

# Case studies on public and occupational exposures to electromagnetic fields

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**Abstract:** *Some examples of public health activities concerning protection of general public and workers against electromagnetic fields, carried out at the Italian National Institute of Health, are presented and discussed.*

## 1. Introduction

The Italian National Institute of Health (Istituto Superiore di Sanità, ISS), technical and scientific body of the Italian National Health Service, pursues promotion and protection of public health through activities performed by several Departments and National Centers. Up to the end of 2016 the Unit of Non Ionizing Radiation of the former Department of Technology and Health, and since 2017 the National Center for Radiation Protection and Computational Physics have been involved, among other activities, in protection of public health against risks deriving from exposures to non-ionizing radiation, from static electric and magnetic fields, Extremely Low Frequency (ELF) fields and radiofrequency (RF) fields (usually called “electromagnetic fields”, or EMFs) to infrared, visible and ultraviolet radiation (“optical radiation”).

Differently from optical radiation, which can pose serious established hazards for human health (e.g. retinal damage from exposure to laser radiation, or skin cancer from exposure to solar and artificial ultraviolet radiation), EMFs can be a matter of concern regarding established health effects just in some occupational settings, while they are very often the subject of widespread worries in population for not established hazards.

In this report, three case studies object of past and on-going activities of ISS are presented and discussed, relating to: 1) general public exposures (health risk assessment of electromagnetic fields emitted by the MUOS satellite earth station in Sicily) [1]; 2) occupational exposures (analysis of regulatory issues in protection of Magnetic Resonance operators exposed to high strength static magnetic fields) [2]; 3) occupational exposures due to common sources of general public exposures like mobile phones (analysis of judicial sentences about electromagnetic fields and tumors) [3].

# Occupational exposure to electromagnetic fields: a look at national research projects

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## **Abstract:**

*This work illustrates some Italian research projects aimed at the protection of workers exposed to electromagnetic fields, also with reference to those bearing active implanted medical devices (AIMD). In particular the Physical Agents Portal and the completed or ongoing research activities developed with the financial support of INAIL are presented.*

## **1. Introduction**

The requirements regarding the protection of workers from the risks arising from electromagnetic fields are set by the Directive 2013/35/EU [1] of the European Parliament and of the Council, published the 26 Jun 2013. In Italy the specific provisions on this topic have been introduced in Chapter IV of Title VIII of Legislative Decree 81/2008 [2], amended in 2016 by Legislative Decree 159/2016 [3], implementing the Directive 2013/35 / EU.

The Decree 159/2016 fully adopts the system of protection of the directive introducing at the same time some more stringent measures aimed at a greater protection of workers. Compared to the first formulation, the current Chapter IV introduces higher complexities in the management of risks arising from exposure to electromagnetic fields (e.g., the derogations system). On the other hand, the decree introduces some novelties in the carry out of the risk assessment aimed at simplifying it whenever possible. Indeed the articulation of Article 209 foresees that the employer may use, at least in the first instance, operational references such as the European Commission's non-binding Practice Guide, relevant European and Italian technical standards as well as information available at INAIL or in regional databases, taking into account also the information provided by the manufacturers for a safe use of the equipment. This formulation qualifies the Italian Physical Agents Portal and validate its content.

Considering the complexity in the risks evaluation and management introduced by the Directive 2013/35/EU, the research activity conducted by INAIL in collaboration with national research institutes and health authorities (ASL) is addressed to the elaboration of procedures for the risk assessment based on standardized protocols for the exposure assessment, in particular regarding the sources of greater interest in the industrial and health environment. The objective is to support the processes of standardization, simplification and reduction of risk according to the provisions of the art. 28 and 29 of the Legislative Decree 81/2008, and to meet the needs of prevention operators and stakeholders, particularly in small and medium enterprises (SMEs). This activity benefits from the experience gained in previous research projects [4-10] both at

# Occupational exposure to electromagnetic fields and prevention of possible adverse effects in workers: results of 20 years of research at the University of Modena and Reggio Emilia

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**Abstract:** *The occupational risk related to electromagnetic fields (EMF) exposure in workplaces is one of the main research fields developed in the last 20 years by the Chair of Occupational Medicine and the Chair of Hygiene of the Public Health Section of the Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia. During this period we have approached several topics in the field of exposure and prevention of EMF risk in occupational settings, including:*

- *the occupational and environmental Extremely Low Frequency – Electromagnetic Fields (ELF-EMF) exposure and effects in different groups of workers;*
- *the possible mechanisms of ELF-EMF effects in biological tissues;*
- *the development of best practices to manage and prevent the EMF related occupational risk in workers according to the European Directives, with particular consideration for health surveillance of exposed workers;*
- *the occupational risk and the health surveillance of Magnetic Resonance Imaging operators;*
- *the epidemiology of proposed adverse long-term effects of occupational EMF exposure.*

## 1. Introduction

Electromagnetic Fields (EMF) are almost ubiquitous in workplaces, and the large majority - almost all - of workers are potentially exposed. Consequently, an adequate evaluation of the occupational risk related to EMF exposure is important to implement an effective prevention, as recognized by authoritative Institutions as the International Labour Organization (ILO) [1] and the World Health Organization (WHO) [2,3]. A specific European Directive, the 2013/35/EU [4], replacing the previous Directive 2004/40/EC [5], has been recently implemented in European Countries, including Italy [6,7], introducing the legal requirement of health surveillance of EMF exposed workers and other important measures for the prevention of EMF related occupational risk. The EU Directive considers only the possible adverse short term effects of EMF exposure in workers, as it states that currently there is no adequate scientific evidence on the possibility of long term adverse health effects, and introduces specific occupational limits based on the results of the works of the International Commission of Non Ionizing Radiation Protection (ICNIRP) [8-10].

# Occupational exposure to electromagnetic fields in healthcare environment

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**Abstract:** *This contribution reports about three projects regarding the evaluation of exposure to electric, magnetic and electromagnetic fields in occupational environments of the healthcare sector. Different aspects of the topic have been addressed throughout the projects: evaluation of biological effects, exposure assessment, and dissemination and education of safety personnel and workers. The activities have been partially supported by INAIL (National Institute for Insurance against Accidents at Work) Campania Region.*

## 1. Introduction

In the last years, our group has been involved in the evaluation of exposure to electric, magnetic and electromagnetic fields in occupational environments of the healthcare sector, by assessing the induction of biological effects, performing exposure assessment, and promoting information and education of safety personnel and workers. The activities have been partially supported by the Regional Technical Advisory Department Risk and Prevention Assessment (CONTARP) of INAIL (National Institute for Insurance against Accidents at Work) Campania Region.

Specifically, two projects were carried out that were focused on workers' exposure in Magnetic Resonance Imaging (MRI) environment, whereas a third one concerned information and

# Electromagnetic Field Propagation in Urban Areas and Exposure Assessment in 5G Scenarios

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**Abstract:** *The fifth generation (5G) of mobile communication systems aims at reaching unprecedented data speed and latency, with limited energy consumption. These goals require a significant increase of the available bandwidth that will be achieved with massive MIMO systems and the use of mm electromagnetic waves. In particular, actual experiments in Europe and United States of America are exploring potentialities and limits of 3.6, 28, 38, 60 and 72 GHz frequencies. This change of paradigm calls for new studies on the exposure of humans to mm waves and the possible biological effects. In this contribution, we present a tool for the evaluation of the electromagnetic field propagation in urban areas, and a layered model as instruments for comprehension of the physical phenomena governing the human exposure in urban areas and the field-tissues interaction at mm waves. The software tool is based on a vertical plane launching algorithm; the layered model on the generalization of the Fresnel coefficients to layered structures. Different significant scenarios will be defined, highlighting the influence of the most significant parameters (urban topology, building size and permittivity, human tissues depths, permittivities and conductivities, and more) on the human exposure in the 5G upcoming environment.*

## 1. Introduction

The design of the fifth generation (5G) of mobile communications is facing fascinating scientific and technological challenges to implement the Internet of Things idea along with several promised band-consuming applications. The new standard is expected to reach data speed up to 20 Gbps with high reliability (latency lower than 1 ms) [1]–[4]. One of the main innovations introduced to achieve the expected performances is the use of millimeter waves electromagnetic fields. This choice, due to the need to use wider bandwidth, requires the reduction of the cell sizes. Indeed, the enhanced free space power loss at high frequencies calls for an ultra-densification of the cells number. Such a change required and still requires intensive

# Microwave Tomography for Monitoring and Diagnosis of Stroke

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**Abstract:** *This chapter presents an overview of the ongoing efforts and the results achieved at CNIT in the framework of the application of microwave tomography for the diagnosis of brain stroke. These research activities are motivated by the current lack of clinical devices able to perform stroke diagnosis before hospitalization, in order to promptly identify the most suitable treatment, as well as by the need of performing continuous monitoring at the patient's bedside during the post-acute stage, in order to implement more effective therapies. The outcomes so far obtained confirm the potential of microwave imaging technology as a candidate to address this clinical need and motivate further developments aimed at the pre-clinical validation of this technology.*

## 1. Introduction

In the last years there has been an intense research activity, both at national and international levels, focused on using alternative diagnostic methodologies for brain stroke detection and monitoring. Indeed, brain stroke is one of the major causes of mortality and permanent disability [1], and its impact on the society is expected to become even more significant in the near future due to the increase in the population age. Key aspects in stroke treatment are represented by the ability of

## 1. Introduction

Thermal Ablation (TA) is a minimally invasive therapeutic technique aimed at destroying pathologic tissues by way of a very high and localized temperature increase. The temperatures needed to destroy the tissue, thus inducing thermal ablation, are about 55–60 °C; in fact, at these temperatures, an almost instantaneous irreversible cellular damage occurs [1], [2]. Such high temperatures can be induced into the pathologic tissue by way of several physical sources, such as ultrasound (US), laser, and radiofrequency (RF) or microwave (MW) electromagnetic field.

Microwave thermal ablation (MTA), which uses electromagnetic fields at microwave (MW) frequencies to induce ablation, gained increasing attention in the most recent years thanks to its low cost, minimal invasiveness, as well as several advantages over the other competing techniques, in particular with reference to RF thermal ablation [3]. Several commercial MTA devices were developed, e.g. Cetrus™, NeuWave; AMICA™ HS Medical; Emprint™, Covidien / Medtronic; Acculis MTA, Angiodynamics / Microsulis, etc. Clinical indications include the treatment of several types of tumours e.g. in the liver, lung, kidney, etc. [4]–[7]. In MTA treatment of tumours, the goal of the therapy is to thermally ablate the entire tumour volume plus a safety margin of healthy tissue, which is about 0.5 – 1.0 cm [2].

MTA set-ups usually include a MW power generator, able to supply up to about 150 W at the operating frequency (typically 915 MHz or 2.45 GHz), an interstitial MW antenna applicator, and a cooling system used to keep the antenna temperature at safe values. The clinical practice consists in positioning the antenna applicator in the centre of the tumour to be treated, usually through image-guided procedures, and in delivering a definite power value for the time of choice. Accordingly, the treatment planning consists in defining the optimum position of the applicator, the microwave power radiated by the antenna, and the time of irradiation needed to cover the whole target area. Several techniques have been used to monitor the development of the thermally ablated area during the treatment. At the very beginning, thermocouples, thermistors, and fibre optic probes were used. Nowadays, non-invasive temperature monitoring methods are explored. They include US, infrared (IR), computed tomography (CT), and magnetic resonance (MR) imaging. However, all mentioned techniques have shown severe drawbacks, such as ambiguity in differentiating ablated, untreated malignant, and untreated normal tissue (e.g. US, IR), or safety concerns with the use of ionizing radiation (CT), and electromagnetic compatibility issues with the MW field (MRI), to cite the more important ones. Thus, the lack of a reliable monitoring system to be used during the procedures is one of the main shortcomings of MTA techniques.

Recently, microwave tomography (MWT) was proposed as an alternative method to monitor MTA during the treatment [8]–[10]. MWT is an imaging technique, which generates images of the human body differentiating the dielectric properties of the different tissues. The imaging device consists of an array of antennas placed outside the region wherein the object to be imaged is located. These antennas act in turn as transmitter and/or receivers. The received signal, which consists in the electromagnetic field scattered by the human body, is then processed to retrieve the target region morphology and the map of its electromagnetic properties. In the framework of medical applications, MWT was mainly developed with reference to the diagnosis of breast tumour [11] but other applications such as for instance brain stroke imaging are nowadays emerging [12].

The proposal of using MWT to monitor MTA procedures relies on the experimentally measured dependence of dielectric properties of tissues from the [13], [14]. In fact, experimental results showed an irreversible decrease of both relative permittivity and electric conductivity at temperatures between 60°C and 90°C, and a dramatic drop as the temperature rose over 90°C.

# Magnetic Nanoparticles Enhanced Microwave Imaging

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**Abstract:** *The recent advancements of nanotechnology are giving a considerable impulse to the development of new biomedical applications as well as to the improvement of the existing ones. One of these applications is the use of nanoparticles as contrast agents in medical imaging. This chapter focuses the attention on magnetic nanoparticle enhanced microwave imaging, a diagnostic modality recently proposed by CNIT researchers that exploits magnetic nanoparticles as modulable contrast agents for the early diagnostic of breast cancer using microwave tomography.*

*In this chapter, we provide an overview on the state of art of magnetic nanoparticle enhanced microwave imaging, starting from the results of the numerical analysis up to the first outcomes of the ongoing experimental assessment, with particular attention to the open questions and the future developments.*

## 1. Introduction

The recent advances in manufacturing a large variety of nanoparticles (NPs), with tuned physical and chemical properties, have opened new exciting possibilities, especially in medicine. To date, NPs of different types have been proposed in several applications, from the diagnostic (as contrast agents) [1-2] to the therapy [3]. Moreover, the use of NPs is also expected to promote the development of new *theranostic* tools, since the same NPs employed as contrast agents at the diagnostic stage can act as therapeutic agents in the subsequent treatment stage. Among the available NPs, Magnetic Nanoparticles (MNPs) are very interesting, as they show some peculiar features which make them particularly suitable for the aforementioned purposes. First of all, they are biocompatible and well tolerated by the human body. Furthermore, they can be coated with a large variety of polymers and biomolecules



# High Permittivity Materials in Magnetic Resonance Imaging

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**Abstract:** *We present an overview, with advantages, drawbacks and challenges of ultra-high field magnetic resonance imaging scanners. Ultra-high field (> 3 Tesla) scanners have the main goal to increase the signal-to-noise ratio (SNR) and, as a consequence, the accuracy of the diagnostic technique. The widespread adoption of these scanners has been so far limited by two main issues: the inhomogeneity of the images due to the interaction between electromagnetic fields and human tissues and the safety concerns related to the exposure of the patients to higher electromagnetic fields.*

*Current research activities are focused on the optimization of the radiofrequency (RF) coils to maximize the SNR and minimize the specific RF energy absorption rate (SAR). In this work, new approaches based on the integration of high permittivity materials (HPM) and RF coils will be discussed, analyzing the effects of HPMs on the magnetic resonance performance. The effects of the HPM characteristics (size, position, permittivity, conductivity, and more) on the magnetic field homogeneity and on the electric field (which is closely related with the SAR) will be presented and discussed with the support of analytical and numerical methods. The activities described here are conducted in the frame of a research and teaching collaboration between New York University and University of Napoli Federico II.*

## 1. Introduction

This chapter describes the research themes related to an ongoing collaboration between the Department of Radiology, School of Medicine, New York University (NYU) and the Departments of Physics and of Electrical Engineering and Information Technology of the University of Napoli Federico II (UNINA).

# Measurement of Breathing Rate and Body Position by Electromagnetic Sensing

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**Abstract:** *In this paper, a novel electromagnetic measurement method for the determination of the respiration frequency and the position of a subject is presented. The apparatus is based on the measurement of a set of reflection coefficients during a frequency scan. Respect to other e.m. systems, based on continuous wave (CW) or Ultra Wide Band (UWB) techniques, the proposed method offers the advantage to use only a single antenna and represents a good compromise between these two consolidated techniques, guaranteeing the advantages of both methods. In particular, the solution proposed resolves the known problem of blind frequencies, which limits the CW approach. The novel measurement technique can provide with a unique apparatus, simultaneously, without contact, and with a robust approach respect to the problem of blind-frequencies, position and respiration rate of the subject. Results from the experimental tests show high correlation respect to the reference instrumentation for the measure of distance and respiration rate. Even if the proposed approach in principle could be used also for different measurement and instrumentation fields, the paper explores its use for the assessment of the respiration frequency and the subject position for use both in clinical and domestic environments.*

## 1. Introduction

Respiratory activity is one of the fundamental physiological functions (also named vital signs) of a human being. The presence of respiration acts, their frequency and the possible interruptions or sudden rate variations are quantities of great interest for monitoring the activity of hospitalized patients, such as the case of subjects recovered in intensive care units. More in general, an important issue in the medical field is the monitoring of the respiratory conditions of patients with respiratory-related pathologies such as the obstructive sleep apnea syndrome (OSAS), affecting 4% of adult males or the sudden infant death syndrome (SIDS), which is the third leading cause of infant mortality.

# Software-Defined Radar Sensor For Biomedical Applications

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**Abstract:** *Non-contact wireless sensing approaches have emerged in recent years to enable novel enhanced developments in the framework of healthcare and biomedical scenarios. One of these technologically advanced solutions is given by Software-Defined Radar platform, a low-cost radar implementation, where all operations are implemented and easily changed via software. In the present Chapter, a Software-Defined Radar implementation with Doppler processing features is presented to be applied for the non-contact monitoring of human respiration signals. A quadrature receiver I/Q architecture is adopted to overcome critical issues related to the occurrences of null detection points, while phase-locked loop components included in the Software Defined Radio transceiver are successfully exploited to guarantee the phase correlation between I/Q signal components. The proposed approach leads to a compact, low-cost and flexible radar solution, whose application abilities may be simply changed via software, with no need for hardware modifications. Experimental results on human target are discussed to demonstrate the feasibility of the proposed approach to vital signs detection.*

## 1. Introduction

The rapid advances in wireless technologies make now feasible the implementation of compact, lightweight and highly integrated systems to improve life quality through early diagnosis and continuous non-invasive monitoring of physiologic parameters [1].

Radar-based techniques are historically employed (since late 1970s) to detect human vital signs, such as respiration and heartbeat, by analyzing the interaction between radiofrequency signals and physiological movements, without requiring any contact with the human body [2].

In particular, Doppler radar sensing devices [3-5] transmit a continuous wave (CW) signal, which is reflected off the human target and successfully demodulated at the receiver stage to provide a signal proportional to the target oscillation. If analyzing the received signal, a time delay with respect to the transmitted wave can be identified. It is determined by both the

# Bio-Integrated Epidermal Wireless Sensors for Human Health Monitoring and Sensation Recovery

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**Abstract:** Originally introduced by the material science community, skin-mounted electronics is nowadays the new frontier for unobtrusive body-centric monitoring systems. Current advances of the Radiofrequency Identification (RFID) technology can boost this emerging class of bio-integrated skin devices exploiting low-power (even passive) wireless communication and sensing interfaces. This contribution resumes the performance of UHF RFID epidermal antennas, their optimal size and the upper bounds in the achievable radiation gain. Finally, three promising applications are introduced. Two of them are devoted to the remote and unobtrusive monitoring of human health, the third one aims at helping impaired people in restoring and enhancing their sensory capabilities.

## 1. Introduction

*Epidermal* or *Skin Electronics* [1] is a currently emerging research trend combining multi-disciplinary backgrounds such as Material science, Mechanics, classic Electronics and Electromagnetics and Communications. Recently published papers [2], demonstrated the possibility to fabricate skin-like electronics and sensors that are suitable to be deployed over thin and bio-compatible conformable membranes for direct placement over living organisms (e.g. tissues), environmental substrates (plants or stems) and foods [3]. The direct “on-skin” sampling of surface temperature, humidity, pH, deformations, skin impedance and electrophysiological potentials by means of plaster-like complex devices may enable a fan of new applications to consumer electronics, human health and wellness as well as to nutrition. In this scenario, the virtuous synergy of Epidermal Electronics with the well-assessed passive Radiofrequency Identification (RFID) technology [4] could boost the usability of skin devices in the real world, providing a further brick of the quickly emerging Internet of Things [5]. The communication through electromagnetic backscattering, as involved in the RFID architectures, requires just a small battery-less IC transponder that is fully compatible with thin and flexible devices. Furthermore, thanks to the intrinsic sensing capabilities of RFID platforms [6], designing epidermal wireless sensors without the need of dedicated and complex electronics integrated into the device, becomes possible. Indeed, strain [7], temperature [8], chemical [9] epidermal battery-less sensors have been recently proposed for the monitoring of fever, breath and physical activity and rehabilitation [10], [11].

# The use of biophysical stimulation in traumatology and orthopaedic practice: electrical stimulation for bone repair and chondroprotection

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**Abstract:** *Biophysical Stimulation (BS) is a local and non-invasive treatment routinely applied in the orthopaedic practice to improve endogenous reparative and anabolic activities of bone and cartilage tissues. Three different BS techniques have been developed: i) electrical energy directly applied to the tissue (capacitively coupled electrical field, CCEF); ii) electromagnetic energy induced using coils (pulsed electromagnetic fields, PEMFs) and iii) mechanical energy directly applied through a mechanical transducer (low intensity pulsed ultrasound system, LIPUS). Pre-clinical research showed that biophysical stimuli trigger a cascade of intracellular events through the cell membrane. In bone cells, BS enhances cellular proliferation and increases synthesis and release of growth factors. In in vivo models, BS has been shown to increase the mineral apposition rate and the formation of the bone callus. BS has been successfully used in clinical settings for the treatment of several skeletal disorders such as fractures, delayed unions and non-unions. In articular cells, PEMF stimulation exerts a strong agonistic effect on  $A_{2A}$  and  $A_3$  adenosine receptors, resulting in a robust anti-inflammatory and chondroprotective effect. In animal models of osteoarthritis (OA), PEMFs stimulation was able to halt the progression of OA and to preserve the quality of the cartilage. In joint pathologies, PEMFs have been effectively applied to control the inflammation, protect the mechanical and biological properties of the cartilage and to prevent chronic pain and functional disabilities. Extensive preclinical and clinical research demonstrates the effectiveness of BS for bone healing and cartilage preservation, thus BS represents a new powerful tool available to orthopaedics to reduce healing time and improve patient functional recovery.*

## 1. Introduction

Clinical biophysics is the branch of medical science that studies the action and the effects of non-ionizing physical stimuli on biological systems. Clinical biophysics applies the essential principles of pharmacological research: it studies the specificity of the physical stimuli, investigates the mechanisms of action and evaluates the employment in pathological conditions. Based on pharmacology principles, the effects exerted by the physical stimulus (“biophysical stimulation”, BS) will be specific to a function rather than being cell or tissue specific, thus anticipating its use in all conditions affected by the modulation of that specific function. Through the cell membrane, the physical signal triggers a series of intracellular events that result in a specific biological response: the mechanisms of signal transduction is different for each type of energy involved. Three different methods for the administration of physical energy for clinical applications have been developed: i) electrical energy directly applied to the tissue (capacitively coupled electrical field, CCEF); ii) electromagnetic energy induced using coils

# Cellular Effects of $\mu$ s to $\text{ms}$ Pulsed Electric Fields: experimental observations and numerical modeling

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**Abstract:** Pulsed Electric Fields (PEF) is an innovative, non-thermal, breakthrough technology relying on electroporation (EP) of cell membranes (human, animal, plant and microbial), that is becoming increasingly popular for biomedical and industrial applications. As an example, in electroporation-based cancer treatments, PEF technology enables enhanced and selective drug permeation in cancer cells (electrochemotherapy), while in food process it represents a highly efficient alternative to conventional treatments for microbial inactivation.

The use of PEF technology is still limited by the lack of complete knowledge on basic mechanisms of EP and resealing of biological membranes, and on the role played by the main electric parameters (pulse duration, repetition rate, electric field amplitude). Here, the emphasis is on the health-related applications of PEF technology. The recent research activities carried out by the Bioelectromagnetic group at CNR –IREA, in cooperation with the Dept. of Information and Electric Engineering and Applied Mathematics of the University of Salerno, are presented, which aim to investigate the interaction mechanisms between PEFs and mammalian cells.

## 1. Introduction

The external application of high intensity, short-duration pulsed electric fields (PEF) to cells and tissues increases the permeability of cell membranes to otherwise impermeant molecules, through the formation of aqueous pores in the lipid bilayer [1]. This phenomenon, termed electroporation (EP), although not completely understood, has been widely studied, and different biotechnological and industrial applications have been developed, spanning from the treatment of cancer tissues [2], to the extraction of valuable compounds [3] and microbial inactivation in food preservation and processing [4].

Successful applications have been developed in cancer therapy, which rely on the applications of PEF with high intensity (kV/cm) and duration in the  $\mu$ s to  $\text{ms}$  range. Such applications include electrochemotherapy (ECT), gene electrotransfer and irreversible electroporation (IRE) [5].

# Magnetic Biomaterials for Hyperthermia and Tissue Engineering

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**Abstract:** *Magnetic biomaterials represent a powerful and attractive therapeutic solution to several biomedical problems. The embedding of magnetic nanoparticles in a biocompatible polymeric or ceramic matrix allow the manufacturing of a synthetic bone implant which can be remotely controlled by an external magnetic field to elicit a specific therapeutic effect in situ. In orthopedic oncology these biomaterials can be employed to treat residual cancer cells after tumor resection/reduction by applying a radiofrequency field and heating the target tissue, thus performing local hyperthermia treatment. The modelling of the heat dissipation dynamic and the multiphysic non-linear problem are managed to assess the effectiveness of magnetic biomaterials for the treatment of Fibrosarcoma and Osteosarcoma. Moreover, these biomaterials have the potential of being used as an in vivo magnet to attract magnetic carriers conjugated with growth factors, which would attract mesenchymal stem cells to the scaffold, thus favoring the bone healing process.*

## 1. Introduction

In the biomedical research field the manufacturing of innovative devices capable of inducing therapeutic actions or facilitating the tissue healing process is a pivotal point [1]. Among the target tissues, bone is a very relevant and peculiar system for which specific, smart, multifunctional and theranostic solutions must be devised [2]. Indeed, when bone tissue is injured and the defect size is higher than 0.5 cm, in clinical practice a synthetic biomaterial is employed to fill the cavity and mechanically support the damaged tissue, while allowing osteoprogenitor cells to seed, proliferate and differentiate [1], [2]. Such prosthetic implants are usually called scaffold and, nowadays, they are designed to control cell microenvironment and exert a direct, controlled physical stimulation of bone tissue, thus being a new and powerful class of therapeutic devices suitable for different clinical purposes in orthopedics [1]-[3].

Multifunctional scaffolds can be synthesized by modifying and functionalizing traditional ceramic or polymeric materials with biomolecules (e.g. growth factors), or by properly tuning their chemical structure to respond to external stimuli (e.g. hydrogels) [2], [3], otherwise incorporating magnetic nanoparticles (MNPs) in biocompatible matrix allows to develop a remotely controlled magnetic object with ad hoc properties [1]. Impregnating polymer with MNPs, or chemically doping with  $\text{Fe}^{2/3+}$  ceramic materials produce a

# Magnetic Nanoparticles as Nano-Heaters and Modulable Contrast Agents in Magnetic and Microwave Hyperthermia

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**Abstract:** *The advances in nano-components design and manufacturing have led to the development of new approaches for improving the performance of Hyperthermia in oncological therapy. Within this framework, this chapter gathers some recent contributions addressing two open clinical challenges.*

*The first regards the Magnetic Hyperthermia, in which the tumor is heated by exploiting magnetic nanoparticles, excited by a low frequency magnetic field. Although the clinical adoption of Magnetic Hyperthermia has been already approved, in particular for the treatment of brain tumors, its implementation is still not optimized, as the choice of the nanoparticles and magnetic field parameters is still based on empirical criteria, while the individuation of the best working conditions is crucial to optimize the effectiveness of the therapy. Hence, we report a rigorous criterion for the optimal choice of the aforementioned parameters, together with the results of numerical studies showing the effectiveness of such criterion and the concrete advantages of its application in the treatment planning.*

*The second contribution deals with the exploitation of magnetic nanoparticles as modulable contrast agents in Microwave Hyperthermia, in order to guide the focusing on the tumor of the field emitted by an antenna array, without requiring any a priori knowledge on the geometry and the electric properties of the region to be treated. This would allow overcoming the drawbacks related to the unavoidable uncertainty in the knowledge of such parameters. In a wider perspective, it would allow to develop a “theranostic” tool, wherein the magnetic nanoparticles are exploited first to image the tumor and then to focus the field for its treatment.*

## 1. Introduction

In recent years, the advances in manufacturing engineered nanoparticles (NPs), with controlled physico-chemical properties, have led to the development of novel biomedical applications. To date, exploitation of many kinds of NPs has been proposed, both in diagnostics [1-2], as contrast agents, and in therapy, mainly in oncological hyperthermia [3] or for drug deliver [4].

Among the available NPs, iron oxide NPs (IONPs) are very appealing as they show some peculiar features which make them particularly suitable for the aforementioned applications. Indeed, they are biocompatible and well tolerated by the human body up to amounts of several



# Towards an Optimal and Personalized Hyperthermia Treatment Planning

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**Abstract:** Hyperthermia is under the way to be considered as a first line cancer treatment in combination with radio- and chemo-therapy. In this respect, personalized and accurate treatment planning represents one of the key goals to achieve. From an engineering perspective, this involves two main ingredients: a reliable patient model and an optimizer able to determine the proper excitations to be used in feeding the applicator, i.e., a phased array. The contribution provides a review of the innovative tools developed at CNIT to address these problems. In particular, they are concerned with a low-cost approach to estimate the electromagnetic tissue parameters needed to build the digital patient model and with a treatment planning which allow to design the excitation coefficients feeding the applicator to shape the power deposition in the target area while avoiding undesired heating of healthy tissues. Some numerical examples are presented to show how the proposed tools work.

## 1. Introduction

Hyperthermia cancer treatments take place when the tumor temperature is elevated to a supra-physiologic temperature 40–44°C for 60-90 min. Clinical trials have demonstrated the therapeutic benefits of this treatment in combination with radio- and chemo-therapy [1]. An enhancement of the clinical effectiveness is induced by increasing the temperature according to the thermal dose-effect relations found in literature [2]. In this framework, the accurate planning of the administered heating is a crucial step for further progress and widespread clinical adoption of hyperthermia [3]. This is especially the case for challenging patients and/or