

Iematol Oncol Clin North Am. Author manuscript; available in PMC 2009 August 1.

Published in final edited form as:

Hematol Oncol Clin North Am. 2008 August; 22(4): 631-viii. doi:10.1016/j.hoc.2008.04.005.

The Value of Acupuncture in Cancer Care

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Keywords

acupuncture; integrative medicine; cancer; symptom management; Complementary and alternative medicine; cancer care

Introduction

In the United States, acupuncture is used to treat a variety of symptoms and conditions associated with cancer and the side effects of cancer treatments. A number of cancer centers in the U.S., including Dana-Farber Cancer Institute (DFCI) in Boston, Memorial Sloan-Kettering Cancer Center in New York, and M.D. Anderson Cancer Center in Houston are integrating acupuncture into cancer care. This trend parallels a broader trend of increasing use of Complementary and Alternative Medicine (CAM) among cancer patients, estimated in some surveys to range between 48% and 83%. ^{1–4} Specific use of acupuncture by cancer patients is estimated to range between 1.7% and 31%. ^{5–7} Despite interest by conventional care providers and the public in the integration of acupuncture into cancer care, the full extent to which acupuncture can be applied to oncology care is limited by research evidence regarding its efficacy and safety in treating and preventing cancer-related symptoms.

There are a few conditions for which sound research has demonstrated acupuncture to be an effective and safe adjunct therapy for cancer care. Randomized clinical trials (RCT) have demonstrated that acupuncture is effective for chemotherapy-induced nausea and vomiting. $^{8-10}$ Research studies also suggest acupuncture may be helpful in managing cancer-related pain, 11 chemotherapy-related neutropenia, 12 cancer fatigue, 13 and radiation-induced xerostomia. $^{14-16}$ Acupuncture, an ancient medical treatment originating in China, is gaining momentum and acceptance as a valid intervention in medical practice. In the past decade acupuncture and other integrative medicine programs have been established in many major

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medical centers in the United States. For example in November 2000, the Leonard P. Zakim Center for Integrative Therapies (Zakim Center) was established at DFCI, a teaching hospital of Harvard Medical School, to provide complementary therapies to patients of DFCI. The Zakim Center is named in memory of Lenny Zakim, a cancer patient and advocate for an integrative approach to cancer treatment. The mission of the Center is to educate and empower patients and staff by integrating the practice of complementary therapies into traditional cancer treatments.

The National Institutes of Health (NIH) has defined acupuncture as "a family of procedures involving stimulation of anatomical locations on the skin by a variety of techniques. The most studied mechanism of stimulation of acupuncture points uses penetration of the skin by thin, solid, metallic needles, which are manipulated manually or by electrical stimulation." ¹⁷

Currently, Traditional Chinese Medicine (TCM) serves as the most prevalent theoretical framework guiding the clinical practice of acupuncture in the U.S., in which clinical decisions are mainly based upon the unique clinical patterns that conform to TCM theory. In order to integrate acupuncture into conventional medical practice successfully, it is critical to develop scientific, evidence-based knowledge of acupuncture through basic and clinical research.

There has been an increase in acupuncture research in the field of oncology in the past twenty years, especially since the 1997 NIH consensus conference on acupuncture ¹⁷. This trend is reflected in the number of acupuncture research articles published on PubMed ¹⁸. From 1987– 2007, PubMed published 8,276 articles that were related to acupuncture, and 320 were specific to acupuncture in oncology. PubMed publications in 2007 grew 96% since 1987. Similarly, acupuncture articles increased 157% from the 323 published in 1987 to 876 released as of the first quarter of 2007, and acupuncture in oncology articles grew 3 ½ times from 12 to 42. Over this twenty-year period, the United States and China published 68 (26%) and 66 (25%) of 255 articles related to acupuncture and oncology, respectively. For the US, 53 (78%) of the 68 were released in the past seven years. The United Kingdom was next most prolific, having released 21 (8%) of the 255 articles. Although absolute numbers remain small, the number of randomized controlled trials (RCTs) also has risen significantly in past years, with 10 studies primarily focused on nausea and vomiting (30%) and 4 (12%) on cancer-related pain. Seven (21%) articles from China focused on acupuncture's anesthetic role in cancer-related surgery. While there were 12 (36%) of the 33 conducted trials on various cancers, 7 (21%) were specific to breast cancer. Overall 63% of the studies reported positive results.

The rise in interest in acupuncture trials could be attributed not only to the National Institute of Health's consensus conference, but also to the increase in federal funding for CAM research since 1999.

Mechanism of Action

The mechanism of action of acupuncture has been of great interest to many researchers. Numerous mechanistic studies of acupuncture in animal models and humans suggest that the effect of acupuncture is primarily based on stimulation to and the responses of the neuroendocrine system involving the central and peripheral nervous systems.

Data from animal research suggests that therapeutic acupuncture is partially mediated through opioidergic and/or monoaminergic neurotransmission involving the brainstem, thalamus, hypothalamic as well as pituitary function. ^{19–24} Human neuroimaging data from functional magnetic resonance imaging (fMRI), positron emission tomography (PET), and electroencephalography (EEG) have demonstrated that acupuncture stimulation moderates a wide network of brain regions, including the primary somatosensory, secondary somatosensory, and anterior cingulated, prefrontal, and insular cortices, amygdale,

hippocampus, hypothalamus, and other areas. $^{25-32}$ The brain response may differ depending on $de\ qi$. $De\ qi$ is a sensation experienced during acupuncture by the acupuncturist during the needle manipulation and by the patient who feels soreness, fullness, heaviness, local distension or other sensations 28 at local needling sites. 33 A pilot study using fMRI suggests a relationship between stimulation of an acupuncture point, LI-2, located at the base of the index finger, and the activation of the brain function area that is responsible for salivary production, suggesting neural transmission. 34

In several animal models, acupuncture and other stimulation methods of acupuncture points, such as thread implantation and point injection, suggest that acupuncture could down regulate the expression of Transforming Growth Factor (TGF). Particularly, two independent studies on rat models of liver fibrosis and chronic renal failure found an inhibition of TGF- β 1 expression in the tissues after acupuncture points were stimulated by either a thread implantation or injection with Chinese herbs. 35,36

It has been suggested that acupuncture stimulates production of granulocyte colony-stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF) in animal models treated with myelosuppressive chemotherapy. 37,38 In one controlled non-randomized human clinical trial, seven patients undergoing chemotherapy were treated with a course of nine daily acupuncture treatments. The serum G-CSF levels were measured before and after acupuncture treatment. There was a significant increase in G-CSF levels post acupuncture (p<0.001), along with an increase in white blood cell (WBC) count level (p<0.01) in this group of patients. 38

Place of Acupuncture in Clinical Cancer Care

Recent advances in acupuncture clinical research suggest that acupuncture may provide clinical benefit for cancer patients with treatment-related side effects such as nausea and vomiting, post operative pain, cancer related pain, chemotherapy-induced leukopenia, postchemotherapy fatigue, xerostomia, and possibly insomnia, anxiety and quality of life (QOL) (Table 1).

Chemotherapy-induced nausea and vomiting

After the NIH Consensus Conference in 1997, several well-designed clinical trials generated promising results. A randomized controlled trial further confirmed acupuncture's antiemetic effect on patients receiving chemotherapy, with a significant reduction of mean emesis episodes (5 vs. 15; P<0.001) compared with pharmacotherapy alone. ¹⁰ The results of the study confirmed the NIH consensus statement about acupuncture: "There is clear evidence that needle acupuncture is efficacious for adult postoperative and chemotherapy nausea and vomiting and probably for the nausea of pregnancy."¹⁷ Methods other than acupuncture needles used to stimulate acupuncture points also have been reported to have a positive effect. These stimulating methods include manual acupressure, a non-needling procedure with manual pressure on acupuncture points, acupressure wrist bands with or without electrical stimulation, and ear acupuncture. $^{9,39-41}$ For example, acupressure wrist bands have shown positive results in controlling chemotherapy-induced nausea and vomiting in a large multicenter study. However, another study indicated that using invasive needle acupuncture at P6, an anti-emesis point, showed no additional effect for the prevention of acute nausea and vomiting in highdose chemotherapy, compared with non-skin-penetrating placebo acupuncture. 42 In addition to chemotherapy-induced nausea and vomiting, acupuncture has been shown to be effective in the prevention of post operative nausea and vomiting.⁴³

The authoritative Cochrane systematic review on this subject states that "data on post-operative nausea and vomiting suggest a biologic effect of acupuncture-point stimulation. Electroacupuncture has demonstrated benefit for chemotherapy-induced acute vomiting, but

studies combining electroacupuncture with state-of-the-art anti-emetics and in patients with refractory symptoms are needed to determine clinical relevance. Self-administered acupressure appears to have a protective effect for acute nausea and readily can be taught to patients though studies did not involve placebo control. Noninvasive electrostimulation appears unlikely to have a clinically relevant impact when patients are given state-of-the-art pharmacologic anti-emetic therapy."⁴⁴

Cancer pain

Pain is a long-standing and unresolved clinical issue among cancer patients. Even after over 20 years since the World Health Organization (WHO) published its recommendation of an analgesic ladder for pain control, ⁴⁵ fifty-five percent of cancer patients still suffer from various forms of pain that significantly impacts their quality of life (QOL). ⁴⁶ One of the reported barriers is the resistance to start opioid therapy either by the patient or the physician. ⁴⁷ Alternatively, inappropriate use of opioids is associated with significant side effects among cancer patients. ⁴⁸

Acupuncture analgesia has been actively studied in the laboratory and clinic for several decades. Several systematic reviews support the use of acupuncture for a wide range of non-cancer-specific pain conditions in clinical practice. These pain conditions include osteoarthritis, ⁴⁹ chronic knee pain, ⁵⁰⁵¹ shoulder pain, ⁵² neck pain, ⁵³ and acute dental pain. ⁵⁴ Although the numbers of acupuncture clinical trials for cancer-specific pain are still small, results of these non-cancer related clinical trials may support benefit for patients with cancer. First, cancer pain may be brought on by a combination of biological, psychological and social components. ⁵⁵ Acupuncture-induced analgesic effects can strongly influence the psychological aspect of pain. ⁵⁶ Second, since the majority of cancer patients are in the older population, a stage when significant numbers are reported to have chronic pain, pain reported from patients with cancer may not necessarily be directly cancer-related and may respond to acupuncture. Third, several RCTs specifically studied acupuncture pain control during surgical procedures and found that acupuncture reduced analgesic requirement of drugs such as morphine, pirinitramide, and alfentanil. ^{57–60} Therefore, it is reasonable to believe that acupuncture could serve as a non-pharmaceutical mediator to assist the WHO analgesic ladder for cancer pain.

In the field of cancer-specific pain management, a randomized placebo-controlled trial demonstrated that auricular acupuncture is effective for cancer patients with various forms of neuropathic pain. Several other randomized controlled clinical trials have suggested that acupuncture can be used for the following conditions to manage pain among cancer patients:

1) chronic constant neuropathic pain in post-cancer therapies; 1 2) post-thoracotomy pain in patients with operable non-small cell lung carcinoma; 61 and 3) other post-operative pain in patients with breast cancer, bladder cancer, prostate cancer, and ovarian cancer. 62

In these clinical settings, acupuncture often is used as a complementary method along with usual care to provide additional pain reduction, as well as to lessen the need for pharmaceutical analgesic medicine.

Symptom relief

Depression and anxiety

A recently published RCT reports that massage combined with acupuncture in post-operative cancer patients can improve the depressive mood of these patients when used in conjunction with usual care (p=0.003). A short-lived improvement in tension and anxiety also was found in this study (p=0.048). 62

Although conducted in non-cancer patients, several RCTs have found acupuncture may significantly reduce patient anxiety during acute physical trauma (e.g., radial fractures, hip fracture), hospital transportation, during or prior to lithotripsy and dental procedures, cataract surgery, and pre-operative parental anxiety. $^{63-68}$ In addition to acupuncture needle stimulation on traditional body acupuncture points, ear acupuncture, ear acupressure and acupressure on other body parts also seems to be effective in providing mild to moderate sedative effects in anxious patients. $^{69-71}$

Hot flashes

Using acupuncture for hot flashes in breast cancer patients is another active area of clinical study. Although empirical reports suggest that acupuncture is beneficial to reduce the number of hot flashes in breast cancer patients, ⁷² a recently published well-controlled clinical trial failed to demonstrate the benefit of active acupuncture as compared to sham acupuncture in reducing hot flashes. ⁷³ Interestingly, hot flash frequency in breast cancer patients in this study was reduced following both true and sham acupuncture. The authors suggest that a longer and more intense acupuncture intervention could produce a larger reduction in all of these symptoms. ⁷³ Another less rigorous RCT from Sweden reported a more than 50% reduction of hot flashes and other associated symptoms in breast cancer patients after receiving a 12 week electroacupuncture intervention. ⁷⁴ There was a suggestion in this study that the symptom reduction effect was durable, lasting up to 6 months.

Leukopenia

Although there is an absence of medical literature in the English language on the use acupuncture for leukopenia, several RCTs conducted in China have suggested that acupuncture could be effective in reducing marrow suppression related leukopenia in patients undergoing chemotherapy. An exploratory meta-analysis of clinical trials conducted in China suggests that acupuncture use is associated with an increase in leukocytes in patients during chemotherapy or chemo-radiotherapy, with a weighted mean difference of 1,221 WBC/ μ L on average (95% confidence interval 636–1,807; p < .0001). A randomized sham-controlled clinical trial exploring chemotherapy induced neutropenia in ovarian cancer patients has been completed at DFCI and preliminary data suggests improved neutrophil counts at the nadir and rebound points after chemotherapy 78,79

Fatigue

Several prospective pilot trials have shown acupuncture may benefit patients with chemotherapy related fatigue. ^{13,80} In patients with persistent fatigue who had previously completed cytotoxic therapy and were not anemic, acupuncture resulted in a 31.3% improvement in the baseline fatigue score. ¹³

Neuropathy

Chemotherapy-induced neuropathy, e.g., from platinum and taxol related compounds, is a common problem. A small pilot study of 5 patients suggested a partial response to acupuncture that could not be explained by any other known neurophysiologic mechanism⁸¹. A positive impact from acupuncture on neuropathy in DFCI clinic patients also has been observed.

Insomnia

Insomnia is one of the most significant symptoms of cancer patients, along with anxiety. Acupuncture has been researched among patients with insomnia with mixed results. A small, non-cancer study found acupuncture may significantly reduce insomnia and anxiety, with clear objective improvements in nocturnal melatonin secretion and in polysomnographic measures. 66 A meta-analysis showed that the improvement rate of insomnia produced by ear acupuncture

was significantly higher than those from diazepam (p < 0.05). 82 The rate of success was particularly higher when ear acupuncture was used for enhancement of sleeping hours, up to 6 hours in treatment subjects (p < 0.05). The authors of this study concluded that ear acupuncture appears to be effective for treating insomnia.

However, in a Cochrane systematic review of acupuncture for insomnia, the authors found that acupuncture or its variants were not more significantly effective than a control (RR = 1.66, 95% CI = 0.68 to -4.03). The current evidence is not sufficiently extensive or rigorous enough to support the use of any form of acupuncture for the treatment of insomnia. Larger high quality clinical trials employing appropriate randomization, concealment, and blinding with longer follow-up are warranted to further investigate the efficacy and safety of acupuncture for the treatment of insomnia.

Radiation-induced xerostomia

Xerostomia, or dry mouth, is considered a significant factor underlying dysphagia. Several pilot clinical studies suggest that acupuncture may improve xerostomia caused by radiation therapy in patients with head and neck cancers. Blom first reported a small RCT with placebo acupuncture control in which acupuncture treatment induced a persistent salivary flow rate among a group of patients with severe xerostomia. A long-term follow up (up to 32 months) further confirmed his findings. \$14,84,85\$ Johnstone and his colleagues used acupuncture for patients with pilocarpine-resistant xerostomia after radiotherapy for head and neck cancer. \$15,86\$ He found a 70% response rate, i.e., an increase of 10% or more from the baseline Xerostomia Inventory. Wong and his colleagues reported a phase I–II study using transcutaneous electrical stimulation. \$16\$ Forty-six patients were randomized among three groups with different acupuncture points. After six weeks of treatment, for 37 patients who completed the treatment course, the salivation increase was statistically significant at both 3-and 6- month follow-ups. Studies using fMRI found a relationship between stimulating acupuncture point, LI-2, located at the base of index finger, and the activation of the brain function area responsible for salivary production. \$34\$

Dyspnea

Although clinical evidence for acupuncture treating dyspnea in cancer patients is yet to come, some preliminary RCTs suggest acupuncture and acupressure may improve respiratory function and quality of life among patients with chronic obstructive asthma, bronchiectasis, and chronic obstructive pulmonary disease. ^{87–89} Therefore, acupuncture/acupressure for dyspnea in cancer patients is a promising area for future studies.

Acupuncture in palliative care

A pilot study demonstrated feasibility of administering acupuncture as adjuvant palliative therapy to patients with advanced cancer. 90 Forty ambulatory patients with advanced ovarian or breast cancer who were receiving conventional palliative care were recruited to receive acupuncture treatment for 8 weeks (12 sessions total). Twenty-six patients (65%) completed all 8 weeks of treatment, thereby achieving the study's main feasibility goal. Over time, a significant decrease in symptom severity was seen for fatigue, pain, and insomnia. QOL measures of pain severity and interference, physical and psychological distress, life satisfaction and mood states showed higher positive scores during acupuncture treatment than before treatment and were sustained at 12 weeks relative to baseline. This pilot study warrants study in a larger population using proper controls.

Clinical Practice

An important criterion to evaluate a therapy in clinical practice is the safety record of that therapy. Several studies on the safety of acupuncture have confirmed that acupuncture is a safe procedure in the hands of competent practitioners. One large study found only 43 minor adverse events associated with 34,407 treatments with no serious adverse events reported. Based upon the criteria proposed by Weiger et al, 20 in which the clinical effectiveness and the risk ratios of CAM therapies are simultaneously weighed, acupuncture for chemotherapy-related nausea and vomiting and for pain have been categorized as "safe and effective" and can be "recommended" as an adjunct to conventional therapy. The assurance of acupuncture safety is further emphasized by the FDA regulation of acupuncture needles as a medical device, the training and licensing of clinical acupuncturists, and continuing education courses and licensing now available to physicians. Medicare has recognized acupuncture by assigning it Current Procedural Terminology (CPT) codes, thereby promoting insurance and health expense account reimbursement.

Despite the wide use of CAM therapies among cancer patients and despite its safety and efficacy, acupuncture use in this population remains low. The prevalence of CAM use varied in range from 48% to 83% among cancer patients in several studies depending on the definition of CAM. ^{1,2,4} One recent study found that among insured cancer patients in Washington State, the acupuncture usage was only 1.7% in the year 2000. ⁶ A survey among 1065 Chinese women with breast cancer found that although 98% of patients had used at least one form of CAM therapy, the utilization rate of acupuncture was only 4.9%. ⁵ Similar findings were reported by Ganz (2.2%) and Burstein (4.0%). ^{94,95} The highest utilization rate of acupuncture in cancer patients was reported by Morris et al as 31% of 617 responses. ⁷ The use of acupuncture is highly associated with the economic status of patients since it requires patients to consult a CAM practitioner whose services generally are not covered by health insurance companies. Although some major cancer centers now provide acupuncture services to cancer patients, the scale of such services is still small. The paucity of referrals from clinicians and the need to self-pay for the acupuncture are considered two main barriers for using acupuncture.

Research Issues

Clinical research of acupuncture in cancer care has been supported by federal and private funding sources. A steady increase in reports from high quality clinical trials is expected in the next few years. This will help improve clinical decision-making about acupuncture, because current available results from many studies suffer from poor study design. The shortcomings of these clinical trials exist mainly in three areas: 1) the design of the clinical trial; 2) the quality control employed in conducting the trial; and 3) the complete, detailed reporting of the clinical trial. As a result, often study results are difficult to interpret. The design of clinical trials of acupuncture should comply with the general principles of clinical trials in medicine, such as adequate sample size, power calculations, randomization, and effective concealment of treatment assignment. Clinicians who have a background in pharmaceutical trials should be made fully aware of the uniqueness of acupuncture clinical studies.

In the past, most clinical trials of acupuncture were designed by clinicians who were not specifically trained in clinical trial design. Therefore, the quality of acupuncture trials was considerably poor. For example, many systematic reviews revealed that most trials reported randomization only, which is only one of three commonly recognized key domains in quality trials; blinding and handling of dropouts and withdrawals were not mentioned. 12,83,96 It is recognized that although quality scales are important tools to assess the integrity of clinical trials, they are poor surrogates of the true quality of a specific trial. Some studies suggested that the poor quality of a trial could lead to inflated results. Trials with inadequate concealment

and ineffective blinding could lead to exaggerated odds ratios by 41% and 17%, respectively. 97

Although inappropriate design of clinical trials of acupuncture is still an issue of concern, many clinician scientists have begun to get involved in the design process of acupuncture trials. However, lack of familiarity with acupuncture technique and the assumption that an acupuncture clinical trial is exactly the same as a pharmaceutical trial potentially may lead to inaccurate results. Currently, the largest issue in clinical trials of acupuncture is the controversy of sham acupuncture as an effective control. Choosing the appropriate control for acupuncture clinical trials is a challenging task. Although several control methods are available, there is still a lack of consensus about which one is the most effective type of sham control. ^{98–100} As many researchers point out, an ideal sham control should mimic verum (true) acupuncture as much as possible, while at the same time not elicit any physiological effect on the study subjects.

A placebo needle (Streitberger needle) has been used in many clinical trials of acupuncture, in which the needle mimics the sensation of needle insertion with its blunt tip and appears to penetrate the skin, but it actually retracts into a hollow shaft. 101 Many studies have reported that this needle produces a very high quality and effective blinding effect on study patients. 42,56 However, critics point out that acupuncture is essentially based upon the sensation of needle insertion, $de\ qi$, while other types of acupuncture variations, such as acupressure and wrist bands, are not required to penetrate the skin, but they still produce the $de\ qi$ sensation in order to produce clinical results. Other sham acupuncture methods, such as superficial acupuncture needling, mock electro-acupuncture stimulation, needling at non-meridians and non-traditional acupuncture points also have been used in many trials. These methods have their shortcomings and limitations as well. Clinical trials have demonstrated that sham acupuncture has different effects on pain than a placebo pill. 56 A study of experimental pain processing also revealed that placebo needling may evoke different types of brain responses than those evoked by more conventional placebos, such as creams or pills. 102

The implementation of clinical trials of acupuncture is another important issue. Since acupuncture is essentially a procedure involving skilled hand manipulation that is highly dependent on the operator's experience and their technique used, minimizing the variations during acupuncture performance is a critical issue to ensure the success of the clinical trials. A careful and meticulous standardization of each procedure should be planned and adequate training for such standardization should be provided before a trial starts.

Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA), ¹⁰³ a CONSORT based recommendation on acupuncture trials, has been published. It focuses on complete reporting of interventions rather than a quality measure scale. Due to the non-pharmaceutical and procedure-like nature of acupuncture trials, a discipline-specific quality measure scale needs to be further developed.

Summary

Clinical research on acupuncture in cancer care is a new and challenging field in oncology. The results of clinical research will continue to provide us with clinically relevant answers for patients and oncologists. The evidence currently available has suggested that acupuncture is a safe and effective therapy to manage cancer and treatment related symptoms, while giving patients the ability to actively participate in their own care plan.

Future research requires the involvement of clinical researchers, clinicians, and patients. Development of innovative research methods is also crucial. It is expected that as more evidence continues to emerge, oncology acupuncture eventually will be integrated into

standard oncology practice. The successful integration of acupuncture at major academic medical and research facilities, such as DFCI and other major cancer centers, underscores the need for and value of acupuncture in cancer care.

Acknowledgements

This work was supported by Grant No. 1K01AT004415-01 from the National Institutes of Health.

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Table1Clinical Trails and Systematic Review of Acupuncture Use in Clinical Cancer Care (2001–2007)

7	Clinical conditions	Author and Study design	Major outcome	Reported adverse events	Study population features
IH-PA Auth	Chemotherapy-induced nausea & vomiting	Roscoe et al. (2003) 9 Randomized controlled multicenter trial (n=739)	Patients in the acupressure group experienced less nausea on the day treatment compared to controls (p<0.05)	No adverse events were discussed	85% breast cancer, 10% hematologic neoplasms patients undergoing chemotherapy
or Manuscript	Post-operative nausea and vomiting	Gan et al. (2004) ⁴³ RCT (n=77) (electro-acupoint stimulation, ondansetron versus placebo)	The complete response rate was 77% vs. 64% and 42% (p=0.01); electro-acupoint stimulation is more effective in controlling nausea.	No difference in adverse events rate among groups	Patients undergoing major breast surgery
	Cancer pain	Alimi et al (2003) 11 Randomized, blinded, controlled trial (n=90)	Pain intensity deceased by 36% at 2 month from baseline in the study group (p<0.0001)	No infection was reported; no other adverse events were reported	Patients with chronic peripheral or central neuropathic pain arising after cancer treatment
NIH-PA A	Postoperative Pain	Mehling et al. (2007) ⁶² RCT (n=138)	Patients in the massage and acupuncture group with usual care experienced a decrease of 1.4 points on a pain scale (p=0.038)	No adverse events were discussed	Patients undergoing cancer- related surgery including breast, bladder, prostate and ovarian cancers
uthor Manuscript	Post-thoracotomy wound pain	Wong et al. (2006) 61 RCT (n=27) (electroacupuncture vs. sham acupuncture)	A trend for lower visual analogue scale pain score in the electroacupuncture group was observed. Postoperative morphine use was significantly lower in electroacupuncture group (p<0.05)	No adverse reactions related to acupuncture were observed	Patients with operable non- small cell lung carcinoma
	Hot flashes	Deng et al. (2007) 73 RCT (n=72) (True acupuncture versus sham acupuncture)	True acupuncture was associated with 0.8 fewer hot flashes per day than sham (p=0.3)	Very minor slight bleeding and bruising at the needle cite were reported	Breast cancer patients
NIH-PA Author	Vasomotor symptoms (hot flashes) and psychological well-being	Nedstrand et al. (2006) ⁷⁴ RCT (electroacupunctur e vs. applied relaxation) (n=38)	Longitudinally, Patients in the electro- acupuncture group experienced a decrease of hot flashes >50% at 12 weeks and at 6 months follow-up	No adverse event were discussed	Patients treated for breast cancer
Manuscri	Chemotherapy-induced leukopenia	Lu et al.(2007) ¹² Systematic review on RCTs (n=682)	WBC counts in study group was significantly higher than that in control group (p<0.05)	No adverse effects were discussed	Patients with non-small cell lung cancer or nasopharynx cancer undergoing chemotherapy
ot	Post-chemotherapy fatigue	Vickers et al. (2004) 13 Uncontrolled	The mean improvement from baseline fatigue	No adverse events were reported	Cancer patients who had completed cytotoxic chemotherapy at least 3

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	Clinical conditions	Author and Study design	Major outcome	Reported adverse events	Study population features
		prospective study (n=37)	score was 31.3% (95% CI: 20.6%– 41.5%)		weeks previously but complained of persisting fatigue.
NIH-PA Author N	Radiation induced Xerostomia	Johnstone et al. (2001) ¹⁵ Uncontrolled prospective study (n=50)	Response rate as improvement of 10% or better from baseline Xerostomia Inventory (XI) was 70%; 48% of patients received benefit of 10 points or more on the XI.	No adverse effects were reported.	Patients with Pilocarpine- resistant xerostomia after radiotherapy for head and neck cancer.