Chapter 3

Estimates of Peak Electric Fields Induced by Transcranial Magnetic Stimulation in Pregnant Women as Patients or Operators Using an FEM Full-Body Model

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3.1 Introduction

Recent studies confirm the efficacy of transcranial magnetic stimulation (TMS) as a noninvasive treatment of medication-resistant depression [1, 2]. Four different devices, the Neuronetics Neurostar Stimulator, Brainsway H-Coil system, Magstim Magnetic Stimulator, and MagVenture Stimulator, have been cleared by the U.S. Food and Drug Administration (FDA) for the treatment of medication-resistant depression [3, 4].

Even though TMS coil holders, and even robots, have been developed that might make the application of TMS more spatially precise and efficient, to date, TMS is often applied by an operator who manually positions and retains the TMS coil over the subject's head. A potential safety concern is thus generated when the operator is a woman and is pregnant. There are no studies to date that assess the safety of TMS

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for a fetus. In the case of a pregnant woman as a TMS operator, we must consider two possibilities:

- Standard operation with the TMS coil held at distances of approximately 1–2 ft from the belly
- Accidental TMS coil discharge when the coil is in direct contact with the belly or in its immediate vicinity

In addition to the scenario of a pregnant woman as a TMS operator, the possibility of a pregnant woman as a TMS patient is also important to consider. TMS can cause a generalized tonic seizure, which can pose a significant risk for the integrity of a pregnancy. Therefore, in most instances, pregnancy will be an exclusion criterion for TMS. However, a considerable percentage of women experience symptoms of depression during pregnancy and develop clinical depression requiring medical intervention. TMS has been proposed as a method to treat maternal depression while avoiding fetal exposure to drugs [5, 6]. So while the risk-benefit profile is argued to be better for TMS than for medications, one must consider that TMS may cause fetal exposure to high induced currents.

In estimating acceptable levels of induced currents, we refer to guidelines from the International Commission on Non-Ionizing Radiation Protection (ICNIRP) [7, 8]. The 2010 ICNIRP basic restrictions for occupational exposure to time-varying electric and magnetic fields for frequencies in the band 1 Hz–100 kHz [8] recommend that the exposure should be limited to electric fields in the head and body of less than 800 mV/m in order to avoid peripheral and central myelinated nerve stimulation. ICNIRP also recommends that the restrictions on electric or magnetic fields including transient or very short-term peak fields (which are encountered during TMS) be regarded as instantaneous values which should not be time averaged.

We assume that the estimate of 0.8 V/m maximum peak field should also apply to the fetal brain, body, and trunk.

3.2 Methods and Materials

3.2.1 Existing Computational Models of a Pregnant Woman

Induction currents in the entire human body (or bodies) of a pregnant subject caused by a TMS coil can be established in every particular case via numerical electromagnetic modeling. One of the primary investigated concerns has been a *significant electric current density*, which may develop in the highly conducting amniotic fluid surrounding the fetus and subject to an external time-varying magnetic field [9, 10]. Table 3.1 lists computational models of a pregnant woman and/or a fetus currently available for electromagnetic and radiological simulations.

These models (except for Refs. [10, 11], which are highlighted in the table) are based on insertion of a fetus into an existing nonpregnant female model. Meanwhile, the models developed from scans of pregnant females include the abdominal region only [10, 11].

Table 3.1 Computational pregnant-woman models (after ~2004)

	Model name	A/H/W	Da	TYPE	RES, mm ^c	FV	D	References
IT'IS Found., Switzerland	PREGNANT WOMAN ^a	3, 7, 9 months fetus	N	V	0.5 x 0.5 x 1.0 h 0.9 x 0.9 x 2b	Y	N	[15, 16]
Natl. Inst. of Inform. and Comm. Technol., Japan	PREGNANT WOMAN (based on non-pregnant model [21])	22/160/53 12, 20, 23, 26, 29, 32 and 33 weeks fetus	N	V	2 x 2 x 2	Y	N	[14, 16, 18]
Imperial College, UK	PREGNANT WOMAN ^b	28 weeks fetus	N	V	1 x 1 x 5	N	N	[11]
Health Protection Agency, UK	PREGNANT WOMAN ^c	23/163/60 8, 13, 26, 38 weeks fetus	N	V	2 x 2 x 2	N	N	[9]
Graz University of Technology, Austria	SILVY	89 kg 30 weeks fetus	N	V	2 x 2 x 7	N	N	[10]
Helmholtz Zentrum Munchen, Germany CST AG, Germany	KATJA	43/163/62 24 weeks fetus	N	V	1.8 x 1.8 x 4.8	N	N	[19]
Rensselaer Poly. Institute, NY, USA	PREGNANT WOMAN ^d	30 weeks fetus	N	V	6 x 6 x 7	N	N	[10]
Rensselaer Poly. Institute, NY, USA	RPI P-3, P-6, P-9 ^e	First, second, third trimesters fetus	N	NURBS, V	6 x 6 x 7 for fetus	N	N	[11]

Notes: A/H/W – age(years)/height (cm)/weight (kg); Da – original image dataset made available for independent evaluation of true model accuracy (Y/N); TYPE (V – voxel; NURBS – CAD model); RES – lowest image resolution (before or after post-processing) of the model declared by the provider (h = head, b = body); FV – free version for research available (Y/N); D – deformable/ posable (Y/N)

^aBased on ELLA [15, 16, 20]
^bAbdominal region only
^cBased on NAOMI [20]
^dAbdominal region only (body from above liver to below pubic symphysis)
^eAnatomical data for the pregnant female and the fetus are gathered from several origins

All models in Table 3.1 are *voxel* models, except for Ref. [11] which used B-splines or NURBS, while some parts of the body are adapted from the Visible Human Project [12, 13]. Figure 3.1 shows a NURBS model from Ref. [11], while Fig. 3.2 shows the voxel model family from Ref. [14].

Fig. 3.1 NURBS model of a pregnant woman [11]

Fig. 3.2 Voxel model of a pregnant woman [16]

3.2.2 Construction of FEM (CAD) Full-Body Pregnant Woman Model and Model Topology

The voxel models listed in Table 3.1 are perfectly fine for radiation dosimetry studies [10, 11, 18] and for high-frequency and RF simulation studies of specific absorption rates [14–16, 18] based on the finite-difference time-domain (FDTD) approach. However, they are not suitable for the finite element method (FEM), which is generally employed by the TMS community [23–33]. This method more accurately

captures complicated coil geometry(s) and curved boundaries between tissues. The NURBS surfaces [11] also have limited value for an FEM solver, which internally operates with geometry primitives: triangular facets and tetrahedra. A conversion from NURBS surfaces to triangular surfaces may require (very) significant additional meshing time.

To enable FEM analysis, a full-body CAD model of a pregnant female in the form of triangular surface meshes has been developed. As an initial dataset, we have chosen the detailed voxel model of a pregnant female by Nagaoka [14, 17, 18]; see second row of Table 3.1. We received the voxel model after signing a licensing agreement with the National Institute of Information and Communications Technology, Japan. This model is based on a 22-year-old pregnant Japanese female (26th week or second trimester) [17]. The original pregnant female voxel model was developed from MRI data collected on a nonpregnant Japanese woman who was 160 cm tall and weighed 53 kg. Further, abdominal MR images of a 26-week pregnant woman were segmented and inserted into this full-body model.

We converted this voxel model into an FEM CAD model using isosurface extraction in ITK-SNAP [35] and MATLAB. Mesh decimation, healing, and smoothing were performed using custom MATLAB scripts and ANSYS SpaceClaim. Standard mesh intersection approaches [36–41] typically result in a large number of triangles close to intersection chains and loops. Furthermore, they leave coincident faces, which might create compatibility problems. Resulting object intersections (which are usually “shallow” intersections) were resolved by locally moving intersecting surfaces in their respective normal directions with a step size of 0.2 mm or so until the intersection was no longer present [42, 43].

A well-known problem with FEM models is object matching in a contact region. Usually, the contact region is not explicitly defined in an imported CAD model and has to be discovered separately by testing for face-to-face overlaps and matching CAD faces/edges [44]. This circumstance may lead to problems for certain CAD kernels such as ACIS. To prevent CAD import errors, a thin gap was introduced between all tissue objects and was filled with “average body properties” of an outer enclosing shell. In some sense, this gap represents membranes separating different tissues. If the gap is reasonably small, it provides a close approximation to reality for different physical processes.

In order to construct the fetus model representing a pregnant female during the first and third trimester, we used the base data for the second trimester and the deformation approach described in Refs. [14, 18].

Figure 3.3 shows three variations of the CAD model constructed for the present study. The corresponding tissue mesh inventory is summarized in Supplement I. To our knowledge, this is the only detailed FEM-compatible model of a pregnant female currently available. The current model contains approximately 100 individual parts. Its distinct feature is a continuous CSF shell around the gray matter for both the mother and the fetus. Creation and testing required about 12 man months and continues as a work in progress. Figure 3.4 illustrates the corresponding fetal volume (second trimester) on a larger scale.

Fig. 3.3 CAD models of a pregnant woman during the first, second, and third trimesters

Fig. 3.4 Detailed view of the fetus for the second trimester model – posterior view with pelvic bones and other nearby tissues removed

Table 3.2 Material properties used in mother/fetus models [11, 51]

Tissue	σ (S/m)/ ϵ_r
Amniotic fluid	Cerebrospinal fluid
Fetus	Mean of muscle, uterus, and blood
Fetal brain	$\left[\left(\frac{\sigma_{\text{fetalbrain}}(64 \text{ MHz})}{\sigma_{\text{fetus}}(64 \text{ MHz})} \right) + \left(\frac{\sigma_{\text{fetalbrain}}(127 \text{ MHz})}{\sigma_{\text{fetus}}(127 \text{ MHz})} \right) / 2 \right] \times \sigma_{\text{fetus}}$ $\left[\left(\frac{\epsilon_{\text{fetalbrain}}(64 \text{ MHz})}{\epsilon_{\text{fetus}}(64 \text{ MHz})} \right) + \left(\frac{\epsilon_{\text{fetalbrain}}(127 \text{ MHz})}{\epsilon_{\text{fetus}}(127 \text{ MHz})} \right) / 2 \right] \times \epsilon_{\text{fetus}}$
Placenta	Average muscle

Other biomechanical CAD models of pregnant women having different degrees of approximation have also been constructed [45–48]. However, these models do not include detailed geometry of the fetus suitable for EM simulation [47–50]. Figure 3.4 demonstrates the corresponding fetal volume (second trimester) on a larger scale.

3.2.3 Tissue Properties

Most tissues were assigned material properties (conductivity and dielectric constant) following the Gabriel & Gabriel database [49], which is further replicated in the IT’IS database [50]. Fetal properties follow Refs. [11, 51] and are outlined in Table 3.2. The conductivity and permittivity of fetal brain are comparable to that of the fetus and also behave similarly. Hence, the fetal brain is assigned scaled fetus material properties; the scaling factor is obtained from the available dataset. The material property values assigned to all tissues are also provided in the supplement.

3.3 Study Design

3.3.1 TMS Coil

Similar to Ref. [26], the base coil is a figure-eight straight coil with a loop radius of 35 mm. However, instead of a stranded conductor, a solid conductor (copper) with a diameter of 8 mm was used.

3.3.2 Pulse Form and Duration

TMS pulse forms vary widely in shape and duration [52–55]. Table 3.3 summarizes the data for four common FDA-approved TMS machines.

In order to take the majority of cases into consideration, we have chosen a simple biphasic harmonic coil pulse current:

$$I(t) = I_0 \sin(2\pi t / \tau), \quad \frac{dI}{dt} = \frac{2\pi}{\tau} I_0 \cos(2\pi t / \tau), \quad (3.1)$$

$$0 \leq t \leq \tau, I(t) = 0 \text{ otherwise}$$

The derivative of the coil current, I , is proportional to the induced electric field/induced electric current in the body. In order to include the majority of cases from Table 3.3, the total pulse duration or length τ was evaluated for two limiting values:

$$\tau = 1 \text{ ms}, \quad \tau = 0.1 \text{ ms} \quad (3.2)$$

Please note that the equivalent frequency of the biphasic harmonic pulse given by (3.1) is

$$f = 1 / \tau \quad (3.3)$$

Other more elaborate pulse forms have also been studied [62].

3.3.3 Coil Current

For every pulse duration and coil position, the coil current amplitude I_0 in (3.1) has been found from the condition of one standard motor threshold (SMT) unit [61, 62]. One SMT means that the electric field at a point 2 cm from the surface of the head beneath the coil center reaches the motor threshold value of approximately 130 V/m [61, 62]. Motor threshold, a measure of the TMS intensity necessary to evoke a peripheral motor response, is variable across individuals but is also remarkably constant in a given individual [63]. For example, the peak coil current for a 0.1-ms-long pulse was found to be approximately 9000 A·turns magnetomotive force (mmf) at 1 SMT unit.

Table 3.3 Pulse widths and SMT values for different TMS setups

#, Pulse form	TMS system	Pulse duration (ms)	Std. motor threshold (SMT)	References
1. Biphasic	Brainsway	0.370	0.60–1.4	[56]
2. Monophasic	Magstim 200 ²	1.000	NA	[57]
3. Biphasic	MagVenture	0.290	0–1.7	[58]
4. Biphasic	Neuronetics	0.185	0.22–1.6	[58, 59]

3.3.4 Coil Positions

Two coil positions for a *pregnant patient* have been considered (see Fig. 3.5). In the first case (Fig. 3.5a), the straight coil is located 10 mm above the top of the head. In the second case (Fig. 3.5b), the straight coil is translated and then tilted by 60 degrees. The first case might represent a standard TMS coil placement for studies aimed at evaluating central motor conduction, though a circular TMS coil would be generally used in such instances. The second case aims to approximate the position of the TMS for the treatment of depression.

A coil positioning map for the *pregnant operator* is shown in Fig. 3.6 for the second trimester. The closest distance from the coil center to the body is 115 mm. We consider three representative polarizations of the major current dipole of the coil:

- A. In the coronal plane (z-polarization in Fig. 3.6, Config. A, labeled as A1-A6)
- B. In the sagittal plane (y-polarization in Fig. 3.6, Config. B, labeled as B1-B6)
- C. In the transverse plane (x-polarization in Fig. 3.6, Config. C, labeled as C1-C4)

For every polarization type, four to six representative coil locations have been tested in the sagittal plane as shown in Fig. 3.6. The operator could achieve any of these positions by moving their right arm along with the coil holder. This results in a total of 16 test cases. For each test case, the eddy current density and the corresponding electric field everywhere in the body were computed. Each test case is conducted for the first, second, and third trimesters. For the first trimester, the closest distance from the coil center to the body is 45 mm (B) or 80 mm (C), 115 mm (B) and (C) for the second, and for the third – 40 mm (B) and 80 mm (C). The remaining topology is the same.

3.3.5 Accidental Coil Discharge

Two extreme cases have also been considered, which are not shown in Fig. 3.6. These are when the coil is moved in the xy-plane until it is as close to the body as possible. These cases will be labeled as B7, B8 and C5, C6, respectively.

Fig. 3.5 Two coil positions used for the pregnant patient study

Fig. 3.6 Coil positioning map for a pregnant operator (second trimester) study. Some tissues are hidden for clarity

3.3.6 Frequency-Domain Computations

All simulations were performed in the frequency domain using ANSYS Maxwell 3D FEM software (v. 16). ANSYS Maxwell 3D is a commercial FEM software package with adaptive mesh refinement and has been extensively used for eddy current computations, similar to the earlier studies [24–26]. The software takes into account both conduction and displacement currents (as well as free and polarization

charges), and solves the full-wave Maxwell equation for the magnetic field, $\mathbf{H}$, in the frequency domain

$$\nabla \times \frac{1}{\sigma + j\omega\epsilon} \times \mathbf{H} = -j\omega\mu\mathbf{H} \quad (3.4)$$

where σ is the local medium conductivity, and ϵ and μ are the local permittivity and permeability, respectively. The major difference from the full-wave case is that the phase is assumed to be constant over the volume of interest. Although Maxwell 3D also has a transient FEM solver, this solver does not take into account the displacement currents and was therefore not used.

All simulations made use of the automated adaptive meshing technology available in Maxwell to iteratively refine the mesh. Five adaptive meshing passes were performed during the calculation, with the final meshes approaching about 2 M tetrahedra. Details of the adaptive mesh refinement procedure have been discussed previously [60].

3.3.7 Time-Domain Computations

Frequency-domain results (coil excitation with a sinusoidal waveform) for fields and currents have been collected for multiple frequencies (a logarithmic frequency sweep) over the band from 300 Hz to 3 MHz in order to generate the required pulse forms via the fast Fourier transform (FFT) and inverse FFT (IFFT) as described in Ref. [60]. The corresponding method has been described in the same reference; it is time-consuming but accurate. The time-domain solution is required for any pulse form including the harmonic pulses given by (3.1) since they are distorted quite differently from the harmonic wave of the same frequency. This solution is also important for other (nonharmonic) pulse forms [60].

3.3.8 Finding Maximum Peak Current Density/Electric Field Strength in Individual Tissues

A uniform $5 \times 5 \times 5$ mm grid of observation points was introduced within a rectangular box, which covers the abdominal area only. This resulted in approximately 150,000 observation points within the body, where the induced current and the electric field are evaluated. For every such point, the pulse form has been restored via IFFT. Then, interpolation of peak pulse values onto a finer $2 \times 2 \times 2$ mm grid was performed, followed by averaging over each small tissue volume as recommended in Ref. [8]. Finally, the absolute maximum peak current/field has been evaluated for every all tissues.

3.4 Results: Pregnant Patient

3.4.1 Qualitative Behavior of Induced Currents in the Body of a Pregnant Patient at Different Frequencies (Pulse Durations)

Figure 3.7 shows eddy current amplitude distribution in a coronal plane of a pregnant patient for three representative frequencies: 3 kHz, 30 kHz, and 300 kHz. The coil current amplitude is 10,000 A (10,000 A-turns mmf). Note that the color scale has been multiplied by the factor of 10 for every subsequent figure.

We observe that the peak current in the fetal area does not exceed 0.1 mA/m², 1 mA/m², and 40 mA/m². Comparing Fig. 3.7a, b, the induced current initially appears to behave as a linear function of frequency. However, the behavior becomes nonlinear after 30 kHz or so as seen in Fig. 3.7c.

We also observe that the bulk of the induced current at any frequency is primarily excited in the amniotic fluid, but not in the fetus. This is to be expected due the very high conductivity of the amniotic fluid.

Fig. 3.7 Eddy current amplitude distribution in a coronal plane for three representative frequencies: 3 kHz, 30 kHz, and 300 kHz (second trimester model). The coil current amplitude is 10,000 A (10,000 A-turns mmf). Note that the color scale was increased by a factor of 10 and 100 for the middle and right-hand figures, respectively

3.4.2 *Quantitative Results for Maximum Peak Electric Field at One SMT Unit*

In the subsequent study, the excitation is always given by a biphasic pulse from Eqs. (3.1)–(3.3) and the TMS intensity is always equal to one SMT unit. Figure 3.8 presents the results for the maximum peak electric field (maximum magnitude of the electric field vector, $E(t)$) for the two coil configurations in Fig. 3.5, respectively, and for every involved tissue. The first, second, and third trimester models were used in this study.

3.4.3 *Comparison with the Recommended Safe Value of Electric Field*

According to the safety requirements discussed in the Introduction, the peak electric field throughout the *fetal volume* (including fetus, placenta, uterus, and amniotic fluid) shall not exceed 800 mV/m. This condition is *certainly met* for all cases given in Fig. 3.8, even using a reduction factor of 10. One obvious reason is that the magnetic field from the coil decays very rapidly far from the head, being approximately proportional to the inverse third power of the distance [64].

3.4.4 *Observations from the Quantitative Solution*

The following observations follow from the analysis of the results given in Fig. 3.8:

- Values of the peak electric field obtained using the condition of one STM unit weakly depend on the pulse duration. This is in contrast to the results shown in Fig. 3.7, where the dependence on frequency is paramount. The reason is the normalization condition of one SMT unit, which means, for example, that the amplitude of the coil current is significantly increased for the 1.0 ms pulse.
- The largest fields are observed in the placenta/uterus.
- The smallest fields are observed in the fetal brain.
- Peak values for two different coil orientations are quite similar.
- The third trimester is characterized by somewhat larger values of the maximum peak electrical field as compared to the first and second trimesters.

These observations suggest that the results given in Fig. 3.8 are rather general and should be valid for a wide variety of coil orientations and pulse durations.

Fig. 3.8 Maximum peak electric field values at two different pulse durations, two different coil positions, and three different stages of pregnancy computed separately for each fetal tissue

3.4.5 Comparison with Upper Analytical Estimate for Electric Fields/Eddy Currents

Using a simplified upper analytical estimate for eddy current/induced electric field in the human body [60], the local electric field anywhere within the body is expressed directly through a time-varying lumped coil current, $I_0 f(t)$, in the following form

$$\mathbf{E} = -\frac{\partial \mathbf{A}^{\text{inc}}}{\partial t}, \mathbf{A}^{\text{inc}}(\mathbf{r}, t) = \frac{\mu_0 I_0 f(t)}{4\pi} \oint_c \frac{d\mathbf{l}}{|\mathbf{r} - \mathbf{r}'(l)|}$$

(3.5)

This estimate does not depend on the specific human model under study. We first apply eq. (3.5) to the coil setup from Fig. 3.5a, assuming an observation point located beneath the coil center and at a distance of 62 mm from the coil (representing the distance from the coil center to the top of the uterus for the present model). The resulting upper electric field estimate is obtained as 90 mV/m at any pulse duration (when normalized to one SMT unit). Neither of the maximum peak values in Fig. 3.8 for the coil from Fig. 3.5a exceeds this value. For the coil from Fig. 3.5b, the same or a more elaborate estimate (with spatial averaging to undo a loci effect) [60] can be applied. Again, neither of the maximum peak values in Fig. 3.8 for the coil from Fig. 3.5b exceeds the value of 90 mV/m. Hence, the upper analytical estimate given by (3.5) is justified for *all* considered cases.

3.4.6

Using the Analytical Estimate for Predicting Maximum Fields for Different Patients

To provide results which may be expected for different patients, we apply the upper analytical estimate of Eq. (3.5) to different distances from the coil center to the top (or a closest point in the general case) of the uterus. The corresponding data rounded to within ± 3 mV/m is summarized in Table 3.4. Although the present results are given for one specific coil type, similar estimates may be expected for other coil geometries according to the study performed in Ref. [60].

Table 3.4 Estimates for the maximum peak field in the fetal volume at one SMT unit

Nearest distance from coil center to uterus	Rounded estimate for the maximum peak electric field in the entire fetal area
50 cm	<170 mV/m
60 cm	<100 mV/m
70 cm	<60 mV/m
80 cm	<40 mV/m
90 cm	<30 mV/m

3.5 Results: Pregnant Operator and Accidental Coil Discharge

3.5.1 *Quantitative Results for Maximum Peak Electric Field at One SMT Unit*

All coil configurations shown in Fig. 3.6 have been studied for three stages of pregnancy and for different pulse durations. Figure 3.9 presents typical data for the second trimester and for the biphasic pulse of 0.1 ms duration. The following observations can be made from these and other relevant computations:

- For coil positions in close proximity to the belly (A-1, A-2, C-1), the peak electric field in the fetal volume may exceed the safe limit of 800 mV.
- When the distance from the coil center to the nearest point of the uterus is less than 60 cm, the maximum peak values in excess of 100 mV/m may be observed (this number is adopted from Table 3.4).
- When the distance from the coil center to the nearest point of the uterus is greater than 60 cm, the upper estimate from Table 3.4 can be applied.

Coil polarization B in Fig. 3.6 creates the smallest values of the peak electric field. This result is to be expected since the equivalent dipole of the figure-eight coil is essentially perpendicular to the abdominal surface.

3.5.2 *Accidental Coil Discharge*

In the two extreme cases (polarization B and C in Fig. 3.6), the coil is placed as close to the body as possible by moving it in the xy -plane. The corresponding cases for polarization B and C in Fig. 3.6 have been labeled as B7, B8 and C5, C6, respectively. The corresponding maximum peak field values for the entire fetal volume are shown in Fig. 3.10. For these cases, the suggested limit of 800 mV/m may be exceeded by a factor of ten or higher. Similar results were obtained for polarization A for similar extreme coil placements.

3.6 Conclusion

At present, safe limits of fetal exposure to TMS electric and magnetic fields are an open subject. This study aimed to perform both numerical and analytical analyses of this important issue.

As a limit of the maximum peak electric field observed in the fetal volume, we have chosen the value of 800 mV/m, which allows us to avoid peripheral and central myelinated nerve stimulation [8].

Fig. 3.9 Maximum peak electric field values for the second trimester for all coil configurations/positions depicted in Fig. 3.6

Fig. 3.10 Maximum peak electric field values for all trimesters and for all coil positions listed in Fig. 3.6

Our numerical and analytical estimates for biphasic TMS pulses of different durations provide similar safety estimates. They reveal that:

1. For the TMS intensity of one SMT unit and when the closest distance between the center of the coil and the uterus is greater than or equal to 60 cm (2 ft.), the maximum peak electric field in the fetal volume (including fetus, placenta, uterus, amniotic fluid) is expected to be less than or equal to 100 mV/m. This value is significantly lower than the recommended safe limit of 800 mV/m.
2. The estimate given above was shown for any stage of pregnancy, for two realistic pulse durations, and for pregnant woman either as a patient or an operator.
3. This estimate appears to scale linearly with TMS intensity. For example, at the TMS intensity of 1.5 SMT unit, the peak field in the fetal volume is less than or equal to $100 \times 1.5 = 150$ mV/m when the closest distance between the coil center and the uterus is still 60 cm or greater.
4. This estimate is scaled approximately proportional to the inverse third power of the distance. For example, at the TMS intensity of one SMT unit, the peak field in the fetal volume is less than $100 \times (6/5)^3 \sim 170$ mV/m when the closest distance between the coil center and the uterus is 50 cm or greater.
5. The following approximate equation for the maximum peak electric field E in the fetal volume is suggested

$$E \leq 100 \left(\frac{60}{d} \right)^3 I [\text{mV/m}] \quad (3.6)$$

where d is the closest distance between the coil center and the uterus in cm and I is the TMS intensity in SMT units. We expect (3.6) to hold at the distances d greater than 30 cm.

6. FDA-cleared TMS devices employ a TMS coil holder. A pregnant operator can (and should) maintain a larger – and thus safer – distance when using a coil holder during TMS treatment. However, the possibility of accidental TMS coil discharge close to the belly has to be considered. In this case, the suggested limit of 800 mV/m may be exceeded by a factor of ten or greater.
7. Given the unknown biological consequences of a large number of pulses in a typical treatment sequence, the decision of whether to use TMS for treatment of depression (the only currently approved indication) should be based on a risk-benefit analysis. In considering the risk-benefit balance, it is important to contemplate the fetal risks posed by pharmacologic treatments for depression in pregnant patients [65, 66]. For more experimental and less evidence-supported indications, a prudent course of action would be to avoid the use of TMS in pregnant women. In any case, appropriate informed consent is critical.

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Japanese Virtual Model (JVM) Finite-Element Model Version 1.1 (6 months)

Table 3.5 List of triangular surface meshes – version 1.1

Hard tissues		Soft tissues		Individual tissues	
Mesh #	Tissue name	Number of triangles	Mesh quality	Min. Edge length, mm	Tissue type
1	JVM amniotic fluid	1286	0.007942	1.850163	Cerebrospinal fluid
2	JVM bile	122	0.272007	2	Bile
3	JVM bladder	420	0.054992	0.273501	Bladder
4	JVM breast fat left	836	0.068894	0.614704	Fat
5	JVM breast fat right	782	0.037711	0.632222	Fat
6	JVM cerebellum	366	0.052604	1.568904	Cerebellum
7	JVM clavicle left	944	0.061578	1.087026	Bone
8	JVM clavicle right	828	0.024572	0.594466	Bone
9	JVM cornea left	76	0.787694	2.000000	Cornea
10	JVM cornea right	76	0.787694	2.000000	Cornea
11	JVM CSF	6514	0.054137	0.446563	Cerebrospinal fluid
12	JVM duodenum	1030	0.004117	0.44492	Duodenum
13	JVM esophagus	756	0.014063	0.429978	Esophagus
14	JVM femur left	2914	0.123556	0.912948	Bone
15	JVM femur right	3216	0.133124	0.408209	Bone
16	JVM fetal brain	854	0.172681	1.861426	Fetal brain
17	JVM fetus	5000	0.007519	1.107346	Fetus
18	JVM fetus CSF	1282	0.039712	0.293805	Cerebrospinal fluid
19	JVM gallbladder	686	0.088411	2	Gallbladder
20	JVM gray matter	5454	0.004558	0.167652	Gray matter
21	JVM heart	1000	0.032791	1.660989	Heart muscle
22	JVM Humerus ulna left	3368	0.007025	0.393429	Bone
23	JVM Humerus ulna right	3558	0.018193	0.093016	Bone
24	JVM jaw	424	0.007359	0.359137	Bone
25	JVM kidney left	568	0.024197	1.163018	Kidney
26	JVM kidney right	636	0.082014	0.314779	Kidney
27	JVM large intestine	3914	0.002854	0.03227	Large intestine
28	JVM large intestine content	5886	1.23E-08	3.05E-05	Large intestine
29	JVM lens left	18	0.787694	2.00000	Lens
30	JVM lens right	18	0.787694	2.00000	Lens
31	JVM liver	2512	0.001358	0.786026	Liver
32	JVM lungs left	1138	0.001854	0.47502	Lung

Hard tissues		Soft tissues		Individual tissues	
Mesh #	Tissue name	Number of triangles	Mesh quality	Min. Edge length, mm	Tissue type
33	JVM lungs right	1146	0.038088	2.120805	Lung
34	JVM ovary left	798	0.207408	0.942092	Ovary
35	JVM ovary right	230	0.170639	0.640317	Ovary
36	JVM pancreas	600	0.015017	0.522665	Pancreas
37	JVM Patella left	304	0.379008	1.276178	Bone
38	JVM Patella right	424	0.005271	1.340134	Bone
39	JVM pelvic	10012	1.6E-05	0.02115	Bone
40	JVM placenta	902	0.008601	2.09859	Placenta
41	JVM rib left 1	194	0.037071	1.501538	Bone
42	JVM rib left 2	246	0.019692	0.874205	Bone
43	JVM rib left 3	298	0.033745	1.198342	Bone
44	JVM rib left 4	376	0.017842	0.792734	Bone
45	JVM rib left 5	552	0.008819	0.223525	Bone
46	JVM rib left 6	482	0.058624	0.928572	Bone
47	JVM rib left 7	516	0.044063	1.117289	Bone
48	JVM rib left 8	498	0.019398	0.611004	Bone
49	JVM rib left 9	438	0.032979	0.525822	Bone
50	JVM rib left 10	594	0.013294	0.127242	Bone
51	JVM rib left 11	282	0.01784	1.493664	Bone
52	JVM rib left 12	158	0.020202	1.013902	Bone
53	JVM rib right 1	194	0.121647	0.908528	Bone
54	JVM rib right 2	252	0.019442	0.85563	Bone
55	JVM rib right 3	298	0.034585	0.900052	Bone
56	JVM rib right 4	374	0.017841	0.917949	Bone
57	JVM rib right 5	624	0.010604	0.159166	Bone
58	JVM rib right 6	474	0.109128	0.928528	Bone
59	JVM rib right 7	516	0.026893	1.025215	Bone
60	JVM rib right 8	502	0.007985	0.541626	Bone
61	JVM rib right 9	564	0.015767	0.125747	Bone
62	JVM rib right 10	596	0.013823	0.193589	Bone
63	JVM rib right 11	282	0.012179	1.474308	Bone
64	JVM rib right 12	156	0.017841	0.320081	Bone
65	JVM salivary gland left	1208	0.036962	2.000000	Salivary gland
66	JVM salivary gland right	1006	0.088411	0.48356	Salivary gland
67	JVM scapula left	1618	0.006059	0.77685	Bone
68	JVM scapula right	1594	0.051858	0.330764	Bone
69	JVM sclera left	556	0.642238	2.000000	Eye (Vitrous humor)
70	JVM sclera right	556	0.642238	2.000000	Eye (Vitrous humor)

(continued)

Hard tissues		Soft tissues		Individual tissues	
Mesh #	Tissue name	Number of triangles	Mesh quality	Min. Edge length, mm	Tissue type
71	JVM skin	8042	0.005529	4.349768	Skin
72	JVM skull	8196	0.005778	0.024727	Bone
73	JVM small intestine	4574	0.000462857	0.121570	Small intestine
74	JVM spine	4694	0.025728	0.503403	Bone
75	JVM stomach	1996	0.00633	0.528757	Stomach
76	JVM stomach contents 1	1388	0.088411	2.000000	Stomach
77	JVM stomach contents 2	968	0.076652	2.000000	Stomach
78	JVM thalamus	574	0.103805	2.000000	Thalamus
79	JVM thyroid	806	0.026187	1.999985	Thyroid
80	JVM tibia fibia left	2686	0.15568	0.965745	Bone
81	JVM tibia fibia right	3332	0.019527	0.407727	Bone
82	JVM tongue	260	0.092234	2.353283	Tongue
83	JVM trachea	870	0.123615	0.597242	Trachea
84	JVM urine	308	0.018274	0.531584	Urine
85	JVM uterus	596	0.300344	8.490075	Uterus
86	JVM white matter	9088	0.000959	0.148079	White matter

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