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The Uterine Epithelium might act as a Protective Barrier for the Embryo against Exogenous Electric Fields: A Computational Study

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ABSTRACT: The purpose of this article is to study the penetration of exogenous electric fields into the womb. It is postulated that the epithelial layer around the womb can act to prevent the penetration of such fields into the uterus, thereby effectively protecting the embryo from hazardous electric fields that have been shown to alter embryonic development. The very thin, low-conductivity epithelial layers are usually ignored in conventional 3D human body models used for dosimetry; i.e. to model electric field penetration in the body. However, these µm-thick layers can significantly influence the field distribution in the body due to their current blocking or barrier function. To evaluate the effect of these layers at low frequencies, the epithelial layer was manually added to the uterine tissue in a 3D human body model. Then, the field distributions across the uterus were compared with and without the epithelial layer. This preliminary study showed that considering this layer at low frequencies can cause a 60% reduction in the electric field strength within the uterus. It is anticipated that if more exact estimations of uterine epithelium resistivity become available, the model could predict yet greater reductions and higher shielding can be assumed to occur in reality.

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1- Introduction

Epithelial layers are one of the main tissue types that make up the body structure; including muscle tissue, connective tissue, and nervous tissues. This tissue carries out a variety of functions that include protection, secretion, absorption, excretion, filtration, diffusion, and sensory reception [1]. It has been shown in [2] that thin membranes that act as barriers against ion movement. The epithelial cells in comparison with other cells are formed as a semi-continuous layer and there is little intracellular space left between them. This allows for the barrier function of the epithelium, which blocks the passage of ions as electric charge carriers. The columnar epithelial tissue is one example of such tissue that can also be found in the uterus: The endometrium (the innermost layer of the uterus) is made of columnar epithelial tissue that plays a role in nutrition and protecting the fetus during pregnancy.

The barrier function of epithelial layers has been investigated rather extensively, as in [3, 4]. However, their protective role against penetrating electric fields has not been sufficiently elucidated. Although the problem of low-frequency exposure during pregnancy has been a matter of concern, computational modeling is usually based on voxel models of the human body [5, 6]. The thin Epithelial layer (several tens of micrometers) can easily “drop out” of the conventional voxel models where voxel sizes are on the order of millimeters [7]. This paper addresses this role in a very important example: the protective function of this barrier for the uterus (Mother’s Womb) where the fetus is formed. The fetus is indeed vulnerable to penetrating electric fields, as shown previously in [2], and especially in [8], where it has been claimed that exposure to power-line frequencies can increase the risk of abortion. High-frequency electromagnetic waves are nominated for effects such as placental barrier disruption [8].

In this study, the distribution of low-frequency electric fields in the human body is examined in the absence and presence of the epithelial layer and the importance of adding this layer manually in the human body voxel model on the field behavior is analyzed.

We show that considering the epithelial layer in the uterine tissue at low frequencies will protect the uterus from external fields to some degree and tends to preserve the intrauterine environment and the embryo from abnormal exogenous fields. It is known that many active electric processes are assumed to occur in this frequency band inside the uterus during embryogenesis and embryo formation [9]. It can thus be hypothesized that such natural protection shall exist at these frequencies. For this reason, we have chosen this frequency range (1-100 Hz) for all computational evaluations.

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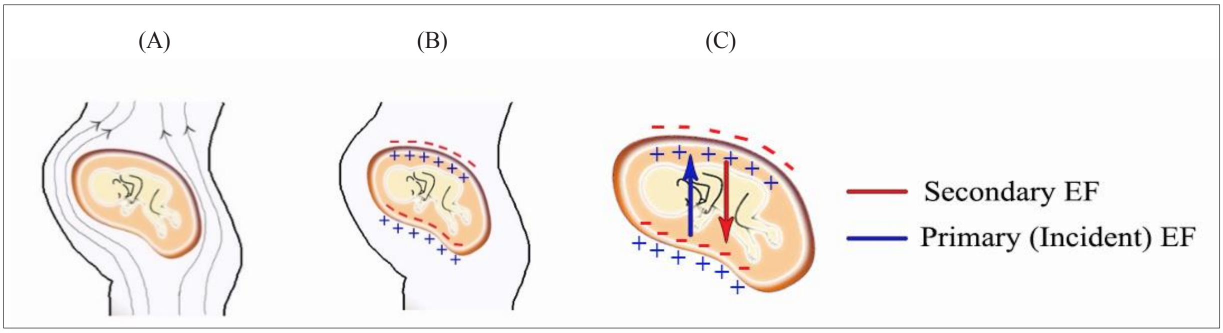

Fig. 1. The role of the epithelial layer in canceling the effect of external fields at low frequencies: (A) Uterus as a closed space with the fetus inside it and the primary electric field. (B) Separation of ions in the body (C) Formation of an opposite electric field (Secondary EF) that cancels the primary electric field

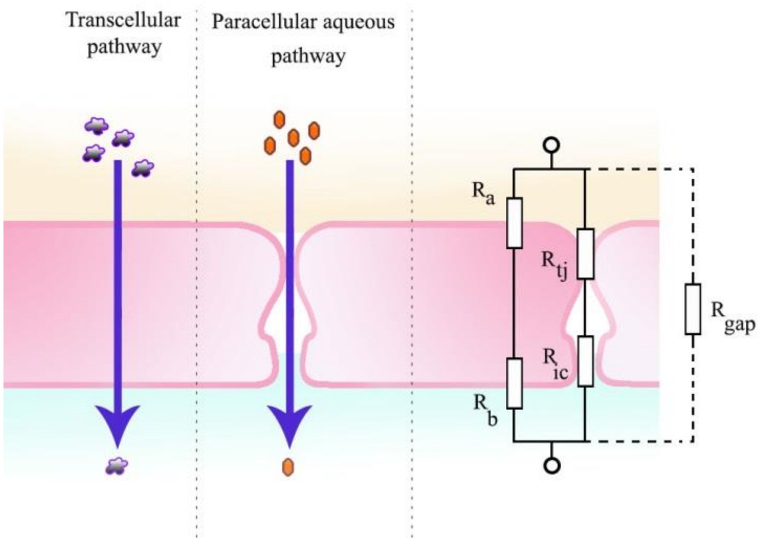

Fig. 2. Electrical modeling of epithelial cell layer and flow pathways: Apical cell membrane resistance (Ra), Basolateral cell membrane resistance (Rb), Transcellular pathway (Ra+Rb), Tight junction resistance (Rtj), Intracellular resistance (Ric), Paracellular pathway resistance (Rtj+Ric), Gap junction resistance (Rgap)[10]

2- Materials And Methods

2- 1- Equivalent electric epithelial circuit and properties estimation

Fig. 2 shows the electrical modeling of epithelial cell layers and flow pathways:

Considering the membrane capacitors and conductivity of the intracellular material, the equivalent circuit of Fig. 3, can be a suitable electrical equivalent to estimate the field behavior of the cell. In this model, the apical and lateral membranes and ion passages (cellular and extracellular flow paths) reflect the field behavior of this cell.

In the equivalent circuit of Fig. 3, the capacitance of the circuit equals 1 μF/cm^2, the intercellular space resistance (Rextra) equals 1000 Ω.cm^{2}d, the cytoplasmic conductivity (σ_{cyto}) is 0.2 s/m, and the cell membrane resistance (Ra and Rb) are assumed to be 500 Ω.cm^2 [11].

2- 2- Simulation Method, and materials properties assignment

The Austin Woman V2.4 female model, developed by the University of Texas Austin [12], is used to evaluate the effect of electrical field changes on uterine tissue. This is a voxel model with voxel sizes of 4 mm, which includes the female organs during pregnancy.

The voxel format of this model contains data on living organs such as skin, meat, bone, blood, and brain. Available models were the whole-body models with voxel dimensions 1×1×1, 2×2×2, 4×4×4, and 8×8×8 mm^3.

Due to the computational load of the existing models, the

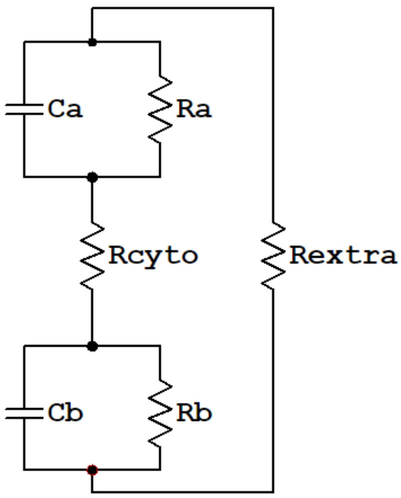

Fig. 3. Electrical equivalent circuit of an epithelial cell

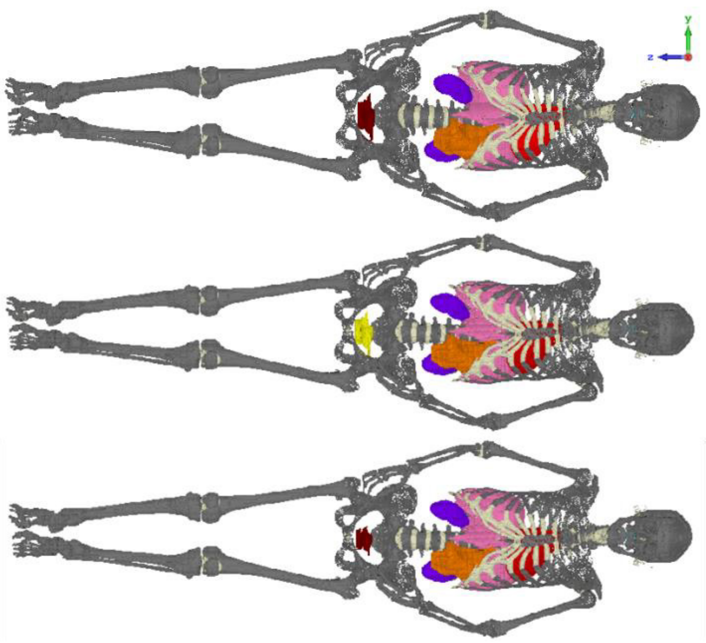

Fig. 4. The model with 2 × 2 × 2 mm3 resolutions. Primary model (top image), with epithelial tissue added (middle and bottom images). Epithelial tissue is shown in yellow (middle) and uterine tissue is brown (bottom)

4×4×4 mm^3 voxel dimensional model was chosen to be of sufficient resolution and thus the most suitable model for this study. The number of voxels used in this model was 1308203.

Due to the high computational load imposed on the simulator system, the model was cut according to Fig. 5. Finally, the simulation was performed only on the red area box.

Therefore, the model with 19 materials including air, bladder, blood vessel, bone cortical, bone marrow, cartilage, cervix, colon, colon internal, fat, muscle, nerve, ovary, dry skin, small intestine, small intestine internal, tendon, uterus, and a new layer was prepared for simulation.

The Impedance Method (IM) was used to compute the internal field distribution. In IM, the whole model is replaced by an interconnected mesh of impedance elements. This is done by replacing every voxel in the model with three impedances which serve to model currents at all directions along x, y, and z. (See Fig. 6). Knowing the voxel properties (Dielectric Permittivity ε_r^c and electric conductivity σ for every tissue type) from previous tissue-level studies (see Table 1), the impedance is calculated as in Eq. (1):

Fig. 5. Simulated model (4 ×4 × 4 mm3 voxel resolution) from the front (left) and side (right) view

Table 1. Tissue Properties [13]

Tissue	Relative Permittivity ε_r (10Hz)	Conductivity σ (S/m) (10Hz)	Relative Permittivity ε_r (100 Hz)	Conductivity σ (S/m) (100 Hz)
Air	1	0	1	0
Bladder	5.10E+06	2.02e-1	192840	2.05e-1
Blood vessel	1.00e+7	2.51e-1	5.09e+6	2.78e-1
Bone cortical	5.52e+4	2.00e-2	5.85e+3	2.01e-2
Bone marrow	1.00e+6	1.48e-3	6.99e+4	2.32e-3
Cartilage	2.01e+7	1.61e-1	4.90e+5	1.72e-1
Cervix	3.98e+7	3.02e-1	2.01e+7	4.11e-1
Colon	3.97E+07	1.22e-1	2.01E+07	1.21e-1
Fat	5.03e+6	3.77e-2	1.52e+5	4.06e-2
Muscle	2.57e+7	2.02e-1	9.33e+6	2.67e-1
Nerve	2.01e+7	1.71e-2	4.66e+5	2.80e-2
Ovary	2.01e+7	3.11e-1	4.87e+5	3.22e-1
Dry skin	1.14e+3	2.00e-4	1.14e+3	2.00e-4
Small intestine internal	2.57e+7	2.02e-1	9.33e+6	2.67e-1
Small intestine	2.05e+7	5.11e-1	8.73e+5	5.22e-1
Tendon	1.99e+7	2.51e-1	1.19e+7	3.05e-1
Uterus	3.51e+7	2.01e-1	2.45e+7	2.90e-1

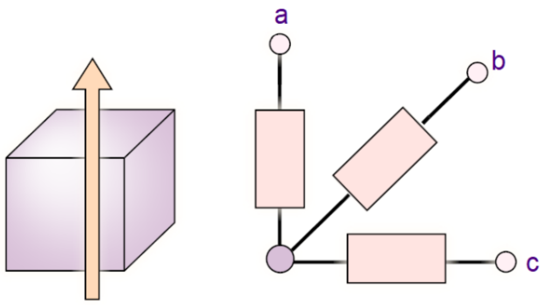

Fig. 6. The cubic voxel and its equivalent node in terms of electrical properties

$$Z = \left[j\omega\varepsilon_0 \frac{A}{d} \left(\varepsilon_r' - j\frac{\sigma}{\omega\varepsilon_0} \right) \right]^{-1} \quad (1)$$

In order to apply a certain electric field to the whole model, the upper and lower sides of the model are covered by PEC, which corresponds to interconnecting all upper nodes by zero-impedance wires. The thus obtained connected impedance network is subsequently delivered to SPICE as a netlist and solved. The model is then solved using HSpice. By selecting the time domain solver of the Hspice software, a 1-volt sine voltage at the desired stimulation frequencies at a log scale (1, 10, and 100 Hz) was applied to the two ends of the model by defining the electrode plates along the z-axis. Thus, the output voltages were calculated in the voxels along the z (defined x and y-axis) and thus, the electric field was calculated using the potential difference of two adjacent voxels divided by the voxel size ($\Delta V_x = E_x .\Delta x$). Due to the large mesh size of whole-body human models for IM, the 4×4×4 mm^3 voxel dimensional model was chosen to be the most suitable model. The number of voxels used in this model was 1308203.

Time-domain simulations were performed at the specified frequency in Hspice software after providing the circuit nodes and the connections used in it. The results are then depicted and drawn by Matlab.

2- 3- Identification of uterine border voxels and assignment of the new layer

Adding a new layer is done using Matlab 2016 software: By inserting the three-dimensional model matrix into the software and finding the boundaries containing the uterine tissue number (#120), a new tissue number (#221) was assigned to the epithelial layer (Fig. 4). The electrical properties of the new voxels (epithelial and uterine composition) are calculated as described below [14].

The barrier function of the epithelia has been studied in [11]. A value of has been used for the epithelial barrier in our simulations. However, since the voxel size (4mm) exceeds the epithelial membrane thickness (30 μm [15]), it is important to provide an effective permittivity/conductivity for the *composite* voxel containing the epithelial layer that is subsequently used to calculate impedance values for simulation by the Impedance method. This is best done by a circuit approach, (see Fig. 7). The diagram shows how a composite voxel (composed of more than one material) is converted to impedance. The epithelial layer is shown in orange. For currents perpendicular to the epithelium, the composite voxel is seen as a series combination of impedances. For currents parallel to the epithelial layer, the composite voxel is seen as a parallel combination of impedances. Due to the rather low volume fraction of the epithelial layer, the parallel combination results in an impedance that is practically the same as a voxel without epithelium.

3- Results

The results reported in figures 8 to 10 were voxels #3 to #40 in the initial model simulation (neighbors tissues: voxel #3 to voxel #18, uterine tissue: voxel #19 to voxel #26, neighbors tissues: voxel #27 to voxel #40).

After replacing the outer layer of the aforementioned tissue with epithelial and considering any node neighbors in the assignment of material properties, voxels 20# to 25# all had uterine tissue properties.

However, voxel #26 was assigned to the combined tissue (combined properties of two tissue; epithelial and uterine).

Voxel #19 also has been assigned with uterine tissue properties with its two neighbors x and y, and in the neighborhood of z, it has combined tissue properties.

As the line integral of E across the womb has to remain the same, attenuation of E inside the womb is compensated by a localized amplification in the walls itself. This mechanism is intuitively depicted in Figure 1, with walls acting as barriers undergoing capacitive charge accumulation. The diagram below (Fig. 11) shows the effect of adding the epithelial

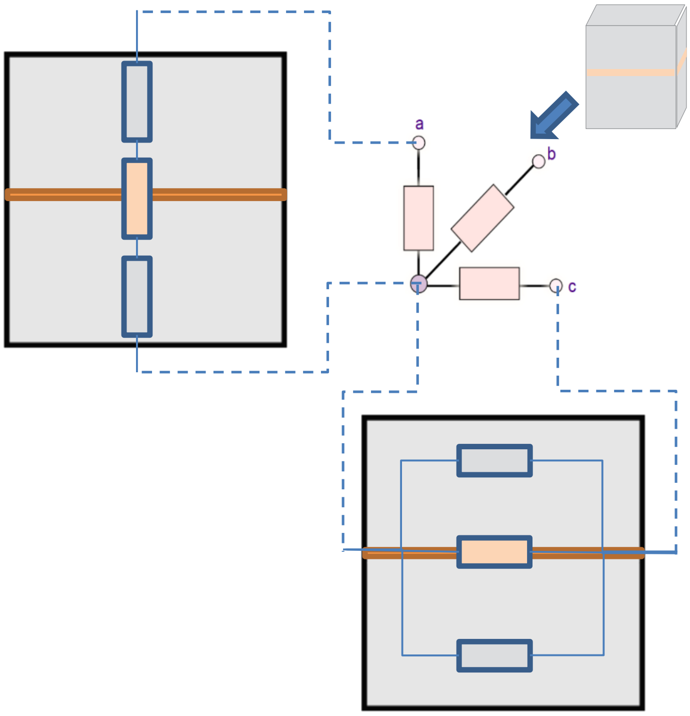

Fig. 7. Equivalent impedances for composite voxels

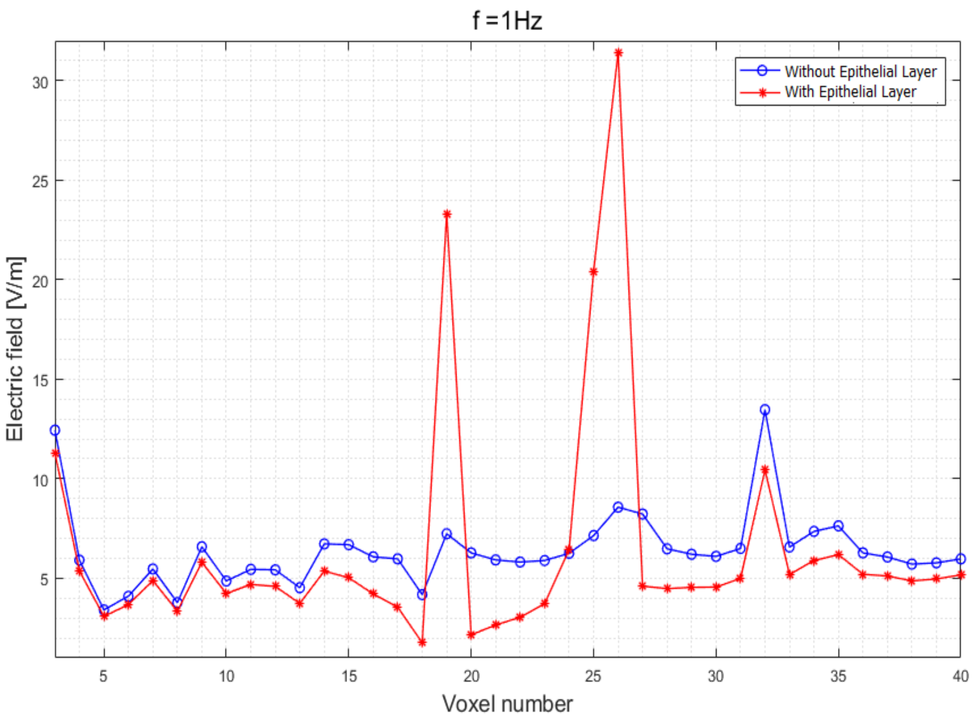

Fig. 8. Induced electric field in specific coordinates (constant x and y) at the frequency of 1 Hz (voxels 19 and 26 are assigned to the combined layer (epithelial and uterine) and voxels 20 to 25 are assigned to the uterine tissue). The ellipsoid is shown above the horizontal axis to indicate voxel numbers corresponding to the uterus internal or uterus wall. As expected (see text) the filed peaks in the walls and is attenuated within the uterus

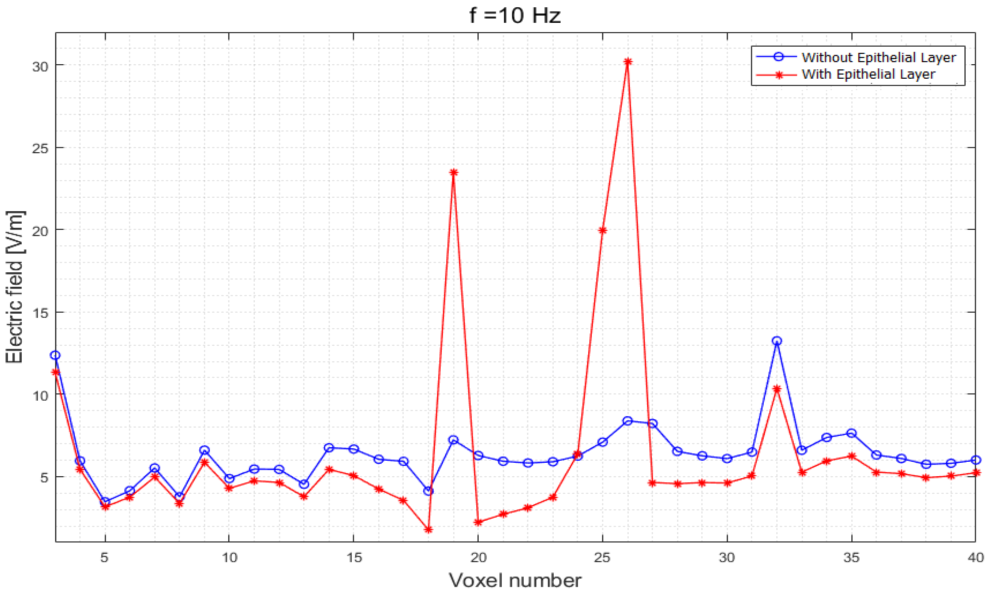

Fig. 9. Induced electric field in specific coordinates (constant x and y) at the frequency of 10 Hz (voxels 19 and 26 are assigned to the combined layer (epithelial and uterine) and voxels 20 to 25 are assigned to the uterus tissue)

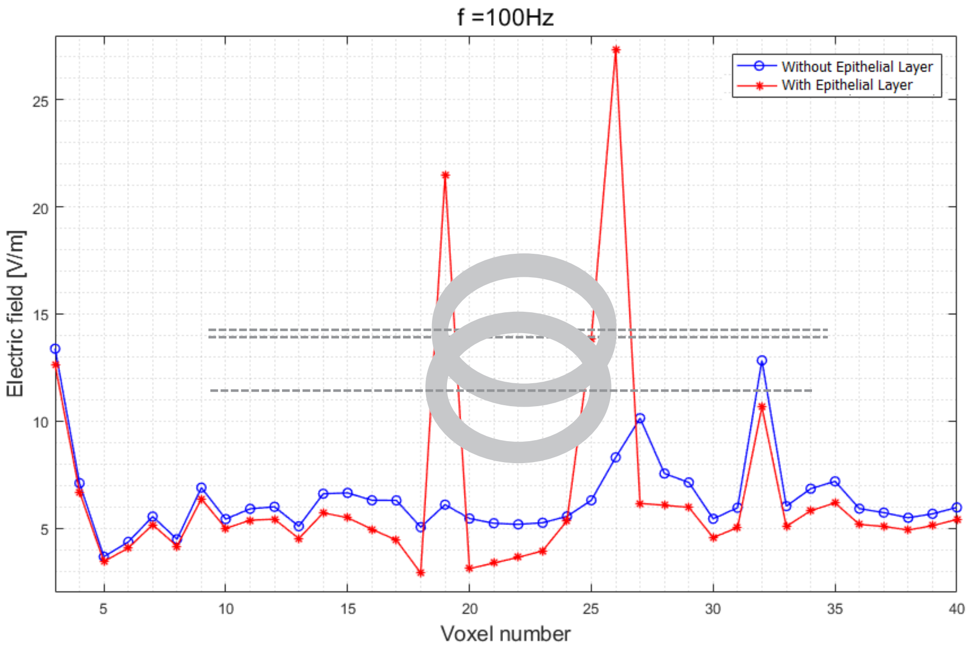

Fig. 10. Induced electric field at specific coordinates (constant x and y) at 100 Hz frequency (voxels 19 and 26 are assigned to the combined layer (epithelial and uterine) and voxels 20 to 25 are assigned to the uterus tissue)

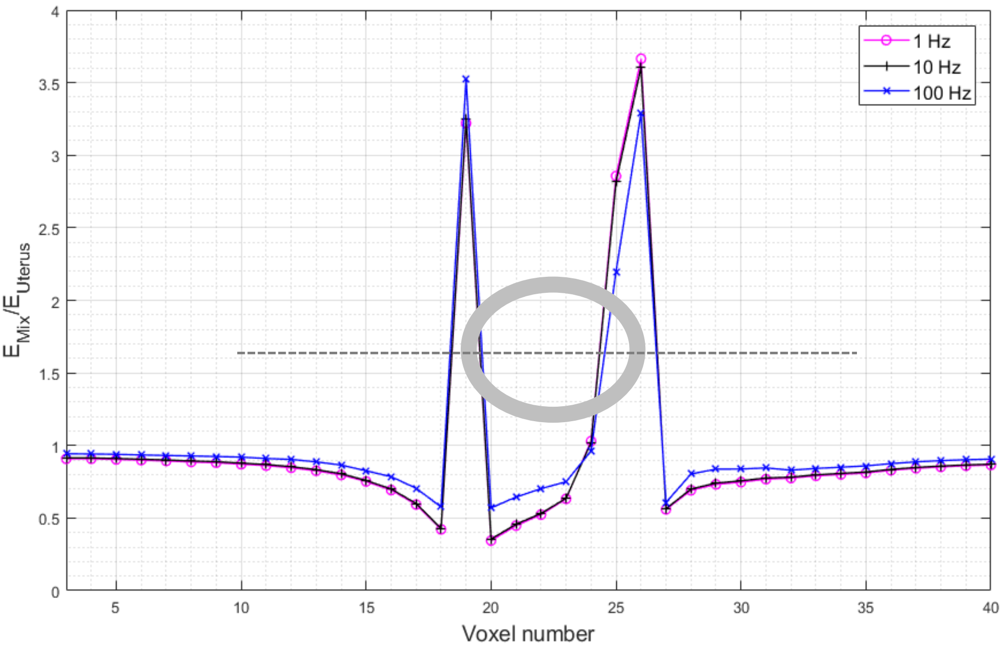

Fig. 11. Ratio of the amplification of the electric field due to the epithelial layer to the initial (raw) model in adjacent voxels at frequencies of 1, 10, and 100 Hz (voxels 19 and 26 are assigned to the combined tissue (epithelial and uterine) and voxels 20 to 25 are assigned to the uterus tissue)

layer (E_{Mix}) relative to the initial state without the layer (E_{Uterus}).Fig. 11 illustrates the attenuation of the field in voxels 20 to 24 (within the uterine tissue) when the epithelial layer is added compared to the state without considering it at the three frequencies studied. The maximum of this attenuation was equal to 0.3444 at 1 Hz frequency in voxel number #20.

For the power-line frequency of 50 Hz, the mean attenuation can be obtained from fig. 11 by interpolation. This gives a value of about 0.6 as averaged across the womb region.

4- Discussion

Numerical results support the hypothesis that the epithelial layer, as the innermost layer of the uterine wall, can act as an electric shield for the uterus and prevent externally generated fields from penetrating into the uterus, thereby protecting the embryo from electric fields of external origin.

As shown in Fig. 11, as frequency increases, the low conductivity effect of the layer in preventing field penetration into the uterine tissue reduces. However, field amplification occurred up to 3.8 times in epithelial-containing voxels.

A discussion of the mechanism for this effect is due here. At lower frequencies, inducing an electric field inside the body; (caused by external radiation), drives the free movement of ions in the inner and outer space of the uterus and causes charge accumulation on the inner and outer faces of the less-conducting epithelial layer. These net charges in turn result in a secondary electric field that is in the opposite direction as compared to the primary electric field and will thereby reduce the total electric field inside the uterus (Fig. 1).

We shall reiterate that the existence of such a protection mechanism shall not be taken as an excuse or justification for excessive exposure of pregnant women to low-frequency electric fields. It has been shown [7] that the induced electric field within the Fetus can exceed conventional “safe” limits under apparently standard conditions.

As regards the limitations of our study, in obtaining the results we have used barrier resistance measurements from available resources. The actual epithelial resistance may be much higher. In that case, the shielding effect will be much more significant, with orders of 10 or 100 of attenuation to be expected. It can be seen, therefore, that the role of this low-conductive layer in preventing electric field penetration into the Uterus can be quite significant This effect is similar to the function that the low-conductivity biological cell membrane performs at low frequencies to protect the internal volume of the cell [16].

References

[1] S.T. Modules, Cancer Registration & Surveillance Modules., in, U.S.Nationa Institutes of Health, National Cancer Institute.

[2] D.L. Miller, Electric fields induced in chicken eggs by 60-Hz magnetic fields and the dosimetric importance of biological membranes, Bioelectromagnetics, 12(6) (1991) 349-360.

[3] B. Srinivasan, A. Kolli, M. Esch, H. Abaci, M. Shuler, J. Hickman, TEER measurement techniques for in vitro barrier model systems. J Lab Autom, (2015).

[4] H. Sackin, L.G. Palmer, Electrophysiological analysis of transepithelial transport, Elsevier Boston, 2013.

[5] P. Dimbylow, Development of pregnant female, hybrid voxel-mathematical models and their application to the dosimetry of applied magnetic and electric fields at 50 Hz, Physics in Medicine & Biology, 51(10) (2006) 2383.

[6] C. Shi, X.G. Xu, Development of a 30-week-pregnant female tomographic model from computed tomography (CT) images for Monte Carlo organ dose calculations, Medical physics, 31(9) (2004) 2491-2497.

[7] R. Cech, N. Leitgeb, M. Pediaditis, Fetal exposure to low frequency electric and magnetic fields, Physics in Medicine & Biology, 52(4) (2007) 879.

[8] M. Ghazanfarpour, Z.A. Kashani, R. Pakzad, F. Abdi, F.A. Rahnemaei, P.A. Akbari, N. Roozbeh, Effect of electromagnetic field on abortion: A systematic review and meta-analysis, Open Medicine, 16(1) (2021) 1628-1641.

[9] R.H. Funk, Endogenous electric fields as guiding cue for cell migration, Frontiers in physiology, 6 (2015) 143.

[10] D.H. Elbrecht, C.J. Long, J.J. Hickman, Transepithelial/endothelial Electrical Resistance (TEER) theory and applications for microfluidic body-on-a-chip devices, Journal of Rare Diseases Research & Treatment, 1(3) (2016).

[11] D.O.N.W. Barrier, function of epithelia, Am. Physiol. Soc., (1981) 275–288.

[12] J.W. Massey, A.E. Yilmaz, AustinMan and AustinWoman: High-fidelity, anatomical voxel models developed from the VHP color images, in: 2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), IEEE, 2016, pp. 3346-3349.

[13] S. Gabriel, R. Lau, C. Gabriel, The dielectric properties of biological tissues: III. Parametric models for the dielectric spectrum of tissues, Physics in medicine & biology, 41(11) (1996) 2271.

[14] M. Saviz, L. Mogouon Toko, O. Spathmann, J. Streckert, V. Hansen, M. Clemens, R. Faraji-Dana, A new open-source toolbox for estimating the electrical properties of biological tissues in the terahertz frequency band, Journal of Infrared, Millimeter, and Terahertz Waves, 34(9) (2013) 529-538.

[15] D.C. Walker, Modelling the electrical properties of cervical epithelium, University of Sheffield., (October 2001).

[16] S. Marzban, M. Saviz, F. Towhidkhah, Significance of biological membranes for accurate computational dosimetry of low frequency electric fields, Journal of Electrical Bioimpedance, 9(1) (2018) 48-51.

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