

# Non-Invasive Detection of Prostate Cancer by Electromagnetic Interaction

Carlo Bellorofonte<sup>a,\*</sup>, Clarbruno Vedruccio<sup>b</sup>, Pietro Tombolini<sup>a</sup>,  
Michele Ruoppolo<sup>a</sup>, Andrea Tubaro<sup>c</sup>

<sup>a</sup>Department of Urology S. Carlo Borromeo Hospital, Milan, Italy

<sup>b</sup>COMSUBIN, Research Office, Italian Navy, La Spezia, Italy

<sup>c</sup>Department of Urology, Sant'Andrea Hospital, 2nd School of Medicine, "La Sapienza" University, Rome, Italy

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## Abstract

**Objectives:** Malignant and normal tissues are known to have different electromagnetic properties, and various attempts have been made to use these information for diagnostic purposes. A nonlinear tuneable oscillator (Trimprob<sup>TM</sup>) generating extremely low energy multiple electromagnetic fields has been developed for non-invasive analysis of electromagnetic anisotropy in humans. Objective of this study was to evaluate the feasibility of prostate cancer detection using the TRIMprob<sup>TM</sup> and to evaluate its diagnostic accuracy.

**Methods:** 757 men were evaluated with the TRIMprob<sup>TM</sup> between July 2002 and May 2003 in a prostate unit. The TRIMprob<sup>TM</sup> was moved over the surface of the patient's perineum while standing, normally dressed, in front of the system receiver. A single operator, blinded to the patient status, conducted the tests. Nonlinear resonance was analysed at 465, 930 and 1395 MHz.

**Results:** Analysis of resonance values at 465 MHz showed a significant difference between controls, patients with benign prostatic hyperplasia and patients with prostate cancer. In our study population, a sensitivity of 95.5% and specificity of 42.7% for the diagnosis of prostate cancer with a positive and negative predictive value of 63.6% and 89.8% was found.

**Conclusions:** The results of this study confirm the possibility of electromagnetic detection of cancer. An extracorporeal scan by the TRIMprob<sup>TM</sup> can identify patients at risk for prostate cancer, and recognise those in whom the risk is extremely low. The results of the present study represent a proof-of-concept, which may open a new field of medicine.

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**Keywords:** Prostate neoplasm; Sensitivity; Specificity; Electromagnetism; TRIMprob<sup>TM</sup>; Biologic resonance

## 1. Introduction

Prostate cancer is the most frequent cancer of the adult male in the United States [1]. The presence of prostate cancer is usually suspected from an abnormal digital rectal examination (DRE) and/or an elevated serum prostate specific antigen (PSA). The definitive

diagnosis is made by prostate biopsy [2]. The introduction of PSA measurement into clinical practice has improved the early diagnosis of cancer to the point that it may be used as a cancer-screening tool [3]. The number of patients found with organ confined disease, possibly amenable of cure by radical prostatectomy, external beam radiation or prostate brachytherapy has increased [4,5]. Nevertheless, PSA remains an organ-specific but not a disease-specific marker because increased PSA levels are found in men with benign prostate enlargement and in inflammatory disorders

\* Corresponding author. Present address: Via Cristina Belgioioso, 2, 20157 Milano, Italy. Tel. +39 02 3564704

E-mail address: carlo.bellorofonte@fastwebnet.it (C. Bellorofonte).



[6,7]. A significant number of patients with elevated PSA levels have a negative prostate biopsy [2].

Analysis of electromagnetic properties of prostate cancer cell lines has been proposed by Smith and co-worker in 2000 although this has not been translated yet into a diagnostic tool [8]. In 1992 Clarbruno Vedruccio, an Italian physicist, invented and patented a device for the electromagnetic (EM) detection of biologic tissues anomalies, based on the principles described below. This equipment is composed by a nonlinear oscillator concealed into a cylindrical probe and a radiofrequency spectrum analyser, and is named TRIMprob™ [9]. Vedruccio's patent stems from research on dielectric properties of biological tissues, a long standing research line in the world of physics. A brief description of the background is reported here.

The response of any material to oscillating electric fields is defined by two frequency dependent functions: the dielectric constant  $\varepsilon$  (relative to vacuum) and the conductivity  $\sigma$ . Schwan and Foster reviewed basic concepts and the main experimental results for biological tissues, while Pethig and Krell discussed possible applications [10–13]. They include the prospect of EM cancer detection, since  $\varepsilon$  and  $\sigma$  display significant differences for malignant and normal tissues. Fricke and Morse compared already in 1926 the electrical properties of malignant tumours of the human breast to those of normal tissue and benign tumours taken from the breast [14]. Their measurements were only performed at 20 kHz, but it appeared very clearly that  $\varepsilon$  was on the average about 10 times larger for actively growing tumours than for normal tissue. Benign or degenerated tumours did yield intermediate results, while  $\sigma$  had always nearly the same value. These features have to result from *membrane effects*, since they are predominant in biological tissues between 3 kHz and 30 MHz. An electric field that polarizes different media will create, indeed, *surface charges* at the interface or on both sides of cell membranes. These surface charges produce a secondary electric field that acts on all charges like an elastic restoring force, and this accounts for the appearance of resonance effects [15]. The increase of  $\varepsilon$  for *actively growing* malignant tumors can thus be attributed to an increased proportion of membrane surfaces per unit volume. The most likely modification concerns *intracellular membranes*, associated with the intensified energy household (in mitochondria) and protein synthesis (at the endoplasmic reticulum). Since cancerous cell proliferation is known to be accompanied by angiogenesis [16,17], we may also have to consider the membranes of capillaries, the high polarizability of the adjacent fluid and the effect of red blood cells.

Chaudhary et al. measured  $\varepsilon$  and  $\sigma$  of breast carcinoma and homologous normal tissue *between* 3 MHz and 3 GHz [18]. They found that  $\varepsilon$  and  $\sigma$  are always greater for tumours in this frequency domain, but  $\varepsilon$  increases towards lower frequencies (below 30 MHz), while  $\sigma$  is growing in the direction of higher frequencies (especially above 300 MHz). The first effect can again be attributed to membranes, but the second effect has to result from *reorientations of dipolar particles*. It has thus been attributed to the increased water content of tumours [19,20]. Joines et al. confirmed that from 30 MHz up to 2 GHz, EM energy absorption is sensibly higher in malignant tumours of various origin than in normal tissues, but they found a broad maximum between 100 and 800 MHz, centred at about 400 MHz [21,22]. Since the resonance frequency for *free* water molecules is 25 GHz at 37 °C, these particles could only account for increased energy absorption above 1 GHz. It was therefore assumed that “bound water” and perhaps even “proteins” are responsible for the increased response at lower frequencies.

It is known that proteins acquire more surface charges in malignant tumours [23]. Since these charges attract water molecules, they can explain the presence of more “bound water”. We believe that it is also necessary to take into account the fact that cancerous cells are characterized by dramatic changes of their metabolism, intercellular communication and adhesion properties. This means that the number and nature of *membrane proteins* has to be modified, but membrane proteins carry dipolar parts, sticking out of the membrane. These dipoles can be reoriented by an oscillating electric field [24].

The existence of significant differences between the electrical properties of malignant and normal tissues was confirmed by other empirical results, but this was to no avail for cancer diagnosis as long as  $\varepsilon$  and  $\sigma$  had to be determined by sophisticated *in vitro* measurements [25–27]. There have been several attempts to simplify this procedure, in particular by pressing an *open-ended coaxial line* against the body surface, to measure the amplitude and phase of the reflected wave, so that  $\varepsilon$  and  $\sigma$  could be determined by model calculations [28,29].

The objective of this study was to evaluate the feasibility of prostate cancer detection using the TRIMprob™ and to evaluate the diagnostic accuracy by establishing the sensitivity, specificity, positive and negative predictive value for the diagnosis of prostate cancer in a single blinded study.

Studies on new diagnostic tools/devices for the diagnosis of prostate cancer are dogged by the difficulty of having a control group in which the risk of having the disease is extremely low. The first part of the

study reflects this difficulty by comparing a group of men with known prostate cancer to a group of normal young men, as well as to those with clinical and ultrasonographic evidence of BPH but with normal levels of PSA. Further groups in which there was likely to be a significant incidence of undetected cancer were also studied. The results of TRIMprob™ scanning in each of these groups was compared. Accuracy was evaluated in patients with either elevated PSA or abnormal digital rectal examination who were submitted to prostate TRIMprob™ test and prostate biopsy. We acknowledge the limitation that sensitivity and specificity values obtained in this study may not be valid when applied to the general population.

## 2. Methods

The study was conducted at a single institution (S. Carlo Borromeo Hospital, Milan, Italy). Ethical approval was obtained from the Italian Ministry of Health. Seven hundred and eighty-three consecutive men were enrolled from July 2002 to May 2003. One hundred and sixty three men volunteers aged less than 35 years without lower urinary tract symptoms or voiding dysfunction having a normal PSA and digital examination were considered as *controls*. Transrectal ultrasound revealed an average prostate volume of 21.4 ml (median 21.8, range 16.2–24.5). PSA values obtained within the last 3 months were considered evaluable, patients were otherwise scheduled for a new consultation after new PSA levels were acquired (IMMULITE DPC, Medical System SPA, Genoa, Italy). Patients with enlarged prostate at digital rectal examination (DRE) but without prostate asymmetry or a palpable abnormality, a PSA value of less than 4.0 ng/ml, were classified as *BPH patients*. Patients with similar characteristic but elevated PSA were described as *BPH with elevated PSA*. Patients with any palpable abnormality of the prostate, which might be suspicious of prostate cancer, were described as *Abnormal DRE*. All patients with a biopsy proven diagnosis of prostate adenocarcinoma were categorized as *Prostate Cancer*. For theoretical safety reasons patients with cardiac pacemaker were excluded as requested by the Italian Ministry of Health.

Analysis of tissue resonance was performed using the TRIMprob™ system (Galileo Avionica, Turin, Italy) consisting of a battery-operated probe, a receiver and a computer display. The probe is about 30 cm long and can easily be held in one hand. It contains a tuneable, autonomous oscillator and an antenna, emitting a very weak EM wave with several frequency components (465, 930 and 1395 MHz multiples). The beam emitted from the probe is narrow, measuring about 0.2 radian. The penetration of the EM wave depends upon its frequency and the dielectric properties of the biological tissues. The 465 MHz frequency has a penetration of 20 cm (calculated for the dielectric properties of striated muscle and the prostate which is quite similar); EM waves in this frequency range travel particularly well in fat tissue so that a higher penetration is expected in fat persons. The biological tissue is situated in the near field, where retardation effects are negligible. The antenna acts there like an “open capacity” and the tested biological tissue is subjected to the resulting electric field. This type of coupling is unusual. It involves a capacity  $C$  that increases when

the probe approaches the tested tissue. Since this capacity favours the passage of high frequency currents, we can call this a dynamic coupling.

The EM field stimulates minute electrical oscillations inside the tissue; when these resonate, an energy transfer can be detected in the wave emitted by the generator, because of the “Non Linear Resonance Interaction” [30]. At the resonance on one, or more of the spectral lines, two effects are detectable: the first is related to the transfer of an amount of radiofrequency from the generator probe to the diseased tissue, that absorbs a part of the signal on the proper frequency line (dynamic coupling), The second effect is related to the deformation of the electromagnetic pattern emitted by the probe, due to the interaction with a resonating agglomerated of cells, as above described, that produces in the “near field” a sort of parasitic resonating element able to deflect, on other spatial direction, the waves, which can be detected on a separate receiver. A receiver, acting as a spectrum analyser, situated about two meters away from the probe, displays three different frequencies. When the probe is brought close to the patient, the interactions of the oscillating electric field with biological tissue induct changes in one or several frequency lines amplitude depending on the pathological state of the tested tissue. Resonance values are representative of power measured on a logarithmic scale but are expressed in arbitrary units ranging between 0 and 255.

TRIMprob™ scanning was performed by a single investigator (CB) after an extensive training performed on a previous series of 245

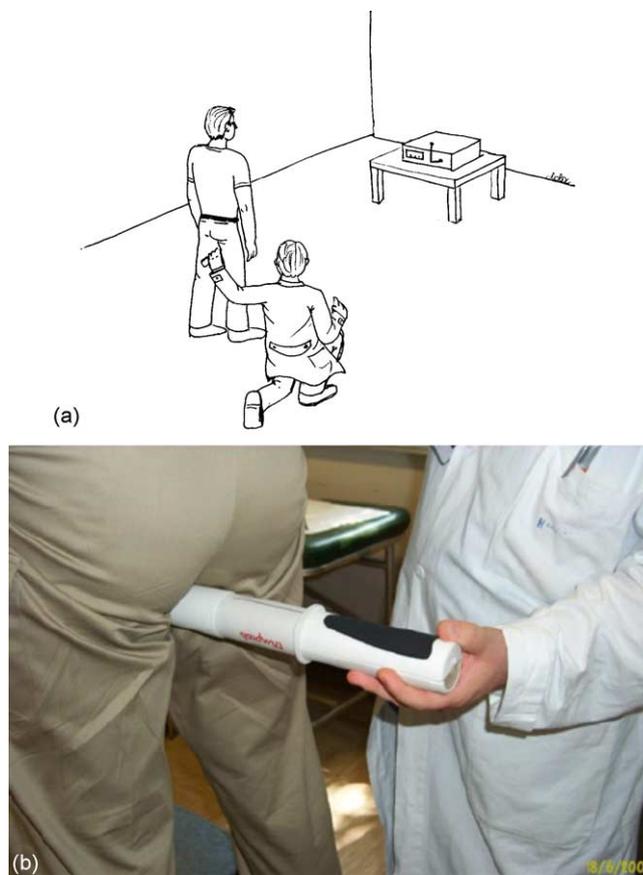


Fig. 1. The prostate area is scanned with the TRIMprob™ while the patient standing, normally dressed, 2 meters in front of the receiver at the level of the prostate (a). The probe is moved in close contact over the perineum (b).

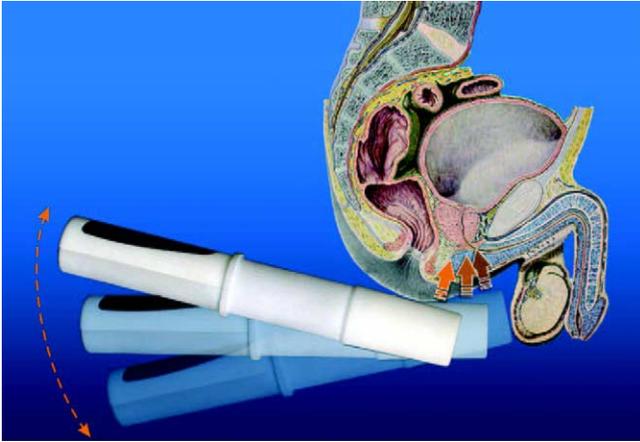


Fig. 2. Tilt scanning of the probe. The probe is moved in close contact over the perineum.

patients which was tested during the industrial development of the diagnostic system. The prostate area was scanned with the TRIMprob™ while the patient standing, normally dressed, 2 meters in front of the receiver at the level of the prostate (Fig. 1). The probe was moved in close contact over the perineum. The prostate gland was scanned in a sagittal plane at an angle of 15° to the left and 15° to the right of the midline; the probe was also tilted so that the beam was aimed at the ventral and the dorsal part of the gland (Fig. 2). Resonance values corresponding to six prostate areas (midline, right and left area of the ventral and dorsal prostate part) were saved on the computer. Great care was taken to find the minimal value for resonance in every area of the prostate. A single investigator who was blind of the patient symptoms and clinical diagnosis performed all TRIMprob™ scans. In a subgroup of 25 patients (10 with a biopsy proven diagnosis of prostate cancer and 15 with a clinical diagnosis of BPH), a preliminary evaluation of intraobserver variability was performed repeating the TRIMprob™ test in the same patient at 24 hours interval. Interobserver variability was estimated in the same group and the TRIMprob™ test was performed by two independent investigators blind of the patient clinical conditions.

In patients with elevated total PSA serum levels and/or abnormal DRE, prostate biopsy was performed and TRIMprob™ accuracy for the diagnosis of prostate cancer calculated. A standard

sextant biopsy technique was used [31]. Biopsy tissue was fixed in formalin and processed accordingly to a standard procedure.

Cut-off values of 4.0 ng/ml and 18% were used for total serum PSA level and free/total serum PSA ratio as suggested by Carter and Christensson respectively [32,33].

Data from the case record forms were entered into an Access database and analysed by VisualStat release 6.0 and Analyse-it + Clinical Laboratory 1.68 software. Analysis of variance were performed by the one-way Anova test with least significant difference post-hoc test. Sensitivity and specificity, positive and negative predicative values were calculated. An alpha value of 0.05 was used as threshold for significance. A 95% confidence interval level was considered.

### 3. Results

Twenty-six patients were excluded from the analysis as their clinical data were found to be incomplete. Data from 757 patients were available for analysis. Mean patient age was  $64 \pm 13$  years. The mean of the lowest signal obtained from the prostate in any area measured at 465, 930 and 1395 MHz in the different patient groups were compared by the one-way Anova test. A significant difference among the various patient groups was found at 465 and 930 MHz ( $p \leq 0.0001$ ) while no difference was seen at 1395 MHz ( $p \leq 0.247$ ) (Table 1, Fig. 3). The variation in field values at 465 MHz for the 5 different categories was much larger than that seen at 930 MHz. In all but 2 patients with a biopsy proven diagnosis of prostate cancer sudden changes in the signal amplitude at 465 MHz was seen, often down to zero level. A similar effect was found in some of the BPH patients with elevated PSA or abnormal DRE. Post-hoc analysis by the least significant difference test showed a significant difference ( $p \leq 0.05$ ) between controls (110.7 (6.4)) and patients with either BPH (94.0 (45.9)), BPH with elevated PSA (51.8 (51.9)), abnormal DRE (10.5 (19.7)) or prostate cancer (19.2 (29.7)). A significant difference was also

**Table 1**

Field level measured by the TRIMprob™ at 465, 930 and 1395 MHz

	No. of patients (757)	Prostate cancer on biopsy	Average (SD)		
			465 MHz	930 MHz	1395 MHz
Controls	163	n.a.	110.7 (36.4)	45.1 (18.2)	49.7 (16.3)
BPH with PSA $\leq 4.0$ ng/ml and normal DRE	228	n.a.	94.0 (45.9)	41.8 (19.4)	48.5 (13.8)
BPH with PSA $> 4.0$ ng/ml and normal DRE	167	31	51.8 (51.9)	37.2 (21.4)	50.7 (16.7)
Abnormal DRE	91	77	10.5 (19.7)	36.2 (18.4)	48.9 (12.5)
Prostate cancer	108	n.a.	19.2 (29.7)	36.0 (19.1)	52.2 (14.7)
One-way Anova			$p \leq 0.0001$	$p \leq 0.0001$	$p \leq 0.247$

Power is measured in arbitrary units ranging between 255 and 0. Mean values and standard deviation data are presented. Analysis of the different patient groups by the one-way Anova shows that the five different patient groups are significantly different at 465 and 930 MHz while no significant difference was seen at 1395 MHz. n.a. (not applicable as patients were not biopsied).

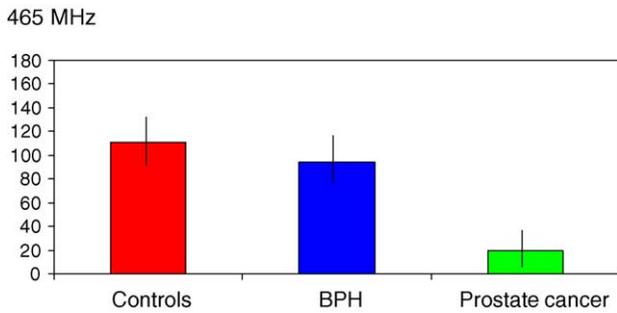


Fig. 3. TRIMprob™ signal amplitude (mean values and standard deviation) at 465 MHz in controls, patients with BPH and PSA <4.0 ng/ml and patients with a biopsy proven diagnosis of prostate cancer.

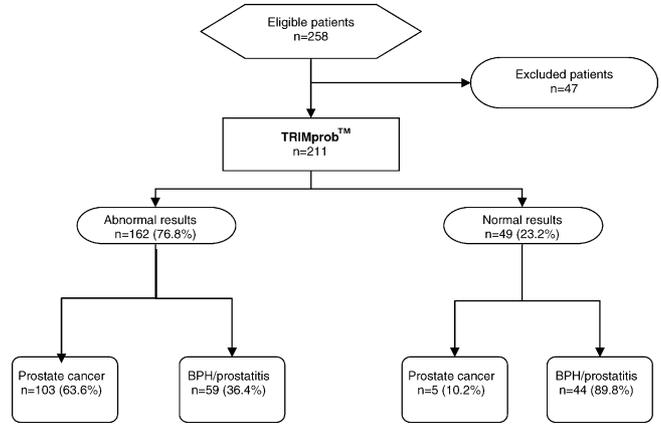


Fig. 4. Flow diagram of patients undergoing prostate biopsy.

found between patients with a know diagnosis of prostate cancer and all the other groups ( $p \leq 0.05$ ).

Preliminary evaluation of intraobserver variability showed a 100% consistency between two TRIMprob™ tests performed by a single investigator at 24 hours interval. An 8% discrepancy (2 of 25 patients)

was found in the results of TRIMprob™ test performed by two separate investigators. Two patients with a clinical diagnosis of BPH were diagnosed as prostate cancer by one of the two investigators, no differences were found in the evaluation of patients with prostate cancer.

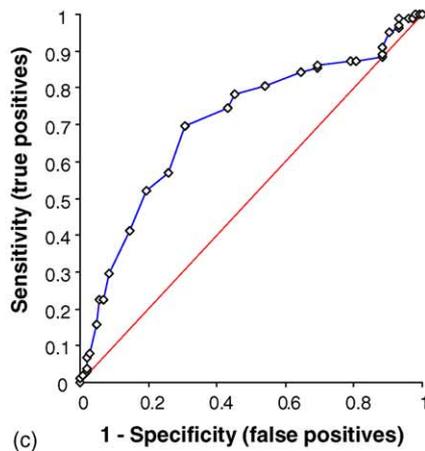
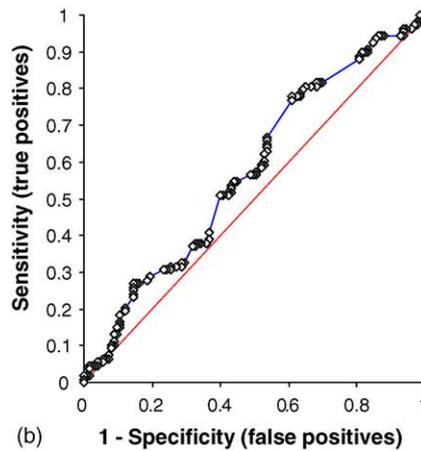
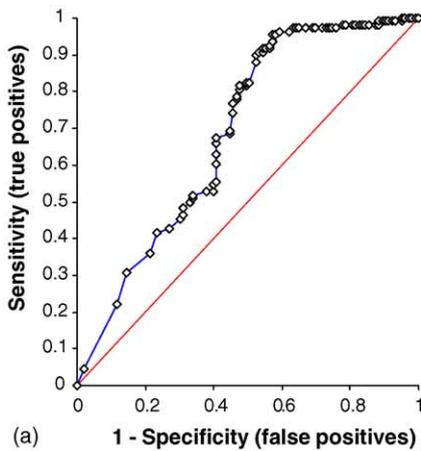


Fig. 5. Receiver Operator Characteristics (ROC) curves. Diagnosis of prostate cancer (biopsy) versus TRIMprob™ [465 MHz] (a), total PSA (b), and free/total PSA ratio (c).

**Table 2**

Sensitivity, specificity, positive and negative predictive value of individual diagnostic parameters

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
TRIMprob <sup>TM</sup> (cut off a 50)	95.4	42.7	63.6	89.8
PSA ( $\geq 4.0$ ng/ml)	94.4	7.3	47.2	60.0
PSA ratio (18%)	80.4	46.2	59.4	70.6
DRE	68.9	80.2	76.0	73.8
TRUS	84.3	52.6	62.3	78.2

Two hundred and fifty-eight patients (all patients included in the categories defined as *BPH with elevated PSA on Abnormal DRE*) were offered a prostate biopsy after TRIMprob<sup>TM</sup> testing, 211 consented. Patient flow diagram is described in Fig. 4. The average total PSA value in this patient cohort was 6.2 ng/ml (median 6.5, range 3.5–38.6). Data were plotted on a receiver operator characteristics (ROC) curve and a cut off value of 50 units was chosen, for resonance at 465 MHz, as the best threshold to distinguish benign from malignant prostate disorders (Fig. 5). One hundred and sixty-two patients were positive on TRIMprob<sup>TM</sup> and 103 had a positive biopsy. Forty-nine patients were negative on TRIMprob<sup>TM</sup> and 44 of them had negative biopsy. Evaluation of core biopsies revealed a Gleason 6 tumour in 55 patients (51%), Gleason 7 and 8 were diagnosed in 36 (33%) and 17 (16%) cases, respectively. Patients with high grade PIN were grouped in the non-cancerous cohort together with those with BPH or chronic prostatitis. Fifty patients (46%) were considered to have stage T1c disease, T2 and T3 disease was diagnosed in 51 (47%) and 7 (7%) respectively. Analysis of data from this patients group resulted in very high level of sensitivity and moderate specificity (95.4 and 42.7%, respectively). The positive and negative predictive values of TRIMprob<sup>TM</sup> testing were 63.6% and 89.8%, respectively. Diagnostic accuracy of total PSA, free/total PSA, DRE and TRUS are summarised in Table 2.

#### 4. Discussion

The results of this study provide the first evidence for the non-invasive EM detection of cancer and represent a proof-of-concept, which may open a totally new field of medicine. Research into the interactions of EM waves with biological tissues goes back to the early decades of 20th century and numerous references can be found in the peer-review literature. Progress in this field paralleled technological development and it was recently summarised by A. Meessen suggesting the possibility of EM cancer detection [30,34]. The dis-

ussion over the mathematics and physics involved in the TRIMprob<sup>TM</sup> function go beyond the scope of this paper. It suffices to understand that the EM waves generated by the TRIMprob<sup>TM</sup> can stimulate minute electrical oscillations in biological tissues and produce resonance effects that depend on the pathological state of these tissues. Coupling of the oscillations of the probe with those from the biological tissues produces the remarkable phenomenon of “nonlinear resonance interaction”. This particular form of resonance can be detected by the receiver of the TRIMprob<sup>TM</sup>. Since the required intensities of the EM wave are very low, there is no health hazard associated to the EM radiation.

The nonlinear resonance interaction at 465 MHz frequency range seems to be important in distinguishing cancerous from benign prostate tissue. No consensus has been reached yet as to the reasons why the 465 MHz frequency is more specific for cancer tissue than 930 and 1395 MHz. It may be that the other frequencies are of importance in the detection of other disease and in different locations. Further work is ongoing for the use of the TRIMprob<sup>TM</sup> in other areas including the detection of breast, kidney, stomach and duodenum as well as bladder cancer [35].

TRIMprob<sup>TM</sup> test performed in 5 patient cohorts (controls, BPH, BPH with elevated PSA, abnormal DRE and prostate cancer) results in significant difference in amplitude at 465 MHz. We felt it was important to observe that patients with a biopsy proven diagnosis of prostate cancer have a very low signal amplitude at 465 MHz compared to young men with normal prostates (as shown by clinical examination, transrectal ultrasound and PSA levels of less than 4 ng/ml) in whom the chance of prostate cancers is virtually nil, because this proves the concept that a significant interaction occurs at this frequency level in patient with prostate cancer compared to controls and patients with BPH [36]. Further testing was undertaken to see if the test could be used to differentiate patients with BPH and seemingly little likelihood of prostate cancer. Significant differences were seen between these groups and those with proven prostate cancer. Those patients with a higher risk of prostate cancer (abnormal DRE or

raised PSA) had an average value for each frequency which was closer to the values obtained for prostate cancer than benign glands, presumably reflecting the incidence of undetected prostate cancer. The very low amplitude found in patients with abnormal DRE is not unexpected as the vast majority of these patients had prostate cancer on biopsy. We have no explanation for the very low amplitude measured at 465 MHz in this group (lower than in the prostate cancer cohort) but we have to consider that no information is currently available as to the relation of the signal amplitude and cancer volume, grading or any other tumour parameter.

Data as to the accuracy of the TRIMprob™ in the diagnosis of prostate cancer are certainly preliminary and remain valid for the patient cohort they were obtained from. We are anyway confident in the reported values, as they can be considered a conservative estimation compared with our present experience. We have to acknowledge that the evaluation of the TRIMprob™ accuracy in the diagnosis of prostate cancer is problematic because the diagnosis is based upon a positive prostate biopsy, and we are aware that even a 16 G biopsy samples less than 1% of the gland, so that a negative set of 6 or 12 biopsies does not rule out completely the possibility of an underlying neoplasm which is eventually diagnosed on further biopsies. Prostate cancer detection currently represents a real challenge for the clinician.

In order to explore the diagnostic accuracy of TRIMprob™ testing for cancer, a subset of 211 patients underwent prostatic biopsy. Analysis of the Receiver Operator Characteristic (ROC) curves for TRIMprob™ data at 465 MHz versus prostate biopsy suggested a cut off value of 50 units as the ideal threshold for diagnosis prostate cancer (best combination of sensitivity and specificity). Using such cut-off value, a sensitivity of 95.4% and a specificity of 42.7% can be expected. The relatively low value of the observed specificity maybe due to the limitations inherent to prostate biopsy, as a negative result does not completely exclude a cancer. These values compare well with the observed values of sensitivity, specificity and positive predictive value for PSA and DRE in the same patient group. Cooner and co-workers, showed that patients with total PSA levels <4 ng/ml had a chance of having a positive biopsy of 9% with a normal DRE and 17% with positive DRE. The chance rises to 25% and 62% in the same patient categories when the total PSA levels were >4 ng/ml [36].

The TRIMprob™ test is currently performed by hand and a certain degree of error can be expected as a result. To ensure that the entire prostate is scanned, a volume well in excess of the gland is studied with

repeated movements across the whole volume, as the beam emitted from the probe is very narrow. Blind scanning of the prostate volume through the perineum carries the theoretical risk of false negative results from failure to analyse the entire prostate volume. Proper training of the TRIMprob™ user is based upon supervised use of the equipment plus a trial and error training on patients with a known diagnosis of prostate cancer, in whom the perineum is examined with the probe until a significant reduction in the amplitude of the 465 MHz signal is observed. The risk of possible interference from rectal or bladder cancer should always be considered. The issue of bladder cancer has been addressed by a study looking at TRIMprob™ test in patients with bladder cancer scheduled for radical cystectomy, this study is now ongoing and will also provide an ideal cohort of age-matched control patients in which pathological examination of the prostate will be carried out irrespectively of PSA or DRE, and histology will be matched with TRIMprob™ results. The issue of rectal cancer will be addressed in a separate study which is also ongoing at the time this manuscript is reviewed. The TRIMprob™ remains an operator-dependent technique, preliminary data on intraobserver and interobserver variability are satisfactory although they have been obtained in a highly trained centre. A very low false negative rate was seen (2%) in patients with an histologically proven diagnosis of prostate cancer (data not shown). At present no information is available as to the lowest volume of prostate cancer which can be detected by the TRIMprob™, although some new information will be available from the ongoing study on patients having the prostate scanned by the TRIMprob™ and subsequently undergoing radical prostatectomy with 3D reconstruction of tumour volume.

We believe the results of the TRIMprob™ test in men have the potential to be used as an adjunct screening tool alongside the recognised tests of digital examination and PSA. The evaluation of non-linear resonance interaction may offer new opportunities in the diagnosis of prostate cancer and open a new field in medicine.

### Conflict of interest statement

Carlo Bellorofonte, Pietro Tombolini, Michele Ruoppolo, and Andrea Tubaro declare no conflict of interest, including employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications, and travel grants or personal relations which may have biased their opinion in the preparation of the paper. Clarbruno Vedruccio is a consultant for

Galileo Avionica S.p.A. The TRIMprob™ system has been kindly provided, free of charge by Galileo Avionica S.p.A., the S. Carlo Borromeo Hospital has gently provided the outpatient facility where the TRIMprob™ tests were conducted and the clinical study has been performed on a voluntary basis by all authors. Mr. Carlo Bellorofonte and Mr. Andrea Tubaro had full access to study database and had final responsibility for the decision to submit for publication.

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## Editorial Comment

C. Bangma, *Rotterdam, The Netherlands*  
[h.j.vanalphen@erasmusmc.nl](mailto:h.j.vanalphen@erasmusmc.nl)

Non-invasive detection of prostate cancer would for sure be a very attractive tool in the hand of the urologists, now we are appreciating the potentially increasing incidence of symptomatic disease in the growing elderly population in Europe. The technique described in this article might be such a tool, however, it does not follow the conventional tract of development. What does the probe actually measure? Following the description of biological and physical properties for the breast (in 1926), it is suggestive that such properties might also be measured in a prostate model, whether in isolated tissues, or even in animal models of 'human' size like the dog. After reading the

article we remain uninformed about the influence of surrounding tissues of the pelvic floor on the detected signals. And it is this proof of the working mechanism on the isolated prostatic tissue (scientific reduction) that might convince the scientist (aren't we all?) that the detected signals are related to the condition of the prostate. For the clinical study, as the authors underline, the gold standard of diagnosis in fact should be the prostate gland removed by radical surgery in order to correlate signals to histologic size and grade of the malignant tumours.

The current evaluation of the probe is little more than looking at a black box, which many of us would like to be opened before jumping on its application. New developments always come as a surprise, but a critical assessment needs to follow these initial observations.