Investigation Of Effective Medium Theory Concerning Applications For Skin Cancer Detection

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Abstract: *Skin cancer detection proves to be complicated and highly dependent on the examiner's skills. Millimeter-wave technologies seem to be a promising aid for the detection of skin cancer. The different water content of the skin area affected by cancer compared to healthy skin changes its reflective property. Due to limited available resources on the dielectric properties of skin cancer, especially in comparison to surrounding healthy skin, accurate simulations and evaluations are quite challenging. Therefore, comparing different results for different approaches and starting points can be difficult. In this paper, the Effective Medium Theory is applied to model skin cancer, which provides permittivity values dependent on the water content.*

1. Introduction

Millimeter-wave (mm-wave) technologies are a promising development to aid in skin cancer detection and classification. According to [1][2] skin cancer shows different electrical properties in comparison to the surrounding healthy skin tissues.

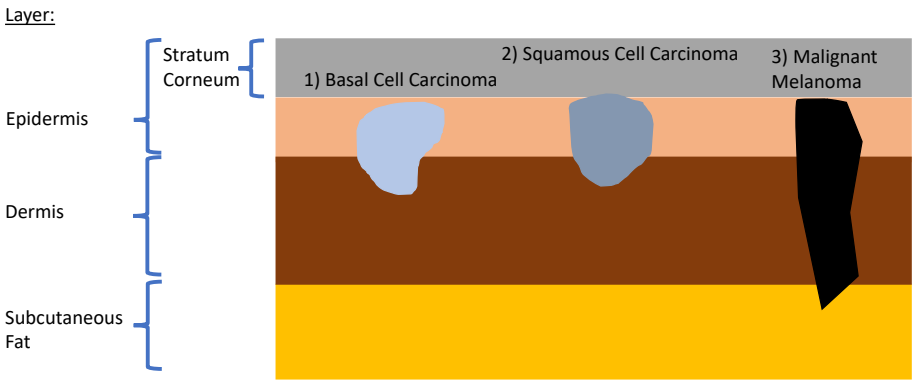

Figure 1: Different layers of the skin and development of skin cancer, cf. [3]

Figure 1 shows the three main layers of the skin: the outermost layer Stratum Corneum, followed by the Epidermis and the last layer the Dermis. The three most common types of skin

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cancer are also depicted. The first one is $1)$ Basal Cell Carcinoma (BCC), which originates at the boundary of the Epidermis and the Dermis. Next is the $2)$ Squamous Cell Carcinoma (SCC) which originates in the Epidermis and lastly the $3)$ Malignant Melanoma (MM), which comes from the pigment cells at the boundary of the Epidermis and Dermis. Most systems measure the effective permittivity of the skin indirectly over the reflectivity with the scattering parameter S_{11} and compare the result with the surrounding healthy skin [3][4]. To develop technologies and devices, which might aid in the detection of skin cancer in the future, models of healthy and cancerous skin need to be available. Especially early-stage evaluation, simulations and development require models and data as a starting point. For healthy skin several studies are available [5][6], whereas in comparison only a limited number of studies are available for skin cancer [7][8]. The Effective Medium Theory (EMT) allows the calculation of an effective permittivity with at least two base materials of known permittivity. It is used in several studies to calculate a single permittivity value for skin cancer [4][9]. Expanding on this, it is proposed to not just focus on a single data value for skin cancer but rather use EMT for the calculation of a whole dataset. It is also suggested here to focus more on the differences in permittivity values of cancer, benign lesions and healthy skin rather than absolute values.
The EMT is well suited for this by allowing an easy calculation of permittivity data for skin cancer, as shown later. A frequency range of 30 GHz to 60 GHz will be considered here, because of the depth at which skin cancer originates and the penetration depth of the electric field in the skin.

2. Limitations of available measurement data of skin cancer

The permittivity describes how a dielectric material polarizes if an external electric field is applied and how the electric field is influenced by this in return. Relative permittivity is a dimensionless value, which is commonly used and defined as:

$$\varepsilon_\mathrm{r} = \frac{\varepsilon}{\varepsilon_0} \tag{1}$$

with the electric field constant $\varepsilon_0 = 8.854 \cdot 10^{-12}\,\mathrm{As/Vm}$. If the material has losses the relative permittivity is complex-valued as follows:

$$\underline{\varepsilon}_\mathrm{r} = \varepsilon_\mathrm{r}' - j\varepsilon_\mathrm{r}'' \tag{2}$$

where ε_r' and ε_r'' describe the real and imaginary part of the relative permittivity, of which the loss factor $\tan\delta = \frac{\varepsilon_\mathrm{r}''}{\varepsilon_\mathrm{r}'}$ can be calculated. In Fig. 2 the real and imaginary part of the relative permittivity of skin cancer data from literature is shown. Mirbeik et al. [7] performed ex-vivo measurements on freshly excised skin cancer tissues. The data is separated into tissues that are histologically confirmed as skin cancer and ones that are benign [7]. Naqvi et al. [8] performed measurements in-vivo of the suspected cancer and surrounding healthy area, before the cancer was excised and histologically investigated [8]. Finally, data from Gabriel et al. [6] for healthy dry skin is also provided for comparison [6].

It is overall visible that the relative permittivity is highly frequency-dependent.

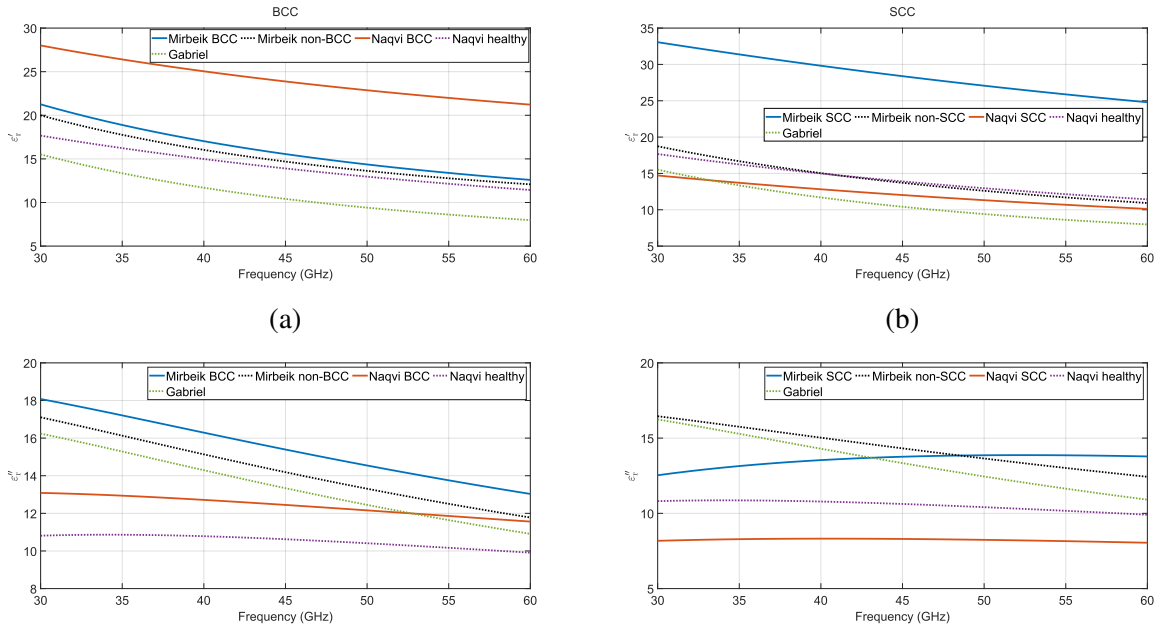

Figure 2: Permittivity for BCC (a & c) and SCC (b & c) separated in real (a & b) and imaginary (c & d) part, literature values for healthy skin are given for comparison [6]-[8]

Real Part of Permittivity (Fig. 2a & Fig. 2b) The real part for healthy and benign data from Naqvi et al. and Mirbeik et al. are in good agreement, which also agrees with the reported fact that benign lesions resemble more closely healthy skin [7][8]. In comparison, to the data from Gabriel et al. and the healthy skin from Naqvi et al. have different values. Overall, the malignant data show large differences. In both Mirbeik et al. and Naqvi et al. results of the shown values for BCC are higher compared to those of healthy skin. The values from Mirbeik et al. show a slight increase in comparison to the results for benign lesions. SCC has according to Mirbeik et al. the highest values overall. In [8], Naqvi et al. the presented results for SCC show lower values than the healthy skin. This agrees with the fact, that it was reported as scaly dry skin patches and excluded SCC lesions which showed as wet/open wounds [8].

Imaginary Part of Permittivity (Fig. 2c & Fig. 2d) The non-malignant data are in good agreement. The reported values from Gabriel et al. are closer to those reported by Mirbeik than the values for healthy skin by Naqvi et al., which show significantly different values. For BCC the values are higher than the respective healthy tissues. The values from Naqvi et al. for SCC are lower than healthy skin, which agrees with the reported lower water content [8]. For SCC reported by Mirbeik et al., the imaginary part of the permittivity is smaller at lower frequencies than the non-malignant tissues but increases for higher frequencies.

The differences in the values of SCC can partially result since Naqvi et al. only choose lesions that showed as dry and scaly, whereas lesions that showed as wet open wounds are excluded

[8]. Secondly, it is to mention that the chosen frequency ranges can also influence the results. Mirbeik et al. for example performed the measurements in the range of 0.5 GHz to 50 GHz [7], while Naqvi et al. measured within 1 GHz to 14 GHz [8]. The fitted Cole-Cole models will not have to extrapolate the data for a larger frequency range. This might cause a larger error for higher frequencies for the data reported by Naqvi et al.

At the same time, Naqvi et al. reported several systematic problems, which might occur by using ex-vivo measurements. One of the main problems is, that the measurements are performed after the cancer has been excised. One major factor is the temperature, which is lower than the normal body temperature by about 10 °C if room temperature is assumed. The permittivity of water is highly dependent on the temperature and will vary greatly, even for small changes. Since water is one of the main components in biological tissues and one of the main contributors to the permittivity [10], a change in temperature will have a major influence on measurement results. Especially, if the measurements of skin are performed at body temperature and the skin cancer measurements are performed at room temperature. In [8], it is also proposed that local anesthetic which is injected ahead of operation might also influence the dielectric properties and further falsify the measurement.
All these factors influence and falsify the measurement results from literature. Comparison or evaluation of systems can vary with used datasets, or even be incomparable if ex-vivo and in-vivo data are used. Therefore, the approach with EMT in this paper is to create several datasets, which might not represent biological tissues on their own but permits to compare and evaluate systems in their regard to measure the contrast $\Delta\varepsilon_\mathrm{r}$, of healthy and cancerous skin.

3. Permittivity of fundamental materials for calculation of skin permittivity

In the following section the used mixing equation is introduced. After that, the permittivity of water and dry biological material as the basic materials for the equation are presented.

3.1. Effective Medium Theory

The EMT allows the calculation of an effective permittivity from several base materials. It is often used in the study of biological tissues to complement and extend existing data [10]. It assumes some properties of the base materials, like shape and percentage of inclusions.

Figure 3: Visualization of the principle of EMT, cf. [10]

The resulting effective permittivity $\underline{\varepsilon}_{\mathrm{r,eff}}$, can be calculated with the Rayleigh equation as following [11]:

$$\frac{\underline{\varepsilon}_{\mathrm{r,eff}} - \underline{\varepsilon}_{\mathrm{r,e}}}{\underline{\varepsilon}_{\mathrm{r,eff}} + 2\underline{\varepsilon}_{\mathrm{r,e}}} = v\frac{\underline{\varepsilon}_{\mathrm{r,i}} - \underline{\varepsilon}_{\mathrm{r,e}}}{\underline{\varepsilon}_{\mathrm{r,i}} + 2\underline{\varepsilon}_{\mathrm{r,e}}} \tag{3}$$

The permittivity of the inclusions is $\underline{\varepsilon}_{\mathrm{r,i}}$ and the permittivity of the surrounding material is $\underline{\varepsilon}_{\mathrm{r,e}}$. The volume percentage which is given by $\underline{\varepsilon}_{\mathrm{r,i}}$ is v and for $\underline{\varepsilon}_{\mathrm{r,e}}$ the volume percentage is $1 - v$. It should be noted that the Rayleigh equation is not symmetrical, i.e., $\underline{\varepsilon}_{\mathrm{r,i}}$ and $\underline{\varepsilon}_{\mathrm{r,e}}$ are not interchangeable.

3.2. Water

The permittivity of water can be calculated with a Debye-Model [5].

$$\underline{\varepsilon}_{\mathrm{r,w}} = \varepsilon_\infty + \frac{\Delta\varepsilon}{1 + j\omega\tau} + \frac{\sigma}{j\omega\varepsilon_0} \tag{4}$$

The used parameters are given in the following Table 1 [5].

Table 1: Debye parameters for water at 32.6 °C [5]

ε_∞	$\Delta\varepsilon$	τ (ps)	σ (S/m)
5.2	70.8	6.9	0

An important aspect to consider is that tissue contains free and bound water. Bound water is part of structures or molecules and its contribution to the total permittivity is comparatively low [5]. This means the value used for water in the mixing equation will be lower than the total amount of water. Since water in biological tissues is not pure, the values can be extended for ionic conductivity, which is mainly due to salts, to represent an electrolyte [10].

$$\underline{\varepsilon}_{\mathrm{r,elec}} = \underline{\varepsilon}_{\mathrm{r,w}} - j\frac{\sigma_{\mathrm{ionic}}}{\omega\varepsilon_0} \tag{5}$$

For the ionic conductivity of water, literature values for the static conductivity of skin can be used. Here a value of $\sigma_{\mathrm{ionic}} = 1.4\,\mathrm{S/m}$ is considered [5].

3.3. Biological Material

For the underlying dry biological material, a constant real permittivity of $\varepsilon_{\mathrm{r}} = 2 \ldots 3$ is usually assumed in literature [10][12]. A value of $\varepsilon_{\mathrm{r}} = 2.5$ is used here, which gives a good agreement with literature values for human skin tissue.

4. Mixing results

The results of the mixing equation are presented in the following. Therefore, the calculated permittivity of electrolyte $\underline{\varepsilon}_{\mathrm{r,e}}$ is used (Section 3.2) and the permittivity of dry biological material

$\underline{\varepsilon}_{\mathrm{r,i}}$ is used (Section 3.3.) for (3). First, permittivity values for healthy skin are calculated by varying v and comparing them with literature values. In the second step, v is changed from the value for healthy skin in accordance with literature values for changes in water content in skin cancer.

4.1. Mixing healthy skin

The following Cole-Cole equation is used with the parameters in Table 2 for the calculation of the permittivity [6].

$$\underline{\varepsilon}_{\mathrm{r}} = \varepsilon_{\infty} + \sum_{\mathrm{n}} \left[\frac{\Delta\varepsilon_{\mathrm{n}}}{1 + (j\omega\tau_{\mathrm{n}})^{1-\alpha_{\mathrm{n}}}} \right] + \frac{\sigma}{j\omega\varepsilon_0} \tag{6}$$

This allows comparing the calculated results to literature values.

Table 2: Cole-Cole Parameter for dry skin [6]

ε_∞	$\Delta\varepsilon_1$	τ_1 (ps)	α_1	$\Delta\varepsilon_2$	τ_2 (μs)	α_2	σ (S/m)
4	32	7.23	0	1100	32.48	0.2	1.4

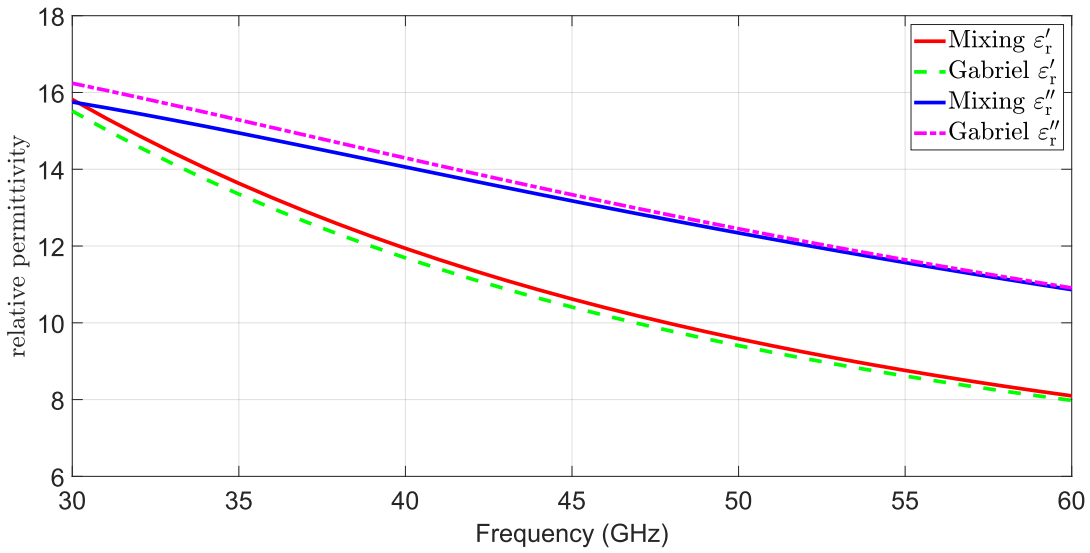

Figure 4: Mixing results compared to values taken from [6] for healthy dry skin.

In Fig. 4, the results of the mixed relative permittivity are shown. The value for $v = (1-0.55) = 0.45$ is used, which corresponds to a water content of $55\,\%$. The mixing results are in good agreement with the values found in literature in the chosen frequency range. The difference for the real and imaginary part of the relative permittivity are < 1 in the frequency range of interest. The used value for the percentage fraction of water is about $10\,\%$ lower than in [10] and [12], both using EMT to approximate the permittivity values for different skin layers separately. The difference of about $10\,\%$ can have several reasons. First, [10] and [12] use both a layered model

of skin, so the Stratum Corneum, Epidermis and Dermis are separated, which will lead to a higher water percentage in the combined Epidermis and Dermis than in a homogeneous model. Second, both use a more complex model for each layer with several mixing steps.

In [5], the water content of skin is reported for measurements at the forearm. The values are given as around 46 % for free water and 65 % to 70 % for total water content, which is a difference of about 10 % in both cases to the 55 % used here. The difference could be that the mixing model does not account for some properties which are compensated by higher free water content, or the bound water has a larger influence in the chosen frequency range than expected. Overall, further investigations into more accurate models and interactions of the E-Field with skin materials can lead to a better model and might allow doing quantitative statements as well.

4.2. Mixing skin cancer

The second step is to use the previous base model for the calculation of skin cancer. In [13], an increase in water content of up to 20 % was found for skin cancer in mice. In [7], similar results are reported.

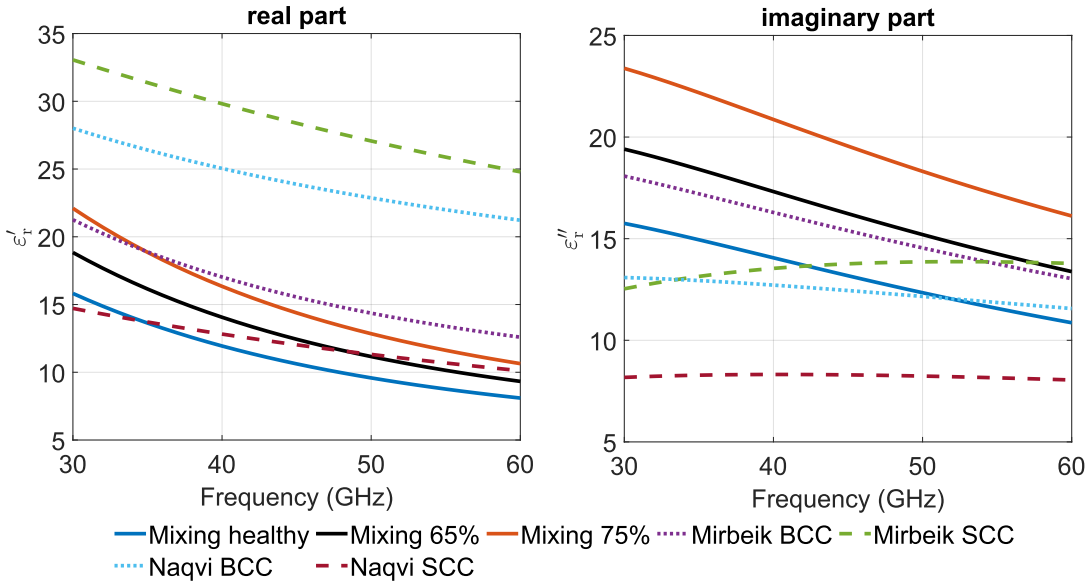

Figure 5: Real part of the permittivity of the mixing calculation compared to literature values for skin cancer [7][8]

Figure 5 shows the result of the mixing algorithm with a water content of 65 % and 75 %. The literature values from Fig. 2 are shown as well. The reasons for the differences in the literature values were discussed in the Section 2.

The changes in real part ($\Delta\varepsilon'_r$) and imaginary part ($\Delta\varepsilon''_r$) of the relative permittivity are shown in comparison to healthy skin (Section 4. 1.) in Fig. 6. In [8], changes in relative permittivity are given with $\Delta\varepsilon'_r = 24.8\,\%$ and $\Delta\varepsilon''_r = 38.6\,\%$ for BCC and with $\Delta\varepsilon'_r = 19.4\,\%$ and

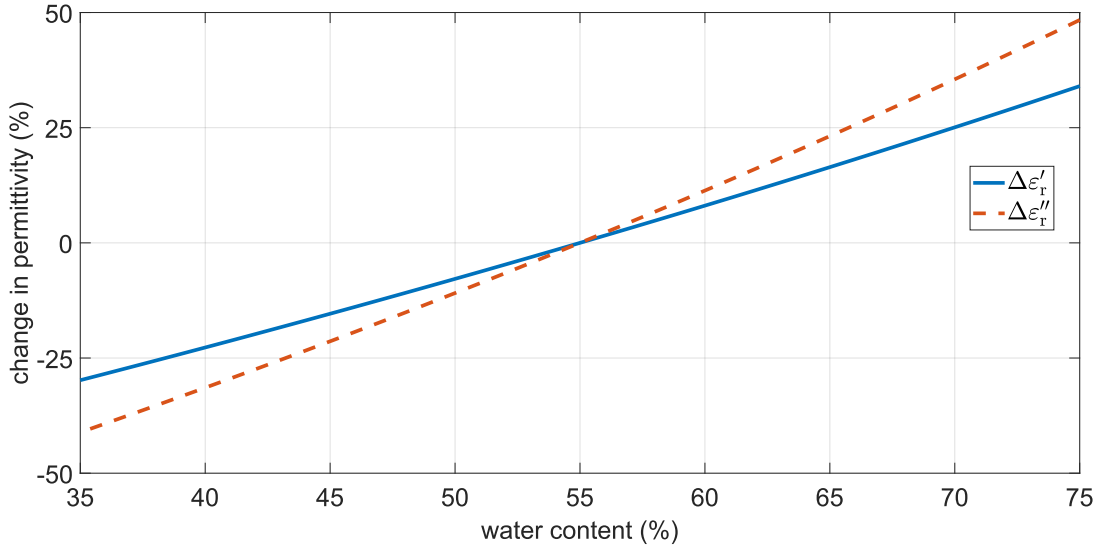

Figure 6: Percentage change of permittivity at 50 GHz for different percentages of water content compared to calculated mixing for healthy skin

$\Delta\varepsilon_r'' = 18.2\,\%$ for SCC as real and imaginary part, respectively. If the increase in relative permittivity is compared to Fig. 6, an increase of 15 % water content to 55 % for healthy skin and 70 % for cancer gives a comparable result for the percentage increase in permittivity of $\Delta\varepsilon_r' = 27.4\,\%$ and $\Delta\varepsilon_r'' = 34.3\,\%$. The increase of 15 % is also comparable to the expectation that cancer has an increased water content by about 10 % to 20 %. If considered that for SCC, [8] reported an overall lower permittivity compared to healthy skin. A comparable result can be achieved for a decrease in water content by about 13 % with $\Delta\varepsilon_r' = 18.3\,\%$ and $\Delta\varepsilon_r'' = 28\,\%$. The real part fits well with the literature data, while the imaginary part has a difference of around 10 %, which might indicate that something else is affecting the permittivity in SCC, which was also concluded in [8]. According to these comparisons, it becomes obvious that more data on the permittivity of SCC is required to draw a conclusion.

This shows that even with the differences of data shown in Fig. 6, EMT can still achieve a similar contrast $\Delta\varepsilon_r$ in comparison to the reported values in [8]. This gives a point of comparison between systems, even using different models.

5. Discussion and Conclusion

The presented EMT method provides a viable approach for simulation and evaluation. The method helps to create several datasets easily for them and allows controlled variation in the data. Although there is no permittivity data available for MM in literature, EMT can still calculate it if the change in water content is known. In the future, more sophisticated models for EMT might allow the creation of models tailored for different types of cancer. Especially because cancer remains highly variable and individual. Furthermore, it was not the goal of this paper to

create a comprehensive model for skin or skin cancer, but the calculated data for healthy skin shows a good agreement with the data from literature. It should still be noted that the results should not be used to make quantitative or medical statements. In general, the focus on contrast or difference in the permittivity values $\Delta\varepsilon_\mathrm{r}$ allows for easier comparison, especially at different frequencies. New studies and the availability of more data within those can also lead to more precise and quantitative statements. This can help in forming assumptions and variations for the development of EMT models.

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