI users listened in quiet to running speech samples and a sentence test on a landline phone and a digital cellular phone with and without the three prototype phone-adapters. Subject performance was assessed using a sentence test, a subjective visual analog scale, and by ranking the best and the poorest listening condition. Compared to the other test conditions, the authors found that listening to a digital cellular phone alone revealed, on average, the poorest

sentence recognition scores (29%) and the poorest results in four different subjective judgments (the amount of disturbances, the clarity of the message, the quality of the sound, overall judgment) with all three phone-adapters tested. The authors concluded that the phone-adapters generally helped the implantees to recognize speech better on the cellular telephone (by 10-21 percent units, on average). Therefore, assistive listening devices could diminish the compatibility problems between CI and digital cellular phones. However, this statement should be interpreted with caution, because only one telephone model and three different phone-adapters with body-worn processors were tested in that study [26]. Nevertheless, both CI and digital cellular phone manufacturers should take EMI problems into consideration. Cochlear implant users could benefit more from existing and future assistive listening devices if the audio inputs (and possible induction coils of the processors) had uniform standards, preferably in common with hearing aids. Furthermore, both for scientific research and product development, international standards for measuring the immunity of hearing devices to EMI are needed. The process of harmonizing these standard assessment techniques is in progress [33].

In the US, the Federal Communications Commission (FCC) has set a final milestone (February 2008), when half of all digital cellular telephones offered by manufacturers and service carriers must produce less interference [34]. However, obviously all the problems probably cannot be eliminated with improved technology. Furthermore, the current digital cellular phones and implant systems, in particular, will be in use for several years.

Only recently, there have been published scientific investigations on the estimation of EMI in CI through phantoms or numerical simulations. Tarusawa *et al*. [35] proposed a test phantom to estimate cellular phone EMI with CI. This test phantom was constructed from a square tank filled with saline solution. The use of a flat phantom provided a level of consistency in duplicating the exposure conditions in the EMI tests. The measurement and calculation results showed that there is no difference in the electric field (E-field) strength near the surface of the phantom when comparing flat and head-shaped phantoms and that the flat phantom is sufficiently thick to disregard the influence of reflective waves near the surface of the phantom. The calculation results also indicated the appropriateness of using physiological saline (0.18 g/l) up to 3 GHz when comparing the E-field strength inside a phantom comprising physiological saline and in a 2/3 muscle model. The results of EMI testing of a CI showed that there is no difference in the maximum interference distance when using either the flat or head-shaped phantom. Based on these results, the authors sustained the validity of using the flat phantom in EMI tests from cellular phone for the CI.

Electrostatic discharge

Large amounts of static electricity could cause the implant memory to reset or, in general could damage its electrical components. For this reason, all implant manufacturers [12-14] warn CI recipients be cautious (or, when possible, to avoid) in situations in which static electricity is created, such as when pulling on and off clothes or when getting out of a vehicle. Children with CI are also advised to avoid plastic playground slides because this creates very high electrostatic discharge (ESD). If static electricity is present, patients should touch something conductive, such as a metal object, before the CI system contacts any object or person. Before a CI recipients take part in activities that create high ESD, such as playing with plastic playground slides, they should remove the speech processor and the headset containing the transmitter coil.

All CI models were subjected by the manufacturers to ESD test. Test procedures used for ESD compliance are different among the manufacturers. For example, for the Nucleus 24 cochlear implant, ESD testing [12] was conducted according to the requirements and indications given in the international standard IEC 801-2 [36]: the implant and the speech processor were tested both for common mode and differential mode discharge at the levels of ± 8 kV for contact discharge and ± 16 kV for air discharge. The implant was compliant (*i.e.*, the testing indicates normal performance within the manufacturer's specification limits) with IEC 801-2 test level 4 for both contact and air discharge; the speech processor was compliant with IEC 801-2 test level 1 for contact discharge and test level 2 for air discharge. The MED-EL Combi 40+ implant was tested for ESD immunity [14] according to the EN60601-1-2 [9] at the ESD levels of ± 6 kV for contact discharge and ± 8 kV for air discharge. All applicable requirements of the standard [9] were fulfilled. For the Clarion multi-strategy cochlear implant (Advanced Bionics, United States) [13], the implant, speech processor, and battery charges were subjected to ESD testing at levels of 5, 10, 15, 20 and 25 kV. No loss of performance (soft failure) was observed up to 15 kV and no component damage (hard failure) was observed up to 25 kV.

Radiotherapy

Ionizing radiation cannot be used directly over the CI system as it may damage the device [12-14]. According to the European standard EN 45502-1 [7] (which is applicable to all active implants), the accompanying documentation of the device shall warn, if appropriate, that electronic components in the implant may be damaged by therapeutic ionizing radiation, and warn that any damage to the device may not be immediately detectable. Compliance shall be checked by inspection. The CI-specific European standard prEN45502-2-3 [8] will provide (when approved) details on the procedure (number of exposures and radiation dose at each exposure)

to follow to test compliance to therapeutic ionizing radiation and the amount of change of the implant output signal (*i.e.*, the stimulating signal) from its value before the first irradiation.

High powers electrical fields applied directly to the patient

Some medical treatments generate induced currents that may cause damage to the tissue or the CI device. Electrosurgical instruments are capable of producing RF voltages of such magnitude that a direct coupling can effectively exist between the cautery tip and the CI electrode array. For all implant models, monopolar electrosurgical instruments must not be used on the head or neck of a CI patient [12-14]. In some implant models [12] bipolar electrosurgical instruments may be used on the head or neck of a CI patient provided that the cautery electrode is not in contact with the implant and is kept more than 1 cm from the extracochlear CI electrodes. Similar warnings are given for diathermy or neurostimulation and electroconvulsive therapy: all implants models warn to use none of these therapies directly over the CI to prevent tissue and implant damage [12-14]. Up to now, there is no standard procedure to test immunity of CI to high power electrical fields applied to the patient. The CI-specific European standard prEN45502-2-3 [8] will provide (when approved) details on the procedure (such as, implant external loads and type of signal generator used to simulate the effect of high power electrical fields) to assess test compliance.

As to scientific investigations on this type EMI, there is only one study which is focused on the compatibility of dental appliances with CI [37]. The electromagnetic field created by dental instruments may present a potential hazard to CI patients. Damage to the electrodes in the cochlea, which lie within 6 cm of the maxillary second molar, would not only irreparably damage the implant, but would also necessitate a surgical procedure to replace it. In fact, not only the implant could be permanently damaged, requiring replacement, but sufficient electrical energy could necrotize vital cells of the basilar membrane, making re-implantation futile. Even if these cells were not damaged, re-implantation would involve significant expense to the patient plus the hazards of another surgery. The study by Roberts *et al*. [37] investigated the effects of EMI with a CI during the operation of the electric pulp tester, apex locator, electrocautery unit, electrosurgery unit and panoramic radiograph machine. A mastoidectomy and cochleostomy were performed on a cadaver, and a CI was implanted. The dental devices were used intraorally and the implant's circuitry was tested after each trial. A second CI was implanted in a human skull, which was then exposed to 50 panoramic radiographs, testing the implant's circuitry after each exposure. The authors [37] concluded that the probability of damage to the CI by any of the devices was negligible, except for the electrosurgery unit operated at level 7, which destroyed the CI's circuitry. Therefore, although the other devices seem safe, they concluded that it is recommended that the electrosurgery unit not be used on a CI patient.

Generic sources of electromagnetic radiation

In addition to the specific EM sources already reviewed in the sections above, non-ionizing radiations from generic sources may affect CI functionality. All CI models are tested by the manufacturers for susceptibility to electromagnetic fields. For two CI models [12-14], EM compliance was tested according to the requirements given in the international standard IEC 60601-1-2 [9]. In particular, immunity to conducted disturbances induced by RF EM fields were assessed at the test level of 3 Vrms (root-mean-squared value) in the range from 150 kHz to 80 MHz; immunity to radiated RF EM fields were assessed at the test level of 3 V/m in the range from 80 MHz to 2.5 GHz. The test results indicate that exposure of the CI device to EM fields will generate some unwanted stimuli but not will result in interference with the normal operation of the device. Exposure will not induce damage to the implant and will not result in intermittent or ceased operation for the duration of the exposure. In other CI models, EM susceptibility was tested according to specific procedures developed directly by the manufacturer. For example, the Clarion multi-strategy cochlear implant was tested [13] with an electric field of 340 V/m in the frequency range 2-500 MHz. Susceptibility at magnetic field was assessed by placing the implant in a magnetic field in the frequency range 2-500 MHz; the strength of the field was increased until the implant stopped working. Susceptibility levels for this implant model ranged from 1.3 to 10.3 A/m. In addition, this implant model was immersed in saline solution to simulate body tissue characteristics. A monitoring system made by a fiber-optic line measured the testing field. Testing was conducted from 10 kHz to 1 GHz at electric field strengths of 0.5 to 7.0 V/m in a shielded room. The implant was properly electrically functioning at the completion of the test.

Examples of EMI from non-ionizing radiation are EAS and metal detection systems, which produce strong electromagnetic fields that may disturb CI functionality. In particular, all CI manufacturers warn that in some cases implant recipients may hear distorted sound when passing near or through these devices. To avoid this disturbance, it is recommended to switch off the speech processor. Also, the materials use in the CI may also activate metal detection systems.

As to scientific investigations on CI compatibility with non-ionizing EM fields, there is a study dealing with EMI with CI in work environment. Hocking *et al*. [38] tested CI patients working in electromagnetic fields. They found that mono-channel implants are more sensitive than multi-channel devices. Interference is also more likely to occur if the frequency of the electromagnetic field is in the

same range of the RF signal transmitted from the external CI transmission coil. The patient should be informed of the possibility of hearing artefacts in order to avoid potentially dangerous situations in the work environment.

CONCLUSIONS

The number of CI recipients as well as the use of EM sources for different applications are increasing very rapidly. EM interaction with CI is very common not only in specific medical treatments (such as with MRI) but also in the everyday life. The most investigated source of EMI in CI is the MRI, due to its dangerous effects both on the patient and on the implant if the implant is not specifically designed for MRI compatibility and safety. The main three manufacturers of the CI devices here reviewed made changes in the design of their implants in order to make them to some extent safe at specified MRI levels. For all implant models and all types of sources of EMI with CI, safety measures were recommended in the implant accompanying documentation. Specific standards on EMC testing in CIs should be provided soon in the European standard prEN45502-2-3 [8] which is currently not yet approved. It will be necessary to perform deeper investigations to achieve more profound knowledge of EMI in CI.

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Experimental and numeric investigation about electromagnetic interference between implantable cardiac pacemaker and magnetic fields at power line frequency

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Summary. The present contribute describes the investigation about the implantable pacemaker (PM) immunity against high level magnetic interfering fields at 50 Hz that a pacemaker wearer could find in his working environment. To this purpose, a test bench has been set up based on a Helmholtz coil for producing extremely low frequency (ELF) magnetic fields and a heart simulator rightly fed by electric signals that simulate atrium and ventricle signals. A widely diffused PM has been tested, under different operation modes and configurations, for both continuous interfering waves (CW) and variously pulsed interfering waves (PW). Pertaining the obtained results, high levels of CW field, only in unipolar mode, produce a behaviour called "asynchronous mode" (not dangerous). For PW fields, under particular and rare conditions, the complete inhibition occurred (the most dangerous effect for PM wearer). In order to validate experimental results, a numerical 3-D model has been developed to simulate the whole bench system formed by Helmholtz coil, human trunk, pacemaker case and its electric leads. In this model the electromagnetic problem is solved by reconstructing the inhomogeneous bench system associating the relative values of conductivity to each cubic cell in which the whole system is discretized. Application of Maxwell's equations in their integral form has allowed to obtain a 3-D electrical network, whose solution gives the current density distribution inside the heart simulator.

Key words: artificial pacemaker, electromagnetic fields, immunity, electric power supplies.

Riassunto *(Studio sperimentale e numerico sull'interferenza elettromagnetica tra pacemaker cardiaci impiantabili e campi magnetici alla frequenza delle linee di alimentazione)*. Il presente contributo descrive una ricerca sulla immunità di pacemaker impiantabili (PM) ai campi magnetici di alta intensità, a 50 Hz, che un portatore di pacemaker potrebbe incontrare nel proprio ambiente di lavoro. Per questo scopo è stato messo a punto un test di prova basato su una bobina di Helmholtz per la creazione di campi elettromagnetici a bassissima frequenza (ELF), e su di un simulatore di camere cardiache in grado di simulare i segnali elettrici tipici di atri e ventricoli. Un modello di pacemaker largamente diffuso sul mercato è stato provato, in diversi modi di funzionamento e configurazioni, sia in presenza di campi interferenti ad onda continua (CW), sia di tipo pulsato (PW). Per quanto riguarda i risultati ottenuti, alti campi magnetici CW, solo nel caso di configurazione unipolare, hanno indotto sul PM un comportamento di tipo "asincrono" (non pericoloso). Per campi pulsati, in condizioni molto particolari e rare, è stata osservata una inibizione totale (la condizione più pericolosa per un portatore di PM). Per confermare i risultati sperimentali, è stato sviluppato un modello numerico 3-D per simulare l'intero sistema di test formato dalla bobina di Helmholtz, il tronco umano, l'involucro del PM e i suoi cateteri. In questo modello il problema elettromagnetico è risolto associando ad ogni cella cubica del sistema discretizzato i valori relativi di conduttività. L'applicazione delle equazioni di Maxwell nella formulazione integrale ha consentito di ottenere una rete elettrica 3-D, la cui soluzione fornisce la distribuzione della densità di corrente all'interno del simulatore di cuore.

Parole chiave: pacemaker artificiale, campi elettromagnetici, immunità, fonti di energia elettrica.

INTRODUCTION

The immunity of implantable cardiac pacemaker (PM) against magnetic fields has been widely investigated in radio frequency (RF) range and there are lots of papers in literature dealing with electromagnetic interaction between PM and RF fields (above all cellular phones and electric security systems) [1-6]. On the contrary, the effects of extremely low frequency (ELF) fields have not been sufficiently considered because the PM wearer, until few years ago,

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was typically an old no-worker person, living in a domestic environment, where strong ELF fields are a rare occurrence [7, 8]. Nowadays, in order to allow to more people to live a normal life, the average age of the PM wearer is considerably lowered, and therefore PM wearer could be a worker operating in a factory near high power machines. This paper deals with the electromagnetic compatibility (EMC) between an implanted cardiac PM and high level magnetic fields at ELF (typically 50 Hz) that can be found above all in industrial environments. Such investigation started with a PM programmed with only one chamber (right atrium or right ventricle), and successively was extended to dual chambers PM (right atrium and right ventricle). In this paper only the results of dual chambers PM are reported, because of the similar behaviors with those obtained for a single chamber one [9].

The principal coupling mechanism between the PM and the external magnetic field, at ELF, is due to the loop formed by the stimulating and sensing electrode system through the human tissues. Such loop area depends on the unipolar and bipolar pacing and sensing (in the following named "polarity system"): for every lead it can be unipolar or bipolar *(Figure 1)*.

In the unipolar system, PM has one electrode that lies within the heart as cathode, whereas the anode is the metallic case of PM itself.

The distance between both can extend up to 25 cm. The loop formed by current path starts from the PM output connection, follows the lead till its tip inside the heart, and returns back to the PM metallic case through the human tissue. In a large human this area can reach a maximum value of 250 cm^2. It is important to observe that through this loop the exogenous field induces a not desired voltage (easily calculated according to Faraday's induction law) that is added to spontaneous heart signal. Obviously such voltage reaches its maximum value if the magnetic flux density is orthogonal to loop area. Moreover loop area depends on the position of PM in human torax.

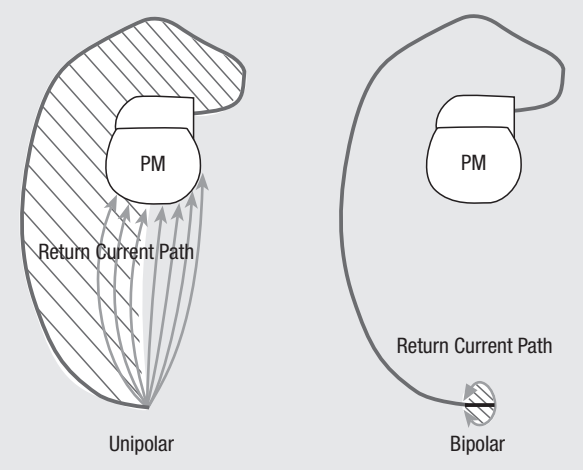

Fig. 1 | *Graphical sketch of current path for the unipolar and bipolar configuration.*

The bipolar system has been realized for reducing PM susceptibility to exogenous signals. In fact, the lead, that exhibits a coaxial structure, has two electrodes very close within the heart (about 3 cm distant), therefore the loop formed is very small (about 15-20 times less than the unipolar system) and electromagnetic interference (EMI) effect is much less than unipolar system. Utilization of this system is not always allowed because its bigger dimensions need a sufficiently large caves vena. Moreover, the clinical experience highlights that bipolar leads require a more frequent substitution. Generally dual chambers PM system has bipolar atrium chamber and unipolar ventricle chamber.

Furthermore, modern PM are provided with hardware filters (generally low-pass filters) and software filters. So if interfering signal rate is included between about 10 Hz and 300 Hz, the signal goes across input circuits and is computed by the internal PM algorithm that should recognize heart signal from exogenous signal. If such acknowledge happens, PM starts to pace at a programmed fixed rate (asynchronous mode), and remains in this condition for all interfering signal time.

The main EMI effects upon PM are:

- standard asynchronous (SA): EMI is recognized and PM switches into a state of periodic pacing at a programmable fixed rate (*e.g.*, 60 beats/min);
- irregular asynchronous (IA): hybrid state in which PM does not recognize always EMI signals and therefore sometimes misses one pulse or delays it;
- complete inhibition (CI): EMI is always confused as heart signal and PM does not produce any stimulation pulse;
- atrium tracking (AT): false atrial sensing inhibits atrial pacing and drives ventricle pacing;
- random inhibition (RI): PM is inhibited only under particular conditions depending on interfering signal start point and on some programmable PM parameters;
- no effect (NE): the PM behaviour is absolutely as expected.

Finally, a numerical 3-D model was used to further confirm the results obtained using the experimental set-up. This model, previously developed and validated [9], is based on a model designed in order to study the stimulation of the brain cortex [10, 11]. Such model provides a discretized description of the volume including the PM metallic body, its insulated leads and the human trunk simulator. The voltages induced at the PM inputs have been calculated and compared to those observed during the experimental tests.

MATERIAL AND METHODS

The PM tested is one of the most diffused on trade and can operate as a single, double or triple chamber device. *Figure 2* shows the used test set-

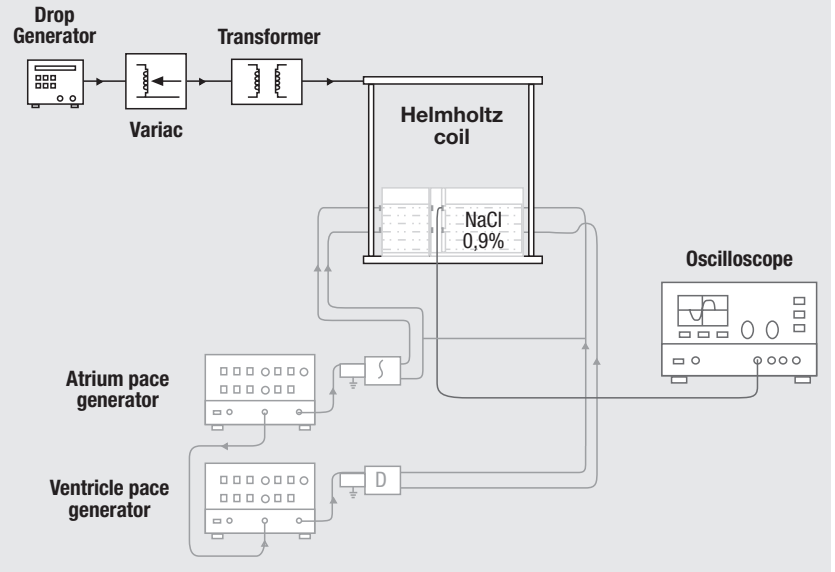

Fig. 2 | *Test set-up bench. Drop generator: Shaffner Model NSG 603 A. Variac: Belotti Model V-20-NC. Oscilloscope: Tektronics TDS-3054. Generators: HP8011A.*

up. The Helmholtz coil is supplied by a variac and a transformer and generates a magnetic field at 50 Hz vertically oriented (the cross-polarized components are at least 26 dB below the main one) allowing to set a whatever value from 0 up to 2 mT (CW mode). The addition of a programmable drop generator allows to produce pulsed fields (PW mode). A plastic box, divided in three chambers (one for the atrium, one for the ventricle and one for the PM lodging), is allocated inside the Helmholtz coil in order to simulate the human heart. For the atrium and the ventricle chambers two rightly synchronized pulse generators simulate electric heart signals. They are applied to two electrode plates on opposite sides. Lastly, the electric signals inside the boxes are detected by two electrodes usually used for electrocardiogram (ECG) analysis and are coupled to an oscilloscope.

A first chamber simulates the right atrium (30 cm × 20 cm), the second chamber simulates the right ventricle (30 cm × 30 cm), and the third is the lateral lodging for PM (15 cm × 15 cm). Further details and a photo of the 3 chamber cardiac simulator can be found in [9]. This box simulator was similar to that previously adopted by Angeloni *et al.* [12]. The boxes dimensions are not critical and are due to detect more easily every electrical signal inside the boxes. The three plastic boxes are filled by a saline solution (NaCl 0.9%) in order to offer an impedance similar to the human one (between 200 and 600 Ohm). Obviously all chambers are electrically connected through proper openings. For positioning the PM and the relative leads every chamber contain a plastic reference grid (adjustable in height) for leads displacements in order to guarantee the right reproducibility of every test. Every chamber is provided with both sensing and stimulating electrodes, and reproduces the electrical activity of one single heart chamber. Simulated heart activity signals were injected in the box by avoiding any ohmic connections between PM leads and instruments wires.

Description of the pacemaker under test

The PM utilized in every test is one of the most diffused on trade. The PM was programmed as follows: atrial and vertical pulse amplitude 3.8 V; pulse duration 400 μs; pacing rate 60 min -1; minimum and maximum atrial sensitivity: 0.5/1.0 mV; minimum and maximum ventricular sensitivity: 1.0/2.0 mV; PM polarity settings: pacing always unipolar and sensing both unipolar and bipolar. The pacemaker was tested in the following operating modes (ICHD code): VVI, AAI and DDD. Details on these operating mode can be found in [9].

Leads configurations

In the tests two different configurations of the leads have been considered to investigate the voltage induced under different orientations with respect to the external field (and consequently the different PM behaviour for the same field value): in configuration 1 the exceeding ventricle part of the lead forms a vertical loop, parallel to the magnetic field, which does not couple to the external; in configuration 2 the same loop is orthogonal to the magnetic field and therefore it is completely coupled with the external field. In both configurations the atrium lead is allocated in the same position because its length (about 380 mm) and flexibility do not allow substantial modifications. On the contrary, the ventricular lead, being usually longer than the necessary length (about 580 mm), can be oriented in various ways.

RESULTS

Results with CW fields

The tests have been carried out using the two previous configurations and increasing external field from

Table 1 | *CW Field: atrium (sensing and pacing unipolar) and ventricle unipolar (only pacing)*

Configuration	1	2	1	2
Atrium sensitivity (mV)	0.5		1.0	
Ventricle sensitivity (mV)	1.0		2.0	
Minimum field for EMI (μT)	58	42	119	91
PM behaviour	SA	SA	SA	SA

SA = standard asynchronous

Table 2 | *CW Field: atrium (sensing bipolar and pacing unipolar) and ventricle unipolar (only pacing)*

Configuration	1	2	1	2
Atrium sensitivity (mV)	0.5		1.0	
Ventricle sensitivity (mV)	1.0		2.0	
Minimum field for EMI (μT)	2000	950	2000	1300
PM behaviour	NE	IA	NE	IA

IA = irregular asynchronous; NE = no effect.

0 μT up to a maximum value of 2000 μT. During the scanning, some PM EMI effects have been recorded. The results are summarized in *Table 1* and *Table 2*. In every table the minimum field value that produces the EMI effect is reported.

Two typical sensitivity values have been chosen for each polarity system. The *Tables* indicate the minimum field value that generates the EMI effect. In *Table 1*, in which both atrium and ventricle are in unipolar mode, the only observed effect was the SA, whereas in *Table 2* the only observed effect was the IA. The field value at which the effect occurs is lower for the configuration 2 in which the field coupling is higher, as we expected. Moreover, the critical field value is proportional to the programmed PM sensitivities. The system polarity with ventricle bipolar provides the same results for atrium both unipolar and bipolar. Furthermore it must be remarked that PM inhibition (that is the most dangerous for wearer's life) was never obtained.

Results with PW fields

Successively, in order to simulate the effects due to intermittent operating machines , the pulsed excitation was considered: in particular three signals with different ratios between period T and time T_{on} were considered, whereas the sinusoidal frequency was always 50 Hz:

- signal 1, whose period T is less than T_{PM};
- signal 2, whose period T is similar to T_{PM};
- signal 3, whose period T is much larger than T_{PM}.

The tests with pulsed fields have been carried out with the same interfering signal already used for CW fields, but interfaced by a drop generator. The obtained results are summarized in *Table 3* and *Table 4*. Only one sensitivity value has been set (the worst).

Generally, it can be remarked that, if the external field pulse (T_{on}) starts before the well defined sensing time, it will be recognized as an EMI signal, otherwise the PM confuses the first sinusoidal wave of interfering signal as a cardiac spontaneous pulse, and consequently PM misses the relative pulse.

In particular in *Table 3* polarity system was unipolar both for the atrium and for the ventricle. With signal 1, there are two effects for two different field values. The first EMI effect is AT. Atrial tracking behavior means that a false atrium sensing drives ventricle pacing, so if the atrium has misinterpreted the interfering signal as a heart signal, the PM paces the ventricle with a period equal to the interfering signal (*e.g.*, 700 ms, that is 85 beats per minute – not dangerous). The second effect was CI. Complete inhibition, has to be considered a potentially lethal effect for the patient.

Table 3 | *Pulsed Field: atrium unipolar and ventricle unipolar*

Configuration	1		2	
Field and EMI effect	B (μT)	PM behavior	B (μT)	PM behavior
Signal 1 T_{on} = 500 ms T = 700 ms < T_{PM}	14 52	AT CI	13 38	AT CI
Signal 2 T_{on} = 100 ms T = 1000 ms = T_{PM}	15	RI	12	RI
Signal 3 T_{on} = 5000 ms T = 10000 ms > T_{PM}	14	RI	11	RI

AT = atrium tracking; CI = complete inhibition; RI = random inhibition.

Table 4 | *Pulsed Field: atrium bipolar and ventricle unipolar*

Configuration	1		2	
Field and EMI effect	B (μT)	PM behavior	B (μT)	PM behavior
Signal 1 T_{on} = 500 ms T = 700 ms < T_{PM}	50	CI	35	CI
Signal 2 T_{on} = 100 ms T = 1000 ms = T_{PM}	50	RI	35	RI
Signal 3 T_{on} = 5000 ms T = 10000 ms > T_{PM}	50	SA	35	SA

CI = complete inhibition; RI = random inhibition; SA = standard asynchronous.

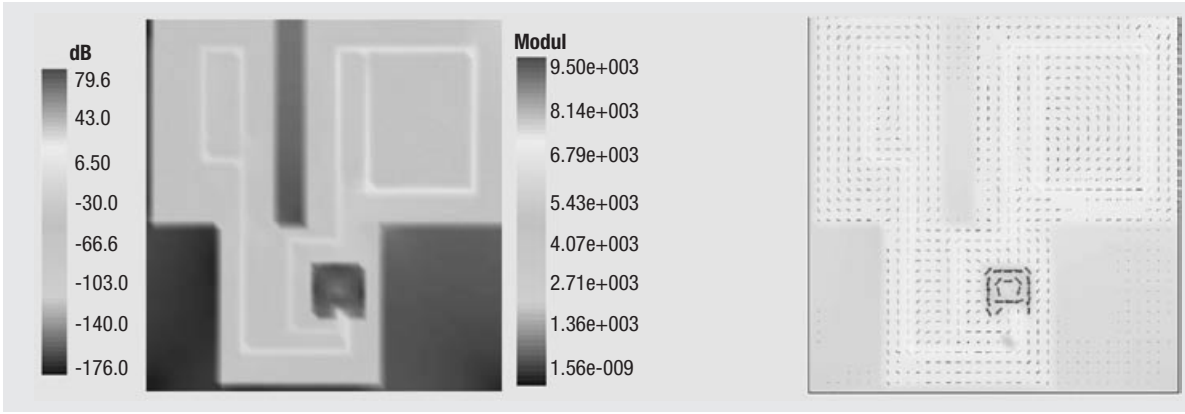

Fig. 3 | *Left panel: amplitude of current density (dBA/m2) in a horizontal section at 10 mm depth for configuration 1. Right panel: corresponding vectorial plot.*

Moreover, if the total period is nearly equal to PM programmed period (*e.g.*, for signal 2), the EMI effect depends on interference starting point and PM inhibition becomes random. Different is the case of a longer Ton (signal 3), where the PM omits the first pacing pulse, but immediately switches into the asynchronous mode for all the remaining T_{on}, as in the CW mode. Obviously, during the T_{off} the PM works as expected. In other words, we can observe that the EMI effects, for short T_{on} signal, strongly depend on interference starting point.

In *Table 4* the polarity system was bipolar for the atrium and unipolar for the ventricle and almost the same EMI effects have been observed for signal 1 and signal 2, whereas for signal 3 SA effect was always obtained.

For the polarity systems with atrium unipolar and ventricle bipolar, we have obtained the same effects recorded with atrium bipolar and ventricle unipolar, but with field values lower than the ones shown before. Lastly, no EMI effect has been observed if both atrium and ventricle are bipolar.

NUMERICAL SIMULATION WITH 3-D MODEL

This tool simulates the whole bench system formed by Helmholtz coil, heart simulator (plastic boxes), pacemaker case and its electrical leads. The aim is to develop a general purpose numerical tool able to analyze different magnetic or electric fields sources, different implanted devices (*e.g.*, defibrillators), different heart simulator (plastic boxes) and different configurations of the leads.

Model theory and development

The electromagnetic problem is to calculate electric fields and current density distribution induced in the biological tissues by a time-varying fields. Human trunk, discretized into cubic cells, is represented with a resistive 3D net characterized by the typical tissue conductivity. The method used to solve this problem consists of the application of one Maxwell's equation and continuity equation, both in their integral form. Since all electric quantities are slowly time-varying in the ELF domain, the quasistatic approach is applied. In particular volume charge density wasn't considered depending on time and, since the minimum wavelength of magnetic field is much greater than cell edge, all electromagnetic quantities can be considered constant inside every cell. The analytical details of the method are described in [9].

3D numerical model

From the knowledge of conductivity of human tissues, the procedure assigns its conductivity to every cell depending on the material, frequency and temperature. In the case of human tissue the Cole-Cole formula is applied [13], in the case of a saline solution the interpolating formula are applied [14, 15]. Successively every object of test bench can be inserted, substituting the proper conductivity in the involved cells. So the three boxes filled with saline solution (conductivity = 1.55 S/m) and with the same experimental dimensions have been inserted within the 3D model. The presence of a a metallic box (pacemaker case) was simulated at 10 mm depth, with two load resistances of 10 k for the electric leads (between the case and every pacemaker in-

Table 5 | *Induced current densities in the lead and voltage levels at PM input, as obtained by the numerical model*

Configuration	1	2
J_{atrial}	2.8 mA/m^2	2.5 mA/m^2
$J_{ventricular}$	2.48 mA/m^2	1.2 mA/m^2
V_{atrial}	2.8 mV	2.5 mV
$V_{Ventricular}$	2.48 mV	1.2 mV

put) in order to simulate the unipolar mode. Lastly, the two insulated wires, representing the leads following the two configurations previously described, are placed in the model.

A proper mathematic software solves the linear system previously obtained and a graphic software shows the results [9]. *Figure 3* left panel shows the J magnitude results for configuration 1 in a horizontal section including the PM at 50 Hz.

An external field with an amplitude of 76.5 μT has been considered. The current span is very large and the currents are concentrated on the metal structure. *Figure 3* right panel shows the same results in a vectorial plot highlighting the current paths. The currents flow through the openings for electrical connection, whose path starts from the outer edge of the greater box and terminates upon titanium case. In general, current path follows the configuration of the leads.

Now, the voltage values have been computed at the PM input impedances for the two analyzed configurations because they represent the final effect of the external field and therefore are responsible for the PM behavior. *Table 5* compares current density values and voltage induced values in the two configurations of the leads. The computed voltage values have the same order of magnitude of the sensitivity values of the PM (between 0.5 mV and 2 mV) and so such voltages are really able to modify PM behaviour, as shown in the experimental tests.

CONCLUSIONS

The bipolar system for EMI effects is always better than the unipolar one, in particular for CW waves which generated only the "standard asynchronous" EMI effect (not dangerous). In the unipolar system, leads orientation in the boxes is very important for EMI effect thresholds.

Pulsed fields are more dangerous than continuous fields, specially if their period is shorter than PM period therefore sensitivity value should be set as high as possible. Some EMI effects occur for field values below the limits suggested by international organizations (*i.e.*, ICNIRP limits are: 100 μT for general public, 500 μT for occupational) [16].

Every EMI effect disappeared when interfering signal has been stopped.

The developed 3D numerical model has demonstrated its capability to reproduce the real experimental situation for both the current distribution inside the human trunk and for the disturbance induced at the PM inputs. Numerical results showed a good agreement with the experimental results.

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Interference between mobile phones and pacemakers: a look inside

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Summary. In this study we analyzed the problem of electromagnetic interference (EMI) between mobile telephones and cardiac pacemakers (PM), by looking at the mechanisms by which the radiated radio frequency (RF) GSM signal may affect the pacemaker function. From a literature review on this topic, we noticed that older pacemakers had a higher rate of being affected by mobile phones when compared to newer ones. This is probably due to the fact that new generation of PM are more protected against electromagnetic field, being equipped with RF feedthrough filters incorporated to the internal PM circuitry. In some experiments conducted by our group, we found that modulated RF signals are somehow demodulated by the PM internal non-linear circuit elements, if no feedthrough assembly is incorporated inside the PM. Such demodulation phenomenon poses a critical problem because digital cellular phones use extremely low-frequency modulation (as low as 2 Hz), that can be mistaken for normal heartbeat. The feedthrough assembly seems instead to prevents the RF signals from accessing the PM enclosure, thus attenuating EMI signals over a broad range of frequencies.

Key words: electromagnetic fields, artificial pacemaker, cellular phone.

Riassunto *(Interferenza tra telefoni cellulari e pacemaker: uno sguardo all'interno)*. In questo studio ci siamo occupati del problema dell'interferenza elettromagnetica tra telefoni mobili e pacemaker cardiaci analizzando i meccanismi con i quali il segnale GSM interferisce con il funzionamento del pacemaker. Dall'analisi della letteratura su questo argomento, si nota come i pacemaker più vecchi hanno un incidenza più alta di interferenza con i telefoni cellulari rispetto a quelli più nuovi. Questo è probabilmente dovuto al fatto che i pacemaker di nuova generazione sono più protetti verso il campo elettromagnetico, essendo equipaggiati con filtri a radiofrequenza (RF) passanti incorporati nel circuito interno del pacemaker. In alcuni esperimenti condotti dal nostro gruppo, abbiamo riscontrato che i segnali a radiofrequenza modulati sono in qualche modo demodulati dai circuiti interni non lineari del pacemaker, se il sistema di filtraggio passante non è incorporato all'interno del pacemaker. Questo fenomeno di demodulazione pone un problema critico perché i telefoni cellulari usano modulazioni a frequenze estremamente basse (fino a 2 Hz), che possono essere erroneamente interpretate come il battito cardiaco. Il sistema di filtraggio passante sembra invece evitare che i segnali RF entrino nell'interno del pacemaker, attenuando i segnali di interferenza elettromagnetica in un vasto campo di frequenze.

Parole chiave: campi elettromagnetici, pacemaker artificiale, telefono cellulare.

INTRODUCTION

Any interference on devices such as pacemakers (PM) and defibrillators (ICD) may have serious consequences for the patient. The earliest generation of cardiac PM did not have the sensing function. Later, PM could sense spontaneous beats and synchronize with them provoking pacing or inhibition. Besides the beneficial effects of the introduction of the sensing function, it also created the potential for inappropriate inhibition of stimuli during pacing when electromagnetic interference (EMI) was mistaken for spontaneous cardiac depolarization. For dual-chamber pacing, EMI sensed in the atrium could trigger inappropriate stimuli in the ventricle, generating palpitations or even tachycardia. The most frequent effects of EMI on PM and ICD are inappropriate inhibition or triggering of stimulation, reversion to asynchronous pacing and spurious tachyarrhytmia detection, and, less frequently, reprogramming of operating parameters. Each of these anomalies is temporary, occurring only while the interference is present.

Patients with PM and ICD live a rather normal life, thus these devices may be exposed to a large number of EMI sources. In daily life patients can interact with cellular phones, electronic article surveillance devices, metal detectors, home appliances (microwave oven, electric razor), high speed train.

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At work patients can stay close to high voltage power lines, transformers, welders, electronic motors, induction furnaces, degaussing coils. In medical environment devices as magnetic resonance scanners, electrosurgical units, defibrillators, neurostimulators, TENS units, radio frequency (RF) catheter ablators, therapeutic diathermy devices could be used on a patient.

To date, Medline search for "interference pacemaker" gives a total of 418 references since 1957. If the search is restricted to the interference caused by telephones, the references become 39 since 1995, about 10 years later the introduction of cellular telephones. Nine of these references concern national studies mainly performed in Europe and in Asia. The others are publications in peer reviewed international journals and concern both *in vivo* and *in vitro* studies conducted on large population and using similar methodologies. Actually, the topic of EMI between mobile phones and PM was recognized in 1994, and since then, prompted several investigations [1-13].

For the scope of this paper, we analyzed the problem of EMI between digital mobile telephones and cardiac PM, by looking at the mechanisms by which the radiated RF GSM signal may affect the PM function.

Interference with cardiac PM by cellular telephones

EMI to PM from mobile phones has been investigated both *in vivo* and *in vitro* by several groups *(Table 1)* [1-13]. The majority of these studies systematically evaluated the PM and ICD models on the market, describing the adverse effects observed and indicating the incidence of EMI. Most of them also suggested a safe separation distance.

Table 1 | *Overview of the* in vivo *and* in vitro *studies about EMI of cellular telephones with cardiac pacemakers*

Authors	Year of publication	Type of experiments	Number of pacemakers tested	Number of pacemaker models tested	Results	
					Incidence of interference per patients	Incidence of interference per test
Barbaro *et al.* [1]	1995	*In vivo*	101	43	26% overall EM interference 10% pulse inhibition 20% ventricular trigger 8% EMI asynchronous pacing	
Naegeli *et al.* [2]	1996	*In vivo*	39	6	18% overall EM interference	3.9% EM interference 2.8% atrial triggering 2.8% ventricular inhibition 5.6% pacemaker inhibition
Irnich *et al.* [3]	1996	*In vitro*		231	31% for C-net 34% for D-net 0% for E-net	
Carrillo *et al.* [4]	1996	*In vitro /In vivo*	65	4 manufacturers		31% overall EM interference 0% for PMs with EMI filter
Chen *et al.* [5]	1996	*In vivo*	29	9	28% overall	
Nowak *et al.* [6]	1996	*In vivo*	31	3	0%	0%
Wilke A *et al.* [8]	1996	*In vivo*	50		4%	
Hayes *et al.* [7]	1997	*In vivo*	980	> 6 manufacturers		20% overall 14.2% atrial interference 7.3% asynchronous pacing 6.3% ventricular inhibition
Ruggera *et al.* [9]	1997	*In vitro*	30	30 models 7 manufacturers	37% overall	
Altamura *et al.* [10]	1997	*In vivo*	200	18	21.5% overall 18% inhibition 5.4 % asynchronous mode 9.4% triggering	
Elshershari *et al.* [11]	2002	*In vivo*	95	6 manufacturers	1% (PM implanted transvenously in a subcutaneous pocket)	
Tandogan *et al.* [12]	2005	*In vivo*	679		5.5% overall	
Trigano *et al.* [13]	2005	*In vivo*	158	> 50 models 7 manufacturers		1.5% overall

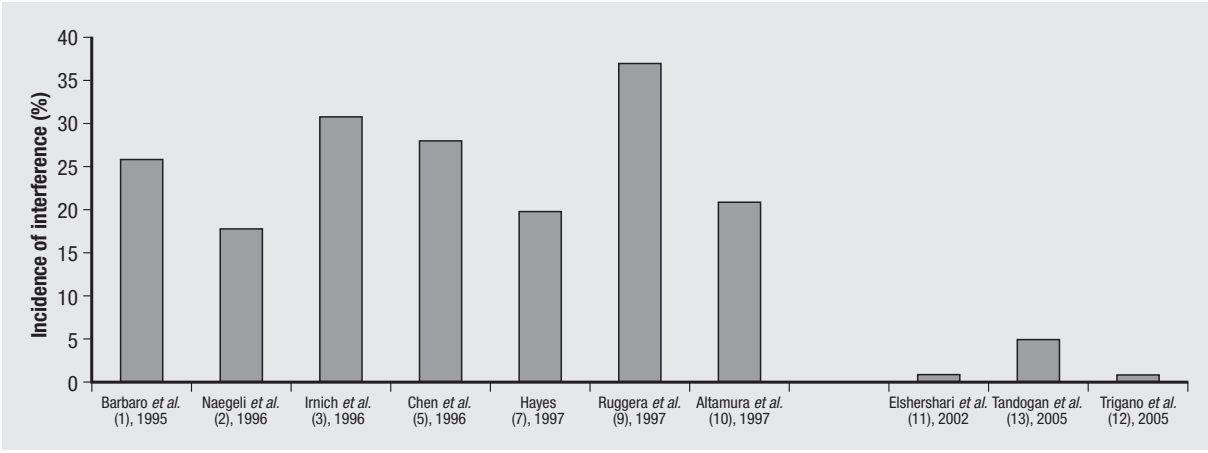

Fig. 1 | *Incidence of interference reported in the most significant published papers.*

The great variability of the findings in the existing literature reflects the complexity of the study design to assess mobile phone interaction with PM. This complexity is attributable to a number of factors such as the rapid evolution of PM and mobile phone technologies, the characteristics of the phone antenna, device implantation and programming, electrode configuration, distance between the device and the radiation source etc. The results obtained so far have shown interference to occur when the phone is very close (less than 5 cm) to the implantable device connection to the cardiac leads (*i.e.*, the PM "header"). Thus it can be concluded that with certain combinations of PM, cellular telephones, patients, and telephone-use habits, EMI can create anomalous PM behaviour with potential clinical consequences.

The number of PM tested in these studies varied from about 30 [6, 9] up to almost 1000 [7]. Until 1997, the reported incidence of EM interference varied form 20% to 30%; the last investigations showed a drastic reduction of EMI incidence to 1-5% [11-13] *(Figure 1)*.

Irnich *et al.* [13] demonstrated that older PM had a higher rate of being affected by mobile phones when compared to newer ones. Tandogan *et al.* made a comparison as to the age of the PM and showed that the rate of being affected significantly increased by age [13]. New generation of PM are reported to be more protected against electromagnetic field, being equipped with RF feedthrough filters incorporated to the circuitry.

In the *in vivo* investigation involving the major number of PM patients (almost 1000), Hayes and coauthors found that PM models without a feedthrough filter had a higher incidence of interference than those with a feed-through filter [7]. Such results are consistent with those found by Carrillo *et al.* on 65 patients [4] and more recently by Trigano *et al.* on 158 patients [12]. Trigano *et al.* found effects of EMI in 4 PM models from a single manufacturers, all implanted before year 2000 and lacking the electromagnetic filters included in more recent devices [12].

The introduction of the feed-through assembly has significantly improved PM immunity [15], giving *a posteriori* evidence that the physical interaction occurs at the lead conductors.

Few studies have investigated the mechanisms through which electromagnetic fields interact with PM. It has been demonstrated that the susceptibility of PM to various sources of EMI depend on the circuitry design. PM have a titanium case acting both as an electromagnetic shield and a barrier against body fluids. Platinum lead wires come out of the case through hermetic terminals and connect with the heart. It is largely believed that the physical interaction between mobile phones and PM is due to the electric coupling with the lead conductors inside the silicon head of the PM, which can act as an antenna and conduct undesirable RF carrier signals to the electronic circuits inside the PM [15, 16]. Most implantable PM employ EMI low pass filters designed with chip or substrate mounted capacitors which should decouple and shield these signals. Such a solution turned out to be inadequate to guarantee a high level of immunity to high-frequency sources such as GSM mobile phones [16]. The incorporation of RF feedthrough filters to the electronical circuit of the PM can strongly reduce EMI from digital cellular telephones.

Feed-through assembly

State-of-the-art PM are protected by input filters, the feedthrough assembly. A feedthrough assembly used to suppress and decouple undesired interference or noise transmission along a terminal pin consists of a coaxial feedthrough filter capacitor. Typically, it comprises a so-called discoidal capacitor similar to

a ceramic monolith. Two sets of electrode plates are embedded in spaced relation within an insulate substrate. One set of the electrode plates is electrically connected at an inner diameter surface of the discoidal structure to the conductive terminal pin utilized to pass the desired electrical signal. The second set of electrode plates is coupled at an outer diameter surface of the discoidal capacitor to a cylindrical ferrule of conductive material, which is in turn connected to the conductive housing of the electronic instrument.

The discoidal capacitor permits passage of relatively low frequency electrical signals along the terminal pin, while shunting and shielding undesired interference signals of typically high frequency to the conductive housing.

As a result, the filter capacitor and terminal pin assembly prevents the RF signals from accessing the PM enclosure, thus attenuating EMI signals over a broad range of frequencies.

It is generally mounted onto the hermetic terminal of the PM and thus acts electrically as a continuous part of the electromagnetic titanium shield (PM housing).

We have recently investigated the mechanisms through which the GSM signal affects the PM function by measuring the signal at the output of the sensing amplifier of PM with various configurations of low pass filters and exposed to modulated and non-modulated RF signals [17], as explained in the next paragraph.

Evaluation of EMI from inside the PM

Our group investigated the mechanisms of EMI between mobile phones and PM using a modified version of a commercial PM [17]: it had an electronic connection with the output of the sensing amplifier, just before the comparator circuit that detects any spontaneous activity of the heart. We used three modified versions of the same PM in order to have an electrical connection to the output of the sensing amplifier: one uses a block capacitor which short-circuits high frequency signals (33nF, resonance frequency at about 20-30 MHz); another one uses a ceramic feedthrough capacitor (4.99nF, resonance frequency at about 2 GHz), consisting of a hermetically sealed mechanism that connects the electronics inside the PM to the connection block outside [17]; the third one uses both.

To avoid any spurious interference from the extra electrical connection, the PM were placed inside an aluminium box. The output of the amplifier buffered by an instrumentation amplifier was connected to an acquisition board through BNC connectors and shielded cables. This configuration guaranteed that only the silicon connection head of the PM and the lead connectors were exposed to RF radiation. A standard catheter was connected to the PM and the catheter was immersed in a 0.9% saline solution in a plexiglass box. All the connections were shielded with aluminium foil.

The noise level was computed on-line by estimating the power spectral density of the signal at the output of the sensing amplifier. The spectral estimation was obtained by averaged periodogram o without windowing or zero-padding. Fifty spectra of PM signal tracks between two consecutive PM spikes were averaged. In order to have the largest possible number of samples between two consecutive spikes, the PM frequency stimulation was set to the lowest value (30 bpm).

All PM were programmed with the same parameters. For each PM, the output of the sensing amplifier was monitored under 4 conditions: no signal delivered to the catheter and no electromagnetic field applied (baseline noise); white noise signal delivered to the catheter, in the presence and absence of non-modulated RF signals (at 900 and 1800 MHz); no signal delivered to the catheter and exposure to GSM signals (at 900 and 1800 MHz). Details on the experimental setup can be found in [17].

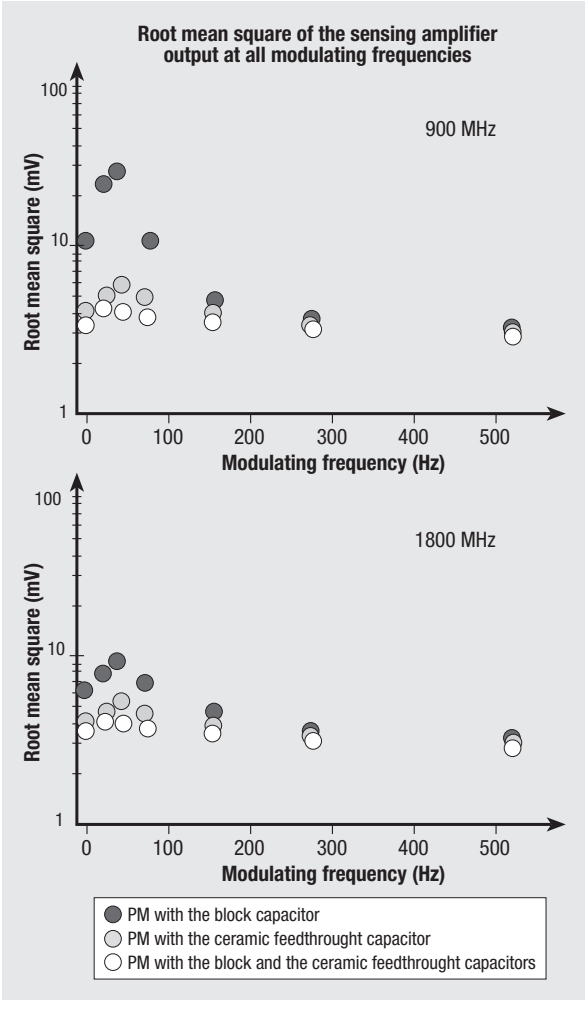

Fig. 2 | *Root mean square at the output of the sensing amplifier in mV for the 3 PM for exposure to all the modulating signals at 900 and 1800 MHz.*

We found that the exposure to RF signals does not alter the response of the PM sensing amplifier: the root mean square of the baseline noise (no signal delivered to the catheter and no electromagnetic field applied) at the output of the PM sensing amplifier was 3.99 mV for the PM with the block capacitor only, 4.04 mV for the PM with the ceramic feedthrough capacitor, and 3.45 mV for the PM having both capacitors. The hypothesis that the saturation and/or non-linear operation of the PM sensing amplifier could be responsible for EMI phenomena does not appear to be consistent with our findings.

The radiated RF fields (non-modulated, 900 MHz and 1800 MHz) did not alter the root mean square of the output of the sensing amplifier of any of the PMs when a white noise was applied to the chloride-silver square plates of the plexiglas box that hosted the catheter.

The spectral density of the output of the sensing amplifier for the PM equipped with the block capacitor only always shows a clear spectral peak at the frequency of the amplitude modulated radiation, indicating an underlying demodulation effect. In order to compare the results of the three PM at the various modulation frequencies and carriers, we computed the total power from the raw spectral data. *Figure 1* shows the root mean square at the output of the sensing amplifier in mV for the 3 PM for exposure to all the modulating signals at 900 and 1800 MHz. Note that the PM equipped with the block capacitor and the ceramic feedthrough showed no effect at 1800 MHz and minimal demodulation phenomena at 900 MHz.

DISCUSSION

Ideally, every possible combination of cellular phone model and PM model should be *in vitro* tested to assess the type and degree of interference to be expected. The number of possible combinations, however, being the product of the number of PM models and the number of cellular phone models, is too large to make this challenge practicable. Instead, PM manufacturers should be encouraged to include appropriate filters in new pulse-generator designs. Specific changes in the design of PM, such as the inclusion of feed-through filters, may limit electromagnetic interference, as was seen in several studies [4, 12, 18, 19] and as has been demonstrated by our investigation [17].

When we exposed the PM equipped only with the block capacitor to modulated RF signals, demodulation products were present at the output of the sensing amplifier. This finding corroborates the hypothesis that the PM functioning can be affected by a RF signal through its modulating components, which may fall within the PM passband and reach the input of the comparator. Once the RF signal is inside the PM case, substrate mounted block capacitors do not succeed in short-circuiting such signal and it is somehow demodulated by PM internal non-linear circuit elements. The PM equipped with the ceramic feedthrough capacitor only showed demodulation products slightly higher than the baseline noise. When both capacitors are installed, the total spectral powers of the output of the sensing amplifier exposed to modulated RF signals are as low as the baseline noise. Thus, the combination of both filters provides an effective attenuation of RF signals, and prevents demodulation phenomena.

The GSM signal utilizes low-frequency RF digital modulation. When exposed to a base-station GSM signal, a 217 Hz component (used by European GSM) appeared at the output of the input stage of the PM equipped with only the block capacitor. We observed demodulation products also at lower frequencies (below 10 Hz), although no specific harmonic components appeared. PM equipped with the feedthrough capacitor did not show demodulation products. These findings demonstrate that RF carriers with digital modulations may originate low-frequency demodulation products in the PM if these carriers are not adequately attenuated by the PM RF filters. Such low-frequency components fall within the typical PM passband; they can be erroneously detected as heart electrical activity and may interfere with the normal PM functions. This finding is consistent with, and can explain, the higher sensitivity of PM to EMI from digital phones than from analog ones, as reported by our and other research groups.

Studies aimed at investigating the mechanisms causing EMI to PM could be useful to prevent EMI effects generated by the large number of electromagnetic sources a PM patient can interact with. Understanding of the path of the electromagnetic signal throughout the PM circuits could improve the PM filtering design.

Since, to date, most PM models have the possibility to record intracardiac electrograms, investigations aimed at understanding the interference mechanisms from inside the PM could be performed easily and on a larger number of cardiac implantable devices.

It is important to note that the likelihood of clinically important symptoms caused by cellular telephone interference with PM operation depends on several aspects: the characteristics of the telephone in terms of the power of the transmitted signals and the use of analogue or digital technology, the pacing mode and implant configuration, the orientation of the telephone respect to the PM electrodes and the patient's underlying heart rhythm. Indeed, PM-dependent patients are at greatest risk from the effects of EMI. However, the patients implanted with PM with inadequate filtering systems should be advised.

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Exposure of humans to electromagnetic fields. Standards and regulations

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Summary. Biological and health effects of electromagnetic fields (EMF) have been investigated for many years. Exposure standards have been developed internationally, that provide adequate protection against all known adverse effects of exposure to EMF. The guidelines developed by the International Commission on Non Ionizing Radiation Protection (ICNIRP) are widely recognized and have formed the basis for national regulations in several countries. The two-level structure, with basic restrictions and reference levels, allows the standards to be adapted to virtually any exposure condition, including complex situations at workplaces. However, concerns for hypothesized, but unproven, long-term effects of chronic exposure to low-level EMF have created a demand for precautionary measures beyond the standards for recognized, acute effects. Such measures, if deemed justified by social considerations, including public anxiety, should be separate from exposure standards, and adopted with special care to avoid undermining the credibility of science-based guidelines, and of health authorities.

Key words: electromagnetic fields, health protection, exposure guidelines, precautionary principle.

Riassunto *(L'esposizione umana ai campi elettromagnetici. Standard e normative)*. Gli effetti sulla salute dei campi elettromagnetici (EMF) sono stati oggetto di ricerche per molti anni. A livello internazionale sono stati sviluppati standard che forniscono una protezione adeguata contro tutti gli effetti avversi da esposizione a EMF noti. Le linee guida sviluppate dalla Commissione Internazionale per la Protezione dalle Radiazioni non Ionizzanti (ICNIRP) sono ampiamente conosciute ed hanno rappresentato la base per regolamenti nazionali in molti Paesi. La struttura a due livelli, con restrizioni base e livelli di riferimento, consente a questi standard di essere adattati virtualmente a ogni condizione di esposizione, incluse situazioni complesse sul posto di lavoro. Tuttavia, la preoccupazione per effetti di lungo periodo, ipotizzati ma non provati, dovuti a esposizione cronica a campi elettromagnetici di bassa intensità, ha creato una domanda di misure precauzionali oltre gli standard per gli effetti acuti accertati. Queste misure, anche se giustificabili da considerazioni di tipo sociale, ivi inclusa la preoccupazione dell'opinione pubblica, devono essere distinte dagli standard di esposizione, e adottate con estrema attenzione al fine di evitare di ledere la credibilità delle linee guida basate su dati scientifici e delle autorità sanitarie.

Parole chiave: campi elettromagnetici, protezione della salute, linee guida all'esposizione, principio cautelativo.

INTRODUCTION

With the rapid development of new technologies, exposure of both workers and the general population to electromagnetic fields (EMF) has enormously increased in recent years. At the same time, concern has been expressed for possible adverse effects of such exposures on human health. Consequently, in several countries national governments and health authorities have been urged to adopt measures to prevent, or to minimize, risks associated to EMF exposure.

Standards on protection against possible health effects of EMF have been developed and updated by various international and national bodies for several decades. Over the years, such standards have evolved from simple recommendations on exposure limits in a limited frequency range to a comprehensive and complex system of protection, covering a large part of the spectrum of non-optical EMF (in general, from 0 Hz to 300 GHz).

At the international level, guidelines for the safe exposure of workers and the general public have been issued by the International Commission on Non Ionizing Radiation Protection (ICNIRP) [1]. A wide consensus exists on these guidelines, that have formed the basis for national regulations in several countries. It should be mentioned however that internationally recognized standards have also been developed by other bodies, in particular the Institute of Electrical and Electronics Engineers in the USA (IEEE) and the National Radiological Protection Board in the UK (NRPB). In spite of few differences of some importance, such as the one- or

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two-tier (workers *vs* general public) structure, or the classification of the environments rather than of the exposed personnel, these standards show close similarities, and are based on the same approach and rationale as ICNIRP guidelines.

A common, basic feature is that all the above standards are firmly based on established science, and aim at protecting against all – and only – the adverse effects that have been clearly indicated by qualified research.

In recent years, however, a culture of precaution has progressively emerged, in all fields of environmental and health protection. Consequently, the demand has increased for policies that go beyond the prevention of established effects, taking in some consideration also partial or preliminary research findings, and health risks not definitely established. This has led to a broader perspective of health protection, in which other factors than scientific findings are taken into consideration, such as socioeconomic implications.

Different systems of protections have been developed, that may be alternative or complementary to one another. Prior to a discussion of the recommendations issued by ICNIRP for the specific case of EMF, a short discussion of these systems is appropriate. More details can be found in a paper that describes the general approach of ICNIRP to the development of exposure guidelines [2].

THE SYSTEMS OF PROTECTION

Different systems of protection are generally adopted for different situations, depending on the nature of the effects and the quality of scientific data. A schematic distinction can be made between:

- *health threshold based systems*, that are adequate when biological effects that might lead to health detriment have been established, and thresholds for such effects have been identified. The protection of physical health is provided through exposure limits (or dose limits, depending on the nature of the agent), in order to assure that exposures are below the thresholds. Such approach allows, in principle, the total prevention of the identified adverse effects;
- *optimization systems*, that may be appropriate in face of a known and accepted hazard, for which a threshold cannot be determined. This is typical of established effects that are stochastic in nature. The knowledge of the hazard includes the identification of a monotonic dose-response relationship, with health risk reducing to zero at zero exposure. Rather than preventing adverse effects, such systems aim at defining – in an objective way – the most acceptable level of risk, *i.e.* the best balance of costs and benefits of measures adopted to reduce the health detriment. A well-known example is the ALARA (as low as reasonably achievable) principle adopted in the area of ionizing radiation;
- *precautionary measures*, that may be adopted in case of uncertainty, *i.e.* to protect against hazards that have been suggested, but not established by scientific research. Most frequently, these measures are implemented – or invoked – in observance of the precautionary principle.

While the two latter systems require economical, social and political considerations to be taken into account, all the three must be based on solid and reliable scientific data. The starting point for the selection, the development, and the implementation of any protection system is therefore an in-depth analysis of the literature, and a scientific assessment of health risks.

SCIENTIFIC ASSESSMENT OF HEALTH EFFECTS

In the evaluation of biological and health effects carried out by ICNIRP, three steps can schematically be identified [2]:

- initially, each study is evaluated in terms of its relevance for the effect being considered, and the quality of methods used. Different weights may be assigned to the studies, depending on the extent to which they meet quality criteria regarding *e.g.,* the experimental techniques used, the assessment of exposure, the control of experimental conditions, possible biases and confounders, the replicability of the experiments and the reproducibility of the results;
- as a second step, all information relevant for each effect is evaluated. This review is normally carried out separately for epidemiological investigations, human laboratory tests, animal studies, and *in vitro* research;
- finally, the outcomes of the above steps are combined in an overall evaluation, taking the consistency of data in proper consideration. ICNIRP recognizes that this process involves some judgements; however, collective participation minimizes bias due to personal attitudes.

Such process of scientific review is at the same time comprehensive and selective. While the totality of science – and not just the most recent research – is taken into consideration, only papers that meet commonly accepted quality standards are retained. Publication in peer reviewed journals is the basic criterion, but further selection may be operated based on crucial aspects such as the quality of the exposure assessment.

In this analysis, a fundamental distinction is made between *biological effects* and *health effects*. EMF exposure may in fact result in different biological responses, with different consequences. Some biological effects have no known consequences, either adverse or beneficial, others may result in diseases, and other still have beneficial health consequences.

When the overall evaluation allows the identification of an effect that is causally related to the exposure, the effect becomes *established*. Leading criteria in the identification of effects are the reproducibility of findings, and the consistency across studies of dif-

ferent nature (*e.g.*, data from laboratory research *in vitro* and *in vivo* that may give biological plausibility to a causal interpretation of statistical correlations indicated by epidemiology).

In general, biological effects without any identified adverse health consequences do not form a basis for limiting exposure. However, effects that might plausibly result in health hazards can be taken into account in the definition of basic restrictions.

The established effects shall be quantitatively related to the exposure. However, the entity of a given effect not only depends on the external field level, but also on the coupling of the field with the exposed body, or selected body organs. The quantitative relationship by which the external exposure affects a biologically effective parameter of the target tissue is unique to a single exposure condition. Therefore, effects are better described by quantities that reflect the efficacy by which the external exposure causes a certain biological effect. These are termed *biologically effective quantities*, or *dosimetric quantities*.

Different dosimetric quantities have been identified as appropriate for different interaction mechanisms and biological effects, and are listed in *Table 1*.

In general – but not always – these quantities are internal to the body and therefore cannot be directly measured. A correspondence shall therefore be established between biologically effective quantities and external fields, taking exposure conditions in due account. This is accomplished through theoretical and experimental modelling techniques that constitute what is called *dosimetry*, in analogy with toxicology and ionizing radiation.

By means of biologically effective quantities, established adverse effects can generally be ranked according to the exposure level at which each effect becomes relevant. The effect that is relevant at the lowest level of exposure is called the *critical effect*, and is the criterion for the definition of exposure limits. The limitation of exposure to levels below the threshold for the critical effect provides, *a fortiori*, protection against any other established adverse effect.

It should be noted that in this process the different sensitivities, and ability to tolerate EMF, of different groups of the population are taken into account. The critical effect is selected with special consideration to categories that might exhibit lower tolerance, including children, the elderly, and some chronically ill people. The guidelines are therefore adequate to protect all the population groups, to the extent to which the corresponding scientific knowledge is adequate.

INTERACTION MECHANISMS

As indicated in *Table 1*, different interaction mechanisms have been established depending on the nature of the field, and on the frequency. These mechanisms are discussed in detail in various scientific reviews, including WHO's Environmental Criteria Documents [3-5], and ICNIRP monographs [6].

Two basic mechanisms are relevant in the low- and the high-frequency region of the spectrum, respectively. Time-varying electric and magnetic fields of frequency up to about 10 MHz induce electric fields and currents inside the body. Such currents and fields

Table 1 | *Relevant mechanisms of interaction, adverse effects, biologically effective physical quantities and reference levels for different parts of the EMF spectrum*

EMF spectral region	Relevant mechanism of interaction	Adverse effect	Biologically effective physical quantity	External exposure, reference level
Time-varying electric fields (up to 10 MHz)	Surface electric charges	Annoyance from surface effects, electric shock and burn	External electric field strength	Electric field strength
	Induction of internal electric fields and currents	Stimulation of nerve and muscle cells; effects on nervous system functions	Tissue electric field strength or current density	Electric field strength
Time-varying magnetic fields (up to 10 MHz)	Induction of internal electric fields and currents	Stimulation of nerve and muscle cells; effects on nervous systems functions	Tissue electric field strength or current density	Magnetic flux density
Electromagnetic fields (100 kHz to 300 GHz)	Induction of internal electric fields and currents; absorption of energy within the body	Excessive heating, electric shock and burn	Specific energy absorption rate	Electric field strength; magnetic field strength; power density
	> 10 GHz: Surface absorption of energy	Excessive surface heating	Power density	Power density
	Pulses < 30 μs, 300 MHz to 3GHz, thermoacoustic wave propagation	Annoyance from microwave hearing effect	Specific energy absorption	Peak power density

Table 2 | *Basic restrictions for time varying electric and magnetic fields for frequencies up to 10 GHz*

Exposure characteristics	Frequency range	Current density for head and trunk ($mA\ m^{-2}$)(rms)	Whole-body average SAR ($W\ kg^{-1}$)	Localized SAR (head and trunk) ($W\ kg^{-1}$)	Localized SAR (limbs) ($W\ kg^{-1}$)
Occupational exposure	up to 1 Hz	40	—	—	—
	1-4 Hz	40/f	—	—	—
	4 Hz-1 kHz	10	—	—	—
	1-100 kHz	f/100	—	—	—
	100 kHz-10 MHz	f/100	0.4	10	20
	10 MHz-10 GHz	—	0.4	10	20
General public exposure	up to 1 Hz	8	—	—	—
	1-4 Hz	8/f	—	—	—
	4 Hz-1 kHz	2	—	—	—
	1-100 kHz	f/500	—	—	—
	100 kHz-10 MHz	f/500	0.08	2	4
	10 MHz-10 GHz	—	0.08	2	4

1. f is the frequency in hertz.

2. Because of electrical inhomogeneity of the body, current densities should be averaged over a cross-section of 1 cm^2 perpendicular to the current direction.

3. For frequencies up to 100 kHz, peak current density values can be obtained by multiplying the rms value by $\sqrt{2}$ (~1.414). For pulses of duration t_p the equivalent frequency to apply in the basic restrictions should be calculated as $f = 1/(2t_p)$.

4. For frequencies up to 100 kHz and for pulsed magnetic fields, the maximum current density associated with the pulses can be calculated from the riselfall times and the maximum rate of change of magnetic flux density. The induced current density can then be compared with the appropriate basic restriction.

5. All SAR values are to be averaged over any 6-minute period.

6. Localized SAR averaging mass is any 10 g of contiguous tissue; the maximum SAR so obtained should be the value used for the estimation of exposure.

7. For pulses of duration t_p the equivalent frequency to apply in the basic restrictions should be calculated as $f = 1/(2t_p)$. Additionally, for pulsed exposures, in the frequency range 0.3 to 10 GHz and for localized exposure of the head, in order to limit or avoid auditory effects caused by thermoelastic expansion, an additional basic restriction is recommended. This is that the SA should not exceed 10 mJ kg^{-1} for workers and 2 mJ kg^{-1} for the general public averaged over 10 g tissue.

cause stimulation of electrically excitable tissues, such as nerves and muscles. The appropriate dosimetric quantities for these phenomena are the induced current density and the internal electric field; while present basic restrictions recommended by ICNIRP are based on the first, it has the recently been suggested that the internally induced electric fields are more closely related to several biological effects.

At frequencies above 100 MHz, a different mechanism becomes increasingly important, namely the absorption of electromagnetic energy and its dissipation in tissues as heating. This absorption results in an increase of body temperature, either general or local. The associated biological effects are related to the temperature increase rather than to EMF *per se,* and for this reason are indicated as *thermal effects.* The appropriate biologically effective quantity is the specific absorption rate (SAR), measured in watts per kilogram (W/kg). However, at frequencies above 10 GHz, the energy absorption is limited to superficial body tissues, and the interaction is better represented by the power density of the electromagnetic wave impinging on the body (measured in watts per square meter).

In the frequency region between 100 kHz and 10 MHz, stimulation and thermal effects co-exist, with their relative importance gradually shifting from the former to the latter as the frequency increases.

In the radio frequency (RF) region, the efficacy of EMF coupling with the human body – and therefore SAR, varies with frequency, showing a typical resonance behaviour. The resonance frequency, where the absorption rate is maximum, basically depends on body size, and posture.

BASIC RESTRICTIONS AND REFERENCE LEVELS

A distinctive feature of the ICNIRP guidelines – as well as of other international standards – is the two-level structure. As already mentioned, the biological and health effects depend on several parameters that characterize exposure. *Basic restrictions* are defined in terms of the appropriate biologically effective quantities, and are set below the threshold for the appropriate critical effects. Due to practical difficulties in measuring or calculating some biologically effective quantities, from basic restrictions *reference levels* are derived, that are expressed in terms of a directly measurable parameter of the external exposure. The correspondence is established through dosimetric techniques, either experimental (based on physical phantoms) or computational (based on numerical models of the whole body or specific organs).

Such procedure makes the guidelines practical and flexible. While the basic restrictions are closely related to the biological mechanisms, the reference levels are easier to evaluate and to relate to the emission levels of different sources.

Table 3 | *Basic restrictions for power density in the frequency range 10-300 GHz*

Exposure characteristics	Power density (W m^{-2})
Occupational exposure	50
General public	10

1. Power densities are to be averaged over any 20 cm^2 of exposed area and any 68/f$^{1.05}$-minute period (where f is in GHz) to compensate for progressively shorter penetration depth as the frequency increases.

2. Spatial maximum power densities, averaged over 1 cm^2 should not exceed 20 times the values above.

The strategy is also conservative. The use of reference levels assures in fact compliance with the basic restrictions, since the relationships between them have been developed under worst-case hypotheses, *i.e.* for conditions of maximum coupling between the external fields and the exposed person. On the other hand, exceeding the reference levels does not necessarily imply that basic restrictions are exceeded; whether this occurs or not should be ascertained through a more detailed investigation.

Both basic restrictions and reference values are affected by uncertainties, due to the intrinsic variability of biological data, experimental errors, uncertainties in the extrapolation of animal data to humans, limitation in dosimetry, biases and confounders. Reduction factors are therefore conservatively introduced, whose magnitude varies depending on the degree of incertitude.

To avoid possible misunderstandings, it shall be clarified that reduction factors are not intended to compensate for gaps in knowledge. In effect, their use as a precautionary measure to account for uncertainty in science has been criticized as inappropriate by standard-setting bodies and health protection agencies. WHO, for example, notes that *"science-based exposure limits should not be undermined by the adoption of arbitrary cautionary approaches. That would occur, for example, if limit values were lowered to levels that bear no relationship to the established hazards or have inappropriate arbitrary adjustments to the limit values to account for the extent of scientific uncertainty"* [7].

Basic restrictions recommended by ICNIRP are listed in *Table 2* and *Table 3*, for frequencies below and above 10 GHz, respectively.

Reference levels for occupational exposure and for general public exposure are listed in *Table 4* and *Table 5*, respectively. The frequency behaviour reflects the different coupling efficiency at different frequencies.

INDIRECT EFFECTS

Besides direct action on biological tissues and physiological functions, two indirect coupling mechanisms of electromagnetic fields exist, that may have an adverse impact on human health.

If a contact occurs either between an individual electrically connected to ground and an ungrounded metal object that has been charged by the external fields, or between a charged individual and a ground-

Table 4 | *Reference levels for occupational exposure to time-varying electric and magnetic fields (unperturbed rms values)*

Frequency range	E-field strength (V m^{-1})	H-field strength (A m^{-1})	B-field (μT)	Equivalent plane wave power density S_{eq} (W m^{-2})
up to 1 Hz	—	1.63 x 10^5	2 x 105	—
1-8 Hz	20 000	1.63 x 105/f^2	1.63 x 105/f^2	—
8-25 Hz	20 000	2 x 104/f	2.5 x 104/f	—
0.025-0.82 kHz	500/f	20/f	25/f	—
0.82-65 kHz	610	24.4	30.7	—
0.065-1 MHz	610	1.6/f	2.0/f	—
1-10 MHz	610/f	1.6/f	2.0/f	—
10-400 MHz	61	0.16	0.2	10
400-2000 MHz	3f1/2	0.008f$^{1/2}$	0.01f$^{1/2}$	f/40
2-300 GHz	137	0.36	0.45	50

1. f as indicated in the frequency range column.

2. Provided that basic restrictions are met and adverse indirect effects can be excluded, field strength values can be exceeded.

3. For frequencies between 100 kHz and 10 GHz, S_{eq}, E^2, H^2, and B^2 are to be averaged over any 6-minute period.

4. For peak values at frequencies up to100 kHz see Table 2*, note* 3.

5. Between 100 kHz and 10 MHz, peak values for the field strengths are obtained by interpolation from the 1.5-fold peak at 100 kHz to the 32-fold peak at 10 MHz. For frequencies exceeding 10 MHz it is suggested that the peak equivalent plane wave power density, as averaged over the pulse width, does not exceed 1000 times the S_{eq} restrictions, or that the field strength does not exceed 32 times the field strength exposure levels given in the Table.

6. For frequencies exceeding 10 GHz, S_{eq}, E^2, H^2, and B^2 are to be averaged over any 68/f$^{1.05}$-minute period (f in GHz).

7. No E-field value is provided for frequencies <1 Hz, which are effectively static electric fields.

Table 5 | *Reference levels for general public exposure to time-varying electric and magnetic fields (unperturbed rms values)*

Frequency range	E-field strength ($V\ m^{-1}$)	H-field strength ($A\ m^{-1}$)	B-field (μT)	Equivalent plane wave power density S_{eq} ($W\ m^{-2}$)
up to 1 Hz	—	3.2 x 104	4 x 104	—
1-8 Hz	10 000	3.2 x 104/f^2	4 x 104/f^2	—
8-25 Hz	10 000	4000/f	5 000/f	—
0.025-0.8 kHz	250/f	4/f	5/f	—
0.8-3 kHz	250/f	5	6.25	—
3-150 kHz	87	5	6.25	—
0.15-1 MHz	87	0.73/f	0.92/f	—
1-10 MHz	87/f1/2	0.73/f	0.92/f	—
10-400 MHz	28	0.073	0.092	2
400-2000 MHz	1375/$f^{1/2}$	0.0037/$f^{1/2}$	0.0046/$f^{1/2}$	f/200
2-300 GHz	61	0.16	0.20	10

1. f as indicated in the frequency range column.

2. Provided that basic restrictions are met and adverse indirect effects can be excluded, field strength values can be exceeded.

3. For frequencies between 100 kHz and 10 GHz, S_{eq}, E^2, H^2, and B^2 are to be averaged over any 6-minute period.

4. For peak values at frequencies up to100 kHz see Table 2, *note* 3.

5. Between 100 kHz and 10 MHz, peak values for the field strengths are obtained by interpolation from the 1.5-fold peak at 100 kHz to the 32-fold peak at 10 MHz. For frequencies exceeding 10 MHz it is suggested that the peak equivalent plane wave power density, as averaged over the pulse width, does not exceed 1000 times the S_{eq} restrictions, or that the field strength does not exceed 32 times the field strength exposure levels given in the Table.

6. For frequencies exceeding 10 GHz, S_{eq}, E^2, H^2, and B^2 are to be averaged over any $68/f^{1.05}$-minute period (f in GHz).

7. No E-field value is provided for frequencies <1 Hz, which are effectively static electric fields.

ed metal object, a contact current flows through the body. The resulting biological response varies from perception to painful shocks and burns. Taking into account the different sensitivities of different population groups (men, women, and children), and conservatively assuming as the criterion the lowest perception thresholds, reference levels on contact currents have also been provided. The reader is referred to the text of guidelines for further details.

The second indirect coupling mechanism is related to electromagnetic interference with medical devices worn by, or implanted in, an individual. Such interference, with possible malfunctioning of the devices, may occur at exposure levels lower that the recommended guidelines. However, ICNIRP considers that this issues can be best dealt with by technical bodies that are responsible for electromagnetic compatibility standards.

PRECAUTIONARY POLICIES

While only acute effects have been scientifically established, the possibility of long-term adverse consequences of chronic exposure below the thresholds for acute effects cannot be dismissed, and extremely low frequency (ELF) magnetic fields have been classified by IARC as "possibly carcinogenic to humans" (group 2B) [8]. In order to prevent or reduce these risks, though hypothetical, some national governments or local authorities have adopted measures that replace or complement science-based exposure limits. In general, the *precautionary principle* is invoked to this purpose.

In spite of its popularity, the principle is not well defined, and is variously interpreted. In addition, a possible conflict between science and the principle has been outlined [9]. An important clarification was provided by the European Commission (EC) [10]; it stressed that a basic condition for the principle to be invoked is that a potentially serious health hazard had been identified and scientifically evaluated. Therefore, science should be the fundamental basis – though not the unique one – for the adoption of precautionary policies.

Other criteria are indicated by EC for the correct application of the principle. The selected measures should be *inter alia*:

- tailored to the chosen level of protection;
- non-discriminatory, *i.e.,* comparable situations should be treated in a similar way;
- comparable to measures already taken in equivalent areas;
- based on an examination of the potential benefits and costs;
- provisional, *i.e.,* subject to review in the light of new scientific data.

Examining in this respect the case of EMF, WHO considers that *"[…] a cautionary policy for EMF should be adopted only with great care and deliberation. The requirements for such a policy as outlined by the European Commission do not appear to be met in the case of either power or radio frequency EMF"* [5].

This position is consistent with the evaluation of both IARC and ICNIRP. The classification of ELF

magnetic fields in the Group 2B is in fact based on a limited evidence of carcinogenicity in humans, and an inadequate evidence of carcinogenicity in animals. ICNIRP, on its side, considers that, in the absence of support from laboratory studies, the epidemiological data are insufficient to allow an exposure guideline to be established for these fields.

The evidence of carcinogenicity is even less convincing for RF EMF: though limited, epidemiological studies are largely negative, as are most of laboratory studies. In the scientific rationale of its guidelines of 1998, ICNIRP noted that the studies available at the date had yielded no convincing evidence that typical exposure levels led to adverse reproductive outcomes or to an increased cancer risk in exposed individuals. The epidemiological findings appeared consistent with the results of laboratory research on cellular and animal models, that showed neither teratogenic nor carcinogenic effects of exposure to athermal levels of RF EMF.

Findings published after the guidelines were issued did not change the overall pattern. Thus, there seems not to be a need to modify the present guidelines to account for the risk of cancer or other long-term adverse effects not scientifically established.

The inapplicability of the precautionary principle does not necessarily mean disregarding any precaution. On the contrary, WHO recommends that in the presence of scientific incertitude (that is unavoidable in principle) any political decision be taken in the context of a *precautionary framework*, where besides scientific evidence of risk, also social and economic factors are taken into account, including public sensitivities.

In this context, health risks of EMF should be put in an appropriate perspective, comparing them with other risks. It is worth to note, for example, that EMF have received only limited attention in comprehensive reviews on cancer and on children's health, carried out by IARC [11] and by the European Regional Office of WHO [12], respectively.

FUTURE DEVELOPMENTS OF THE ICNIRP GUIDELINES

The development of safety guidelines is a dynamic process, that evolves with the progress of knowledge. ICNIRP continuously checks the validity of its recommendations by monitoring both the advancement of research on biological and health effects of electromagnetic fields, and the development of emerging technologies that may involve the introduction of new sources and new modalities of exposure. While there seems not to be an urgent need to change basic restrictions and reference levels, an update of the scientific rationale that includes the most recent research findings is appropriate. ICNIRP is in the process of revising its recommendations for the whole frequency range covered by the present guidelines, *i.e.* from 0 Hz to 300 GHz. Such activity is coordinated with other international bodies, in particular with WHO and IARC. The three organizations have established tight links, in order to avoid redundant activities and to create the most effective synergies.

A specific sequence of actions has been established in order to provide to authorities, workers, and the public the best possible advice on all health issues related to EMF. On commitment by WHO, ICNIRP carries out a comprehensive review of the scientific literature concerning exposure assessment and dosimetry, biological effects, and epidemiology. On its side, IARC evaluates the available data regarding a possible role of EMF in the development of cancer, with the final goal of classifying the different types of electromagnetic fields on the basis of their carcinogenic power. Using the conclusions of ICNIRP and IARC as input, WHO globally evaluates any possible health risk of EMF exposure, and publishes its review as an Environmental Health Criteria (EHC) document. Finally, ICNIRP revises and updates its guidelines as appropriate.

For low-frequency fields (up to 100 kHz), the IARC monograph was published in 2002 [8], and ICNIRP published its review in 2003 [6]. The EHC document, presently in press, is available online at WHO's website [13]. A revision of ICNIRP guidelines based on this risk assessment is in progress.

The process is necessarily longer for RF fields (100 kHz-300 GHz). An international epidemiological study on mobile phone users is in fact in progress, that is expected to provide important information on a possible association between RF fields and cancer, in particular brain tumours. Only after completion of this study, IARC will convene the expert group for the classification of RF fields with respect to human carcinogenicity. Further steps of risk assessment by WHO and revision of guidelines by ICNIRP will follow, and the whole process will probably take a few years.

CONCLUSIONS

Comprehensive systems of protection have been developed at the international level, and adopted in a large number of countries. They are conservative, flexible, and based on solid science, so providing adequate protection against all known health effects of EMF.

In response to the concerns of the public, and given some uncertainties that still exist in some areas of scientific knowledge, consideration of precautionary measures could be warranted in some cases. A basic requirement is that these measures are adopted in such a way as not to undermine the credibility of the international standards, and consequently the trust in health authorities and in science.

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Electromagnetic immunity of medical devices: the European regulatory framework

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Summary. In this paper, the international standards and the European Regulation on medical devices are discussed, with attention to the collateral standards and the particular standards concerning the electromagnetic compatibility and immunity of medical devices. In addition, recommended guidelines to be used by health care organizations to assess the immunity of medical devices to radiated electromagnetic fields from portable radio frequency transmitters are indicated and discussed. As far as electromagnetic immunity of active implantable devices are concerned, the difference between United States and European Union (EU) regulatory frameworks is presented (standard ANSI/AAMI PC69:2000 for US and EN45502-1 framework in EU). Finally, some considerations on how to address the risk assessment of workers with implanted devices are discussed.

Key words: medical devices, equipment and supplies, directives, reference standards, electromagnetic compatibility.

Riassunto *(Immunità elettromagnetica dei dispositivi medici: il quadro di riferimento normativo europeo)*. In questo lavoro vengono discussi gli standard internazionali e la regolamentazione europea sui dispositivi medici, con particolare attenzione agli standard collaterali e particolari riguardanti la compatibilità e l'immunità elettromagnetica dei dispositivi medici. Inoltre, sono indicate e discusse le linee guida per le organizzazioni ospedaliere al fine di valutare l'immunità dei dispositivi medici ai campi elettromagnetici irradiati da trasmettitori portatili a radio frequenze. Per quanto riguarda l'immunità elettromagnetica dispositivi medici impiantabili attivi, si riporta la differenza tra il quadro normativo in vigore in Europa e negli Stati Uniti (standard ANSI/AAMI PC69:2000 per gli USA e EN45502-1 nella Comunità Europea). Infine sono riportate alcune considerazioni su come affrontare la determinazione del rischio di lavoratori con dispositivi impiantabili.

Parole chiave: dispositivi medici, apparecchiature e forniture, direttive, standard di riferimento, compatibilità elettromagnetica.

INTRODUCTION

Medical devices are regulated by the EC directives, which define the "essential requirements", *e.g.*, protection of health and safety that goods must meet when they are placed on the market. The European standards bodies have the task of drawing up the corresponding technical specifications meeting the essential requirements of the directives, compliance with which will provide a presumption of conformity with the essential requirements. Such specifications are referred to as "harmonised standards". There are three directives for medical devices [1-3]: the active implantable medical device (AIMD) directive - 90/385/EEC; the medical device directive (MDD) - 93/42/EEC; the *in vitro* diagnostic device directive (IVD) - 98/79/EC [1-3].

In particular, electromagnetic immunity is an essential requirements for both not implantable and implantable medical devices, as it is clearly stated in the EC directives: *"Devices must be designed and manufactured in such a way as to remove or minimize as far as is possible: risks connected with reasonably foreseeable environmental conditions, such as magnetic fields, external electrical influences, electrostatic discharge, pressure, temperature or variations in pressure and acceleration; the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given"*.

Problems with electromagnetic compatibility (EMC) of medical devices have been known for some time in hospitals. Research groups, manufacturers, and governmental and non-governmental agencies have reported incidents related to electromagnetic interference (EMI) to medical devices. Some of them had life-threatening consequences, others could have had, others can be considered just a nuisance. From 1979 to 1993 the Food and Drug Administration received more than one hundred reports related to EMI. These reports prompted the need for an increased attention to medical device EMC by users, manufactures, and standard organizations.

There are several motivations behind the increasing researches and efforts in this field:

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- deaths and severe injuries have occurred due to EMI on life-supporting medical devices;
- the ambient electromagnetic environment continues to intensify (*e.g.*; mobile phones, wireless local area networks, paging system);
- use of higher carrier frequencies the medical devices have not been tested for;
- increase in electronic sensors, actuators, and microprocessors based medical devices (*e.g.*, ventilators and infusion pumps);
- increased number of patients with electrical active implanted devices (pacemaker and cardioverters/defibrillators);
- widespread of new EM sources such as anti-theft systems and metal detectors, due to the increased need for security in public areas and buildings.

Most of the reported incidents before 1993 involved EMI originated from sources such as electrosurgical units, other medical devices and power line interferences. In the report of Silberberg, 3% of the reports involved mobile phones and 6% hand-held transceivers [4]. It should be observed that in 1993 the usage of mobile phones was much less prevalent than today.

The large number of different medical devices, the peculiarity of some of them (*e.g.*, implantable *vs* non-implantable or diagnostic *vs* therapeutic), and the gravity of the potential consequences in case of EMI make difficult to regulate this matter in a unique way. The wide number of potential sources of interference and their associated mechanism (*e.g.*, conducted vs radiated) make the problem even more complex. These differences are also reflected in the international standards on EMC for medical devices. According to these standards, three groups of devices may be considered:

- electrical active implantable devices (*e.g.*, pacemakers, implanted defibrillators, nerve stimulators);
- life-support devices (*e.g.*, ventilators, external defibrillators, electrosurgical units, infusion pumps, monitors);
- non life-support devices (*e.g.*, ECG, EEG, ultrasound scanner, MRI, CT-SCAN).

The topic of EMI between mobile phones and pacemakers (PM) and implantable defibrillators (ICD) has raised much interest among physicians since 1995, when several research data were reported on the adverse effects of electromagnetic fields (EMF) radiated from mobile phones on implantable PM [5-12]. Later on, studies were extended to ICD [13] and to the mechanisms involved and the solution to be adopted [14, 15] More recently, other sources of interference such as electronic surveillance systems and metal detectors have been investigated [16].

In the following the international standards and the European Regulation on medical devices and implantable devices will be discussed (*Table 1* and *Table 2*). At international level, such standards are issued by the International Electrotechnical Commission (IEC) and/or by the the European Committee for Electrotechnical Standardization (CENELEC).

The IEC is the international standards and conformity assessment body for all fields of electrotechnology, including electromagnetic compatibility and immunity. Each National Committee of the IEC handles the participation of experts from its country. Norms and standards issued by the International Electrotechnical Commission are easily recognized by the prefix IEC followed by a number indicating the particular field.

In the European Union (EU), CENELEC is preposed to issue harmonized standards. These standards are named using the EN prefix, followed by a number indicating the particular field.

To avoid duplication of efforts, speed up standards preparation and ensure the best use of the resources available and particularly of experts' time, a joint working agreement exists between IEC and CENELEC (Dresden Agreement, 1996), covering nearly 30 IEC National Committees. If the results of parallel voting are positive in both the IEC and CENELEC, the IEC will publish the international standard, while the CENELEC Technical Board will ratify the European standard. In this case the standard will bear both IEC and EN prefixes.

The typical structure of IEC/EN standards comprehends a "parent" standard which establishes the "default" set of requirements in the particular field. There are 2 types of "sibling" standards related to the "parent": the "collateral standards" and the "particular standards".

A collateral standard contains requirements that are an addition to the parent. Collaterals are referred to as "dash-one" standards and are numbered IEC/EN AABBB-1-X. Collateral standards cover topics

Table 1 | *International standards and European directives related to electromagnetic compatibility and immunity of non-implantable medical devices*

MDD 93/42: Medical device directive	European Union directive
IEC EN 60601-1-2 Medical electrical equipment. Part 1: General requirements for safety 2. Collateral standard: electromagnetic compatibility - requirements and tests	Harmonized standard
EN ISO 14971:2004 Application of risk management to medical devices [27]	Harmonized standard
ANSI C63.18-1997 Recommended practice for an on-site, ad hoc test method for estimating radiated electromagnetic immunity of medical devices to specific radiofrequency transmitters	Guidelines

Table 2 | *International standards and European directives related to electromagnetic compatibility and immunity of implantable medical devices*

AIMD 90/385 Active implantable medical device directive	European Union directive
DIRECTIVE 2004/40/EC Minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (electromagnetic fields)	European Union directive
Council recommendation 1999/519/EC of 12 July 1999 on the limitation of exposure of the general public to electromagnetic fields (0 Hz to 300 GHz) [28]	Recommendation
EN 45502-1:1997 CEN/CLC/JWG AIMD Active implantable medical devices. Part 1: General requirements for safety, marking and information to be provided by the manufacturer	Harmonized standard
EN 45502-2-1:2003 CEN/CLC/JWG AIMD Active implantable medical devices. Part 2-1: Particular requirements for active implantable medical devices intended to treat bradyarrhythmia (cardiac pacemakers) 6060 90/385/EEC	Harmonized standard
prEN 45502-2-2:2006 CEN/CLC/JWG AIMD Active implantable medical devices. Part 2-2: Particular requirements for active implantable medical devices intended to treat tachyarrhythmia (includes implantable defibrillators) 5020 90/385/EEC	Harmonized standard
prEN 45502-2-3:2006 CEN/CLC/JWG AIMD Active implantable medical devices. Part 2-3: Particular requirements for cochlear implant systems 4020 90/385/EEC	Harmonized standard
ANSI/AAMI PC69:2000 Active implantable medical devices - Electromagnetic compatibility - EMC test protocols for implantable cardiac pacemakers and implantable cardioverter defibrillators	Guideline
EN ISO 14971:2004 Application of risk management to medical devices	Harmonized standard

applicable to all equipments. They may be published separately due to the unique nature of the topic, like EMC, or may simply be an issue that was not considered or not complete when the parent was last revised. As the parent is revised, existing collaterals are occasionally absorbed into the parent.

The "particular" standard contains requirements that are exceptions to both the parent and the collateral standards. Particular standards are written for specific types of devices. Particulars are referred to as "dash-two" standards and are numbered IEC/EN AABBB-2-X.

THE IEC EN 60601 MEDICAL ELECTRICAL EQUIPMENT SAFETY STANDARDS: PARENTS, COLLATERALS AND PARTICULARS

The IEC EN 60601-1: Medical electrical equipment. Part 1: general requirements for safety [17] (parent standard) establishes general safety requirements for all aspects of medical devices from light boxes to beds to high-end diagnostic equipment like ultrasound or magnetic resonance (MR). It includes test requirements, documentation, protection from electrical hazards, protection from mechanical hazards, protection against excessive or unwanted radiation, protection against temperature, fire prevention, ingress of liquids, disinfection, biocompatibility etc. At present there are 8 collateral standards including medical systems, programmable systems, EMC, alarms etc. As the parent is revised, existing collaterals are occasionally absorbed into the parent (IEC EN 60601-1, *Figure 1*).

The topics relevant to EMC are covered in the collateral standard IEC EN 60601-1-2: Medical electrical equipment. Part 1: general requirements for safety - 2. Collateral standard: electromagnetic compatibility - Requirements and tests [18].

Within the IEC EN 60601 framework, particular standards are written for specific types of devices such as X-ray, MR, computed tomography (CT) and the like. Particulars are referred to as "dash-two" standards and are numbered IEC 60601-2-X. At present, there are more than 50 particular standards. Particular standards identify changes to the parent standards and any applicable collateral standard, which are unique to that particular technology. In the case of EMC, a particular standard may increase the required immunity.

EMC FOR MEDICAL ELECTRICAL DEVICES: IEC EN 60601-1-2

Several standards worldwide pertain to the permissible levels of electromagnetic power that can be radiated by a medical device and to the level of immunity from EMI a device must demonstrate. As for electrical medical devices, the most comprehensive one is the IEC EN 60601-1-2. Medical electrical equipment. Part 1: general requirements for safety - collateral standard: electromagnetic compatibility - requirements and tests. The IEC EN 60601-1-2 is a collateral standard of the major safety standard for medical electrical equipment (IEC EN 60601-1, *Figure 1*).

As mentioned above, as far as the EMC immunity level are concerned, the up-to-date revision of the

IEC EN 60601-1-2:2003 distinguishes between life-support and non life-support medical device. In addition, EMC of active implantable devices is regulated by different norms (*e.g.*, ANSI PC69 in the US [19] and EN 45502-1 [20], in the EU).

The IEC EN 60601-1-2 standard specifies test limits for emissions, immunity, electrostatic discharge (ESD), radiated radio frequency (RF) EMF bursts, and surges. As for radiated RF EMF, the first version of this collateral standard required a minimum immunity of 3 V/m, over a frequency range of 26 MHz to 1 GHz. This standard has been updated (2nd edition, 2001). This second edition expands RF immunity requirements in three areas. First, the highest frequencies used are increased from 1.0 to 2.5 GHz. The second important change is the modulation of the signal to which the equipment is exposed: the first edition required the signal be amplitude modulated at 1000 Hz, while the second edition requires equipment that controls or monitors physiological parameters (*e.g.*, heart rate) be tested with signals modulated at 2 Hz (closer to the frequencies of such biological parameters). Equipment that does not fall into this category is tested at a modulation frequency of 1000 Hz. The first edition did not specify the modulation level; however, the new standard sets it at 80%. Finally, life-support equipment, such as ventilators or infusion pumps, must now be tested for immunity to RF at a field strength of 10 V/m; all other equipment is still tested at 3 V/m.

Compliance with the requirements of the norms is confirmed if the device performs as intended, irrespective of the interfering signals. For those devices involving measurements of low level physiological signals, compliance level can be lower than the IEC EN 60601-1-2 test level. If this is the case, the manufacturer is required to disclose (in the instructions for use) the levels at which the device meets the performance requirements of this standard and to specify the electromagnetic characteristics of the environment in which the device will perform as intended.

In addition the norm provides formulas to calculate the recommended separation distance from portable and mobile RF communications equipment, given the compliance level of the equipment and the rated maximum output power of RF transmitter. *Table 3* summarizes the RF requirements: conducted RF, radiated RF, compliance levels and separation distances (calculated assuming far-field conditions).

Testing the immunity of medical devices as described in the EN 60601-1-2 requires specialized facilities, extensive knowledge on electromagnetics and expensive instrumentation (*e.g.*, anechoic chambers). The test set-up for radiated fields is described in the EN 61000-4-3. It requires the following types of equipment: anechoic chamber, EMI filters, RF signal generators, power amplifiers, and transmitting and monitoring antennas.

This kind of testing is generally performed by the device manufacturers or by specialized companies. In

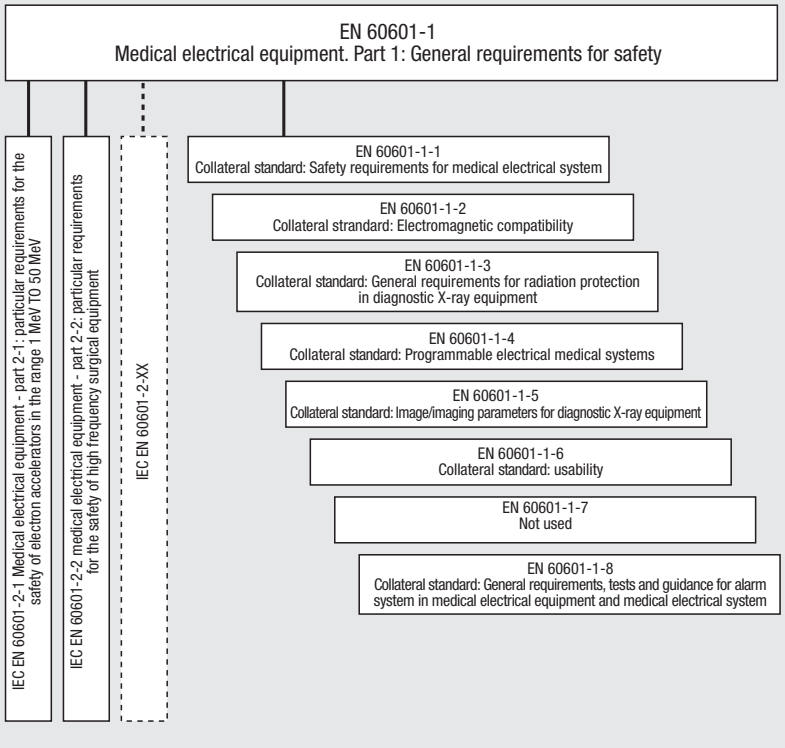

Fig. 1 | *The IEC-EN 60601 medical electrical equipment safety standards: parents, collaterals and particulars.*

Table 3 | *Life-supporting and not life-supporting devices: immunity tests and levels, in accordance with the IEC EN 60601-1-2:2003*

Immunity test	Life-supporting device			Not life-supporting device		
	IEC EN 60601-1-2 test level	Compliance level	Recommended separation distance	IEC EN 60601-1-2 test level	Compliance level	Recommended separation distance
Conducted RF (150 kHz – 80 MHz)	3 V (rms) (outside ISM band)	V_1 (V)	$d = \frac{3.5}{V_1}\sqrt{P}$	3 V (rms)	V_3 (V)	$d = \frac{3.5}{V_3}\sqrt{P}$
	10 V (rms) (inside ISM band)	V_2 (V)	$d = \frac{12}{V_2}\sqrt{P}$			
Radiated RF (80 MHz – 2.5 GHz)	10 V/m	E_1 (V/m)	$d = \frac{12}{E_1}\sqrt{P}$ 80 MHz-800 MHz; $d = \frac{23}{E_1}\sqrt{P}$ 800 MHz-2.5G0Hz	3 V/m	E_2 (V/m)	$d = \frac{3.5}{E_2}\sqrt{P}$ 80 MHz-800 MHz; $d = \frac{7}{E_2}\sqrt{P}$ 800 MHz-2.5G0Hz

ISM: industrial, scientific and medical bands.

addition it is worth noting that, in the evaluation of EM immunity, devices are exposed to far-fields: such testing may thus not be representative of particular EM interference as those arising from mobile emitters at close distances (near field). In the far-field (distance greater than several wavelengths of the transmitter carrier frequency) and for typical antennas, the field strength varies proportional to the inverse of the distance from the transmitter *(Figure 2)*. Note that for distances lower than 1 meter, field strength can exceed the immunity level indicated by the norm. In addition, the typical exposure from mobile emitters hardly matches the conditions of far-field.

The above considerations are the basis for the developments of guidelines and standards for electromagnetic immunity of medical devices, to be used by health care organizations. An example of such guidelines is the America National Standard Institute (ANSI) publication entitled *Recommended practice for an on-site,* ad hoc *test method for estimating radiated electromagnetic immunity of medical devices to specific radio-frequency transmitters* (C63.18) [21].

GUIDELINES FOR *AD HOC* TESTING IN HEALTH FACILITIES: ANSI C63.18-1997

The ANSI C63.18-1997 [21] recommended practice was developed in response to a need expressed by clinical and biomedical engineers for a technical guide to aid them in assessing the immunity of medical devices to radiated EMF from portable RF transmitters. The test modality suggested in this document differs from that described in the IEC EN 60601-1-2. If anechoic chamber is not available, medical devices can be tested in a proper dimensioned clear area. RF transmitters can be selected among commercial

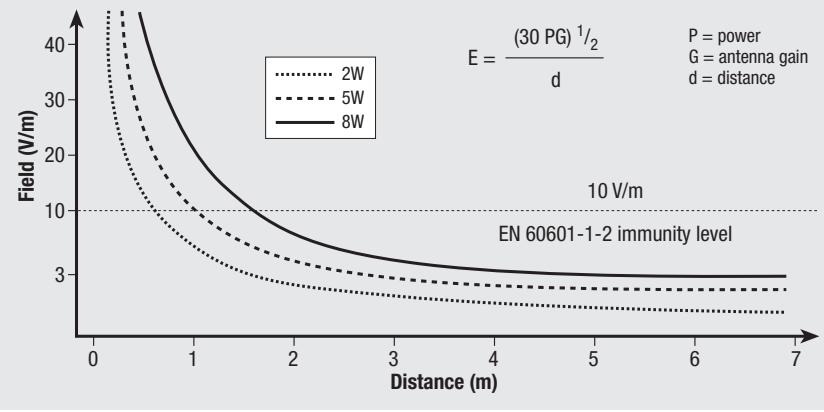

Fig. 2 | *Electric field (E [V/m]) as a function of distance (d [m]) generated by an antenna having gain G = 1.64, with emitting power P[W] of 2 W, 5 W and 8 W (according to the reported formula). The IEC EN 60601-1-2 immunity level for life supporting equipments of 10 V/m is also indicated (gray line).*

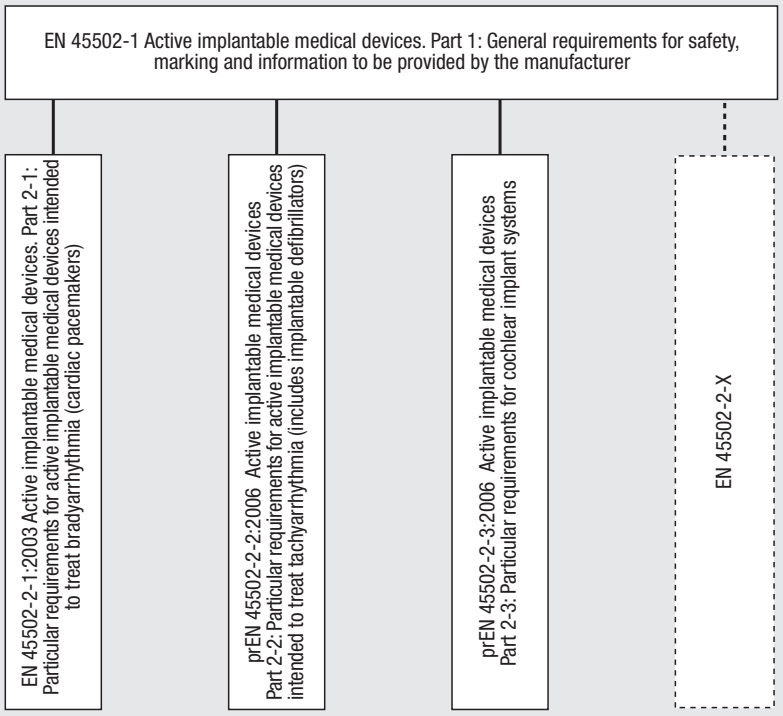

Fig. 3 | *The EN 45502 active implantable medical devices standards.*

equipment used in the health facilities. Care should be paid to set the transmitters to their maximum output power.

Tests are carried out during normal operation of the transmitter (*e.g.*, making and receiving calls) located at an initial distance which would expose the medical device to fields strengths of approximately 3 to 7 V/m. During the test transmitter is moved progressively closer to the medical device up to a minimum recommended test distance, which would expose the medical device to no more than approximately 22 V/m.

As a matter of fact, this guideline complements the 60601-1-2 by exploring EM immunity of medical devices at distances shorter than the recommended separation distance indicated by the 60601-1-2. As far as mobile transmitters are concerned, this approach accounts for the actual situation of RF transmitters frequently used in the vicinity of medical devices. It should be also noted that this standard was designed assuming an immunity level of 3 V/m, thus not taking into account the higher immunity level recommended for the life-supporting medical devices, which was introduced after ANSI C63.18 publication.

STANDARDS ON ELECTROMAGNETIC COMPATIBILITY OF IMPLANTABLE DEVICES

The standards addressing the electromagnetic immunity of active implantable devices differs between US and EC.

In the US, active implantable device should comply with the ANSI/AAMI PC69:2000 [19], while in the EU active implantable devices should comply with the EN45502-1 [20], and its particular device-specific norms: EN45502-2-1 (for pacemakers) [22], prEN 45502-2-2:2006 (for defibrillators) [23], prEN 45502-2-3:2006 (for cochlear implants) [24] *(Figure 3)*. For frequency higher than 450 MHz, these vertical standards partially adopt the testing procedures of the ANSI/AAMI PC69:2000.

The EN 45502 family cover several topics related to the safety of active implantable devices, besides the electromagnetic compatibility. As far as this field is concerned, assessment of EMC includes tests on both conducted and radiated fields.

The tests of the European standards for implantable pacemakers and defibrillators EM immunity are summarised in *Table 4*. Compliance is achieved if the device at all times functions in its set mode irrespective of the application of the EM signal. For frequency up to 1 kHz, however, compliance is achieved even if there are sensitivity settings causing malfunctioning, provide that an appropriate warning is given in the accompanying documentation.

Immunity to radiated field requires compulsory testing up to 40 mW, and voluntary testing up to 8 W. The specified test requirement of a 40 mW emitted power ensures compatibility of implanted cardiac devices with handheld wireless and personal communication services phones when the transmitter is maintained a minimum of 15 cm from the implanted device, and it is consistent with the

Table 4 | *Implanted active cardiac devices: EMC tests with modulated electromagnetic fields. In accordance with EN45502-2-1:2005 and prEN45502-2-2:2006*

Frequency (carrier)	Test	Type of signal	Amplitude	
16.6 Hz – 150 kHz	Conducted	Square wave amplitude modulation	2 mV 2 mV*(f/1kHz)^2 6 mV*f/1kHz	for 16.6 Hz ≤ f ≤ f kHz for 1 kHz ≤ f ≤ 3kHz for 3 kHz ≤ f ≤ 150kHz
150 kHz – 10 MHz	Conducted	Sinusoidal amplitude modulation at 130 Hz	6 mV*f/1kHz 1V 1V*f/1MHz	for 150 kHz ≤ f ≤ 167 kHz for 167 kHz ≤ f ≤ 1 MHz for 1 MHz ≤ f ≤ 20 MHz
10 MHz – 450 MHz	Conducted	Sinusoidal amplitude modulation at 130 Hz	10 V	
450 MHz – 3 GHz	Radiated	AAMI PC69 (amplitude modulation)	40 mW*	

**voluntary testing at 8W in the frequency range 450 MHz ≤ f < 1000 MHz, and at 2W in the frequency range 1000 MHz ≤ f ≤ 3000 MHz.*

device labelling and patient guidance adopted by the producers. The voluntary testing level of 8 W are intended to ensure compatibility of implanted cardiac devices with handheld wireless phones that are operated without restrictions near the implantable device. In this standard, the test for the radiated fields can be skipped if the PM is equipped with a feed-through filter with an attenuation of at least 30 dB. The rationale behind this clause is that for PM it is known that this solution is effective for radiated EMI in this band.

Protection from exposure to weak and strong static magnetic fields and to varying magnetic fields which patients may encounter in the general public environment is addressed according to the test reported in *Table 5*. A major difference between the electromagnetic and the magnetic tests concerns the mechanism of coupling with the device: the major influence of EMF is through induced voltages and currents in the leads; magnetic fields could cause malfunctions due to direct effects on the internal circuitry of the device.

Scope of the 45502 family of standards is to standardize the testing procedures to be use by the manufacturers and notified bodies to assess the compliance to the applicable essential requirements. The essential requirements on EM immunity of implantable devices guarantees an high level of safety in several conditions, although, in a number of specific exposure conditions, interferences due to external EMF may occur. For example, the working environment is a typical condition which may require appropriate precautions and protective measures, as described in the next paragraph.

PROTECTION OF WORKERS BEARING ACTIVE IMPLANTABLE DEVICE

The European Directive 2004/40/EC deals with the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (EMF) [25].

The 2004/40/EC Directive sets exposure limits and action values which provide a high level of protection as regards the established health effects that may result from exposure to EMF. These limits come from the maximum occupational exposure limits of the ICNIRP guidelines [26], and are based on direct effects of EMF exposure to the human body. For the low frequency range the induced current density in the nervous system is the limiting factor whereas in the higher frequency area tissue heating by absorption has to be limited. Thus, adherence with these limits may not necessarily avoid interference problems with, or effects on the functioning of, implanted medical devices such as metallic prostheses, cardiac PM and defibrillators, cochlear implants and other implants; interference problems especially with PM may occur at levels below the action values. Therefore appropriate precautions and protec-

Table 5 | *Implanted active cardiac devices: EMC tests with static and time-variable magnetic fields, in accordance with EN 45502-2-1:2005 and prEN 45502-2-2:2006*

Frequency	Type of signal	Amplitude		Compliance if:
DC	Constant	1 mT		Unaffected
DC	Constant	10 mT		Recovery within 5 s
1 kHz – 140 kHz	Sinusoidal	150 A/m 150 A/m*100 kHz/f	for 1 kHz ≤ f ≤ 100 kHz for 100 kHz ≤ f ≤ 140 kHz	Unaffected

tive measures are needed. The occupational exposure directive 2004/40/EC in article 4.5 obliges the employer to investigate during the risk assessment process also indirect effects like interference with medical electronic equipment and devices (including cardiac PM and other implanted devices). To help the employer to carry out the risk assessment for workers with implanted devices, CENELEC gave mandate to technical committees to prepare harmonized standard to produce standardised simple mechanisms for assessing possible risks to implanted workers exposed to EMF.

CONCLUSIONS

Up to date the collateral standard IEC EN 60601-1-2 on EMC is the International standard to which the medical device manufacturers (eventually through specialized companies) should refer to provide the presumption of conformity with the essential requirement on EMC.

The ANSI C63.18-1997 recommended practice is instead a technical guide to be used by health care organizations to assess the immunity of medical devices to radiated EMF from portable RF transmitters.

The standards addressing the EM immunity of active implantable devices differs between US and EC. In the US, active implantable device should comply with the ANSI/AAMI PC69:2000, while in the EU active implantable devices should comply with the EN 45502-1, and its particular device-specific norms: EN 45502-2-1 (for PM), prEN45502-2-2:2006 (for defibrillators), prEN45502-2-3:2006 (for cochlear implants). For some frequencies (higher than 450 MHz), these particular standards partially adopt the testing procedures of the ANSI/AAMI PC69:2000. Particular attention should be paid for the risk assessment of workers with implanted devices, for which the CENELEC set technical committees to prepare standardised simple rules for assessing possible risks.

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Criteria and terms for certified suitability of organ donors: assumptions and operational strategies in Italy

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Summary. Limited access to scarce resources, such as organs for transplantation, has increasingly prompted the use of elderly donors, with a consequent growth of possible risk factors linked to their particular features. Acceptable organ quality must therefore be guaranteed, without exposing recipients to unacceptable risks. For this reason, a set of guidelines for assessing donor suitability has been drawn up. This document standardizes the operative steps in the donor evaluation process and provides precise instructions for center staff. A pool of experts is available round the clock to offer advice on doubtful clinical cases. Such measures have allowed more effective use of available donors for transplantation.

Key words: infectious risk, neoplastic risk, donor, recipient, transplantation.

Riassunto *(Criteri e modalità per la certificazione di idoneità del donatore di organi: presupposti e strategie operative in Italia)*. L'accesso a risorse inevitabilmente scarse, quali quelle degli organi per trapianto, ha spinto il sistema verso un esponenziale utilizzo di donatori anziani con un contestuale aumento dei possibili fattori di rischio legati alle peculiarità di questi soggetti. Si è quindi posto il problema di come garantire al ricevente una qualità accettabile dell'organo senza esporlo a rischi inaccettabili. Allo scopo sono state realizzate le linee guida per la valutazione di idoneità del donatore che, uniformando le modalità operative nel processo di valutazione, danno un preciso riferimento comportamentale agli operatori del sistema. A sostegno dell'iniziativa opera un pool di esperti reperibili ventiquattro ore su ventiquattro per i casi clinici di dubbia interpretazione. Tali misure hanno permesso un maggiore e migliore utilizzo dei donatori per trapianto.

Parole chiave: rischio infettivo, rischio neoplastico, donatore, ricevente, trapianto.

INTRODUCTION

The original patient pathology is clearly the most powerful and direct predictor of clinical outcome. The more serious the patient's clinical condition the higher the risk of a negative outcome. Moreover, the results of a cadaveric donor transplantation also depend on other factors linked to both donor and single organ features [1-5]. Inadequate donor procurement, the risk/benefit ratio in transplantation, the time needed for diagnosing and certifying death coupled with the necessity of shortening ischemia time for retrieved organs have a strong impact on terms and timing of suitability evaluation of the potential donor. Despite such limits and the fact that even a good clinical practice behaviour cannot eliminate the risk of transmission of infectious or neoplastic pathologies, any retrieved organ should have an acceptable quality and should not expose the recipient to unacceptable risks.

MATERIALS AND METHODS

In 2001 the Italian National Transplant Centre (Centro Nazionale Trapianti) set up a national commission of experts in order to lay down a reference document for all personnel involved in the evaluation process of potential organ donor. The Commission was formed by infectious disease experts, immunologists, clinical experts, surgeons, coordinators, anatomopathologists, medical examiners and oncologists. During the preparation phase, which lasted one year, the text underwent a series of changes and supplements resulting in a final version shared with the scientific community and approved by the Italian National Transplant Centre as technical annex (guidelines) to the Ministry Decree of August 2, 2002 [6].

These Guidelines focus on two main aspects:

- the definition of acceptable/unacceptable risks for donor suitability or single organ utilization;

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- the establishment of practical steps for the risk evaluation process.

The first aim was to identify the different risk levels and as a result five risk levels have been defined:
1. unacceptable risk;
2. increased but acceptable risk;
3. calculated risk;
4. not assessable risk;
5. standard risk.

Unacceptable risk. The donor classified under this category should be excluded from donation and no organ can be used for transplantation. HIV1 or 2 positive donors fall into this category as well as HbsAg and HDV contemporaneous seropositivity; current neoplastic conditions with the following exceptions: carcinoma *in situ*, basal cell carcinoma, cutaneous squamous cell carcinoma without metastases, carcinoma *in situ* of the cervix, carcinoma *in situ* of vocal cords, urotelial papillary carcinoma (T0 according to the TNM classification). Eventually systemic infections caused by agents for which treatments are not feasible and documented prior disease must also be considered as exclusion criteria.

Increased but acceptable risk includes cases for which use of organs is justified by urgency or by special clinical conditions of recipients. In these cases, although the evaluation process evinces the presence of pathogens or transmissible disease, organ utilization is allowed in the light of a risk benefit assessment, as in case of patients struck by fulminant hepatitis, or retransplants for liver primary non function or of patients who underwent hepatectomy for trauma with complete organ function loss. In all these cases, transplantation is the only chance of survival for the patient and therefore the use of an organ with increased risk of transmission of infectious or neoplastic disease is justified by the clinical urgency status of the recipient who receives adequate prophylactic therapy.

Calculated risk includes all cases where the presence of a specific pathogen or a serological status of the donor (HBsAg+, or anti-HCV+ or HbcAb+) is compatible with transplantation recipients with the same disease or serological status, independently from recipient's health conditions. Donors with meningitis who have been administered targeted antibiotic therapy for at least 24 hours and those bacteremia-affected who started targeted antibiotic therapy are included in this category of risk.

Not assessable risk includes cases for which the evaluation process does not allow an appropriate risk assessment for transmittable diseases for lack of one or more assessment elements (*e.g.* failure to collect an accurate medical history for lack of relatives, unavailability of microbiology data despite a well-grounded suspicion of infectious pathology). In such cases, tests and checks have to be performed in order to consider the donor as suitable and exclude those conditions that represent an absolute or relative contraindication to donation (biomolecular tests carried out by laboratory with adequate specialized skills for reducing the "window period" as much as possible, autopsy). If such exams give negative results, the donor can be considered as in the standard risk rated. If they cannot be performed, donor organs can only be used in case of emergency, after informed consent of the recipient.

Standard risk includes cases for which the evaluation process did not identify any risk factor for transmittable disease. It is the most frequent condition in the assessment of donors and grafts. It is commonly defined as standard risk since, in this field, *null risk* does not exist, and infectious or neoplastic pathologies can still be transmitted even if guidelines and good clinical practice are followed.

The second aim was to define and code the operational steps in the risk assessment process, stressing its multiphasic and multidisciplinary approach and that the evaluation of donor suitability has to be based on:
- medical history;
- physical examination;
- instrumental and laboratory tests (lab tests must be conducted on samples collected before procedures which required haemodilution);
- histological examination and/or post mortem examination on the basis of results of previous evaluation steps.

After having certified brain death, elements that have not yet been explored are further investigated.

Medical history must take in due account at least the following aspects: sexual behaviour; illicit drug abuse; pre-existing illnesses such as autoimmune, infectious, neoplastic or diseases with partially or completely unknown aetiology. If it is not possible to obtain a medical history, it is necessary to perform the tests required to exclude those conditions that represent an absolute or relative contraindication to donation (*e.g.* biomolecular viral serum tests for HIV, HCV, HBV), in order to consider a donor suitable (*i.e.* with a "standard risk"). If such tests are negative, donor can be considered as standard risk. If they cannot be performed donor organs can only be used in case of urgencies, after informed consent of the recipient. Should a previous neoplasia be evinced from medical history, accurate information has to be gathered whenever possible from the healthcare facility where pathology was diagnosed, with details about diagnosis date, histological test, administered therapy, subsequent controls and follow-up.

The donor evaluation process avails itself of biochemical testing through routine examinations and physical external examination with the aim of highlighting indicators of infectious or neoplastic transmittable disease. External physical examination should at least investigate the items listed in *Table 1*.

Table 1 | *Signs to be evaluated during external physical examination*

Cutaneous scars
Cutaneous or mucous pigmented lesions
Jaundice
Tattoo, for the risk of infections
Exanthemas (paediatric transplants)
Signs of illicit substance abuse
Palpation of thyroid, breasts, testicle, superficial lymphadenopaty
Digital rectal examination for donor aged more than 50 years old

If external physical examination gives rise to any suspicion about donor suitability, further specific laboratory or instrumental examinations are required and if necessary, the expert opinion of the National Transplant Centre could be required. The evaluation process is completed by examination in the operating theatre during retrieval, where possible previous suspicions are verified; inspection and palpation of thorax organs, including lymphonodes; abdominal organs inspection and palpation including kidneys after removal of the capsule of Gerota and the pararenal tissue and inspection of the convex kidney surface up to the hilus fatty tissue.

The guidelines also identify some special situations that concern two main aspects, neoplastic risk and infectious risk.

Concerning neoplastic risk, if, at the time of death, the potential donor has a neoplastic condition, he can be considered as a standard risk donor only if affected by carcinoma *in situ*, basal cell carcinoma, cutaneous squamous cell carcinoma without metastases, carcinoma *in situ* of the cervix, carcinoma *in situ* of vocal cords, urotelial papillary carcinoma (T0 according to the TNM classification)

The assessment of *standard risk* has also been extended to low grade prostate carcinoma, intraprostatic carcinomas (Gleason score ≤ 6), and such thyroid tumours as encapsulated papillary thyroid carcinoma and follicular carcinoma with incipient infiltrative aspects. For other tumors, when epidemiological studies indicate that tumor transmission risk is much lower than potential transplant benefit, the transplant centre can decide to use grafts after obtaining informed consent from the recipient in case of clinical emergencies. Relatively frequent cases, such as donors affected by low grade renal carcinoma (G 1-2 s Fuhrman) or prostate tumor of intermediate grade (Gleason score 7) are defined as *non standard* risk. In other exceptional situations the transplant centre can decide to use a life-saving organ even when other malignant neoplasias are detected, in agreement with the national second opinion expert for safety of neoplastic donors. A donor is always considered as unacceptable risk when leukemia/lymphoma, malignant melanoma, breast cancer, lung carcinoma is detected.

Table 2 | *Tumors of brain system at low grade (I or II according to WHO classification) judged suitable for the organs donation*

Glial neoplasms	Anaplastic astrocytoma (II) Pilocytic astrocytoma (I) Xantoastrocytoma pleomorphic (II) Subependymal giant cells astrocytoma (I) Oligodendroglioma (II) Oligoastrocytoma (II) Ependymoma (II) Myxo-papillary ependymoma (I) Subependymoma (I) Choroid plexus papillomas (I) Third ventricular chordoid glioma (II)
Neuronal and mixed neuronal-glial neoplasms	Gangliocytoma (I) Dysplastic Gangliocytoma of cerebellum Astrocytoma/desmoplastic infantile ganglioglioma (I) Neuroembryonal desmoplastic tumor (I) Ganglioglioma (I) Central neurocytoma (II) Liponeurocytoma of cerebellum (II)
Meningiomas	Meningiomas (meningothelial, fibrous, transitional, with psammoma bodies, angiomatous, microcistic, secretory, lymphoplasmacellular, metaplastic) (I) Atypical meningioma Clear cell meningioma Choroid meningioma
Miscellaneous	Craniopharyngiomas (I) Hemangioblastomas (not associated to the Von Hippel-Lindau Syndrome) (I) Acoustic Schwannomas (I) Pinealocytoma (II) Mature teratomas

Table 3 | *High grade brain tumors (III or IV). Subjects affected by one of these neoplasias must be considered as "donors at increased risk", so they have to be used only for patients in urgent clinical conditions*

Glial tumours	Anaplastic astrocytoma (III) Anaplastic Oligodendroglioma (III) Anaplastic oligoastrocytoma (III) Anaplastic Ependymoma (III) Choroid plexus tumor (III) Gliomatosis cerebri (III)

In general, the specific risk profile of a cancer defined as "at risk so low that it can be considered negligible" refer to biological features of cancer in conventional patients. In addition it is supported by the absence of cases in literature where the tumour was transmitted to transplanted subjects.

Central nervous system (CNS) tumours deserve a separate chapter. According to the last classification of brain cancers published by WHO in 2000, the grading (I, II, III, IV) refers to the level of malignancy. In particular, low grade tumours are those categorised as I and II group while high grade are those categorised as III and IV group. Data from literature show that the systemic dissemination of a brain tumour can follow a CNS diversion. This can happen in tumours of low grade as well as high grade [7-10]. For this reason, subjects affected by a CNS primitive brain tumour that underwent a ventricular-systemic diversion cannot become donors [11].

Table 4 | *Malignant intracranical tumors. Subjects affected by one of these neoplasias must be excluded as potential donors*

Glial tumors	Multiform Gliobastoma (IV)
Embryonal tumors	Pineoblastomas (IV) Medulloblastoma (IV) Primitive neuroectodermal supratentorial tumor (PNET) (IV) Atypica theratoid/rabdoid tumors (IV) Medulloepithelioma Ependymoblastoma
Tumors of germinal cells	Germinoma Embryonal tumors Tumor of the vitellin sac Choriocarcinoma Immature teratomas Teratomas with malignant trasformation
Other frequently metastatic tumors	Malignant meningiomas Hemangiopericytomas Meningeal sarcoma Chordomas Malignant lymphomas

Taking this into account, in the guidelines subjects with CNS grade I and II tumours are considered as donors *(Table 2)*. Tumours of CNS grade III and IV *(Table 3)* are considered as "increased risk" that is not standard and therefore can be used only under proven clinical emergency. Donors affected by brain tumours as listed in *Table 4* are finally excluded from donation.

As regards the detection of a potentially transmissible neoplastic disease and the donor medical history, organs are not useable for transplantation when:

1) less than 10 years have passed from the date of recovery. In this case only life-saving organs can be used for patients in emergency conditions or with specific medical situations;
2) the diagnosis was of breast cancer, melanoma, leukaemia; lymphoma, lung microcytoma.

As concerns infections, special attention has been devoted to the following cases: donor with HCV infection; donor with HBV infection (HBsAg positivity); donors with anticore IgG antibodies against B virus (HBcAb). In such cases the guidelines impose the adoption of the following procedures.

Organs from a donor with HCV infection should be used only in emergency situations and after having obtaining a signed informed consent from recipient.

Transplantation of organs from a donor positive for HCV antibodies to a recipient positive for idem is allowed, after informed consent, provided that the transplant execution be monitored and transplanted patients be followed up according to a common national protocol established by the National Transplant Centre. Data are recorded in a National Registry.

If a donor turns out to be HBsAg positive, transplantation is allowed in a HBsAg positive recipient, after informed consent, provided that the following conditions are met:

a) the donor has a negative HDV antigen, negative IgM anti HDV antibodies, negative IgG anti HDV antibodies or with a titre < 1:100 or below the significant level according to the assay used; the absence of IgM anti HDV does not exclude delta virus chronic infection;
b) the liver recipient is not co-infected by delta virus;
c) the patient follow-up can be monitored on the basis of a common national protocol established by the National Transplant Centre and to record data on a National Registry.

If the recipient is HBsAg negative, he has no anti-HBV antibodies or has a protective anti-HBsAg titre (≥ 10 mUI/ml), transplantation could be performed, after informed consent, provided that:

a) the donor has a negative HDV antigen, negative IgM anti HDV antibodies, negative IgG anti HDV antibodies or with a titre < 1:100 or below the significant level according to the used assay;

b) the patient follow-up can be monitored on the basis of a common national protocol established by the National Transplant Centre and to record data on a National Registry.

Donors with anti-HBcAg positivity. The liver of these donors has an high risk of HBV transmission to the recipient (approximately 50%) [12, 13]. Hence it is necessary to provide an informed consent and to monitor the recipient over time according to a common national protocol established by the National Transplant Centre. Transplants of kidney, heart and lung from HBsAg negative, anti-HBcAg positive donors is allowed if the recipient is HBsAg positive or HBsAg negative previously vaccinated for HBV. In these cases informed consent is not necessary, however it is important to follow-up transplanted patients over time. If the donor is anti-HBcAg positive, the risk of HBV transmission to transplant recipients unvaccinated or not-responders to vaccination for HBV is extremely low for kidney, heart and lung transplants but the risk is not null [14]. It is however necessary to provide an informed consent and to monitor the recipient over time according to a common national protocol established by the National Transplant Centre. The importance of HBV vaccination for transplant candidate on the waiting list shouldalso be emphasized.

As a supplement to these measures the Italian National Transplant Centre has deemed as proper to support further transplant network health workers, through adhoc developed information tools and an expert task force (second opinion) for evaluation of doubtful cases. In practice this safety project features two different integrated and linked activities:

1) the appointment of an expert task force (second opinion);
2) the implementation of a safety information network (Tel-Bios project).

The second opinion task force is formed by a panel of professional experts nominated by a Ministerial Decree dated October 27, 2004 [15]. It is composed of two medical doctors from the Italian Transplant Centre, a medical examiner, an infectious disease expert and a pathologist. This group provides around-the-clock support to the national transplant network, with high expertise and is a consulting tool used by the local coordinator during the evaluation of the donor or of single organs. In addition, it acts as a reference point for transplant surgeons in monitoring calculated risk transplants. So far, all regional transplant centres (CRT), the three interregional reference centres and the National Transplant Centre as well as the second opinion experts are connected by the safety network. All these users are authorised to use the network and have access to the information system on ongoing donor evaluation process; as do the local coordinator who manages the donor and the entry of data into the system; the Interregional transplant centre of the coordinator; the National Transplant Centre, one expert or the experts of the second opinion group involved in donor assessment. In detail, the health worker of the coordinating centre receives from the local coordinator or intensive care unit the report on potential donor with annex documents and opens a donor file in the information system and informs the involved transplant centre that the process has started. At the end, he/she is the only person entitled to close the process. The staff of the interregional reference centre receives such communication from the coordinator who is responsible for the donor and, if required, sends information about the donor to other interregional reference centres. In each phase of the process the need can arise to request a second opinion expert who is allowed to enter the system and acquire all necessary data for evaluation, to express an opinion. Since one of the safety network's aims, as stated above, is to document the chronological order of procedures, each document (medical reports, images, etc.) is saved and filed in the system. The safety network architecture is also supplemented with three microscope services (located at each interregional centre) enabled to electronically transmit histological images; a multipoint videoconference system connecting six sites; and satellite mobile phones for second opinion members.

RESULTS

From the date of guidelines coming into force (September 30, 2003) to December 31 2006, 7954 potential cadaveric donors were reported out of which 1375 presented a neoplastic or infectious risk. Over the whole considered period, 4326 donors were used for transplantation, equal to 54.38% of reported donors. Through the application of safety guidelines and taking advantage of second opinion expert advice, it has been possible to assess the suitability of the 1375 donors that had been diagnosed as risk donors. In detail of these, 580 were neoplastic-disease affected donors and 795 infection-disease affected donors. Three hundred and ninety-four of the 580 reported as neoplastic donors were excluded from donation for absolute contraindications, whereas 186 were considered as standard risk or increased but acceptable risk and were therefore utilised for transplantation. Of the 795 infection-affected donors, 67 were excluded from donation and 728 were classified as calculated risk donors and therefore utilised for transplantation.

The incidence of neoplasias detected in reported donors concerned the following apparatus or organs: 49.09% of donors had urogenital and reproductive apparatus (out of these 56.61% refers to prostate carcinoma with an average donor age equal 64.8 years); 12.09% of donors had central nervous system; 11.19% digestive apparatus; 4.69% breast; 3.97% thyroid; 2.88% breathing apparatus; 15.16% leukaemia and lymphomas.

The incidence of donors with neoplastic risk factors in the three interregional areas has been increasing

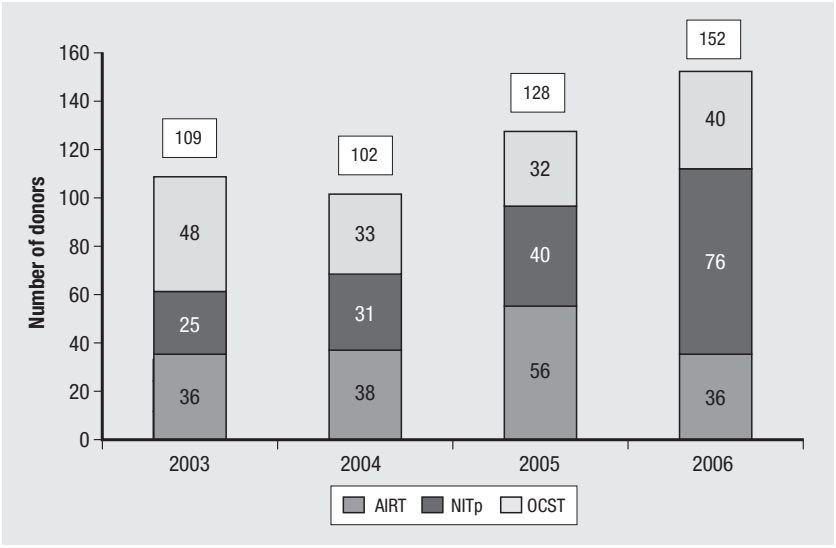

Fig. 1 | *Incidence of cadaveric donors with neoplastic risk factors over the years distributed in three interregional areas.*
AIRT: Associazione Inter Regionale Trapianti
NITp: Nord Italia Transplant Program
OCST: Organizzazione Centro-Sud Trapianti.

in these last four years, 109 reported donors in 2003 against 152 donors in 2006. This means that the application of guidelines and the support supplied by second opinion group allows us to reassess an increasing number of potentially useable donors over the years *(Figure 1)*, thus making it possible to transplant 167 livers; 128 kidneys; 7 lungs and 29 hearts for a total of 331 transplanted patients. At the same time the general capability to detect such donors in due time during the donation-retrieval-transplant process is the real gold standard that has been achieved. Indeed no neoplasia was detected in 2006 after transplantation, whereas the diagnosis capability improved during previous phases, that is when it is still possible to stop the process without exposing the potential recipient to the risk of disease transmission.

In 728 infection-affected donors who were used for transplantation, the following risk factors were detected: 75.8% of donors were virus B anticore antibody IgG positive donors (HBcAb); 11.8% of donors HCV+ donors; 8.1% of donors affected by bacterial meningitis or other systemic infections; 4.3% of donors were HBV infected individuals (HBsAg+) but negative for antigen HDV, for IgM anti-HDV for IgG anti-HDV. Organs divided by risk category are shown in *Table 5*. These cadaveric donors have been used in the total respect of the guidelines or following the directions given by infectious disease second opinion. In detail the evaluation strategies presently in force have allowed the retrieval and transplant of 1026 kidneys, 618 livers, 182 hearts, 25 lungs and 13 pancreas from cadaveric donors with infectious risk factors. The recipients of such organs have been steadily monitored after transplantation according to guidelines which enforce an adhoc follow-up program till the fifth post-transplant year. The results of this monitoring show that no cases of reinfection or donor-recipient disease transmission were reported by December 2006.

DISCUSSION AND CONCLUSIONS

What has been done in Italy in terms of safety in the evaluation process of the cadaveric donors leads us to make various remarks.

Firstly, guidelines are an essential need for professionals from different medical disciplines who should consider thousands of unsorted information items that may be difficult to be put into practice. Therefore, they are a precious reference tool for a professional practice that is increasingly ruled by a variability of different possible solutions to tackle single problems. And yet, they pertain more to medical art striving to become science than to science itself sincethey are recommendations and general methodological tools for physicians, whose main goal is toat manage frequent situations and help to

Table 5 | *Kind of carried out transplants divided by donor serological and/or bacterial status*

Serological and bacterial status of donor	Kidney	Liver	Heart	Lung	Pancreas
anti HCV+	8.7%	9.2%	6.8%	4.3%	0.0%
HBsAg+	3.5%	3.9%	4.2%	0.0%	0.0%
antiHBcAb+	79.4%	77.5%	80.2%	85.1%	84.6%
Bacteremia/Meningitis	8.4%	9.4%	8.9%	10.6%	15.4%
Total performed transplants	1026	618	182	25	13

choose the most effective and appropriate solution, on the basis of discussions among experts and professionals supported by international literature.

Secondly, in the transplant field, multifactoriality and multidisciplinarity generate subjective situations and dynamics that can not always be foreseen in a reference guide. Despite that, in our experience, the strict application of the guidelines for the evaluation of donor suitability has dwarfed possible risk factors or at least highlighted them in due time when it was still possible to better evaluate and manage them. Furthermore, standardization and objectives of the donor evaluation process have made everybody aware of the clinical behaviour based on experience and fostered the operational and decision-making capability of every network professional.

Third, in the donation-transplantation process, as mentioned several times in this paper, even if there is a behaviour consistent with good clinical practice principles, some risk of transmission of pathologies from the donor to the recipient is still present.

In the light of this, the setup of the safety network and Second Opinion group can be considered as a real turning point. The group, now operating in the national territory for more than two years, has further contributed to give safe support to the whole system, reducing the risk of transmitting disease through transplantation and bettering the use of offered organs. The cultural, scientific and care-related implications of such approach are therefore very clear: the comparison, the discussion and the sharing of one's own actions not only improve the skills of those who make use of such tool, but also tend to foster a steady circulation of ideas and opinions. In this way a continuous education is guaranteed and even professionals working in outlying areas are actively involved. The goal of this initiative is to create an expertise in management and decision-making steps of the organ evaluation process, thus reducing the risk of transmissible diseases from donor to recipient through shared and good clinical practice procedures. Aside, the aim is to support health workers making them aware of clinical evidence-based codes of practice, without reducing their decision making, since they remain the leading actors responsible to choose the best solution, after having carefully evaluated single cases.

At the same time, the need and aim of the "Safety Network" are on one hand the necessity of an Information Technology support, at all the different network levels, for exchanging information collected during potential donor evaluation process; and, on the other, the possibility to allow such exchange in real time among the different transplant system involved actors. Eventually, such Information Technology support allows the consultation and the filing of the whole donation process data, from donor report to performed transplantation, allowing to trace back the chronological order of the different received information. In conclusion, the *end-point* of the "safety network", project is to increase the transplant opportunities for the patient on the waiting list through the use of donors that would previously have been discarded, without exposing the recipients to unacceptable risks. This has been made possible by acquainting health workers with the most accredited scientific evaluation methodologies and validated through the consensus *conference* system. In this framework, the reference to the evidence-based medicine (EBM) can be considered as a reliable invitation to a documented choice of diagnostic and therapeutic paths commonly agreed and to the punctual recording of the adopted option.

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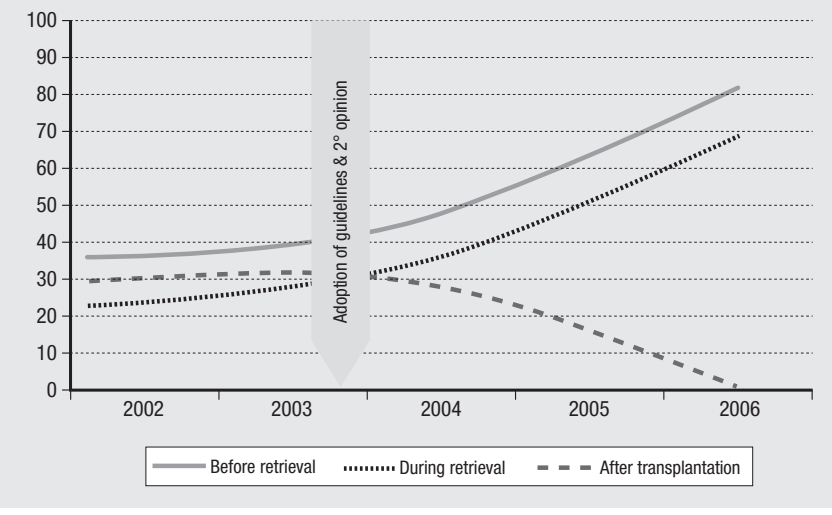

Fig. 2 | *Timing of neoplasia identifications*

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Surveillance of toxic exposures: the pilot experience of the Poison Control Centers of Milan, Pavia and Bergamo in 2006

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Summary. Between 1 February and 31 March 2006, the Poison Control Centers (PPC) active in Lombardy collaborated with an integrated surveillance system carried out in Piedmont during the Olympic Games 2006. The collaborating PPC notified to the system 697 human cases of exposure occurred in Piedmont during the observation period. Among these cases, 70% were exposed accidentally, 40% were 6 years old or younger, and 45% reported at least a clinical effect. The agents more frequently reported were: cleaning substances (household) (110 cases), fumes/gases/vapors (63 cases, comprising 38 cases accidentally exposed to carbon monoxide), and sedative/hypnotics/antipsychotics (53 cases). Although very limited, the available observations focused the attention on specific hazards and were able to highlight the potential of a toxic exposure surveillance system based on the information reported by the Italian PPC.

Key words: poison control centers, surveillance, toxic exposures.

Riassunto *(Sistema di sorveglianza integrata: un'esperienza pilota dei Centri antiveleni di Milano, Pavia e Bergamo nel 2006)*. Nel periodo 1 febbraio-31 marzo 2006 i Centri antiveleni (CAV) lombardi hanno collaborato ad un sistema di sorveglianza integrata messo in atto per la Regione Piemonte durante le Olimpiadi Invernali 2006. Complessivamente, i CAV hanno preso in esame 697 casi di esposizione umana verificatisi in Piemonte. Di questi, circa il 70% ha subito un'esposizione accidentale, il 40% ha presentato un'età inferiore ai 6 anni ed il 45% ha riportato almeno una manifestazione clinica. Gli agenti con il numero più elevato di casi sono stati i detergenti per uso domestico (n. = 110), fumi/gas/vapori (n. = 63), comprendenti 38 casi di esposizione accidentale a monossido di carbonio e sedativi/ipnotici /antipsicotici (n. = 53). Sebbene limitata, la casistica analizzata ha permesso di focalizzare l'attenzione su alcune problematiche specifiche ed ha evidenziato la potenzialità di un sistema di sorveglianza delle esposizioni pericolose basato sui CAV italiani.

Parole chiave: Centri antiveleni, sorveglianza, esposizioni pericolose.

INTRODUCTION

Poison Control Centers (PCC) are centers operating on a 24-hours-a-day basis in the framework of the National Health System to provide specialized services in the field of clinical toxicology and, in particular, to ensure proper diagnosis and management of poisonings. The exposure cases examined by the PCC involve a number of different agents and can be indicative of widespread and underestimated hazardous conditions. A systematic analysis and examination of the cases selectively reported to the PCC is extremely important for an adequate description and prevention of a wide range of events, such as pediatric poisoning, drug poisoning, household, environmental and workplace exposures and food poisoning. A careful examination of the findings of the PCC is also essential to verify the actual safety of marketed pharmaceutical and non-pharmaceutical products. More recently, the findings of the PCC have contributed to a prompt

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identification of unusual events which could be associated with the intentional or unintentional release of toxic agents [1-4].

In view of the above and using as a reference the work carried out by the PCC in the United States since the early 1980s [1-3], a working plan for the development of a surveillance system based on the information provided by the PCC was recently started at the National Health Institute (Istituto Superiore di Sanità, ISS) in agreement with the Italian Center for Disease Control (ICDC) of the Health Ministry and in cooperation with Region Lombardy. The first step in the implementation of this project was the definition of standard procedures for collection and classification of the information handled by the PCC. Indeed, preliminary observations showed that each PCC in Italy has its own data collection system, which renders difficult the integration and analysis of all the cases identified by these centers. Nevertheless, like the PCC operating in the USA [1, 2], the Italian PCC systematically collect (although with different procedures) relevant information including: type of the requested advice, patient information, exposure informatin, clinical effects and recommended therapy. The activities carried out by the PCC of Milan, Pavia and Bergamo in the framework of the health surveillance plan promoted and coordinated by Region Piedmont during the 2006 Winter Games provided a first opportunity to verify the applicability of the standard procedures proposed by the ISS [5, 6]. Indeed, during the Winter Games, the PCC of Region Lombardy, which are the reference centers also for Region Piedmont, transmitted the data regarding all the cases reported by patients from Piedmont to the Regional service for the surveillance of infectious diseases (SeREMI) and to the ISS on a daily basis. At the ISS, the information collected by the three participating centers was systematically verified and classified using standard reference categories. Analyses were carried out by the ISS and the SeREMI on a daily and weekly basis to identify any unusual condition requiring further examination and verification; at the end of the observation period, an overall analysis of all the identified cases was also carried out by the ISS. In this report, the results of that final analysis are described with a view to providing a sample of Italian data testifying to the potentials of a toxic exposure surveillance system based on the information reported by the PCC.

MATERIALS AND METHODS

Between February 1 and March 31, 2006, the PCC of Milan, Pavia and Bergamo notified to the ISS, on a daily basis, all relevant information (stored in their own databases) concerning the professional advice provided the day before. Such information was made available in the form of Microsoft Excel tables. The data included:

1. Details of the advice provided
   - date and time
   - type of advice
   - advice-seeker
   - site of the call
2. Patient information
   - gender
   - sex (in human exposure cases)
   - age (in human exposure cases)
3. Exposure information
   - geographical location where the exposure occurred
   - time interval between exposure and advice-seeking
   - agent
   - reasons for exposure
   - route of exposure
   - frequency
   - site of exposure
4. Clinical effects
   - latency between exposure and clinical effects
   - signs and symptoms

At the ISS, the professional advice provided by the PCC was initially classified into the following categories: "case of exposure", including all cases of exposure handled for the first time by the PCC; "follow-up", including any follow-up advice provided with regard to a previously reported case of exposure but recorded in one or more entries other than the original one; "information calls", including requests for further information on toxicological issues rather than actual exposures. Eventually, all of the records regarding the same exposure case were unified and the original "follow-up" category was eliminated. In case of exposures involving more than one individual (multiple exposures), the actual correspondence between the number of affected individuals and that of identified cases was systematically verified requesting, whenever possible, the retrieval of data regarding cases handled but not reported in details by the PCC. Each of the individuals involved in multiple exposures was recorded in a separate record maintaining the indication of the original incident. For all the exposure cases identified by the PCC, the date when the incident occurred was calculated subtracting the time interval between exposure and advice-seeking from the date and time in which advice was sought. On this basis, only exposures occurred during the period at issue (1 February - 31 March) were considered for further examination. Most reasons for exposure were coded according the following definitions: "unintentional", including accidental exposures or exposures resulting from mistakes (general incidents, unintentional misuse, occupational incidents, environmental incidents, incapacity, therapeutic error, animal bites and stings); "intentional", including intentional abuse or self-destructive purposes; "malicious", including condition in which a patient is victim of another person's intent to harm him; "adverse reaction", including adverse effects occurring with normal use of farmaceutical or non farmaceutical products; "food poisoning", including suspected or confirmed ingestion of food

contamitated with microorganisms or chemical. The agents involved in the exposures were classified into two main groups: "pharmaceuticals" and "non-pharmaceuticals". The first group included all the agents used for therapeutic purposes and provided for in the plus the "substances of abuse", including street drugs and other stimulants. The drugs which were found to be associated with human exposure cases were originally classified according to the Anatomical Therapeutic Chemical (ATC) classification system and eventually grouped in the categories adopted by the US PCC in the framework of the Toxic Exposure Surveillance System (TESS) [2, 3]. The non-pharmaceutical substances were also classified according to the categories adopted by the American Association of Poison Control Centers TESS. Clinically relevant signs and symptoms were identified using a standardized nomenclature and grouped in 12 categories (cardiovascular, cutaneous, hematological, hepatic, gastrointestinal, metabolic, neuromuscular, ocular, oropharyngeal, renal, respiratory and related to the nervous system). The patients exhibiting at least one sign or symptom whose association with their exposure to the reported agent was not excluded by the PCC were classified as symptomatic. At the end of the review and classification processes, the data collected by the three PCC were transferred to a single file to find out all separate entries regarding the same case reported to more than one participating center. The variables used to identify any duplicate report included: date and site of exposure, agent, sex and age. In cases of confirmed duplicate reports, all the information provided by the separate PCC was integrated into a single record.

A descriptive analysis of the available data was made possible using the EpiInfo statistical software.

RESULTS

Over the period at issue, the three participating PCC received 776 requests for professional advice from patients living in Region Piedmont, which accounted for

Table 1 | *Human exposure cases occurred in Piedmont over the period February 1- March 31 2006 and examined by the PCC of Lombardy (Italy)*

	PCC									
	Milan		Pavia		Bergamo		More PCC		Total	
	n.	(col. %)	n.	(col. %)	n.	(col. %)	n.	(col. %)	n.	(col. %)
Province										
Alessandria	21	6.0	58	20.4	1	25.0	2	14.3	82	12.5
Asti	15	4.3	15	5.3	1	25.0	0	0.0	31	4.7
Biella	10	2.8	34	11.9	0	0.0	1	7.1	45	6.9
Cuneo	51	14.5	26	9.1	1	25.0	1	7.1	79	12.1
Novara	56	15.9	14	4.9	0	0.0	3	21.4	73	11.1
Turin	153	43.5	120	42.1	0	0.0	5	35.7	278	42.4
Verbania	25	7.1	5	1.8	0	0.0	0	0.0	30	4.6
Vercelli	21	6.0	13	4.6	1	25.0	2	14.3	37	5.6
Total Region	**352**	**100.0**	**285**	**100.0**	**4**	**100.0**	**14**	**100.0**	**655**	**100.0**
Advice-seeker										
Hospitals	233	66.2	244	85.6	1	25.0	12	85.7	490	74.8
Others										
Private invidual	94	26.7	24	8.4	3	75.5	2	14.3	123	18.8
Doctor/health care operator	20	5.7	7	2.5	0	0.0	0	0	27	4.1
Emergency service	5	1.4	5	1.7	0	0.0	0	0	10	1.5
Unknown	0	0.0	5	1.8	0	0.0	0	0.0	5	0.8
Latency between exposure and consultation with PCC (in hours)[a]										
≤ 1	188	53.0	120	41.2	0	0.0	8	57.1	316	47.5
2-12	87	24.5	106	36.4	0	0.0	4	28.6	197	29.6
> 12	35	9.9	28	9.6	2	40.0	1	7.1	66	9.9
Unknown	45	12.7	37	12.7	3	60.0	1	7.1	86	12.9
One	347	98.6	269	94.4	4	100.0	14	100.0	634	96.8
More than one	5	1.4	16	5.6	0	0.0	0	0.0	21	3.2
Total consultations	**352**	**100.0**	**285**	**100.0**	**4**	**100.0**	**14**	**100.0**	**655**	**100.0**

[a]*includes 10 cases reported in February but occurred in January and excluded from analysis work.*

Table 2 | *Main features of human exposure cases occurred in Piedmont over the period February 1 - March 31 2006 and examined by the PCC of Lombardy (Italy)*

	PCC									
	Milan		Pavia		Bergamo				Total	
	n.	(col. %)	n.	(col. %)	n.	(col. %)	n.	(col. %)	n.	(col. %)
Symptoms										
Not observed/associated	216	60.3	148	46.1	2	50.0	8	57.1	374	53.7
Observed	134	37.4	173	53.9	2	50.0	6	42.9	315	45.2
Unknown	8	2.2	0	0.0	0	0.0	0	0.0	8	1.1
Age groups										
≤ 6	164	45.8	92	28.7	2	50.0	10	71.4	268	38.5
6-19	36	10.1	29	9.0	0	0.0	0	0.0	65	9.3
19+	141	39.4	195	60.7	1	25.0	4	28.6	341	48.9
Unknown	17	4.7	5	1.6	1	25.0	0	0.0	23	3.3
Reasons for exposure										
Unintentional	274	76.5	199	62.0	4	100.0	11	78.6	488	70.0
Intentional	76	21.2	110	34.3	0	0.0	3	21.4	189	27.1
Criminal/malicious	0	0.0	6	1.6	0	0.0	0	0.0	6	0.9
Food poisoning	3	0.9	1	0.3	0	0.0	0	0.0	4	0.6
Adverse reaction	1	0.3	2	0.7	0	0.0	0	0.0	3	0.5
Unknown	4	1.1	3	0.9	0	0.0	0	0.0	7	1.0
Site of exposure										
Residence	332	92.7	297	92.5	3	75.0	14	100.0	646	92.7
Workplace	10	2.8	6	1.9	0	0.0	0	0.0	16	2.3
Other	14	3.9	15	4.7	0	0.0	0	0.0	29	4.2
Unknown	2	0.6	3	0.9	1	25.0	0	0.0	6	0.9
Agents										
Non-pharmaceuticals	212	59.2	168	52.3	1	25.0	6	42.9	387	55.5
Pharmaceuticals	137	38.3	140	43.6	3	75.0	8	57.1	288	41.3
More than one category	9	2.5	13	4.0	0	0.0	0	0.0	22	3.2
Total individuals	358	100.0	321	100.0	4	100.0	14	100.0	697	100.0

6% of all the counseling provided in the same period (n. = 13 760 requests). In particular, 419 of the 776 requests for advice (54%) were handled by the PCC of Milan, 295 (38%) by the PCC of Pavia and 48 (6%) by the PCC of Bergamo. Consultations regarding new human exposure cases accounted for 84% of all the counseling work (n. = 655); 14 of these cases were examined and reported by more than one PCC. Seven animal exposure cases were reported, while information calls represented less than 15% of the total (n. = 114). As for human exposures *(Table 1)*, about 42% of all the requests for assistance came from the province of Turin which is home to some 50% of the whole population of Region Piedmont.

Most requests for assistance came from hospitals (n. = 490, or about 75% of all the exposures). The time interval between the exposure and its reporting to a PCC was one hour or less in about 47% of the cases, and 12 hours or less in about 77% of the cases. Most of the reported exposure cases (about 97%) involved only one individual. Overall, 21 multiple exposures were reported involving a total of 63 individuals. The human exposure cases amounted to 697, which result in an estimated average of 11.4 cases per 10 000 inhabitants reported annually to the PCC of Lombardy from Region Piedmont, ranging from 9.0 cases per 10 000 inhabitants in the province of Turin to 15.6 cases per 10 000 inhabitants in the provinces of Alessandria and Biella.

As shown in *Table 2*, clinical effects were reported in about 45% of the cases (n. = 315) and children younger than 6 years accounted for 38% of the total (n. = 268). 70% of all the reported exposures (n. = 488) were unintentional, while 27% (n. = 189) were intentional. The remining 2% (n. = 20) included 6 cases of suspected malicious exposure, 4 cases of food poisoning and 3 cases of adverse reaction to drugs. The most frequently reported site of exposure was the victim's own residence (646 cases, or 93% of the total) followed by the workplace (16 cases, or 2% of the total). The sites of exposure classified as "other" (about 4% of the total) included civil buildings (hospitals and schools) (14 cases), open spaces (6 cases), public premises (6 cases) and transports

Table 3 | *Main features of human exposure cases examined by the PCC of Milan, Pavia and Bergamo in February - March 2006 at the request of Region Piedmont (Italy)*

Type of agents	Exposures		Clinical effects		Age (years)				Reason for exposure		
	n.	col. %	None	Present	< 6	6-19	> 19	Unknown	Unint.	Int.	Other
NON-PHARMACEUTICALS											
Household cleaning substances	115	29.7	56	59	50	7	53	5	101	14	0
Fumes/gases/vapors	[a]63	16.3	19	44	6	10	40	7	61	1	1
Cosmetics/personal care products	36	9.3	22	14	23	4	8	1	32	4	0
Toys/foreign bodies	30	7.8	24	6	27	2	1	0	29	1	0
Food/beverages (excl. ethanol)	22	5.7	12	10	3	5	13	1	11	0	[b]11
Colors/office supplies	13	3.4	12	1	12	1	0	0	13	0	0
Fertilizers	10	2.6	10	0	2	2	6	0	10	0	0
Pesticides	7	1.8	6	1	4	0	3	0	6	1	0
Glues/adhesives	7	1.8	7	0	6	1	0	0	7	0	0
Plants	7	1.8	6	1	5	0	2	0	7	0	0
Hydrocarbons	6	1.6	1	5	0	2	4	0	5	1	0
Ethanol beverages	3	0.8	0	3	0	2	1	0	1	2	0
Tobacco	3	0.8	1	2	3	0	0	0	2	0	0
Matches/explosives/fireworks	5	1.3	4	1	5	0	0	0	5	0	0
Fire extinguishers	4	1.0	2	2	0	3	0	1	2	2	0
Bites/stings	4	1.0	1	3	0	0	3	1	4	0	0
Batteries	4	1.0	4	0	3	1	0	0	4	0	0
Non-drinking water	3	0.8	3	0	1	2	0	0	3	0	0
Room deodorizers/air fresheners	3	0.8	3	0	3	0	0	0	3	0	0
Mushrooms	3	0.8	2	1	0	0	2	1	3	0	0
Essential oils	2	0.5	2	0	1	0	1	0	2	0	0
Other	14	3.6	8	6	3	0	10	1	12	2	0
Exposure to more than one categ.	5	1.3	1	4	0	0	4	1	0	5	0
Unknown	18	4.7	7	11	4	2	11	1	15	0	3
Total n. of non-pharmaceuticals	**387**	**100.0**	**213**	**174**	**161**	**44**	**162**	**20**	**338**	**33**	**16**
% of non-pharmaceuticals	100.0		55.0	45.0	41.6	11.4	41.9	5.2	87.3	8.5	4.2
% of all substances	57.3		56.5	58.4	60.1	67.7	50.8	87.0	69.4	19.6	80.0
PHARMACEUTICALS											
Sedatives/hypnotics/antipsychot.	53	18.4	17	36	7	3	42	1	12	39	[c]2
Analgesics	32	11.1	27	5	20	1	11	0	24	7	[c]1
Gastrointestinal preparations	15	5.2	10	5	9	1	5	0	12	2	[c]1
Antidepressants	13	4.5	6	7	1	4	8	0	2	11	0
Antiepileptics	12	4.2	8	4	1	1	10	0	4	8	0
Cardiovascular drugs	12	4.2	9	3	8	0	4	0	11	1	0
Street drugs and stimulants	10	3.5	1	9	0	0	10	0	0	10	0
Vitamins	9	3.1	9	0	9	0	0	0	9	0	0
Antimicrobials	8	2.8	7	1	3	2	3	0	6	2	0
Eye/nose/throat preparations	8	2.8	8	0	6	0	2	0	8	0	0
Cold and cough preparations	8	2.8	8	0	7	0	1	0	7	1	0
Asthma therapies	8	2.8	8	0	6	1	1	0	8	0	0
Hormones and horm. antagonist	6	2.1	6	0	6	0	0	0	6	0	0
Topical preparations	5	1.7	3	2	3	0	2	0	4	1	0
Antihistamines	3	1.0	3	0	2	1	0	0	3	0	0
Diuretics	2	0.7	1	1	2	0	0	0	2	0	0
Anticoagulants	1	0.3	1	0	1	0	0	0	1	0	0
Antineoplastics	1	0.3	1	0	1	0	0	0	1	0	0
Electrolytes and minerals	1	0.3	1	0	0	1	0	0	1	0	0
Homeopathic preparations	1	0.3	1	0	1	0	0	0	1	0	0
Veterinary drugs	1	0.3	1	0	0	0	1	0	1	0	0
Others	14	4.9	10	4	9	1	3	1	14	0	0
Drug mixtures	55	19.1	13	42	0	4	51	0	4	51	0
Unknown pharmaceuticals	10	3.5	5	5	5	1	3	1	8	2	0
Total n. of pharmaceuticals	288	100.0	164	124	107	21	157	3	149	135	4
% of pharmaceuticals	100.0		57.0	43.1	37.2	7.3	54.5	1.0	51.7	46.9	1.3
% of all substances	42.7		43.5	41.6	39.9	32.3	49.2	13.0	30.6	80.4	20.0

[a]38 cases of human exposure to carbon monoxide and 13 cases of human exposure to fire smoke; [b]includes 4 cases exhibiting symptoms of "histamin fish poisoning" as a result of fish ingestion and 6 cases of suspected malicious exposure following consumption of bottled water; [c]one case of adverse reaction.

(3 cases). Non-pharmaceutical agents were found to be involved in about 55% of the reported exposure cases (n. = 387) and pharmaceutical agents in 41% (n. = 288) of the exposure cases. Both non-pharmaceutical and pharmaceutical agents were found to be involved in 3% (n. = 22) of the exposures.

The most frequently reported non-pharmaceutical agents *(Table 3)* included: household cleaning substances (115 cases), fumes/gases/vapors (63 cases), cosmetics/personal care products (36 cases), toys/foreign bodies (30 cases), food and beverages (22 cases). Findings in individuals exposed to fumes/gases/vapors were slightly different from those described, in general, for the cases exposed to non-pharmaceutical agents: in particular, about 97% of those individuals were exposed accidentally to the said agents, only 9% of them were younger than 6 years and some 70% exhibited at least a sign or symptom associated with the exposure. The most frequently reported compound, among the agents classified into the "fumes/gases/vapors" category, was carbon monoxide (38 cases, 31 of which as a result of multiple exposures). Other agents in this category included fire smoke (13 individuals exposed, 8 of whom as a result of occupational incidents), and chlorine vapors (6 individuals exposed as a result of improper mixing of household cleaning substances). Six of the cases exposed to food and beverages were of a suspected malicious nature: in particular, 3 cases were found to have consumed bottled water contaminated with a pesticide and 3 other cases bottled water suspected to be contaminated with an unknown agent. This category also included 4 cases of individuals who exhibited symptoms usually associated with the condition known as "histamine fish poisoning" as a result of fish ingestion. As shown in *Figure 1*, the clinical effects most frequently observed in individuals exposed to non-pharmaceutical agents were gastrointestinal illness (93 cases, or about 50% of all the symptomatic cases).

The highest number of intentional exposures was observed among exposures to pharmaceutical agents *(Table 3)* (135 cases, or about 47% of all drug-related exposures). The most frequently reported agents were those belonging to the "sedatives/hypnotics/antipsychotics" category, with 53 exposure cases, about 74% of which were found to be intentional. In this category, about 79% of all the cases involved adults (19 years old or older). Other drug categories associated with a high number of exposures included analgesics (32 cases) and gastrointestinal preparations (15 cases): in particular, a high proportion of all the cases of exposure to these categories were unintentional (75% of the cases for analgesics and 80% for gastrointestinal preparations) and involved children (about 60% of the cases were 6 years old or younger). Finally, it should be pointed out that one case of adverse reaction was observed for each of the three most frequently reported drug categories. About 90% of all

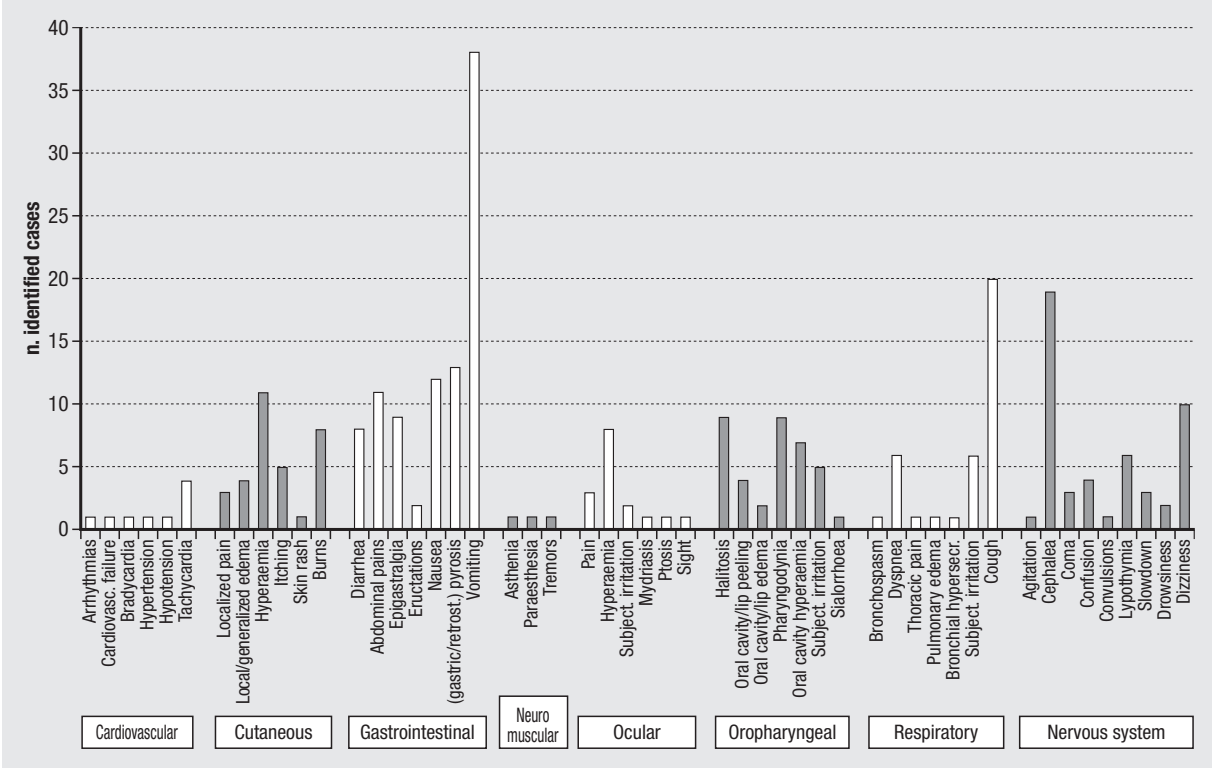

Fig. 1 | *Signs/symptoms observed in cases of exposure to non-pharmaceutical agents examined by the PCC of Milan, Pavia and Bergamo in February-March 2006 at the request of Region Piedmont (Italy).*

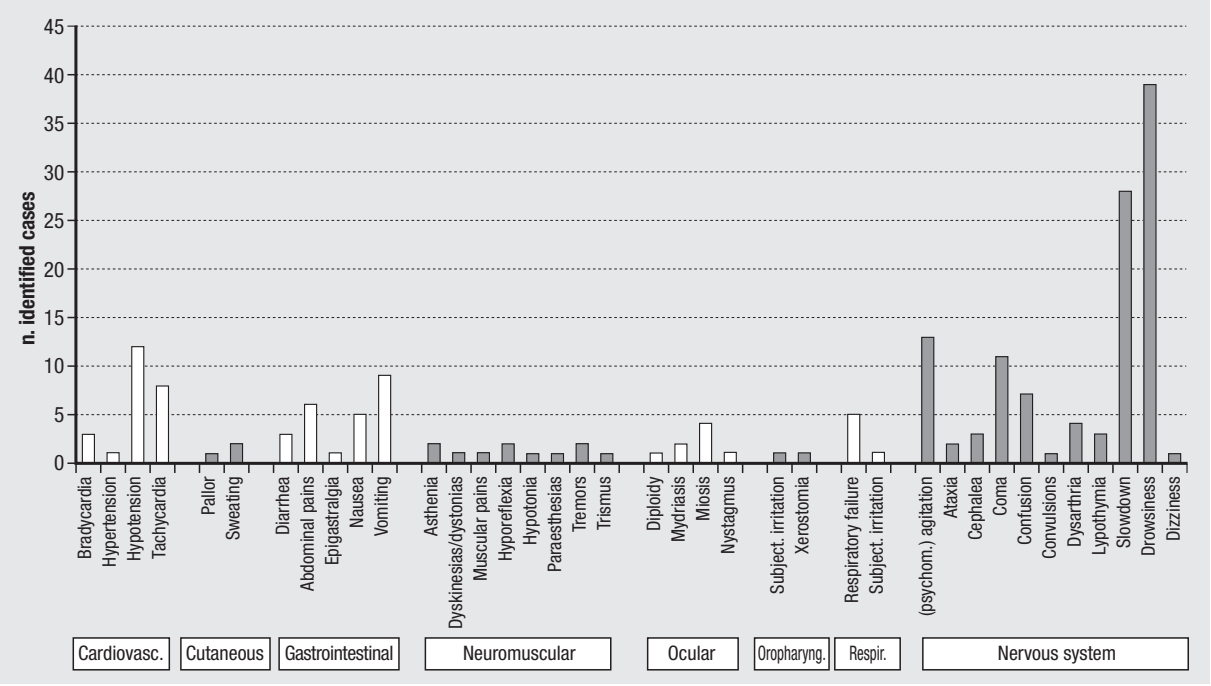

Fig. 2 | *Signs/symptoms observed in cases of exposure to pharmaceutical agents examined by the PCC of Milan, Pavia and Bergamo in February-March 2006 at the request of Region Piedmont (Italy).*

symptomatic patients reported clinical effects related to the nervous system (112 cases) *(Figure 2)*.

DISCUSSION AND CONCLUSIONS

About 70 000 human exposure cases are reported on an annual basis to the PCC operating in Italy [7]. An integrated analysis of these data, although extremely interesting, is still something difficult to achieve because each PCC active in Italy uses its own data collection system and does not share with other centers uniform definitions to capture data. A first attempt to define and apply standard operating procedures was made in the framework of the pesticide-related poisoning surveillance plan promoted by the ISS [8-10]. The operating procedures originally identified for the implementation of this working plan were eventually used, on an experimental basis, by the PCC of Milan, Pavia and Bergamo to notify the cases of Piedmont region detected during the 2006 Winter Games. Subsequent controls contributed to the better definition of a data collection system capable of providing a uniform database which would best suit both the counseling work carried out by the PCC and specific surveillance goals, without entailing increased workload for the operators. Moreover, the nomenclature and definitions adopted by the PCC for the variables at issue were standardized. Such results acted as a first operational reference point paving the way for adoption of shared data collection and management procedures. In particular, with regard to the categories used in this experience for the classification of the various exposure cases, it should be pointed out that the planned level of detail requires the adoption of a computerized data management system ensuring the automatic classification of all the agents or commercial products entered into the database and indicating the agents of toxicological interest composing each commercial product as well as their relative concentrations. In order to achieve this objective, which is of interest also for the routine management of exposure cases by the PCC, a matrix should be developed matching each identified category of agents with updated lists of commercial products in use. Matching functional and chemical classes, agents and commercial products is not difficult for drugs because lists of all the marketed products accompanied by their own ATC code are made available through the Health Ministry. Developing procedures for the management of non-pharmaceutical products is a more difficult. As for pesticides, however, it should be emphasized that the ISS is currently developing a database of all commercial products intended for use in agriculture, containing information on their specific agents and main toxicological characteristics [11]. This database is updated through the systematic collection of information regarding newly granted marketing authorizations and a regular consultation of the results of toxicological review and classification activities carried out by various international organizations for all active ingredients. At present, the database does not include information on pesticides intended for use at

home or other civil purposes; as a result, neither updated lists of the marketed products nor procedures ensuring the systematic reporting of newly granted authorizations are currently available. Another database that could be used for the acquisition of data regarding non-pharmaceutical commercial products is the Archivio Preparati Pericolosi (a database of dangerous preparations) implemented by the ISS which can be accessed by the PCC subject to the authorization of the Ministry of Health [12]. When it comes to developing procedures for the management of commercial product data, it is important to remember that such procedures should be regularly updated and reviewed in order to be effective. The updating and reviewing processes must be such as to ensure the immediate acquisition of information on newly marketed products and a prompt detection of any change in the composition of products already on the market and not accompanied by a change in the product's name.

The findings relative to the human exposure cases from Piedmont reported by the PCC of Lombardy, although representative of a single region and of a limited period of time, turned out to be substantially comparable with the results observed in the USA on an annual basis (about 2 400 000 cases detected by 62 PCC in 2005) [3]. Moreover, those findings contributed to highlight emerging problems, such as the high frequency of intentional exposures to carbon monoxide, and press for further investigation and controls at the local level to increase prevention. The detection of six cases of human exposure to contaminated water and 4 cases of food poisoning proved especially interesting. Indeed, these findings demonstrated that the real-time analysis of the data collected by the PCC can contribute to a prompt identification of events of a suspected malicious or accidental nature requiring quick intervention and investigations.

Therefore, the work done by the PCC of Lombardy region during the 2006 Winter Games made a qualified contribution to the surveillance system dedicated to this specific event [5, 6] and highlighted the importance of a systematic review and analysis of the data collected by the PCC.

What is more, reviewing and classifying the variables at issue, prior to the actual analysis work, proved essential for a better definition of the standard procedures to be proposed to the PCC with a view to standardizing data collection and management procedures and making them comparable with each other. A direct result of both the work done and the related considerations was the development by the ISS of a prototypical computerized system available online and capable of acquiring and integrating the data collected from different poison centers in one database. There are plans to improve this prototype through further examinations so as to turn it into a mechanism capable of both meeting the data management needs of the PCC and ensuring adequate support for regional and national surveillance activities.

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Estimating river pollution from diffuse sources in the Viterbo province using the potential non-point pollution index

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Summary. This paper describes the application of the Index of Potential Non-point Pollution (PNPI) to the territory of the Viterbo Province (Central Italy). PNPI is a GIS tool that allows managers to assess the pressure on surface aquatic ecosystems deriving from diffuse sources of pollution. The index aims to assemble the available environmental datasets and specialists' expertise to set up a user-friendly and informative tool that can support decision-making processes and foster a multi-disciplinary approach. The index calculation is described and results are reported in order to give an overview of PNPI possible applications.

Key words: hydrographic basin, GIS, land use management, surface water bodies.

Riassunto *(Valutazione dell'inquinamento fluviale da sorgenti diffuse nella provincia di Viterbo per mezzo dell'indice di inquinamento diffuso potenziale)*. L'articolo descrive l'applicazione dell'indice di inquinamento diffuso potenziale (IDP) alla Provincia di Viterbo (Italia centrale). L'IDP è uno strumento GIS che permette ai responsabili della gestione ambientale di valutare e controllare la pressione esercitata sugli ecosistemi acquatici superficiali da parte di sorgenti diffuse di inquinamento. L'indice mira a sfruttare i dati ambientali e territoriali disponibili e le conoscenze di esperti del settore delle acque per la definizione di uno strumento semplice da utilizzare e di grande capacità comunicativa ed informativa, il quale possa supportare i processi decisionali e promuovere un approccio multidisciplinare. Nel testo vengono presentate le metodologie per il calcolo dell'indice ed i risultati ottenuti, al fine di fornire una visione generale delle sue possibili applicazioni.

Parole chiave: bacino idrografico, GIS, gestione dell'uso del suolo, corpi idrici superficiali.

INTRODUCTION

Sound policies for the management of water resources must be grounded in a deep knowledge of the environment and of the affected ecosystems. An integrated approach is essential to reach a multidisciplinary and comprehensive knowledge. Coordinated contributions from a variety of specialized technicians and scientists (biologists, naturalists, chemists, engineers, economists) can be highly beneficial. The National Institute of Health (Istituto Superiore di Sanità, ISS) and the councillorship for the environment of the Viterbo Province implemented a project with the goal of putting such an integrated approach into practice [1]. The main objective of the project was the application of the index of potential non-point pollution (PNPI) for the assessment of the pressure exerted by diffuse sources on surface water ecosystems. Within the project, many other aspects of the management and protection of water resources were addressed; among the project activities we mention the application of the fluvial functioning index (FFI) to estimate the integrity and identify alterations in fluvial ecosystems [2, 3], the use of the model SWAT (soil and water assessment tool) [4] on a pilot river basin for a different perspective on diffuse pollution assessment, and the study of the ornithic community, that contributed to the research on biodiversity. Last, guidelines for an economic analysis were defined in order to foster the achievement of restoration objectives by means of a "costs-benefits" analysis.

The method applied within the project "Development and deployment of a GIS based decisions support system for the control of water bodies' pollution from non-point sources" is in line with the ecosystem health approach to environmental management, which is in turn a keystone of all activities of the ISS Department of Environment and Primary Prevention [5, 6].

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The present paper describes in detail the line of activity concerning the assessment of pollution from diffuse sources. It aims at providing a novel insight into the complex interactions between fluvial ecosystems, land use management and environmental health; it also tries to show how readily available tools and datasets can be exploited with a view to fostering a more informed and knowledge-based decision making process.

MATERIALS AND METHODS

Assessment of water bodies' pollution from non-point sources is a complex, data-intensive and time-consuming task. The potential non-point pollution index (PNPI) is a tool designed to assess the global pressure exerted on rivers and other surface water bodies by different land use practices across the watershed [7, 8]. One key feature of PNPI is the ready availability of the input data needed to run the model. Highly detailed input maps, often lacking for many areas, are not required for the calculation of the PNPI. As a consequence of the input data chosen, the modelling of physical processes is simplified. The model applies an "expert system" approach; it bypasses the accurate representation of the physical reality to assess globally the pollution potential of different land uses, as estimated by scientists dealing with different aspects of watershed management. PNPI is a GIS-based, river basin-scale tool designed to inform decision makers and public opinion about the potential environmental impacts of different land management scenarios. PNPI calculation applies the multi-criteria approach to the description of pollutants dynamic and assessment of water bodies' health. It broadly follows the approach used in the environmental impact assessment. Diffuse pressure on water bodies deriving from different land units is expressed as a function of three indicators: land use (LCI), run-off (ROI) and distance from the river network (DI). They are calculated from land cover/land use datasets, geological maps and a digital elevation models (DEM). The meaning of each Indicator is explained below:

1) LCI (land cover indicator): refers to the potential generation of non-point pollution, as determined by the land use of the different parcels;
2) ROI (run-off indicator): takes into account pollutants mobility and possible filtering due to terrain slope, land cover/land use and geology/pedology;
3) DI (distance indicator): permits to account for the effect of the hydraulic distance between the source of pollution and the receiving water body.

The weights assigned to the three indicators and to the different land uses allow to calculate the value of the PNPI on each node of a grid representing the watershed: the higher the PNPI of the cell the heavier the potential impact on the river network.

LCI indicator is the most important of the set (in this regard, see also the weights given to the indicators as reported in *Table 1*); it allows to estimate the environmental consequences of different planning scenarios. Part of the research activities presented in this paper deal with the definition of the weights for the three indicators and for the land uses classes. To this purpose, several specialists with different backgrounds were consulted; the experts are biologists, natural scientists, ecologists and environmental engineers. The outcomes of the consultation are presented in the section "Results".

The calculation of the ROI on the cell *i* requires the preliminary definition of the Run-off coefficient for each cell along the hydraulic path between the cell *i* and the river network. The values for the Run-off coefficients are found in *Table 2*. The coefficient depends on the land use and permeability classes. Permeability ranges from A (high permeability) to D (low permeability). If permeability maps are not available, estimates of this parameter can be made through geological, lithological or pedological maps. For the present work, the permeability levels were retrieved from the lithological map of Lazio on a scale of 1:50 000 (which includes the Viterbo province); within the lithological map permeability classes had already been determined. The values in *Table 2* must be corrected for the effect of slope. This is done by adding the values in *Table 3* [9] (if the corrected value is higher than 1, the Run-off coefficient is set at 1). Once the Run-off coefficient for each cell is set, the Run-off indicator of the cell *i* can be calculated as the average of the Run-off coefficients of all cells between the cell *i* and the river network (along the hydraulic path).

The DI is calculated as the normalized distance between the cell *i* and the river network. The normalization was done by means of an exponential function expressed by the formula $DI_i = Exp(-([D_i]*k)$, where D_i is the distance of the cell *i* from the river measured in number of cells, and k is a constant value set at 0.090533.

Table 1 | *Indicators used to measure three key aspects shaping the land-based, diffuse pressure on surface water bodies [7]. The indicators, weighted according to the outcome of an experts' consultation, are combined to calculate the potential non-point pollution index (PNPI). The average values that resulted from of the consultation were normalized, therefore their sum is 10*

Indicator	Weight of the indicator (average)	Weight of the indicator (standard deviation)
LCI (Land cover indicator)	4.8	0.71
ROI (Run-off indicator)	2.6	0.52
DI (Distance indicator)	2.6	0.71

Table 2 | *Run-off coefficients by land use class (Corine land cover) and by permeability class (A: high permeability, D: low permeability). For the present study, the permeability levels were retrieved from the lithological map of Lazio (scale 1:50 000)*

Land use class (Corine land cover)	Permeability Classes			
	A	B	C	D
Continuous urban fabric	0.77	0.85	0.90	0.92
Discontinuous urban fabric	0.57	0.72	0.81	0.86
Industrial or commercial units	0.89	0.90	0.94	0.94
Road and rail networks and associated land	0.98	0.98	0.98	0.98
Port areas	0.89	0.92	0.94	0.94
Airports	0.81	0.88	0.91	0.93
Mineral extraction sites	0.46	0.69	0.79	0.84
Dump sites	0.46	0.69	0.79	0.84
Construction sites	0.46	0.69	0.79	0.84
Green urban areas	0.39	0.61	0.74	0.80
Sport and leisure facilities	0.39	0.61	0.74	0.80
Non-irrigated arable land	0.70	0.80	0.86	0.90
Permanently irrigated land	0.70	0.80	0.86	0.90
Rice fields	0.90	0.90	0.90	0.90
Vineyards	0.45	0.66	0.77	0.83
Fruit trees and berry plantations	0.45	0.66	0.77	0.83
Olive groves	0.45	0.66	0.77	0.83
Pastures	0.30	0.58	0.71	0.78
Annual crops associated with permanent crops	0.58	0.73	0.82	0.87
Complex cultivation patterns	0.58	0.73	0.82	0.87
Land principally occupied by agriculture with significant areas of natural vegetation	0.52	0.70	0.80	0.85
Agro-forestry areas	0.45	0.66	0.77	0.83
Broad-leaved forest	0.36	0.60	0.73	0.79
Coniferous forest	0.36	0.60	0.73	0.79
Mixed forest	0.36	0.60	0.73	0.79
Natural grasslands	0.49	0.69	0.79	0.84
Moors and heathland	0.49	0.69	0.79	0.84
Sclerophyllous vegetation	0.49	0.69	0.79	0.84
Transitional woodland-shrub	0.36	0.60	0.73	0.79
Beaches. dunes. sands	0.76	0.85	0.89	0.91
Bare rocks	0.77	0.86	0.91	0.94
Sparsely vegetated areas	0.49	0.69	0.79	0.84
Burnt areas	0.77	0.86	0.91	0.94
Glaciers and perpetual snow	1.00	1.00	1.00	1.00
Inland marshes	1.00	1.00	1.00	1.00
Peat bogs	1.00	1.00	1.00	1.00
Salt marshes	1.00	1.00	1.00	1.00
Salines	1.00	1.00	1.00	1.00
Intertidal flats	1.00	1.00	1.00	1.00
Water courses	1.00	1.00	1.00	1.00
Water bodies	1.00	1.00	1.00	1.00
Coastal lagoons	1.00	1.00	1.00	1.00
Estuaries	1.00	1.00	1.00	1.00
Sea and ocean	1.00	1.00	1.00	1.00

If $D_i = 0$ then $DI_i = 1$, while if $D_i = \infty$ then $DI_i = 0$.

For the Viterbo Province the PNPI [7] was adapted to match the characteristics of the available datasets. For the purpose of watershed delineation, a 75 meters resolution DEM was used together with the hydrological network on the scale of 1:250 000 produced APAT (Italian Agency for Environmental Protection and Technical Services) [10]. The permeability was derived from a lithological map on a scale of 1:50 000. The land use map derives from the "Corine land cover 2000" project [11].

In order to define protection or restoration policies

Table 3 | *Slope correction coefficients for the calculation of the Run-off indicator [9]. The coefficient is added to the Run-off coefficient as derived from* Table 2*; if the total is bigger than 1 it is nonetheless equalized to 1*

Slope classes (degrees)	Correction coefficient
< 2°50'	0
2°50'-3°41'	0.1
3°41'-4°32'	0.2
4°32'-5°23'	0.3
5°23'-6°14'	0.4
6°14'-7°05'	0.5
7°05'-7°56'	0.6
7°56'-8°47'	0.7
8°47'-9°38'	0.8
9°38'-10°29'	0.9
> 10°29'	1.0

it can be very useful to know which river stretches suffer the highest pressure from diffuse sources. While the PNPI as it is shown in *Figure 1* describes how diffuse sources are scattered across the watersheds, it is possible to focus on one single basin and estimate the pressure affecting the different parts of its river network. To do so, the river network can be divided into segments and for each segment the sum of all related pressures can be calculated. This allows the creation of a map that can support studies of hydrological network vulnerability. In *Figure 2* it is shown this type of output for the Mignone river basin, which is partly within the Viterbo Province. For this exercise, the river network was divided into portions 5 kilometres long and the relative quality classes were depicted using the usual representation (darker segments correspond to higher pressure).

RESULTS

An extremely important part of the project dealt with the experts' consultation through which the core of the knowledge base was created. Some of the experts selected had a specific knowledge of the study area while some others had not. In addition to the authors of the paper, seven experts were consulted (see acknowledgements below). They expressed their opinion on the weights for the three indicators (LCI, ROI, DI) and they also estimated the potential pollution generated by the different land uses.

In *Table 1* we present the average weights given to the three indicators by the experts and the relevant standard deviations. It is clearly shown that land use is considered to be the most important indicator among the three and the relatively low values of the standard deviations are proof of the substantial agreement among the consulted experts.

In *Table 4* it is shown the potential generation of pollution for different land use classes as evaluated by the experts; the potential ranges from 0 to 10. We should stress that densely built areas and intensively cultivated fields score the highest coefficients whereas natural and unaltered zones are, not unexpectedly, placed at the opposite end of the scale.

The output of the calculation can be presented in the form of maps depicting areas that are more likely to produce pollution (darker areas in *Figure 1*). PNPI works at watershed level, in this case results from adjacent basins were put together on a GIS system for display purposes. One clear feature in *Figure 1* is the concentration of high pressure areas (black areas in the Figure) along the river network. This is due to the relatively high weight assigned by experts to the Distance Indicator; in the map it is made evident to land use planners and decision makers that the territory in the vicinity of the rivers plays a key role in generating diffuse pollution.

As proof of concept, in *Figure 2* it is shown how it is possible to aggregate the PNPI index so as to identify the segments of the river network that undergo the highest pressure in terms of diffuse pollution. In this representation, darker areas are more at risk of diffuse pollution. This does not directly entails that they are more vulnerable; if a continuous and substantial riverine vegetation is present, the pressure can be largely absorbed and the impact may be limited.

DISCUSSION

The use of land cover maps to monitor and control sources of diffuse pollution appear very promising. Other sources of diffuse pollution such as atmospheric depositions can play a significant role in the overall nutrient budget of a watershed, but such sources are more homogeneous in space than the land-based ones; in addition, the spatial resolution of the available datasets of atmospheric depositions is normally very coarse (*e.g.*, in Italy the resolution is 50 km) which makes them unfit for an accurate GIS-based analysis. Besides, the authors decided to concentrate on the land based sources because they are much more dependent on local policies and therefore they can be more easily integrated in decision making processes.

In the calculation of the PNPI the experts' judgment is highly critical. This work and the related experts' consultation substantially confirmed the weights originally assigned by the index developers in a previous work on the Tevere river basin [7, 8] thus testifying to the soundness of the assumptions. However, the weights remain eminently subjective in nature and there is a need to assess the sensitivity of the index to the weights used. Some tests, not presented in this paper, were made for the Viterbo Province by using the values assigned by individual experts. On the whole, it appeared that the macro-pattern of the pollution sources remained unchanged, differences being very limited in space. It seems reasonable to assume that decisions on which areas to tackle first to reduce diffuse pollution

would not be affected to a large extent by the use of weights given by different experts.

In the results section it is also underlined the close association between hydrological network used as input and the PNPI map. This implies that the use of GIS-layers for the river network at a differed resolution (and detail) would give different results. PNPI users are encouraged to adopt the hydrological network that is more relevant at the scale of the intervention: if the objective of the study is to identify

Table 4 | *Estimated diffuse pollution generation of Corine land cover classes as resulted from an experts' consultation. The table reports the average values of the consultation and the relevant standard deviations. Experts were asked to assign a score ranging from 0 (minimum pollution) to 10 (maximum pollution)*

Corine land cover class	Score - Average value (0 - 10)	Score - standard deviation
Continuous urban fabric	8.22	2.22
Discontinuous urban fabric	6.89	1.36
Industrial or commercial units	7.78	2.49
Road and rail networks and associated land	5.67	2.55
Port areas	7.00	3.10
Airports	5.56	1.67
Mineral extraction sites	7.78	1.72
Dump sites	8.11	2.32
Construction sites	7.22	2.54
Green urban areas	2.33	1.66
Sport and leisure facilities	3.00	1.66
Non-irrigated arable land	6.33	2.50
Permanently irrigated land	8.89	2.03
Rice fields	7.67	1.80
Vineyards	7.00	2.24
Fruit trees and berry plantations	7.89	2.26
Olive groves	5.22	1.99
Pastures	4.00	2.35
Annual crops associated with permanent crops	7.44	2.24
Complex cultivation patterns	6.89	1.96
Land principally occupied by agriculture. with significant areas of natural vegetation	5.67	1.94
Agro-forestry areas	2.89	2.03
Broad-leaved forest	0.56	1.13
Coniferous forest	0.56	0.88
Mixed forest	0.44	0.88
Natural grasslands	1.94	2.27
Moors and heathland	0.56	1.01
Sclerophyllous vegetation	0.22	0.44
Transitional woodland-shrub	0.78	1.09
Beaches, dunes, sands	0.78	1.64
Bare rocks	0.00	0.00
Sparsely vegetated areas	0.89	1.96
Burnt areas	2.67	2.24
Glaciers and perpetual snow	0.11	0.33
Inland marshes	0.89	1.17
Peat bogs	1.00	1.50
Salt marshes	0.44	0.88
Salines	0.43	1.13
Intertidal flats	0.43	1.13
Water courses	0.14	0.38
Water bodies	0.88	1.81
Coastal lagoons	0.14	0.38
Estuaries	0.43	1.13
Sea and ocean	0.14	0.38

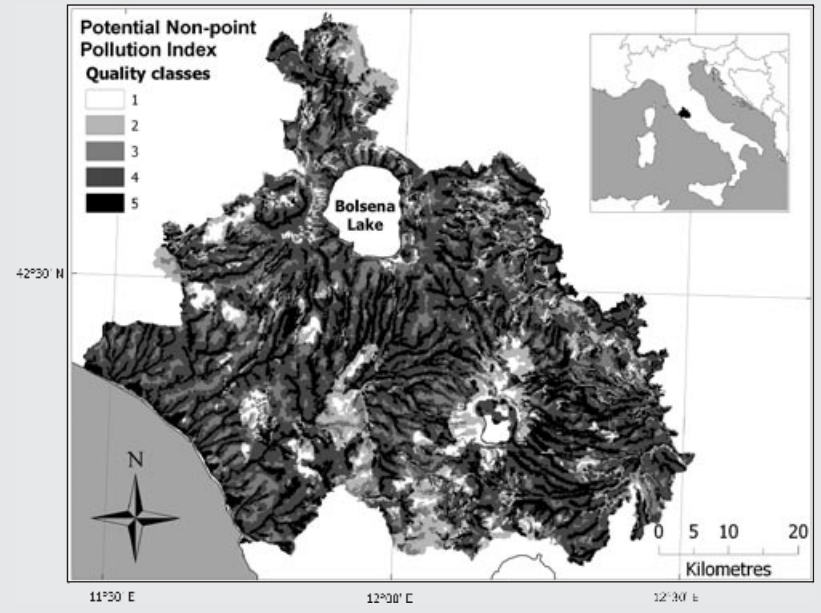

Fig. 1 | *Spatial distribution of the diffuse sources of pollution across the province of Viterbo. Darker areas are characterized by a higher potential for diffuse pollution. In this figure, the results of all watersheds in the province of Viterbo are combined.*

the watersheds more at risk, a coarse river map can be sufficient; on the contrary, a more detailed layer could help select the river stretches or small tributaries that need a wider and more continuous riparian vegetation to balance the higher pollution input.

CONCLUSIONS

Both national and continental legislation on surface water management recently pushed environmental protection authorities toward a deeper commitment to diffuse pollution defence. Nevertheless, tools and skills currently available within mandated control and planning authorities are very often insufficient. Data availability is also a serious constraint to the application of sophisticated models. In this context, PNPI is believed to be a valid support to the monitoring of the aquatic environments and related restoration programmes in accordance with the targets set by the Italian regulations and the European directives [12-14]. A major advantage of such a tool is the capability to investigate the pollution drivers and their spatial distribution, thus making it possible to depict current situation and assess the likely impact of alterative intervention options. The index emphasises the indissoluble link between the river

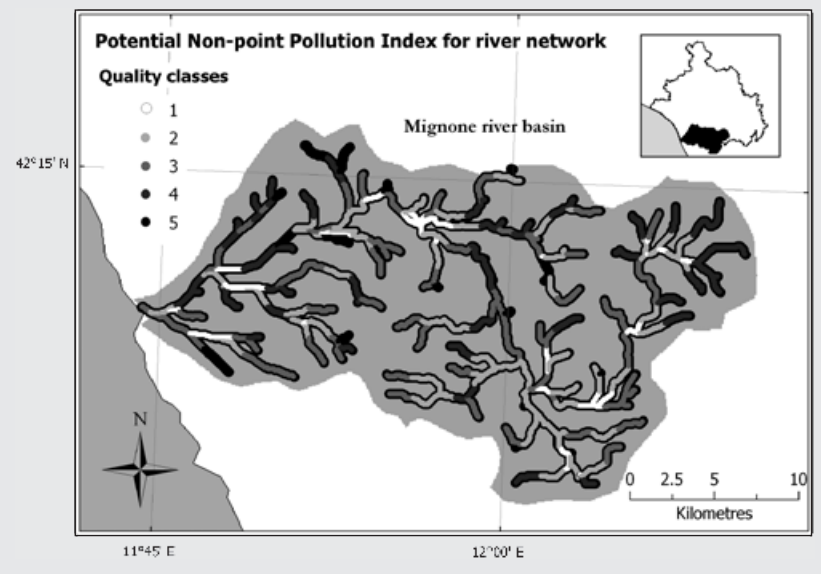

Fig. 2 | *River network vulnerability classes (Mignone basin). Darker stretches are estimated to suffer a more severe pressure from diffuse sources of pollution.*

and its territory and it is meant to facilitate the integration of waterbodies protection into the decision making process and land planning activities. Local authorities such as Viterbo Province could use the PNPI as a synthetic tool for sounder management of river diversions and wells exploitation.

While PNPI as it is displayed in *Figure 1* is more directly concerned with land planning and the strategic environmental assessment, *Figure 2* brings back the focus on the riverine ecosystem and provides an example of how the index can be used to assist the river management and the related monitoring activities; river stretches that undergo a major pressure from diffuse pollution can be identified so that targeted control and protection actions can be taken. In conclusion, it seems that PNPI can effectively support the development of new multidisciplinary methods for riverine ecosystem assessment and it can complement the results of well-established methods such as FFI [2, 3].

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