General Psychiatry

Caliper-based precise positioning of the target (CALIPPOT) for transcranial magnetic stimulation without neuronavigation system

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To cite: Hu Y, Zeng R, Yue J, *et al*. Caliper-based precise positioning of the target (CALIPPOT) for transcranial magnetic stimulation without neuronavigation system. *General Psychiatry* 2024;**37**:e101262. doi:10.1136/gpsych-2023-101262

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/gpsych-2023-101262).

Received 07 August 2023
Accepted 08 January 2024

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To the editor:

Transcranial magnetic stimulation (TMS) is a non-invasive brain modulation technique. One important usage of TMS is the transient interruption of cognitive brain function (also named virtual lesion) for investigating precisely where and when a specific cortical region contributes to a specific cognitive function.[1] A more important usage of TMS is the treatment of brain disorders by repetitive TMS (rTMS). The spatial accuracy of the 'Figure-8' coil could be up to 3 mm with a TMS robot.[2] Functional magnetic resonance imaging (fMRI) has been used to guide neuronavigation systems for precise positioning of TMS targets.[3–6] While rTMS is a routine treatment approach in many hospitals, few practitioners are using neuronavigation systems. One major reason is the expense of neuronavigation systems which is usually more than CN¥350 000 (US$50 000) and more expensive than the TMS machine itself. Another reason is the complexity of its usage.

Here, we proposed a simple, precise and cheap method, named Caliper-based precise positioning of the target (CALIPPOT) for TMS without a neuronavigation system. After MRI scanning with two or more imageable marks, experimenters use two outside callipers to precisely locate the stimulation target on the scalp. Each outside calliper costs about CN¥200 (US$28) and is reusable. The imageable marks are disposable and cost about CN¥0.6 (US$0.08) for each participant. The positioning duration is less than 10 min. Two experimenters tested the accuracy in 10 participants. The mean error was 2.32 mm. All participants signed informed consent before scanning.

The following introduces the positioning steps and then the verification experiment.

STEPS FOR SCALP TARGET POSITIONING

Step 1. Marks on the scalp

MRI imageable marks were purchased from an e-shop (https://shop196017839.taobao.com)—this is a kind of anti-collision silica gel (round, 10 mm diameter, 2 mm thickness) with glue on one side. Before putting the marks on the scalp, we drew a point at the centre of the mark for positioning in order to measure the distances more accurately. At least two marks are needed to locate the scalp target. But in practice, we recommend using three marks (M1, M2 and M3): two (eg, M1 and M2) for positioning and another two (eg, M1 and M3) for validation. Additionally, to ensure that the markers do not detach during the localisation process, adhesive tape can also be applied simultaneously as an auxiliary measure to guarantee the stability of the markers. If the validation step shows an error of more than 3 mm, we suggest redoing the process. Another purpose for the redundant marks is that, if one mark is occasionally lost during scanning or positioning, the other two marks will still work (figure 1).

Step 2. MRI scanning and target measurement

After MRI scanning and data analysis (eg, fMRI task activation and/or resting-state fMRI functional connectivity analysis), a cortical stimulation target in the superficial cortex could be defined. It should be noted that these targets were predefined scalp targets rather than cortical targets. The current study focus lay in demonstrating the localisation of scalp points so

we did not encompass the process of converting cortical to scalp. And thereafter, the scalp target (ie, T in figure) was defined on the MRI images by using Euclidean distance from the cortical target. Then the Euclidean distances from the scalp target to the centre of marks were calculated.

Step 3. Positioning the scalp target

First, set the distance of the outside callipers as measured on the MRI images. Then, two experimenters simultaneously placed one end of the outside calliper at the centre of two marks (eg, M1 and M2), drew an arc with the other end of the outside calliper simultaneously on the scalp, and then could find out the intersection point. This intersection point was the scalp target, that is, T1'. This scalp target T1' was then marked on the scalp with a marker pen. Since the current method relies on calculating the Euclidean distance between at least two marks and the target for localisation, it necessitates the use of at least two callipers for measurements. It is not feasible for a single operator to simultaneously perform measurements on the scalp to find the intersection, which could pose potential safety risks to the subjects and lead to inaccurate localisation. Therefore, our method currently requires the involvement of two operators.

Step 4. Validation of the scalp target

This step was just like step 3 but used the other two marks (eg, M1 and M3) and to find the intersection point, that is, the scalp target T2'. If the distance between T1' and T2' (ie, location error) is more than 3 mm, redo step 3 and step 4. If this location error is less than 3 mm, just use the midpoint between T1' and T2' as the scalp target for TMS.

STEPS FOR VERIFICATION OF POSITIONING ACCURACY

We recruited 10 healthy adults (five men and five women, aged 24 (2.1) years). Two experimenters performed the verification steps as follows (online supplemental figure S1).

Step 1. Marks on the scalp

Six imageable marks were pasted on the scalp, including (1) M1–M4 on the forehead for positioning purposes and (2) T1 and T2 taken as the predefined scalp targets on roughly the vertex.

Step 2. MRI scanning and target measurement

3D-T1 was scanned for each participant. On the T1 image, the Euclidean distance from the scalp targets (T1 and T2) to the marks (M1–M4) was measured, including T1-M1, T1-M2, T1-M3, T1-M4, T2-M1, T2-M2, T2-M3 and T2-M4.

Step 3. Verification points and verification distances

Two marks were labelled using a marker pen beside each of the two scalp targets (A1 and B1 for T1, A2 and B2 for T2). Then the distances between the scalp targets and verification points were measured, that is, A1-T1, B1-T1, A2-T2 and B2-T2, using a Vernier calliper.

We used a Vernier calliper instead of an outside calliper to measure the verification distance. Vernier calliper measurement is highly accurate when the distance is not very long. To test the measurement error of the Vernier calliper, three participants were measured by two experimenters (ie, raters) on the distances, including A1-T1, B1-T1, A2-T2 and B2-T2. The inter-rater error was 0.03–0.89 mm, with an average of 0.13 mm (online supplemental table S1).

Step 4. Positioning and verifying the scalp targets

The predefined marks on the scalp targets (ie, T1 and T2) were first removed. Then two experimenters used outside callipers to define and a Vernier calliper to verify the scalp targets. The following is an example of using marks M1 and M2 to define and verify the scalp target T1.

As was done in the positioning step (figure 1), two experimenters used outside callipers and positioned the scalp target T1'. Then, one experimenter used a Vernier calliper to measure the distance from A1 and B1 to the measured scalp target T1'. After one experimenter completed this step, the scalp target T1' mark was erased. Then the other experimenter repeated this step.

Two experimenters performed the above positioning and verifying steps twice for each scalp target of each participant. In each verification procedure, the marks of 'M1 and M2' or 'M3 and M4' were used for positioning. The error of each positioning is shown in online supplemental table S2. Generally, the mean error was 2.32 mm. It should be noted that, although there were a few big errors (eg, 6.55 mm), we did not intend to reduce the error by repeated measurement. In practice, we suggest using three marks, with two marks for positioning and the third mark for validation. If the distance error is larger than 3 mm, redo the positioning step. Currently, our approach to addressing this issue is to mark both the markers and the target with a marker pen. Before and after each stimulation, we used a marker pen to reinforce the trace of the target. In several days of stimulations, it is feasible to remark any traces before each treatment. Based on our experience, if participants do not intentionally clean off the marked areas, these markings will last for days.

SUMMARY

This CALIPPOT method can precisely (mean error <3 mm) locate the scalp target defined by fMRI. Two reusable outside callipers cost about CN¥400 (US$56). The marks cost <CN¥1 (US$0.1) for each participant. The whole procedure takes less than 10 min. This method could be widely used in MRI-guided precise rTMS treatment. As compared with the TMS neuronavigation system, one drawback of the current CALIPPOT method is that it lacks continuous monitoring, although continuous monitoring is seldom used in treatment. Nowadays, the theta burst TMS (TBS) is increasingly used,[7 8] which delivers hundreds of pulses within a very short period of

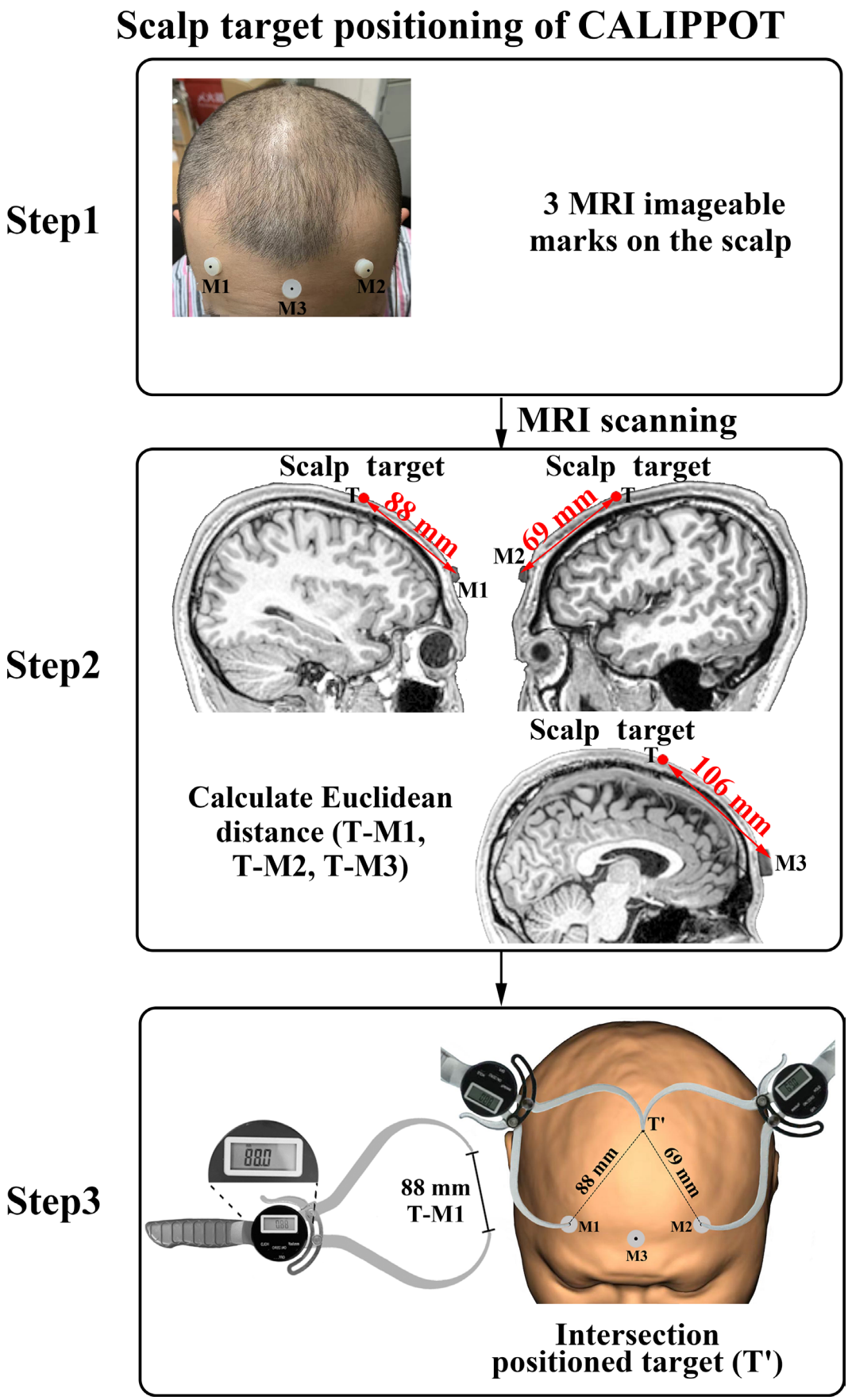

Figure 1 The scalp target positioning procedure of CALIper-based Precise POsitioning of the Target (CALIPPOT). M1–M3, imageable marks for positioning; MRI, magnetic resonance imaging; T, the predefined scalp target that needs to be positioned by CALIPPOT; T', positioned target by CALIPPOT.

time (eg, 600 pulses in 40 s). In such a short period, head motion is not a big problem. In such situations, continuous monitoring may not be necessary. Therefore, not having continuous monitoring may not be a big problem for the current CALIPPOT.

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Contributors YH, JW and YZ analysed the data and wrote the paper. RZ, JY and QG collected and processed the data. HW and ZF collected the data. All authors designed the experiments.

Funding Ministry Key Project (JW0890006), Key Realm R&D Program of Guangdong Province (2019B030335001), Department of Science and Technology of Sichuan Province (2022NSFSC0808), Key Medical Discipline of Hangzhou, The Cultivation Project of the Province-leveled Preponderant Characteristic Discipline of Hangzhou Normal University (18JYXK046, 20JYXK004).

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Ethics Committee of the Center for Cognition and Brain Disorders (CCBD) at Hangzhou Normal University (HZNU). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

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Supplementary material

Steps for verification of positioning accuracy (Figure. S1)

We recruited 10 healthy adults (5 males and 5 females, aged 24 ± 2.1 years old). Two experimenters performed the verification steps as follows.

Step 1. Markers on the scalp

Six imageable markers were pasted on the scalp, including 1) M1-M4 on the forehead for positioning purpose and 2) T1 and T2 taken as the predefined scalp targets on roughly the vertex.

Step 2. MRI scanning and target measurement

3D-T1 was scanned for each participant. On the T1 image, the Euclidean distance from the scalp targets (T1 and T2) to the markers (M1 – M4) were measured, including T1-M1, T1-M2, T1-M3, T1-M4, T2-M1, T2-M2, T2-M3, and T2-M4.

Step 3. Verification points and verification distances

Two markers were labelled by using marker pen besides each of the two scalp targets (A1 and B1 for T1, A2 and B2 for T2). Then the distances between the scalp targets and verification points were

measured, i.e., A1-T1, B1-T1; A2-T2, and B2-T2 by using Vernier caliper.

We here use Vernier caliper instead of outside caliper to measure the verification distance. Vernier caliper measurement is very accurate when the distance is not very long. To test the measurement error of Vernier caliper, three subjects were measured by two experimenters (i.e., raters), the distances including A1-T1, B1-T1, A2-T2, and B2-T2. The inter-rater error was 0.03 - 0.89 mm, with an average of 0.13mm (Table S1).

Step 4. Positioning and verifying the scalp targets

The predefined markers on the scalp targets (i.e., T1 and T2) were firstly removed. Then two experimenters used outside calipers to define and used Vernier caliper to verify the scalp targets. The following is an example of using markers M1 and M2 to define and verify the scalp target T1.

As did in the positioning step (Figure. 1), two experimenters used outside calipers and positioned the scalp target T1'. Then, one experimenter used Vernier caliper to measure the distance from A1 and B1 to the measured scalp target T1'. After one experimenter completed this step, the scalp target T1' marker was erased. Then the other experimenter repeated this step.

Two experimenters performed the above positioning and verifying steps twice for each scalp target of each participant. In each verification

procedure, the markers of "M1 and M2" or "M3 and M4" were used for positioning. The error of each positioning was shown in Table S2. Generally, the mean error was 2.32 mm. It should be noted that, although there were a few big errors (e.g., 6.55 mm), we did not intend to reduce the error by repeated measurement. In practice, we suggest use 3 markers, with two markers for positioning and the third marker for validation. If the distance error is larger than 3 mm, redo the positioning step.

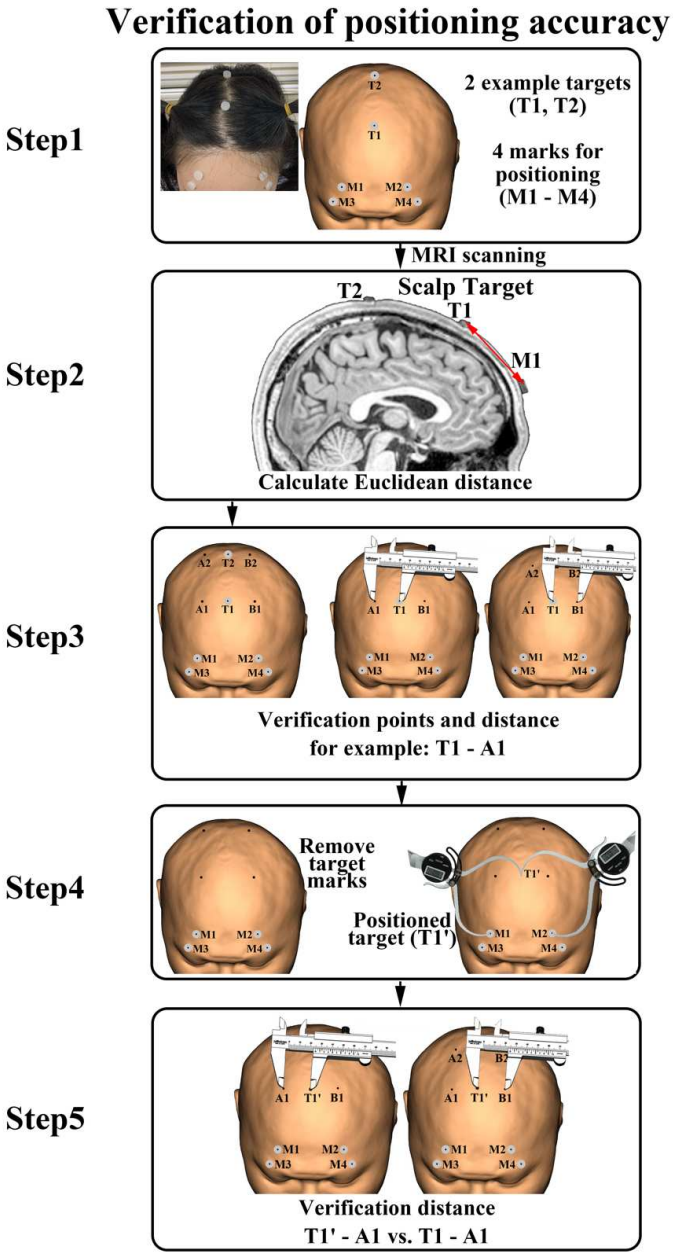

Figure S1. The verification procedure of CALIPPOT. M1-M4: imageable markers for positioning; T1 and T2: the predefined scalp targets; A1 and B1: verification points for T1 target; A2 and B2: verification points for T2 target.

Table S1. The measurement (mm) with Vernier caliper of two experimenters.

Subject	Experimenter	A1 – T1	B1 – T1	A2 – T2	B2 – T2
Subject 01	Experimenter 1	44.75	49.33	44.10	49.50
	Experimenter 2	44.66	49.17	44.93	49.01
	error	0.09	0.16	0.83	0.49
Subject 02	Experimenter 1	39.67	51.23	48.00	56.32
	Experimenter 2	39.64	51.92	47.63	56.94
	error	0.03	0.69	0.37	0.62
Subject 03	Experimenter 1	47.46	61.92	45.48	41.99
	Experimenter 2	47.88	61.88	45.56	42.12
	error	0.42	0.04	0.08	0.13

The population mean value: 0.32mm; T1, T2: The predefined scalp targets; A1, B1, A2, B2: The verification points.

Table S2. The positioning error (mm) of ten participants.

		verification 1 of T1 (*d* - *d*')		verification 2 of T1 (*d* - *d*')			verification 1 of T2 (*d* - *d*')		verification 2 of T2 (*d* - *d*')		
Marker	Sub	E_{A1}	E_{B1}	E_{A1}	E_{B1}	Mean (SD)	E_{A2}	E_{B2}	E_{A2}	E_{B2}	Mean (SD)
M1 and M2	Sub01	1.45	2.7	3.21	4.88	2.32 (1.43)	2	3.47	1.69	1.07	2.43 (1.52)
	Sub02	1.58	5.1	1.85	4.21		2.1	0.63	0.31	0.74	
	Sub03	4.34	2.26	3.53	1.26		4.59	0.53	2.65	3.86	
	Sub04	3.08	2.01	1.68	1.92		1.82	1.38	1.88	1.1	
	Sub05	2.49	0.11	2.6	1.26		3.92	0.08	4.48	2.32	
	Sub06	0.1	1.25	2.27	1.55		4.6	3.98	2.2	2.18	
	Sub07	1.16	2.09	2.69	1.38		4.47	0.62	2.04	0.57	
	Sub08	0.38	0.8	1.4	0.12		2.62	1.86	2.89	2.51	
	Sub09	3.6	5.07	4.29	3.73		4	3.72	0.45	5.31	
	Sub10	4.23	3.31	1.92	0.11		4.5	5.19	0.72	2.12	
M3 and M4	Sub01	0.34	1.9	1.93	0.3	2.13 (1.48)	0.71	1.68	2.72	0.35	2.40 (1.57)
	Sub02	0.52	0.75	2.25	2.92		1.44	2.69	0.78	2.61	
	Sub03	5.72	0.78	2.78	1.15		6.55	1.09	5.54	0.94	
	Sub04	1.78	0.66	1.63	0.75		1.7	0.35	2.24	1.25	
	Sub05	3.3	1.18	3.75	0.34		4.78	2.24	5.14	3.76	
	Sub06	1.11	0.32	1.75	1.04		1.21	4.55	2.26	2.38	
	Sub07	2.03	2.19	4.55	5.1		4.47	3.49	3.07	2.8	
	Sub08	2.69	0.97	1.05	0.49		1.25	2.28	2.04	2.47	
	Sub09	4.33	3.66	4.08	3.23		0.09	1.61	4.31	3.67	
	Sub10	4.58	1.74	2.85	2.85		0.37	2.63	0.44	2	
	mean(SD)					2.23 (1.45)					2.42 (1.54)

Verification 1: Two experimenters positioning and verify two predefined scalp targets for the first time; verification 2: Two experimenters positioning and verify two predefined scalp targets for the second time; *d*: verification distance before target positio*ning; d'*: verification distance after target positioning; E_{A1}: absolute error value measured by A1 of T1 target; E_{B1}: absolute error value measured by B1 of T1 target; E_{A2}: absolute error value measured by A2 of T2 target; E_{B2}: absolute error value measured by B2 of T2 target.