

Clinical Application of Spectral Electromagnetic Interaction in Breast cancer: Diagnosis Results of a Pilot Study

*De Cicco C, Mariani L¹, Vedruccio C², Ricci C³, Balma M⁴, Rotmensz N⁵, Ferrari M⁶, Autino E⁴,
Trifirò G, Sacchini V⁷, Viale G⁸ and Paganelli G*

Divisions of Nuclear Medicine, European Institute of Oncology, Milan, Italy.

*Epidemiology and Biostatistics, European Institute of Oncology and National Cancer Institute,
Milan, Italy¹*

COMSUBIN Research Office, Italian Navy, La Spezia, Italy²

Consulting Engineer, Medicina, Bologna, Italy³

Galileo Avionica S.p.A., S. Maurizio C. se, Turin, Italy⁴

Epidemiology and Biostatistics, European Institute of Oncology, Milan, Italy⁵

Physics Unit, European Institute of Oncology, Milan, Italy⁶

Department of Breast Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY⁷

Pathology Division of European Institute of Oncology and University of Milan, Milan, Italy⁸

Concetta De Cicco, MD(📧)

European Institute of Oncology,

Via Ripamonti, 435 – 20141 Milano, Italy

concetta.de-cicco@ieo.it

Fax no. +39 02 57489040

Phone no. + 39 02 57489044

ABSTRACT

Aims and background: There is a need for a cost-effective method to safely reduce the number of diagnostic procedures women undergo for breast cancer. We tested a new procedure for breast cancer diagnosis based on breast tissue response to low level electromagnetic incident waves.

Methods: We tested 101 patients with suspicious palpable breast lesion detected by mammography or ultrasonography, who were scheduled to receive open biopsy. Using an electromagnetic field generator (tissue resonance interaction method probe [TRIMprob™]), we passed the TRIMprob™ over the breast area and recorded the signal variation of 1 or more spectral lines (dB1, dB2, dB3). The results were compared with a control group as well as with pathologic data obtained from excisional biopsy.

Results: No adverse effects of the test were observed. Pathology revealed 86 malignant breast cancers (72 invasive, 14 in situ) and 15 benign conditions. We achieved the best discrimination between normal breasts and lesions using dB1 (dB1 AUC-ROC=0.8; dB2 AUC-ROC=0.61; dB3 AUC-ROC=0.76). With a specificity of 75% to 95%, the sensitivity ranged from 49% to 84%. Tumor or patient variables did not influence the results.

Conclusions: TRIMprob test was able to provide some degree of discrimination between normal breast tissue and lesions but not between benign and malignant lesions. The lack of an influence of patient age and tumour size on test results might be advantageous in terms of early diagnosis in young women. These preliminary results need to be verified and extended in a preclinical-stage disease setting before clinical applicability can be envisaged.

INTRODUCTION

Nowadays, breast cancer screenings detect abnormalities in breast parenchyma with increased frequency (1). Diagnostic tests include mammography, ultrasound, scintimammography, magnetic resonance imaging (MRI), and fine-needle aspiration. However, these tests have varying levels of unreliability and some of them are expensive. Mammography is the best imaging modality for the detection of breast abnormalities due to its high sensitivity; it may also contribute to a reduction in advanced breast cancer cases (2,3). However, its sensitivity and specificity may be reduced in young subjects because of the presence of dense parenchyma (4). Mammography also employs radiation, which makes frequent repetition of the procedure difficult in cases of doubtful findings.

Ultrasound is a safe test, but its accuracy in breast cancer screening still must be proven (5). Scintimammography is limited by its low sensitivity and positive predictive value in nonpalpable lesions (6,7). Compared with these tests, MRI is a highly sensitive procedure, but it has a considerable false positive rate (4,8). Because of their high cost and low availability, scintimammography and MRI are not primary tools for investigation and are used after the first examination.

It has been proposed that cancer exposed to a low level electromagnetic incident waves (9,10,11) may behave differently than healthy tissue; the specific resonances of involved charges (macromolecular dipoles, ionic currents) in pathological states can be used to investigate the tissue's biophysical properties by means of a weak electromagnetic interaction (12,13). Encouraging results have been recently obtained in the diagnosis of prostate cancer using a device based on electromagnetic emission (TRIMprob™) (14). This prospective study was designed to evaluate the TRIMprob™ capability to correctly reveal the presence of cancer in subjects with palpable breast lesions. We tested this new diagnostic method by analyzing the response of breast parenchyma when it is exposed to low levels of electromagnetic radiation (ER).

MATERIALS AND METHODS

Patients

At the European Institute of Oncology from January to December 2002, we studied a group of 101 consecutive women with a suspicious palpable lesion of the breast detected by mammography or ultrasonography that were scheduled to receive open biopsy.

A control group of 71 women without breast abnormalities also underwent clinical examination, mammography, and/or ultrasound. Subjects were chosen at random among institute personnel and patients' companions. Written informed consent was obtained from all subjects.

Women were excluded from the study who were less than 18 years old or had experienced psychiatric illness,, pregnancy, lactation, breast surgery, core biopsy, chemotherapy, and radiotherapy. To rule out possible interferences between the electromagnetic field and altered tissues like scar or inflammatory infiltration, subjects with previous operations or active flogistic processes were excluded from the study.

The study protocol was approved by the Ethics Committee of the European Institute of Oncology.

Description of test procedure

A tissue resonance interaction method probe (TRIMprob™ Galileo Avionica, Turin, Italy), an electromagnetic generator, was used to produce an extremely low-energy, multiple frequency electromagnetic field (11, 12) to radiate the breast area. The sudden signal variation in negative sense, corresponding to a sudden attenuation of 1 or more spectral lines, constitutes the basis for diagnosing radiated tissues and structures. Physical characteristics of the method are described in appendix section. Both of the breasts were examined by a skilled operator, who was unaware of the subject's clinical and instrumental diagnosis.

The test was performed while the patient stood about 2 meters from the receiver. The operator was placed on the opposite side of the breast that is being tested (Fig.1). No metallic objects were allowed on the patient; electronic devices were also not admitted in test area.

The detector was kept at close contact to the breast surface covert with a thin vestment and moved through the 2 orthogonal planes, obtaining a scan of the whole breast volume.

The scan was performed looking for any modifications of the emitted signals in terms of amplitude changes in 1 or more lines of the established frequencies (see appendix). The signal's variations were recorded and stored in a PC file as value of spectral lines expressed in decibel. Three numerical values were obtained for each breast (dB1, dB2, dB3). Patients underwent operation the day after their examination. The lesion of the affected breast was excised surgically under general anesthesia. The results were compared with the histological findings.

Pathology

Intraoperative frozen section examination was usually performed only in solid, nonpalpable lesions larger than 1 cm; in all other cases, permanent hematoxylin and eosin sections were prepared. If an invasive carcinoma was diagnosed, the resection was enlarged to quadrantectomy. Histological classification was according to the Rosen and Oberman modification of the World Health Organization classification (15).

Statistical analysis

Simple descriptive statistics (mean, median, minimum, maximum, standard deviation) were computed for dB1-dB3 variables separately for patients with invasive cancer, benign conditions, and healthy controls.

To evaluate the diagnostic performance of dB1-dB3 variables, receiver operating characteristic curves (ROCs) were developed nonparametrically for each variable, and areas under receiver operating characteristic curves (AUC-ROC) were obtained thereof together with corresponding standard error (SE)s (16). AUC-ROC may vary from 0.5 (a value denoting the lack of diagnostic discrimination) to 1 (denoting perfect discrimination). P- values were obtained from simple and multiple discriminant logistic models testing whether estimated AUC-ROCs significantly differed from 0.5.

Measurements of dB1-dB3 taken from cancer patients were compared across strata defined by age and the most important tumor characteristics: the Wilcoxon rank-sum or the Kruskal-Wallis tests, as appropriate. In all the analyses, two-sided P values were considered to be significantly below the conventional 5% threshold.

RESULTS

From January to December 2002, 86 women with malignant breast cancers (either in situ or invasive), 15 women with benign conditions, and 71 with normal breast control subjects were investigated. In all subjects, only 1 breast was considered, namely the breast with the malignant or benign lesion, or 1 randomly chosen in normal breast controls.

No adverse effects of the test were observed. The procedure was always performed easily, in a short time (around 5-10 minutes), and was well accepted by all women.

Median age was 52 years (range, 32-74 years) in breast cancer patients, 47 years (range, 28-71 years) in women with benign conditions, and 37 years (range, 18-74 years) in control subjects. A balanced distribution of the side of the investigated breast was observed in all the 3 sets of women.

The totality of breast lesions was palpable and all patients underwent excisional biopsy or conservative surgery. Out of the 86 breast cancers, 14 were in situ lesions, and the remaining 72 were invasive cancers. Table 1 shows the distribution of main tumor characteristics.

Descriptive statistics for dB1-dB3 variables are shown in Table 2. Compared to normal breasts, cancer lesions showed on average lower dB1 and dB3 values, and slightly higher dB2 levels. None of the 3 signals showed a meaningful difference between malignant and benign lesions.

The results of the AUC-ROC analysis are shown in Table 3. In terms of statistical significance, all dB1-dB3 variables were able to provide some degree of discrimination between normal breasts and cancer lesions, but not between benign and malignant lesions. By looking at AUC-ROC figures, the best discrimination between normal breasts and cancer lesions was achieved using dB1 (0.83; see Fig 1), followed by dB3 (0.76) and dB2 (0.61). Combining the information of dB1 and dB3, discrimination increased to 0.88 ($P < .0001$ for the difference with the discrimination achieved using only dB1). AUC-ROC estimates for the comparison between benign and malignant lesions were close to 0.5, a figure denoting poor discrimination, according to the previously mentioned lack of statistical significance.

Sensitivity and specificity were computed considering different thresholds for the classification of dB1 as negative (above the threshold) or positive (below the threshold). The results, summarized in Table 4, showed that by keeping specificity within an interval ranging from 75% to 95%, the sensitivity ranged from 84% to 49%.

Finally, descriptive statistics were computed for signal levels according to a number of invasive tumor characteristics for which we had information, and the medians were compared statistically across strata. The results achieved, shown for dB1 in Table 5, denoted the lack of significant and clinically meaningful associations with any of the investigated characteristics. In other words, dB1 (and the other variables) did not seem to be affected by tumor characteristics, which therefore cannot influence the diagnostic performance. Similar results (not shown in detail) were obtained considering patient age ($P=0.1790$), the side of the lesion ($P=0.4701$), or the in situ versus invasive nature of the tumor ($P=0.1876$). As regards the latter characteristic, however, there was a trend toward higher median dB1 measurements in situ lesions (16.2) than in invasive cancers (12.5).

DISCUSSION

The objective of this study was to evaluate the ability of a new method based on the electromagnetic emission in revealing breast parenchymal alteration in subjects scheduled for surgical intervention because of a suspicious lesion.

Our findings show that TRIMprob is an easy and fast procedure, with an excellent degree of acceptance by the patient, which is able to discriminate between subjects with normal breast tissue and patients affected by pathological conditions. The best results were achieved in particular with dB1, 1 of the 3 signal measures obtained with TRIMprob, or combining dB1 and dB3 measures. However, in consideration of the slight gain achieved with the combination and for the sake of simplicity, we focus our attention here on the dB1 variable.

Another positive indication of this study is that in subjects with cancer, signal measures were not affected by patient's and tumour's characteristics such as age, menopausal status, the in situ or invasive nature of the lesion, side and size of the tumour, histological grading, axillary involvement, presence of perivascular invasion, estrogen and progesterone receptors status. The histological type could not be investigated because of the high prevalence of ductal invasive carcinoma in this series.

In particular, the lack of an influence of patient age and tumour size on test results might be advantageous in terms of early diagnosis when young women with dense or predominantly glandular breast parenchyma are evaluated. It is well-known, in this condition mammography is affected by poor sensitivity. Moreover, the possibility to diagnose an intraductal carcinoma with the same accuracy achieved in the presence of an infiltrating tumor might represent an advantage in terms of clinically occult carcinomas detection. Of course, all the above considerations need to be verified in further studies.

This pilot investigation gave also some indications on suboptimal TRIMprob performance. First of all, the discriminant power of the technique, as quantified by the area under the ROC curve (0.83 for dB1), was such to imply that some trade-off comes into play between test sensitivity and specificity, as shown by Table 4. In our opinion, considering that sensitive methods are already applied for breast cancer screening and in order to avoid under-diagnosis, the threshold for test positivity should be kept relatively high, in order to achieve high sensitivity. This would be at the cost of low specificity and, consequently, a high number of false-positives. Even in this case, however, the number of more costly investigations, necessary to exclude or confirm the presence of disease, would be diminished. Second, the procedure did not apparently distinguish benign from malignant disease of the breast. However, the low prevalence of benign lesions in this series might affect the results. Actually, benign lesions were found in only 15 cases, which do not allow a detailed analysis of the results on the basis of lesion severity indicators like presence of proliferation, atypia, or hyperplasia.

Some important issues that were not investigated in this study deal with TRIMprob reproducibility, i.e. the assessment of intra-observer and inter-observer variability of test results, and, more importantly, the performance of this technique in the presence of non-palpable malignant lesions. Finally, no comparison between our findings and literature data on TRIMprob is possible, since this study is the first of this kind. In conclusion, this study provides indication that the interaction between breast matter and the electromagnetic field might be investigated for diagnostic purposes in oncology. The TRIMprob test appears to be safe and noninvasive. The required intensity of the electromagnetic waves is very low (the power is similar to a mobile phone), thus allowing repeated examinations.

The results on the diagnostic performance of the technique in detecting breast cancer are promising. However, as previously outlined, such results must be considered preliminary and need to be verified and extended in a preclinical-stage disease setting, before clinical applicability can be envisaged.

REFERENCES

- 1) Tabar L, Vitak B, Chen HH, Yen MF, Duffy SW, Smith RA. Beyond randomized controlled trials: organized mammographic screening substantially reduces breast carcinoma mortality. *Cancer*. 2001 May 1;91(9):1724-31.
- 2) Fracheboud J, Otto SJ, Van Dijck JA, Broeders MJ, Verbeek AL, De Koning HJ. Decreased rates of advanced breast cancer due to mammography screening in The Netherlands. *Br J Cancer*. 2004. Aug 31;91(5):861-7.
- 3) Coburn NG, Chung MA, Fulton J, Cady B. Decreased breast cancer tumor size, stage, and mortality in Rhode Island: an example of a well-screened population. *Cancer Control*. 2004 Jul-Aug;11(4):222-30.
- 4) Van Goethem M, Schelfout K, Dijckmans L, Van Der Auwera JC, Weyler J, Verslegers I, Biltjes I, De Schepper A. MRI mammography in the pre-operative staging of breast cancer in patients with dense breast tissue: comparison with mammography and ultrasound. *Eur Radiol*. 2004 May;14(5):809-16.
- 5) Kopans DB. Sonography should not be used for breast cancer screening until its efficacy has been proven scientifically. *AJR Am J Roentgenol*. 2004 Feb;182(2):489-91.
- 6) Tolmos J, Cutrone JA, Wang B, Vargas HI, Stuntz M, Mishkin FS, Diggles LE, Venegas RJ, Klein SR, Khalkhali I. Scintimammographic analysis of nonpalpable breast lesions previously identified by conventional mammography. *J Natl Cancer Inst*. 1998 Jun 3;90(11):846-
- 7) De Cicco C, Trifiro G, Baio S, Sierra ML, Pizzamiglio M, Cassano E, Prisco G, Gatti G, Galimberti V, Luini A, Paganelli G. Clinical utility of ^{99m}Tc-Sestamibi scintimammography in the management of equivocal breast lesions. *Cancer Biother Radiopharm*. 2004 Oct;19(5):621-6.
- 8) Heywang-Kobrunner SH, Viehweg P, Heinig A, Kuchler C. Contrast-enhanced MRI of the breast: accuracy, value, controversies, solutions. *Eur J Radiol* 1997;24:94-108.
- 9) Foster K R, Epstein BR, Gealt MA. Resonances in the dielectric absorption of DNA. *Biophys. J* 1987. 52:421-425.
- 10) Frolich H. Long range coherence and energy storage in biological systems. *Int. J. Quantum Chem* 1968. 2 :641-649.
- 11) Adair, RK, *Vibrational Resonances in Biological Systems at Microwave Frequencies*, Biophysical Journal 2002. Volume 82, March
- 12) Vedruccio and A.Meessen, *EM Cancer Detection by Means of Non Linear Resonance Interaction*, Proceedings of PIERS2004, Progress in Electromagnetics Research Symposium, Pisa, Italy, March 28-31 2004 : 909-912.
- 13) C. Vedruccio, A. Meessen, *Nuove possibilità diagnostiche tramite onde elettromagnetiche*, *Fisica in Medicina (AIFM)*, 3: 225-230, 2004.
- 14) C. Bellorofonte, C.Vedruccio et al.: *Non-invasive detection of prostate cancer by electromagnetic interaction*, *European Urology*, 47: 29-37 (2005).
- 15) WHO. *Histological Typing of Breast Tumours*, 2nd ed. International Histological Classification of Tumours N 2. Geneva: WHO, 1991.
- 16) Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic ROC curve. *Radiology* 1982. 143:29-36.

Table 1: Main tumor characteristics

	Patients effected (N=72)	%
Tumor size (cm)		
≤ 1	23	32.4
1.1-2.0	32	45.1
> 2.0	16	22.5
NA	1	--
Histology		
Infiltrating ductal carcinoma	53	73.6
Infiltrating lobular carcinoma	6	8.3
Infiltrating cribriform carcinoma	7	9.7
Others	6	8.3
Axillary nodes status		
Negative	38	59.4
Positive	26	40.6
NA	8	--
Histologic grade		
1	12	17.1
2	33	47.1
3	25	35.7
NA	2	--
IVP		
Negative	49	71.0
Positive	20	29.0
NA	3	--
Estrogen receptor status		
Negative	10	14.5
Positive	59	85.5
NA	3	--
Progesterone receptor status		
Negative	26	37.7
Positive	43	62.3
NA	3	--

Table 2: Descriptive statistics for dB1-dB3 variables

Group	N	Variable	Median	Minimum	Maximum
Controls	71	dB1	27	1	33
		dB2	17	-6	31
		dB3	14	-1	19
Benign lesions	15	dB1	11	0	34
		dB2	20	4	31
		dB3	11	0	14
Malignant tumors	86	dB1	14	0	34
		dB2	18	3	32
		dB3	9	0	22

Table 3: Areas under the ROC curve (corresponding P values) quantifying the discrimination between malignant tumors and controls or benign lesions using dB1-dB3 variables

Comparison group:	dB1	dB2	dB3
Controls	0.83 (<.0001)	0.61 (0.0039)	0.76 (<.0001)
Benign lesions	0.58 (0.4948)	0.52 (0.8362)	0.50 (0.8455)

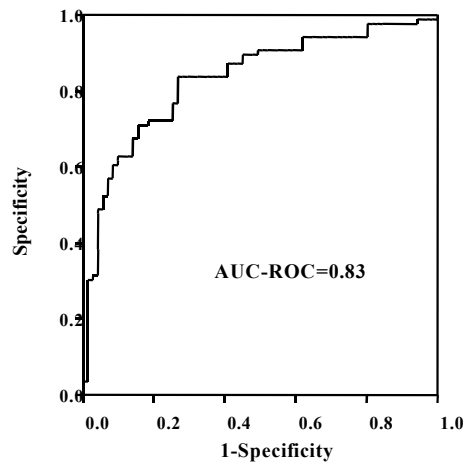
Table 4: Sensitivity and specificity considering different thresholds for the classification of dB1 as negative (above the threshold) or positive (below the threshold)

Specificity (%)	Threshold	Sensitivity (%)
≈ 75	< 24	84
≈ 90	< 17	63
≈ 95	< 14	49

Table 5: dB1 levels (median, minimum and maximum) according to invasive tumor characteristics and P values for testing the overall association between dB1 levels and each of the characteristics considered

	Median	Minimum	Maximum	P
Tumor size (cm)				0.0627
≤ 1	12	0	29	
1.1-2.0	16	2	32	
> 2.0	12	0	34	
Axillary nodes status				0.0977
Negative	12	0	31	
Positive	15	4	34	
Histologic grade				0.6357
1	11	0	26	
2	14	0	32	
3	15	4	34	
IVP				0.9419
Negative	12	0	34	
Positive	14	0	32	
Estrogen receptor status				0.3567
Negative	11	5	23	
Positive	14	0	34	
Progesteron receptor status				0.8579
Negative	15	5	32	
Positive	13	0	34	

Fig 1: Receiver operating characteristic (ROC) curve, and corresponding area under the ROC curve (AUC-ROC).



Appendix

The TRIMprob™ system consists of a battery-operated detection probe, a receiver, and a computer display. The detection probe contains a nonlinear oscillator that generates a complex electromagnetic wave of low intensity with several frequency components and with a high degree of spatial and temporal coherence (patent n° WO 01/07909A1). The beam from the probe is narrow measuring no more than 0.5 cm across.

The electromagnetic field drives oscillations inside the tissue; when the internal oscillations are in a resonant state, an energy transfer can be detected in the wave emitted by the generator, and the resonance interaction phenomena can be detected on a spectrum analyser situated about 2 meters away from the probe. The spectrum shows the different frequency emission levels. When the probe is brought close to biological disease, strong power amplitude changes (more than -20 dB) can be identified in 1 or several lines of different frequencies[1,2].

The sudden signal variation in the negative sense, corresponding to a sudden attenuation of 1 or more spectral lines, constitutes the basis for diagnosing radiated abnormal tissues and structures.

The main requirement to allow exploration of breast tissue is the use of a specific electromagnetic field that is able to penetrate into the area to be tested.

By expressing the tissue characteristics in terms of macroscopic permittivity, conductivity and losses due to the particular structures present in the area, we can obtain the penetration depth, which allows the complete investigation of the whole breast volume.

To calculate how much the incident wave penetrates into the body, we have expressed the complex wave number k in a real part, k_r , and in an imaginary part, k_i , such as [3]:

$$k = k_r - jk_i \quad (1)$$

and the penetration depth δ , that is the body thickness able to reduce the intensity of incident field of a $1/e$ factor, as the reciprocal of k_i :

$$\delta = (k_i)^{-1} \quad (2)$$

Indicating the permittivity with \mathcal{E} and the permeability with μ , it is possible to come out the real and the imaginary part of k , such as:

$$k_r = \frac{\omega}{c} \sqrt{\frac{\mathcal{E} \mu_r}{2}} \left\{ \left[1 + \left(\frac{\sigma}{\omega \mathcal{E}_0 \mathcal{E}_r} \right)^2 \right]^{1/2} + 1 \right\}^{1/2} \quad (3)$$

$$k_i = \frac{\omega}{c} \sqrt{\frac{\mathcal{E} \mu_r}{2}} \left\{ \left[1 + \left(\frac{\sigma}{\omega \mathcal{E}_0 \mathcal{E}_r} \right)^2 \right]^{1/2} - 1 \right\}^{1/2} \quad (4)$$

where σ represents the conductivity of the tissues under test.

Since the considered biological system is much smaller than the wavelength of microwave radiation, which is by definition greater than 1 mm, any absorption of energy by the system must take place through the interaction of the field with dipole moment charge distribution of the system [4].

The frequencies emitted by the device had been previously optimized during the studies in prostate cancer[5], stomach and duodenum as well as bladder cancer, obtaining the values of 460, 920, and 1380 MHz because they appeared to respond, in the appropriate way, to the resonances of the system [6, 7, 8].

The following table shows the experimental values of permittivity and conductivity measured at the frequencies of the TRIMprob™ device.

Table 1

<i>Frequency [MHz]</i>	<i>Wavelength [m]</i>	<i>Conductivity [S/m]</i>	<i>Relative permittivity</i>
460	0.28	0.036	5.5
920	0.14	0.050	5.4
1380	0.09	0.070	5.4

Inserting these data in the equations (4) and (2) we obtained the computed penetration depth shown in the second column of table (2)

Table 2

<i>Frequency [MHz]</i>	<i>Penetration depth [m]</i>
460	0.35
920	0.24
1380	0.18

During the diagnostic test the incident beam was oriented toward the breast area. When the incident beam, during its propagation within the body, encounters a diseased state, the electromagnetic field interacts with the tissue components at molecular level and, by means of a resonant mechanism[1,2,9], the response is detected by the receiver of TRIMprob™ and data registered as number of decibel (dB) .

References

1. C.Vedruccio and A.Meessen, *EM Cancer Detection by Means of Non Linear Resonance Interaction*, Proceedings of PIERS2004, Progress in Electromagnetics Research Symposium, Pisa, Italy, March 28-31 2004 : 909-912.
2. C. Vedruccio, A. Meessen, *Nuove possibilità diagnostiche tramite onde elettromagnetiche*, Fisica in Medicina (AIFM), 3: 225-230, 2004.
3. Ulaby, et al. *Microwave remote sensing – Active and Passive*, Addison-Wesley Publishing Company, 1981
4. Adair RK. *Vibrational Resonances in Biological Systems at Microwave Frequencies*, Biophysical Journal, Volume 82, March 2002
5. C. Vedruccio, E. Mascia, V. Martines, *Ultra High Frequency and Microwave Non-linear Interaction Device for Cancer Detection and Tissue Characterization*, a Military Research approach to prevent Health Diseases, International Review of the Armed Forces Medical Services (IRAFMS), vol. 78/2: 120-126(2005) .
6. C. Bellorofonte, C.Vedruccio et al.: *Non-invasive detection of prostate cancer by electromagnetic interaction*, European Urology, 47: 29-37 (2005)
7. G.Leucci, C.Vedruccio et.al., *Studio pilota per la diagnosi del carcinoma vescicale mediante l'utilizzo del Trimprob*, Proc. of XI National Congress AURO_{IT}, Lecce, Italy, Oct. 6- 9, 2004.
8. Pokorny J, Jelenek F, Trkval V, Lamprecht I, Holtzel R. 1997. Vibrations in microtubules. J Biol Phys. 48:261
9. C. Vedruccio, *Ultra High Frequency and Microwave Non-linear Interaction Device for Cancer Detection and Tissue Characterization*, Proc. of Augmented Reality in Surgery, 1st European Summer School (ARISER) IFC-CNR, Lecce, Italy, July 4th-8th 2005: 8-12.