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Data Article

Dataset on the quality of life and neurocognitive effects of prophylactic cranial irradiation, with and without hippocampal avoidance, in small-cell lung cancer patients

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ABSTRACT

This article presents data collected from 15 patients diagnosed with small-cell lung cancer who received prophylactic cranial irradiation (PCI), with or without hippocampal avoidance. Patient assessments included two specific questionnaires related to quality of life and an extensive neurocognitive evaluation. The evaluation covered various domains: verbal short-term memory, working memory, visuoconstructive abilities, visuospatial memory, semantic memory, verbal fluency, cognitive flexibility, inhibitory control, selective and divided attention, and processing speed. Assessments were conducted prior to PCI and at 3, 6, 12, and 24 months post-treatment.

Despite the limited sample size due to challenges in patient recruitment and comprehensive follow-up, the data presented may help to identify the neuropsychological domains most affected in this population and can be useful in the design of future larger-scale studies. At present, there is limited information regarding the neuropsychological profiles of these patients and most studies focus on only one or two

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neuropsychological domains, typically emphasizing working memory assessments.

Specifications Table

Subject	Health Sciences – Radiotherapy - Neuropsychology.
Specific subject area	Quality of life and Neurocognitive effects of prophylactic cranial irradiation
Type of data	Data format: Raw Table (.csv format) Supporting materials (codebook .csv format).
Data collection	Data were collected by a specialized neuropsychologist at the Hospital Sant Joan de Reus, Spain. The reference hospital's oncologist asked patients to participate in the data collection, and they were scheduled for assessments before treatment and at 3, 6, 12, and 24 months later. All tests were administered in the same order and at the same location to avoid unexpected sources of variability.
Data source location	Country: Spain; Province: Tarragona
Data accessibility	Repository name: Mendeley Data Data identification number: 10.17632/3vx6xsf8kz.1 Direct URL to data: https://data.mendeley.com/datasets/3vx6xsf8kz/1
Related research article	None.

1. Value of the Data

- The data presented in this article are valuable given the challenge of collecting such extensive information from patients with this type of cancer. Studies involving cancer patients often experience high experimental attrition.
- Currently, there are no data on such comprehensive assessments of neurocognitive performance in these patients, particularly in relation to different therapeutic options. The neurocognitive assessments conducted provide valuable insights into the areas most likely to be affected in patients undergoing radiotherapy.
- The data can be reused to calculate the sample size needed for larger studies or incorporated into other databases, allowing for more robust and comprehensive statistical analyses. Given that such studies are typically expensive and pose clear ethical implications, data sharing is considered best practice and can significantly contribute to advancing knowledge in this field.
- Additionally, the dataset includes information on patients' quality of life over a two-year period. This data could be useful for identifying the domains most frequently impacted.
- The data could also be useful for generating hypotheses in exploratory studies, particularly given the rarity of such comprehensive neuropsychological evaluations in patients with limited life expectancy. These datasets can help identify early trends or patterns in neurocognitive decline, which might inform future research designs or therapeutic interventions for similar populations.

2. Background

Patients with small cell lung cancer (SCLC) are at a high risk of developing brain metastases. Prophylactic cranial irradiation (PCI) is recommended for this population to reduce the incidence of brain metastases and to improve overall survival. In this context, PCI is considered

the standard of care for patients with limited-stage SCLC, while its use in extensive-stage disease remains a topic of ongoing debate [1]. However, PCI is associated with a significant risk of neurocognitive decline, particularly in verbal memory performance, and has been linked to whole-brain volume loss [2,3]. Various strategies have been proposed to mitigate this risk, such as hippocampal avoidance (HA) during PCI, but previous studies have yielded inconsistent results [4]. Furthermore, PCI has been shown to negatively impact patients' quality of life. The challenge of conducting comprehensive cognitive assessments, coupled with high attrition rates in these studies, has led to a significant gap in our understanding of the neuropsychological profile and quality-of-life progression in these patients. The present data aim to guide the design of future studies in this field and contribute to bridging this knowledge gap.

3. Data Description

The files associated with this data-in-brief article include:

(1) The raw data from the tests in .csv file format (Dataset_Neuroonco.csv). The file contains six variables related to demographic data and experimental design (Subject, Sex, Age, Years of Schooling, Group, and Month). Moreover, it also contains the data collected from neuropsychological tests, encompassing 46 variables (see Table 1).
(2) The codebook in .csv format (Codebook_Neuroonco.csv), which includes information about variable labels, their codifications, ranges, units, and notes to better understand the conditions under which the data were collected.

The dataset comprises the assessments of 15 patients suffering SCLC. They are divided into two groups depending on the type of radiotherapy received (without or with hippocampus avoidance; PCI and HA-PCI respectively). The initial number of participants were nine for PCI and six for HA-PCI groups. In the subsequent assessments at 3, 6, 12, and 24 months, the number of participants decreases due to attrition and mortality. Additionally, the dataset includes various descriptive variables about the participants, specifically sex, age, and years of education.

4. Experimental Design, Materials and Methods

4.1. Experimental design and participants

Adult patients ($\geq$ 18 years of age) with confirmed histologic or cytologic diagnoses of SCLC (limited disease or extensive disease without brain metastases) candidate for PCI were eligible and randomly assigned 1:1 to receive HA-PCI or PCI. Eligibility criteria were as follows:
Inclusion criteria:

- Karnofsky Index $\geq$ 80%.
- Negative brain MRI within one month of enrollment.
- Able to give informed consent.

Exclusion criteria:

- Prior radiotherapy to the brain.
- Brain metastases or primary brain tumors.
- Evidence of progressive extracranial metastatic disease.
- Previous malignancy $<$ 5 years ago except for adequately treated basal cell carcinoma of the skin and carcinoma in situ of the cervix.
- Any systemic anticancer treatment during PCI or within 3 weeks before start PCI.
- Pregnant women or women of childbearing potential who are sexually active and not willing or able to use medically acceptable forms of contraception.

Table 1
Tests and neurocognitive variables included in the dataset.

TEST	VARIABLE
Digit span test (Barcelona test II)	Digits forward
	Digits backward
Rey-Osterrieth Complex Figure	Time of copy
	Quality of copy
	Inmediate recall
	Delayed recall
	Recognition
Free and cued selective reminding test	Free recall first assay
	Total free recall
	Total recall
	Total delayed free recall
	Total delayed free and cued
Fluency test (Barcelona test II)	Semantic fluency
	Phonological fluency
Trail making test	Part A
	Part B
Symbol digit modalities test	SDMT
Stroop color and word test	Word
	Color
	Word-Color
Brain cancer module (QLQ)	Future uncertainty
	Vision disorder
	Motor dysfunction
	Communication deficit
	Headache
	Seizures
	Drowsiness
	Hair loss
	Pruritus
	Leg weakness
	Bladder
EORT QLQ-C30	Physical
	Rol
	Emotional
	Cognitive
	Social
	Global quality of life
	Fatigue
	Pain
	Nausea and vomiting
	Sleep disturbance
	Dyspnea
	Appetite loss
	Economical impact
	Constipation
	Diarrhea

Patients and radiation oncologist was not blinded to treatment condition, however, the neuropsychologist who scored the neurocognitive tests was masked. The Protocol was approved by the ethical committee of Hospital Universitari Sant Joan de Reus (14-7-31/7obs3) and all participants gave their voluntary participation consent.

4.2. Radiation simulation and treatment

Patients underwent a cranial computed tomography (CT) scan for treatment planning while immobilized. Within one month of initiating the study, each patient had a high-resolution, three-dimensional T1-weighted post-gadolinium MRI brain scan to determine their eligibility for the study. This MRI was then coregistered with the simulation CT scan. The hippocampus and

the hippocampal avoidance structure (defined as the hippocampus with a 5-mm radial expansion) were delineated according to the contouring atlas for RTOG 0933 [5]. The clinical target volume included the entire brain, while the planning target volume was created by expanding the clinical target volume by 5 mm, excluding the hippocampal avoidance zone (HAZ) in the experimental arm.

Patients received a total dose of 25 Gy, delivered in 2.5 Gy fractions, administered five days a week. For the HA-PCI group, a volumetric modulated arc therapy (VMAT) plan was developed.

4.3. Neurocognitive function and quality of live assessments

The following tests were administered in the same order prior of the irradiation and 3, 6, 12, and 24 months later.

Digit Span test from NEURONORMA project: Digit Span test is an assessment tool designed to evaluate verbal short-term and working memory, available in two formats: Forward Digit Span and Reverse Digit Span. This verbal task involves auditory presentation of stimuli, with participants responding verbally. During the task, participants receive a sequence of digits and are instructed to repeat them either in the order they were presented (forward span) or in reverse order (backward span). Although these tasks may appear quite similar, they engage different cognitive processes. The forward span task primarily assesses verbal working memory and attention, whereas the backward span task also evaluates cognitive control and executive functioning [6,7].

Rey-Osterrieth complex figure: The Rey–Osterrieth complex figure test is used to assess perceptual organization, visuocontructive abilities, and visuospatial memory. This test also implies executive functions as it requires the subject to plan how to best copy the complex figure. In this test, subjects have to copy a detailed drawing first and then reproduce it from memory (3 min after copying it). Approximately 30 min later, subjects draw the figure again from memory. Finally, after the Delayed Recall trial, a recognition response sheets with some designs included in the larger figure are presented and participant must recognize the correct answers. In copy and recall stages of the test, two measures of performance were recorded: quality of copy (range of possible scores = 0–36), which reflects the accuracy of reproduction of the original figure and it is a measure of visuoconstructive abilities, and the amount of time taken in the reproduction process. The score in the recognition phase ranges from 0 to 24 [8,9].

Free and cued selective reminding test (FCSRT): The Free and Cued Selective Reminding Test (FCSRT) is a commonly utilized assessment tool designed to differentiate the various processes involved in new memory formation. It was be developed and validated by Peña-Casanova et al. [6] and Tamayo et al. [7]. This test aims to evaluate whether memory deficits impact the consolidation phase by implementing a learning paradigm that encourages deep semantic processing of words. Initially, participants are tasked with categorizing words into predefined semantic groups. Subsequently, these category cues are employed to aid the recall of items that were not retrieved through free recall. This approach allows to discern whether memory impairment arises from issues with consolidation or other influences, such as inattention during the word presentation or difficulties in retrieving previously consolidated information via free recall. The assessment consists of five distinct phases: (1) reading and identifying words, (2) an interference task (counting backward by threes for 20 s to prevent subvocal repetition), (3) free recall, (4) cued recall and (5) a delayed free and cued recall after 30 min. Phases II to V are repeated three times throughout the learning process.

Fluency test from NEURONORMA project: The categorical evocation and verbal fluency subtests of the NEURONORMA project [10,11] are used to assess the verbal fluency variable. The test is divided into two parts: the semantic verbal fluency test, which requires the participant to name as many animals as they can within 1 min, and the verbal phonological fluency test, which requires the participant to produce as many words as they can beginning with the letter "p" within 1 min. These two tests involve executive function, which means they require participants to put the processes underlying vocabulary development (semantic-lexical memory) into

operation. The total number of correct answers (correct name of an animal or real word that starts with P) was recorded for both parts of the test.

Trail making test (TMT): The Trail Making Test (TMT) [6,7] is one of the most widely utilized neuropsychological assessments and consists of two subtests: TMT-A and TMT-B. In TMT-A, participants are instructed to draw a line connecting the numbers 1 to 25, which are randomly arranged on a sheet, in the correct ascending order as quickly as possible. In TMT-B, participants must alternate between numbers and letters while following the alphabetical sequence. The score is measured in seconds taken to complete the task, with longer times indicating poorer attentional capacity. TMT-B is related also with cognitive flexibility and working memory performance.

Symbol digit modalities test (SDMT): The Symbol Digit Modalities Test (SDMT) [6,7] is a short, easily administered cognitive test which exists in both written and oral forms, of which the written form is used in the cognitive assessments. The participant is presented with a coding key of nine geometrical symbols, each representing a digit. After an initial 10 trial practice period, the subject is asked to recode as many symbols into digits as possible in 90 s using the key. The score is one point per correct digit, and the maximum result is 110 points. The performance in this test is related to divided attention, visual scanning and processing speed.

Stroop color and word test: The Stroop test is used to assess mental flexibility and inhibitory control [12,13]. For each participant, the total number of correct answers for each condition within 45 s (P: word, C: color naming, and PC: word-color interference) was recorded. Scores in the P and C conditions are related to processing speed. Scores in the PC condition is related to mental flexibility and inhibitory control.

Brain cancer module (QLQ-BN20): The QLQ- BN20 brain tumor module is a questionnaire to evaluate the effects of the tumor and its treatment on symptoms, functions and health-related quality of life of brain tumor patients. It was developed and validated by Osoba et al. [14] and consist in 20 items assessing the following disturbances: worry about future uncertainty, vision disorder, motor disfunction, communication deficit, headache, seizure, drowsiness, hair loss, pruritus, leg weakness and bladder disturbances. The items of the questionnaire can be accessed at https://qol.eortc.org/questionnaire/qlq-bn20/.

EORT QLQ-30: The EORTC QLQ-C30 is a comprehensive instrument designed by Aaronson et al. [15] to evaluate the quality of life of cancer patients. This 30-item questionnaire focuses on various dimensions of health-related quality of life, capturing both the physical and psychological impacts of cancer and its treatment. The questionnaire includes 15 variables related to possible disturbances: Physical, Rol, Emotional, Cognitive, Social, Global quality of life, Fatigue, Pain, Nausea and vomiting, Sleep disturbances, Dyspnea, Appetite loss, Economical impact, Constipation and Diarrhea. It was developed by the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Group, drawing from over a decade of research. The items of the questionnaire can be accessed at https://qol.eortc.org/questionnaire/eortc-qlq-c30/.

Limitations

The main limitation of the dataset is the high rate of experimental attrition recorded due to the severity of the participants' pathology.

Ethics Statement

Protocol was approved by the ethical committee of Hospital Universitari Sant Joan de Reus (reference number: 14-7-31/7obs3). The procedures used in this study adhere to the tenets of the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

Data availability

Dataset on the Impact of Prophylactic Cranial Irradiation, with and without hippocampal avoidance, on Quality of Life and Neurocognitive Function in Small-Cell Lung Cancer Patients (Original data) (Mendeley Data)

CRediT Author Statement

Luis Heredia: Writing – original draft, Writing – review & editing, Data curation; **Mauricio Murcia-Mejía:** Methodology, Investigation, Writing – review & editing; **Margarita Torrente:** Methodology, Investigation, Supervision, Writing – review & editing.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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