SYNOPSIS (English)	
Title	Pain monitoring after breast biopsy: benefit of e-health
Acronym	BIO-PSY
Pathology	Breast cancer
Protocol codes	Sponsor Code : PRO ICM 2020-06 BIO ID-RCB: 2020-A00836-33 N° NCT : NCT04456920
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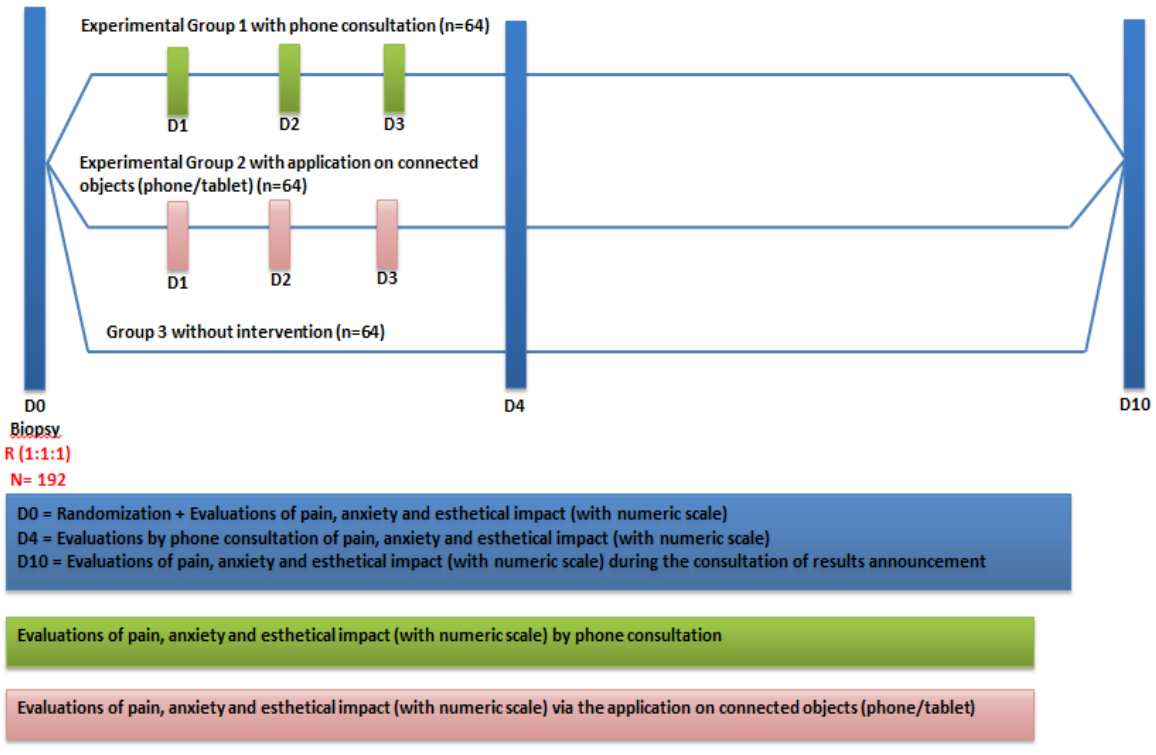
Study design	Monocentric, prospective, open-labeled, randomized controlled trial
Trial sites	1 participating center
Number of planned patients	Expected number of patients : 192

Background and Rationale	Each year, approximately 1500 breast biopsies (1000 microbiopsies and 500 macrobiopsies) are performed in the radiologic department of the Montpellier Cancer Institute (ICM). This exam, which is relatively easy for the radiologist, can however lead to major anxiety for patients. Indeed, previous studies show that about 50% of women undergoing a breast biopsy have significant anxiety affects. Anxiety associated with the risks of biopsy, potential breast cancer diagnosis and/or lack of routine sedation procedures increase patient concerns. Distress prior to biopsy is associated with greater pain and discomfort during the procedure. The psychological distress that persists after the biopsy is related to a worse psychological management of side effects of the biopsy breast (*e.g.,* sensitivity, skin irritation). Limiting apprehension, worry and anxiety induced by the uncertainty linked to the biopsy results and the biopsy-related pain should be an integral part of the medical care through the patient follow-up during, after and until the diagnosis is announced. In light of these challenges, new alternative methods are emerging to enhance patient knowledge, develop procedural skills, improve confidence and mitigate procedural anxiety. However, to our knowledge, few methods have been developed during this period of 'waiting-time'. Currently, only care instructions and a consultation to announce the results (about 10 days after the procedure) are proposed to patients at the end of biopsy. Patients are also encouraged to call if they suspect complications such as infection or bleeding. In this context, we propose to integrate a pain management after biopsy via e-health system through the patient's medical care. Radiologist/patient communication could have an impact on patients' anxiety and health-related issues, given the challenging nature of discussions around need for breast biopsy and potential implications of the results. Indeed, paying attention and focusing on symptoms as patients experience them improves their empowerment and their adjustment to the disease. Web-based systems that can provide electronic-Patient reported Outcomes (e-PRO) have been shown to prompt clinicians to intensify symptom management, to improve symptom control and to enhance patient-clinician communication patient satisfaction, as well as well-being. In addition, it is known that improved communication between patients and medical staff to less anxiety after a biopsy and that anxiety is related to pain. Taken as a whole, these elements encourage the integration of e-health and e-PRO for the management of pain and anxiety in patients undergoing a biopsy. The benefits of e-PRO are still being discussed in terms of quality of life (Qol) and psychological distress. We thus propose to integrate two types of e-health intervention: 1/e-PRO collected by connected objects (smartphone or tablet) as they were used in previous studies, and 2/ e-PRO collected by a phone consultation, which values human communication between the medical staff and the patient. In case of significant pain, the collection of e-PRO by any of these e-health interventions will generate an alert and a reactive and responsive care. *In fine*, the purpose of this research is to improve the medical organization and care of post-biopsy patients by proposing an innovative connected patient technology, regardless of their remoteness from the hospital. Social inequalities will be reduced by lending a tablet to patients who do not have such a device with a 4G key.

Study Objective(s)	**Primary objective** To compare the benefit of intervention by e-health (phone consultation with a professional or connected objects (smartphone or tablet)) with the standard follow up of the pain intensity of patients 4 days (D4) after un breast biopsy. **Secondary objectives** - To compare the benefit of intervention by e-health (phone consultation with a professional or connected objects) with the standard follow up of the pain intensity of patients during the consultation of results announcement (about D10) after a breast biopsy. - To compare the benefit according to the type of intervention by e-health (phone consultation with a professional or connected objects) on the pain intensity of patients at 4 days (D4) and during the consultation of results announcement (about D10), after a breast biopsy. - To compare the benefit of intervention by e-health (phone consultation with a professional or connected objects) with the standard follow up of the anxiety intensity of patients at 4 days (D4) and during the consultation of results announcement (about D10), after a breast biopsy. - To compare the benefit according to the type of intervention by e-health (phone consultation with a professional or connected objects) on the anxiety intensity of patients at 4 days (D4) and during the consultation of results announcement (about D10), after a breast biopsy. - To compare the benefit of intervention by e-health (phone consultation with a professional or connected objects) with the standard follow up of the esthetic impact of patients at 4 days (D4) and during the consultation of results announcement (about D10), after a breast biopsy. - To compare the benefit according to the type of intervention by e-health (phone consultation with a professional or connected objects) on the esthetic impact of patients at 4 days (D4) and during the consultation of results announcement (about D10), after a breast biopsy. - To compare the benefit of intervention by e-health (phone consultation with a professional or connected objects with the standard follow up of the insomnia of patients at 4 days (D4) and during the consultation of results announcement (about D10), after a breast biopsy. - To compare the benefit according to the type of intervention by e-health (phone consultation with a professional or connected objects) on the insomnia of patients at 4 days (D4) and during the consultation of results announcement (about D10), after a breast biopsy. - To compare the benefit of intervention by e-health (phone consultation with a professional or connected objects) with the standard follow up of patient's management - To compare the use of a biopsy-related drug intervention (analgesics, anxiolytics, antidepressants, anti-inflammatory and hypnotics) in patients with e-health interventions (phone consultation or smartphone), with the standard follow-up, during the consultation of results announcement (about D10) after a breast biopsy. - To compare adverse events in patients with e-health interventions (phone consultation with a professional or connected objects), with the standard follow-up, during the consultation of results announcement (about D10) after a breast biopsy.

	- To reduce social and territorial inequalities. - To assess satisfaction with specific study management. - To assess compliance.
Study endpoints	**<u>Primary endpoint</u>:** Pain score assessed (by phone) via a numeric pain scale completed 4 days after biopsy (D4). **<u>Secondary endpoints</u> :** - Pain score assessed using a numeric pain scale administered after to biopsy and during the consultation of results announcement (approximately D10). - Anxiety score assessed using a numeric anxiety scale administered after to biopsy, at 4 days (D4) and during the consultation of results announcement (approximately D10). - Esthetic impact score assessed using a numeric esthetic scale administered after to biopsy, at 4 days (D4) and during the consultation of results announcement (approximately D10). - Insomnia score assessed using the Index of Severity of Insomnia administered during the baseline visit and the consultation of results announcement (approximately D10). - Number of alerts that generated a phone call or number of phone calls generated directly by the patient and patient care accordingly. - Quantity, nature and dose of analgesics, anxiolytics, anti-depressants, anti-inflammatory and hypnotics used for the biopsy and its aftermath. - Adverse event in particular bleeding and infection due to biopsy recorded at 4 days (D4) and during the consultation of results announcement (about D10) by NCI-CTCAE 5.0 - Geographical distance from the reference center. - Number of tablets/4G keys made available to patients who do not benefit from them at home. - Number of positive responses to satisfaction questions related to the number of solicitations for the study and how interventions are communicated - Rate of completion questionnaire and numeric scale.
Benefit	Focusing on symptoms as patients experience them improves their empowerment and their adjustment to the disease. e-PRO prompt clinicians to intensify symptom management, to improve symptom control and to enhance patient-clinician communication patient satisfaction, as well as well-being. In addition, it is known that improved communication between patients and medical staff to less anxiety after a biopsy and that anxiety is related to pain. Taken as a whole, all these elements encourage to integrate e-health and e-PRO in the management of pain and anxiety in patients undergoing a biopsy. In case of significant pain, the gathered e-PRO will generate an alert and a reactive and responsive care. *In fine*, this research aims to improve the medical organization and management of post-biopsy patients by proposing an innovative connected patient technology, regardless of their remoteness from the hospital.

Eligibility criteria	**1) <u>Inclusion criteria</u>** - Patient with diagnostic breast biopsy at ICM - Age > 18 years - Informed patient and signed informed consent received - Affiliation to a social security system **2) <u>Non inclusion criteria</u>** - Patient without phone number - Patient with previous biopsy in 6 months prior to study - Pregnant and breastfeeding woman - Patient whose regular follow-up is initially impossible for psychological, family, social or geographical reasons - Patient under legal protection (guardianship, curatorship or safeguarding of justice)
Enrolment Procedure	After the patient has given her informed consent to participate in the study, and after verification of all inclusion/ non-inclusion criteria, the investigator will proceed to the patient registration via a dedicated form to be sent to the Biometrics Unit of the center.
Treatment modalities	After breast biopsy and randomization (random bloc method and ratio 1:1:1), patients will either be in the: - Experimental Group 1: PRO gathered via a phone consultation - Experimental Group 2: e-PRO self-completed via connected objects (tablet/phone) - Group 3: Control group without e-PROs (standard care) 

	At D1, D2 and D3, patients in the experimental group 1 will receive a call from a neuro-psychologist during which pain, anxiety and esthetical biopsy impact will be assessed using numeric or visual analog scales during a semi-direct interview. During this call, any adverse events related to the breast biopsy will also be noted, as well as the amount, nature and dose of analgesics, anxiolytics, anti-depressants, anti-inflammatory and hypnotics taken linked to the biopsy. If detected, pain or significative distress would be specifically managed. Patients in the experimental group 2 will be asked by SMS or notification to connect to the application in order to complete online the numeric and visual anog scales of pain, anxiety and esthetical impact. Any adverse events related to the breast biopsy will also be noted online, as well as the amount, nature and dose of analgesics, anxiolytics, anti-depressants, anti-inflammatory and hypnotics taken for the biopsy. If detected, pain or significative distress would be specifically managed. At D4 post biopsy, all patients (of the 3 groups) will receive a phone call from a neuro-psychologist to assess pain, anxiety and esthetical impact, using numeric scales, and to collect adverse events. If detected, pain or significative distress would be specifically managed. And at D10 (+/- 3 days), all patients will have the consultation of biopsy results announcement. This visit will be held either on-site or by videoconference At the beginning of this consultation, pain, anxiety and esthetical impact will be assessed using numeric scales. The adverse events related to the breast biopsy will be collected as well as the amount, nature and dose of analgesics, anxiolytics, anti-depressants, anti-inflammatory and hypnotics taken for the biopsy and its findings. Insomnia will be evaluated by the Insomnia Severity Index. If detected, pain or significative distress would be managed as usually in the center. If the consultation is to be done by telephone, it is essential that this data collection be done before the results are announced.
Statistical considerations	<u>Sample size.</u> A pilot study has been performed in the radiology department including 25 patients in order to determine the pain level on average: mean = 5 and standard deviation = 3. Assuming a mean pain score on day 4 equals to 5 points with a standard deviation equals to 3 in the control group, with α (two-sided) = 2.5%, power= 90%, it is necessary to include 58 patients per group (174 patients in total), to detect a difference of 2 points (according algology criteria and good practice recommendations) between control arm and each experimental arm. Finally, 192 patients will be included considering 10% non-evaluable patients. <u>Statistical analyses.</u> A statistical analysis plan (SAP) will be written before the closed database. All statistical analyses will be performed on ITT population and on PP (per-protocole) population for primary endpoint. All collected data will be described. Descriptive analyses will be performed using frequency (N) and percentage (%) for categorical variables, mean / standard deviation or median / range for continuous parameters.

	The Pearson's chi-square or the Fisher's exact test will be performed for categorical variables and the Student test or Wilcoxon / Kruskal-Wallis test for continuous parameters. The primary endpoint, pain score assessed by phone 4 days after biopsy, will be compared between control and experimental arms (telemedicine vs control and smartphone vs control). The secondary endpoints will be compared between control and experimental arms (telemedicine vs control and smartphone vs control) and between the two e-PRO interventions (telemedicine vs smartphone). All statistical analyses will be performed with the Stata software v16.0 and a statistical report will be provided according to the current model.
Study period	Starting date of inclusion: February 2021 Duration of inclusion: 34 months Duration of participation: 10 days (+/- 2 days) Date of end of patient follow-up: December 2023