TECHNICAL NOTES

Diagnosis of Rectal Cancer by Electromagnetic Interactions: Preliminary Results

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OBJECTIVES: Although colonoscopy is effective in screening for colorectal cancer, its high cost and low compliance rates have encouraged a search for different methods. Our study was designed to evaluate the feasibility of rectal cancer detection using a nonlinear tuneable oscillator (TRIMprob™), a recently developed device for detecting differences in electromagnetic properties of cancerous and normal tissues.

METHODS: We tested 228 patients (115 male and 113 female) between March and September 2006: 114 patients with rectal cancer diagnosed on colonoscopy and 114 patients with negative colonoscopy results. The TRIMprob™ probe was moved over the surface of the pelvic area from the back and the front, with the patient standing, normally dressed, between the operator and the system receiver. The signal variation of three spectral lines, for 465-MHz, 930-MHz, and 1395-MHz frequencies was recorded for each of six probe positions.

RESULTS: Analysis of resonance values showed that only the 465-MHz frequency differentiated patients with rectal cancer from those without cancer at all six probe positions ($P < 0.001$). With a cutoff value of 50 arbitrary units, the area under the receiver operating characteristic curve was 0.94 (specificity, 85 percent; sensitivity, 94 percent).

CONCLUSIONS: The TRIMprob™ test discriminates well between patients with normal rectal tissue and those with malignant lesions. These preliminary results confirm that electromagnetic detection of rectal cancer is possible and suggest this method of extracorporeal scanning may be useful as a first-level screening tool.

KEY WORDS: Cancer screening; Nonlinear tuneable oscillator; Rectal cancer; TRIMprob; Tissue Resonance InterferoMeter Probe.

With its high incidence and mortality, colorectal cancer constitutes a public health burden in most industrialized countries, increasing the importance of proper screening and early diagnosis.[1] During 1998–2002, colorectal cancer was the fourth most frequently diagnosed cancer among males (11.3 percent of all cancers) and the third among females (11.5 percent). Among cancer deaths, it was the second most relevant among both males (10.4 percent of all cancer deaths) and females (12.4 percent). Data from the Italian Network of Cancer Registries[2] show an average of 88.8 new colorectal cancer diagnoses in Italy per year per 100,000 males and 70.3 per 100,000 females. It was estimated that 20,457 new colorectal cancer diagnoses are made in Italy every year among males and 17,276 among females. There were 10,526 deaths because of colorectal cancer among males and 9,529 among females.

Because of this high prevalence, as well as a long asymptomatic phase and treatability of precancerous lesions, colorectal cancer is an ideal target for screening. Several screening tests are available, but none is ideal. Previous studies have investigated the cost-effectiveness of colonoscopy, flexible sigmoidoscopy, and fecal occult blood testing as screening alternatives.[3] Flexible sigmoidoscopy was less cost-effective than fecal occult blood testing and colonoscopy. Fecal occult blood testing is a simple, low-cost screening method, but colonoscopy was more effective in saving lives. However, high costs and low compliance rates for colonoscopy have encouraged a search for different methods.

It has been proposed that cancer exposed to a low level of electromagnetic incident waves may behave differently than healthy tissue.[4] The phenomenon of "nonlinear resonance interaction," which is produced when the oscillations of an electromagnetic probe are coupled with those from biological tissue,[5] can be used to test for differences between healthy and cancerous tissues.

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A device containing a nonlinear tuneable oscillator (TRIMprob™) has been used with encouraging results in the diagnosis of prostate cancer[5–7] and breast cancer.[8] The aim of the present study was to test the ability of the TRIMprob™ device to detect rectal cancer.

MATERIALS AND METHODS

Patients

Of 1,792 patients admitted to our outpatient clinic from March to September 2006 because of gastrointestinal disease, 756 patients underwent colonoscopy and were evaluated for possible participation in the TRIMprob™ study. Exclusion criteria consisted of age younger than 18 years, history of psychiatric illness, and preoperative radiotherapy. To rule out possible interference with the electromagnetic field, we also excluded patients with active phlogistic processes, such as inflammatory bowel disease, anal abscess, or fistulas. To rule out possible interference from other types of altered tissues, we included only the rectum, with a cutoff 15 centimeters from the anal verge. A total of 228 patients (113 females and 115 males) were selected for participation in the study: 114 patients with negative colonoscopy results and 114 patients with colonoscopy positive for rectal cancer. Written informed consent was obtained from all subjects. The study protocol was approved by the Institutional Review Board of the Istituto Nazionale dei Tumori.

Test Principle

The TRIMprob™ system (Galileo Avionica, Turin, Italy), also called a Tissue Resonance InterferoMeter Probe, consists of a hand-held, battery-operated detection probe, a receiver, and a computer display. The system has been previously described.[4,5,8] Briefly, the probe, which is about 30 cm long, contains a nonlinear oscillator that generates a complex electromagnetic wave of low intensity with three frequency components (465, 930, and 1395 MHz) and a high degree of spatial and temporal coherence. According to Bellorofonte *et al.*[5], malignant and normal tissues may differ in the way they interact with such electromagnetic waves because proteins acquire more surface charges in malignant tumours,[9] and the attraction of these charges for water molecules results in the presence of more "bound water." Furthermore, dramatic changes in metabolism, intercellular communication, and adhesion properties of cancer cells result in modification of the number and nature of membrane proteins. The dipolar parts of the membrane proteins, which protrude from the membrane, can be reoriented by an oscillating electric field.[10] The electromagnetic field produced by the nonlinear oscillator of the TRIMprob™ stimulates oscillations inside the tissue. When these oscillations begin to resonate, an energy transfer can be detected in the wave emitted by the probe.[8] The receiver situated a short distance from the probe detects the change and acts as a spectrum analyzer. When the probe is brought near cancerous tissue, interaction with the oscillating electric field causes a negative amplitude change in one or more of the spectral lines. The reduction in signal amplitude indicates the presence of abnormal tissues and structures. The frequencies 465, 930, and 1395 MHz were previously determined to be optimal because they appeared to respond in the appropriate way to the resonances of the system.[8]

Test Procedure

The test was performed for each individual patient according to the procedure shown in Figure 1. The patient stood between the operator and the receiver, at a distance of 120 cm from the receiver. There was a single operator, who was not blinded to the results of the colonoscopy, because the endpoint was the feasibility of this device. The patient was dressed normally, but no

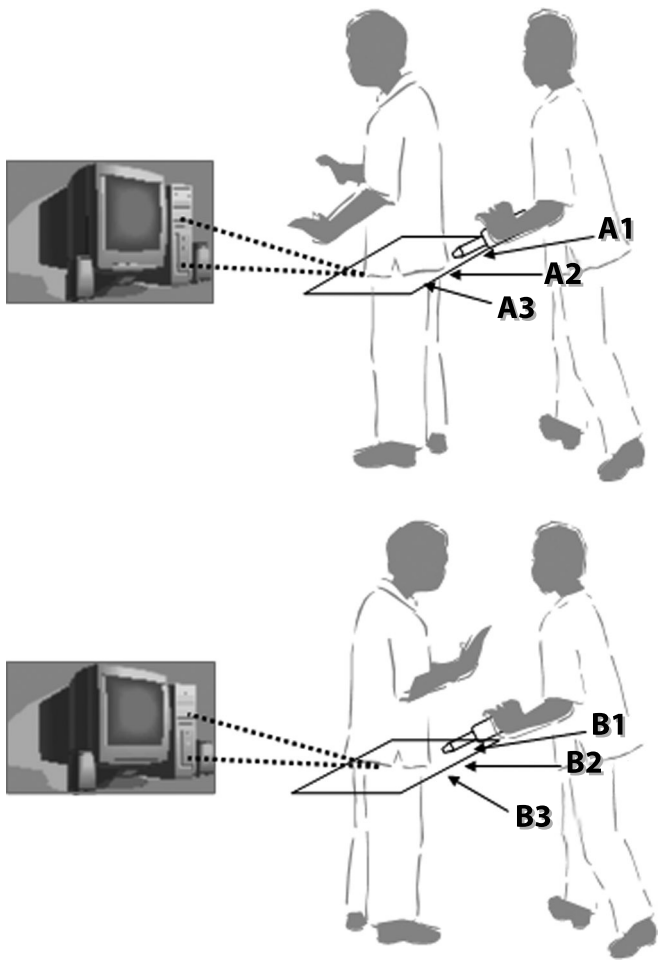

FIGURE 1. TRIMprob™ procedures. The detector was kept in close contact with the pelvic surface and was moved through six planes: A1, posterior right lateral; A2, posterior median; A3, posterior left lateral; B1, anterior right lateral; B2, anterior median; B3, anterior left lateral.

TABLE 1. Characteristics of tumors found in patients with positive colonoscopy

Tumor	*No. of patients (n = 114)*	*%*
Length from anal verge (cm)		
15–11	26	22.8
10–7	50	43.9
<7	38	33,3
Astler-Coller category		
A	12	10.5
B1	18	15.8
B2	25	21.9
C1	35	30.7
C2	14	12.3
D	10	8.8
Perivascular infiltration		
Negative	54	47.4
Positive	60	52.6

metallic objects were allowed on his or her person, and no electronic devices were admitted in the test area. The pelvic area was scanned by moving the detector at close contact over the pelvic surface through six planes, first in three directions (axial, left, and right) with the patient facing the receiver and then repeating the process with the patient turned to face the operator. In this way, a scan of the whole pelvis volume was obtained with signal acquisition at six positions: posterior median, left lateral, and right lateral; and anterior median, left lateral, and right lateral. Each change in amplitude of the emitted signals at the established frequencies was recorded and stored in an electronic file as a value of the corresponding spectral line expressed in arbitrary units between 255 and 0. Thus, three numeric values, corresponding to the signal amplitude of the spectral lines for the frequencies 465, 930, and 1395 MHz, were obtained for each position.

Statistical Analysis

Descriptive statistics (mean value, standard deviation, minimum, maximum, and range) were calculated for the signal amplitude values of the three frequencies for the six positions of signal acquisition. For each position and frequency, patients with positive results on colonoscopy were compared with those with negative results by means of Student's *t*-test. To evaluate the diagnostic performance of the TRIMprob™ test, we calculated receiver operating characteristic (ROC) curves for each of the three frequencies, using the mean of the two lowest signal values from the six acquisition positions in each patient for the individual TRIMprob™ values and the results of colonoscopy as the standard. Afterwards, the value of the area under each of the three different curves was calculated.

For all analyses, P values < 0.05 were considered significant. All statistical tests were performed with the SPSS 13.0 software for Windows (SPSS, Milan, Italy).

RESULTS

No adverse effects of the TRIMprob™ procedure were observed. The procedure was performed in a short time (approximately 10 minutes) and was well accepted by all patients.

Data from 114 patients with negative colonoscopy results and 114 patients with positive colonoscopy results were available for analysis. The mean patient age was 60.1 (range, 30–85; SD, 11.8) years for the negative colonoscopy group and 59.7 (range, 30–85; SD, 12.5) years for the positive colonoscopy group ($P = 0.67$). All patients with positive colonoscopy were admitted to the hospital with a diagnosis of adenocarcinoma and submitted to surgery. Table 1 shows the distribution of the main tumor characteristics.

Descriptive statistics for the signal amplitude values at each probe position and frequency are shown in Table 2. The results of Student's *t*-test performed on the comparison of values from patients with negative

TABLE 2. Descriptive statistics for signal amplitude values[a] of spectral lines for 465-MHz, 930-MHz, and 1395-MHz frequencies

	Results of colonoscopy											
	Negative						*Positive*					
	First line 465 MHz		*Second line 930 MHz*		*Third line 1395 MHz*		*First line 465 MHz*		*Second line 930 MHz*		*Third line 1395 MHz*	
Position	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Posterior												
Right	98.9	29.11	111.54	43.13	124.92	30.08	52.14	22.53	98.44	35.56	116.85	26.39
Median	95.67	31.55	109.96	42.48	121.08	31.30	51.61	27.12	96.79	36.34	117.7	24.41
Left	98.84	30.14	108.93	45.14	122.12	32.79	52.65	21.05	98.25	36.20	116.02	27.04
Anterior												
Right	95.05	32.28	110.67	44.09	123.84	29.46	55.37	20.24	101.32	33.11	119.49	25.13
Median	93.92	29.36	105.92	43.14	121.7	31.22	48.73	23.57	99.89	33.76	116.45	26.20
Left	99.32	28.89	112.18	42.30	122.25	30.69	56.19	21.73	99.54	31.82	115.79	26.04

SD = standard deviation.
[a]Expressed in arbitrary units.

TABLE 3. Student's *t*-test[a] of comparison of mean signal amplitude values from patients with negative vs. positive colonoscopy

Position	Student's t-test	
	T	*P value*
Posterior right		
465 MHz	13.06	<0.001
930 MHz	2.05	0.01
1395 MHz	2.02	0.03
Posterior median		
465 MHz	11.03	<0.001
930 MHz	2.52	0.01
1395 MHz	0.91	0.37
Posterior left		
465 MHz	13.40	<0.001
930 MHz	0.11	0.05
1395 MHz	1.53	0.13
Anterior right		
465 MHz	11.01	<0.001
930 MHz	1.08	0.07
1395 MHz	1.20	0.23
Anterior median (465 MHz)		
465 MHz	12.08	<0.001
930 MHz	1.17	0.24
1395 MHz	1.04	0.17
Anterior left		
465 MHz	12.07	<0.001
930 MHz	2.05	0.01
1395 MHz	1.07	0.09

[a]Equality of variance assumed.

colonoscopy vs. those with positive colonoscopy are shown in Table 3. Only the first spectral line, at the 465-MHz frequency, differentiated the group with positive colonoscopy from that with negative colonoscopy in all six probe positions ($P < 0.001$). At 930 MHz, the two groups differed significantly only in the posterior right, posterior median, posterior left, and anterior left positions; no significant differences were seen at 1395 MHz.

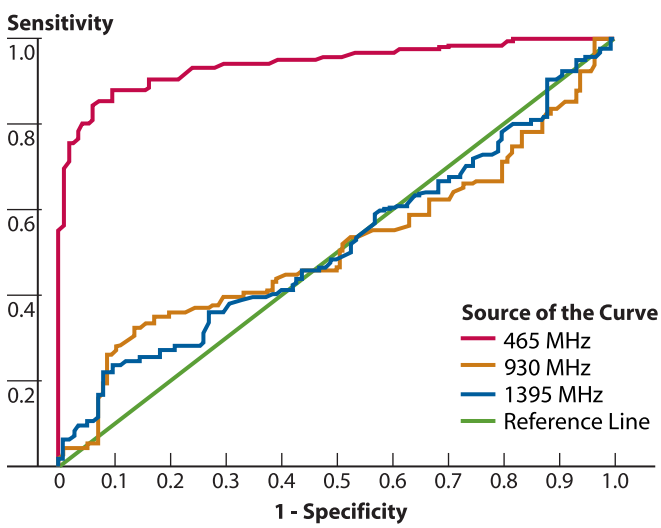

FIGURE 2. Receiver operating characteristic (ROC) curves and corresponding areas under the ROC curve (AUC-ROC) calculated for each frequency (465 MHz, 930 MHz, and 1395 MHz) using the mean of the two lowest signal values from the six acquisition positions in each patient for the individual TRIMprob™ values and the results of colonoscopy as the standard. Diagonal segments are produced by ties.

TABLE 4. Area under the curve of receiver operating characteristics curve (AUC-ROC)

Spectral line	AUC-ROC	SE[a]	P[b]	Asymptotic 95% CI	
				Lower boundary	Upper boundary
465 MHz	0.94	0.02	<.001	0.91	0.97
930 MHz	0.51	0.04	0.75	0.44	0.59
1395 MHz	0.52	0.04	0.65	0.44	0.59

95% CI = 95% Confidence interval; AUC-ROC = Area under the curve of receiver operating characteristic curve; SE = Standard error.
[a]Under the nonparametric assumption.
[b]Null hypothesis: true area = 0.5.

Figure 2 shows the ROC curves calculated for each frequency. The corresponding area under the ROC curve (AUC-ROC) is shown for each frequency in Table 4. Only the 465-MHz frequency had an AUC-ROC value close to 1 (0.94), indicating good discrimination between positive and negative colonoscopy at this frequency. In contrast, 930 MHz and 1395 MHz had AUC-ROC values close to 0.5, indicating poor discrimination.

Table 5 shows the diagnostic performance of the TRIMprob™ test when a cutoff of 50 arbitrary units was chosen for the 465-MHz frequency.

DISCUSSION

Recent interest has focused on use of the phenomenon of nonlinear resonance interaction coupling of the oscillations of a probe with those from biological tissues for diagnosis of disease.[13–15] Our study shows that this technique may be useful in the detection of rectal cancer. In our experience, the TRIMprob™ procedure can be easily and quickly performed and is well accepted by patients. Our finding that the 465-MHz frequency was the most accurate of the three frequencies in identifying patients affected by rectal cancer (AUC-ROC, 0.94) was consistent with results obtained by Bellorofonte *et al.*[5] in patients with prostate cancer.

Because the TRIMprob™ is a handheld device and the beam emitted from the probe is narrow, proper

TABLE 5. Diagnostic accuracy of TRIMprob™ with a cutoff of 50 arbitrary units for the 465-MHz frequency

True positive	True negative	False positive	False negative
n	*n*	*n*	*n*
107	97	17	7
Sensitivity 0.94 (0.88–0.98)		Specificity 0.85 (0.77–0.91)	

training of the operator is important to avoid error.[5] Operators should be trained to scan a volume well in excess of the bowel to ensure that the entire rectum is included, with repeated movements across the whole volume. Novice operators should be supervised and should undergo trial-and-error training with patients who have a known diagnosis of rectal cancer. The risk of possible interference from prostate or bladder cancer should always be considered. If in doubt, it is easy to check the bladder or the prostate with the probe in one shot. Although the TRIMprob™ remains an operator-dependent technique, preliminary data on intra- and inter-observer variability obtained with highly trained operators appear satisfactory.[5,8]

The ROC curves in Figure 2 reflect the trade-off that comes into play when the cutoff value is raised, increasing test sensitivity at the expense of specificity. We believe that the cutoff value should be kept relatively high to achieve high sensitivity. Approximately 50 percent of patients with colorectal cancer who are diagnosed on the basis of clinical symptoms could be cured by surgery, and early diagnosis before the appearance of symptoms would likely increase the number of patients who could be cured. Therefore, screening a sensitive screening method appears to be the simplest way to decrease mortality from colorectal cancer. The sensitivity of fecal occult blood testing is only 26 percent, and the predictive value of a positive test is 8.2 percent.[16] Colonoscopy has high sensitivity and predictive value, but its high cost and low compliance rates preclude its use in widespread screening.[17] Our findings of 94 percent sensitivity and 85 percent specificity for the 465-MHz frequency were consistent with values found in other studies.[5,6,7]

The usefulness of the TRIMprob™ test as a screening tool needs to be verified in further studies. However, this probe appears promising in the diagnosis of rectal cancer and presents an opportunity for a new screening strategy characterized by simplicity, efficacy, and good patient compliance.

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