

Article

Using Virtual Reality During Chemotherapy to Support Emotional Regulation in Patients: Adding an Olfactory Reinforcement or Not?

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Abstract: Introduction: In line with previous research conducted during chemotherapy to explore whether virtual reality (VR) can support patients' emotional regulation, this study examines the relevance of adding olfactory reinforcement to VR sessions during breast cancer treatment. Methods: An experimental protocol assessed the impact of VR sensoriality in 50 patients over three chemotherapy sessions. Each patient experienced a 10-min immersion in a natural environment under three randomized conditions: Contemplative VR, Participatory VR, Participatory VR with olfactory reinforcement. The sense of presence measured immersion, while anxiety, depression, and emotional state were evaluated using a within-subject design to compare the effects of each VR modality. Results: A reduction in anxiety and depression was observed in patients regardless of the type of VR immersion experienced. The interactive and multimodal nature of VR may support patients in their emotional regulation. Conclusions: This study provides preliminary evidence for the usefulness of olfactory enhancement in VR during chemotherapy sessions in breast cancer patients. The multimodal potential of VR contributes to the reduction of anxiety and depression by inducing a positive emotional experience in a soothing natural environment. The reported results highlight the value of sensorimotor VR, which also stimulates the sense of smell, in improving supportive care.



Academic Editor: Christos J. Bouras

Received: 27 February 2025

Revised: 2 April 2025

Accepted: 14 April 2025

Published: 16 April 2025

Citation: Buche, H.; Michel, A.; Blanc, N. Using Virtual Reality During Chemotherapy to Support Emotional Regulation in Patients: Adding an Olfactory Reinforcement or Not? *Virtual Worlds* **2025**, *4*, 16. <https://doi.org/10.3390/virtualworlds4020016>

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Keywords: virtual reality; olfaction; breast cancer; emotional regulation; anxiety; chemotherapy

1. Introduction

The use of VR to reduce anxiety, induce positive emotions and alleviate emotional distress in patients undergoing chemotherapy has proven relevant thanks to the multisensory virtues of virtual immersion [1]. It is now accepted that multisensory immersion spontaneously directs attention to pleasant stimuli in the environment, resulting in a more intense sense of presence in this virtual environment [1,2]. According to the model of Buche, Michel and Blanc, (2022) [1], the induction of positive emotions would be enhanced by the variety of immersive properties of the virtual device. Discovering through VR a natural environment composed of visual and auditory elements is particularly popular in oncology [3,4]. This stimulating environment is thought to promote relaxation and reduce anxiety, eliciting a positive state that helps decreasing negative emotions during cancer treatment [5–7]. To further enhance the VR experience, the addition of a sensory modality, particularly through olfactory stimulation, could enhance the vividness of environmental

information conveyed by the visual and auditory modalities [8] and accentuate the salience of certain environmental stimuli [9].

1.1. Emotions and Olfaction

There is a close relationship between olfactory and affective information [10–12]. Indeed, the olfactory bulb has the advantage of being directly connected to the amygdala and hippocampus, two cortical structures in the limbic system responsible for processing and controlling emotions [13]. Olfaction may help to reduce anxiety and improve emotional states [14,15]. Pleasant ambient odors are thought to modulate mood, cognition and behavior [10,11]. For example, a study investigating the effects of olfactory stimulation via a nasal cannula during magnetic resonance imaging in oncology found that exposure to heliotropin (i.e., a vanilla scent) helped reduce anxiety in MRI patients by 63% compared to a placebo [16].

1.1.1. Olfaction, VR and the Sense of Presence

Despite its advantages, olfaction appears to have been exploited in VR much later than the other sensory modalities [9,17]. The potential benefits of integrating the olfactory component into a virtual environment were first outlined in 1996 by Barfield and Danas, (1996) [2]. Since then, pioneering research has shown that certain odors (i.e., unpleasant ones) would be able to increase the salience of the sense of presence in VR [18]. Moreover, the pleasantness of an odor correlated with the visual representation of the natural environment would enhance the sense of reality (i.e., plausibility). Indeed, Baus, Bouchard and Nolet, (2019) [19] showed that perceiving cinnamon apple pies in a virtual kitchen while being exposed to the smell of this dessert significantly increased the sense of plausibility. According to these authors, this sense of plausibility may depend more on the conscious recognition of the smell than on the match between the visual and olfactory stimuli [19].

In terms of emotional regulation, a study investigating the benefits of VR related to olfactory diffusion argues that synchronizing relaxing olfactory stimuli with natural scenarios in the virtual environment could improve the emotional experience and increase the sense of escape during immersion [20]. To go one step beyond, the authors suggest collecting autobiographical odors to personalize the immersive experience for patients, in order to reactivate multisensory memory traces charged with positive emotions and intensify the relaxing experience in a more personalized environment [20].

1.1.2. Olfaction and the Practice of Relaxation

As far as relaxation practices are concerned, olfactory stimuli in VR have proven their effectiveness by offering the possibility of increasing emotional relaxation in the daily lives of healthy participants. The regular diffusion (i.e., every 10 s) of lavender essential oil during virtual immersion increased the subjective perception of relaxation by 26.1% compared to the absence of olfactory stimuli [11].

1.1.3. Olfaction and Clinical Practice

In clinical practice, this olfactory component has provided an additional benefit to VR exposure therapies. In the treatment of post-traumatic stress disorder [21–23], phobias [24–26], pleasant odors are thought to facilitate the extinction of classical conditioning and emotional desensitization procedures by transmitting reassuring signals to the brain when the patient is exposed to trauma or high stress in the virtual scenario [20].

1.2. From Interactivity to Olfactory Reinforcement

The clinical application of the olfactory component in VR for therapeutic purposes remains very little studied in oncology, as pointed out by Pizzoli et al., (2022) [20]

and Freeman et al., (2017) [27]. Researchers have mainly focused on visual, auditory and sometimes haptic stimuli to improve the care and rehabilitation of cancer patients [27–30]. In particular, a recent study conducted in chemotherapy highlighted the benefits of VR in this acute phase of breast cancer care by comparing two immersive modalities (i.e., contemplative vs. participative) with a classical music listening situation or a distraction-free care situation. VR proposed a multisensory immersion offering patients active or passive strategies in the environment (i.e., contemplative vs. participative VR), aimed at focusing their attention on the pleasant stimuli of the virtual experience [31]. In this context of chemotherapy, the use of VR helped to reduce anxiety and alleviate emotional tension. The multisensory and immersive nature of VR appeared more effective than music in inducing positive emotions, even more so when the immersion was interactive. Also, VR could compensate for the relative availability of caregivers by allowing patients to take control of their emotional wellbeing by creating their own interactive and relaxing environments.

In line with this study [31], the aim of the present research is to investigate the benefits of VR in chemotherapy by examining whether the degree of sensation can be increased by the diffusion of essential oil (i.e., contemplative VR vs. participatory VR vs. participatory VR with olfactory enhancement). If the interest in mobilizing the olfactory senses in VR has been noted in the context of exposure therapies or relaxation practices [26], it would now be interesting to consider combining the benefits of olfaction with interactive VR during the breast cancer care. Based on Pavlovian theory, (1960) [32], it is thought that the response to specific odors in chemotherapy may manifest as reactive nausea and emotional distress in breast cancer patients [33]. Isolating patients through olfactory reinforcement could counteract the unpleasant effects of medical odors, but also provide additional comfort to patients during the immersive experience, and enhance their sense of emotional presence by creating their own interactive and relaxing environment.

1.3. Emotional Distress

In oncology, the effects of VR on depressed mood have not been systematically investigated. The contributions of three studies are noteworthy. A first study evaluating the effectiveness of three sessions of compassion-focused therapy in VR measured symptoms of emotional distress using the DASS-21 [34] in 21 patients undergoing cancer treatment. The data showed a significant reduction in distress levels between baseline and the end of the third session of compassion-focused VR, but no significant reduction in the depression subscore was observed [35]. A second study evaluated the effectiveness of VR in managing symptoms of emotional distress in 68 breast cancer patients undergoing chemotherapy. HADS scores [36] showed significant effects in reducing anxiety and depression after immersion compared to a non-VR group [37]. A third study evaluating the contribution of VR in the homes of women with metastatic breast cancer found significant improvements immediately after VR and/or 48 h later in quality of life, fatigue, pain, depression, anxiety and stress [38].

However, no study has investigated the potential of olfactory augmentation VR on the emotional distress of patients undergoing chemotherapy.

1.4. The Present Study

Would it be possible to increase the benefits of virtual immersion in oncology by integrating the already proven effectiveness of odors for relaxation with active distraction strategies for emotional regulation in VR? If multiple sensory modalities stimulated simultaneously can contribute to the regulation of emotional states, then the addition of an olfactory stimulus should enhance the positive effect of VR on the emotional state (i.e., anxi-

ety, depressive mood, intensity and emotional valence) of breast cancer patients undergoing chemotherapy. To test this hypothesis, the effectiveness of three immersion modalities was compared on the same sample of patients during three chemotherapy sessions included in their care pathway: contemplative VR (i.e., passive exploration of the environment); participative VR (i.e., possibility to perform some actions in the environment); participative VR with olfactory enhancement (i.e., possibility to perform some actions in the environment combined with olfactory stimulation).

2. Materials and Methods

2.1. Sample

The initial study sample consisted of 58 female patients aged between 30 and 81 years (mean age = 53.06 ± 11.26 years) (see Table 1). Participants were recruited at the Breast Institute of Montpellier (i.e., Montpellier Institut du Sein) in the chemotherapy department of the Clémentville clinic. Inclusion and exclusion criteria were identical to those of one previous study conducted on VR in chemotherapy (see Buche, Michel & Blanc, 2023 [31]).

Table 1. Characteristics of the sample.

Variables	Participants	%
Age: Mean (SD *)	53.06 (11.26)	
Marital status		
Married/couple	N = 30	60
Single/separated/divorced	N = 20	30
Employed		
Yes	N = 13	26
No	N = 37	74

* SD, Standard deviation.

Of the 58 patients who took part in the experiment, 50 participated in all immersion conditions (i.e., contemplative VR vs. participatory VR vs. participatory VR augmented with olfactory stimulation). Six patients did not wish to continue with the study (i.e., lack of interest, headset-related discomfort, nausea). Two patients did not return to complete their chemotherapy sessions during the recruitment period. We therefore treated 86.21% of the baseline population. The socio-demographic characteristics of the participants are shown in Table 1.

2.2. Materials

This study follows on from a previous study carried out during a chemotherapy session with breast cancer patients [31]. Given the patients' preference for natural environments [3,4], Greener Gamer's *Nature Treks VR* relaxation application [39] was used (cf. Buche et al., 2021, 2023 [31,40]). Tools from previous methodologies [31,40] were used to assess patients' mood state (i.e., SAM) [41], sense of presence (i.e., ITC-SOPT) [42], tendency of immersion (i.e., ITQ) [43], and to monitor any negative effects (i.e., QC) [44,45] generated by each virtual immersion modality. All measurements used and the corresponding questionnaires are listed in Table 2.

With regard to the measurement of anxiety, the STAI [46] was replaced by the *Hospital Anxiety Depression Scales (HADS)* [36] in order to obtain an additional measure (i.e., depressed mood) and to optimize the speed of administration required in the clinical context (i.e., chemotherapy). In addition, the HADS is a 14-item self-report measure specifically designed to detect the presence of emotional distress related to hospital care. The first seven

items assess anxiety, two of which are indices of fear and five of which measure tension and agitation. The last seven items assess depression, two of which relate to motor slowing and the other five are markers of anhedonia [47]. Each item is scored on a four-point scale (i.e., from 0: lowest level of distress to 3: highest level of distress) for a total score ranging from 0 to 21 for each subscale.

Table 2. Measurement tools used during the three chemotherapy sessions.

Name of the Measure	Corresponding References	Number of Items	Targeted Measures
<i>Self Assessment Manikin (SAM)</i>	Bradeley et Lang (1994) [41]	2 items	Mood state: Emotional valence, Emotional arousal
<i>Hospital Anxiety Depression Scales (HADS)</i>	Zigmond & Snaith, (1983) [36]	14 items	Hospital Anxiety Depression
<i>Independant Television Commission-Sense Of Presence Inventory (2000) (ITC-SOPI) [42]</i>	Lessiter et al., (2001) [43], translated by Cyberpsychology from UQO (2006)	28 items	Sens of presence: The spatial presence, Engagement
<i>Questionnaire on Cybersickness (QC)</i>	Laboratory of Cyberpsychology at UQO (2002) [44], French translation of the Simulator Sickness Questionnaire (Kennedy et al., 1993) [45]	16 items	Symptoms which may be caused by VR: Oculomotor, Nausea
<i>Tendency of Immersion French version (ITQ)</i>	Laboratory of Cyberpsychology at UQO (2002) [44]	18 items	Tendency to immerse in distraction
<i>Immersive preference</i>		1 standardized qualitative question	Preference for interactive and sensory modalities

2.3. Apparatus

To ensure optimal immersion and to minimize the risk of discomfort associated with the VR device, the Meta Quest 2[®] headset was used, as in one previous chemotherapy study [31]. To isolate the patients from the auditory medical context, a headset was also integrated into the virtual device in each immersion condition [31]. For olfactory immersion, a simple olfactory diffusion process consisted of placing three drops of essential oils (e.g., ginger, citrus, pine, vanilla) on a sterile compress placed near the virtual device. Ginger essential oil is thought to relieve nausea caused by motion sickness, sweet orange oil is thought to improve psycho-emotional state and reduce anxiety, lemon oil is thought to stabilize mood and grapefruit oil is thought to have relaxing properties [48]. Vanilla essential oil is thought to help reduce anxiety by inducing a state of calm [16]. The pine scent was used to evoke the forests of the green meadow environment described by Kawai and Noro (1996) [49], while the citrus and vanilla scents were used in the blue ocean environment associated with the beach.

2.4. Procedure

The procedure used in the study by Buche et al., (2023) [31] was reproduced during three chemotherapy sessions (see Figure 1). However, to investigate the benefits of VR in terms of interactivity and sensory experience, participatory immersion and contemplative immersion were compared with participatory immersion augmented with an olfactory stimulation thanks to the simultaneous diffusion of natural essential oils. To assess the benefits of the different sensory experiences, patients were randomly assigned to each immersion condition during three chemotherapy sessions. In this way, patients were able to experience VR in all its diversity (i.e., contemplative; participative; participative with olfactory enhancement).

Given the nature of our study, implementing a fully double-blind design presented methodological challenges, particularly because patients were aware of the olfactory stimulation during participatory VR with odor. However, to minimize expectancy effects, we

proceeded as follows: (i) Patients were not informed of the specific hypothesis comparing olfactory-enhanced VR to the other conditions; (ii) The study followed a within-subject design, where each participant experienced all three immersion conditions in a randomized order, reducing potential biases linked to individual predispositions; (iii) Prior to exposure, participants were asked whether any of the proposed scents were unpleasant to them, ensuring that negative reactions did not confound the emotional regulation measures.

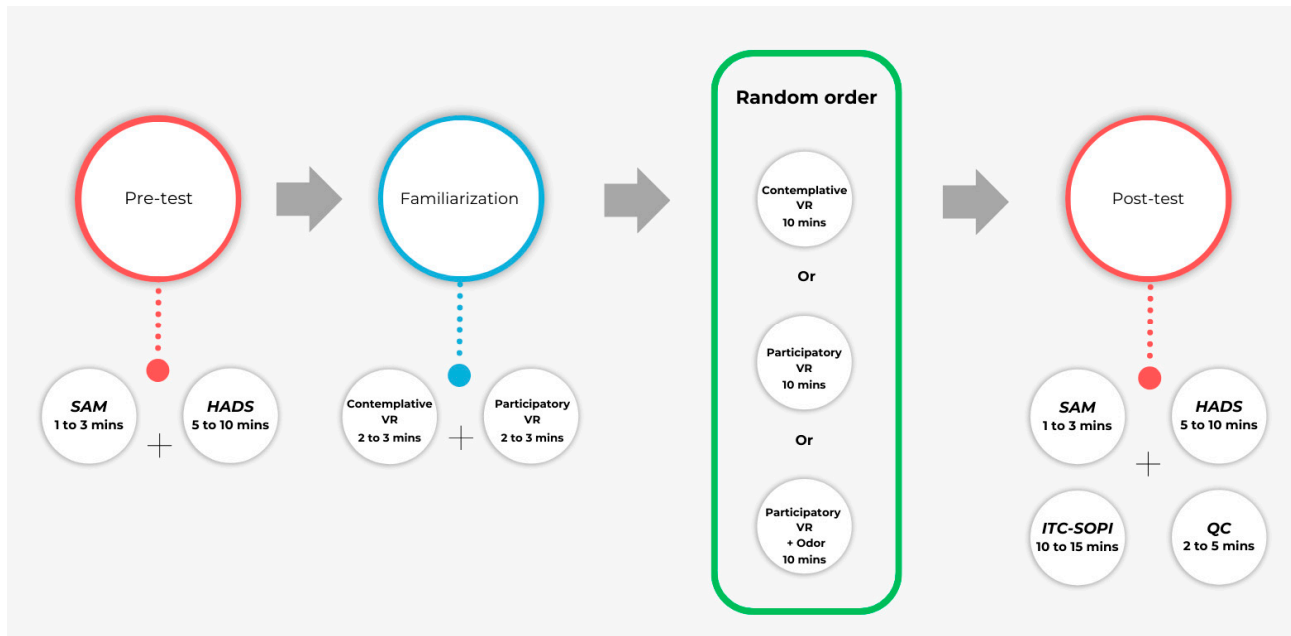


Figure 1. Experimental design of the study (i.e., phases and measures).

The VR sessions were all carried out in the chemotherapy department of the Clémentville clinic in Montpellier. Patients were informed in advance about the possibility of taking part in this study and were approached during treatment on the recommendation of the oncology nurses.

To facilitate the completion of the questionnaires, a specific booklet for each patient was created to collect their responses and was used for each immersive experience. Prior to their participation, patients who were volunteered signed the informed consent form and completed the demographic questionnaire.

Once seated in the individual treatment room, patients were systematically informed about the proposed immersion (i.e., contemplative VR vs. participatory VR vs. participatory VR augmented with olfactory stimulation) before completing the first set of questionnaires (i.e., *SAM*, *HADS*). In line with the expectations of the Ethics Committee that approved this study (CER UPVM—Université Paul Valéry—Montpellier III. IRB00013686- 2023-23-CER UPVM—Université Paul Valéry—Montpellier III France IRB #2), data collection was carried to ensure patient anonymity. Nurses provided standard care and administered intravenous chemotherapy. Each chemotherapy session lasted between 45 and 90 min. The VR experiment (i.e., contemplative VR vs. participatory VR vs. participatory VR augmented with olfactory stimulation) took place after a reminder of the device handling instructions for the different distraction conditions.

Each VR session was preceded by a period of familiarization with the virtual device, which gave each patient the opportunity to get used to handling the device, so that the relaxing experience was not compromised by navigational difficulties during immersion. During familiarization, the experimenter explained the different environments offered and then demonstrated how to use the VR equipment: the contemplative and participatory

immersions consisted of exploring the chosen environment without requiring any physical movement. Exploration was performed using two joysticks, which the patients pointed in the desired direction. In addition to exploration, participatory immersion allowed patients to control the weather, plant trees or flowers to shape their own environment, and feed the animals. Familiarization took between two and seven minutes, depending on the patient's needs.

During the experimental sessions, the experimenter helped the patients to put on the programmed VR headset in the desired environment to directly access the relaxing immersive experience. Patients used the equipment for ten minutes during each session. In the participatory VR condition involving olfactory stimulation, a cotton pad infused with three drops of essential oil was strategically placed on the armrest of the patient's chair, at a standardized distance of approximately 30 cm from their face. This placement was designed to ensure a consistent and controlled diffusion of the olfactory stimuli while preventing excessive exposure that could potentially induce discomfort.

At the end of the immersion, all patients were asked to complete the final set of questionnaires (i.e., *SAM*, *HADS*, *ITC-SOPI*, *QC*). At the final session, patients completed a last questionnaire (i.e., *ITQ*) and a standardized immersion preference question before being thanked for their participation.

3. Results

JAMOVI, version 2.3.21, software was used for all statistical analyses. With regard to the intended benefits on patients' emotional state, measures of anxiety, depressive mood, emotional valence and arousal levels were analyzed using repeated measures *ANOVAs*. Indicators of quality of virtual immersion, spatial presence and level of engagement were processed using *ANOVAs* [31,40]. As in the first study [40], a *Student's t-test* was used to compare the patients' tendency to immerse themselves in the virtual environment according to the standards of the Laboratory of Cyberpsychology at UQO (2002) [44]. All statistical analyses have a significant level set at 0.05 by applying Tuckey's correction.

3.1. Anxiety

To assess the effect of virtual immersions on anxiety reduction, data were coded and transformed according to *HADS* standard guidelines. A repeated measures *ANOVA* was calculated according to the time of measurement (i.e., before vs. after) and according to the immersion condition (i.e., contemplative VR vs. participatory VR vs. participatory VR augmented with olfactory stimulation) in order to analyze anxiety (see Table 3).

A main effect of the time of measurement was observed $F(1, 49) = 56,759, p < 0.001, \eta^2p = 0.537$. The anxiety level was lower after the VR sessions than before. However, the analysis showed no significant difference between the three immersion modalities on patients' anxiety $F(2, 98) = 1.469, p = 0.235, \eta^2p = 0.029$. Thus, whatever the immersive parameters proposed (i.e., contemplative VR, participatory VR and participatory VR augmented with odor stimulation), a reduction in anxiety after each chemotherapy session was observed.

The interaction between measurement time and immersion condition was not significant, $F(2, 98) = 0.498, p = 0.609, \eta^2p = 0.010$. The type of immersion had no effect on the timing of the anxiety measurement.

Post hoc tests calculated revealed there was a significant difference between before and after each immersive experience. Patients were less anxious after contemplative immersion than before, $t(49) = 4.965, p < 0.001$. They were less anxious after participatory immersion than before, $t(49) = 5.349, p < 0.001$. Similarly, they were less anxious after participatory immersion augmented with odor stimulation than before, $t(49) = 6.219, p < 0.001$. Overall,

patients experienced a reduction in anxiety regardless of the type of immersion. In addition, patients reported a relatively constant level of anxiety before each chemotherapy session.

Table 3. Mean and standard deviation of each measure of emotional state for each immersion condition as a function of measurement time, mean and significant differences by pairwise comparison.

Measures	Immersion Condition	Before	After	Difference	p-Value
		Mean (SD)	Mean (SD *)		
Emotional valence	Contemplative VR	6.16 (1.84)	7.28 (1.78)	1.12	0.002
	Participative VR	6.32 (1.99)	7.9 (1.49)	1.58	<0.001
	Participative VR with odor	6.26 (1.98)	7.84 (1.60)	1.58	<0.001
Arousal	Contemplative VR	3.84 (2.03)	2.38 (1.76)	−1.46	<0.001
	Participative VR	3.14 (2.29)	2.50 (1.88)	−0.64	0.11
	Participative VR with odor	3.04 (1.78)	2.28 (1.64)	−0.76	0.007
Anxiety	Contemplative VR	7.70 (3.97)	5.44 (4.14)	−2.26	<0.001
	Participative VR	6.88 (3.70)	4.56 (3.55)	−2.32	<0.001
	Participative VR with odor	7.48 (3.92)	4.74 (3.59)	−2.74	<0.001
Depressive mood	Contemplative VR	5.04 (3.65)	4.10 (3.54)	−0.94	0.066
	Participative VR	4.42 (3.57)	3.34 (2.83)	−1.08	0.014
	Participative VR with odor	5.48 (3.32)	3.52 (2.80)	−1.96	<0.001

* SD, Standard Deviation.

3.2. Depressive Mood

To account for the effect of immersion on reducing patients' depressed mood, data were coded and transformed according to standard *HADS* guidelines. A repeated measures ANOVA was calculated according to the time of measurement (i.e., before vs. after) and according to the immersion condition (i.e., contemplative VR vs. participatory VR vs. VR augmented with olfactory stimulation) to assess the level of depressed mood (see Table 3).

A main effect of time of measurement was obtained, $F(1, 49) = 39.08$, $p < 0.001$, $\eta^2 p = 0.444$. The level of depressed mood was lower after the immersions than before. However, the immersion condition did not reach the significance threshold: no significant difference was observed between the three immersion modalities on the patients' depressed mood $F(2, 98) = 1.79$, $p = 0.172$, $\eta^2 p = 0.035$. In other words, regardless of the immersive parameters used (i.e., contemplative VR vs. participatory VR vs. VR augmented with olfactory stimulation), a reduction in depressed mood was observed after each chemotherapy session.

The interaction between time of measurement and immersion condition was significant, $F(2, 98) = 4.10$, $p < 0.020$, $\eta^2 p = 0.077$. The type of immersion had an effect on the time of measurement of depressed mood. The post hoc test showed a reduction in depressed mood after the VR experience mainly for participatory immersions, whether associated with diffusion of essential oils $t(49) = 7.04$, $p < 0.001$, or not $t(49) = 3.453$, $p < 0.014$, only a tendency being observed for contemplative VR $t(49) = 2.848$, $p = 0.066$. In sum, VR improved depressed mood in breast cancer patients during chemotherapy sessions. Patients' depressed mood tended to improve after contemplative VR while improved significantly after the two participatory immersion sessions, with a larger difference when VR was associated with the diffusion of a pleasant odor.

3.3. State of Mood

For the measure of emotional induction, differences were observed in the valence and intensity scores on the *SAM scale* (see Table 3). For each measure, we calculated a repeated measures ANOVA according to the time of measurement (i.e., before vs. after) and the

immersion condition (i.e., contemplative VR vs. participatory VR vs. participatory VR augmented with olfactory stimulation).

For the emotional valence measure, only an effect of time of measurement was observed, $F(1, 49) = 83.10$, $p < 0.001$, $\eta^2p = 0.629$. After the immersive experience, the patients were in a more pleasant emotional state than before. Analysis of variance revealed no significant difference between the three immersion modalities on emotional feeling $F(2, 98) = 1.44$, $p = 0.242$, $\eta^2p = 0.029$, nor any interaction between time of measurement and condition $F(2, 98) = 1.42$, $p = 0.247$, $\eta^2p = 0.028$.

The post hoc test showed a significant difference between before and after each type of immersion. When patients used contemplative VR, they felt more positive after the immersion than before, $t(49) = -4.164$, $p < 0.002$. When using participatory VR, patients again felt more positive after immersion than before, $t(49) = -7.451$, $p < 0.001$. When they used participatory VR with odor diffusion, they felt more positive after immersion than before, $t(49) = -6.702$, $p < 0.001$. The patients' emotional feelings were more positive after each virtual immersion.

For emotional intensity, the results also showed a main effect of time of measurement, $F(1, 49) = 37.11$, $p < 0.001$, $\eta^2p = 0.431$. Emotional intensity was higher before than after the experiment. As the SAM scale associates the lowest value with the adjective 'calm', these results seemed to reflect a calming effect. No effect of condition on emotional intensity was observed $F(2, 98) = 1.54$, $p = 0.219$, $\eta^2p = 0.031$, while an interaction between time of measurement and condition was observed $F(2, 98) = 4.88$, $p = 0.010$, $\eta^2p = 0.091$.

Post hoc test analyses showed statistically significant differences only between before and after contemplative immersion and participatory immersion with odor. Patients felt more peaceful after contemplative immersion than before, $t(49) = 6.43$, $p < 0.001$. The patients felt the same emotional intensity after the participatory immersion as before, $t(49) = 2.63$, $p < 0.011$, whereas they felt calmer after the participatory immersion accompanied by pleasant olfactory stimuli, $t(49) = 3.67$, $p < 0.001$.

Post hoc analyses showed statistically significant differences after each immersion. Patients felt more peaceful after contemplative immersion than before, $t(49) = 6.43$, $p < 0.001$ as after participative immersion $t(49) = 2.63$, $p < 0.011$, and participative immersion accompanied by pleasant olfactory stimuli, $t(49) = 3.67$, $p < 0.001$.

Regardless of the type of immersion proposed (i.e., contemplative VR, participative VR, participative VR augmented with olfactory stimulation), an increase in positive emotional state was found after each chemotherapy session. On the other hand, the patients' level of arousal decreased in the contemplative immersion or when the participative immersion was accompanied by an olfactory stimulation.

3.4. Sense of Presence

Only spatial presence and engagement were measured using the ITC-SOPI (see Table 4). In line with experts' recommendations for this scale, we performed two one-way ANOVAs (one per factor) with the type of immersion (i.e., contemplative VR vs. participative VR vs. participative VR augmented with olfactory stimulation) as the within-subject factor.

The analysis of variance revealed an effect of immersive interactivity on spatial presence, $F(2, 98) = 35.9$, $p < 0.001$, $\eta^2p = 0.423$. More specifically, spatial presence observed with the post hoc test was higher during participatory immersion with olfactory stimulation, $t(49) = 7.28$, $p < 0.001$, than during contemplative immersion. Similarly, spatial presence was higher during participatory immersion, $t(49) = 6.10$, $p < 0.001$, than during contemplative immersion. In line with our hypothesis, interactive and multimodal immersion with olfactory stimulation (i.e., the odor of essential oils) induced a more intense sense of presence than contemplative immersion. Contrary to our expectations, olfactory

enhancement did not increase the sense of presence compared to participatory immersion, $t(49) = 1.23, p = 0.440$.

The analysis of variance also revealed an effect of immersive interactivity on patient engagement, $F(2, 98) = 16, p < 0.0001, \eta^2 p = 0.246$. In line with our expectations, patients' engagement observed in the post hoc test were higher during participatory immersion with olfactory stimulation, $t(49) = 4.96, p < 0.001$, than during contemplative immersion. The level of engagement was higher in the participatory immersion, $t(49) = 3.87, p < 0.001$, than in the contemplative immersion. Not surprisingly, interactive and multi-modal immersions were more efficient to involve patients in the environment. However, olfactory reinforcement did not seem to be more engaging than participatory immersion, $t(49) = 1.26, p = 0.18$.

Table 4. Mean and standard deviation of spatial presence and engagement as a function of immersive modalities.

	Contemplative VR	Participative VR	Participative VR Augmented with Olfactory Stimulation
	Mean (SD)	Mean (SD *)	Mean (SD)
Spatial presence	3.48 (0.65)	4.05 (0.57)	4.13 (0.52)
Engagement	3.87 (0.59)	4.14 (0.50)	4.20 (0.44)

*SD, Standard Deviation.

3.5. Cybersickness

The negative effects of virtual immersion were examined using three ANOVAs (one for each variable we considered: oculomotor, nausea, total) according to the immersion modality (i.e., contemplative VR vs. participatory VR vs. participatory VR augmented with olfactory stimulation). The possible VR-induced discomforts identified by the QC are presented in Table 5.

Table 5. Mean and standard deviation of negative effects observed in the three types of chemotherapy immersion.

	Contemplative VR	Participative VR	Participative VR Augmented with Olfactory Stimulation
	Mean (SD)	Mean (SD *)	Mean (SD)
Total cybersickness	1.04 (1.78)	1.16 (1.84)	1.46 (2.3)
Oculo-motor	0.6 (1.25)	0.52 (1.20)	0.66 (1.65)
Nausea	0.42 (0.86)	0.62 (0.97)	0.8 (1.14)

*SD, Standard Deviation.

The analysis revealed no main effect of immersion on the intensity of total cyber discomfort $F(2, 98) = 0.882, p = 0.417, \eta^2 p = 0.018$. In this study, the differences observed between participatory VR with or without olfactory stimulation and contemplative VR were not significant. The same is true for the oculomotor subfactor, $F(2, 98) = 0.201, p = 0.818, \eta^2 p = 0.004$. On the other hand, the analysis showed a main effect of nausea, $F(2, 98) = 3.07, p = 0.051, \eta^2 p = 0.026$. According to the post hoc test, the tendency to experience nausea was higher in participatory VR with olfactory stimulation than in contemplative VR, $t(49) = 2.32, p < 0.062$. As the mean scores were less than five in each immersive modality, the negative symptoms produced by the VR devices were again negligible.

3.6. Tendency to Immerse

To determine to what extent the patients would be predisposed to immerse themselves in a virtual environment, 4 *Student's t-tests* were calculated to compare the means of the immersion tendency subscales (i.e., focus, engagement, emotion, games and the total mean) with the norms provided by the Cyberpsychology Laboratory of the UQO (2002) [44] (see Table 6).

Table 6. Mean and standard deviation of patients' tendency to immerse by subfactors vs. norm.

	Patients	Norms
	Mean (SD *)	Mean (SD)
Total	81.6 (16.9)	64.11 (13.11)
Focus	25.3 (4.86)	24.81 (7.54)
Engagement	23.2 (6.28)	15.33 (8.67)
Emotions	18.2 (5.29)	14.25 (6.70)
Games	10.5 (5.29)	6.56 (4.95)

* SD, Standard Deviation.

Patients' ability to maintain focus and disregard external distractions was not significantly different from the norm $t(49) = 0.655$, $p = 0.515$. Patients' tendency to focus their attention on virtual immersion stimuli was not different from the norm. The difference between the mean score for patients' engagement and the norm was significant $t(49) = 8.84$, $p < 0.001$, *Cohen's d* = 1.25, the effect size is strong. Since $t_{cal} > 0$, the patients felt very involved in the virtual experiences. This result was consistent with the high levels of involvement observed with the *ITC-SOPI*. The difference between the patients' mean emotion score and the norm was significant $t(49) = 5.31$, $p < 0.001$, *Cohen's d* = 0.75, effect size was medium. Since $t_{cal} > 0$, the patients were willing to feel the emotions induced in the natural immersions. The observed result was consistent with the data obtained using the SAM Scale.

The frequency with which the participants devoted time to screens was significantly different from the norm, $t(49) = 5.89$, $p < 0.001$, *Cohen's d* = 0.83. The effect size was strong. The patients who took part in this study were thus highly interested in multimedia distractions. Additionally, the difference between the mean score of the patients' general tendency to immerse themselves in an activity and the norm was significant, $t(59) = 3.071$, $p < 0.001$, *Cohen's d* = 1.04. The effect size was strong. Since $t_{cal} > 0$, patients were able to immerse themselves in the relaxing environment.

3.7. VR Benefits According to Immersive Preference

The immersive preferences collected concerned interactivity and sensoriality: The majority of patients preferred interactive VR (86%, $n = 43/50$, 40% with olfactory stimulation and 46% without olfactory stimulation). Those who favored interactivity augmented with olfactory stimulation reported feeling more immersed in the environment, which appeared more realistic and pleasant. The patients who preferred interactivity alone reported that they were insensitive to odors or too sensitive to odors. Only 14% of patients preferred contemplative immersion ($n = 7/50$).

To deepen our understanding of the contribution of multi-sensoriality in VR, a factorial ANOVA was then performed, particularly among the majority of patients who preferred interactivity ($n = 43$). Anxiety levels after the two interactive immersions (Participatory VR vs. Participatory VR augmented with olfactory stimulation) were measured within subjects, according to their immersive preferences (without odor vs. with odor) introduced as a between-subject variable (See Figure 2).

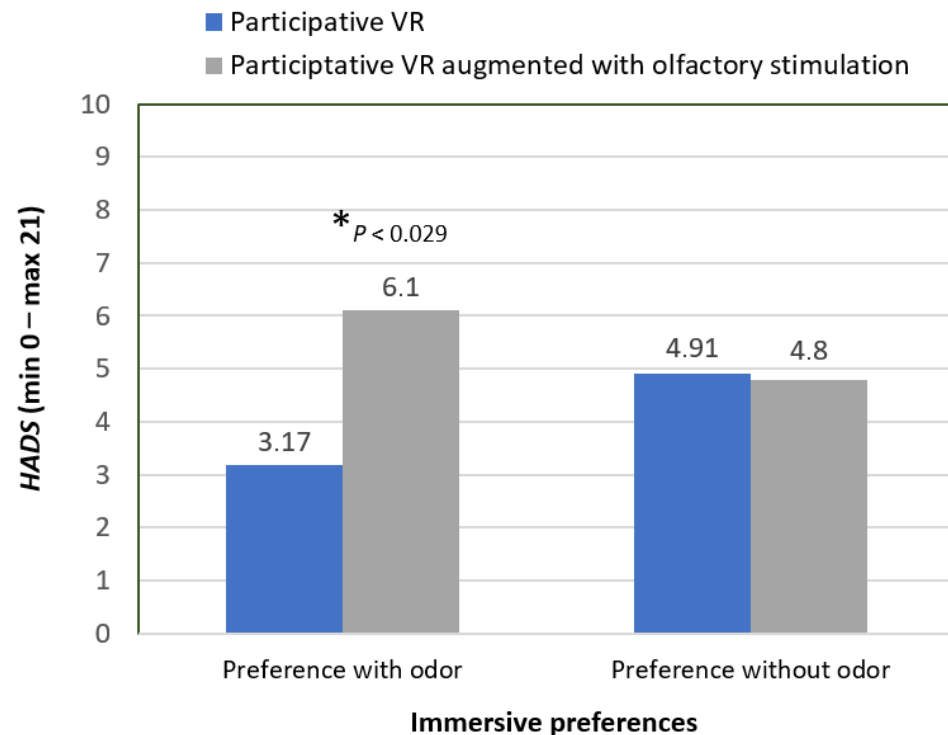


Figure 2. Anxiety after interactive immersions (participatory VR vs. participatory VR augmented with olfactory stimulation) according to patients' immersive preferences (with vs. without odor).

Factor analysis revealed a significant interaction between immersion modality and immersive preferences on the anxiety measure, $F(1, 41) = 9.631, p < 0.003$.

The post hoc test revealed that following participative immersion without odor, the anxiety level was higher among women who prefer immersion with odors ($M = 6.10 \pm 3.57$) compared to those who prefer immersion without odor ($M = 3.17 \pm 3.05$), $t(1, 41) = -2.90, p < 0.029$. Patients who stated that they did not prefer odors during immersion reported a higher level of anxiety when VR was enhanced with an odor.

Similarly, patients with a preference for participatory immersion without odor tended to have lower levels of anxiety after this type of immersive experience ($M = 3.17 \pm 3.05$) than after immersive experience augmented with odor stimulation ($M = 4.91 \pm 3.57$), $t(1, 41) = 2.60, p = 0.059$.

Among the patients who preferred immersive experience with odor, it can be seen that the benefits of VR on anxiety were not influenced by the diffusion of essential oils during immersion $t(1, 41) = 1.82, p = 0.28$.

These results provided evidence that the effect of VR on anxiety reduction was not enhanced with the addition of essential oil scents, if this olfactory stimulation is not desired by the patients.

4. Discussion

The use of VR in challenging care contexts is increasingly being considered by medical institutions. In light of this growing interest, it has become necessary to ensure its effectiveness for patients and, more importantly, to investigate which immersive conditions are best suited to reduce anxiety and emotional distress while inducing a positive emotional experience. To date, no study has evaluated the relevance of olfactory stimulation within interactive VR for breast cancer patients by comparing this condition with the traditionally used immersions [31,40] (i.e., participatory VR vs. contemplative VR). To this end, a recurrent methodology [1,50–52] with a quasi-experimental protocol was implemented in

an oncology unit to assess the sense of presence in the virtual environment (*ITC-SOPI*), the emotional state of patients (*HADS*; *SAM*) and cybersickness (*QC*).

The results of the present study confirm the effectiveness of VR as a tool to support emotional regulation in women with breast cancer undergoing chemotherapy [40]. In line with the existing literature, the strength of VR lies in improving psychological well-being through its calming and distracting properties. Consistent results have been reported in other studies of women with breast cancer [52], and even a reduction in the intensity and frequency of hot flushes associated with breast cancer [53].

Contrary to expectations, the hypothesis that olfactory enhancement in VR might enhance the emotional support benefits associated with VR was not confirmed. Each immersive modality demonstrated benefits in reducing anxiety and distress by eliciting positive emotional responses in patients during the acute phase of cancer. Similar to the findings of Serrano et al., (2016) [54], the hypothesis that olfaction could enhance a more positive emotional response was not supported [54]. Other diffusion methods that are more controllable through olfactory interfaces delivering synchronized and consistent scents could enhance the effectiveness of the emotional support tool [20,54].

A particularly subtle finding of this study is the marginal impact of olfactory stimulation on depressive mood regulation. While all immersive VR conditions contributed to an overall reduction in anxiety and emotional distress, participatory VR combined with olfactory stimulation resulted in the most pronounced improvement in depressive mood. This effect suggests that olfactory cues may enhance the affective benefits of VR immersion by engaging neural mechanisms associated with mood regulation, particularly through the olfactory-limbic pathways involving the amygdala and hippocampus [13]. Furthermore, the olfactory-enhanced VR condition was associated with a greater decrease in arousal, suggesting an augmented capacity to modulate emotional responses and promote a more profound state of relaxation.

According to qualitative measures, the interactive possibilities offered by VR continue to be preferred by the majority of patients undergoing chemotherapy. Also, almost half of the patients preferred interactivity augmented with olfactory stimulation to have a positive effect on their emotional well-being. Conversely, quantitative measures indicated that the olfactory modality could reduce the beneficial effects of interactive VR on anxiety in patients who did not have a particular preference for odors.

In line with previous studies [31,40,55], the sense of presence is more pronounced when patients have the opportunity to interact with and shape their natural relaxing environment. The significantly higher levels of spatial presence and engagement observed during interactive and multimodal immersion underscore the value of sensorimotor VR in maintaining patients' attention within the relaxing environment. In addition, the VR tool used during chemotherapy was generally well tolerated, regardless of the type of immersion experienced. Olfactory stimuli and interactivity did not generate cybersickness, although the risk of nausea was higher with olfactory VR [55].

Limitations and Perspectives

Despite these promising findings, several limitations must be acknowledged. First, the sample size remains a constraint, as a larger cohort would allow for greater statistical power and more robust generalizability of the findings. Additionally, the absence of a control group limits the ability to precisely isolate the effects of the intervention and rule out other potential influencing factors. This methodological choice was made to reduce the burden on patients undergoing chemotherapy and to ensure the study remained as non-intrusive as possible in a sensitive clinical context. Introducing an additional no-intervention group could have increased fatigue or discomfort, which we aimed to avoid in accordance with

ethical considerations. This within-subject design allowed each patient to serve as her own control, thereby reducing interindividual variability and strengthening the internal validity of the observed effects despite the absence of an external control group. Future studies should aim to replicate these results with a more extensive and diverse patient population while incorporating a control group to refine the conclusions drawn [56].

Second, the study did not control for the potential influence of chemotherapy drug regimens on patients' emotional states. Given that different pharmacological treatments may variably impact mood, anxiety, and overall well-being, future research should consider integrating this variable into the analysis to dissociate the specific contributions of VR from those of the pharmacological agents administered during chemotherapy. A finer-grained approach, considering patient-reported side effects and drug-induced emotional fluctuations, would provide a more comprehensive understanding of VR's impact in this context [57].

Third, the lack of long-term follow-up data limits the ability to assess whether the observed emotional benefits persist beyond the immediate chemotherapy sessions [38,56]. While the study provides compelling evidence of VR's short-term efficacy in reducing anxiety and distress, it remains unclear whether these benefits translate into prolonged emotional resilience or improved psychological adjustment throughout the cancer treatment trajectory. Longitudinal studies are warranted to evaluate the durability of these effects and to explore whether repeated VR exposure could generate cumulative psychological benefits over time [38,56].

Finally, the study lacks physiological measures that could provide an objective assessment of VR's impact on emotional regulation. The addition of biometric indicators such as heart rate variability or electrodermal activity would constitute a meaningful methodological improvement alongside self-reported data. These measures could help validate subjective experiences, detect unconscious affective responses, and offer real-time insights into autonomic nervous system activity during immersion. Their inclusion would strengthen the reliability of emotional assessments and contribute to a more nuanced understanding of the psychophysiological mechanisms through which immersive environments support patients' well-being and emotional adjustment in oncology settings [6]. Moreover, recent advances in emotion-aware artificial intelligence have highlighted the importance of integrating attention-based mechanisms and fine-grained emotional monitoring in digital mental health interventions [58]. In line with this, future studies could explore the use of eye-tracking and attentional metrics in VR to better capture the mechanisms underpinning emotional engagement during immersive exposure.

5. Conclusions

This preliminary study has the advantage of confirming the results of previous research on the contribution of VR to emotion management in difficult health contexts. It also paves the way for further investigation into the potential role of adding olfactory stimulation for those who request it, in order to respond more accurately to patients' needs and preferences.

Author Contributions: Conceptualization, H.B., A.M. and N.B.; methodology, H.B., A.M. and N.B.; software, H.B., A.M. and N.B.; validation, H.B., A.M. and N.B.; formal analysis, H.B., A.M. and N.B.; investigation, H.B., A.M. and N.B.; resources, H.B., A.M. and N.B.; data curation, H.B., A.M. and N.B.; writing—original draft preparation, H.B., A.M. and N.B.; writing—review and editing, H.B., A.M. and N.B.; visualization, H.B., A.M. and N.B.; supervision, H.B., A.M. and N.B.; project administration, H.B., A.M. and N.B.; funding acquisition, H.B., A.M. and N.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee (CER UPVM—Université Paul Valéry—Montpellier III. IRB00013686- 2023-23-CER UPVM—Université Paul Valéry—Montpellier III France IRB #2) at 6 September 2023, for studies involving humans.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

VR Virtual reality
SD Standard deviation

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