




# BMJ Open Influence of chemotherapy on postural control and quality of life in women with gynaecological cancer: a protocol of a prospective observational study

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## ABSTRACT

**Introduction** Chemotherapy-induced peripheral neuropathy is a frequent side effect of some chemotherapies that can cause postural control disorders and has a serious impact on quality of life (QoL). An enhanced understanding of postural control dysfunction could help build a systematic and accurate assessment as well as specific exercises to limit the impact on QoL. This study aims to assess the influence of chemotherapy on postural control and the QoL for women with gynaecological cancer.

**Methods and analysis** This prospective observational study will include 37 participants with cancer treated using neurotoxic chemotherapy. Their postural control in various conditions (rigid and foam surfaces, eyes open and closed, with and without tendon vibration, and dual tasks), limits of stability, QoL and modified Total Neuropathy Score will be assessed. A linear mixed model will compare postural control pre-chemotherapy and post-chemotherapy.

**Ethics and dissemination** This study was approved by an ethical review board in Geneva (CCER-2020-01639). The study findings will be disseminated through conference presentations and publications in peer-reviewed journals.

**Trial registration number** NCT04692168.

## BACKGROUND AND RATIONALE

Chemotherapy-induced peripheral neuropathy (CIPN) is a frequent side effect of chemotherapy treatments.<sup>1</sup> More than 60% of patients with cancer experience CIPN within one month of completing their therapy. Due to a multifactorial process that includes nerve fibre damage, oxidative stress, and inflammation,<sup>2</sup> CIPN generates sensory symptoms (neuropathic pain, tingling, numbness, and hypo/hypersensitivity) as well as motor (weakness, hyporeflexia, and cramps), gait, and postural control impairments.<sup>3</sup>

Postural control disorders are among the most frequent posturodynamic impairments described by cancer survivors.<sup>3</sup> Postural control is defined as the ‘act of maintaining,

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The main strength of this study lies in its evaluation of various conditions of postural control with sensory input disturbance to obtain an enhanced understanding of postural control adjustment strategies after chemotherapy.
- ⇒ This study considers static and dynamic stability.
- ⇒ As a test session is relatively long, some fatigue may be experienced.
- ⇒ Specific inclusion criteria are applied (age, comorbidities and treatment type), so the study population may not represent all people with gynaecological cancer.

achieving or restoring a state of balance during any posture or activity’,<sup>4</sup> whereas balance is ‘the ability to keep the body’s centre of mass within the limits of the base of support’.<sup>5</sup> This complex physical capacity includes ‘static stability’, namely ‘the ability to control the centre of mass when the base of support does not change’, and ‘dynamic stability’, namely ‘the ability to weight shift, controlling the centre of mass within the base of support’.<sup>5</sup> Studies assessing postural control using a force platform have demonstrated that chemotherapy patients have increased centre of pressure (CP) parameters compared with healthy individuals.<sup>6–12</sup> The increased CP root mean square (RMS), ellipse area, and velocity found in people with cancer indicate the reduced accuracy of position control, the delayed detection of imbalance and more corrective actions required for maintaining stability.<sup>6–8–10–12–13</sup>

These disturbances can be observed in a static balance task with eyes open and in a balance task with disturbed sensory input (i.e., eyes closed or on an unstable surface),<sup>11</sup> making postural control more difficult. The eyes-closed condition limits the availability of

visual input, and an unstable surface such as foam disrupts the somatosensory system by altering proprioceptive feedback in the feet and reducing the muscle response efficiency at the ankles.<sup>14</sup> Therefore, the vestibular system is mainly used to develop an efficient postural strategy for managing postural control.<sup>12</sup>

Among all patients treated with chemotherapy, those with CIPN tend to exhibit more pronounced postural control disorders.<sup>8 15</sup> These disturbances have been predominantly found in test conditions relying on the vestibular and somatosensory systems (i.e., on a rigid surface).<sup>8</sup> A possible explanation is that the pain, paraesthesia, and loss of sensitivity found in the CIPN may limit somatosensory feedback and prevent adequate postural adjustment.<sup>8</sup>

However, the link between the CIPN-associated decrease in peripheral sensory capacities and postural disorders is unclear. Whereas some authors<sup>12 16</sup> have reported a link between CIPN and impaired postural control capacity, others have not.<sup>13 17</sup> Thus, the roles of the somatosensory system and CIPN in postural control disorders in patients with cancer remain unclear. According to a recent review by Wang *et al*,<sup>3</sup> further work is required to clarify the involvement of the different systems—namely the CIPN-altered somatosensory, vision, and vestibular systems—in postural control disorders.<sup>3</sup>

This study will perform postural control tests by disturbing different sensory inputs, individually and in combination, to provide information on the sensory inputs preferentially used by patients and the coping mechanisms employed when one or more systems are disrupted by treatment. To date, no longitudinal design study has assessed postural control under conditions of a somatosensory system disturbance. The somatosensory system can be disturbed, for example, with a foam surface or a vibration system. A vibration system, recommended in experimental settings,<sup>18</sup> involves inducing an illusion of movement by stimulating the neuromuscular spindles of afferent Ia fibres of the sural triceps tendon, thus disrupting somatosensory feedback. So far, unstable surfaces have been chosen in all oncology studies, but the smaller amplitudes of disturbances generated by vibrations make this system appropriate on individuals with postural control disorders. The consequences of performing a common daily dual task on posture will also be investigated in this study to determine whether using a common cognitive and fine motor task, such as texting (potentially impaired by CIPN), may disrupt postural control and increase the risk of falling.

Finally, this study will assess dynamic stability to complement the limited data in the literature on post-chemotherapy patients who appear to have impaired dynamic balance.<sup>12 19</sup> An improved understanding of the alterations in postural control may help establish the need for a systematic evaluation of postural control after chemotherapy, specifying the appropriate evaluation. Based on this assessment, an adapted and specific exercise programme could be designed to limit the multiple

impacts of impaired postural control in the daily lives of these patients. Indeed, with postural control disorders, the fear of falling increases,<sup>20</sup> the physical activity level decreases leading to deconditioning, daily living activities become difficult, and autonomy becomes limited.<sup>21</sup> Overall, these patients' quality of life (QoL) is severely impaired.<sup>22</sup> Thus, an enhanced understanding of CIPN-related postural control disorders and compensatory strategies for maintaining balance is essential for helping to alleviate CIPN's impact on the QoL.

## Objectives

### Primary objective

This study aims to compare postural control prior to and after neurotoxic chemotherapy in women with gynaecological cancer under various conditions (open/closed eyes, rigid/soft surface, with/without vibration and dual tasks). The hypothesis is that following 12 weeks of chemotherapy, the participants' postural control ability will be diminished due to the side effects of the treatments.

### Secondary objectives

The study also aims to compare the modifications of postural control according to the conditions tested, thus identifying the underlying sensorimotor dysfunction. The hypothesis is that postural control will be particularly altered in conditions where somatosensory input is necessary (rigid surface and visual disturbance) since the decrease in sensory feedback caused by CIPN should result in reduced postural control that cannot be compensated for with vision.

The modifications of standing dynamic stability (the limits of stability (LOS)) and the QoL of individuals with gynaecological cancer after chemotherapy will also be assessed. The hypothesis is that the treatment will negatively impact the LOS and the QoL due to CIPN-related symptoms, the loss of function, and autonomy.

This study also aims to investigate the association between the severity of CIPN (mild, moderate, severe) and the postural control, dynamic balance and QoL of individuals with gynaecological cancer. This study hypothesises that the postural control, dynamic balance and QoL will deteriorate with the increasing severity of CIPN.

## METHODS AND ANALYSIS

### Study design and setting

This prospective observational study will be conducted from October 2020 to December 2022 at the Geneva University Hospitals in Switzerland in the oncology department.

### Study participants

#### Eligibility criteria

Women with an oncological disease about to start chemotherapy known to be neurotoxic will be recruited. **Table 1** details the inclusion and exclusion criteria. The upper age limit is set to minimally influence the results with the

**Table 1** Eligibility criteria

Inclusion criteria	Exclusion criteria
Women <ul style="list-style-type: none"> <li>▶ Between 18 and 65 years;</li> <li>▶ With a gynaecological cancer about to start chemotherapy known to be neurotoxic (paclitaxel, docetaxel, nab-paclitaxel or paclitaxel-carboplatin);</li> <li>▶ Able to stand upright for 30 s on a flat surface without assistance;</li> <li>▶ Able to provide written consent.</li> </ul>	Women <ul style="list-style-type: none"> <li>▶ With pre-existing vestibular, uncorrectable visual, or somatosensory disorders or other pathologies altering postural control that would influence testing;</li> <li>▶ With exposure to known neurotoxic chemotherapy (paclitaxel, docetaxel, nab-paclitaxel, vinorelbine, trastuzumab-emtansine, eribulin or paclitaxel-carboplatin) that may have caused previous CIPN;</li> <li>▶ With an inability to perform the test due to poor comprehension of instructions or psychological problems.</li> </ul>
CIPN, chemotherapy-induced peripheral neuropathy.	

natural age-related deterioration of postural control and muscle mass.<sup>23</sup>

### Recruitment procedure

Potential participants will be screened consecutively among patients in the hospital's oncology department to determine whether they meet the eligibility criteria. Oncologists will ask their patients for their consent to be contacted about the study. In case of agreement, a research assistant who is not involved in routine care will call the participants and provide them with all the necessary information (i.e., the nature of the study, its purpose, procedures involved, expected duration, potential risks and benefits and any potential discomfort). An information sheet will be provided after the phone call by mail or post. The research assistant will then call the participants back after a minimum period of 24 hours to allow them to make a decision and ask questions. In case of acceptance to participate in the study, two appointments will be scheduled concurrently with another hospital appointment (e.g., medical evaluation, blood test) to avoid adding an extra hospital visit. Consent will be obtained before the participants undergo any study procedures.

### Blinding

During the second test, the participants and the assessor will be blinded to the results of the first postural control test.

### Outcomes

#### Primary outcome

##### Postural control

Participants will be asked to stay as still as possible for three trials of 30 s in different sensory disturbances conditions on a force platform to assess postural control. The mediolateral RMS of the CP will be measured to provide information on the excursion of CP from the mean position.<sup>24</sup> The higher the RMS, the further the CP moves away from the mean position towards the base of support, indicating a decrease in postural stability.

### Secondary outcomes

#### Other parameters of postural control

The following CP parameters will be measured to assess postural stability, the accuracy of control of the position, the ability to detect imbalance, and the extent of corrective actions for maintaining balance: total RMS, anteroposterior RMS, area, total length, anteroposterior and mediolateral length, anteroposterior and mediolateral delta (maximal-minimal value), maximal velocity, mean velocity and anteroposterior and mediolateral variability. Regarding the ground reaction forces, force peaks (maximal and minimal values); anteroposterior, mediolateral and vertical deltas; the number of oscillations; and force variability will be measured.

#### Dynamic standing balance

The same parameters as for postural control will be used to measure the LOS reflecting dynamic stability. The anteroposterior and mediolateral deltas of the CP length will be normalised to the mean size of the foot (the distance between the heel and hallux without shoes) according to the following formula :

$$\text{LOS}_{\text{normalised}} = \frac{\text{Measured value (mm)}}{\left( \frac{\text{Size left foot (mm)} + \text{Size right foot (mm)}}{2} \right)} \times 100$$

#### Quality of life

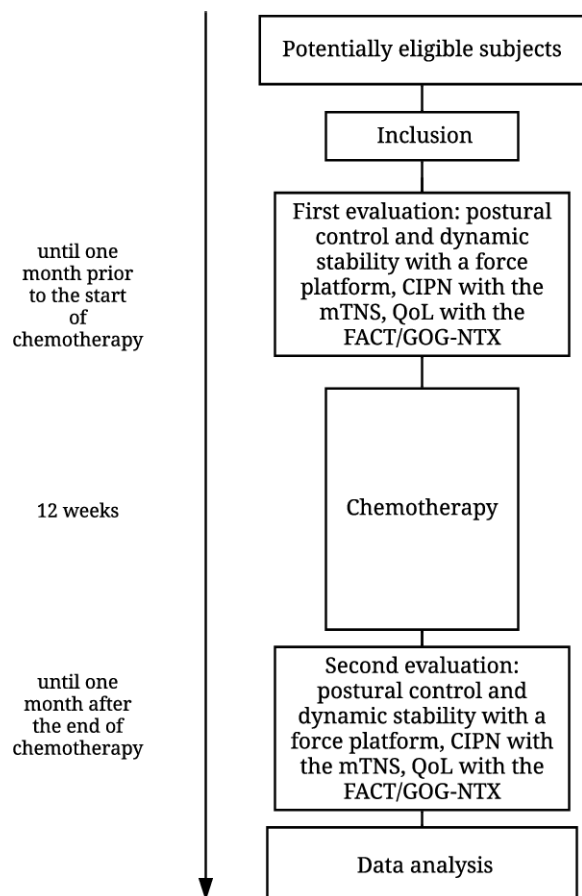
Physical, social/family, emotional and functional well-being will be assessed through patient-reported outcomes.

#### CIPN assessment

The severity of CIPN will be assessed using a composite score based on participants' symptoms and signs.

#### Assessment procedure

Two 75 min assessments will be scheduled: one before chemotherapy (baseline) and one during the first month following the end of neurotoxic chemotherapy (approximately 12 weeks of treatment, [figure 1](#)). A specifically trained physiotherapist will conduct all tests in a quiet room. Appointment reminders will be sent to participants.



**Figure 1** Experimental procedure. CIPN, chemotherapy-induced peripheral neuropathy; FACT/GOG-NTX, Functional Assessment of Cancer Therapy/Gynaecologic Oncology Group Neurotoxicity; QoL, quality of life; mTNS, modified Total Neuropathy Score.

Participants' characteristics and lifestyles will be collected during the baseline appointment. At both test sessions, individuals will perform the modified Total Neuropathy Score (mTNS) to assess CIPN,

be tested on a force platform to assess postural control and fill in the Functional Assessment of Cancer Therapy/Gynaecologic Oncology Group-Neurotoxicity (FACT/GOG-NTX) questionnaire to assess QoL. All participants will follow the same procedure. The score, tests, and questionnaire have been chosen according to our objectives and their clinimetric qualities (table 2).

### Postural control

Postural control will be measured by a 600 × 500 mm force platform (Biomechanical Force Plate Systems type 9260AA6, Kistler Instrument AG, Winterthur, Switzerland). This equipment will record the three components of ground reaction force—anteroposterior, mediolateral and vertical—and the modification of the CP at 100 Hz, as recommended<sup>25</sup> and used in oncology.<sup>13</sup> As in the study by Fino *et al.*<sup>26</sup>, the feet will be 10 cm apart between the heels and 15 cm apart between the halluces.<sup>26</sup> Participants will be instructed to stand as still as possible for 30 s<sup>27</sup> while looking at a fixed point on a wall at eye level at a distance of 0.9 m.<sup>28</sup> Participants will perform the procedure three times with a rest period of 10 s between the trials.<sup>27</sup> If a loss of balance results in the test being stopped, participants will restart the trial. A maximum of five attempts will be allowed. The mean of the successful trials will be recorded for the data analysis in all postural control tests. Data collection will start 5 s after participants are positioned to avoid perturbations linked to the trial initiation.<sup>13</sup>

Participants will be asked to maintain balance under the conditions of sensory disturbance described in table 3. The various conditions will be performed randomly according to a previously defined randomised list to avoid fatigue and learning bias.

**Table 2** Clinimetric qualities of the tests

Clinimetric quality	Postural control with a portable force platform	LOS test	FACT/GOG-NTx	mTNS
Validity	Inground force platform, CP RMS: ICC = 0.73, p<0.05 CP length: ICC = 0.86, p<0.05	MDRT forward, $r = 0.35$ , p<0.01 backward, $r = 0.16$ , p>0.05 right, $r = 0.75$ , p<0.01 left, $r = 0.64$ , p<0.01 Cronbach's $\alpha = 0.75$ (internal consistency)	NCI-CTC, $r = 0.6 - 0.76$ Cronbach's $\alpha = 0.8 - 0.85$ (internal consistency)	TNS, $r = 0.99$ , p<0.001 SOT, $r = -0.64$ , p<0.01 TUG, $r = 0.65$ , p<0.01 FACT/Tax, $r = -0.62$ , p<0.01
Reliability:				
Intra-rater		ICC = 0.86		TNS: ICC = 0.99
Test-retest	CP area: ICC = 0.94 (0.81 - 0.98) CP range: ICC = 0.88 (0.55 - 0.96) CP velocity: ICC = 0.84 (0.55 - 0.95) CP velocity max: ICC = 0.8 (0.29 - 0.94)		Korean version, four items of NTX: ICC = 0.84	
Reference	Validity <sup>50</sup> Test-retest reliability <sup>27</sup>	Validity <sup>51</sup> Intra-rater reliability <sup>36</sup>	Validity <sup>52</sup> Test-retest reliability <sup>53</sup>	Validity <sup>41</sup> Intra-rater reliability <sup>54</sup>
-, no studies found; CP, centre of pressure; FACT/GOG-NTX, Functional Assessment of Cancer Therapy/Gynaecologic Oncology Group-Neurotoxicity; ICC, intraclass correlation coefficient; LOS, limits of stability; MDRT, Multi-Directional Reach Test; mTNS, modified TNS; NCI-CTC, National Cancer Institute Common Toxicity Criteria; NTX, neurotoxicity; RMS, root mean square; SOT, Sensory Organisation Test; TNS, Total Neuropathy Score; TUG, Timed Up and Go.				

**Table 3** Conditions tested for postural control assessment with sensory input disturbance

Condition	Eyes	Surface	Vibration	Cognitive task	Altered sensory information	Unaltered sensory information
EO	Open	Rigid	No	No	–	Somatosensory, vestibular, vision
EC	Closed	Rigid	No	No	Vision	Somatosensory, vestibular
EOF	Open	Foam	No	No	Somatosensory	Vestibular, vision
ECF	Closed	Foam	No	No	Somatosensory, vision	Vestibular
EOV	Open	Rigid	Yes	No	Somatosensory	Vestibular, vision
ECV	Closed	Rigid	Yes	No	Somatosensory, vision	Vestibular
DT	Open	Rigid	No	Yes	–	Somatosensory, vestibular, vision

C, close; DT, dual task; E, eyes; F, foam; O, open; V, vibration.

#### Foam surface conditions (EOF, ECF)

A 6 cm high piece of foam (48 × 40 × 6 cm) will be added under participants' feet to modify the proprioceptive feedback (Airex, Airex AG, Sins, Switzerland).<sup>14</sup>

#### Vibration conditions (EOV, ECV)

As the sural triceps are the predominant muscles for standing postural control,<sup>29</sup> vibrators (Vibrasens, Technoconcept, Manosque, France) will be positioned on the Achilles tendons to create an illusion of muscle elongation and disturb the somatoproprioceptive feedback.<sup>30</sup> A frequency of 80 Hz with an amplitude of approximately 0.5 mm will be predefined to allow greater responses.<sup>31</sup> After the test, participants will pause while sitting for 30 s to allow the effects of the vibration to disappear.<sup>32</sup>

#### Dual-task condition (DT)

Participants will be asked to write the following unusual text message on a smartphone while maintaining balance: 'la vache noire saute par-dessus la barrière en métal et mange l'herbe verte',<sup>33</sup> which means 'the black cow jumps over the metal fence and eats the green grass'. This task is a cognitive-motor nonverbal task used in everyday life.<sup>34</sup> Participants will be asked to perform both tasks simultaneously without prioritising either.

#### Dynamic balance

As participants' performance during a quiet stance may not directly correspond to their performance during more dynamic tasks,<sup>35</sup> a LOS test on a force platform will be performed to complete the tests (Biomechanical Force Plate Systems type 9260AA6, Kistler Instrument AG, Winterthur, Switzerland). Participants, standing on the force platform with arms at their sides, will bend as far as possible in four directions (anterior, posterior, right and left) without falling. They will be asked not to bend their hips during the test and not to lift any part of their feet off the platform.<sup>36</sup> The position will be systematically controlled and corrected by the assessor. Participants will perform this procedure three times, and the average of the three trials will be recorded.<sup>36</sup> The recorded parameters will be the same as those for standing postural control. Prior, participants will practise by performing two unrecorded tests in each direction to avoid learning

bias.<sup>37</sup> If the test is stopped in case of balance loss, the participants may retry the test a maximum of five times.

#### Quality of life

The FACT/GOG-NTX questionnaire will assess physical (0–28 points), social/family (0–28 points), emotional (0–24 points) and functional (0–28 points) well-being and other areas of concern (0–44 points) corresponding to the specific components of neurotoxicity to obtain subscores and a total score. This questionnaire's good clinimetric qualities support its use for assessing the negative consequences of chemotherapy and their impact on patients' QoL.<sup>38</sup> Moreover, this questionnaire was validated in French in a previous study.<sup>39</sup> The participants will respond to the different statements on a scale between 0 (not at all) and 4 (a lot), considering the previous seven days.

#### CIPN assessment

The mTNS is a component score from 0 to 24 used to accurately classify CIPN.<sup>17 40</sup> The score is composed of the following components: patient-reported sensory and motor symptoms, superficial sensitivity, vibratory sensitivity, strength and tendon reflexes.<sup>41</sup> Each component is individually scored on a scale between 0 (no symptoms) and 4 (most severe symptoms; table 4).<sup>42</sup> The final score is obtained by summing the various components. A score below 9 indicates mild CIPN, between 9 and 16 moderate CIPN, and above 16 severe CIPN.<sup>40</sup>

#### Sensory and motor symptoms

Participants will be asked if they experienced sensory (tingling, pins and needles, pain, burning) or motor (weakness, numbness, mobility) symptoms in the last seven days.<sup>43</sup>

#### Superficial sensitivity

The superficial sensitivity will be tested with a cotton swab cut at the tip to make it protrude as carried out by Smith *et al*<sup>44</sup> and easily performed in the clinic.<sup>44</sup> The different areas to be tested are as follows: the dorsal aspect of the hallux interphalangeal joint, medial malleolus, antero-inferior part of the leg, patella, anterosuperior part of the thigh, fingertips, dorsal surface of the hand, head of the

**Table 4** Parameters assessed in the modified Total Neuropathy Score

Parameters	Score				
	0	1	2	3	4
Sensory symptoms	None	Symptoms limited to fingers or toes	Symptoms extend to the ankle or wrist	Symptoms extend to the knee or elbow	Symptoms above the knee or elbow or functionally disabling
Motor symptoms	None	Slightly difficult	Moderately difficult	Require help/assistance	Paralysis
Superficial sensitivity	Normal	Reduced in fingers or toes	Reduced up to the wrist or ankle	Reduced up to the elbow or knee	Reduced to above the elbow or knee
Vibratory sensitivity	Normal	Reduced in fingers or toes	Reduced up to the wrist or ankle	Reduced up to the elbow or knee	Reduced to above the elbow or knee
Strength	Normal	Mild weakness (MRC 4)	Moderate weakness (MRC 3)	Severe weakness (MRC 2)	Paralysis (MRC 0–1)
Reflexes	Normal	Ankle reflex reduced	Ankle reflex absent	Ankle reflex absent, others reduced	All reflexes absent

Adapted from Cavaletti *et al.*<sup>42</sup>  
MRC, Medical Research Council.

ulna, lower-anterior part of the forearm, olecranon and the anterosuperior part of the arm. Participants will be asked whether they feel the stimulation.<sup>44</sup> The tests will be conducted distally to proximally.<sup>44</sup>

#### Vibratory sensitivity

A Rydel-Seiffer 128 Hz tuning fork will measure vibration sensitivity. Participants will be asked to close their eyes and indicate when they can no longer feel the vibration.<sup>44</sup> Vibration sensitivity will be considered normal if they score 7 or 8.<sup>43</sup> The tuning fork will be placed in the same areas as the superficial sensitivity test.<sup>44</sup>

#### Muscular strength

The muscular strength of the toe extensors/flexors, tibialis anterior, sural triceps, quadriceps and hamstrings will be tested for the lower limbs with manual muscle testing (from 0 = no visible contraction to 5 = normal strength).<sup>45</sup> For the upper limbs, the flexor/extensor muscles of the fingers, flexor/extensor muscles of the wrist, and flexor/extensor muscles of the elbow will be selected.<sup>42</sup> The muscle with the worst score will be retained.<sup>42</sup>

#### Tendon reflexes

A reflex hammer will assess the Achilles, patellar, biceps and triceps brachii tendons. They will be scored as normal, reduced, or absent.<sup>42</sup>

#### Monitoring

As this study presents no more risks than the usual patient care in an oncological context, only internal monitoring is planned to ensure that participants' rights and welfare are respected, that the reported data are accurate and verifiable from the source documents, and that the study is conducted per the protocol, procedures and applicable regulations.

#### Withdrawal and discontinuation

Participants will be free to withdraw from the study at any time. The criteria for participant withdrawal will be a deterioration of medical stability, a procedure being stopped for safety reasons, and the withdrawal of informed consent. All data collected before that point will be considered in the analyses.

Each adverse event will be registered and reported to medical staff throughout the procedure.

#### Statistical analysis

Statistical analysis will be performed with the Stata V.15 software package (StataCorp, Texas, USA, 2017).

#### Sample size calculation

Sample size calculation was performed using the G\*Power V.3.1 software package and a two-sided *t*-test for paired data (HHU Düsseldorf, Germany, 2017).<sup>46</sup> With the significance level set at 0.05, a power of 90%, and an effect size of 0.61, the number of participants required for this study is 31. The assumption of the effect size is based on a previous study that evaluated the effect of chemotherapy on postural control, which found mediolateral RMS CP values of  $3.3 \pm 1.1$  mm at the baseline and  $4.3 \pm 1.9$  mm at the last follow-up after chemotherapy.<sup>16</sup> We assume a correlation of 0.5 between the baseline and the last follow-up. With a conservative assumption that this correlation is null, the power is still 89% for detecting a mean difference of 1.3 mm in CP RMS ( $3.3 \pm 1.1$  mm at the baseline and  $4.6 \pm 1.9$  mm at the last follow-up) with the calculated sample size.

We anticipate a 16% drop-out rate as occurred in a study with a similar population<sup>35</sup>; therefore, 37 participants should be included to reach the 31 participants

according to the following calculation:  $(1 / (1 - 0.16)) = 1.19$ , so  $1.19 \times 31 = 37$  participants.

### Data management

The study data will be collected and managed using Research Electronic Data Capture (REDCap) tools hosted at HES-SO.<sup>47</sup> The data will be backed up frequently.

### Data treatment

All CP data from the postural control tests will be treated with a fifth-order low-pass Butterworth filter at 30 Hz before being analysed.

### Descriptive statistics

Participants' clinical data will be described in terms of demographic, medical and lifestyle information. Qualitative variables will be expressed in frequency, while continuous variables will be expressed via the mean and standard deviation.

### Statistical analysis

#### Primary outcome

To compare the postural control pre-chemotherapy and post-chemotherapy, a linear mixed model with a random effect on the intercept due to the participant cluster will be performed. The primary analysis will compare the mediolateral RMS of the CP adjusted for the conditions tested and potential confounding factors. In this model, the dependent variable will be the CP RMS under the seven conditions (i.e., EO, EC, EOF, ECF, EOv, ECV, DT) and pre–post. The independent variables will be the conditions tested, the periods (pre–post), and potential confounding factors (i.e., smoking status, age, body mass index).

In the secondary analysis of the primary outcome, a modification of the pre–post differences across the conditions tested will be investigated. For this purpose, an interaction term between the conditions and pre–post will be added to the previous model.

#### Secondary outcomes

1. The other postural control parameters will be analysed using similar methods for the primary outcome.
2. Similar methods will be used to analyse the LOS parameters and the QoL total score.
3. The association between the severity of CIPN (i.e., mild, moderate, severe) and the pre–post change in postural control (CP parameters) will be investigated in two specific conditions (where postural control was most affected by chemotherapy) using linear regression models with mixed effects (one model per condition). An interaction term between the severity of CIPN (i.e., mild, moderate, severe) and pre–post will be introduced to the model. The model will be adjusted for potential confounding factors (i.e., smoking status, age, body mass index).

The conditions of application of each model will be verified. A threshold value of  $p < 0.05$  will be adopted for statistical significance. All statistical tests will be two-sided.

### Patients and public involvement

Patients and public involvement were not applied in this project. However, oncology clinicians were included in the conception and design of the study since the project is a co-production between researchers and clinicians.

### ETHICS AND DISSEMINATION

#### Recruitment and consent

All participants will give their written consent.

#### Amendment

Each significant amendment to the protocol will be communicated to all relevant parties after approval is received from the ethics committee.

#### Data collection, storage and access

Data will be de-identified and stored in a secure folder and electronic database. Only the investigators and the statistician will have access to the final dataset.

#### Dissemination strategy

Outcomes will be disseminated through publications in peer-reviewed journals and presentations at international conferences. Data will be available on request with reasonable justification.

### DISCUSSION

This observational study aims to improve the knowledge of the objective characterisation and underlying causes of CIPN-related postural control dysfunction.<sup>3</sup> It will incorporate a comprehensive postural control assessment with various visual and somatosensory disturbance test conditions. This study should also provide more information about stability limits. Currently, few data are available on patients with CIPN regarding how far they can move without falling or disturbing their balance.<sup>48</sup>

An improved understanding of postural control dysfunctions will help determine the value of systematic screening for these disorders after chemotherapy and identify the most relevant tests to use according to the test conditions affected by chemotherapy. In addition, it could help establish the interest of setting up personalised exercises. CIPN management remains challenging for the oncology team because therapeutic options for restoring or maintaining patients' function have not been thoroughly delineated.<sup>49</sup> Whereas structured exercise programmes have provided promising results on CIPN functional consequences, the modalities and content remain to be determined.<sup>49</sup> Thus, an improved understanding of the mechanisms linked to postural control impairments and coping strategies for maintaining balance after chemotherapy is required to offer specific physical activity programmes and alleviate the negative consequences of postural control disorders in patients' daily lives.

This study has limitations. The comprehensive postural control assessment, including different test conditions as well as a subjective and objective evaluation of CIPN,<sup>3</sup> will

take time. The whole study procedure will last 75 min, so participants may experience fatigue. However, the order of the tests will be randomised, and breaks will be planned to limit the impact of fatigue.

Furthermore, the study population will be limited to women aged under 65 years with gynaecological cancer treated with taxanes and without pre-existing disorders affecting postural control. Therefore, study's results may not apply to older patients who are undergoing other treatments or who have comorbidities.

Despite these limitations, the results should contribute to new scientific knowledge to further understand chemotherapy-related postural control disorders.

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