



## Integrating Acupuncture into Cancer Care

Tsai-Ju Chien<sup>1,2</sup>, Chia-Yu Liu<sup>1,3,4</sup>, Chung-Hua Hsu<sup>1,3,4</sup>

<sup>1</sup>Institute of Traditional Medicine, National Yang-Ming University, Taipei, Taiwan.

<sup>2</sup>Department of Internal Medicine, Division of Hemato-Oncology, Branch of Zhong-xing, Taipei City Hospital, Taipei, Taiwan.

<sup>3</sup>Department of Traditional Chinese Medicine, Branch of Linsen and Chinese Medicine, Taipei City Hospital, Taipei, Taiwan.

<sup>4</sup>Taiwan International Traditional Chinese Medicine Training Center, Taiwan.

### ABSTRACT

Oncology acupuncture has become a new and promising field of research because more and more cancer patients have sought non-pharmacological alternatives for symptom management. While different mechanisms have been proposed to explain its efficacy, including theories of the neural system, endocrine cytokine or immunological regulation, its eventual role has become that of alleviating the side effects induced by chemotherapy or radiotherapy. In this paper, we have reviewed the related articles focusing on acupuncture mechanisms and applications in cancer care to provide a quick sketch of acupuncture in cancer care. A detailed search was performed to identify the randomized controlled trials (RCTs) and systematic reviews on acupuncture in oncology, using PUBMED and Cochrane. The search terms included: Acupuncture, acupressure, and cancer. Additional terms were used to target specific symptoms (i.e., breast cancer, hot flash, xerostomia, nausea, vomiting, cancer pain, insomnia, fatigue). Two authors independently extracted data for analysis and review. Ultimately, 25 articles underwent full-text review. Recent trials made efforts in studying (a) hot flashes in breast cancer, (b) xerostomia induced by radiotherapy in head and neck cancer, (c) nausea and vomiting post-chemotherapy, (d) cancer pain, and (e) fatigue and insomnia in cancer patients. Controversial results for acupuncture application in cancer care appeared in different categories, but a trend emerged that acupuncture can palliate cancer-related symptoms. The research to date certainly offers us a valid complementary therapy in treating cancer-related symptoms. Meanwhile, practical strategies with safe measures for enhancing the efficacy are needed in further interventions, as well as continuing research with a validated methodology.

**Key words:** Acupuncture, Cancer, Oncology

### INTRODUCTION

With the increasing incidence of cancer and major advances in cancer treatment in recent decades, acupuncture has become a popular complementary treatment in oncology. One European survey highlighted over a third of cancer patients are utilizing complementary therapies for treating their cancer symptoms and/or the side effects of their treatment.<sup>[1]</sup> Since different cancer patients often share similar symptoms, most complementary therapies are

focused on the symptoms rather than the disease itself. Oncology acupuncture is a new field of research. Recent advances from published clinical trials have added evidence to support the use of acupuncture for management of symptoms such as pain, nausea and vomiting, xerostomia, hot flashes, fatigue, anxiety, depression, and insomnia. Acupuncture is based on the meridian theory of Traditional Chinese Medicine and stresses “Qi.” From the viewpoint of western medicine, the mechanism of acupuncture may be explained by neurotransmitter release or modulation of autonomic

### Correspondence to:

Dr. Chung-Hua Hsu, Institute of Traditional Medicine, National Yang-Ming University, 155, Li-Nong St, Sec 2, Peitou, Taipei, Taiwan.  
Tel: 886-2-2826-7050; 886-920630090; Fax: 886-2-28201461; E-mail: owlherbs@yahoo.com.tw

DOI: 10.4103/2225-4110.119733

nervous system (ANS). Recent studies also used sham acupuncture control groups to validate the efficacy of acupuncture.<sup>[2]</sup> Applying acupuncture in oncology requires constant dialog and communication between qualified practitioners and the oncology team.

Here, we review some review articles and clinical trials including patient-administered acupuncture, electroacupuncture (EA), acupressure, and auricular acupuncture applied in cancer-related symptom treatment. Most studies indicate acupuncture has the potential to act as an adjunctive care in palliating symptoms.<sup>[2]</sup> This has encouraged deeper investigations and clinical practice to apply this technique in cancer care because of its low side-effect profile and economic cost benefits.

### Theory and mechanism

In Traditional Chinese Medicine theory, acupoints are defined as the visceral reaction points on the body surface where the Qi of the viscera and meridians are transfused.

Triggering these acupuncture points promotes the flow of Qi and blood, and regulates visceral function.<sup>[3]</sup>

In the last half of the 20<sup>th</sup> century, many studies conducted in animals and humans have demonstrated multiple biological responses related to acupuncture, including (a) neural regulation, (b) endocrine regulation, and (c) immunological regulation.<sup>[4]</sup>

In neural regulation, some experiments have indicated the relationship between acupuncture and the ANS.<sup>[5]</sup> According to Traditional Chinese Medicine, “acupuncture is believed to restore the balance of Yin and Yang,” which may correspond to the modern definition that “acupuncture modulates the imbalance between the parasympathetic and sympathetic activity.”<sup>[6]</sup>

In endocrine regulation, EA evokes serotonin release from the upper brain stem region and hypothalamus and stimulates endogenous opiate release ( $\beta$ -endorphin, enkephalin, endomorphin, and dynorphin) which then alleviates cancer pain.<sup>[7]</sup> In addition, some neurohormones like  $\gamma$ -aminobutyric acid and glutamate, neuropeptide Y, and brain-derived neurotrophic factors can lead to euphoric sensations and treat the psychological problems of the cancer patients.<sup>[8,9]</sup>

From the view point of immune modulation, EA may stimulate leukocytes’ (granulocytes and lymphocytes) growth via the hypothalamus–pituitary–adrenal axis.<sup>[10]</sup> Improvements in T-lymphocyte and Natural Killer cell function to promote the recovery of immune function in cancer patients were observed in some studies.<sup>[11,12]</sup>

## METHODS

Our search for articles of acupuncture in the management of each symptom was carried out on 15 September 2012 in the database PUBMED and in the Cochrane Central Register of Controlled Trials. Language restricted to English were applied. Key search terms were: Acupuncture, electroacupuncture, acupressure, and cancer. Additional terms were used to target specific symptoms (i.e., breast cancer, hot flashes, xerostomia, nausea, vomiting, cancer pain, insomnia, fatigue). References of all the included studies were also searched.

### Selection criteria

We included only the recent reviews and randomized controlled

trials (RCTs) investigating acupuncture applied in cancer-related symptoms within the past 8 years.

### Data collection and analysis

Two independent reviewers screened the abstracts and titles of all the articles for eligibility. When the reviewers felt that the abstract or title was potentially useful, full copies of the article were retrieved and considered for eligibility by all reviewers.

When discrepancies occurred between reviewers, the reasons were identified and a final decision was made based on the agreement of all reviewers. In the end, 25 articles, including RCTs and systemic reviews, were retrieved for the final analysis [Figure 1]. And the major conclusions of included RCTs and systemic reviews in acupuncture applied in cancer-related symptoms would be summarized in Table 1. The common acupoints applied in oncology-related problem would be list in Table 2.

## ACUPUNCTURE APPLIED IN ONCOLOGY-RELATED PROBLEM

### Hot flashes

Hot flashes are a common complaint in nearly 70% of breast cancer patients.<sup>[13]</sup> They may be related to abrupt menopause or anti-estrogen therapy (tamoxifen or aromatase inhibitors). Acupuncture (a complementary modality) plays some role in reducing the hot flashes in breast cancer patients on treatment

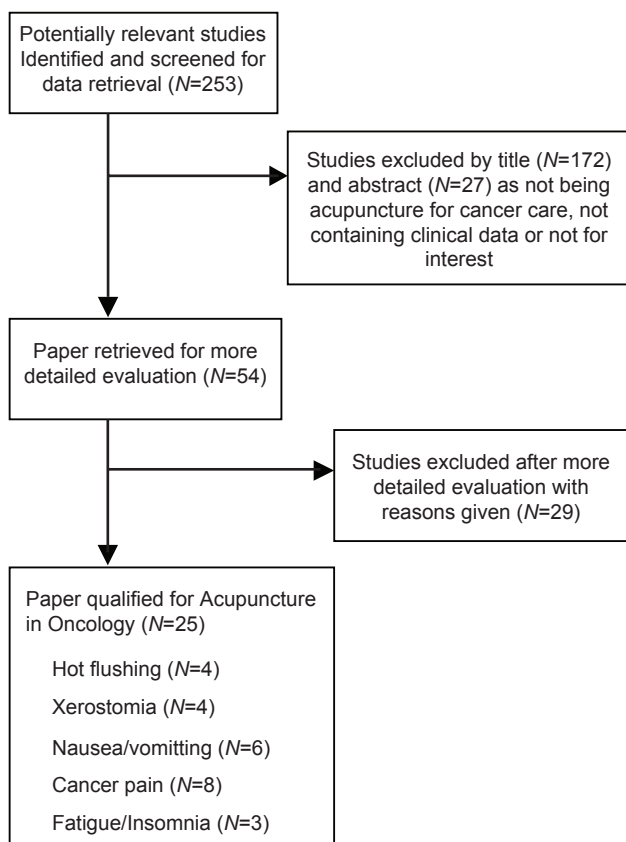


Figure 1. Reviewing process flowchart

**Table 1.** Recent RCT and systemic reviews in acupuncture applied in cancer-related symptoms

Cancer related symptom (review studies number)	Method	Major conclusion	Reference
Hot flushing	RCT (3) systemic review (1)	Two RCT studies: The flush frequency reduced following acupuncture, but no statistical significance was found when compared with sham acupuncture. One study confirmed acupuncture's role in reducing hot flush frequency and postmenopausal complaints Systemic studies show equivocal results for acupuncture in reducing hot flushes	14-17
Xerostomia	RCT (2) Systemic review (2)	RCT: One study concluded acupuncture can stimulate salivary flow, and the other confirmed its role in palliating the xerostomia Systemic reviews: Limited role for the heterogeneity of acupuncture techniques	19-21,23
Nausea/Vomitting	RCT (4) Systemic review (2)	P6 has significant effects in reducing CINV A significantly reduced potency of CINV was observed in acupuncture applied in cisplatin or cyclophosphamide related CINV, but no benefits were found in high dose chemotherapy before stem cell transplantation Inconclusive data as to the benefit of acupuncture used in radiotherapy related nausea/vomitting	27,28,32-35
Cancer pain	RCT (4) Systemic reviews (4)	The RCT confirmed the role of acupuncture in breast cancer AI treatment related joint pain and post-operation pain Auricular acupuncture also significantly reduced cancer pain Controversial data about TENS used in cancer pain from the two systemic reviews due to a lack of large multi-centre RCTs	39-46
Fatigue/Insomnia	RCT (1) Systemic review (2)	Auricular acupuncture may be useful in improving sleep quality May need stronger evidence based data for the fatigue and insomnia issue	47,50,51

RCT: Randomized controlled trial; CINV: Chemotherapy-induced nausea/vomiting; TENS: Transcutaneous electric nerve stimulation

**Table 2.** Common acupoints applied in cancer care

Cancer-related symptom	Acupoints	Location
Hot flashes	LIV3	In the depression distal to the junction of the 1 <sup>st</sup> and 2 <sup>nd</sup> metatarsal bones
	Gb20	Below the occiput, in the hollow between the sternomastoid and trapezius muscles
	Lu7	Superior to the styloid process of the radius
	Ki3	In the depression between the tip of the tibial medial malleolus and the Achilles tendon
	SP6	On the medial side of lower leg, 3 cun superior to the medial malleolus
	REN4	On the midline of the abdomen, 3 cun below the umbilicus
	P7	Between the palmaris longus and flexor carpi radialis at the wrist
	LIV8	At the medial end of the traverse popliteal crease at the knee
Xerostomia	LI4	On the dorsum of the hand, between the 1 <sup>st</sup> and 2 <sup>nd</sup> metacarpal bones, in the middle of the 2 <sup>nd</sup> metacarpal bone on the radial side In the depression of the radial side, distal to the 2 <sup>nd</sup> metacarpophalangeal joint when a loose fist is made
	LI2	On the medial side of the lower leg, 3 cun superior to the medial malleolus
	SP6	On the head, 5 cun directly above the midpoint of the anterior hairline at the midpoint of the line connecting the apexes of both ears
Nausea/vomiting	GV20	On the instep of the foot in the depression of the posterior end of the 1st interosseous metatarsal space
	PC6	Located on the anterior surface of the forearm, about 2 inches proximal of the wrist crease between the tendons of the muscle
	TE6	On the dorsal side of the forearm and on the line connecting Yangchi (SJ4) and the tip of the olecranon, 3 cun proximal to the dorsal crease of the wrist, between the radius and ulna
Cancer pain	ST36	3 cun below ST 35, one finger width lateral from the anterior border of the tibia
	LI4	On the dorsum of the hand, between the 1 <sup>st</sup> and 2 <sup>nd</sup> metacarpal bones, in the middle of the 2 <sup>nd</sup> metacarpal bone on the radial side
	LU7	Superior to the styloid process of the radius
	ST36	3 cun below ST 35, one finger width lateral from the anterior border of the tibia
Fatigue/insomnia	TE8	On the dorsal side of the forearm, 4 cun proximal to the dorsal crease of the wrist, between the radius and the ulna
	HT7	At the wrist crease, on the radial side of the flexor carpi ulnaris tendon, between the ulna and the pisiform bones
	PC4	5 cun above the wrist crease between the tendons of the palmaris longus and flexor carpi radialis
	Auricular	The Shen Men point is located near the inferior lateral wall of the triangular fossa of the ear Shen Men

with accompanying side effects. Two recent RCT studies showed acupuncture may decrease the frequency of hot flashes, but not to a statistically significant level when compared with sham acupuncture.<sup>[14,15]</sup> Another RCT enrolled breast cancer patients who had all taken tamoxifen for more than 3 months, and compared the Kupperman index and frequency of hot flashes between the patients who received true acupuncture (TA) and those who received sham acupuncture (SA). A significant benefit was found in this study.<sup>[16]</sup> A systemic review indicated evidence from sham-controlled RCTs for the limited effects of acupuncture in treating hot flashes in breast cancer patients, and more pharmacologic agents, including megestrol acetate, clonidine, and selective serotonin reuptake inhibitors (SSRI), need to be tested.<sup>[16,17]</sup> Although the mechanism is uncertain, it is hypothesized that neurotransmitters are involved in thermoregulation.<sup>[18]</sup>

### Xerostomia

Radiation-induced xerostomia is a common symptom in patients with head and neck cancer (HNC) because radiotherapy fields frequently encompass the major salivary glands. Once the accumulated dose exceeds 26 Gy, the radiation damage to salivary gland tissue is difficult to reverse. The dry mouth sensation definitely influences a patient's quality of life (QoL). Thus, some conventional modalities that have been applied include (a) salivary replacement treatment, (b) mechanical and pharmacological stimulants, (c) cholinergic muscarinic agonist (pilocarpine), and (d) improved radiation dosimetry. In recent years, "acupuncture" has received much more attention stemming from a hypothesis that acupuncture may stimulate salivary flow accompanied by corresponding central nervous system (CNS) functional magnetic resonance imaging (fMRI) changes in radiation-induced xerostomia.<sup>[19]</sup> Some systemic reviews have given evidence indicating that acupuncture's benefit in irradiation-induced xerostomia is limited and further high-quality RCTs are still needed.<sup>[20,21]</sup> A recent non-RCT study showed preventive acupuncture led to significantly improved salivary flow rates and decreased xerostomia-related symptoms,<sup>[22]</sup> and another RCT by David reported significant reduction in pain, dysfunction, and xerostomia with good tolerance.<sup>[23]</sup> The possible mechanism for palliating xerostomia using acupuncture may be related to the neuropeptides modulating the salivary secretion in a complex process orchestrated by both the sensory and the autonomic nervous systems.<sup>[24]</sup>

### Nausea/vomiting

Both ASCO (American Society of Clinical Oncology) and NCCN (National Comprehensive Cancer Network) state the 5-hydroxytryptamine (5HT<sub>3</sub>) antagonists and neurokinin 1 (NK1)-receptor antagonist can reduce chemotherapy-induced nausea/vomiting (CINV). However, there are still many patients who cannot tolerate these symptoms because they deeply impair the patients' QoL and delay the chemotherapy course.<sup>[25]</sup> Application of acupuncture in cancer-related nausea/vomiting has been studied since 1990s.<sup>[26]</sup> In 1998, the National Institutes of Health Consensus Statement on Acupuncture noted that promising results have emerged showing the efficacy of acupuncture in adult postoperative and chemotherapy-induced nausea and vomiting. A review

article indicated the benefits of EA in chemotherapy-induced acute vomiting, but studies combining EA with state-of-the-art antiemetics and in patients with refractory symptoms are needed to determine the clinical relevance.<sup>[27]</sup> The most popular acupoints applied in this problem are P6 and S36, both of which belong to the Chinese stomach meridian.<sup>[28]</sup> Improving vagal modulation and HRV (Heart rate variability) change were observed to be related to reducing post-chemotherapy nausea/vomiting.<sup>[29]</sup> Several acupuncture studies have applied different chemotherapy regimes such as cisplatin or cyclophosphamide. They revealed that acupuncture combined with antiemetics can effectively decrease the incidence and degree of cisplatin- and cyclophosphamide-induced delayed nausea and vomiting and that the effect of acupuncture is better than that of sham acupuncture.<sup>[30,31]</sup> Two multicenter longitudinal RCTs have also shown significant benefits of acupuncture in alleviating the severity of both acute and delayed vomiting.<sup>[32,33]</sup>

However, there have still been negative results of acupuncture on CINV. A randomized controlled single-blind trial that focused on high-dose chemotherapy and autologous peripheral blood stem cell transplantation showed no benefit from acupuncture.<sup>[34]</sup>

Therefore, the effect in radiotherapy-induced nausea/vomiting is not conclusive, as there are both positive and negative results.<sup>[35,36]</sup>

### Cancer pain

Cancer pain is a refractory symptom in oncology. The World Health Organization suggested managing pain should begin with the use of time-honored opioids, but it also recommends the use of adjuvant therapies such as acupuncture and other complementary and alternative modalities early in the management process.<sup>[37]</sup> The main mechanism of the analgesic effect of acupuncture may be related to its effect in decreased substance P and upregulating plasma  $\beta$ -endorphin levels.<sup>[38]</sup> Since there are various manual approaches to acupuncture, there is no definite conclusion as to its effectiveness. A systemic review of RCTs evaluating any type of invasive acupuncture for cancer pain indicated insufficient evidence to judge whether acupuncture is effective, due to methodological limitations, small sample sizes, poor reporting, and inadequate analysis.<sup>[39]</sup> Meanwhile, a meta-analysis showed Transcutaneous Electric Nerve Stimulation (TENS) may have a role in pain management, but there was insufficient available evidence to determine its effectiveness in treating cancer-related pain.<sup>[40,41]</sup> However, closer inspection shows positive results, for example, a randomized controlled blind study with 90 patients found auricular acupuncture may significantly reduce pain intensity from cancer patients who are in pain, despite stable analgesic treatment.<sup>[42]</sup> Providing massage and acupuncture in addition to usual care also resulted in decreased pain among postoperative cancer patients, when compared with usual care alone.<sup>[43]</sup> Similar significant benefits were also observed in RCTs comparing true body and auricular acupuncture with the sham group, concluding acupuncture can relieve Aromatase inhibitors induced arthralgia and joint stiffness.<sup>[44,45]</sup> This is because cancer pain may arise not only from cancer itself, but also from cytokine or other related treatments. More focused and rigorous, methodological quality studies are necessary to assess the clinical efficacy of acupuncture for cancer pain.<sup>[46]</sup>

### Fatigue/insomnia

Cancer-related fatigue is a multidimensional phenomenon that is self-perceived, and includes physical, emotional, cognitive, and behavioral components. It is usually accompanied by symptoms such as depression and insomnia. As part of complementary therapy, acupuncture has been studied in this field for several decades. A methodologically feasible RCT compared acupuncture, acupressure, and sham acupressure in post-chemotherapy fatigue patients and found positive results in enhancing patients' general fatigue ( $P < 0.001$ ), physical fatigue ( $P = 0.016$ ), activity ( $P = 0.004$ ), and motivation ( $P = 0.024$ ).<sup>[47]</sup> A single-arm, phase II pilot study showed clinically meaningful results in improving post-chemotherapy fatigue with acupuncture.<sup>[48]</sup> On the other hand, insomnia may lead to fatigue and depression, which are also commonly observed in cancer patients. A recent RCT evaluated 80 patients and revealed acupuncture can effectively reduce malignant-related depression and improve the sleep quality of cancer patients.<sup>[49]</sup> A meta-analysis also indicated auricular acupuncture may improve sleep quality better than medications such as diazepam.<sup>[50]</sup> However, studies focused on cancer-related fatigue and insomnia are difficult to clearly understand because many confounding factors need to be considered. A Cochrane systematic review of acupuncture for insomnia concluded, "The current evidence is not sufficiently extensive or rigorous enough to support the use of any form of acupuncture for treating insomnia."<sup>[51]</sup> The data so far show acupuncture causes sedative and hypnotic effects in cancer patients when used for treating nervousness and insomnia. Further methodologically strong, randomized controlled studies with a large sample size are needed to assess the usefulness of acupuncture for cancer-related fatigue and insomnia.

### Side effects and complication management

The safety issues concerning oncology acupuncture practice have become imperative, since cancer patients usually have a more complicated medical status and are at higher risk of developing adverse reactions from acupuncture. Patients with coagulation dysfunction or severe thrombocytopenia with a bleeding tendency should be paid special attention. In patients with a cardiac pacemaker or intracardiac defibrillator, EA should be avoided. Direct insertion of needle into a tumor nodule or ulcerated wound, as well as lymphedematous limbs should be avoided. Sterile needles are obligatory. Severe adverse effects of acupuncture are rare and easily handled, such as a small hemorrhage, fainting, or syncope, bruising, dizziness, needle breakage, pneumothorax, or nerve damage. A multicentric survey from Germany observed that if it is used according to the established safety rules and carefully at appropriate anatomic regions, it is a safe treatment method.<sup>[52]</sup>

Based on our experience, patients with sepsis or those in shock are unsuitable for acupuncture. Other conditions caused due to treatment, such as cancer-related neutropenia [absolute neutrophil count (ANC)  $< 500/\mu\text{l}$ ] or thrombocytopenia (platelet  $< 20,000/\mu\text{l}$ ), as well as immune-compromised condition or major co-morbidities should always be kept in mind. Before the first visit, approval and communication should be obtained from the patients and the primary oncologist.

## THE PERSPECTIVE ROLE OF ACUPUNCTURE IN ONCOLOGY

The increase in the overall survival of cancer patients is attributed to the rapid progress of cancer treatment modalities. More and more attention has been focused on complementary and alternative medicine. Acupuncture is a well-established technique in this field. Many studies showed benefits of the technique to multiple cancer-related symptoms, as discussed above. Note, however, that the study design with respect to the study population, sample size, methodological quality, mode of TENS, treatment duration, method of administration, and outcome measures used was not uniform and some equivocal conclusions were reached. Based on the holistic cancer care viewpoint and current RCT data, the clinical application and study of acupuncture in oncology should be simultaneously evaluated. To be more persuasive, standardized clinical protocols, and the types and points of acupuncture for each symptom should be elucidated and investigated further. As encouraging evidence continues to emerge, acupuncture could play a more prominent role in integrative cancer care.

## ACKNOWLEDGMENTS

The authors would like to thank the team members of the National Yang-Ming University, School of Medicine, Institute of Traditional Medicine for their participation.

## REFERENCES

1. Molassiotis A, Fernandez-Ortega P, Pud D, Ozden G, Scott JA, Panteli V, *et al.* Use of complementary and alternative medicine in cancer patients: A European survey. *Ann Oncol* 2005;16:655-63.
2. Sagar SM. Acupuncture as an evidence-based option for symptom control in cancer patients. *Curr Treat Options Oncol* 2008;9:117-26.
3. Rong P, Zhu B, Li Y, Gao X, Ben H, Li Y, *et al.* Mechanism of acupuncture regulating visceral sensation and mobility. *Front Med* 2011;5:151-6.
4. Moritaka K, Zereto JL, Kimoto M, Nasution FH, Hirano T, Toda K. Response properties of nucleus reticularis lateralis neurons after electroacupuncture stimulation in rats. *Am J Chin Med* 2010;38:869-80.
5. Carpenter RJ, Dillard J, Zion AS, Gates GJ, Bartels MN, Downey JA, *et al.* The acute effects of acupuncture upon autonomic balance in healthy subjects. *Am J Chin Med* 2010;38:839-47.
6. Takahashi T. Mechanism of acupuncture on neuromodulation in the gut: A review. *Neuromodulation* 2011;14:8-12.
7. Lin JG, Chen WL. Acupuncture analgesia: A review of its mechanisms of actions. *Am J Chin Med* 2008;36:635-45.
8. Yu LL, Liu RP, Gao XY, Liu K, Li L, Ben H, *et al.* Development of studies on neurochemical mechanism of acupuncture underlying improvement of depression. *Zhen Ci Yan Jiu* 2011;36:383-7.
9. Wang XJ, Wang LL. A mechanism of endogenous opioid peptides for rapid onset of acupuncture effect in treatment of depression. *Zhong Xi Yi Jie He Xue Bao* 2010;8:1014-7.
10. Mori H, Nishijo K, Kawamura H, Abo T. Unique immunomodulation by electro-acupuncture in humans possibly via stimulation of the autonomic nervous system. *Neurosci Lett* 2002;320:21-4.
11. Zhang SY, Du YQ. Effects of warming needle moxibustion on improvement of gastrointestinal and immune function in patients with postoperation of colorectal cancer. *Zhongguo Zhen Jiu* 2011;31:513-7.
12. Kim SK, Bae H. Acupuncture and immune modulation. *Auton Neurosci*

- 2010;157:38-41.
13. Carpenter JS, Andrykowski MA, Cordova M, Cunningham L, Studts J, McGrath P, *et al.* Hot flashes in postmenopausal women treated for breast carcinoma: Prevalence, severity, correlates, management, and relation to quality of life. *Cancer* 1998;82:1682-91.
  14. Kim DI, Jeong JC, Kim KH, Rho JJ, Choi MS, Yoon SH, *et al.* Acupuncture for hot flushes in perimenopausal and postmenopausal women: A randomised, sham-controlled trial. *Acupunct Med* 2011;29:249-56.
  15. Deng G, Vickers A, Yeung S, D'Andrea GM, Xiao H, Heerdt AS, *et al.* Randomized, controlled trial of acupuncture for the treatment of hot flashes in breast cancer patients. *J Clin Oncol* 2007;25:5584-90.
  16. Hervik J, Mjaland O. Acupuncture for the treatment of hot flashes in breast cancer patients, a randomized, controlled trial. *Breast Cancer Res Treat* 2009;116:311-6.
  17. Lee MS, Kim KH, Choi SM, Ernst E. Acupuncture for treating hot flashes in breast cancer patients: A systematic review. *Breast Cancer Res Treat* 2009;115:497-503.
  18. Borud EK, Alraek T, White A, Fonnebo V, Grimsgaard S. The effect of TCM acupuncture on hot flushes among menopausal women (ACUFLASH) study: A study protocol of an ongoing multi-centre randomised controlled clinical trial. *BMC Complement Altern Med* 2007;7:6.
  19. Deng G, Hou BL, Holodny AI, Cassileth BR. Functional magnetic resonance imaging (fMRI) changes and saliva production associated with acupuncture at LI-2 acupuncture point: A randomized controlled study. *BMC Complement Altern Med* 2008;8:37.
  20. O'Sullivan EM, Higginson IJ. Clinical effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia in patients with head and neck cancer: A systematic review. *Acupunct Med* 2010;28:191-9.
  21. Jedel E. Acupuncture in xerostomia: A systematic review. *J Oral Rehabil* 2005;32:392-6.
  22. Braga FP, Lemos Junior CA, Alves FA, Migliari DA. Acupuncture for the prevention of radiation-induced xerostomia in patients with head and neck cancer. *Braz Oral Res* 2011;25:180-5.
  23. Pfister DG, Cassileth BR, Deng GE, Yeung KS, Lee JS, Garrity D, *et al.* Acupuncture for pain and dysfunction after neck dissection: Results of a randomized controlled trial. *J Clin Oncol* 2010;28:2565-70.
  24. Dawidson I, Angmar-Mansson B, Blom M, Theodorsson E, Lundeberg T. The influence of sensory stimulation (acupuncture) on the release of neuropeptides in the saliva of healthy subjects. *Life Sci* 1998;63:659-74.
  25. Osoba D, Zee B, Warr D, Latreille J, Kaizer L, Pater J. Effect of postchemotherapy nausea and vomiting on health-related quality of life. The Quality of Life and Symptom Control Committees of the National Cancer Institute of Canada Clinical Trials Group. *Support Care Cancer* 1997;5:307-13.
  26. Dundee JW, Ghaly RG, Bill KM, Chestnutt WN, Fitzpatrick KT, Lynas AG. Effect of stimulation of the P6 antiemetic point on postoperative nausea and vomiting. *Br J Anaesth* 1989;63:612-8.
  27. Ezzo JM, Richardson MA, Vickers A, Allen C, Dibble SL, Issell BF, *et al.* Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. *Cochrane Database Syst Rev* 2006;2:CD002285.
  28. Ezzo J, Streitberger K, Schneider A. Cochrane systematic reviews examine P6 acupuncture-point stimulation for nausea and vomiting. *J Altern Complement Med* 2006;12:489-95.
  29. Streitberger K, Ezzo J, Schneider A. Acupuncture for nausea and vomiting: An update of clinical and experimental studies. *Auton Neurosci* 2006;129:107-17.
  30. Lao L, Zhang G, Wong RH, Carter AK, Wynn RL, Berman BM. The effect of electroacupuncture as an adjunct on cyclophosphamide-induced emesis in ferrets. *Pharmacol Biochem Behav* 2003;74:691-9.
  31. Sima L, Wang X. Therapeutic effect of acupuncture on cisplatin-induced nausea and vomiting. *Zhongguo Zhen Jiu* 2009;29:3-6.
  32. Dibble SL, Luce J, Cooper BA, Israel J, Cohen M, Nussey B, *et al.* Acupressure for chemotherapy-induced nausea and vomiting: A randomized clinical trial. *Oncol Nurs Forum* 2007;34:813-20.
  33. Molassiotis A, Helin AM, Dabbour R, Hummerston S. The effects of P6 acupressure in the prophylaxis of chemotherapy-related nausea and vomiting in breast cancer patients. *Complement Ther Med* 2007;15:3-12.
  34. Streitberger K, Friedrich-Rust M, Bardenheuer H, Unnebrink K, Windeler J, Goldschmidt H, *et al.* Effect of acupuncture compared with placebo-acupuncture at P6 as additional antiemetic prophylaxis in high-dose chemotherapy and autologous peripheral blood stem cell transplantation: A randomized controlled single-blind trial. *Clin Cancer Res* 2003;9:2538-44.
  35. Enblom A, Johnsson A, Hammar M, Onelov E, Steineck G, Borjeson S. Acupuncture compared with placebo acupuncture in radiotherapy-induced nausea: A randomized controlled study. *Ann Oncol* 2012;23:1353-61.
  36. Enblom A, Lekander M, Hammar M, Johnsson A, Onelöv E, Ingvar M, *et al.* Getting the grip on nonspecific treatment effects: Emesis in patients randomized to acupuncture or sham compared to patients receiving standard care. *PLoS One* 2011;6:e14766.
  37. Running A, Seright T. Integrative Oncology: Managing cancer pain with complementary and alternative therapies. *Curr Pain Headache Rep* May 2012;16:325-31.
  38. Lee HJ, Lee JH, Lee EO, Lee HJ, Kim KH, Lee KS, *et al.* Substance P and beta endorphin mediate electroacupuncture induced analgesic activity in mouse cancer pain model. *Acupunct Electrother Res* 2009;34:27-40.
  39. Paley CA, Johnson MI, Tashani OA, Bagnall AM. Acupuncture for cancer pain in adults. *Cochrane Database Syst Rev* 2011;1:CD007753.
  40. Robb K, Oxberry SG, Bennett MI, Johnson MI, Simpson KH, Searle RD. A cochrane systematic review of transcutaneous electrical nerve stimulation for cancer pain. *J Pain Symptom Manage* 2009;37:746-53.
  41. Hurlow A, Bennett MI, Robb KA, Johnson MI, Simpson KH, Oxberry SG. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. *Cochrane Database Syst Rev* 2012;3:CD006276.
  42. Alimi D, Rubino C, Pichard-Leandri E, Ferman-Brule S, Dubreuil-Lemaire ML, Hill C. Analgesic effect of auricular acupuncture for cancer pain: A randomized, blinded, controlled trial. *J Clin Oncol* 2003;21:4120-6.
  43. Mehling WE, Jacobs B, Acree M, Wilson L, Bostrom A, West J, *et al.* Symptom management with massage and acupuncture in postoperative cancer patients: A randomized controlled trial. *J Pain Symptom Manage* 2007;33:258-66.
  44. Crew KD, Capodice JL, Greenlee H, Brafman L, Fuentes D, Awad D, *et al.* Randomized, blinded, sham-controlled trial of acupuncture for the management of aromatase inhibitor-associated joint symptoms in women with early-stage breast cancer. *J Clin Oncol* 2010;28:1154-60.
  45. Crew KD, Capodice JL, Greenlee H, Apollo A, Jacobson JS, Raptis G, *et al.* Pilot study of acupuncture for the treatment of joint symptoms related to adjuvant aromatase inhibitor therapy in postmenopausal breast cancer patients. *J Cancer Surviv* 2007;1:283-91.
  46. Choi TY, Lee MS, Kim TH, Zaslowski C, Ernst E. Acupuncture for the treatment of cancer pain: A systematic review of randomised clinical trials. *Support Care Cancer* 2012;20:1147-58.
  47. Molassiotis A, Sylt P, Diggins H. The management of cancer-related fatigue after chemotherapy with acupuncture and acupressure: A randomised controlled trial. *Complement Ther Med* 2007;15:228-37.
  48. Vickers AJ, Straus DJ, Fearon B, Cassileth BR. Acupuncture for postchemotherapy fatigue: A phase II study. *J Clin Oncol* 2004;22:1731-5.
  49. Feng Y, Wang XY, Li SD, Zhang Y, Wang HM, Li M, *et al.* Clinical research of acupuncture on malignant tumor patients for improving depression and sleep quality. *J Tradit Chin Med* 2011;31:199-202.
  50. Chen HY, Shi Y, Ng CS, Chan SM, Yung KK, Zhang QL. Auricular acupuncture treatment for insomnia: A systematic review. *J Altern Complement Med* 2007;13:669-76.
  51. Cheuk DK, Yeung WF, Chung KF, Wong V. Acupuncture for insomnia. *Cochrane Database Syst Rev* 2007;3:CD005472.
  52. Ernst G, Strzyz H, Hagmeister H. Incidence of adverse effects during acupuncture therapy—a multicenter survey. *Complement Ther Med* 2003;11:93-7.