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Transcranial Magnetic Stimulation Coil with Electronically Switchable Active and Sham Modes

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Abstract—**Blinded studies with transcranial magnetic stimulation (TMS) require a valid sham condition. A wide range of sham approaches have been implemented but they have various limitations including residual electric field in the brain, inadequate reproduction of auditory and cutaneous sensations, and/or need for electrical stimulation with scalp electrodes. We propose a quadrupole TMS coil configuration that can be electronically switched between active and sham modes. In active mode, the quadrupole coil has electric field characteristics similar to a conventional figure-8 coil. In sham mode, the quadrupole coil compared to the reverse-current sham figure-8 coil has 50% less electric field penetration depth, is 97% more focal, produces 35% less intense field in the brain, and induces scalp electric field characteristics closer to those of active TMS.**

I. INTRODUCTION

TRANSCRANIAL magnetic stimulation (TMS) is a noninvasive method of brain stimulation that uses brief, strong magnetic pulses to induce an electric field to modulate neural activity. TMS is used as a tool for studying the brain and as a therapeutic intervention. Both psychophysiological and clinical studies with TMS require a valid sham stimulation condition, which allows for the differentiation between placebo and treatment effects. The ideal sham condition should reproduce the ancillary aspects of TMS without producing significant direct brain stimulation. The sham TMS system should therefore be identical in appearance to the active system. In addition, the auditory (coil clicking) and somatic (coil vibration and scalp nerve and muscle activation) sensations should be comparable between active and sham modes.

The most common form of sham manipulation involves tilting the coil at a 45° or 90° angle from its "active" placement tangential to the head, in order to divert the maximum field intensity away from the brain. However, the 45° coil-tilt sham condition was shown to be about half as potent as active TMS in eliciting motor-evoked potentials [1],[2] and can induce observable changes in cerebral glucose metabolism [3]. Intracerebral voltage measurements in the rhesus monkey [2] and electric field simulation in a human head model [4] suggest that the 45° coil-tilt sham conditions can induce 40%–76% of the brain stimulation strength of active TMS. In addition, the active and coil-tilt sham conditions produce considerably different scalp sensations, which can compromise patient blinding in crossover studies [1]. Furthermore, the person administering TMS is aware of the stimulation condition due to the difference in coil positioning, which jeopardizes double-blind studies.

More advanced approaches use a dedicated sham coil that looks and sounds identical to the active coil, but does not emit a strong magnetic field. One strategy is to integrate a conductive plate on the coil face to block the magnetic field [5]; however, this abolishes both scalp and brain stimulation. Another approach is to house a smaller coil in identical looking casing, which can provide some scalp stimulation and discharge noise [6]—a strategy followed in the sham counterpart to the Magstim Co. (Whitland, U.K.) 70 mm figure-8 active coil (P/N 3190) [6]. However, Sommer and colleagues found that this Magstim sham coil fails to mimic the characteristic clicking sound associated with active TMS [7]. The Magstim air-cooled, figure-8 sham coil reportedly produces clicking of similar intensity as the active coil (though not necessarily at matched stimulator output settings) [8]. Nevertheless, replicating the scalp sensation experienced during active TMS remains a challenge.

One proposed sham procedure to overcome this challenge is the use of synchronous electric stimulation of the scalp [9]. This type of sham strategy typically requires a dedicated passive coil [8],[10]–12], and in some cases, an additional active coil placed near the subject to reproduce the sound of coil discharge [9]. However, it has been reported that non-TMS-naïve subjects were able to discriminate between electrical and magnetic stimulation, as the former was felt as more focal [8]. Although a titration procedure was introduced to match the scalp sensation of the electrical stimuli to that of active TMS [11], it remains unclear whether this procedure can effectively blind non-TMS-naïve subjects [11],[12].

A promising sham TMS strategy employs electronically switchable coils that have the ability to deliver active and sham TMS without physically reconfiguring the coil. For example, the "sandwich" complex proposed by Sommer et al. consists of a back-to-back stack of two active figure-8 coils, sandwiching a mu-metal shield [7]. Active and sham TMS are delivered by discharging either the coil nearest the head or the coil behind the mu-metal shield, respectively. However, subjects were able to discriminate between the active and sham stimuli [7], probably because the sham configuration did not produce significant scalp stimulation. Ruohonen et al. introduced an electronically switchable figure-8 coil in which

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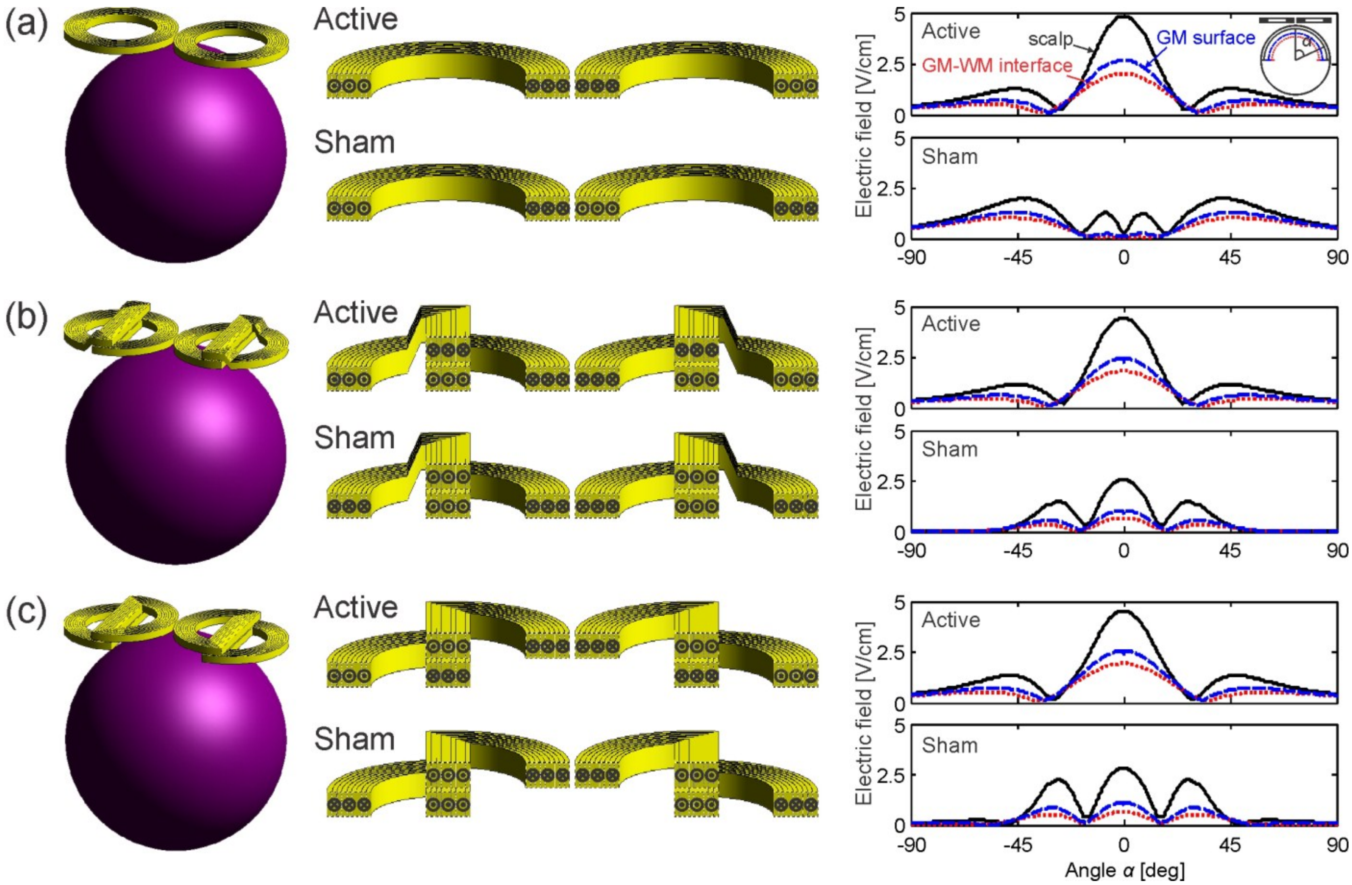

Fig. 1 Simulations of TMS coils in active and sham mode: (a) figure-8 coil, (b) quadrupole coil with coplanar windings, and (c) quadrupole coil with stepped windings. The coil current directions for active and sham modes are indicated by dot/cross symbols on the coil cross-section (middle column). The electric field strength contours (right column) were evaluated at depths of 0.25 cm (mid-scalp), 1.5 cm (gray matter surface), 2 cm (gray matter–white matter interface) from the surface of the head. The electric field was simulated for maximum pulse amplitude of a Magstim 200 device.

the coil current in one of the windings can be reversed [13]. In active mode, the coil current directions in the two windings are opposite, such that the electric field sums at the center where the windings meet. In sham model, the coil current directions are the same, and the resultant electric field cancels at the coil center. In sham mode, the coil was unable to induce motor-evoked potentials even at maximum stimulator output [14], but induced similar auditory-evoked potentials as active TMS [13]. Furthermore, subjects were not able to discriminate between the active and sham conditions at high intensities of 70% or 90% of maximum stimulator output [14]; although these intensities may not necessarily reflect realistic stimulation conditions. The non-electronically switchable, reverse current sham design was adopted by Magstim as the air film figure-8 placebo coil (P/N 3950). The main limitation with this approach is that the peak electric field shifts to the coil periphery in sham mode, which can still stimulate a broad brain volume in the vicinity of the target and can affect scalp sensation.

We present an electronically switchable quadrupole coil design with improved sham-mode electric field characteristics compared to the reverse-current figure-8 coil, including lower field penetration depth, preserved focality, and better replication of the active-mode scalp electric field pattern.

II. METHODS

A. *Electric field simulation*

Coil and electric field modeling were performed using the finite element method package MagNet and its 3-D electromagnetic time-harmonic solver (Infolytica, Inc., Canada). The human head was modeled by a homogeneous conducting sphere with 8.5 cm radius, with electrical conductivity of 0.33 S m^{-1} [15]. The electric field was simulated at the maximum output of a Magstim 200 stimulator.

B. *Coil configurations*

We modeled three coil configurations: the switchable figure-8 coil [13] [Fig. 1(a)] and two implementations of the proposed quadrupole coil [Fig. 1(b,c)]. The figure-8 coil had two adjacent windings each with inner diameter of 56 mm, outer diameter of 87 mm, and 9 turns [6]. The coil windings were modeled as solid copper wires with cross section of 6 mm × 1.75 mm. The coil conductors were placed 5 mm from the surface of the head model to account for the thickness of the insulating casing.

The quadrupole coil topology was derived by splitting each winding of the figure-8 coil into two semicircular (D-shaped) loops. The straight segments of the D-windings overlap either by introducing a bend in the outer D-windings ["coplanar windings," Fig. 1(b)] or by stepping the outer D-windings beneath the inner windings [Fig. 1(c)]. The current direction in the outer D-windings is reversible. In active mode, the currents in the straight segments of the D-windings are opposite. In sham mode, the currents in the straight segments of the D-windings are parallel [Fig. 1(b) and (c)].

C. *Electric field characterization*

We considered the maximum electric field strength at depths of 0.25 cm (mid-scalp), 1.5 cm (cortical surface), and 2 cm (gray matter–white matter interface) from the surface of the head model as representative of the strength of scalp and cortical stimulation [16]. We also quantified the intrinsic electric field penetration depth by the distance from the cortical surface to the point where the field strength decreased to half of its maximum value, $\mathrm{depth}(E = E_{\max}/2)$. Further, we quantified the intrinsic focality of each coil by the percentage of brain volume that is exposed to an electric field larger than the half-maximum electric field, $\mathrm{vol}(E \geq E_{\max}/2)$ [17].

III. RESULTS

The figure-8, quadrupole coplanar, and quadrupole stepped coils have inductances of 15.8, 17.4, and 17.2 µH in active, and 14.4, 18.8, and 18.6 µH in sham mode, respectively.

Fig. 1 depicts the electric field contours in the scalp and cortex induced in active and sham modes for the three coils. During the active mode, the three coils produce similar electric field distribution. However, for the sham-mode figure-8 coil, the electric field maxima shift approximately 45º to the periphery, while for the sham-mode quadrupole coils, the electric field maxima remain under the center of the coil.

Fig. 2 summarizes the electric field characteristics for the three coils. In active mode, the figure-8 and quadrupole coils have nearly identical electric field penetration depth [Fig. 2(a,b)] and focality [Fig. 2(c)]. In sham mode, the quadrupole coils have substantially faster field decay in depth [Fig. 2(a,b)] and higher focality [Fig. 2(c)] than the figure-8 coil. Furthermore, in sham mode the quadrupole coils induce approximately 60% of the active mode electric field strength in the scalp, compared to only 40% for the figure-8 coil [Fig. 2(d)]. Finally, in sham mode the quadrupole coils induce 34%–37% of the active mode electric field strength in the cortex, compared to 53% for the figure-8 coil [Fig. 2(d)].

IV. DISCUSSION

A. *Coil performance*

One of the properties of an optimal sham condition is to replicate the scalp sensation associated with active TMS. As shown in Fig. 1 and 2(d), in sham mode the quadrupole coils induce electric field characteristics closer to those of active TMS compared to the figure-8 coil. For example, the figure-8 coil induces the strongest field strength at different locations in the scalp in active and sham modes [Fig. 1(a)]. In contrast, the quadrupole coils induce electric field maxima under the center of the coil in both modes. The sham mode scalp field strength is also higher with the quadrupole coils than with the figure-8 coil. It has been reported that the perceptual discrimination is poor between active and sham figure-8 coil TMS at high stimulator intensities [14]. Therefore, we expect even better blinding with the quadrupole coil. Further, the auditory and vibration sensations from the quadrupole coils

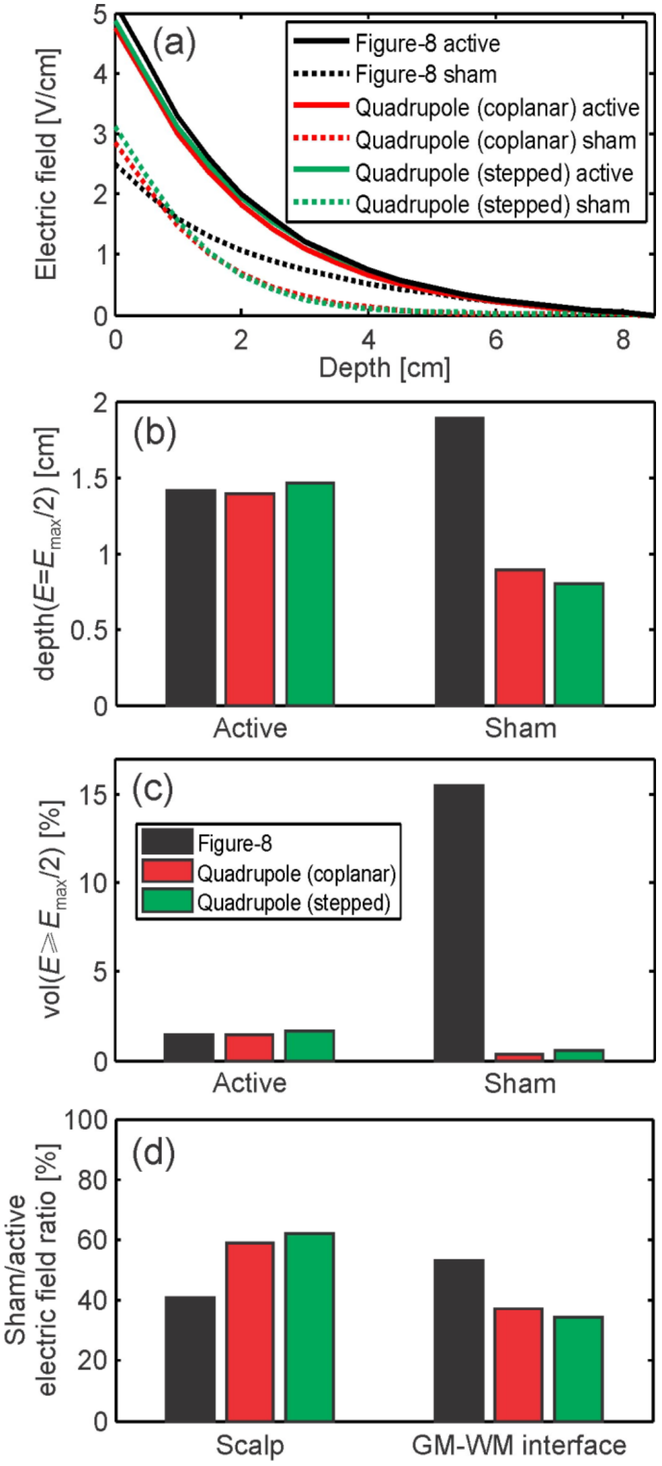

Fig. 2 Electric field characteristics of the figure-8, quadrupole coils (coplanar and stepped) in active and sham modes: (a) maximum electric field as a function of depth in the head, (b) the depth from the cortical surface to the point where the electric field strength decreases to half of its maximum value, $\mathrm{depth}(E = E_{\max}/2)$, (c) the percentage of brain volume that is exposed to an electric field larger than the half-maximum, $\mathrm{vol}(E \geq E_{\max}/2)$, and (d) maximum electric field strength of sham relative to active TMS in scalp and gray matter–white matter interface.

would likely be similar between active and sham modes since the coil current is the same, as is with the figure-8 coil [14].

A disadvantage of both the figure-8 and quadrupole coils is that the maximum electric field strength in the brain in sham mode remains a sizable fraction of the active field strength (53% for figure-8, 34%–37% for quadrupole). This could result in subthreshold stimulation effects in the brain. However, in sham mode the quadrupole coil induces weaker field in the brain than the figure-8 coil, which is an important advantage. Furthermore, the brain volume stimulated at subthreshold intensities by the sham mode quadrupole coil is smaller compared to the figure-8 coil in both active and sham mode. In sham mode, the figure-8 coil effectively becomes a large ellipsoidal coil since the field cancels at the center, which explains its higher field penetration depth and loss of focality [Fig. 2(b,c)]. In contrast, the quadrupole coil provides more focal stimulation in sham mode, i.e., a smaller brain volume is exposed to sizable subthreshold electric field. Thus, the combination of lower field intensity and higher focality in sham mode of the quadrupole coil compared to the figure-8 coil could be a major advantage in terms of overall impact on brain activity. Finally, the quadrupole field maximum is in the same location in the brain in sham mode as in active mode, whereas the sham figure-8 configuration shifts the field maximum under the periphery of the coil. This may be an advantage or a disadvantage depending on the objectives of the experimental paradigm. The figure-8 coil is advantageous if subthreshold stimulation of wide regions beyond the active target is considered acceptable, whereas the quadrupole coil is advantageous if residual subthreshold stimulation of the active target is acceptable.

It should be noted that the inductance of the figure-8 coil decreases, while the inductance of the quadrupole coil increases from active to sham mode. The differential changes in inductance for the three coils will affect the stimulus waveform pulse widths, which in turn affect the level of neural stimulation [17]. Additional analysis (not presented here) showed that the effect of inductance changes on the neural stimulation strength is less than 4%.

B. *Implementation considerations*

As shown in Fig. 1(b,c), only the outer D-windings of the quadrupole coil changes current direction between active and sham mode. When the outer windings are connected in series, they can be switched as a single winding. Therefore, the quadrupole coil system can use the same switching circuit as described by Ruohonen et al. for the figure-8 coil [13].

In a practical implementation with identical coil size constraints, the quadrupole coils will have higher electrical losses than the figure-8 coil. Specifically, the straight segments of the D-windings in the quadrupole coil will add approximately 64% more total wire length and resistance compared to the figure-8 coil, and will increase proximity effect losses in active mode because of the presence of copper in high magnetic field regions. Proximity effect losses can be mitigated by the use of litz wire for the coil construction (litz wire is already used in a number of commercial TMS coils). The impact of the increased losses on the induced electric field strength can be compensated by appropriate increase of the voltage applied to the coil. Finally, the sharp bends in the D-windings may experience stronger local forces [18]. Appropriate reinforcement of the windings (e.g., epoxy potting customary for TMS coils) can mechanically stabilize the coil.

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