# **ORIGINAL ARTICLE**



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# Characterizing the tissue dielectric constant of skin basal cell cancer lesions

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# Abstract

**Background**: Measuring tissue dielectric constant (TDC) of cancer tissues to distinguish them from normal or non-cancerous tissues has been an active area of research that has targeted several different cancer types usually using in vitro specimens. The goal of this study was to determine if and to what extent TDC values measured in vivo at 300 MHz using a simple hand-held measuring device might differentiate between skin cancer lesions and non-cancerous skin.

**Materials and Methods**: Triplicate TDC measurements were made in 32 patients who were subsequently diagnosed with skin basal cell carcinoma (BCC) and in 14 patients subsequently diagnosed as having non-cancerous lesions. Lesion TDC values were compared to contralateral unaffected skin and between lesion types.

**Results**: A significantly lower TDC value (mean ± SD) of BCC lesions (TDC<sub>L</sub>) vs TDC values of contralateral non-affected skin (TDC<sub>C</sub>) was found (22.4 ± 16.2 vs  $38.1 \pm 15.2$ , *P* < .00001). A similar pattern was found for non-cancerous lesions with lesion TDC values less than non-affected skin (14.5 ± 9.0 vs 29.1 ± 9.0, *P* < .0001). However, TDC values were not statistically different between BCC lesions and non-cancerous lesions (22.4 ± 16.2 vs 14.5 ± 9.0, *P* = .096) and calculated TDC<sub>L</sub>/TDC<sub>C</sub> ratios between BCC lesions and non-cancerous lesions also were not significantly different (0.596 ± 0.345 vs 0.501 ± 0.261, *P* = .364).

**Conclusions**: (1) Main results do not support using TDC measurements to differentiate in vivo skin cancer lesions from non-cancerous lesions. (2) TDC values strongly suggest reduced water content of both cancerous and non-cancerous lesions. (3) Lesion TDC measurements provide reference values for future studies.

### KEYWORDS

basal cell carcinoma, cancer cell permittivity, cancer differentiation, dielectric constant, skin cancer, skin permittivity, skin water

# 1 | INTRODUCTION

Assessment of the tissue dielectric constant (TDC) of cancer tissues as a means to distinguish them from normal or non-cancerous tissues has been an active area of research that has targeted several different cancer types. TDC measurements over the range of 500 MHz to 8000 MHz have recently been made of excised normal breast tissue vs non-malignant breast tumors vs breast cancer tumors.<sup>1</sup> Results indicated cancer tissue to have a significantly greater TDC than either of the other tissue types. Similar results have been reported using lower frequencies.<sup>2</sup> Part of these differences may be related to the lower water content of normal breast tissue since the permittivity of water plays an important role in the TDC value.<sup>3</sup> However, similar measurements of thyroid cancers, which have also indicated a greater TDC for malignant than normal tissue<sup>4</sup> may indicate additional roles for cell size, shape and orientation within malignant tissue that contributes to impedance spectra differences among skin cancers and normal tissue.<sup>5-7</sup> The goal of the present study was to determine if and to what extent TDC values measured at 300 MHz using a simple hand-held measuring device might differentiate between skin cancer lesions and non-cancerous skin. The purpose of these measurements was to determine if such TDC measurements have a possibility of subsequently being used in a clinical setting to help differentiate between cancer and normal tissue. Because there is virtually no published information we could identify regarding in vivo skin lesion dielectric permittivity at this operating frequency, the present research may be termed a pilot study with the specific aim to help characterize basic skin lesion TDC properties. The focus of the present report is skin basal cell carcinoma (BCC) as compared to non-cancerous skin tissue.

# 2 | METHODS

### 2.1 | Subjects

Persons who presented at a dermatology practice for the evaluation of a skin lesion were asked to participate if clinical judgment determined that a biopsy of the lesion in question was indicated. The nature of the research study was explained and those who elected to voluntarily participate signed a university institutional review board approved consent form. This report is based on a total of 32 patients in whom lesion biopsies were made with the histological diagnosis of basal cell carcinoma (BCC) and 14 patients who had the histological diagnosis of the lesion being non-cancerous. This BCC evaluated group consisted of 12 women and 20 men. The women's age (mean  $\pm$  SD) was  $78.1 \pm 10.7$  years and body mass index (BMI) was  $28.9 \pm 7.7$  kg/m<sup>2</sup>. The men's age was  $68.7 \pm 16.0$ with a BMI of  $27.8 \pm 4.5$  kg/m<sup>2</sup>. The non-cancerous lesion group consisted of 5 women and 9 men. The age of women in this group

# **TABLE 1** Anatomical locations of evaluated lesions

was 76.1  $\pm$  9.5 years and their BMI was 31.4  $\pm$  6.5 kg/m<sup>2</sup>. The men's age was 74.2  $\pm$  6.4 and their BMI was 29.9  $\pm$  3.4 kg/m<sup>2</sup>. The distribution of anatomical locations of the evaluated lesions is indicated in Table 1.

### 2.2 | Measurements

TDC measurements were done using the MoistureMeterEpiD (Delfin Technologies, Kuopio Finland) that has a sensor tip contact diameter of 8 mm (Figure 1) and a stated effective measurement depth of 0.5 mm. This device was chosen for its small sensor diameter allowing measurement of lesions with diameters as small as 10 mm with the inclusion of little or none of the surrounding skin in the measurement. The use of TDC values to assess skin properties has been widely reported in the literature,<sup>8-12</sup> however the present application is unique. Briefly, the probe acts as an open-ended coaxial transmission line<sup>13-17</sup> through which a 300-MHz signal is transmitted. Reflections depend on the tissue's complex permittivity, which in-turn depends on the signal frequency and the tissue dielectric constant (the real part of the complex permittivity). At the frequency used, the contribution of conductivity to permittivity is small, so TDC is determined by water molecules (free and bound) and the other tissue constituents. Although the device used in this study internally converts the measured TDC value to a percentage water, all values herein reported are expressed as the unconverted true TDC value. The TDC measurement procedure requires that the device sensor be placed in contact with the skin for 6-7 seconds (Figure 1) whereupon the reading is displayed on the device digital display. A built-in pressure sensor allows for reasonably consistent applied pressures to be achieved. Triplicate measurements were taken on the lesion and also on a non-affected anatomically similar contralateral site.

	Basal cell cancer lesions			Non-cancer lesions	
Locations	Number	Percent	Locations	Number	Percent
Total	32	100	Total	14	100
Arm	5	15.6	Arm	3	21.4
Back	1	3.1	Back	1	7.1
Cheek	1	3.1	Cheek	1	7.1
Chest	2	6.3	Eyebrow	1	7.1
Chin	2	6.3	Forehead	1	7.1
Ear	2	6.3	Hand	1	7.1
Forehead	2	6.3	Leg	1	7.1
Jaw	1	3.1	Nose	1	7.1
Lip	1	3.1	Rib	1	7.1
Neck	4	12.5	Shin	1	7.1
Nose	9	28.1	Thigh	2	14.3
Shin	1	3.1			
Shoulder	1	3.1			

One lesion per patient was included in the location distribution so the number of lesions corresponds to the number of patients. The anatomical specifications were based on chart statements and photographs.



FIGURE 1 Tissue Dielectric Constant (TDC) Measuring Device. A, Full view with dimensions, B, Sensor view C, Sensor in contact with skin

	Basal cell carcinoma diagnosis		Non-cancer diagnosis		
	Lesions	Contralateral skin	Lesions	Contralateral skin	
Ν	32	32	14	14	
TDC value	22.4 ± 16.2	38.1 ± 15.2	14.5 ± 9.0	29.1 ± 9.0	
P -value	<.00001		<.0001		
TDC Ratio Lesion/ Contralateral	0.595 ± 0.345		0.501 ± 0.261		
P -value	.364				

**TABLE 2** Tissue dielectric constant (TDC) values

TDC values are based on triplicate values at each site that are averaged. TDC values and Lesion/ Contralateral TDC ratios are given as mean  $\pm$  SD. Lesion TDC values are significantly less than nonaffected contralateral skin for both BCC lesion diagnosis and for benign lesion diagnosis. There is no statistically significant difference in TDC ratios (Lesion/Contralateral) between BCC and noncancerous lesions.

The average of the three measurements at each site was used and taken as representative of the lesion and non-affected skin site TDC values. Room temperature during measurements was  $21.6 \pm 1.2$  °C.

### 2.3 | Analysis

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The average of the triplicate TDC values measured at each lesion  $(TDC_l)$  and control skin  $(TDC_c)$  site was used to determine differences between lesion and control sites and between BCC lesions and non-cancerous lesions. Lesion/control TDC ratios  $(TDC_l/TDC_c)$ 

were also calculated Values measured on lesions compared to those measured on non-affected control skin (TDC<sub>C</sub>) were compared using a paired T test (SPSS v16). BCC lesion values were compared to non-cancerous lesions using independent t tests.

### 3 | RESULTS

The main quantitative result for BCC lesion demonstrates are summarized in Table 2. A highly significant difference between TDC



**FIGURE 2** Cancerous and Non-Cancerous Lesions with Various Lesion/Contralateral Ratios. A-C are cancerous lesions (BCC) and D-E are non-cancerous (benign lesions). A, Shoulder with ratio = 0.365, B, Face with ratio = 0.411, C, Neck with ratio = 1.255, D, Arm with ratio = 0.243, E, Leg with ratio = 0.639, F, Arm with ratio = 0.980

values as measured on the BCC lesion vs TDC values measured at the non-affected skin site, with the lesion having a lower TDC<sub>L</sub> value as compared to TDC<sub>C</sub> (22.4 ± 16.2 vs 38.1 ± 15.2, *P* < .00001). Of the 32 BCC lesions measured in the 32 patients, TDC<sub>L</sub> was less than TDC<sub>c</sub> in 29 patients (90.6%). The calculated TDC<sub>L</sub>/TDC<sub>c</sub> ratio ranged from 0.081 to 0.938 and had an average ratio of 0.522 ± 0.268. The overall TDC<sub>L</sub>/TDC<sub>c</sub> ratio including all 32 patients was 0.595 ± 0.345. The three lesions for which TDC<sub>L</sub> > TDC<sub>c</sub> were located on the neck and each had a visual appearance of considerable erythema and in one case ulceration. TDC<sub>L</sub>/TDC<sub>c</sub> ratio for these three lesions was 1.304 ± 0.086. Figure 2 (A-C) illustrates three BCC lesions with different locations and different TDC<sub>L</sub>/TDC<sub>c</sub> ratios.

The main quantitative result for non-cancerous lesions also demonstrates a highly significant difference between TDC values as measured on these lesions vs TDC values measured at the non-affected skin site, with the lesion having a lower TDC<sub>L</sub> value as compared to TDC<sub>C</sub> (14.5 ± 9.0 vs 29.1 ± 9.0, *P* < .0001). Of the 14 non-cancerous lesions measured in the 14 patients, TDC<sub>L</sub> was less than TDC<sub>c</sub> in all patients (100%). The calculated TDC<sub>L</sub>/TDC<sub>c</sub> ratio ranged from 0.081 to 0.980 and had an average ratio of 0.501 ± 0.261. Figure 2 (D-F) illustrates three non-cancerous, benign lesions with different TDC<sub>L</sub>/TDC<sub>c</sub> ratios.

Comparisons of TDC values between BCC lesions and noncancerous lesions reveal no statistically significant difference between them although there appears to be a tendency for BCC lesions to have a greater TDC value ( $22.4 \pm 16.2$  vs  $14.5 \pm 9.0$ , P = .096). Comparing the TDC<sub>L</sub>/TDC<sub>C</sub> ratios between BCC lesions and non-cancerous lesions also reveals no significant difference ( $0.595 \pm 0.345$  vs  $0.501 \pm 0.261$ , P = .364).

## 4 | DISCUSSION

The primary aim of this study was to investigate the possibility of using TDC measurements of skin lesions as a way to differentiate malignant lesions from non-malignant tissue. As a first step in that process TDC values were measured and compared on skin lesions that were subsequently histologically assessed and determined to be basal cell carcinoma or benign lesions.

A new finding was that TDC values on lesions, whether cancerous or noncancerous lesions, were significantly lower than corresponding TDC values measured on contralateral non-affected skin. On average the BCC lesions were 42.2% less than corresponding control skin and the non-cancerous lesions were 50.2% less than corresponding control skin. However, despite these clear and substantial differences between lesions and normal skin, there was no statistically significant difference between lesion types whether assessed in absolute terms or in terms of lesion/control ratios. These pilot study findings suggest that lesion TDC measurements are not useful to differentiate between lesion types.

Despite this apparent negative outcome with respect to the primary study aim, the present results do provide previously unavailable data relevant to in vivo lesion TDC-related features. Firstly, is the finding of a lower TDC value of lesions independent of type. This would appear to be at odds with almost all other reported dielectric constant and conductivity measurements made on tumors measured in vitro. Measurements of thyroid tissue also indicate greater values for malignant tissue than for normal tissue with values measured at 500 MHz being 68.7 vs 24.0.<sup>4</sup> This yields a more modest cancer/normal permittivity ratio of 2.86. Similar measurements on breast cancer tissue and non-cancerous breast tissues have comparable directional differences, with cancer tissue dielectric permittivity being greater.<sup>1</sup> The pioneering work of Schepps and Foster<sup>3</sup> has demonstrated in normal tissue and in several cancer types that the dielectric constant value as a function of frequency positively correlates with the water volume fraction in the tissue. Based on extensive measurements, they report an empirical predictive equation for the dielectric constant ( $\varepsilon'$ ) that depends on both frequency (f) and tissue water volume fraction (W) that can be expressed as  $\varepsilon' = 1.71 \text{ f}^{-1.13} + [\varepsilon_{water} (2W-1) - 4] / [1 + (f/25)^2] + 4.$ 

At a frequency of 300 MHz (0.3 GHz) as used in the present study, this equation can be used to estimate the approximate water volume fraction in the measured skin and lesions using the dielectric constant of water ( $\varepsilon_{water}$ ) at 34°C which is approximately 75 x.<sup>18</sup> Doing this calculation for both lesion types (BCC and non-cancerous) and for the corresponding non-affected skin indicates an average skin water percentage of between 65%-71% which would be consistent with values determined using a variety of other methods.<sup>19,20</sup> In contrast, the calculated water percentages for the BCC and non-cancerous lesions are 61% and 45%, respectively. These approximate calculations indicate that the relative water content of in vivo skin lesions is in fact less than normal skin and also less than values variously reported for nonskin cancer tissues measured under in vitro conditions. Although the source of this difference is not known with certainty, it may be that the presence of the lesions on the skin surface permit an effective partial dehydration as compared to normal skin which is protected from significant water loss via intact skin barrier function. Such an explanation would be consistent with the fact that in this study design TDC values were measured to a depth of 0.5 mm.

In conclusion, the present results do not support the use of tissue dielectric constant measurements as a way of differentiating skin cancer lesions from non-cancerous lesions. Moreover, the results indicate a strong possibility of large differences in water content of skin exposed lesions as compared with those excised and measured in vitro. These findings along with the tabulated absolute TDC values may prove to be useful reference in future studies.

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