JAWATANKUASA ETIKA UNIVERSITI UNTUK PENYELIDIKAN MELIBATKAN MANUSIA (JKEUPM)
UNIVERSITI PUTRA MALAYSIA, 43400 UPM SERDANG,
SELANGOR, MALAYSIA

FORM 2.4: RESPONDENT'S INFORMATION SHEET AND INFORMED CONSENT FORM

Please read the following information carefully and do not hesitate to discuss any questions you may have with the researcher.

1. STUDY TITLE :

Effectiveness and Tolerability of Repetitive Transcranial Magnetic Stimulation for Preventive Treatment of Episodic Migraine: A Single Centre, Randomised, Double-Blind, Sham-Controlled Phase 2 Trial (MAGNET-EM).

2. INTRODUCTION:

You are invited to participate in a research study because you have migraine that requires treatment of a non invasive device that delivers pulsed magnetic fields on the scalp. The treatment with the device is called repetitive transcranial magnetic stimulation (rTMS) because it is done repetitively in several sessions. The details of the research trial are described in this document. It is important that you understand why the research is being done and what it will involve. Please take your time to read through and consider this information carefully before you decide if you are willing to participate. Ask the study staff if anything is unclear or if you like more information. After you are properly satisfied that you understand this study, and that you wish to participate, you must sign this informed consent form. To participate in this study, you may be required to provide your doctor with information on your health history, you might harm yourself if you are not being truthful with the information provided.

Your participation in this study is voluntary without any compensation or emolument. You do not have to be in this study if you do not want to. You may also refuse to answer any questions you do not want to answer. If you volunteer to be in this study, you may withdraw from it at any time. If you withdraw, any data collected from you up to your withdrawal will still be used for the study. Your refusal to participate or withdrawal will not affect any medical or health benefits to which you are otherwise entitled.

This study has been approved by the Jawatankuasa Etika Universiti Melibatkan Manusia (JKEUPM).

3. WHAT WILL YOU HAVE TO DO?

1. You are required to be present at the Neurophysiology Laboratory located at the Faculty of Medicine and Health Sciences UPM.

2. You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. Neither you nor your doctor can choose the group you will be in.

You will have an equal chance of being placed in any group. You will receive either an active rTMS treatment or a sham coil in a 50-50 chance based on a fair draw.

3. For the active rTMS treatment, a magnetic stimulation device will be placed on the top of your head. The detailed procedure has been explained in previous section.

4. For the sham treatment, a similar TMS device but without the magnetic coil will be placed on the top of your head. Both active and sham TMS device looks exactly the same and you would not know which treatment you have. There is no risk associated with the sham rTMS.

5. For both groups, treatment is non invasive without oral or intravenous medications or procedure done. All the study procedures and follow-ups will be the same for both groups.

6. Participants will receive rTMS treatment for a total of 5 sessions days within 2 weeks. Only one treatment session will be given per day. Participants will receive 3 consecutive sessions per week in the 1st week and 2 consecutive sessions in the 2nd week. This means that the participants are required to present themselves to the headache research clinic 5 times within 2 weeks for the treatment phase.

7. The follow-ups will be conducted after 1 month, 2 months and 3 months. There will be questionnaires to be answered by the participants and also some neurophysiological tests such as transcranial doppler and electroencephalography to see if there are any changes after the rTMS treatment.

8. Participants will be given a headache diary to record the occurrence of headaches on daily basis for every month. The information from this headache diary should be handed over to the research officer at each follow-up treatment session.

9. You are advised to continue taking medicines as normal and continue your follow-up with your previous doctor. Participants should continue all their medications as prescribed by their doctors. Participants will receive a memo to notify their doctors about their participation in this study.

10. Study visits schedule and procedures are summarised in the table below:

Screening & Run in period 1 month (Visit 1)	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10
M0	M1	M1 T1	M1 T2	M1 T3	M1 T4	M1 T5	M2	M3	M4
Check eligibility Informed consent Headache diary Questionnaires	Check eligibility Informed consent Questionnaires Blood test EEG TCD	Blood taking Randomisation Study treatment (TMS)	Study treatment (TMS)	Study treatment (TMS)	Study treatment (TMS)	Study treatment (TMS)	Efficacy assessment (Headache diary)	Efficacy assessment (Headache diary)	Efficacy assessment (Headache diary) Questionnaires Blood test TCD EEG

M = Month, T = Treatment

4. WHO SHOULD NOT PARTICIPATE IN THE STUDY?

One who are not meet the inclusion criteria should not participate in the study.

The exclusion criteria are:

1. Patients with previous history of repetitive Transcranial Magnetic Stimulation treatment.
2. Onset of headache at more than 50-year-old .
3. Headache with red flags symptoms that may suggest organic secondary headaches.
4. Pregnant or lactating women.
5. Patients with contraindications to TMS such as metallic implant and pacemaker based on the Screening 13-item Questionnaire for rTMS candidate. The questions are:

1) Do you have epilepsy or have you ever had a convulsion or a seizure?
2) Have you ever had a fainting spell or syncope? If yes, please describe on which occasion(s)?
3) Have you ever had a head trauma that was diagnosed as a concussion or was associated with loss of consciousness?
4) Do you have any hearing problems or ringing in your ears?
5) Do you have cochlear implants?
6) Are you pregnant or is there any chance that you might be?
7) Do you have metal in the brain, skull or elsewhere in your body (e.g., splinters, fragments, clips, etc.)? If so, specify the type of metal.
8) Do you have an implanted neurostimulator (e.g., DBS, epidural/subdural, VNS)?
9) Do you have a cardiac pacemaker or intracardiac lines?
10) Do you have a medication infusion device?
11) Are you taking any medications? (please list)
12) Did you ever undergo TMS in the past? If so, were there any problems.
13) Did you ever undergo MRI in the past? If so, were there any problems.

7. Patients with medical conditions such as severe hypertension, infections, malignancy, cardiovascular and cerebrovascular diseases, epilepsy, degenerative central nervous system diseases, renal failure, hepatic failure, bleeding diathesis and serious mental illnesses .

5. WHAT WILL BE THE BENEFITS OF THE STUDY:

(a) TO YOU AS THE SUBJECT?

There may or may not be any benefits to you. Patients are informed that TMS is not intended to provide a cure for migraine and that reduction in symptoms may be modest.

You will receive certification as appreciation and RM100 honorarium upon completion of the study. However, no reimbursement will be given to patient to cover for travel expenses and food.

b) TO THE INVESTIGATOR?

This study may reveal to detect the genetic and biochemical factors of migraine and information obtained from this study will help improve the treatment or management of other participants with the same disease or condition.

6. WHAT ARE THE POSSIBLE RISKS?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop the treatment. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the study. You are covered with insurance in this study. However, any cost of treatment or procedure related to complication of procedure including hospitalization will bear with patient's own expenses.

Risks and side effects related to the rTMS device include those which are:

Likely	**Less likely**	**Rare but serious**
Headache	Neck pain	Seizure
Nausea	Hearing impairment	
Vomiting	Scalp burns	
Dizziness	Difficult to concentrate	
	Cognitive impairment	
	Acute mood changes	

The side effect of this research product on the fetus / content is unknown. Therefore, you should not conceive or make your partner pregnant.

A last menstrual period (LMP) date will be obtained on potential women to conceive and patient must declare that they are not pregnant. Throughout this research, if you have the potential to get pregnant, it is very important that you practice effective pregnancy prevention methods continuously and correctly. The research doctor will discuss with you about some family planning techniques. Tell your doctor as soon as possible, if you suspect that you are pregnant. If this happens, the treatment will be discontinued immediately and your participation in this research will be terminated.

Please ask your study doctor if you need more information on risks and side effects. The trial staff will inform you in a timely manner about any new findings or changes about the study product which may affect your health or willingness to continue in this study. Subjects will be informed if new information relevant to consent becomes available. Where necessary, you may be asked to re-consent to participate.

7. WILL THE INFORMATION THAT YOU PROVIDE AND YOUR IDENTITY REMAIN CONFIDENTIAL?

All your information obtained in this study will be kept and handled in a confidential manner, in accordance with applicable laws and/or regulations. When publishing or presenting the study results, your identity will not be revealed without your expressed consent. Individuals involved in this study and in your medical care, qualified monitors and auditors, the sponsor (UPM) or its affiliates and governmental or regulatory authorities may inspect and copy your medical records, where appropriate and necessary. Since this study will not reveal individual results, all the results will be kept confidential unless the subjects requested the result personally.

Your biospecimens may be sent to the local university laboratories or other laboratories in the country for testing. If this is required, your biospecimens will be coded and information that can identify you will be removed. Only your study doctor and study staff will be able to link the code with you. In addition to the biochemical analysis, genetic testing will also be done on the biospecimens. A separate optional consent will be obtained from you for the genetic testing of those biospecimen. The subjects will not be informed of personal genetic findings unless the subjects requested the result personally.

Some of your biospecimens may be stored by the sponsor for 2 years for future testing. Your biospecimens will be coded and information that can identify you will be removed. Only your study doctor and study staff will be able to link the code with you. The sponsor may share those biospecimens with other researchers. The future studies on biospecimens is optional. Should you agree, a separate optional consent will be obtained from you for the storage and use of those biospecimens. You can withdraw your consent and the specimens will be destroyed. Or you can request for the stored excess biospecimens to be destroyed.

The sponsor will still use any information obtained from the biospecimens up until the time you withdraw consent. These excess biospecimens will be stored at the medical laboratory, UPM.

All the future research on your biospecimens will need another ethical committee approval.

Data from the study will be archived and may be transmitted outside the country for the purpose of analysis, but your identity will not be revealed at any time. Publications and/or presentations that result from this study will not identify you by name.

With your permission your family doctor will be informed of your participation in the study.

8. WHO SHOULD YOU CONTACT IF YOU HAVE ADDITIONAL QUESTIONS DURING THE COURSE OF THE RESEARCH?

If you have any questions about the study or if you think you have a study related injury and you want information about treatment, please contact the study doctor, Dr [redacted] at telephone number [redacted] or Research Officer, Miss [redacted] or Miss [redacted]

Please initial here if you have read and understood the contents of this page

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9. CONSENT

I …….....

I/C No. …….....

address……..

…….....

hereby voluntarily agree to take part in the research stated above *(clinical trial / drug trial / video recording / focus group / interview-based / questionnaire-based).

I have been informed about the nature of the research in terms of methodology, possible adverse effects and complications (as written in the Respondent's Information Sheet). I understand that I have the right to withdraw from this research at any time without giving any reason whatsoever. I also understand that this study is confidential and all information provided with regard to my identity will remain private and confidential.

I* wish / do not wish to know the results related to my participation in the research

I agree/do not agree that the images / photos / video recordings / voice recordings related to me be used in any form of publication or presentation (if applicable)

* delete where necessary

Signature: ……..…… *(Respondent)*

Signature: ……..…….. *(Witness)*

Date :……..

Name : ……..…..

Time: ……..

(24 hour Format)

I/C No. : ……..…..

I confirm that I have explained to the respondent the nature and purpose of the above-mentioned research.

Date: ……..……

Signature: ……..…….. *(Researcher)*

Time: ……

(24 hour Format)

I/C No. :……..…..