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ORIGINAL RESEARCH

Investigating the Analgesic Mechanisms of Acupuncture for Cancer Pain: Insights From Multimodal Bioelectrical Signal Analysis

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Purpose: Cancer pain management remains a significant clinical challenge. While acupuncture has shown potential in alleviating cancer pain, its underlying mechanisms are not yet fully understood. This study investigates the neurophysiological mechanisms underlying acupuncture's analgesic effects using multimodal bioelectrical signal analysis.

Patients and Methods: Fifteen cancer pain patients underwent acupuncture while wearing portable, multi-sensor devices to capture bioelectrical signals. Pain levels were assessed using the Numerical Rating Scale (NRS) before and during needle retention. Neurophysiological changes were evaluated using Principal Component Analysis, Joint Time-Frequency Analysis, power spectrum analysis, spectral analysis, and dynamic functional network analysis.

Results: There was a significant reduction in NRS scores from pre-treatment to the retention period, indicating pain relief. Principal component analysis showed significant differences in bioelectrical signals between these periods. Power spectrum analysis revealed decreased signal power during retention. Functional network analysis demonstrated a reduction in connectivity strength between electroencephalography and electromyography signals. Spectral analysis identified distinct real-time and staged characteristics of bioelectrical signals, with correlation analysis confirming a positive relationship between NRS score changes and bioelectrical signal alterations.

Conclusion: Acupuncture alleviates cancer pain by reducing functional connectivity between injured tissues and the brain, with immediate effects. Prolonging needle retention may enhance therapeutic outcomes. These findings provide new insights into the neurophysiological basis of acupuncture's analgesic effects, supporting its role in cancer pain management.

Keywords: cancer pain, acupuncture, multimodal bioelectrical signals, analgesic mechanism, deep learning

Introduction

Cancer pain is a complex and multifaceted condition, resulting from a combination of inflammatory, neuropathic, and cancer-specific mechanisms.[1,2] It can manifest at any stage of the disease, with over 70% of cancer patients experiencing pain during their illness. Even within the first three months following successful cancer treatment, the incidence of pain remains as high as 36%.[3] Moreover, with the increasing variety of cancer treatment modalities, persistent pain caused by therapeutic interventions has become more common.[4] Cancer pain not only adversely impacts emotional well-being and cognitive function but also significantly diminishes quality of life, contributing to reduced survival rates.[5] While the World Health Organization's three-step analgesic ladder offers a structured approach to cancer pain management, nearly

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half of patients still report inadequate pain control.[6] Additionally, the ongoing opioid crisis complicates pain management decisions, underscoring the need for alternative therapies.[7]

Acupuncture has a long history of use in pain management due to its efficacy, ease of application, and minimal side effects. It provides a holistic approach by modulating pain sensation, emotional responses, and pain cognition.[8,9] Since the early 20th century, acupuncture has been employed as an adjunct to anesthesia in various surgical procedures. For example, when the acupuncture - drug combined anesthesia technique was used in conjunction with tracheal intubation, the intraoperative usage of sufentanil was reduced by approximately 20%. In cardiac surgeries without tracheal intubation under acupuncture - drug combined anesthesia, only about 30% of the anesthetic dosage required for conventional tracheal intubation was needed.[10] In cancer pain management, acupuncture has demonstrated efficacy in alleviating both tumor-related pain and pain associated with treatments like chemotherapy and radiotherapy. This analgesic effect is also associated with a reduced reliance on conventional analgesics.[11,12] Moreover, over 47.9% of cancer patients are willing to undergo acupuncture therapy.[13] Despite these promising results, the underlying physiological mechanisms of acupuncture's effect on cancer pain remain incompletely understood, leading to ongoing debates about its routine clinical use.

Electrophysiological processes play a crucial role in the development and perception of cancer pain. As cancer cells invade surrounding tissues, nociceptive signals are transmitted to the central nervous system, resulting in pain perception.[14] Acupoints, which possess specific electrical properties, have been shown to regulate bioelectrical imbalances in injured tissues, thereby exerting analgesic effects.[15] For example, electroacupuncture has been found to alleviate pain by reducing Na^+ channel currents in animal models,[16] and stimulation of the "Zusanli (ST36)" acupoint has been shown to reduce acid-sensing ion channel currents, alleviating mechanical hyperalgesia.[17] Moreover, another study proposes a hypothesis that electroacupuncture exerts an analgesic effect by inhibiting the activity of wide-dynamic-range neurons, which are induced by C-fibers in the trigeminocervical complex. This mechanism regulates the transmission of migraine pain signals from the periphery to the central nervous system.[18] This indicates that electroacupuncture's analgesic effects are multifaceted, involving distinct physiological pathways at both cellular and neural levels. However, there is a lack of clinical studies exploring the electrophysiological mechanisms of acupuncture in cancer pain management.

Electroencephalography (EEG) has been used to examine the neural mechanisms of pain perception in the human brain,[19] while electromyography (EMG) measures pain-related changes in muscle activity, including altered amplitude, frequency, and waveforms.[20] Skin electrical activity (EDA) is another indicator of pain response, capturing rapid changes in electrical conductivity during painful stimuli.[21] Despite the insights provided by each bioelectrical signal, limitations remain due to variations in sampling frequency and application contexts, making it difficult to capture comprehensive pain-related information.[22]

In recent years, remarkable breakthroughs have been made in deep learning. Advanced neural network architectures, such as the Transformer, have emerged continuously. Meanwhile, multimodal fusion technology has been developing steadily and can integrate various types of data more efficiently. These technological advancements enable the seamless integration of multimodal information, such as text, images, and bioelectrical signals, bringing hope for overcoming the challenges in acupuncture analgesia research. For example, researchers can leverage multimodal fusion technology to integrate EEG and EMG data, comprehensively understanding changes in brain neural activities, muscle responses, and the brain regions related to pain perception during acupuncture.[23] Significantly, multimodal fusion not only facilitates the data integration process but also enhances the accuracy and depth of analysis, thereby allowing for a more comprehensive understanding of the mechanisms behind acupuncture's analgesic effects.[24] This study utilizes portable, wearable multi-sensor devices to record a combination of EEG, electrooculogram (EOG), EMG, and EDA signals, coupled with advanced bioelectrical signal analysis. The primary objective is to elucidate the neurophysiological mechanisms through which acupuncture alleviates cancer pain, using a medico-engineering integration approach. Ultimately, this research aims to contribute to a deeper understanding of cancer pain management and advance the therapeutic use of acupuncture.

Materials and Methods

Study Design

This study employed a single-group, pre- and post-treatment observational design at the Shenzhen Traditional Chinese Medicine Oncology Center. The objective was to assess the neurophysiological effects of acupuncture on cancer pain using multimodal bioelectrical signal analysis. The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Guangzhou University of Chinese Medicine Shenzhen Hospital (Futian) (Approval number: GZYLL(KY)-2023-020-01). All participants provided informed consent before inclusion in the study. The trial was registered with the International Traditional Medicine Clinical Trial Registry (ITMCTR2024000225).

Eligibility Criteria

Inclusion Criteria

(1) Patients with malignant tumors, confirmed by pathological examination;
(2) Patients who had received standardized pharmacological treatment for 1–2 weeks but continued to experience inadequate pain control or intolerable side effects, with an
(3) NRS score ≥4 or suffering from breakthrough pain at least three times per day;
(4) Participants aged 18 years or older;
(5) Patients capable of providing informed consent.

Exclusion Criteria

(1) Patients with communication difficulties or impaired consciousness;
(2) Patients unwilling to undergo acupuncture as an adjunct analgesic therapy;
(3) Patients with severe infections or organ dysfunction, particularly involving the liver or kidneys;
(4) Patients with non-removable electronic devices or metallic implants that could interfere with bioelectrical signal collection.

Experimental Device

The Biosignals-Plux multi-channel biosignal acquisition system (PLUX Wireless Biosignals, Portugal) was employed for this study. The system recorded bioelectrical signals across six channels, including one for EEG, two for EMG, one for EDA, and two for EOG. The sampling frequency was set at 1000 Hz. A total of 16 active electrodes were used, with one serving as the reference electrode. EEG sensors were placed bilaterally on the participants' frontal regions, and the reference electrode was positioned behind the ear. EMG sensors were attached to the forearms and calves near the acupuncture points to measure local muscle activity. The EDA sensor, equipped with two electrodes, was placed on the thenar eminence to monitor skin conductance. Horizontal and vertical EOG signals were recorded using electrodes positioned around the left eye. To ensure optimal signal quality, impedance was maintained below 20 kΩ for all electrodes. Disposable electrode patches (Model: 81.1245.21) from Shenzhen Nanbei Pharmaceutical Co. Ltd were utilized during signal acquisition.

Experimental Procedure

The experiment was conducted in a shielded environment to minimize electromagnetic interference from external sources. Participants were instructed to avoid using electronic devices and to remain still during data collection to reduce motion artifacts. Before each session, all bioelectrical signal acquisition devices were rigorously calibrated to ensure measurement accuracy. Additionally, we implemented advanced noise reduction algorithms, including a Butterworth zero-phase bandpass filter (1–150 Hz, 5th order), to eliminate baseline drift and high-frequency noise. Through multiple experimental trials, we systematically optimized the filtering parameters to maximize the signal-to-noise ratio (SNR) for reliable data acquisition. Furthermore, we manually inspected the raw signals post-collection to identify and exclude segments with significant interference, ensuring the integrity of the final dataset. Pain levels were assessed using the validated Numeric Rating Scale (NRS) before and after acupuncture treatment. Participants lay in a supine position with their eyes closed and remained still throughout the bioelectrical signal collection process. Electrode sites were disinfected with 75% alcohol before applying disposable electrode patches. Two minutes of baseline bioelectrical signals were recorded before acupuncture treatment.

The acupuncture treatment protocol followed the "Acupuncture for Cancer Pain: Evidence-Based Clinical Practice Guidelines".[25] The selected acupoints included Hegu (LI4), Taichong (LR3), ST36, Sanyinjiao (SP6), Yanglingquan (GB34), and Ashi points bilaterally. After disinfection, sterile disposable needles (0.3 mm × 40 mm) were inserted to a depth of 20–25 mm at each acupoint. Standardized acupuncture manipulation, including uniform lifting, thrusting, and twisting, was performed for 1 minute at each acupoint until participants reported the "acupuncture sensation". The needles were retained for 20 minutes. Following the treatment, pain levels were reassessed using the NRS, and an additional two minutes of bioelectrical signals were recorded to capture post-acupuncture changes. The entire acupuncture treatment procedure was performed by an experienced practitioner to ensure consistency and accuracy (Figure 1a–d).

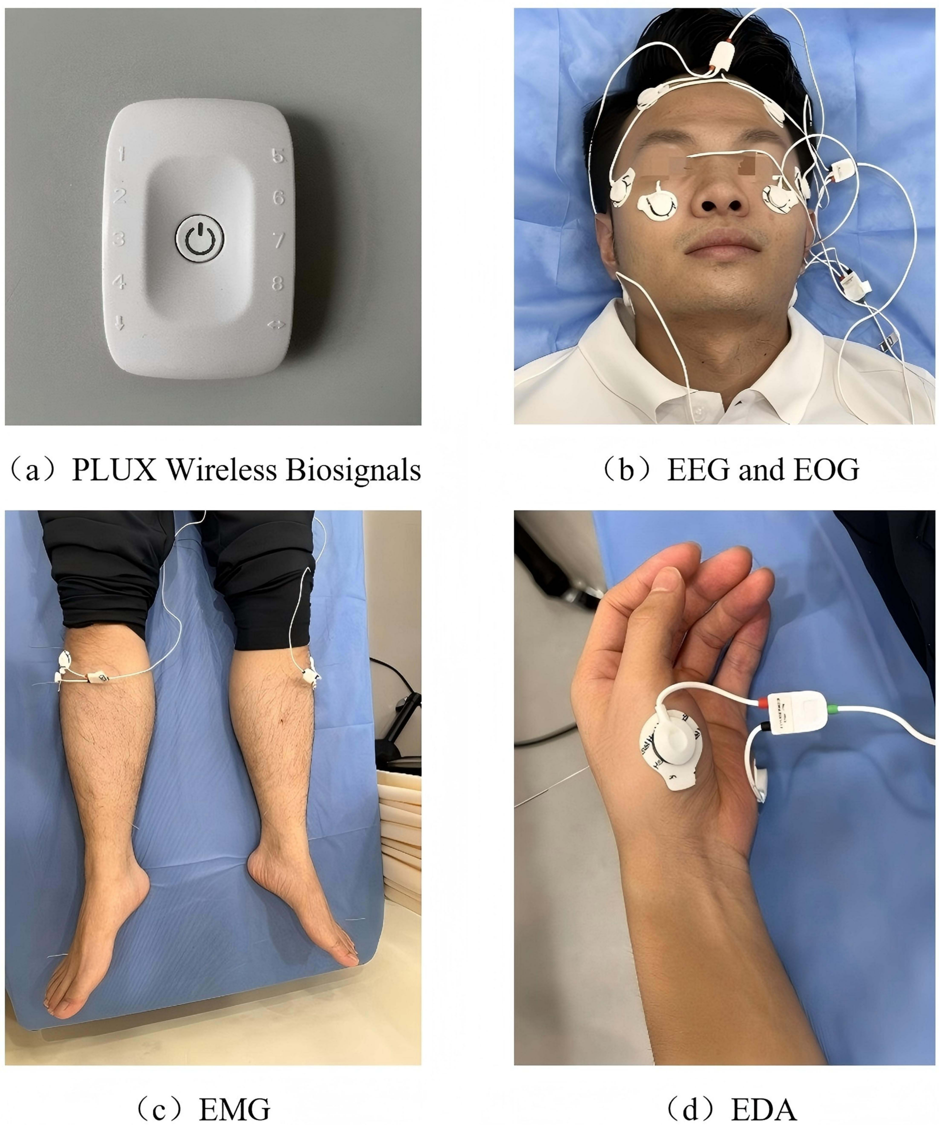

Figure 1 Multi-channel bioelectrical signal acquisition in cancer pain acupuncture using PLUX Wireless Biosignals. Figure (**a**) demonstrates the Biosignals-Plux multi-channel biosignal acquisition system. Figure (**b**) presents the electrode placement for EEG and EOG: the EEG sensors are bilaterally attached to the frontal regions of the participants, with the reference electrode positioned behind the ear; EOG records horizontal and vertical electro-oculogram signals via electrodes around the eyes. Figure (**c**) shows the placement of the EDA sensor, where its two electrodes are attached to the thenar eminence of the hand to monitor skin conductance. Figure (**d**) illustrates the attachment positions of EMG sensors—electrodes are placed on the forearms and calves (near acupoints) to measure local muscle activity.

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Written informed consent was obtained from the individual depicted in Figure 1b for the publication of their image. After the acupuncture treatment, we conducted a comprehensive quality assessment of the data from each subject. For data with an extremely low signal - to - noise ratio, severe data loss, or a large number of outliers, we carried out further analysis to determine whether they were unusable due to signal interference. Only the data that passed the strict quality assessment were included in the subsequent analysis.

Signal Analysis

Bioelectrical signals were continuously collected from 23 patients across four distinct phases: before acupuncture treatment, during manual needling, during the needle retention period, and post-acupuncture treatment. Signal collection was conducted using six channels. As illustrated in Figure 2, we analyzed the median power and Principal Component Analysis (PCA) results from the signals recorded before acupuncture treatment and during the retention period. Subsequently, the power spectrum, functional connectivity, and Joint Time-Frequency Analysis (JTFA) were calculated from the fused signals.

The median power represents the frequency at which the total power in a defined window is equally divided into two parts, ensuring equal power in both parts of the spectrum.[26] This provides a key indicator of the signal's central frequency components. The power spectrum analysis offers a detailed view of how the power of bioelectrical signals is distributed across different frequency components, which is essential for understanding variations in signal activity across time.

The application of PCA aimed to reduce the dimensionality of the bioelectrical signals, highlighting key features while removing noise to enhance signal clarity. PCA helps isolate the most significant components of the data, making it easier to interpret the results.

JTFA was used to visualize how the power spectrum of the bioelectrical signals changes over time. This graphical representation captures both the time and frequency domains simultaneously, providing a comprehensive view of signal dynamics during acupuncture treatment.

Functional connectivity refers to the temporal correlation between neurophysiological activities occurring in spatially distinct brain regions. By analyzing functional connectivity, we assessed the strength of connections between different areas of the brain and muscles, particularly focusing on changes induced by acupuncture.

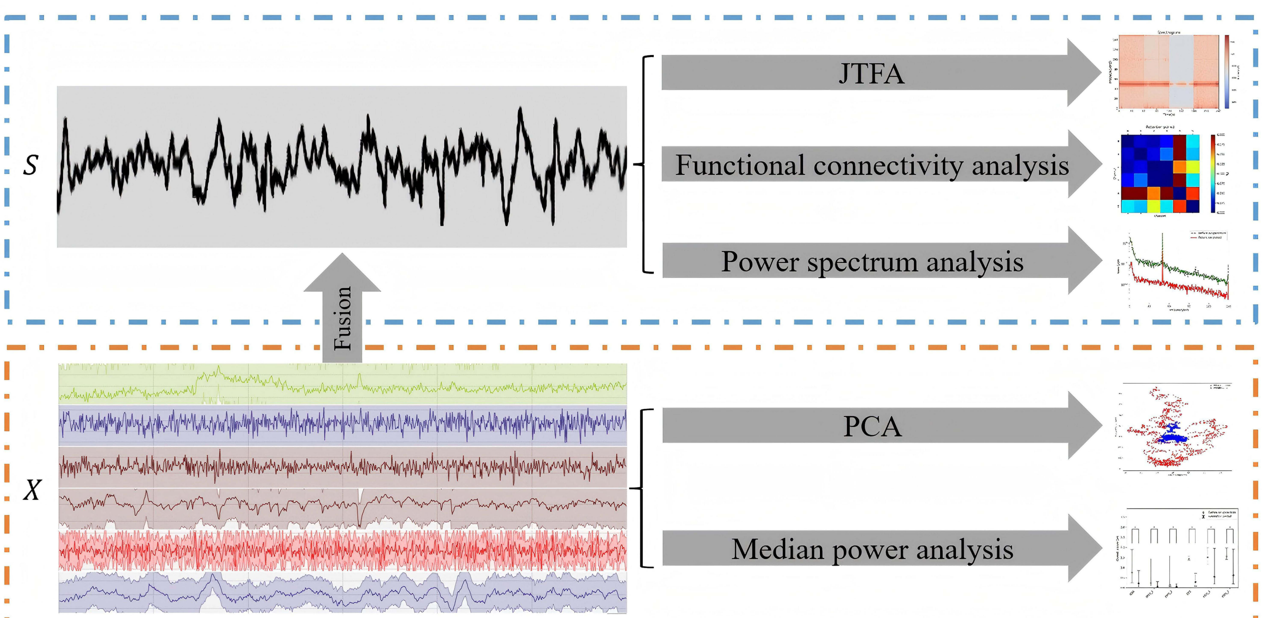

Figure 2 Analysis methods.

Signal Analysis Methodology

For each patient, the bioelectrical signals recorded in each period were represented as $X = \{x_1, x_2, x_3, \ldots, x_c\}$, where $X \in R^{c \times n}$, c represents the number of channels, and n represents the length of the signals. The FastICA method was used to fuse signals from the c channels into a single signal S. The process can be described as follows:

Centering the Data

The signals were first centered by subtracting the mean value from X:

$$X_{centered} = X - \overline{X},$$

where $\overline{X}$ is the mean value X of.

Signal Fusion via FastICA

We applied the FastICA algorithm to fuse the centered signals. This was done using the formula:

$$S = WVD^{-\frac{1}{2}}V^{T}X_{centered,}$$

where V and D represent the eigenvectors and eigenvalues of the covariance matrix of $X_{centered}$, respectively, and W is the unmixing matrix that maximizes the non-Gaussianity of the independent components S. The unmixing matrix W was obtained iteratively. Where, the number of signal channels extracted is 1, parallel algorithm is used to perform data whitening, and the maximum number of iterations is 200.

Power Spectrum Calculation

The median power of the fused signal was calculated, as it is a more reliable measure than peak power or peak amplitude. Research indicates that not all patients exhibit a dominant peak in their FFT spectrum, which makes peak frequency difficult to determine. Thus, median power was chosen for its robustness in such cases.[26,27] The frequency windows for each signal type were empirically determined: EEG (1–50 Hz), EMG (50–500 Hz), EDA (1–150 Hz), and EOG (1–40 Hz).[26,27] The mean peak frequency was calculated within these ranges, and the lower and upper limits were defined by the mean ± two standard deviations. Median power was computed for each patient within these windows, representing the sum of the values in each range. The fusion signal S is preprocessed using a Butterworth zero-phase bandpass filter, maintaining a frequency between 1 and 150 Hz with an order of 5 as:

$$S_{filtered} = F^{-1}\{H_{bp}(S) \cdot F(S)\},$$

where $H_{bp}(S)$ is the band-pass filter's transfer function, F(S) denotes the Fourier transform, and F^{-1} is the inverse Fourier transform. The filtered signal was then segmented into 4-second epochs, with no epochs discarded due to artifacts. Fast Fourier Transform (FFT) was applied to each epoch using a Hanning window, and the FFT results were averaged across all epochs for each patient.

PCA

PCA is a widely used statistical technique for dimensionality reduction and we aim to transform a large set of variables into a smaller one that still contains most of the information in the bioelectrical signals. By projecting the high-dimensional data onto a lower-dimensional space, PCA helps to visualize the inherent structure of the data and discern the differences between the two periods more effectively. About signal X, we normalize X and calculate the covariance matrix:

$$C = \frac{1}{n-1}XX^{T}$$

Calculating the eigenvalues and eigenvectors of the covariance matrix:

$$CW = W\Lambda,$$

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where Λ is the diagonal matrix of eigenvalues and W is the matrix of eigenvectors. Then we select the first two principal components and choose the eigenvectors corresponding to the two largest eigenvalues to form the projection matrix W, thereby projecting the data onto the principal component space Z:

$$Z = W^{T}X.$$

JTFA

It is computed using Short-Time Fourier Transform (STFT) to reveal the frequency distribution of the signal over different time segments. STFT divides the signal into multiple short segments and applies Fourier Transform to each segment. Let the original signal be S(t), the window function be w(t), the window length be M, the frequency is f, and the time step be Δt. The STFT formula is:

$$S(t, f) = \sum_{m=-\infty}^{\infty} S(m)w(m - t)e^{-j2\pi fm}$$

JTFA typically display power spectral density in decibels (dB). Power spectral density P(t, f) is calculated as the squared magnitude of STFT:

$$P(t,f) = 10\log_{10} |S(t,f)|^{2}.$$

Functional Connectivity

Functional connectivity network analysis derives the Phase Lag Index (PLI) by calculating the asymmetry of the instantaneous signal phase difference between two electrodes. PLI reflects the degree of synchronous oscillation between signals in different regions, indicating the connection between physiological signals in the human body:

$$PLI = |\langle \text{sign}(\Delta\phi(t)) \rangle|,$$

where $\langle\cdot\rangle$ denotes averaging over time, $\Delta\phi(t)$ is the phase difference between the time series information of any two electrode leads at time t and sign is the sign function:

$$\text{sign}(x) = \begin{cases} 1 & if\ x > 0 \\ 0 & if\ x = 0 \\ -1 & if\ x < 0 \end{cases}$$

Statistical Analyses

All statistical analyses were performed using SPSS for Windows (version 27). The Shapiro–Wilk test was applied to assess the normality of the data distribution for each variable. Variables that followed a normal distribution were reported as mean ± standard deviation, and comparisons between groups were made using the *t*-test. For variables that did not conform to a normal distribution, results were presented as medians and interquartile ranges, and the rank-sum test (Mann–Whitney *U*-test) was used for analysis.

A significance threshold of $P \leq 0.05$ was applied to determine statistical significance. Additionally, bivariate Pearson correlation analysis was performed to evaluate the relationship between changes in Numerical Rating Scale (NRS) scores and the amplitude differences in multimodal bioelectrical signals. This analysis helped to identify any potential correlations between pain relief (as measured by NRS) and the corresponding bioelectrical activity changes induced by acupuncture. The significance level for all statistical tests was set at $P \leq 0.05$.

Cohen's d was a widely used effect size metric in quantitative research, designed to precisely measure the magnitude of differences between two groups. It effectively complemented significance testing by revealing the practical significance of research findings. A Cohen's d value of less than 0.2 indicated a small difference between the two groups.

A value around 0.5 suggested a medium effect size, and a value greater than 0.8 signified a large difference between the groups.

Results

Characteristics of Participants

Between June 1, 2024, and August 1, 2024, a total of 23 patients meeting the inclusion criteria were recruited for the study. However, due to various circumstances, only 15 participants (7 males and 8 females) completed the study and were included in the final analysis. Four patients experienced intolerable breakthrough pain during acupuncture treatment, preventing them from maintaining the required static supine position for bioelectrical signal acquisition. Two additional patients withdrew due to severe changes in their medical condition that required immediate intervention. Moreover, data from three patients were excluded due to significant signal interference, which compromised the quality of the collected electrical signals. The mean age of the 15 patients who completed the study was 56.06 ± 0.83 years, and the mean disease duration was 21.3 ± 15.54 months. The types of cancers showed a diversified distribution. Gastric cancer had the highest proportion, with 3 cases, accounting for 20% of the total sample. Multiple myeloma ranked second, with 2 cases, accounting for 13.3%. The remaining 10 types of cancers each had 1 case, accounting for 6.7% respectively. Specifically, these included 1 case of uterine leiomyosarcoma (postoperative pathological stage pT1NxM1 stage IV, with secondary pulmonary malignancy), 1 case of colon cancer, 1 case of sigmoid colon cancer, 1 case of lung cancer, 1 case of pleomorphic undifferentiated sarcoma of the right thigh, 1 case of nasopharyngeal malignant tumor, 1 case of renal clear cell carcinoma, 1 case of colorectal cancer (colorectal cancer, CRC; specific location not specified), 1 case of cervical squamous cell carcinoma, and 1 case of cholangiocarcinoma. A detailed summary of the baseline demographic and clinical characteristics of the participants is provided in Table 1.

Changes in NRS Scores Before Acupuncture Treatment and During the Retention Period

As the NRS scores did not follow a normal distribution, a paired-samples Wilcoxon signed-rank test was performed. The median NRS score before acupuncture treatment was 7 (IQR: 6, 8), while the median score during the retention period was 4 (IQR: 3, 5). The results indicated a statistically significant reduction in NRS scores following acupuncture treatment (Wilcoxon signed-rank test, $Z = -3.471$, $P \leq 0.01$). This suggests that acupuncture was effective in reducing pain levels in cancer pain patients.

Changes in Bioelectrical Signals Before Acupuncture Treatment and During the Retention Period: PCA Analysis

PCA was applied to reduce the complexity of the high-dimensional bioelectrical signal data, isolating two primary components representing the signals before acupuncture treatment and during the retention period. A scatter plot was

Table 1 Baseline Demographic and Clinical Characteristics of the Included Participants

Characteristics	Total sample (n = 15)
Sex, No. (%)	
Female	8(53.3)
Male	7(46.7)
Age, mean (SD), y	56.03(0.83)
Course of the disease, mean (SD), m	21.3(15.54)
Cancer Types	Gastric cancer (3, 20%); Multiple myeloma (2, 13.3%); Others (10 cases, 66.7%, including 1 uterine leiomyosarcoma with pT1NxM1 IV and lung metastasis, 1 colon cancer, 1 sigmoid colon cancer, 1 lung cancer, 1 right - thigh sarcoma, 1 nasopharyngeal cancer, 1 renal cell carcinoma, 1 undefined colorectal cancer, 1 cervical cancer, 1 cholangiocarcinoma)

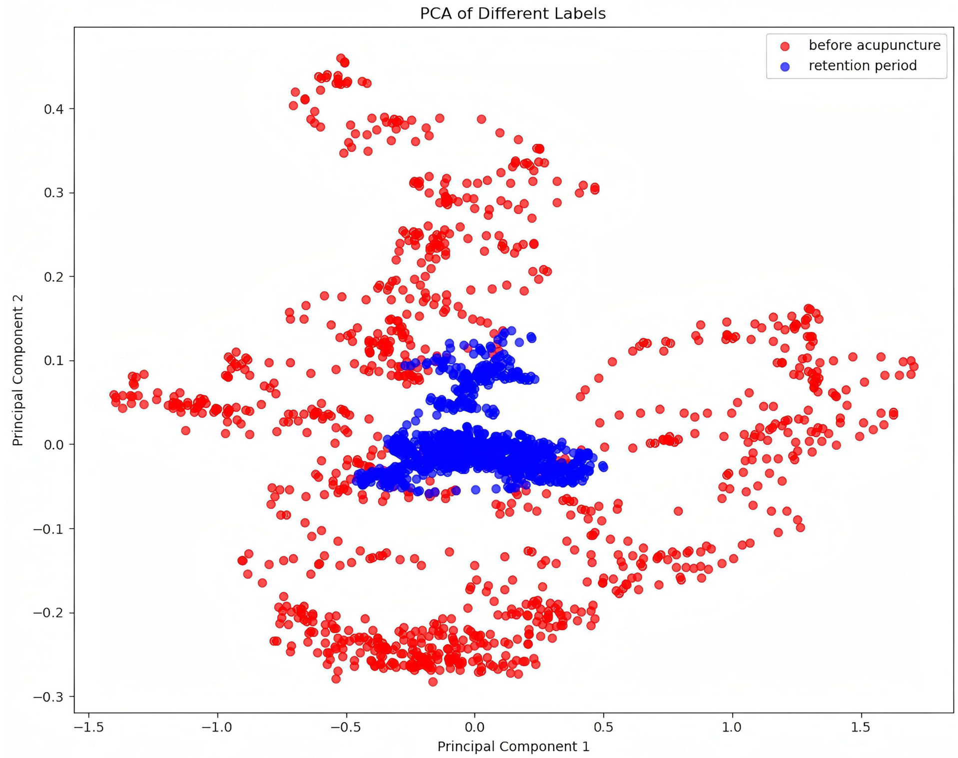

Figure 3 Comparison Chart of Principal Component Analysis Before Acupuncture and Retention.

constructed based on these principal components (Figure 3). Upon comparison of the data points, a clear distinction between the two phases emerged. The bioelectrical signals collected before acupuncture treatment (represented by red points) showed a more dispersed distribution, whereas the signals from the retention period (represented by blue points) exhibited a more concentrated distribution. This marked difference indicates that the bioelectrical signals during the retention period are significantly different from those collected before acupuncture treatment, suggesting a notable effect of acupuncture on neurophysiological patterns in cancer pain patients.

Changes in Bioelectrical Signal Power Before Acupuncture Treatment and During the Retention Period

Using Fourier transform techniques, time-domain bioelectrical signals were converted into the frequency domain to analyze power distribution across different frequency components. A power spectrum was generated to visualize the power variations in bioelectrical signals before acupuncture treatment and during the retention period (Figure 4). The red line represents the power spectrum before acupuncture treatment, while the green line represents the spectrum during the retention period. Comparative analysis revealed a general reduction in power across the entire frequency range during the retention period compared to the pre-acupuncture treatment phase. Specifically, a pronounced reduction in power was observed at around 51 Hz. This suggests that bioelectrical activity at this frequency during the retention period of acupuncture treatment may be particularly beneficial for alleviating cancer pain.

Changes in Overall Power Before Acupuncture Treatment and During the Retention Period

This section examines the effect of acupuncture on bioelectrical signals across four modalities: EEG, EOG, EMG, and EDA. Bar charts were created to depict the power changes before acupuncture treatment and during the retention period (Figure 5). Cohen's *d* was employed to quantify the magnitude of the observed changes. The dots in the charts represent

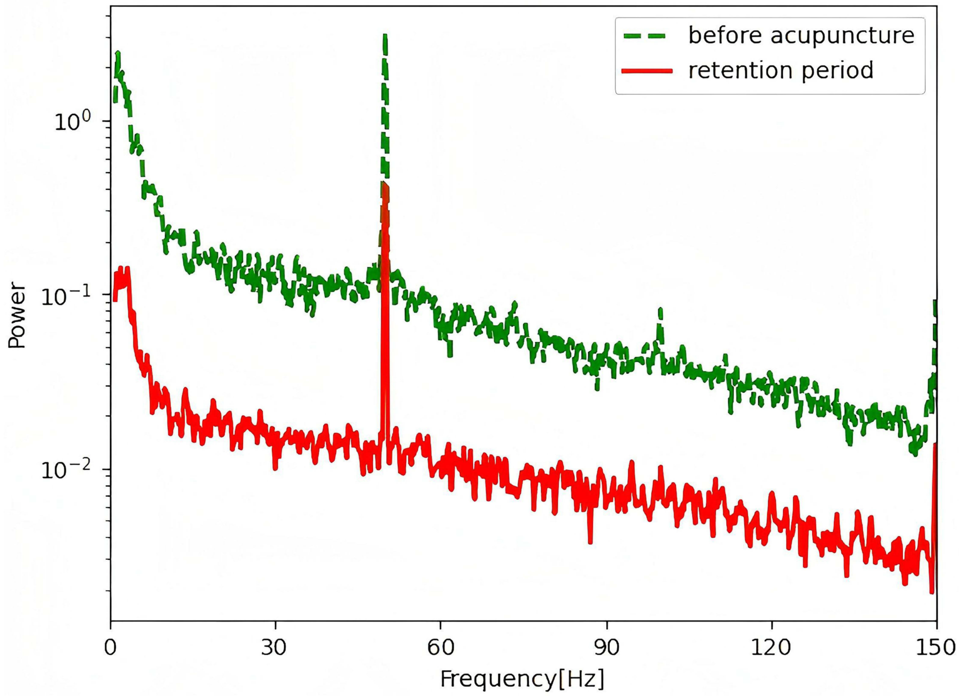

Figure 4 Comparison chart of power spectrum before acupuncture and retention period.

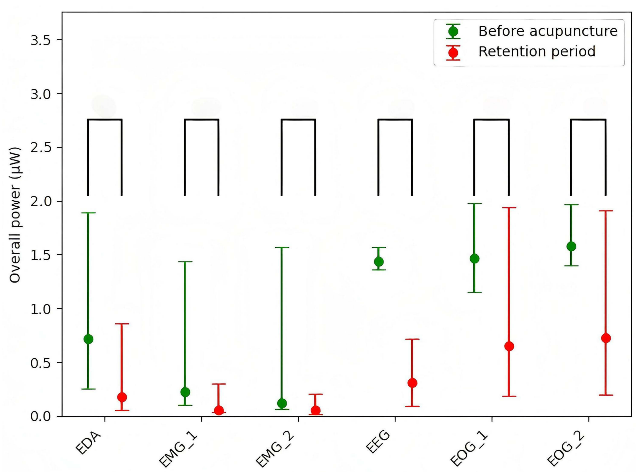

Figure 5 The median power amplitude (and interquartile range) of the six channels for the four bioelectrical signals, both before and during acupuncture retention, were presented.

median values, while the horizontal lines indicate the interquartile ranges. Our findings indicate that prior to acupuncture treatment, the power of EEG and EOG signals was relatively high. However, during the retention period, there was a decrease in the overall power of all four bioelectrical signal types compared to the pre-acupuncture treatment levels. Specifically, EEG power exhibited the most substantial reduction, followed by EOG, then EDA, with EMG showing the smallest decrease. During the retention period, EOG signals displayed the highest overall power among the four modalities. Table 2 provides detailed power values for the four bioelectrical signals during both the pre-acupuncture treatment and retention periods, along with the corresponding Cohen's *d* values.

For EDA, the Cohen's d value was 1.38, indicating a large effect size ($d > 0.8$). This suggests a highly significant difference in electrodermal activity between the pre-acupuncture and retention periods. For EEG, the Cohen's *d* value

Table 2 Four Types of Bioelectric Signal Power Values and Cohen's d Values Before Acupuncture and the Retention Period ($\bar{x} \pm$ SD)

	EDA	EMG1	EMG2	EEG	EOG1	EOG2
Before acupuncture (μW)	0.72±0.52	0.22±0.46	0.12±1.10	1.43±0.05	1.46±0.22	1.57±0.18
Retention period (μW)	0.17±0.22	0.05±0.07	0.05±0.08	0.31±0.16	0.64±0.65	0.72±0.54
Cohen's d	1.38	0.52	0.09	9.45	1.69	2.11

was.45, also indicating a large effect size (*d* > 0.8). This demonstrates an extremely significant change in brain electrical signals induced by acupuncture, reflecting its strong regulatory effect on specific brain regions. On the other hand, this may also be related to the relatively high stimulation intensity of acupuncture in this study. For the EMG1 module, the Cohen's *d* value was 0.52, indicating a moderate effect size in bioelectrical signal changes during the retention period. In contrast, the EMG2 module had a value of 0.09, suggesting that the acupuncture intervention had no practical significance on the bioelectrical signals in this region. This difference may reflect the specific regulatory effects of acupuncture on local tissues, consistent with previous studies describing the neuromuscular activation mechanisms of acupuncture. Future research should combine anatomical localization to clarify the bioelectrical transmission pathways of the intervention. For EOG1 (*d* = 1.69) and EOG2 (*d* = 2.11), both exhibited large effect sizes, suggesting that acupuncture may significantly influence oculomotor-related neural activities, such as the oculomotor nerve or vestibular system. Overall, these findings indicate that acupuncture has a significant impact on multiple bioelectrical signals.

The reliability of our findings is supported by the consistent results across multiple analytical methods, including principal component analysis, power spectrum analysis, and functional network analysis. Furthermore, the reproducibility of the study is enhanced by the detailed description of the experimental protocols and the use of standardized procedures for data collection and analysis.

The Effect of Acupuncture Treatment on Functional Connectivity of Bioelectrical Signals in Cancer Pain Patients

To assess changes in functional connectivity, we employed dynamic functional network analysis and complex network parameters. A heatmap was generated to visually represent changes in functional connectivity between bioelectrical signal channels before acupuncture treatment and during the retention period (Figure 6). In the heatmap, darker colors indicate stronger connectivity, while lighter colors represent weaker connectivity. Before acupuncture treatment, the heatmap showed a relatively disorganized distribution, reflecting variations in connectivity strength among different channels. Notably, the functional connectivity between EDA and EMG was weaker, while the connectivity between EMG, EEG, and EOG was stronger. During the retention period, there was a marked reduction in functional connectivity strength between EEG and EMG. This suggests that acupuncture may alleviate cancer pain by decreasing the efficiency of information transmission between injured tissues and the brain.

Intensity Changes of Bioelectrical Signals During Different Stages of Acupuncture Treatment

The acupuncture treatment process was divided into four stages: before acupuncture treatment, manual needling, retention period, and post-acupuncture treatment. To explore the differences between these stages, we created a spectrogram to illustrate the temporal changes in multimodal bioelectrical signals in the frequency domain (Figure 7). The horizontal axis of the spectrogram represents time, the vertical axis represents frequency, and the color shading indicates the signal intensity at specific frequencies and time points, with darker colors signifying stronger intensities. The spectrogram revealed distinct real-time and stage-specific characteristics in bioelectrical signal intensity. Before acupuncture treatment, signal intensity ranged from −80 to −115 dB. During manual needling, intensity increased to −80 to −100 dB, likely due to the Deqi sensation induced by acupuncture manipulation. The frequency range of high-

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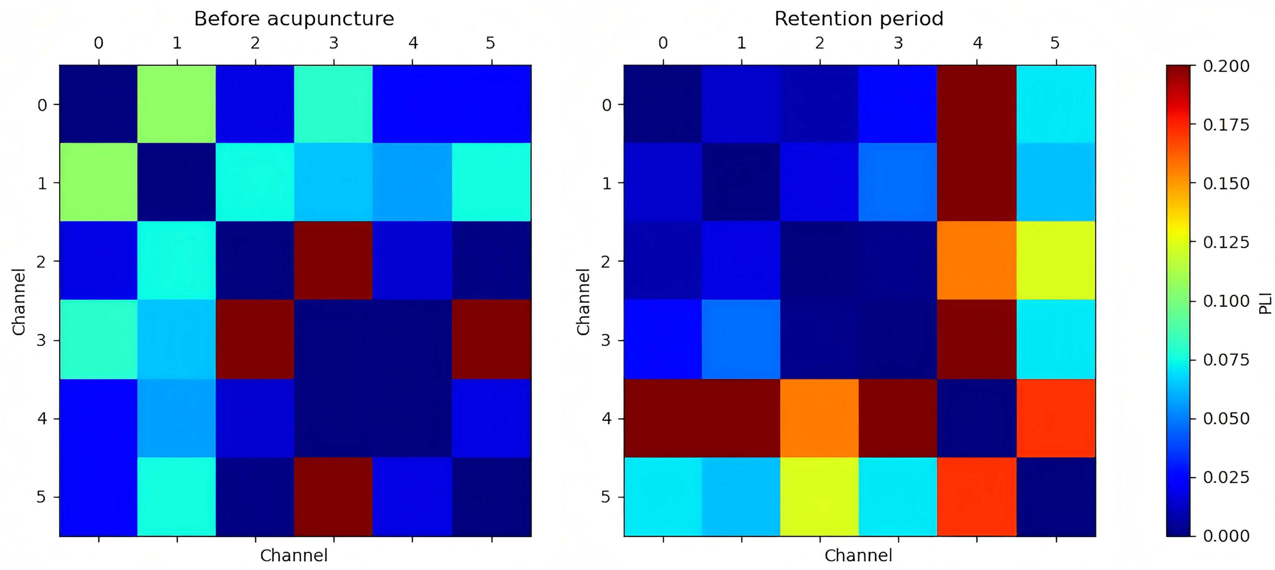

Figure 6 Heatmap of functional connectivity between different bioelectrical signals before acupuncture and needle retention.

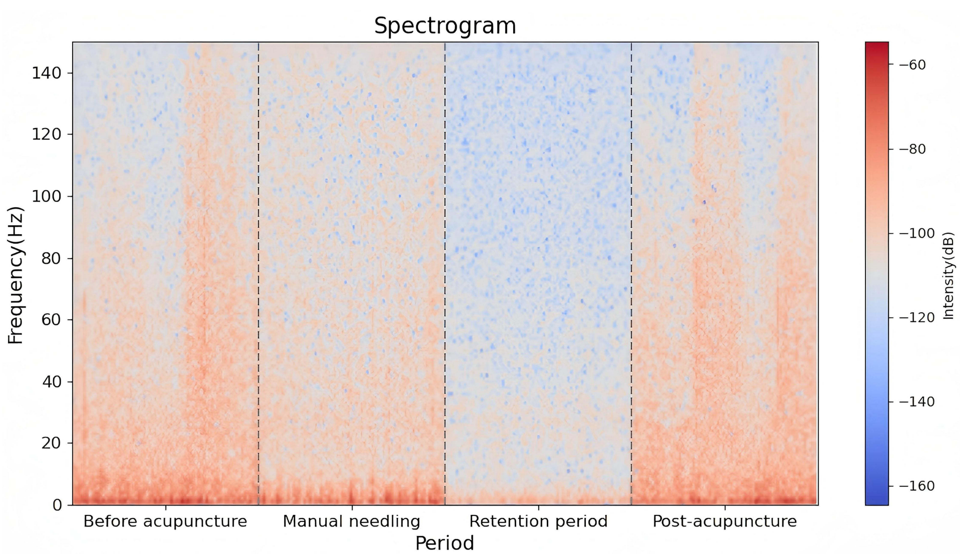

Figure 7 Spectrogram of multimodal bioelectrical signals during the four stages of acupuncture.

intensity signals also broadened, reflecting increased bioelectrical activity. During the retention period, as pain levels decreased, signal intensity dropped to −120 to −130 dB. In the post-acupuncture treatment stage, the intensity rose again to −80 to −110 dB, gradually returning to pre-acupuncture treatment baseline levels.

Correlation Analysis Between Bioelectrical Signal Changes and Pain Scores

Given the observed differences in pain scores and bioelectrical signal power before acupuncture treatment and during the retention period, correlation analysis was conducted to investigate the relationship between these variables. The calculated Spearman correlation coefficient was $r = 0.52$, with a $P = 0.047$, which is below the significance threshold of 0.05 (two-tailed test). This indicates a positive correlation between the change in pain scores and the variation in bioelectrical signal power. These findings provide new evidence for the impact of acupuncture treatment on bioelectrical signals in cancer pain relief, further supporting the hypothesis that pain and bioelectrical activity are closely connected.

Discussion

Instant Effects and the Deqi Response of Acupuncture in Cancer Pain Management

Our study demonstrated that acupuncture has significant immediate effects in alleviating cancer pain. This efficacy can be attributed to two main factors. First, the acupoints selected for this study are widely recognized for their strong analgesic properties, often used in acupuncture anesthesia.[28] Second, the use of the lifting-thrusting and twisting manipulation technique ensured that all patients experienced the characteristic sensations of soreness, numbness, distention, and pain—collectively known as the deqi response. Achieving the deqi state is considered a critical prerequisite for maximizing acupuncture's therapeutic effects.[29] While previous studies have explored deqi sensations.[30] Most have relied on subjective rating scales, and consensus has yet to be reached. Our findings contribute to the objectification and quantification of the deqi state, revealing that the information intensity of multimodal bioelectrical signals during the deqi state increases by 15–20 dB compared to pre-acupuncture treatment levels. This provides a potential objective measure for future studies.

Mechanism of Acupuncture in Cancer Pain: Reducing Functional Connectivity Between Injured Tissue and the Brain

Acupuncture's analgesic effects are thought to result from the interaction and integration of afferent impulses from both acupoints and painful areas within the central nervous system, acting similarly to a distraction mechanism.[31] This theory has been supported by evidence showing an increase in bioelectrical signal energy,[32] but challenges the notion of acupoint specificity. However, our research suggests a different mechanism: acupuncture reduces the power of bioelectrical signals, and notably weakens the functional connectivity between EEG and EMG in cancer pain patients. This indicates that acupuncture may alleviate pain by reducing communication between injured tissues and the brain, rather than merely providing a counteractive distraction. These findings are supported by previous research suggesting that acupuncture inhibits the transmission of pain signals by activating different patterns of afferent fibers.[33] Additionally, since fear of pain can reduce eye movements,[34] the increased activity in eye movements following acupuncture may indicate a reduction in pain intensity and an enhancement of EOG connectivity.

Extending Needle Retention Time in Acupuncture for Cancer Pain Management

While most studies focus on pain changes before and after acupuncture treatment, they often neglect the impact of other stages, such as the retention period, on pain relief.[35] Our results revealed distinct, stage-specific characteristics in multimodal bioelectrical signals throughout the acupuncture treatment process. Specifically, bioelectrical signal intensity increased during manual needling but declined during the retention period. This fluctuation in signal intensity correlates with changes in pain intensity. Consequently, our findings suggest that prolonging needle retention time after achieving the deqi sensation may enhance the analgesic effects of acupuncture treatment in clinical practice.

Bioelectrical Signals: A Highly Promising Multidimensional Pain Assessment Tool

The NRS is a simple and widely used pain assessment tool that enables patients to quickly and intuitively quantify pain intensity. Its advantages, such as ease of operation and understanding, provided essential data on changes in pain intensity in this study. However, its limitations cannot be overlooked. The NRS primarily focuses on pain intensity and neglects other critical dimensions of pain, such as the nature of pain, its impact on patients' daily life functions, and their emotional states. Additionally, in special situations like consciousness disorders, subjective scales like the NRS become ineffective.

Given these limitations, the use of multidimensional pain assessment tools is highly necessary. Our study found a positive correlation between changes in pain intensity and changes in the power of multimodal bioelectrical signals, suggesting that bioelectrical signals could serve as a promising objective measure for pain assessment. Further investigations should explore the specific mechanisms underlying this correlation and identify relevant biomarkers to optimize the clinical efficacy of acupuncture in cancer pain management. Furthermore, future studies should investigate the long-term effects of acupuncture on cancer pain using bioelectrical signal analysis and extend this approach to other types of pain, such as neuropathic pain and inflammatory pain, to validate its broader applicability and mechanisms.

Advantages and Limitations

This study is the first clinical investigation to explore the mechanisms of acupuncture treatment for cancer pain using multimodal bioelectrical signals. A key strength of the study lies in the use of a wearable wireless sensing device, allowing for real-time, non-invasive assessment of acupuncture's neurophysiological effects in a clinical setting. By integrating multidimensional bioelectrical signals, we enhanced the comprehensiveness and reliability of our data. However, several limitations must be acknowledged. First, the relatively small sample size may limit the generalizability of our findings. Second, the intense and variable nature of cancer pain made long-term follow-up impractical. Finally, the absence of a control group makes it difficult to rule out potential placebo effects. Future studies should address these limitations by including larger sample sizes, control groups, and extended follow-up periods to further validate the findings.

Conclusion

This study demonstrates that acupuncture alleviates cancer pain primarily by modulating the functional connectivity between injured tissues and the brain, rather than merely providing a counteractive distraction. Specifically, acupuncture may regulate neural pathways, influence neurotransmitter release, and normalize brain network dynamics, thereby reducing pain perception. These findings provide novel insights into the neurophysiological mechanisms of acupuncture in cancer pain management.

Notably, acupuncture produces significant immediate analgesic effects, and extending the needle retention time after the deqi sensation appears can further enhance therapeutic outcomes. The measurable changes in bioelectrical signals before and after acupuncture treatment, as demonstrated in our study, provide objective evidence supporting its efficacy. This underscores the potential of acupuncture as a non-pharmacological intervention with minimal side effects, offering a viable alternative to conventional analgesics.

From a clinical perspective, acupuncture not only enhances the quality of life for cancer patients but also enables a more comprehensive approach to patient care. By reducing reliance on medications, acupuncture mitigates risks associated with long-term drug use, such as tolerance and adverse effects. These findings align with traditional Chinese medicine principles, which emphasize the holistic regulation of body functions, while being validated by modern scientific methods.

Future research should focus on identifying cancer pain-related biomarkers to further elucidate the neurophysiological mechanisms underlying acupuncture's effects. To strengthen the evidence base, future studies should also consider designing randomized controlled trials with larger sample sizes and longer follow-up periods. These trials would provide more robust data on acupuncture's efficacy and help validate the relationship between bioelectrical signal changes and pain relief.

Abbreviations

NRS, Numerical Rating Scale; EEG, Electroencephalography; EMG, electromyography; EDA, electrical activity; EOG, electrooculogram; PCA, Principal Component Analysis; JTFA, Joint Time-Frequency Analysis; FFT, Fast Fourier Transform; STFT, Short-Time Fourier Transform; VAS, Visual Analog Scale.

Data Sharing Statement

All the processed data were included in the current study. If reviewers or readers have any questions regarding our published data, they can contact the corresponding author, Dian Zhang.[Email: zhangd@szu.edu.cn] for access to the original data.

Ethical Statement

Although there was a brief delay in the registration of our study, all necessary ethical and regulatory requirements were strictly adhered to prior to patient recruitment.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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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