Effect and Safety of Smart Bra (PUMCH)

Protocol

NCT number:

Version: V3

Version Date: 9 Fab 2021

Founder: Wang Xuefei

Title and Investigators:

Effect and Safety of Smart Bra (PUMCH)
Principle Investigator: Xuefei Wang
Co-invetigators: Qiang Sun

Abstract:
This is a multicenter, prospective clinical study, and was conducted to evaluate the safety and effectiveness of PUMCH smart bra for breast disease screening in outpatients. According to the patients' wishes and written informed consent, they were randomly assigned to the study group. A total of 2000 patients were expected to be enrolled. The training group: validation group = 1:1. The subjects wore smart bras in the outpatient department, took photos and kept the data. The project team further studied artificial intelligence. The main endpoint and secondary endpoint was Sensitivity and Specificity at baseline，using $\chi 2$ test. During the follow-up, the safety of the product was evaluated with number of participants with smart-bra related adverse events as assessed by CTCAE v4.0. Data and Safety Monitoring Board will periodically review, evaluate and give recommendations to this study in various aspects.

Specific aims:
To evaluate the Effect and Safety of Smart Bra (PUMCH).

Significance:
According to China cancer status and trend report released in 2019 by the National Cancer Center, the incidence rate of breast cancer is 7.74% in China, ranking the highest in female malignant tumors, with 304 thousand new deaths and 70 thousand [1] deaths annually. Early detection and early treatment can greatly reduce the mortality, the cure rate of early breast cancer patients can reach more than 80%. With the promulgation of the "healthy China 2030" program [2], the gateway of breast disease diagnosis and treatment has moved forward, which has laid the foundation of national policy for early diagnosis and treatment of breast disease. In order to meet the needs of early diagnosis and treatment of breast diseases, breast disease screening has become an important research direction.
However, China's per capita high-quality medical resources are limited, and the number of people and the number of people covered by the conventional screening and diagnosis mode are extremely limited. Now the monthly breast self-examination advocated by popular science, because patients can not distinguish between normal hyperplasia and new tumors, it can only be on paper. For decades, there is no other way to screen breast diseases except large-scale physical examination of doctors, B-ultrasound and infrared examination of breast in hospitals. However, new screening methods for breast diseases are being explored all over the world, especially the cross application of previous examination and artificial intelligence [3]. Although the world's major medical institutions are trying to explore, there are still many problems

(1) The current status of breast disease screening challenges the existing disease screening model

The breast surgery department of Peking Union Medical College Hospital first verified and formulated the breast cancer screening model PUMCH model in line with China's national conditions, which significantly improved the early detection rate of breast cancer. PUMCH model technology was used to screen and follow up more than 200000 healthy people. Combined with the analysis of health economics, a screening model suitable for Chinese women was developed for the first time in China, that is, a standardized screening process with ultrasound and infrared detection as the main and molybdenum target as the auxiliary [4-5]. However, in practical work, we found that although mammography and ultrasound are the most commonly used screening methods, they are difficult to detect tumors in dense breast tissue. At present, the sensitivity of standard mammography is low for women with dense breast images. The sensitivity of dense breast is only 48%, and the sensitivity is 62.9%. This is worse than the 87% sensitivity of fat type breast. Most Asian women have dense breasts. In addition, with the increasing pressure of outpatient treatment, due to the barrier of time and space, the conventional screening methods are not suitable for radiation and compression, and the privacy of the breast, few women can really come to the hospital for regular breast B ultrasound, infrared detection or molybdenum target screening.

Therefore, how to make women use a more convenient way for breast disease screening is an urgent problem to be solved. So we propose a Concorde breast smart bra system based on infrared detection.

(2) the high incidence rate of breast cancer challenges the existing functions of bra.

Over the past 200 years, bras that cover privacy, support breasts and increase comfort and mobility have developed rapidly in appearance. But in terms of function, there is no breakthrough except massage and shaping. With the increasing incidence rate of breast cancer and the increasing concern of the public on breast health, the existing common bra has been unable to meet the requirements of modern women for breast health. The report on the competition pattern and future development trend of China's underwear market [6-7] shows that women's demand for underwear has begun to diversify. With the increasing demand of women for bra health function, the functional demand for underwear has become the main standard for consumers to choose underwear. Comfort, functionality and fashion are the main factors for women to buy underwear.

Combined with women's health and medical needs, Concorde smart bra system opens the door to the diagnosis and treatment of breast diseases from the perspective of people-friendly screening, making it possible for the diagnosis and treatment of breast diseases to follow the natural diagnosis and treatment process, with screening and follow-up as two systems, including screening, follow-up, prevention, health care, diagnosis and treatment. Finally, the bra realizes diagnosis and treatment through the Concorde breast artificial intelligence big data platform which has been built by the project team, and connects with the whole process management platform of breast diseases, so as to truly realize the whole process management of breast, and endow the intelligent bra with richer extension and connotation. The project of this subject is the

bra body part [8-20].
(3) The specialization of bra function challenges the professionalism of R & D team
With the screening (auxiliary examination) function, more scientific, professional and accurate bra has put forward high requirements for the R & D team, regulatory departments and the professionalism of docking diagnosis and treatment. The existing bras are rarely independently developed by surgeons, so there is a lack of evidence-based medical data to measure breast health indicators, let alone research and development with screening (auxiliary examination) function. Therefore, in the world, the bra with screening function is still a blank. Thus, we have established a PUMCH intelligent bra team with PUMCH breast surgeon as the main team, Computer Department of Tsinghua University as the auxiliary team, and medical device manufacturers as the media, which has laid a solid foundation for the professionalism of the team.
Smart bra, originated from the actual needs and technical difficulties, has important theoretical and practical significance and high application value. Now we plan to conduct a clinical trial on the effectiveness and safety of bra.

Methods:
Concorde smart bra, including bra entity and AI app. The app end belongs to the whole process management application software of PUMCH. Follow these steps:
Step 1: download the whole process management application software of Xiehe mammary gland and set and register it
1. Open the mobile phone and use the link or application platform to download the software.
2. Registration: input the name, telephone number, e-mail address and personal password according to the prompt, and confirm the same personal password.
3. After reading and selecting the "terms of use and privacy policy", complete the personal information and medical records and fill in the questionnaire.
Step 2: bra initialization
1. CRC should fill in the "corresponding information" section of CRF form for patients to register.
2. Make sure the mobile phone is connected to the Internet.
Step 3: wear smart bra
1. After registration and information entry, CRC introduced smart bra to patients, obtained informed consent, reviewed research procedures, and informed patients how to wear smart bra.
2. The size of the bra depends on the patient's previous bra size. Refer to the size table and select the closest appropriate size. Note: if the patient is between sizes, it is recommended to choose a smaller size.
3. Ask the patient to take off his coat and wipe the skin thoroughly with a towel (a small amount of soap and water can be used). In this process, CRC can provide privacy space for patients.
4. CRC determines the bra to wear.
Note: at this time, the cable will only end with USB and switch.

Step 4: upload photos using the photo function of the app
1. CRC will open the application program in the above way, turn on the worn bra switch at the same time, and turn off the indoor light;
2. Use the app to take photos or upload the taken photos to the app (pay attention to turn off the flash);
3. The photos should be taken from position.
Step 5: device removal
Step 6: background data processing
1) Open from the background of the application software to export patient information and photos.
2) We will carry out artificial intelligence learning on the data of training stage.
3) We will conduct AI learning on the data in the verification phase.

Study subjects:

patients in breast surgery department clinic

- Inclusion criteria:

1. The patients who went to the breast surgery clinic and planned to have double breast ultrasound and molybdenum target;
2. Female patients (18-80 years old);
3. Signed written informed consent approved by the relevant institutional review board (IRB) or independent ethics committee (IEC).

- Exclusion criteria:

1. The subjects were pregnant or lactating;
2. Patients with nipple discharge;
3. Known allergy to bra materials;
4. Patients who have received breast surgery or breast puncture within half a year;
5. Patients with skin diseases.

Plans for sampling, recruiting and retaining subjects：

- Sample type: Convenience sample
- Recruitment method: When patients presented our hospital, we will review these patients' medical records to find out the potential subjects for this study according to the inclusion and exclusion criteria. The eligible subject who is willing to participate in this study will be enrolled and consented.

Measurements:

- Predictor variables:

The predictor variable we are assessing is whether use statins. According to which, we established the intervention group and control group.

- Outcome variables:

Primary outcome: Sensitivity at baseline;

Secondary outcome: Specificity at baseline;

Other Pre-specified Outcome Measures: Number of adverse events assessed by CTCAE v4.0.

Plans for blinding, run-in period as needed:

- Blinding

The clinicians and patients will be blinded to the intention of the group divided. Since the patients' and clinicians' subjective motion may affect the outcomes.

- Run-in design

We would like to recruit patients from the breast surgery department. Clinic doctors in this department will help us to find appropriate patients. Then appraiser will do the diagnostic evaluation. If patients meet the included standard, we will ask them to sign informed consent and the registration form (questionnaire). Meanwhile we will make a calendar for their supervision.

Statistical Analysis Plan:

(1) Effectiveness analysis

The main evaluation indexes were the sensitivity and specificity of breast ultrasound and/or pathology at baseline. ROC curve was drawn and the accuracy of quantitative response diagnosis was calculated according to the area under the curve. Chi square test or Fisher's exact was used, and paired design was used. The method was paired chi square test Bowker test. If the baseline value was not balanced between groups, stratified analysis was used based on the baseline variable (classification or grade variable).

(2) Safety analysis

The safety analysis was conducted in the safety population. Adverse events include symptoms and signs. All the reported adverse events were divided into all and those related to the use of the instrument. Number of participants with smart-bra related adverse events as assessed by CTCAE v4.0 at baseline and 3 months later. All reported adverse events were listed in detail. In addition, the relevant indicators in the feedback form will also be described.

Data safety & monitoring:

The members of DSMB are 3 professors in the breast surgery department, 6 attending doctors and 3 residents. DSMB members will meet:
1) before the start of the trial to discuss the study protocol,
2) at early stage of about 10-20 patients are enrolled. In order to monitor **enrollment** efficacy, **adverse effects** that might have happened, the efficacy of **blinding** strategy, the current **outcome variables** in control and interventional group (only known to DSMB members), **protocol** compliance and quality control issues.
3) Subsequent DSMB meetings will be hold regularly (at least every three months) or anytime when there are safety issues, need to stop the program earlier and so on.
If DSMB find that the bra is causing harm, they could discuss whether to end the study early after balancing between ethical responsibility to the participants and the advance of scientific knowledge.

Ethical considerations:

In our study, the major ethical issue is that may do harm for patients with known allergy to bra materials. In order to mitigate this situation, we:
1) Set exclusion criteria: Known allergy to bra materials.
2) Inform the patients with this potential risk comprehensively, have them better understood the potential risk of this study, and write it in the informed consent.
3) Use DSMB to monitor any risk related to the intervention.

Reference:

[1] Zheng rongshou, sun Kexin, Zhang Sihua, et al. Analysis of cancer prevalence in China in 2015 [J]. Chinese Journal of oncology, 2019,41 (1): 19-28 DOI:10.3760/cma.j.issn.0253-3766.2019.01.005.
[2] Zeng Zhao, Liu Juan. Outline of "healthy China 2030" plan issued by the State Council of the CPC Central Committee [J]. Bulletin of the State Council of the people's Republic of China, 2016 (32): 5-20
[3]The National Artificial Intelligence Research and Development Strategic Plan. In: Council NSaT, editor. United States: Networking and Information Technology Research and Development Subcommittee; 2016. p. 1 - 40. *Comprehensive AI research and development report.
[4]Turati F, La Vecchia C. Risk factors for breast cancer in China: similarities and differences with western populations. Arch Med Sci. 2012 May 9;8(2):179-82. doi: 10.5114/aoms.2012.28542.
[5]Xu YL, Sun Q, Shan GL, et al. A case-control study on risk factors of breast cancer in China. Arch Med Sci. 2012 May 9;8(2):303-9. doi: 10.5114/aoms.2012.28558.
[6] Zhiyan Consulting Group, "2016-2022 China underwear market competition pattern and future development trend report"
[7] Zhiyan consulting group. Research Report on market depth analysis and investment strategy of China's underwear industry from 2018 to 2024

[8] Gao Z, Ma Z, Chen X et al. Enhancement and Denoising of Near-Infrared Image with Multiscale Moephology [J]. IEEF, Bioinformatics and Biomedical Engineering. 2011.1-4
[9] Sheng Jie, Gao Jie, Qian Pengfei. Comparative study of mammography and high frequency color Doppler ultrasound in the diagnosis of early breast cancer [J]. Chinese Journal of clinical medical imaging, 2012, 23 (3): 206-207.4, Wang Qiang, Hu Guodong, Kuang Jun, et al. Comparative study of MRI and full digital mammography in breast lesions [J]. Journal of Southern Medical University, 2009, 29 (2): 292-294
[10] Li Zhengguo, Zheng Jinghong, Zhu Zijian et al. Weighted guided image filtering[J]. IEEE Transactions on Image Processing A Publication of the IEEE Signal Processing Society, 2015, 24(1):120-129.
[11] Gao Yuanhong, Dong Yan. Application of infrared breast scanning, color Doppler ultrasound and mammography in breast physical examination [J]. China convalescent medicine, 2012,21 (1): 1013-1014
[12]Li K, Xiang Y, Yang X et al. Extracting Pathologic Patterns from NIR Breast Images with Digital Image Processing Techniques[M]. Medical Imaging and Augmented Reality. Springer Berlin Heidelberg, 2004:62-69.
[13] Bai Xiaoping. Application of manual examination and infrared scanning in general survey of women's breast diseases [J]. Chinese and foreign medical, 2010,29 (25): 65
[14] Yang HY. Clinical value of near-infrared scan and molybdenum target photography in diagnosing mammary gland disease.
[15] Jiang S, Pogue BW, Mc Bride TO and Paulsm KD. Quantitative analysis of near-infrared tomography: sensitivity to the tissue-simulating precalibration phantom[J]. Journal of Biomedical Optics 2003,08:308-315.
[16] Zhang Bin, Cheng HW, you Li. Application of color Doppler ultrasound and infrared scanning in breast physical examination [J]. China convalescent medicine, 2009,18 (9): 846
[17] Cao Yali, Wang Guoqing, Wu Xiaobo, et al. Diagnostic value of three methods in breast diseases [J]. Journal of practical cancer, 2009,24:165-167
[18] Wang Haiyan, Zhang Aiqin. Analysis of 3709 cases of breast diseases diagnosed by infrared scanning [J]. Chinese community physicians (Medicine), 2009,11 (16): 199
[19]Nioka S, Chance B. NIR spectroscopic detection of breast cancer[J]. Technology in Cancer Research & Treatment, 2005, 4(5):497.
[20] Shang linhui, Xiao Gang, Guo Daqing. Comparative imaging study on breast cancer [J]. Chinese PLA Journal of medicine, 2011,23 (4): 51-53

Effect and Safety of Smart Bra (PUMCH)

Informed Consent

NCT number:

Informed Consent Version: V3

Informed Consent Version Date: 9 Fab 2021

Founder: Wang Xuefei

Effect and Safety of Smart Bra (PUMCH)

Informed consent

Respected patients:

We invite you to participate in a clinical study. Before you decide whether to participate in this study, it is important to understand the impact of the purpose of the study on you. Please read the following information carefully. You can discuss with your family, friends and family doctor about your participation in this study. Once all the questions have been answered, you are satisfied with the explanation of the study, and you decide to participate, you will be invited to sign this informed consent form.

Name of research project:

Effect and Safety of Smart Bra (PUMCH)

Research leader: Wang Xuefei

Contact number: 13001289600

SETTING: Peking Union Medical College Hospital, Chinese Academy of Medical Sciences

1. Research background and purpose:

Background:

According to China cancer status and trend report released in 2019 by the National Cancer Center, the incidence rate of breast cancer is 7.74% in China, ranking the highest in female malignant tumors, with 304 thousand new deaths and 70 thousand [1] deaths annually. Early detection and early treatment can greatly reduce the mortality rate, and the cure rate of early breast cancer patients can reach more than 80%. With the promulgation of "healthy China 2030" program [2], the key point of breast disease diagnosis and treatment has moved forward, which has laid the foundation of national policy for early diagnosis and treatment of breast disease. In order to meet the early diagnosis and treatment of breast disease, breast disease screening has become an important research direction.

However, China's per capita high-quality medical resources are limited, and the conventional screening and diagnosis mode covers a very limited number of people. Now the popular science advocates monthly breast self-examination, because patients can not identify normal hyperplasia and new tumor, but only on paper. For decades, there is no other way to screen breast diseases except for large-scale medical examination by doctors and breast B-ultrasound and infrared examination in hospitals. However, the whole world is exploring new breast disease screening methods, especially the cross application of previous examination and artificial intelligence [3]. Despite the great efforts of the world's major medical institutions, there are still many problems: 1. The current situation of screening for breast diseases challenges the existing screening models; 2, the rising incidence rate of breast cancer challenges the functions of bra, and 3, the specialization of bra function challenges the professional quality of R & D team.

Concord smart bra, originated from practical needs and technical difficulties, has

important theoretical and practical significance and high application value. Now we plan to carry out a clinical trial on the effectiveness and safety of bra.

2. Research contents, methods and procedures:

This study is a randomized, open, multicenter clinical study. It will be conducted in Peking Union Medical College Hospital, Shanxi Provincial People's Hospital, Beijing Third Hospital, Zhalantun ZhongMeng hospital, Chongqing Medical University affiliated university town hospital, Shenzhen People's Hospital and other national hospitals. A total of 2000 subjects are expected to participate.

The patients in the group wore the device for about 3 minutes, and took photos of 5 breast sites. After that, the artificial intelligence learning was carried out on the photos of the training group. For the photos of the verification group, the algorithm obtained by the training group was compared with the existing artificial intelligence algorithms of ultrasound and molybdenum target. During the follow-up, the safety of the product was evaluated. According to the basic principles of safety and performance of medical devices (sg1-n020r5), which is the international general purpose of who (Appendix 2).

Selection criteria:

All the following conditions should be met before they can be enrolled in the group:

1. The patients who went to the breast surgery clinic and planned to have double breast ultrasound and molybdenum target;
2. Female patients (18-80 years old);
3. Signed written informed consent approved by the relevant institutional review board (IRB) or independent ethics committee (IEC).

If you participate in the research, you will need to do the following work:

(1) First of all, you need to understand the whole process of the study and volunteer to participate, and sign the informed consent form at the same time:

λ the doctor will ask and record your medical history and give you a physical examination / sign / physical fitness score.

λ based on the results, the study doctor will assess whether you meet the inclusion criteria and do not meet the exclusion criteria.

(2) If you pass the above inspection, the research will be conducted according to the following steps:

Union smart bra, including bra entity and artificial intelligence app. The bra body is composed of bra, switch, battery and detection probe. The app side belongs to Xiehe breast whole process management application software. Follow these steps:

Step 1: Download union breast whole process management application software and set up and register

1. Open the mobile phone and download the software using the link or application platform.
2. Registration: enter the name, telephone number, email address, personal password according to the prompt content, and confirm the same personal password.
3. After reading and selecting the "terms of use and privacy policy", improve personal information and medical records, and fill in the questionnaire.

Step 2: bra initialization

3. CRC should fill in the "corresponding information" part of CRF form for patient registration.
4. Make sure the mobile phone is connected to the network.
Step 3: wear smart bra
5. After registration and information entry, CRC introduces smart bra to patients, obtains informed consent, reviews research procedures, and tells patients how to wear smart bra.
6. The size of the bra depends on the patient's previous bra size. Refer to the dimension table (as shown in Figure 2) and select the closest appropriate size. Note: if the patient is between sizes, a smaller size is recommended.
7. Ask the patient to take off his coat and thoroughly dry and disinfect the skin with a towel (a small amount of soap and water can be used). In this process, CRC can provide privacy space for patients.
8. CRC determines the bra to wear (as shown in Figure 3).
9. Each chest aligned near the center has a cable to the USB connector.
Note: at this point, the cable will only end with USB and switch.
Step 4: upload photos by using the camera function of app
1. CRC will open the application in the above way, and turn on the bra switch to turn off the indoor light;
2. Use the app to take photos or upload the photos to the app terminal (pay attention to turn off the flash);
3. Photos should be taken from 5 locations at 3, 1, 12, 9 and 6 o'clock.
The battery has a shelf life of one year and is designed to withstand a total scanning time of 24 hours. After selecting the scan period, the application will determine if the 24-hour battery scan life is still available. If the battery fails to scan for a full 24 hours, the app will provide a shorter wearable time for CRC. The battery is rechargeable.
Step 5: equipment removal
When the patient returns to the test site after completing the test, the power is turned off, the patient slowly and carefully takes it off and puts it into the original packaging bag. The CRC asks the patient about her experience and records any feedback about the experience. CRC provided post monitoring questionnaire to patients. After completing the questionnaire, the questionnaire and "patient activity log" will be placed in the patient's clinical study file.
Step 6: background data processing
1) Open from the background of the application software to export patient information and photos.
2) Tsinghua University carries on the artificial intelligence learning to the training group data.
3) Tsinghua University conducts artificial intelligence learning on validation data.

3. Possible risks (or discomfort, inconvenience) and benefits (benefits to individuals or social groups) of participating in the study:
(1) Risk:
We do not expect significant adverse reactions. Although the incidence rate is very low,

patients may be allergic to bran contact with skin. If the bra pressure is not enough, it may not work. If this happens, please inform your doctor immediately.
(2) Benefits:
The product is still in the trial stage, and patients may not get any direct benefits from participating in this study. The data collected in this study can provide a safer and more effective choice for future women to diagnose breast diseases.
(3) Alternative therapy:
Participation in this study is entirely voluntary and there is no alternative program for this project if you choose not to participate or opt out at any stage of the study. This study is a supplement to your routine care, not a substitute. Whether you participate in the study or not, the recommended care you receive is the same.
(4) Personal information storage:
Your medical records (case report form, examination report, etc.) will be kept completely in the hospital, and the results of laboratory examination will be recorded in your outpatient or inpatient medical records. The investigator, the sponsor's representative, the ethics committee and the drug administration will be allowed to access your medical records. Any public report on the results of this study will not disclose your personal identity.

4. Consultation on relevant contents:
You have the right to consult on the research content (researcher's telephone number: 17310976820); and you have the right to consult on issues related to your rights or related risks (Tel. of ethics review committee): 010-69154494.

5. The right to withdraw from the study
Your participation in this study is entirely voluntary. For no reason, your unwillingness or unwillingness to continue to participate in this study will not have any impact on your rights and interests. In addition, you have the right to withdraw from the study at any time. Or drop out of the study as directed by your doctor, if not for your doctor's request.
Participation in the study is entirely up to you. You may refuse to participate in the study, or withdraw from the study at any time during the course of the study. This will not affect the relationship between you and your doctor, nor will it affect the loss of your medical treatment or other benefits.
If you withdraw from the study for any reason.
If you do not participate in the study, or drop out of the study, it will not affect the doctor to give you other appropriate treatment.
If you choose to participate in this study, we hope you will be able to adhere to the whole research process.
Whether or not to participate in this study is up to you. You can discuss with your family or friends before making a decision. Before you make a decision to participate in the study, please ask your doctor as much as possible until you fully understand the study.

6. Compensation for the study:

You will not be paid for your participation in this study. You will not be required to pay any additional fees for participating in this study. If you have some side effects or damage, please inform your research doctor immediately. The clinician will give active treatment and corresponding treatment measures, and ensure that you can receive appropriate treatment in time. Doctors and researchers will do their best to prevent and treat the possible injury caused by this study. If an adverse event occurs in a clinical trial, the medical expert committee will determine whether it is related to the product. In case of serious adverse events related to this study, the sponsor will provide corresponding economic compensation for serious damage related to the clinical trial in accordance with the relevant laws and regulations of China and the supplementary principle of clinical observation patients, and patients can obtain relevant compensation and free treatment. At the same time, in case of grade 3 or above adverse events (especially serious adverse events), it will be reported to Peking Union Medical College Hospital within 24 hours, and the breast surgery department of Peking Union Medical College Hospital will carry out investigation and further treatment.

7. Confidentiality system:

The medical information you receive from participating in this research institute will be kept confidential. The results of the study, published in academic journals, do not reveal any information that identifies you personally. The Peking Union Medical College Hospital will keep all the records of your research and the relevant hospital and office records. No one is authorized to obtain such information.

Under no circumstances will your personal identity be disclosed. We will make every effort to protect the privacy of your personal medical data within the limits permitted by law.

8. This informed consent is in duplicate, one for each subject and one for each researcher, and is valid upon signature by both parties.

Subjects' informed consent:

I have read the above in detail and fully understood it, and seriously considered the above contents, especially my rights, risks and benefits of participating in this research. I volunteered to participate in this research and would like to cooperate with researchers. At the same time, I declare that I can withdraw from this study for any reason at any time without losing any legal rights.

Subject name: Subject signature: date: year, month, day

Researcher's Name: Researcher's Signature: Date: Year, Month, Day

Statements and signatures of legal representatives (if applicable)

I confirm that the researcher has explained to the participants and me the details of the study, including its powers, possible benefits and risks, and will provide us with a signed copy of the informed consent. I agree to participate in the study on behalf of the participants.

Official letters of legal representatives:_____

Signature by legal representative:_____

Relations with subjects:_____

Date:_____

Statements and signatures of witnesses (if applicable)

Subjects have shown that he or she is unable to read. One or more researchers have read and explained this informed consent, including its power and possible benefits and risks, discussed with the subjects, given them the opportunity to ask questions and fully explained it, and will provide a signed copy of the informed consent for the subjects. I have witnessed the process of informed consent.

Witnesses in block letters:_____

Witness's signature:_____

Date:_____