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The Treatment of Anxious-Depressive Disorders among Breast Cancer Patients Integrating the EMDR Psychotherapy: From Pilot Study Results to the Development of a Randomized Trial

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Abstract

In recent years, the literature has shown the efficacy of EMDR with cancer patients in reactional disorders such as post-traumatic, depressive and anxious symptoms. However, those studies have several methodological limitations. This pilot study aims to test the feasibility and acceptability of the EMDR approach among female patients with invasive breast cancer, in order to adjust the intervention to the target population, to validate and adopt the standardized protocol before any large-scale randomized trials. Fifteen patients were included between December 2017 and May 2018 and were treated by EMDR therapists. Following the feedback from therapists, patients and the medical team, adaptations were made regarding the organization of the sessions, patient inclusion criteria, measured variables and EMDR standard protocol. With that design, the aim is to implement a trial starting from the reality of clinical practice with a rigorous methodology. The randomized trial is ongoing.

Keywords

Anxious-Depressive Disorders, Breast Cancer, EMDR Psychotherapy, Feasibility Pilot Study

1. Introduction

Breast cancer is, without doubt, the commonest type of cancer and the main cause of cancer mortality among women (DeSantis et al., 2017). Despite recent clinical and therapeutic improvements, breast cancer remains a life-changing experience for patients. It appears that those receiving a cancer diagnosis feel the same emotions as the victims of violent crimes or natural disasters (Cordova et al., 2007), and thus can experience post-traumatic symptoms (Mehnert & Koch, 2008). Although the diagnosis of PTSD (Post-Traumatic Stress Disorder) among cancer patients has been controversial since the classification of the DSM-V (Cordova et al., 2017), cancer patients suffer from cancer-related PTSD—from 7% to 14% of them according Abbey et al. (2015). In reaction to such a life-threatening medical condition, they experience high psychological distress, ranging between 29% and 59.3% (Gao et al., 2010; Zabora et al., 2001), and most are anxious and depressive symptoms. For instance, Hopwood et al. (2010) estimated a prevalence of anxiety disorders of 32.4% among breast cancer patients at the time of diagnosis and 30.8% six months after. Similarly, other studies have shown that anxiety is associated with deterioration in breast cancer patients' quality of life (Härtl et al., 2010).

Considering the symptomatology of cancer patients, psychotherapies such as Cognitive-Behavioural Therapy (CBT) and Eye Movement Desensitization and Reprocessing (EMDR) therapy-based interventions are associated with reduced post-traumatic symptoms (Dimitrov et al., 2019). More specifically to EMDR, which was initially intended to treat patients who have experienced traumatic events, that approach was later developed towards indications in the treatment of several psychopathological disorders such as anxious-depressive symptoms including with cancer patients (Capezzani et al., 2013; Pomeri et al., 2021). Carletto et al. (2019) have shown the efficacy of EMDR among cancer patients on anxious, post-traumatic or depressive symptoms using Shapiro's protocol (Shapiro, 2018) or EMDR specific protocol for oncological patients (Faretta & Borsato, 2016). Thus, considering cancer as an accumulation of pathogenic and traumatic events (Capezzani et al., 2013) that need to be dealt with, EMDR psychotherapy appears very useful to help patients to face illness.

Before any Randomized Controlled Trial (RCT) studying the efficacy of EMDR psychotherapy among breast cancer patients, a feasibility pilot study was necessary. The aim of this first French pilot study was to test the feasibility and acceptability of the EMDR approach among female patients with invasive breast cancer, in order to adjust the intervention to the target population, to adapt and validate the standardized protocol, to explore its acceptability and finally, to test its feasibility before any large-scale RCT. This article presents the results from this pilot study and the adjustments made to the design of the randomized trial implemented thereafter.

2. The Pilot Study

Materials and methods of the pilot study

The PSYCANCER-EMDR pilot study was a mixed-method interventional study, in which patients agreeing to participate underwent EMDR treatment. Questionnaires were administered to the patients and qualitative interviews were carried out with volunteering psychotherapists and patients at the end of their treatment.

Sample

Recruitment took place over a 6-month period during consultations in the oncology unit of the regional hospital.

All patients meeting the inclusion criteria were invited by the investigating oncologists to take part in the study before the start of adjuvant treatment. The inclusion criteria verified by the oncologist were: 1) being a woman aged 18 years or over; 2) having primary breast cancer, without relapse, and having undergone breast surgery for the primary invasive breast cancer; 3) not having started adjuvant treatment following surgery; 4) not having physical poly-pathologies; and 5) being able to complete self-administered questionnaires.

After inclusion by an oncologist, patients were seen by an inclusion psychologist within the next two weeks. The psychologist aims to confirm inclusion after checking different psychological inclusion criteria: 1) not having any contraindications for EMDR psychotherapy (neurological disorders, dissociative states, oculomotor problems); and 2) not having any history of psychiatric disorder (including anxious-depressive disorders). The psychiatric history evaluation was conducted using the MINI (Sheehan et al., 1998).

Intervention

The 8-phase EMDR protocol was guided by Shapiro's Adaptive Information Processing (AIP) model (Shapiro, 2018) (see **Table 1**). This model is based on the idea of a system of information processing that assimilates and integrates various aspects of an experience (somatic, sensory, cognitive, behavioral and emotional). In highly stressful conditions such as traumatic events, that system seems to be destabilized, thus hampering the integration of experiences into the subject's autobiographical memory: initial perceptions are therefore stored in their initial form with distortions triggered by a high level of stress. EMDR could enable the retrieval of those "frozen" memories and the stimulation of adaptive information reprocessing, so that appropriate connexions and associations are re-established.

EMDR sessions were carried out by 5 psychotherapists trained to use EMDR psychotherapy. Therapists were asked to practice according to the standard protocol (Shapiro, 2018) as they usually do. The patients had 8 weekly sessions: two sessions to establish individual histories and 6 EMDR sessions (Visit 1 (V1) to Visit 8 (V8)). An initial session for the validation of the patients' psychological inclusion criteria (V0) was carried out in the place of treatment (regional hospital) by the inclusion psychologist, and the other sessions (V1 to V8) took place at the psychotherapists' premises. This venue for psychotherapeutic treatment was beneficial to the patients: they could be treated closer to their homes, thus avoiding extra tiredness linked to commuting.

Table 1. Overview of the eight-phase eye movement desensitization and reprocessing (EMDR) therapy (Shapiro, 2012).

Phase	Purpose	Procedure
Medical history collection	Obtain background information; Identify suitability for EMDR treatment; Identify reprocessing targets from events in the patient's life according to standardized three-pronged protocol	Standard medical history-questionnaires and diagnostic psychometrics; Review of selection criteria; Questions and techniques to identify : 1) past events that have laid the foundations for the pathology; 2) current triggers; and 3) future needs
Preparation	Prepare suitable patients for EMDR reprocessing of targets	Education based on the symptom profile; Metaphors and techniques to foster stabilization and a sense of personal control
Assessment	Access the target for EMDR reprocessing by stimulating primary aspects of the memory	Elicit body image, negative beliefs currently held, desired positive belief, current emotions, physical sensations and baseline measures
Desensitization	Reprocess experiences toward an adaptive resolution (no distress)	Standardized protocols incorporating eye movements (taps or tones) that allow the spontaneous emergence of insights, emotions, physical sensations, and other memories
Installation	Improve connections to positive cognitive networks	Enhance the validity of the desired positive belief and fully integrate the positive effects within the memory network
Body scan	Complete reprocessing of any residual disturbance associated with the target	Concentration on and reprocessing of any residual physical sensation
Closure	Ensure patient stability on completion of an EMDR session and between sessions	Use of guided imagery or self-control techniques if needed; Briefing on expectations and behavioral reports between sessions
Reassessment	Ensure maintenance of therapeutic outcomes and patient stability	Evaluation of treatment effects; Evaluation of integration within broader social system

Data collected

Medical data (type of surgery and axillary node dissection, stage, adjuvant treatments planned, complementary treatments (pain treatments, psychotropic drugs, etc.) and patient socio-demographic data (age, marital status, family situation, educational level and professional status) was collected at the beginning and the end of the study.

At each psychotherapy session, the psychotherapists collected data on the presence of pain, sleeping problems, treatments, lifestyle habits such as physical activity or the presence of a home help, and difficulties encountered during the sessions. Questionnaires were completed by the patients at the psychologist's inclusion time and during the 3rd (V5) and 6th (V8) EMDR sessions.

The questionnaires used were:

- The STAI (State-Trait Anxiety Inventory) STAI Y-A, developed by Spielberger et al. (1993), measuring "state" anxiety, defined as a transitory emotional condition. Patients are invited via 20 items to express what they feel at the present moment (state) on a 4-point Likert scale, 1 meaning the lowest level of anxiety. Scores fall into 5 categories: over 65 (very high), from 56 to 65 (high),

from 46 to 55 (average), 36 to 45 (low), and below 35 (very low).

- The PCLS (Post-traumatic stress disorder Checklist Scale) developed in 1993 by a team from the National Center for Post-Traumatic Stress Disorder, was translated into French by Yao et al. (2003). It is a relatively short, self-administered scale that evaluates the 17 symptoms of a state of post-traumatic stress included in the DSM-IV. Although in its new version the DSM-V includes criteria for post-traumatic stress disorder, this scale uses the diagnostic criteria for post-traumatic stress used in the DSM-IV. The present study therefore retained the DSM-IV criteria. The 17 items in the PCLS are assessed on a 1 - 5 scale (1 = not at all, 2 = a little, 3 = sometimes, 4 = often, 5 = very often). The items can be grouped into 3 sub-scales corresponding to the 3 main syndromes of PTSD, reexperiencing (items 1 to 5), avoidance (items 6 to 12), and neuro-vegetative hyperactivity (items 13 to 17). A score over 50 is considered as a very strong indication of the presence of PTSD (McFall et al., 1990).
- The QLQ-C30 (Quality of Life Questionnaire-Core 30) from the EORTC (European Organization for Research and Treatment of Cancer) version 3 was developed by Aaronson et al. (1993). It comprises 30 items and is intended for cancer patients, whatever the localization. Patients answer the questions by circling the number from 1 ("not at all") to 4 ("a lot") that best corresponds to their situation at the time of questionnaire administration. It provides 15 scores, derived from the 5 functional domains (physical, daily activities, cognitive functions, emotional and social well-being), 3 symptom domains (fatigue, pain, nausea and vomiting), and one domain covering general health and quality-of-life. It also contains single items focusing on different symptoms or problems. The QLQ-C30 comes with its breast cancer module, the QLQ-BR23. It comprises 23 items enabling the evaluation of breast cancer symptoms and adverse reactions to treatment. It explores 8 different dimensions (4 functional dimensions: body image, sexual functioning, sexual enjoyment, future perspectives, and 4 symptom dimensions: systemic therapy side effects, arm symptoms, breast symptoms and upset by hair loss). All the scores dimensions and single item scores are converted to linear scores from 0 to 100. A high score on the functional dimensions means a good functioning level and a high score for the general health and quality-of-life domain means good quality of life, whereas a high score on the symptom dimensions reflects a high level of symptoms.
- The Centre for Epidemiologic Studies-Depression (CES-D) questionnaire in its short 10-item version, developed in English by Andresen et al. (1994), was used to assess depressive symptoms. Each item is coded on a scale from 0 to 3. The score ranges from 0 to 30 and is calculated by adding an item scores. A high score means a high level of depressive symptoms. Based on previous research, a score of 10 or more identifies patients with a high risk of significant depressive symptoms.

Feedback from the EMDR psychotherapists was collected from individual interviews. They were performed by a postgraduate Master's degree student in psychology, working on the adjustment of the EMDR protocol to cancer patients for implementation in the RCT following this study.

In addition, phone calls were made to patients to collect their feedback on care and levels of satisfaction.

Analyses

Clinical and socio-demographic variables and data derived from the questionnaires were described. To explore patient participation and adherence to the intervention, several indicators were studied: the percentage of patients agreeing to take part in the study; the percentage of patients actually taking part; the average number of sessions attended per patient; the number of patients who discontinued the study/were lost to follow-up; the patient satisfaction data collected by phone one month after the last session.

Clinical and socio-demographic variables and data from the questionnaires were also described.

To ensure the suitability of the intervention to the field, adherence among medical teams and feedback from the EMDR psychotherapists were examined.

3. Results from the Pilot Study

Sample description and study of patient participation and adherence

The pilot study was offered to 26 patients at regional hospital in eastern France between December 2017 and May 2008. 15 patients were included and followed by an EMDR psychotherapist from the study. Among non-included patients, 77% refused to participate because they were living too far from the psychotherapist's office.

The included patients were 57.8 years old on average (range 37 to 76 years). 80% of them had a partner, 40% were working, 60% had an educational level corresponding to the French *Baccalauréat* (high school diploma). Half of them stated they did regular physical exercise such as walking.

All the patients underwent total mastectomy. 3 patients underwent axillary node dissection and 11 patients were offered the sentinel lymph node technique, associated with axillary node dissection for 4. 67% of patients had stage II breast cancer. 73% received adjuvant chemotherapy followed by radiotherapy.

Among the 15 patients, 2 left the study just after their inclusion because they no longer wished to take part.

The patients who were followed attended an average of 6.3 sessions (range 3 to 8) out of the 8 planned. Six patients completed all sessions. Three patients left the study after the 2 sessions on medical history, which the psychotherapists thought resulted from a poor selection policy, as certain patients did not present clear signs of depression or anxiety or any particular difficulties concerning the illness. The analysis of the questionnaires at inclusion (**Table 2**) showed that 20% of the patients had a low anxiety score (<45), 47% of patients had a CES-D

Table 2. Description of questionnaires scores.

	Inclusion (n = 15)		T1 (n = 9)		T2 (n = 7)		T3 (n = 3)	
	Moy	ET	Moy	ET	Moy	ET	Moy	ET
Anxiety score STAI Y A	49.0	5.2	46.4	4	46.6	4.3	44.7	2.9
Depression score CES-D	9.9	4.7	10.7	5	7.4	5.3	9.3	2.1
Health and QoL on QLQ-C30	64.8	20.3	61.1	17.5	70.4	20.5	81	8.7
PCLS score	36	12.1	37	10.9	28	10.2	26	8.7
Reexperiencing	10.6	4	10.7	3.9	7	6.3	6.3	1.2
Avoidance	14	5.9	15	5.1	13	5.4	10	3.2
Dysautonomia	11.2	3.7	11.1	3.1	8.9	2.3	9.3	4.9

depression score under 10, *i.e.*, low risk of presenting depressive symptoms, and 87% had a low score for PTSD (PCLS score < 50).

Study of the appropriateness of the intervention to the field

Feedback from the medical team on patient inclusion highlighted difficulties in including patients during their post-surgery consultation, just before the start of adjuvant treatment because it entailed very few visits. In addition, certain patients refused to take part in the study because the psychotherapist's private office was too far from their home.

The interviews conducted at the end of the pilot study with the psychotherapists enabled a few relevant points to be highlighted, such as too many EMDR sessions programmed and a too short time-lapse between EMDR sessions (weekly). Therapists indicated difficulties to focus on past targets with their patients as they usually do in their own practice according to the standard protocol. Consequently, they were asked to focus now on more recent targets, in recent past or in present, specifically to cancer history (diagnosis announce, surgery…) as some authors have already proposed (Faretta & Borsato, 2016). After reaching that objective, patient's other possible difficulties are assessed to identify further potential targets to improve the patient's experience, thoughts and behaviors towards the illness.

In their feedback, patients reported that psychotherapy had been useful in their experience of cancer and in their daily lives. They considered that the sessions were too close to one another and often too close to chemotherapy sessions, which led to difficulties.

4. Development of the RCT

The main objective of the PSYCANCER-EMDR RCT is to assess and compare anxiety among women treated for invasive breast cancer receiving EMDR psychotherapy, and anxiety among women receiving supportive psychotherapy.

Materials and Methods of the RCT

The study is a two-arm, interventional, open, RCT: a control group where pa-

tients receive standard supportive psychotherapy, and an intervention group where patients receive EMDR psychotherapy. Inclusion has been underway since December 2018 in the oncology unit of regional hospital and is set to run 48 months; inclusion started in September 2019 at the regional oncology institute.

Sample

Results from the pilot study enabled 2 inclusion criteria to be added: a psychological criterion following feedback from the psychotherapists—"presenting a minimum level of state anxiety (STAI Y-A inclusion score > 35)", and a medical criterion—"Having primary breast cancer that is currently being treated, is about to start treatment, or has completed treatment within the last 6 months", following feedback from the oncologists.

Interventions

The oncologists are in charge of assessing the medical criteria, and the inclusion psychologist validates the psychological criteria within the following two weeks and randomizes the patients at the end of the randomization session into one of the 2 groups, referring them to the psychotherapist specific to their group and whose office is the closest to the patient's home. The number of participating psychotherapists has been increased, as the RCT involves larger numbers of patients. Following feedback from the medical team, particular attention is given to the geographical localization of the offices. Indeed, therapists from each group cover the whole regional territory (8 psychotherapists in the EMDR group and 9 in the support group) for patients included in the regional hospital, and for Meurthe et Moselle (5 psychotherapists in the EMDR group and 7 in supportive psychotherapy) for patients included in the regional oncology institute (*Lorraine Oncology Institute*). For patients with travel difficulties (severe fatigue or mobility problems), psychotherapists could go to their homes. In EMDR group, therapists have several years of experience with EMDR and have committed to respect Shapiro's (2018) standard protocol. Regular meetings and initial training days in each group are organized in order to harmonize clinical practices. If necessary, a supervisor in each group can be called in.

All the patients undergo 7 sessions irrespective of their group. The sessions take place every two weeks, rather than weekly as in the pilot study. This alteration was made following feedback from psychotherapists and patients.

The patients randomized to the control group receive support psychotherapy. That widely implemented approach supports and helps the patient without any deep psychotherapeutic action (Douglas, 2008) with active listening and advices.

The patients randomized to the EMDR group follow two sessions to establish their history followed by 5 EMDR sessions rather than 6, given psychotherapists feedbacks.

Finally, to assess the efficacy of EMDR psychotherapy in the longer term, two follow-up sessions including questionnaires are organized at 3 and 6 months after the last psychotherapy session.

Data collected

The medical and socio-demographic data collected is similar to that for the pilot study. Only one open-question has been added for EMDR group: therapists have to precise desensitization length and describe briefly the different EMDR targets. That addition allows a more detailed view of the standard protocol.

Concerning the questionnaires administered, the PCLS questionnaire has been replaced by the Post-Traumatic Growth Inventory developed by Tedeschi & Calhoun (1996) and adapted into French in 2015 by Cadell et al. (2015). In the pilot study, poor results were obtained with the PCLS. It seems that traumatic symptomatology in cancer patients takes on a particular form, evolving with the illness (diagnosis, stages of the illness, treatments, prognosis, etc.) (Borio & Torta, 2007). Furthermore, somewhat surprisingly, some studies have shown that a high percentage of cancer survivors reports positive changes after cancer treatment (Jansen et al., 2011) resulting from coping with extremely difficult life conditions (Tedeschi & Calhoun, 2004). For instance, Szpringer et al. (2018) have shown a significant improvement of the sense of coherence (defines as the sense of the quality and meaningfulness of life) after EMDR treatment among 18 patients with brain cancer compared to 19 patients control group where it decreases. That positive reshaping of the cancer experience can been described by the concept of Post-Traumatic Growth (PTG) (Tedeschi & Calhoun, 1996). With desensitization and reprocessing negative cognitions and emotions, the effect of EMDR treatment could potentiate a transformation of the relationship of patients with the world, rather than only reducing symptoms. PTG is an indicator of that resource, which should be activated by EMDR therapy.

The PTGI questionnaire comprises 21 items and 6 response options on a Likert scale ranging from (0) "I have not felt this change following the critical incident" to (5) "I have felt this change very strongly following the critical incident". In the case of the present study, the phrase "critical incident" has been replaced by "following the announcement of my cancer". The 21 items in the scale are divided into 5 sub-dimensions: "new possibilities", "relationships with others", "personal strengths", "enjoyment of life" and "spiritual changes". The sum of the 21 items gives a score ranging from 0 to 105. For the global score and the sub-dimension scores, the higher the score, the more positive change the patient feels.

Finally, one of the consequences of post-traumatic development is optimism, characterized by a general tendency to expect positive results (Carver & Scheier, 2014), which is important to integrate into the assessment of positive adaptation following the occurrence of breast cancer. The Life-Orientation Test-Revised (LOT-R) questionnaire developed by Scheier, Carver, & Bridges (1994), adapted into French in 2008 by Trottier et al. (2008) has therefore been added. It comprises ten items and five response choices on a Likert scale, ranging from (0) "Totally disagree" to (4) "Totally agree". The scores range from 0 to 24, and the higher the score, the greater the optimism exhibited by the patient.

All the self-administered questionnaires (STAI Y-A, LOT-R, QLQ-C30, followed

by QLQ-BR23, PTGI and CES-D) are administered 5 times: during inclusion validation by the psychologist (V0), during the 3rd (V5) and 5th sessions (V7), and 3 and 6 months after the sessions by post.

Analyses

Number of subjects required

The number of subjects required was calculated to validate the hypothesis of a decrease in the mean score for STAI state anxiety of about 5 points in favour of the EMDR group after 6 EMDR psychotherapy sessions. This difference is clinically relevant according to results from a study by Tarquinio et al. (2012) comparing EMDR to another, eclectic, post-treatment care regimen (after 6 psychotherapy sessions) among women having undergone domestic violence. With a *p*-value fixed at 0.05 (bilateral), 90% power and a standard deviation of 10, a minimum of 86 patients per intervention group is required, *i.e.*, 172 patients to detect any score difference of at least 5 points between the 2 groups (EMDR psychotherapy and supportive psychotherapy). However, to compensate an estimated ineligibility or lost-to-follow-up rate of 10%, 95 patients will be included per psychotherapy group (EMDR vs. supportive), *i.e.*, a total of 190 patients.

Statistical analyses

Main judgement criterion

A longitudinal analysis of the STAI Y-A scores will be carried out using a mixed-effect linear model, with random effect on patient and time, taking the measures into account.

A univariate analysis will be conducted first, introducing a treatment arm effect (supportive vs. EMDR psychotherapy). All the clinical and socio-demographic data collected at inclusion will also be tested in univariate analysis to identify potential predictive factors for better response to EMDR psychotherapy. All the variables with a $p \leq 0.20$ will be introduced into a multivariate model. The treatment arm will be forced into the multivariate analysis and the "psychotherapist" effect will also be measured and integrated into the model.

Secondary judgement criteria

A longitudinal analysis of each score for quality-of-life (QLQ-C30 and BR23), depression (CES-D), optimism (LOT-R) and post-traumatic growth (any positive psychological changes occurring after a traumatic event, measured by the PTGI) will be carried out using a mixed-effect linear model, with random effect on patient and time, taking the measurements into account.

5. Discussion

This pilot study has enabled the feasibility of the EMDR psychotherapy to be tested on female patients with breast cancer and currently undergoing treatment, with a view to adjusting the logistics and the resources required for a larger-scale RCT. Inclusion for the RCT has been ongoing since the end of 2018. This trial has several hypotheses: a substantial decrease in anxiety and depression scores is expected following EMDR compared to standard psychotherapeutic treatment; improvements in quality-of-life, in perceptions of positive change following trau-

ma (post-traumatic growth) and in optimism within this group are expected; finally, results should be observed after the first sessions and maintained over 3 and 6 months after the end of the sessions.

In our study, we only chose to include female patients with breast cancer because it is the most common cancer in women in France. Breast cancer accounts for one-third of all new cancer cases in women and is the leading cause of cancer deaths in women. Of course, even if they are in the minority, male patients with breast cancer could be included in future research. However, it should be noted that breast cancer in men doesn't involve the same upset as in women in terms of identity, particularly because it affects their femininity.

The pilot study results highlight the required adaptation of Shapiro's standard protocol for cancer patients, and more particularly for patients with breast cancer currently undergoing adjuvant treatment, focusing on recent past and present EMDR targets related to cancer history, as some authors had already proposed that clinical strategy (Faretta & Borsato, 2016). In the field of EMDR, a lot of specific protocols had been developed for different populations or psychopathological disorders, modifying some aspects of the protocol including the choice of the targets. But considering those adaptations—certainly very important from a clinical point of view—as specific protocols without rigorous methodological validation can be the subject of controversy because actually, it is still EMDR (Rydberg, 2017, 2019). Shapiro F. herself proposed in the EMDR training manual to adapt our target plan according to patients' needs (Shapiro, 2012). The objective was to build a pilot study with clinical practice as a starting point. Then, we aim to evaluate these practice-based elements with the strongest methodology, as proposed by the randomized controlled trial. With the RCT, we hope to define precise guidelines for EMDR therapists working with cancer patients.

The psychotherapeutic setting of cancer patients is much more complicated than simple PTSD patients. Cancer can be considered as a succession of psychotraumatisms from the announcement of the disease to its remission. While the determination of EMDR targets is more complex and may refer to life history or difficult moments that the disease reactivates, it is common to see that patients are still strongly mobilized to fight against the disease and often put aside their fear and anxiety. But it is not uncommon that cancer patients are able to find internal resources and transcend themselves, becoming stronger than they ever were. So, it is difficult to do an appropriate research design because of those clinical features.

Cancer is an illness that is rarely defined in time, it upsets the patient on at least three levels: in terms of temporality, identity, and changes in values. EMDR psychotherapy appears to be a relevant clinical approach not only as a therapeutic technique for the treatment of reactional symptoms (depressive, anxious, post-traumatic, etc.), but also for the new psychopathological paradigm it proposes. Indeed, recent studies have shown the association between Adverse Childhood Experiences (ACEs) and health, including the development of cancer (Alcalá et al., 2017; Hughes et al., 2017). The efficacy of EMDR on psychological and physi-

ological symptoms stemming from ACEs has already been studied, among others by Francine Shapiro herself (Shapiro, 2014). EMDR can repair the fractures in terms of identity and temporality. The EMDR therapist can work on optimistic projections, remobilize the individual in his or her daily life and give hope to get out of the unbearable powerlessness imposed by cancer. Moreover, the idea is to make the patient grow from this ordeal (post-traumatic growth) which allows them to access a new understanding of their world and of themselves, in an ultimately spiritual and deeply resilient dynamic. Here are probably the most important implications for all clinicians working with cancer patients.

With our design, the aim was to propose a stronger methodological framework that is often highlighted as lacking in the scientific literature with very interesting research but with several methodological limits such as high-risk bias or no calculation of sample size (Pomeri et al., 2021). To our knowledge, only two RCT studied EMDR and cancer (Borji et al., 2019; Capezzani et al., 2013), one non-randomized controlled trial studied EMDR among patients with glioblastoma multiforme (brain cancer) (Szpringer et al., 2018). No one is specifically to breast cancer. Our pilot study has provided many answers that have enlightened clinicians and researchers, thus allowing the development of a research programme that is more in line with the situation of cancer patients. And so on, the interest was to conduct a larger RCT in order to have a high level of prediction of the effectiveness of EMDR therapy in oncology. In that way, the PSYCANCER-EMDR study aims to keep the rigorous methodology of the RCT but in relation to daily clinical reality.

To conclude, the PSYCANCER-EMDR study aims: to open perspectives for psychological care of cancer patients with EMDR therapy, regarding specifically psycho-traumatic impact; to cater for anxious-depressive disorders more promptly; and to enable a positive reshaping of the cancer experience to help patients adapt to their illness.

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Ethical Approval Statement

This research was registered on the French national drug safety agency website: 2017-A00119-44 and received approval from the Paris-1 Committee for individual privacy on 20/06/2017. The pilot study was registered on the ClinicalTrials.gov website (https://clinicaltrials.gov/ct2/show/NCT03271476) as well as the RCT (https://clinicaltrials.gov/ct2/show/NCT03898453).

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Data Availability Statement

The quantitative data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

All authors have no conflicts of interest to declare.

References

Aaronson, N. K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N. J., Filiberti, A., Flechtner, H., Fleishman, S. B., & de Haes, J. C. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: A Quality-of-Life Instrument for Use in International Clinical Trials in Oncology. *Journal of the National Cancer Institute, 85,* 365-376. https://doi.org/10.1093/jnci/85.5.365

Abbey, G., Thompson, S. B. N., Hickish, T., & Heathcote, D. (2015). A Meta-Analysis of Prevalence Rates and Moderating Factors for Cancer-Related Post-Traumatic Stress Disorder. *Psycho-Oncology, 24,* 371-381. https://doi.org/10.1002/pon.3654

Alcalá, H. E., Tomiyama, A. J., & von Ehrenstein, O. S. (2017). Gender Differences in the Association between Adverse Childhood Experiences and Cancer. *Women's Health Issues: Official Publication of the Jacobs Institute of Women's Health, 27,* 625-631. https://doi.org/10.1016/j.whi.2017.06.002

Andresen, E. M., Malmgren, J. A., Carter, W. B., & Patrick, D. L. (1994). Screening for Depression in Well Older Adults: Evaluation of a Short Form of the CES-D (Center for Epidemiologic Studies Depression Scale). *American Journal of Preventive Medicine, 10,* 77-84. https://doi.org/10.1016/S0749-3797(18)30622-6

Borio, R., & Torta, R. (2007). I disturbi psichici in oncologia. In R. Torta, & A. Mussa (Éds.), *Psiconcologia* (pp. 58-62). Centro Scientifico Editore.

Borji, M., Tarjoman, A., Abdi, A., & Otaghi, M. (2019). Efficacy of Implementing Home Care Using Eye Movement Desensitization and Reprocessing in Reducing Stress of Patients with Gastrointestinal Cancer. *Asian Pacific Journal of Cancer Prevention, 20,* 1967-1971. https://doi.org/10.31557/APJCP.2019.20.7.1967

Cadell, S., Suarez, E., & Hemsworth, D. (2015). Reliability and Validity of a French Version of the Posttraumatic Growth Inventory. *Open Journal of Medical Psychology, 4,* 53. https://doi.org/10.4236/ojmp.2015.42006

Capezzani, L., Ostacoli, L., Cavallo, M., Carletto, S., Fernandez, I., Solomon, R., Pagani, M., & Cantelmi, T. (2013). EMDR and CBT for Cancer Patients: Comparative Study of Effects on PTSD, Anxiety, and Depression. *Journal of EMDR Practice and Research, 7,* 134-143. https://doi.org/10.1891/1933-3196.7.3.134

Carletto, S., Porcaro, C., Settanta, C., Vizzari, V., Stanizzo, M. R., Oliva, F., Torta, R., Fernandez, I., Moja, M. C., Pagani, M., & Ostacoli, L. (2019). Neurobiological Features and Response to Eye Movement Desensitization and Reprocessing Treatment of Posttraumatic Stress Disorder in Patients with Breast Cancer. *European Journal of Psychotraumatology, 10,* Article ID: 1600832. https://doi.org/10.1080/20008198.2019.1600832

Carver, C. S., & Scheier, M. F. (2014). Dispositional Optimism. *Trends in Cognitive Sciences, 18,* 293-299. https://doi.org/10.1016/j.tics.2014.02.003

Cordova, M. J., Giese-Davis, J., Golant, M., Kronenwetter, C., Chang, V., & Spiegel, D. (2007). Breast Cancer as Trauma: Posttraumatic Stress and Posttraumatic Growth. *Journal of Clinical Psychology in Medical Settings, 14,* 308-319.

https://doi.org/10.1007/s10880-007-9083-6

Cordova, M. J., Riba, M. B., & Spiegel, D. (2017). Post-Traumatic Stress Disorder and Cancer. *The Lancet Psychiatry, 4,* 330-338. https://doi.org/10.1016/S2215-0366(17)30014-7

DeSantis, C. E., Ma, J., Sauer, A. G., Newman, L. A., & Jemal, A. (2017). Breast Cancer Statistics, 2017, Racial Disparity in Mortality by State. *CA: A Cancer Journal for Clinicians, 67,* 439-448. https://doi.org/10.3322/caac.21412

Dimitrov, L., Moschopoulou, E., & Korszun, A. (2019). Interventions for the Treatment of Cancer-Related Traumatic Stress Symptoms: A Systematic Review of the Literature. *Psycho-Oncology, 28,* 970-979. https://doi.org/10.1002/pon.5055

Douglas, C. J. (2008). Teaching Supportive Psychotherapy to Psychiatric Residents. *The American Journal of Psychiatry, 165,* 445-452. https://doi.org/10.1176/appi.ajp.2007.07121907

Faretta, E., & Borsato, T. (2016). EMDR Therapy Protocol for Oncological Patients. *Journal of EMDR Practice and Research, 10,* 162-175. https://doi.org/10.1891/1933-3196.10.3.162

Gao, W., Bennett, M. I., Stark, D., Murray, S., & Higginson, I. J. (2010). Psychological Distress in Cancer from Survivorship to End of Life Care: Prevalence, Associated Factors and Clinical Implications. *European Journal of Cancer (Oxford, England: 1990), 46,* 2036-2044. https://doi.org/10.1016/j.ejca.2010.03.033

Härtl, K., Engel, J., Herschbach, P., Reinecker, H., Sommer, H., & Friese, K. (2010). Personality Traits and Psychosocial Stress: Quality of Life over 2 Years Following Breast Cancer Diagnosis and Psychological Impact Factors. *Psycho-Oncology, 19,* 160-169. https://doi.org/10.1002/pon.1536

Hopwood, P., Sumo, G., Mills, J., Haviland, J., Bliss, J. M., & START Trials Management Group (2010). The Course of Anxiety and Depression over 5 Years of Follow-Up and Risk Factors in Women with Early Breast Cancer: Results from the UK Standardisation of Radiotherapy Trials (START). *Breast (Edinburgh, Scotland), 19,* 84-91. https://doi.org/10.1016/j.breast.2009.11.007

Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., Jones, L., & Dunne, M. P. (2017). The Effect of Multiple Adverse Childhood Experiences on Health: A Systematic Review and Meta-Analysis. *The Lancet Public Health, 2,* e356-e366. https://doi.org/10.1016/S2468-2667(17)30118-4

Jansen, L., Hoffmeister, M., Chang-Claude, J., Brenner, H., & Arndt, V. (2011). Benefit Finding and Post-Traumatic Growth in Long-Term Colorectal Cancer Survivors: Prevalence, Determinants, and Associations with Quality of Life. *British Journal of Cancer, 105,* 1158-1165. https://doi.org/10.1038/bjc.2011.335

McFall, M. E., Smith, D. E., Mackay, P. W., & Tarver, D. J. (1990). Reliability and Validity of Mississippi Scale for Combat-Related Posttraumatic Stress Disorder. *Psychological Assessment, 2,* 114-121. https://doi.org/10.1037/1040-3590.2.2.114

Mehnert, A., & Koch, U. (2008). Psychological Comorbidity and Health-Related Quality of Life and Its Association with Awareness, Utilization, and Need for Psychosocial Support in a Cancer Register-Based Sample of Long-Term Breast Cancer Survivors. *Journal of Psychosomatic Research, 64,* 383-391. https://doi.org/10.1016/j.jpsychores.2007.12.005

Pomeri, A. P., La Salvia, A., Carletto, S., Oliva, F., & Ostacoli, L. (2021). EMDR in Cancer Patients: A Systematic Review. *Frontiers in Psychology, 11,* Article ID: 590204. https://doi.org/10.3389/fpsyg.2020.590204

Rydberg, J. A. (2017). Protocoles EMDR spécialisés. In C. Tarquinio, M.-J. Brennstuhl, H. Dellucci, M. Iracane-Blanco, J. A. Rydberg, M. Silvestre, & E. Zimmermann (Éds.), *Pratique de la psychothérapie EMDR: Introduction et approfondissements pratiques et psycho-*

pathologiques (p. 117-127). Dunod. https://doi.org/10.3917/dunod.tarqu.2017.01.0117

Rydberg, J. A. (2019). Protocoles EMDR spécialisés. In C. Tarquinio, M.-J. Brennstuhl, H. Dellucci, M. Iracane-Blanco, J. A. Rydberg, M. Silvestre, P. Tarquinio, & E. Zimmermann (Éds.), *Aide-mémoire de l'EMDR en 46 fiches* (p. 119-132). Dunod. https://doi.org/10.3917/dunod.tarqu.2019.01.0119

Scheier, M. F., Carver, C. S., & Bridges, M. W. (1994). Distinguishing Optimism from Neuroticism (and Trait Anxiety, Self-Mastery, and Self-Esteem): A Reevaluation of the Life Orientation Test. *Journal of Personality and Social Psychology, 67,* 1063-1078. https://doi.org/10.1037/0022-3514.67.6.1063

Shapiro, F. (2012). *EMDR Therapy Training Manual*. EMDR Institute.

Shapiro, F. (2014). The Role of Eye Movement Desensitization and Reprocessing (EMDR) Therapy in Medicine: Addressing the Psychological and Physical Symptoms Stemming from Adverse Life Experience. *The Permanente Journal, 18,* 71-77. https://doi.org/10.7812/TPP/13-098

Shapiro, F. (2018). *Eye Movement Desensitization and Reprocessing (EMDR) Therapy, Third Edition: Basic Principles, Protocols, and Procedures*. Guilford Press.

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., & Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): The Development and Validation of a Structured Diagnostic Psychiatric Interview for DSM-IV and ICD-10. *The Journal of Clinical Psychiatry, 59,* 22-33. https://doi.org/10.1037/t18597-000

Spielberger, C. D., Bruchon-Schweitzer, M., & Paulhan, I. (1993). *STAI-Y: Inventaire d'anxiété état-trait forme Y*. Éditions du centre de psychologie appliquée, DL 1993.

Szpringer, M., Oledzka, M., & Amann, B. L. (2018). A Non-Randomized Controlled Trial of EMDR on Affective Symptoms in Patients with Glioblastoma Multiforme. *Frontiers in Psychology, 9,* Article No. 785. https://doi.org/10.3389/fpsyg.2018.00785

Tarquinio, C., Brennstuhl, M.-J., Rydberg, J. A., Schmitt, A., Mouda, F., Lourel, M., & Tarquinio, P. (2012). Eye Movement Desensitization and Reprocessing (EMDR) Therapy in the Treatment of Victims of Domestic Violence: A Pilot Study. *European Review of Applied Psychology, 62,* 205-212. https://doi.org/10.1016/j.erap.2012.08.006

Tedeschi, R. G., & Calhoun, L. G. (1996). The Posttraumatic Growth Inventory: Measuring the Positive Legacy of Trauma. *Journal of Traumatic Stress, 9,* 455-471. https://doi.org/10.1002/jts.2490090305

Tedeschi, R. G., & Calhoun, L. G. (2004). Posttraumatic Growth: Conceptual Foundations and Empirical Evidence. *Psychological Inquiry, 15,* 1-18. https://doi.org/10.1207/s15327965pli1501_01

Trottier, C., Mageau, G., Trudel, P., & Halliwell, W. R. (2008). Validation de la version canadienne-française du Life Orientation Test-Revised. *Canadian Journal of Behavioural Science/Revue Canadienne Des Sciences Du Comportement, 40,* 238-243. https://doi.org/10.1037/a0013244

Yao, S.-N., Cottraux, J., Note, I., De Mey-Guillard, C., Mollard, E., & Ventureyra, V. (2003). Evaluation of Post-Traumatic Stress Disorder: Validation of a Measure, the PCLS. *L'Encephale, 29,* 232-238.

Zabora, J., BrintzenhofeSzoc, K., Curbow, B., Hooker, C., & Piantadosi, S. (2001). The Prevalence of Psychological Distress by Cancer Site. *Psycho-Oncology, 10,* 19-28. https://doi.org/10.1002/1099-1611(200101/02)10:1<19::AID-PON501>3.0.CO;2-6