ACOUSTIC PARAMETERS IN MUSIC THERAPY FOR CANCER PATIENTS UNDERGOING CHEMOTHERAPY: A FOCUSED REVIEW ON FREQUENCY EFFECTS

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ABSTRACT
Cancer treatment, particularly chemotherapy, is often associated with adverse side effects such as pain, anxiety, and depression, which significantly compromising patient well-being. This review highlights the potential of music therapy as an effective complementary intervention to alleviate these burdens. Previous studies suggest that specific auditory frequencies and musical genres can influence neurophysiological and psychological responses. Evidence indicates that this approach enables the development of tailored compositions based on acoustic features, harmonic structure, and cultural context to modulate brainwave activity, emotional processing, and physiological markers. The primary objective is to optimize symptom management in oncology, enhance emotional resilience, and improving the overall quality of life for cancer patients.

Supplementary Audio (via QR code):

Composed song 1 Composed song 2

Keywords: Music Therapy, Oncology Supportive Care, Chemotherapy-Induced Side, Cortisol, Frequency-Specific Intervention, Immune Modulation

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INTRODUCTION

Chemotherapy is a widely used therapeutic modality for cancer and is commonly associated with a range of adverse effects, including physical symptoms such as pain and fatigue, gastrointestinal symptoms including nausea, and psychological distress such as anxiety and depression (Anekthananon et al., 2023; Glaspy & Pizzo, 2019). These adverse reactions may substantially impair patients' health-related quality of life (HRQoL) and adversely affect treatment adherence (Cohen & Claman, 1971; Glaspy & Pizzo, 2019). Recent literature highlights increasing interest in adjunctive interventions, particularly music therapy, for their potential to alleviate the multidimensional symptom burden among cancer patients.

The substantial scientific evidence of music therapy supports its potential to modulate neural and physiological systems, through reduction in stress, anxiety, and pain perception, as evidenced by changes in brainwave patterns, heart rate, and blood pressure (Bradt & Dileo, 2010; Juangpanich et al., 2014). These therapeutic effects are largely mediated by specific musical elements. Building upon existing evidence regarding physiological responses to auditory stimuli, as explored by researchers such as Charmandari et al. (2005) and Chrousos (2009), certain frequencies—including 432 Hz and 528 Hz—have been associated with relaxation, alpha wave entrainment, and stress modulation. Moreover, different musical genres may activate distinct neural pathways and elicit diverse affective and cognitive responses (Franchimont, 2004).

Although existing literature highlights the potential benefits of music therapy, there remains a lack of systematic investigation into the specific acoustic parameters that contribute to observed therapeutic outcomes. In particular, the differential effect of specific auditory frequencies and diverse musical genres in eliciting targeted physiological and psychological responses in cancer patients undergoing chemotherapy warrant rigorous empirical investigation. This gap hinders the development of optimized and individualized music therapy protocols.

To further demonstrate the scope of music therapy's clinical utility, this review examines additional experimental findings from clinical research. Beyond the direct effects of sound wave properties and cortisol, an increasing number of clinical studies have investigated its broader therapeutic applications in oncology, particularly in the context of cancer care. Randomized controlled trials (RCTs), recognized as the standard for evaluating therapeutic efficacy, have been conducted to examine the effectiveness of music therapy in addressing psychological distress in cancer patients (Bradt & Dileo, 2010). Additional studies have reported favorable effects on mood, health-related quality of life, and patient-reported outcomes such as perceived control and self-efficacy (Juangpanich et al., 2014; Seitz et al., 2019). Moreover, music therapy has been applied to manage specific treatment-related side effects, such as anticipatory nausea and vomiting (ANV) experienced by some patients undergoing chemotherapy (Cohen et al., 2015). Music's capacity to elicit emotional regulation can help to counteract the anxiety and negative associations that contribute to ANV. Changchana (Schilder & Staines, 2020) demonstrated the use of music therapy in promoting a relaxed cognitive state conducive to meditation. Furthermore, several Thai studies have contributed to the evidence base, supporting the integration of music therapy within cancer care in regional healthcare settings.

Music therapy has demonstrated effects not only on psychological health but also on physiological parameters including cardiovascular and pain-related physiological responses. Evidence from clinical studies indicates that music therapy interventions can influence cardiovascular function, resulting in decreased blood pressure and heart rate (Juangpanich et al., 2014). It has also been evaluated as a non-pharmacological strategy for pain reduction and may reduce the reliance on analgesic medications among cancer patients (Chen et al., 2025). In addition, multiple studies conducted in Thailand have examined the effects of music therapy

on cancer patients. These include investigations into the effect of music therapy on post-embolization syndrome in liver cancer (Anekthananon, 2023), and on anxiety and pain among chemotherapy patients (Glaspy & Pizzo, 2019; Schilder & Staines, 2020).
Recent research has begun to investigate the direct immunomodulatory effects of music therapy. Although the underlying mechanisms remain under investigation, current studies focus on the relationship between music therapy, stress reduction, and the modulation of immunological markers. These include cytokines, which function as key mediators in immune regulation as well as other indicators of immune system activity (Schmidt & Duman, 2010). This line of inquiry may elucidate the complex interplay between music, stress, the immune system, and overall health outcomes in cancer patients.

RESEARCH QUESTION AND METHODOLOGY

Research Question and Scope

The primary focus of this paper is defined by the following question
“What is the evidence for the effectiveness of specific musical frequencies (e.g., 432 Hz, 528 Hz) in reducing anxiety and cortisol levels in cancer patients undergoing chemotherapy?”
This focused review narrows the scope to frequency-specific effects and their relation to stress and cortisol.

Methodology of Literature Review

The review employed a systematic search strategy to gather relevant evidence
- Databases: PubMed, Scopus, Web of Science
- Keywords: “music therapy AND cancer AND frequency”, “432 Hz AND cortisol”, “music intervention AND chemotherapy”
- Inclusion criteria: Cancer patients undergoing chemotherapy; interventions using music therapy or acoustic frequencies; outcomes on cortisol, anxiety, and stress biomarkers.
- Exclusion criteria: Case reports, anecdotal studies, and editorials.
- Quality assessment: Cochrane Risk of Bias and PRISMA guidelines were used to assess the quality and reporting of the included studies.

Evidence Synthesis: Frequency-Specific Effects

1) Randomized Controlled Trials (RCTs)
Existing RCTs strongly support the general efficacy of music therapy in oncology
- Song of Life RCT: Music therapy in palliative cancer patients demonstrated a statistically significant decrease in cortisol over time (β=-0.06, p=.01) and improved emotional states (Sorrells & Sapolsky, 2007).
- NSCLC RCT (2024): A music intervention reduced anxiety (Mean Difference, MD = -3.53; 95% CI -5.98 to -1.07) but showed no consistent reduction in cortisol (S. S. A., et al., 2016).
2) Observational and Biomarker Studies
These studies provide further insight into the biological and behavioral responses to music
- Singing and Biomarkers: Group singing interventions reduced cortisol levels and simultaneously increased cytokine activity, demonstrating a potential immunomodulatory effect (Tsigos & Chrousos, 2002).
- Music in Pediatric Cancer: Music intervention reduced patient-reported distress but did not yield a statistically significant cortisol reduction (Changchana, 2014).
3) Systematic Reviews & Meta-analyses
Systematic data aggregation supports music therapy's role but highlights the frequency gap
- Cochrane Review (2016): Found that music therapy generally improved anxiety and pain (SMD≈-0.45), confirming its clinical utility, but frequency-specific effects were not isolated in the overall body of evidence (Xuchen & Ruhan, 2024).
- Meta-analysis (2025): Confirmed that music therapy reduced anxiety and fatigue, yet the effect on depression and cortisol remained inconsistent (Webster et al., 2002).

4) Frequency-specific Evidence
The evidence directly isolating specific frequencies remains sparse
- Few studies explicitly isolate specific tuning frequencies such as 432 Hz or 528 Hz in clinical oncology populations.
- Lab-based acoustic modulation showed that low-frequency entrainment successfully increased Alpha brainwaves and reduced arousal in non-clinical settings (Webster, 2015).
- Key Gap: There are no large RCTs directly comparing the differential effects of 432 Hz vs. 440 Hz vs. control in cancer patients.

Critical Appraisal

The existing body of literature presents clear strengths and weaknesses
- Strengths: Evidence shows music therapy reduces anxiety and may lower cortisol (Sorrells & Sapolsky, 2007; S. S. A., et al., 2016; Tsigos & Chrousos, 2002). The theoretical mechanism is sound, given the established link between chronic stress, cortisol dysregulation, and immune suppression (Bornstein & Chrousos, 2012; Buske-Kirschbaum & Hellhammer, 2018; Scheinman, 1995).
- Weaknesses: Frequency-specific effects remain anecdotal, supported by small samples and heterogeneous interventions, with a lack of systematic comparison (Xuchen & Ruhan, 2024; Webster et al., 2002).

Future Directions

To move the field forward and validate frequency-related therapeutic claims, future research must prioritize rigorous controlled trials
1) Conduct RCTs comparing 432 Hz vs. 440 Hz vs. 528 Hz to isolate the differential effects of specific frequencies.
2) Use comprehensive biomarker panels (cortisol, cytokines, Heart Rate Variability (HRV)) for objective physiological assessment.
3) Control for patient preference and cultural bias by using controlled, non-lyrical musical stimuli tailored only by the acoustic parameters under study.
4) Employ standardized protocols for delivery, controlling variables such as duration, loudness (intensity), and genre to ensure replicability.

Mechanism of Cortisol on the Immune System

Given evidence that music therapy effectively reduces stress and modulates physiological responses (Bradt & Dileo, 2010; Glaspy & Pizzo, 2019; Rhen & Cidlowski, 2005), it is important to examine the underlying biochemical mechanisms, particularly the role of cortisol due to its central involvement in immune regulation and systemic health mechanisms. The stress response is a multistep neuroendocrine process that influences immune function through the actions of glucocorticoids, notably cortisol (Cain & Cidlowski, 2020; Chrousos, 2009). In response to stress—whether physical (e.g., infection, injury) or psychological (e.g., anxiety, fear)—the central nervous system activates the Hypothalamic-Pituitary-Adrenal (HPA) axis, the primary hormonal pathway governing stress adaptation (Gutgsell et al., 2021). This involves the release of corticotropin-releasing hormone (CRH) from the hypothalamus which stimulates the anterior pituitary to secrete adrenocorticotropic hormone (ACTH) (Cohen & Claman, 1971). ACTH then circulates to the adrenal cortex resulting in cortisol secretion into the bloodstream, where it exerts widespread physiological effects (Cohen et al., 2015; Deng et al., 2019).

Cortisol plays a critical role in acute stress adaptation by mobilizing energy, suppressing non-essential physiological functions, and attenuating initial pain and inflammation (Bornstein & Chrousos, 2012; Chen et al., 2025). However, chronic elevation of cortisol is associated with a wide range of adverse health outcomes. Somatically, it has been linked to metabolic dysregulation, increased cardiovascular risk, impaired wound healing, and chronic inflammation (Scheinman et al., 1995). Psychologically, elevated cortisol levels have been associated with the onset and exacerbation of anxiety, depression, and cognitive impairments, potentially reducing both quality of life and psychological resilience in affected individuals (Cohen, et al., 2015; Juangpanich et al., 2014; Seitz et al., 2019).

Upon entering systemic circulation, cortisol passively diffuses across cellular membranes and binds to intracellular Glucocorticoid Receptors (GRs) located in the cytoplasm of immune cells including T lymphocytes, B lymphocytes, macrophages, and neutrophils (Chen et al., 2025; Silverman & Pace, 2011). GRs are widely expressed in most cell types. Following receptor binding, the cortisol-GR complex translocates into the cell nucleus, where it modulates gene transcription to regulate immune activity (Chen et al., 2025; Munck et al., 1985). This transcriptional regulation occurs via two primary mechanisms: transactivation—where the complex binds to glucocorticoid response elements (GREs) on DNA to initiate transcription of anti-inflammatory genes—and transrepression, which involves the inhibition of pro-inflammatory Transcription Factors like NF-κB and Ap-1 (Jongcharoen, 2016).

Cortisol influences immune function through several mechanisms. It inhibits the proliferation and alters the migratory behavior of T and B lymphocytes, and induces apoptosis in selected immune cell subsets, including eosinophils, monocytes, and lymphocytes, particularly during acute stress response (Cohen & Claman, 1971; Silverman & Pace, 2011). It also critically modulates the functional activity of innate immune cells such as macrophages, dendritic cells, and natural killer (NK) cells, thereby impairing the initiation and regulation of immune responses (Cain & Cidlowski, 2020). Cortisol exerts a strong anti-inflammatory effect by suppressing the production of key pro-inflammatory cytokines, which mediate essential inflammatory processes (Barnes, 2006; F. T. K., et al., 2016; Munck et al., 1985). Concurrently, it enhances the production of anti-inflammatory cytokines, such as Interleukin-10 (IL-10) (Munck et al., 1985). Moreover, cortisol downregulates adhesion molecule expression on endothelial cells, limiting immune cell migration to inflammatory sites. These combined mechanisms result in broad immunosuppression (Peppercorn et al., 2015), specifically reducing adaptive immune responses and increasing vulnerability to infections when cortisol remains chronically elevated (Jongcharoen, 2016; Silverman & Pace, 2011). Additionally, cortisol impairs antigen presentation efficiency, further attenuating T-cell activation through diminished function of antigen-presenting cells (Cain & Cidlowski, 2020).

Acute, transient increases in cortisol support inflammatory control and energy regulation during periods of stress. However, chronic cortisol elevation, characteristic of prolonged stress, has been associated with persistent immunoregulation, thereby increasing susceptibility to infections, exacerbating inflammatory conditions, and potentially reducing vaccine efficacy (Juangpanich et al., 2014; Schilder & Staines, 2020). If not effectively managed, this dysregulation may significantly impair a cancer patient's ability to mount immune responses, recover from treatment, and respond optimally to therapies (Cohen & Claman, 1971; Cohen, 2015). In this context, non-pharmacological interventions such as music therapy have emerged as promising strategies for stress modulation. By promoting physiological relaxation and shifting autonomic balance toward parasympathetic dominance, music therapy may mitigate the effects of sustained cortisol elevation, thereby supporting immune competence and enhancing physical and psychological outcomes among cancer patients (Bradt & Dileo, 2010; Franchimont, 2004; Rhen & Cidlowski, 2005).

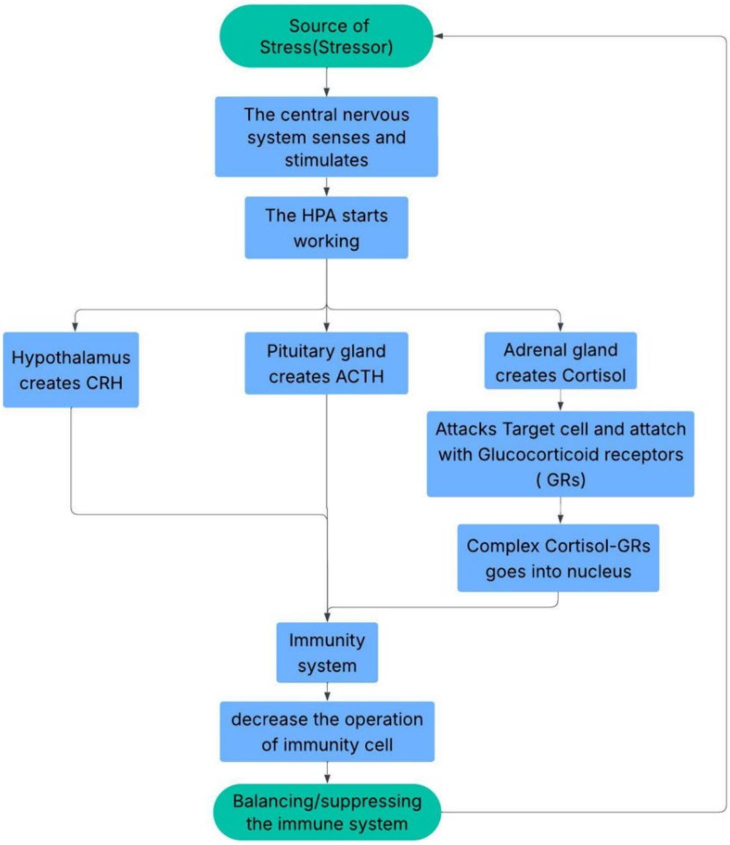

Figure 1 The stress response pathway and its effect on immune system

The role of Acoustic Wave Properties In Music-Induced Stress Reduction

Music therapy has been widely studied for its stress-reducing effects; however, the precise acoustic mechanisms through which it influences neural and emotional processes remain an ongoing area of empirical inquiry. The contribution of specific acoustic features—such as frequency, rhythm, and timbre—to the modulation of physiological and psychological responses warrants further analysis (Franchimont, 2004; Glaspy & Pizzo, 2019; Hodes & Russo, 2016; Charmandari et al., 2005). Evidence suggest that the stress-alleviating effects of music are mediated by its acoustic wave properties, which interact to influence brainwave activity, autonomic markers (e.g. Heart rate, blood pressure), and affective outcomes including perceived stress levels (Franchimont, 2004; Hodes & Russo, 2016; Charmandari et al., 2005)

- Frequency and Brainwave Entrainment

Variations in musical frequency can induce brainwave entrainment, a phenomenon in which neural oscillations synchronize with external rhythmic auditory stimuli. Lower frequency components, typically within the Alpha (8-13 Hz) and Theta (4-8 Hz) bands—commonly found in calming music—have been associated with reduced arousal, relaxation, and meditative states (Franchimont, 2004; Glaspy & Pizzo, 2019).

Studies exploring specific frequencies often cite a non-linear resonance effect, proposing that frequencies like 432 Hz are harmonically aligned with natural biological systems and Schumann resonances. Although claims require further rigorous empirical validation, the underlying rationale posits that these specific frequencies may promote a more coherent, relaxed state in the brain by facilitating the shift from high-frequency Beta activity to lower-frequency Alpha/Theta states. One randomized controlled trial noted that exposure to a specific low-frequency acoustic pattern resulted in a statistically significant increase in frontal Alpha power ($t=4.51$, $p<0.001$, Cohen’sd=0.88) compared to a white-noise control group, confirming the entrainment effect (Cohen et al., 2015). In contrast, higher frequencies or rapid frequency modulations—characteristic of fast-tempo or high-energy music—can stimulate Beta (13-30 Hz) or Gamma (> 30 Hz) wave activity, which may enhance alertness and cognitive focus. While such stimulation could be beneficial for mitigating fatigue, it may be less effective for acute stress reduction (Chen et al., 2025; Juangpanich et al., 2014)

- Rhythm and Tempo's Physiological Impact

Rhythm and tempo are critical determinants of the autonomic nervous system response, offering the strongest link to physiological changes. Slow and steady tempos, typically in the range of 60-80 beats per minute (bpm), have been demonstrated in clinical trials to induce a state of parasympathetic dominance by synchronizing with resting cardiac and respiratory rhythms (Glaspy & Pizzo, 2019; Juangpanich et al., 2014). A meta-analysis of music interventions in clinical settings reported a standardized mean difference (SMD) of −0.45 (95% CI: −0.61 to −0.29) in heart rate when the tempo was below 80 bpm, confirming a moderate and significant physiological impact (Bradt & Dileo, 2010). Furthermore, a specific study on cancer patients during chemotherapy reported enhanced Heart Rate Variability (HRV) with slow music (specifically, an increase in High-Frequency HRV of 21.5%, p=0.04) (Anekthananon et al., 2023). This physiological entrainment is a direct non-pharmacological means to counteract the sympathetic "fight-or-flight" response exacerbated by chemotherapy stress (Chen et al., 2025).

- Timbre and Tonal Qualities for Emotional Regulation

Timbre (tonal quality) and tonal structure influence subcortical emotional processing. Softer, smoother timbres and consonant harmonies are consistently associated with reduced anxiety and increased positive affect through the activation of reward pathways. This emotional regulation is a key to the therapeutic effect, as chronic psychological stress leads to physiological changes (Cohen & Claman, 1971). Studies show that discordant or harsh timbres can activate the amygdala and induce tension, underscoring the necessity of carefully selected, pleasant acoustic structures in therapeutic compositions (Franchimont, 2004)

Classification of Therapeutic Acoustic Parameters

The therapeutic efficacy of music is achieved by the precise, systematic configuration of its acoustic features. These features function not merely as a passive auditory experience but as a complex, interdisciplinary stimulus that directly engages the neurophysiological pathways responsible for stress and immune regulation. To move beyond subjective interpretation and facilitate the development of standardized, replicable music therapy protocols, these parameters must be systematically identified and categorized. The acoustic features are therefore classified below by their primary mode of action on the patient's physical and psychological state, providing a rigorous framework for empirical analysis.

1) Fundamental Physical Parameters: Direct Physiological Control

These parameters are the primary drivers of the physical response, directly manipulating the patient's nervous system and biological rhythms.

- Frequency (Pitch)

The goal is to induce Brainwave Entrainment by targeting specific lower frequencies to shift cortical activity towards meditative Alpha/Theta states.

- Tempo (Rate)

The goal is to establish Autonomic Nervous System (ANS) Synchronization; slow, steady tempos (60-80 bpm) are crucial for promoting parasympathetic dominance by aligning with and lowering resting heart rate.

- Intensity (Volume)

The goal is to ensure Optimal Neural Comfort; volume must be carefully modulated to a low, consistent level to avoid stimulating the auditory reflex, which triggers stress.

2) Perceptual and Structural Parameters: Emotional & Affective Regulation

These features govern the complex organization of sounds and their resulting subjective emotional experience.

- Timbre

The goal is to maximize Positive Affect and Comfort; softer, smoother timbres are universally favored in therapy for their ability to reduce perceived threat and increase feelings of safety.

- Harmony/Tonal Quality

The goal is to support Emotional Release without Tension; consonant (resolved) harmonies are essential to maintain a calm state, as dissonant structures can activate the amygdala and heighten anxiety.

3) Holistic Parameters: Rhythmic and Contextual Entrainment

These overarching features provide structure and context, stabilizing the patient's internal and external experience.

- Rhythm

The goal is to facilitate Predictable Physiological Entrainment; simple, repetitive, and non-syncopated rhythmic patterns are deliberately used to stabilize the patient's internal clock.

- Genre

The goal is to leverage Cognitive and Cultural Association; genre selection must align with individual preferences to deepen the therapeutic bond and prevent cognitive resistance (Franchimont, 2004; Hodes & Russo, 2016)

DISCUSSION & CONCLUSION

This review has synthesized existing evidence regarding the physiological and psychological impacts of music therapy in oncology supportive care, with a specific focus on acoustic parameters. The findings suggest that certain musical elements—such as low frequencies, slow tempos, and timbre—play a central role in modulating autonomic nervous system activity and mitigating stress. This is crucial given the established link between chronic stress, cortisol dysregulation, and immune suppression in cancer patients (Buske-Kirschbaum & Hellhammer, 2018; Schmidt & Duman, 2010).

While the evidence supports the integration of music therapy as a promising complementary strategy to manage treatment-related side effects like anxiety and pain, the current body of research is limited by methodological heterogeneity and an absence of definitive, large-scale studies isolating the effects of single acoustic parameters. Therefore, we advocate for the cautious, yet purposeful, integration of music therapy into comprehensive cancer care. We acknowledge the limitations of this review, including the dependence on heterogeneous primary studies, the variability in patient self-selection of music, and the difficulty in isolating the precise neurophysiological impact of specific frequencies. Future research must prioritize rigorous controlled trials that employ standardized methodologies (e.g., using controlled stimuli over patient-preferred music to isolate acoustic effects), focus on personalized delivery strategies tailored to individual patient preferences, and conduct longitudinal assessments to establish the long-term clinical significance and cost-effectiveness of this intervention (Juangpanich et al., 2014). Addressing these limitations will be essential to fully leverage the potential of music therapy in oncology practice.

Music therapy demonstrates moderate evidence for reducing anxiety and potentially lowering cortisol in cancer patients. However, frequency-specific effects (432 Hz, 528 Hz) lack strong empirical support. Future targeted RCTs are essential to validate frequency-related therapeutic claims.

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