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Experimental Framework for Magnetic Nanoparticles Enhanced Breast Cancer Microwave Imaging

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ABSTRACT Magnetic nanoparticles (MNP) enhanced microwave imaging could provide an effective approach for an early stage diagnosis of breast cancer, if encouraging results coming from accurate and realistic numerical studies are confirmed by an experimental proof of concept framework. To this end, an ad hoc laboratory setup has been designed and built up to verify the possibility of detecting the low signal scattered by MNP when embedded into a simplified but realistic breast phantom. This paper describes the developed measurement setup and the results coming from a first run of experiments, which confirm the possibility to detecting realistic amounts of accumulated nanoparticles. Moreover, the experimental results analysis allows addressing the future developments required to determine the ultimate detection limits of the technique, giving relevant information to plan the preclinical assessment.

INDEX TERMS Contrast enhanced microwave imaging, breast cancer, magnetic nanoparticles.

I. INTRODUCTION

The use of microwave imaging (MWI) for breast cancer diagnosis has been investigated for many years [1], but unfortunately without achieving the expected clinical breakthrough, notwithstanding some clinical evidence of the effectiveness of MWI in detecting and imaging locally advanced breast tumors [2], [3]. One reason for such a state of things is due to the relatively high error rate that can occur when the electric contrast between malignant and healthy tissues is not sufficiently large, as in the case of tumors in fibroglandular tissue [4], [5]. As a matter of fact, this not only dramatically reduces the specificity of a microwave based diagnosis, but also limits its usefulness, given the fact that most breast cancers are located in this kind of tissue.

To overcome such an issue, the use of contrast agents is gaining an increasing interest [6], [7]. In particular, the use of magnetic nanoparticles (MNP) has been proposed to take advantage of their specific features with respect to dielectric contrast agents [8]. As a matter of fact, MNP are already approved for clinical use and can be properly functionalized with antigens specific to tumor cells receptors, so that they can specifically target the malignancy. In addition, the microwave magnetic response of the MNP can be properly modified by applying an external polarizing magnetic field (PMF), which does not influence the response of the surrounding scenario, being human tissues nonmagnetic. As a result, by exploiting a proper differential measurement strategy, one can separate the response of the background from that of the MNP (i.e., the "useful" signal), which, if present, is unambiguously associated to the presence of a malignant lesion [8].

The feasibility of this technique has been investigated, with encouraging results, in the single frequency case by means of accurate and realistic numerical studies [9]–[11], whose main outcomes can be summarized as follows:

- the measurement conditions (in terms of noise level and dynamic range) required to detect the useful signal due

to realistic MNP concentrations are fully consistent with the performance of standard MWI devices [9];
- once the signal is reliably detected, the imaging task can be carried out without requiring patient specific information (e.g., the breast properties) [10];
- 24 properly allocated probes are sufficient for achieving satisfactory imaging results [11].

Notably, the above statements rely on full-wave electromagnetic models and experimentally measured response of MNPs at microwaves [12], [13], so that, in principle, they fully support the expectations for a successful assessment at preclinical level. Nevertheless, before approaching such a challenging stage, the presentation of an experimental proof-of-concept is certainly appropriate, in order to demonstrate that the aforementioned measurement requirements still hold true when dealing with a real system, and that it can be actually met by exploiting standard MW apparatuses. Furthermore, an experimental framework can be strongly useful to identify possible critical aspects that may have been overlooked in the simulations.

According to the above statements, in the present paper the results of an initial set of experiments are presented which are aimed to prove the concept underlying MNP enhanced MWI. They have been carried out by means of a laboratory measurement system specifically designed and built to target such a task. It is worth noting that this work is actually the conclusion of a broad research effort carried out by the authors, whose intermediate outcomes have been partially discussed in a series of papers [14]–[16] presented in the last years at specialized conference. As such, here we are reporting the complementary in depth material not contained in the cited previous communications. In this respect, besides presenting in a unitary way the framework of this design, realization and demonstration effort, reporting the main characteristics of the realized apparatus, the paper conveys a number of original contributions. In particular, thanks to a detailed analysis of the instrumental drift, a new processing strategy to extract the useful signal is presented, which allows a more refined estimate of the detection limits. Moreover, a possible way to overcome the negative influence of both instrumental drifts and possible variations of the electrical scenario is suggested. Finally, we provide a more insightful interpretation of the obtained results, by comparing the experimental results with those achieved by full wave numerical simulations. Notably, this allows to put in evidence some points which are still open and deserve attention before moving to the pre-clinical validation.

Finally, it is worth recalling that the study herein presented is completely different from [17], since detection experiments exploiting a UWB radar system have been therein reported, whereas herein we deal with monochromatic case with respect to which the technique has originally been developed [8] and for which a proof of concept is not yet available. Nevertheless, the promising results presented in [17] has increased the confidence in the success of our study.

The paper is structured as follows. Section II describes the experimental set-up, recalling the idea underlying its design and its components (the phantom, the coupling medium and the antennas). Section III reports the experimental results, obtained by counteracting (as much as possible) the unavoidable instrumental drift. The results are then discussed in Section IV, by making use of the results from the numerical simulations, to address the next steps needed to assess the detectability limits. Conclusions follow.

II. DESCRIPTION OF THE EXPERIMENTAL SET-UP

A device for MNP enhanced microwave breast cancer imaging conceptually consists of two main blocks. The first one is a standard MWI device in which an array of antennas, possibly hosted in a coupling medium, probes the region of interest (ROI) and gathers the backscattered signal. The second block is instead specific of the technique, and consists of an electromagnet that supplies the PMF, whose amplitude modulation induces the variation of the magnetic contrast. This variation, in turn, gives rise to the differential signal needed by the imaging procedure [8], [10].

The proof-of-concept we are aiming at is meant to show that it is possible to detect (at a single frequency and with the needed accuracy) the expected variation of the scattering parameters due to the PMF amplitude modulation that drives the microwave response of MNP. This has to be done in almost actual conditions, that is, with realistic accumulation of MNP, and for a scenario having the typical dimension of the breast and mimicking its electromagnetic characteristics.

The experimental set-up we designed, built and characterized to this end is shown in Fig.1.(a) and is briefly described in the following. For the generation of the PMF, we exploited the electromagnet EMU 75 from SES Instrument PVt. Ltd., capable of generating a PMF having strength of 160 kA/m, at the maximum air gap of 8 cm and input current of 3 A. Due to the limited size of the available air gap, it is not possible to host within the poles of this electromagnet a full scale breast phantom. Hence, our choice has been that of modeling a ‘‘slice’’ (parallel to the chest) of an actual prototype. As such, the MWI part is made of a copper box, which supports the antennas and contains the breast phantom and the surrounding coupling medium. The poles of the electromagnet are placed in such a way to generate a PMF in the central portion of the box, wherein the breast phantom, with a plastic cuvette hosting the MNP, is properly positioned. Note that the copper box also acts as a shield from external interferences. Of course, in the full scale system it will not be possible to confine the breast into a closed box, but the human body itself will act as a shield from the upper direction.

According to the above, the breast phantom mimics a transversal slice of the breast. The phantom is made of two concentric cylinders, 6.4 mm high and 3 mm thick, made of plexiglass (relative permittivity hlequal to 3.6 and negligible losses). The inner cylinder, representing the fibroglandular tissue, has an external radius equal to 10 mm and it is filled with a mixture of 30% Triton X-100 and 70%

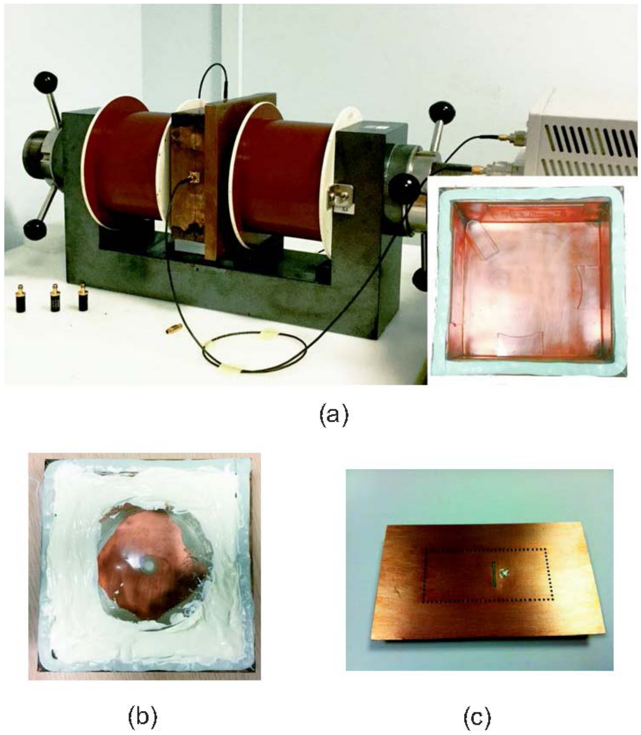

FIGURE 1. **The experimental set up. (a) The copper box which hosts the phantom and the coupling medium is placed between the poles of the electromagnet. The two cavity backed slot antennas mounted on its sides are connected to the VNA. The inside of the copper box is shown in the inset on the right. Note the plexiglass phantom holders and the two antennas on the upper and left sides. The electromagnet is connected to its power supply, not shown. (b) The phantom hosted in the copper box filled with the coupling medium. (c) The cavity backed slot antenna.**

water, having relative permittivity relative permittivity ε_r equal to 48 and conductivity σ equal to 1.5 S/m over the band $2.2 - 2.4$ GHz [18]. The outer cylinder, of radius equal to 60 mm, is filled with pure Triton X-100, having $\varepsilon_r = 5$ and and $\sigma = 0.1$ S/m, over the same band, so to approximate the breast adipose tissue properties. It is worth noting that, while having dimension comparable to an actual breast, the phantom is obviously a rough schematization, as it is circularly symmetric and lacks a layer of skin-mimicking material. However, due the fact that the measurement procedure is intrinsically differential (and the skin is not affected by the PMF), we can safely assume that the phantom sufficiently accounts for the relevant electromagnetic aspects that come into play in the technique.

To simulate the tumor, a 1.5 mL cuvette is put inside the inner cylinder of the phantom. The cuvette is filled with a suspension of 10 nm MNP (Liquid Research Ltd, product code WHKS1S9 (whose microwave response is reported in [12]), in phosphate-buffered saline (PBS, $\varepsilon_r = 80$, $\sigma = 1.7$ S/m), at a concentration of 40 mg/mL. Given the size of the cuvette, this corresponds to a MNP mass of 60 mg. Let us notice that the considered concentration is larger than the one that could be actually reached *in-vivo* with currently available targeting techniques, which is instead in the order of some tens of mg of iron /mL of tumor volume at most [19], [20]. The reason for using such a large MNP is related to the fact that the cuvette containing the MNP would have been no longer accessible once the phantom had been assembled. Hence, we have considered a concentration capable to guarantee a useful signal well above the noise level of the employed measurement apparatus. On the other hand, thanks to the linear dependence of the level of the useful signal on the MNP concentration, this choice does not impair the goal of our study, since the detection limits can be still analyzed by comparing the level measured for the useful signal with the noise level (see Section IV).

The matching medium should have low losses and a relative permittivity in the range [10, 30] [21]. In a first instance, following [22], a water-oil emulsion (36% distilled water, 60% corn oil, 4% HBL10), exhibiting $\varepsilon = 18$ and $\sigma = 0.26$ S/m has been exploited. Unfortunately, such an emulsion is not stable in time, rapidly turning into two separate phases. Hence, to minimize possible changes during the measurements, a commercially available sun cream (Coppertone s.f.p. 50+) has been adopted as a stable coupling medium. The electric properties of this medium have been measured with a standard coaxial cable technique, exploiting the apparatus described in [12], and are quite constant in the $2-3$ GHz band. In particular, at the frequency of interest (see below), we have $\varepsilon_r = 32$ and $\sigma = 0.68$ S/m. Fig.1.(b) shows the phantom hosted in the copper box filled with the coupling medium.

The adopted antenna is a cavity-backed slot, shown in Fig.1.(c), whose design and details have been presented in [14] and [15]. Such a kind of antenna allows to accommodate crucial requirements, namely, a reduced width (for an easy integration with the set-up), the capability of radiating a H-field polarized along the direction of the PMF (to maximize the differential scattered field) [9] and a minimal sensitivity to the variations of the electromagnetic properties of the scenario. To realize the cavity, a substrate integrated waveguide (SIW) approach has been adopted. The antenna is printed on a dielectric substrate having thickness equal to 0.762 mm and relative permittivity $\varepsilon_s = 10$. The SIW cavity is delimited by 1.5 mm spaced via-holes, all having diameter equal to 1 mm. The dimension and the position of the radiating slot, together with the position of the feeding probe, have been properly optimized to achieve good matching conditions in the considered environment.

As the feasibility proof concerns the detectability of the level of the differential signal, only two antennas, located on two adjacent sides of the copper box have been exploited.

The experimental characterization in actual working conditions confirms that the antenna faithfully matches the design goals and shows that numerical simulations very satisfactorily describe the antenna behavior [15]. In particular, at the frequency of 2.32 GHz, wherein the mutual coupling is maximum ($|S_{21}| = -47$ dB), the numerical result matches the experimental one within 1.5 dB accuracy. This is fully compatible with the incertitude in the knowledge of the actual values of the electromagnetic parameters and with the fact that, for simplicity, the presence of the cuvette has not been taken into account in the simulations. From the simulated tangential electric field distribution over the slot aperture, exploiting a plane wave expansion, it has been possible to estimate the antenna efficiency, namely the ratio between the power radiated into the box and that delivered to the antenna, leading to an efficiency of 0.86.

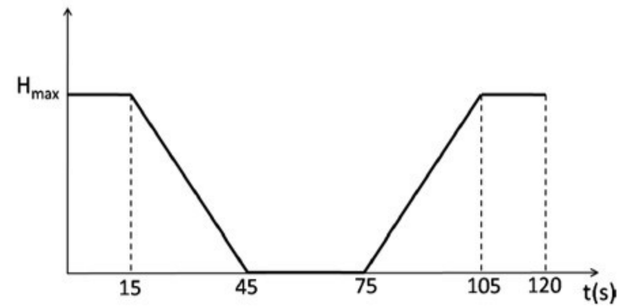

FIGURE 2. The adopted ON-OFF modulation law.

III. EXPERIMENTAL RESULTS: DETECTION OF THE PMF MODULATED SIGNAL

In this first experimental validation, the same PMF modulation law considered in the numerical analysis [9], [10] has been adopted, namely a simple ON-OFF law, with maximum and minimum intensity of the PMF equal to 160 and 0 kA/m, respectively.

With our electromagnet, the time required to switch between the above field values is equal to about 30 s, with a smooth, linear, variation of the field during the transition. This quite naturally leads to the modulation law depicted in Fig.2, namely a duration of the ON and OFF conditions equal to the transition time, with an overall measurement time of 120 s.

The duration of the measurement interval allows to adopt the minimal IF bandwidth (10 Hz), thus minimizing the noise, while allowing to collect many points (1001) within the measurement time span. The corresponding noise floor level is −123 dBm, allowing a SNR of 133 dB, if the highest available input power, equal to 10 dBm, is adopted.

We performed five distinct measurements at the frequency of 2.32 GHz, under the ON-OFF PMF modulation introduced above. The amplitudes of the measured S_{21} are shown in Fig.3. As can be seen, there is a neat separation among the measured traces, due to the instrumental drift. Moreover a drift, well above the noise level, is also present within each measurement. This would induce errors well above the noise level, concealing the response variations due to PMF modulation.

To counteract, at least in part, such a detrimental effect, we have eliminated the linear component of the drift from each trace by performing a linear least square fitting of S_{21} in the ON time interval, $[0, 15] \cup [105, 120]$ and subtracting such linear fit from the measured signal. As can be seen

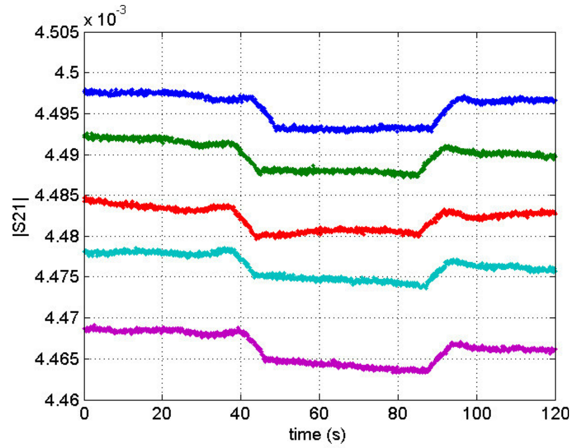

FIGURE 3. ON-OFF S_{21} measurements. The temporal order in which measurements are gathered is from the top to the bottom of the graph.

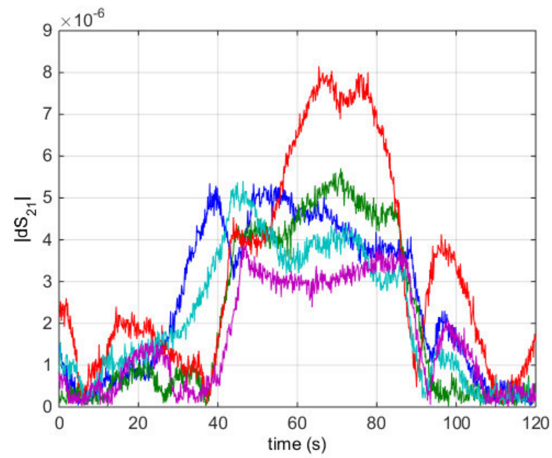

FIGURE 4. The measured S_{21} parameters after the estimated linear component of the drift has been filtered out from each trace.

from Fig. 4, the resulting signals, dS_{21}, are still affected by a significant residual drift. Actually, as shown in [16], the mean square value of the residual drift (in the absence of PMF modulation), is equal to about −118 dB, namely 15 dB higher than the noise level. Hence, we conclude that, in the considered measurement conditions, the minimum detectable signal is actually dictated by the residual instrumental drift, say δS_{21}.

To better understand the nature of such residual drift, we have analyzed the behavior of the complex values of δS_{21} when the PMF is switched off and when it has the maximum achievable amplitude (i.e., 160 kA/m), obtaining the plot reported in Fig.5. As can be seen, the values of the real and imaginary parts of δS_{21} are clustered along a line with a -45^{o} slope, thus exhibiting a strong negative correlation. As such, the mean square value of their sum should be significantly lower than that of δS_{21}. As a matter of fact, it turns out to be about 4 dB lower. This suggests that, in order to reduce the influence of the residual drift, it is convenient to consider

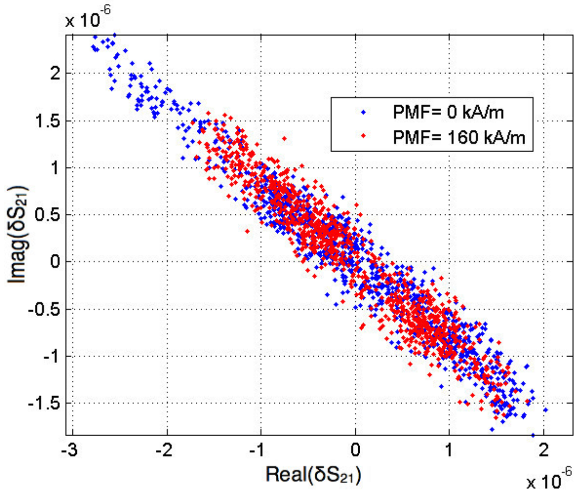

FIGURE 5. Plot of the complex residual drift component dS_{21}.

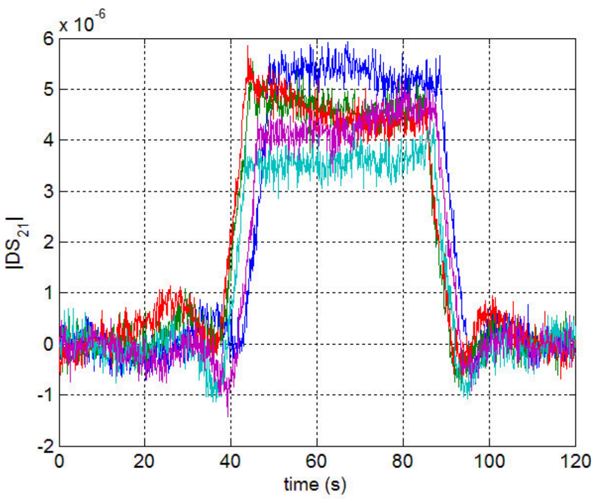

FIGURE 6. ON-OFF measured DS_{21}.

the quantity:

$$DS_{21} = Re(dS_{21}) + Im(dS_{21}), \quad (1)$$

that is, the ''transverse'' part of the scattering parameter dS_{21}.

The obtained traces are reported in Fig. 6, which not only shows that it is possible to successfully reveal the presence of the MNP by modulating their microwave response, but also that, thanks to the processing done to get rid (as much as possible) of the effects of instrumental drift, the dispersion between the measurements has been significantly reduced, as compared to the ''raw'' data (see Fig.3). In the next Section, we exploit such results to appraise the minimal amount of MNP that can be actually detected in the considered experimental conditions.

IV. DISCUSSION AND INTERPRETATION

To assess the actual detectability limits of our experimental set-up, let us recall that as DS_{21} is linearly related to S_{21}, the amplitude of its modulation, induced by the PMF, is proportional to the MNP mass [8]. Hence, as long as the value of DS_{21} in the ON state is separated from the value of of DS_{21} in the OFF state, it will be possible to detect the corresponding MNP mass.

Accordingly, Fig. 6 allows to estimate the amount of MNP that can be actually detected in the considered experimental conditions. To this end, we have to evaluate the modulation amplitude from the available measurements. To counteract the effect of noise, we have performed, for each measurement, the average of DS_{21} over the 201 points centered on the center of the measurement interval (in the OFF condition). The so obtained five amplitude values have a mean equal to 4.5×10^{-6} and a standard deviation equal to 6.7×10^{-7}. It is worth explicitly noting that, as expected, the mean value of the signals in the ON interval is practically zero.

Taking into account the ratio between the mean amplitude and the estimated standard deviation when the PMF is off, it follows that we could lower the modulation amplitude up to a factor of about 6 and still be able to qualitatively appraising the variation of the measured signal induced by the PMF modulation. Since the above results have been achieved with the considered MNP mass of 60 mg, and given the proportionality with the MNP mass, we can conclude that a mass of about 10 mg can be still detected, with a *single measurement*, which compares very well with the amounts which could obtained in tumors of 1 mL volume via active targeting [20]. Notably, without the envisaged processing of the raw signal, to achieve a similar result requires to average all the five measurements [16], with a corresponding increase of the overall measurement time. Viceversa, if performed on the processed measurements, such an average would bring to a standard deviation $\sqrt{N}$ times smaller, with N equal to 5 in our case (and $\sqrt{N} \simeq 2.25$). This means that, the detectable MNP mass (given by the ratio between the average and standard deviation)can be reduced to less than 5 mg.

Although the above MNP amount is well inside the range of an actually achievable delivery, looking at Fig.6, we realize that the residual drift is still significantly higher than noise. This means that if we could envisage some way to overcome the instrumental drift, we could lower the detectability limit up to the noise level, allowing to detect tumors less than one cm in size [9], which would be a substantial clinical achievement.

To this end, it is worth recalling that in our case the drift is slow compared to the single point measurement time (0.12 s). Hence, its spectrum must be confined to frequencies much lower than $0.5/0.12 = 4.17$ Hz. This is confirmed by Fig.7, which shows the power spectra of dS_{21} and DS_{21} for the case of zero PMF. As it can be seen, even in the worst case, namely that of dS_{21}, the spectrum is much larger than the noise at very low frequencies, but it merges in the noise for frequencies larger than 1 Hz.

This circumstance shows the pitfall of the adopted modulation law, namely its extremely low frequency, equal to $1/120$ Hz, which entails that the spectrum of the modulated

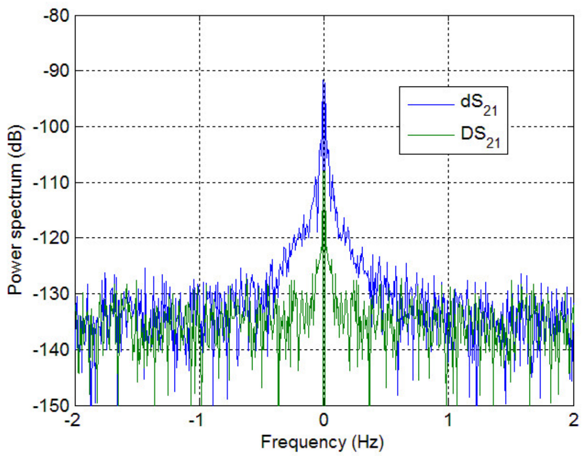

FIGURE 7. Power spectra of dS_{21} and DS_{21}. No PMF.

S_{21} is well inside the drift bandwidth. As such, it follows that improving the detectability limit requires to increase the frequency of the modulation law beyond the drift bandwidth. Notably, choosing such frequency significantly larger than 1 Hz, also allows to avoid the effects of the unavoidable variations of the electric scenario during the actual clinical measurement, due to the vital activity of the patient. However, at such higher frequencies, an on-off modulation is clearly impractical and difficult to achieve, so that a sinusoidal modulation of the PMF becomes more convenient preferable, followed by a coherent detection of the scattered signal through a proper spectral filtering.

To conclude the discussion on the obtained results, we provide a comparison between the measured value of the differential scattering parameter and the one theoretically predicted. As shown in the Appendix, in absence of instrumental drifts and variations of the electrical scenario, the differential scattering parameter can be computed as

$$dS_{21} = \frac{j\omega\mu_0}{4}\Delta\chi V < h^2 >, \tag{2}$$

where ω is the pulsation corresponding to 2.32 GHz, μ_0 is the magnetic permeability in vacuum, $\Delta\chi$ is the variation of the complex magnetic contrast induced by the PMF, V is the volume of the cuvette and $< \cdot >$ denotes the mean value over V and h is the magnetic incident field generated by the antennas for unit incident power.[1] From the results reported in [12], $\Delta\chi = -0.0256 - j0.0155$.

The magnetic field generated by the antennas inside the cuvette has been simulated by using CST Microwave Studio. In these simulations, the presence of the actual cuvette and its holder has not been taken into account, i.e., only its PBS filled interior has been considered in the numerical model. The obtained magnetic field amplitude distribution in the two principal planes is shown in Fig. 8. From these results we obtained $< h^2 >= -0.018 - j0.048$ A^2/m^2 , which leads to $|DS_{21}| = 12.2 * 10^{-6}$, which is almost three times larger than the experimental finding.

[1] Note h is the same for both antennas given the symmetry of the system

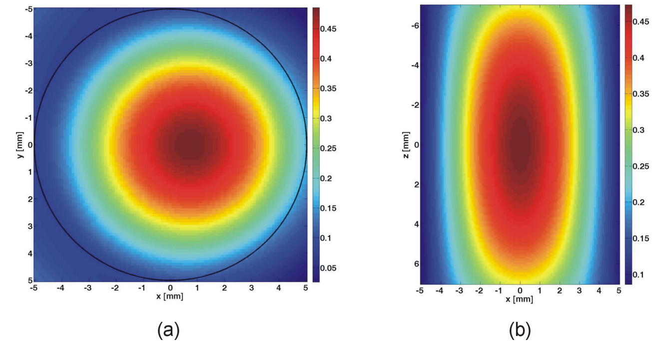

FIGURE 8. Simulated amplitude of the magnetic field inside the cuvette hosting the MNP. (a) equatorial cut; (b) meridian cut.

While such a discrepancy is not very relevant from the practical point of view, as it does not impair the capability of detecting the modulated signal, it is larger than expected, given the incertitude on the electric scenario. A possible reason could be the severe simplification adopted for simulating the cuvette, which is expected to significantly affect the computation of the field at its interior.

Finally, another aspect that an insightful *a posteriori* analysis should take into account is the presence of magnetic effects not accounted for in the theoretical analysis. As a matter of fact, due to the extremely low level of the useful signal, effects of the PMF that are usually completely negligible could come into play and require proper attention. At least two of such effects can be envisaged. The first is the (anisotropic) modulation of the conductivity of the involved media (hence of the equivalent permittivity) due to the Lorentz's force exerted by the PMF on the charge carriers. The second is the presence of unwanted or unforeseen magnetic materials in the measurement set-up, which could modulate the response even in absence of MNP. The presence of these, or possibly other, unwanted weak effects is practically impossible to assess a priori. Hence, we can conclude that, while the reported experimental results fully demonstrate the actual feasibility of MNP enhanced MWI, the assessment of the actual detectability limits requires not only the adoption of proper modulation laws and the development of optimal detection algorithms, but also an experimental, quantitative, investigation of the possible presence of the above-mentioned side effects.

V. CONCLUSIONS

In this paper, we have presented an experimental study aimed at assessing the capability of detecting the microwave signal scattered by a MNP mass when modulated by an external PMF. This principle is the one underlying MNP enhanced MWI, a novel and promising technique for early stage breast cancer diagnosis, whose feasibility is preliminarily demonstrated through our experiments.

To pursue our goal, we have designed and realized an ad hoc set-up. As shown by experimental results the obtained measurements are dominated by drift rather than noise, so that, achieving the ultimate detection limits (which are ideally only dictated by noise) requires to overcome the presence of drift. To this end, the adoption of a sinusoidal modulation will be exploited in the future, as this latter allows to filter out both the drift and the effects of vital signs by simply choosing a high modulation frequency (for instance, > 5 Hz).

In addition, since this system had been previously numerically characterized [16], we have been able to compare the outcomes of the experiments with the values predicted from simulations. This comparison has suggested that some magnetic effect we assumed to be negligible at the design stage is present and may have an influence on the actually detectable amount of MNP. Possible source of "spurious" magnetic modulation could be given by the presence of magnetic materials in the components of the measurement system (cables connectors, etc.), or the presence of Lorentz's force exerted by the PMF on the charge carriers of conductive materials. Hence, to assess the actual detection limits, an accurate investigation of these aspects will have to be carried out.

As a final remark, it is worth mentioning that the most challenging aspect for the actual exploitation of MNP enhanced MWI in the early diagnosis of breast cancer, is linked to the actual possibility of target a sufficient amount of MNP into the tumour via systemic injection. On the other hand, besides the specific diagnostic purpose for which the experimental set-up has been designed, the same concept herein presented could be useful for other applications of microwave in medicine, in which the targeting of MNP is overcome (or it is less crucial). As an example, the estimation of MNP amount accumulated in human tissues could be of interest in magnetic hyperthemia [19], [23], where a higher concentration of nanoparticles is expected, or for the detection of sentinel lymph-nodes [24], where the local injection of contrast agent allows to overcome the very low accumulation of nanoparticles in target tissues.

APPENDIX

The field scattered by the MNP can be seen as due to equivalent magnetic currents, say $\mathbf{M}$, induced by the incident field and radiating in the surrounding dielectric environment. Due to the small magnitude of the magnetic contrast induced by the MNP, such a current can be expressed through the distorted wave Born approximation [25] as

$$\mathbf{M}_1 = j\omega\mu_0\Delta\chi\mathbf{H}_1 = j\omega\mu_0\Delta\chi\mathbf{h}_1\sqrt{P_1}, \tag{A.1}$$

where $\mathbf{H}_1$ is the magnetic field generated by the antenna 1 in absence of the MNP, with an incident power equal to P_1, while $\mathbf{h}_1$ is the magnetic incident field generated by the antenna 1 for unit incident power. By exploiting the reciprocity theorem it is easy to show that the corresponding voltage at the (matched) antenna 2 is given by:

$$V_2 = \frac{1}{2}\sqrt{\frac{Z_0}{2\,P_2}}\int_V \mathbf{H}_2\cdot \mathbf{M}_1\,dV = \sqrt{\frac{Z_0}{8}}\int_V \mathbf{h}_2\cdot\mathbf{M}_1 dV, \tag{A.2}$$

where Z_0 is the characteristic impedance of the feeding cables and $\mathbf{H}_2$ is the magnetic field radiated by the antenna 2 when fed with power P_2 and V is the cuvette volume.

By substituting (A.1) in (A.2) and dividing by the incident voltage on antenna 1 (which is equal to $\sqrt{2Z_0\,P_1}$), we get:

$$dS_{21} = \frac{j\omega\mu_0}{4}\int_V \Delta\chi\mathbf{h}_1\cdot\mathbf{h}_2 dV, \tag{A.3}$$

where $\Delta\chi$ denotes the variation of the magnetic susceptibility. By observing that, in our case, such a variation is in the cuvette and zero outside, while the magnetic fields are linearly polarized and equal by symmetry, we finally get Eq.(2).

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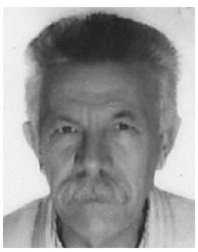

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