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## REVIEW ARTICLE

# Acupuncture Research at Memorial Sloan Kettering Cancer Center



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### Abstract

Acupuncture may help treat specific cancer-related symptoms. Here, we summarize our clinical trials that sought to determine acupuncture's role in managing cancer-related symptoms. Trials have been conducted to determine acupuncture's ability to mitigate cancer-related symptoms including dyspnea, fatigue, xerostomia, lymphedema, hot flashes, postoperative ileus, pain and dysfunction after neck dissection, and postthoracotomy pain. Published studies indicate that acupuncture versus placebo acupuncture failed to reduce cancer-related dyspnea. Both true and sham acupuncture alleviated fatigue slightly, but no significant differences between groups emerged. Compared with sham acupuncture, our research showed that acupuncture significantly improved saliva production in patients with xerostomia and significantly reduced lymphedema patients' arm circumference in a pilot study. However, acupuncture failed to significantly reduce hot flashes and was no more successful than sham acupuncture in reducing postoperative ileus. Significant reductions in pain and dysfunction occurred in cancer patients after neck dissection. In a feasibility study, acupuncture was found to be acceptable to lung cancer patients and did not interfere with standard postoperative care. In summary, acupuncture is a potential candidate for the treatment of some important cancer-related symptoms. Large clinical trials and research to investigate mechanistic pathways are warranted.

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## 1. Introduction

Cancer patients experience a variety of symptoms that diminish quality of life. Pain, reportedly the most common symptom among cancer patients, affects many, including approximately two-thirds of those with metastatic cancer. Common treatments such as opioids or neurosurgical procedures fail to provide full symptom relief and, used long-term, can cause constipation, nausea, and other side effects [1]. Other common symptoms include depression and anxiety, sleep disturbance, diarrhea, lymphedema, xerostomia, and joint or muscle dysfunction [2]. Standard treatments for these cancer-related symptoms may not provide full relief. Patients seek complementary therapies to address the side effects of cancer and cancer treatment, often when symptoms are not fully managed with mainstream interventions. Acupuncture is preeminent among them.

An increasing body of evidence supports the use of acupuncture for the control of cancer-related symptoms [2]. Here we summarize the acupuncture research conducted by the Memorial Sloan Kettering (MSK) Integrative Medicine Service, New York City, NY, USA.

## 2. Common cancer-related symptoms treated with acupuncture

### 2.1. Dyspnea

Dyspnea (shortness of breath) is often experienced by cancer patients, especially those with advanced disease [3]. Although most common in lung cancer patients, dyspnea is observed also in patients with breast or other cancers that affect the lungs [4,5]. Treatments such as opioid administration and supplemental oxygen are not always effective [6,7]. The objective of one MSK study was to determine whether we can relieve cancer-related dyspnea. In this trial, 47 patients with lung or breast cancer experiencing dyspnea were randomized to a single session of true versus placebo acupuncture in addition to mainstream dyspnea treatment. Semipermanent acupuncture “studs” were then inserted and the patients were instructed to apply pressure to these studs twice a day in order to provide constant stimulation to the acupuncture points. The patients’ subjective sensation of dyspnea was assessed immediately before and after acupuncture treatment daily for a week using a 0–10 numerical rating scale. Study results showed that acupuncture did not improve cancer-related dyspnea compared with placebo. We found no further publications on acupuncture for cancer-related dyspnea following our 2005 study described here [8]. A future potential trial with repeated acupuncture treatment might produce a cumulative effect. It is also possible that a different acupuncture technique, such as modifying the point prescriptions for each patient’s specific pathology, might produce better results.

### 2.2. Postchemotherapy chronic fatigue

An overwhelming majority of cancer patients experience fatigue [9]. Although most prevalent among patients

undergoing therapy or with advanced disease, fatigue is also common among cancer survivors [10]. Currently administered pharmacologic agents include modafinil or corticosteroids. Patients also seek nonpharmacologic treatments such as cognitive-behavioral interventions, lifestyle changes, and complementary medicine modalities such as acupuncture [11]. In an MSK study, 37 patients experiencing significant fatigue for at least 2 months following chemotherapy were randomized to receive true versus sham acupuncture once a week for 6 weeks. Patient fatigue was evaluated before and after each treatment.

Both true and sham acupuncture were found to alleviate fatigue slightly, but there were no significant differences between the two groups [12]. However, a 2007 randomized trial demonstrated that true acupuncture showed substantial improvement (36%) in fatigue levels compared with sham acupuncture and acupressure [13]. Two studies conducted after our trial show mixed results. In a randomized trial comparing acupuncture with sham acupuncture and with wait list controls, a significant reduction in fatigue was found for patients receiving acupuncture versus controls after 2 weeks [14]. However, in a randomized trial of self-needling as a maintenance therapy for cancer-related fatigue after therapist-delivered acupuncture, a nonsignificant reduction in fatigue was observed after treatment [15]. A major limitation of our MSK study was that a considerable number of patients were lost to follow up. In a future trial, a more intensive treatment regimen (e.g., 3 times weekly as opposed to once weekly) may be more effective.

### 2.3. Xerostomia

Radiation-induced salivary gland damage produces xerostomia (dry mouth) due to impaired saliva production [16]. Past clinical trials indicate that acupuncture may alleviate radiation-induced xerostomia [17–19]. The objective of an MSK study was to employ functional magnetic resonance imaging (fMRI) technology to investigate the neural substrates affected by acupuncture. In a randomized, controlled, participant-blinded trial, 20 healthy volunteers received true versus sham acupuncture. fMRI was used to evaluate the cortical regions activated or deactivated during treatment and saliva production was measured. Results showed that areas activated by true acupuncture at the acupoint LI-2 overlapped areas involved in gustation/salivation. Sham acupuncture was not associated with such neural activations. Moreover, true acupuncture induced significant saliva production compared with sham acupuncture [20]. These results corroborate past results and establish a foundation for further research into the mechanisms of acupuncture treatment for xerostomia.

## 3. Acupuncture for the relief of breast cancer related symptoms

### 3.1. Lymphedema

Lymphedema is the chronic swelling of a limb following lymph node removal. It is a frequent complication of breast

cancer treatment [21]. Patients must undergo regular intensive physical therapy to reduce lymphatic fluid volume in the affected arm [22]. Treatment must be continuous in order to prevent fluid reaccumulation and patients are obligated to wear tight, uncomfortable elastic stockings to prevent increased swelling [23]. In addition to being difficult to treat, lymphedema is costly to manage [24]. Previous clinical trials indicated that acupuncture can decrease lymphedema symptoms as well as limb swelling in both upper and lower extremities [25,26].

In 2011, a pilot study was conducted at MSK to evaluate the safety and effectiveness of acupuncture in women with chronic lymphedema after breast cancer surgery. Nine patients received acupuncture twice a week for 4 weeks. Four patients showed at least a 30% reduction in the affected versus unaffected arm. It was concluded that acupuncture is safe and may be able to reduce lymphedema in breast cancer patients [27].

Another MSK pilot study of breast cancer-related lymphedema (BCRL) was conducted in 2003. Eligible individuals ( $N = 33$ ) had experienced lymphedema for 0.5–5 years and had an affected arm circumference of 2 cm or larger than the unaffected arm. Participants received acupuncture treatment twice weekly for 4 weeks prior to evaluation. Needles were placed in the affected arm, a practice previously considered contraindicated but shown to be safe in modern research, including our previous publication and as was the case in this study [28]. Circumference differences between the affected and unaffected arm were assessed. Patients were followed monthly for 6 months after treatment to document complications and to obtain self-reported lymphedema status. Results showed that acupuncture significantly reduced the circumference in the affected arm. There were no reports of infections or other complications throughout treatment and follow-up. A high treatment adherence rate was noted. We found no further publications on acupuncture for breast cancer related lymphedema following our 2013 study noted here [28]. These results corroborate past findings and suggest that acupuncture may be considered a potential treatment modality for BCRL patients.

### 3.2. Hot flashes

Hot flashes (or hot flushes) are sensations associated with increased temperature and profuse sweating. Patients with hot flashes may also experience anxiety, palpitations, and sleep difficulties [29]. Patients undergoing treatment also may experience hot flashes due to abrupt menopause or estrogen ablation therapy [30]. Current treatment options for hot flashes include pharmacologic agents such as selective serotonin reuptake inhibitors (SSRIs), but these produce adverse effects and are considered undesirable options for most women [31,32]. Acupuncture may be a potential treatment modality as current treatment options for hot flashes are limited, especially for breast cancer patients on hormonal therapy. Previous studies suggest that acupuncture may relieve hot flashes in breast cancer patients [33–37].

An MSK study attempted to determine the effects of true versus sham acupuncture on hot flash frequency in women

with breast cancer. A group of 72 women with breast cancer experiencing three or more hot flashes daily were randomly assigned to receive either true versus sham acupuncture twice weekly for 4 weeks. Hot flash frequency was evaluated at baseline, at 6 weeks, and at 6 months posttreatment. Patients receiving sham acupuncture began receiving true acupuncture starting at Week 7. Results showed that hot flash frequency was reduced in breast cancer patients following both true and sham acupuncture, but the reduction associated with true acupuncture treatment was not statistically significant compared with the sham acupuncture group [38]. Future research may show that longer and more intense acupuncture intervention can evoke a stronger reduction in hot flash experience. Studies conducted after our 2007 trial show mixed results. Some demonstrated that, compared with sham, true acupuncture does not significantly reduce hot flashes [39–41], but others suggest that true acupuncture can reduce hot flashes and related symptoms [42,43].

## 4. Acupuncture for the relief of symptoms related to other cancer diagnoses

### 4.1. Postcolectomy ileus in colon cancer patients

Postoperative ileus (POI) commonly develops in patients after abdominal surgery and manifests in transient bowel dysfunction and reduced intestinal tract motility. POI can lead to other complications that prolong hospital stay, imposing a financial burden. POI is difficult to treat as interventions such as epidural local anesthetics are very costly [44]. Acupuncture may be potentially valuable as it is known to improve gastrointestinal motility in animal models [45,46]. The objective of our MSK study was to evaluate whether true acupuncture reduces POI more effectively than sham acupuncture. A group of 90 colon cancer patients undergoing colectomy were randomized to receive 30 minutes of true versus sham acupuncture twice daily for their first 3 postoperative days. GI function as well as pain, nausea, and vomiting were evaluated daily for the 3 postoperative days. Results showed that true acupuncture did not reduce POI more significantly than did sham acupuncture [47]. However, two other studies demonstrate that acupuncture is a potential candidate for mitigating postoperative ileus [48–50] as well as postoperative gastroparesis syndrome in abdominal surgical patients [51]. A major limitation of our study was a larger than expected standard deviation. Future trials should include larger sample sizes.

### 4.2. Pain, dysfunction, and xerostomia after neck dissection in head and neck cancer patients

Neck dissection is often required to prevent the spread of disease to the lymph nodes [52]. The removal of the spinal accessory nerve in this procedure leads to neck or shoulder pain and dysfunction, which is common, occurring in ~30–70% of patients after radial neck dissection [53,54]. Patients relying on physical therapy exercises and anti-inflammatory drugs report low efficacy and incomplete

**Table 1** Summary of MSK clinical acupuncture research.

Symptom	Population evaluated	MSK study	Methods	Results
Dyspnea (shortness of breath)	45 lung or breast cancer patients with dyspnea	[8]	Patients were randomized to true vs. placebo acupuncture. Semipermanent acupuncture "studs" were used by patients to provide ongoing stimulation. Dyspnea was assessed with a 0–10 numerical rating scale.	Acupuncture did not improve cancer-related dyspnea compared with placebo immediately after acupuncture treatment and for daily 1-week follow-up ( $p > 0.05$ ).
Fatigue	74 cancer patients with fatigue postchemotherapy	[12]	Patients were randomized to receive either true or sham acupuncture once a week for 6 weeks. Fatigue was assessed before and after treatment.	Both true and sham acupuncture alleviated fatigue slightly with no significant differences between the two ( $p > 0.05$ ).
Xerostomia (dry mouth)	20 healthy volunteers	[20]	Volunteers were randomized to true vs. sham acupuncture. Cortical regions activated or deactivated were evaluated by functional magnetic resonance imaging (fMRI). Saliva production was measured.	True acupuncture induced significant saliva production compared with sham acupuncture ( $p = 0.02$ ).
Lymphedema	33 women with breast cancer-related lymphedema	[28]	Patients received acupuncture treatment twice weekly for 4 weeks. Arm circumference for both arms was measured before and after each treatment. Positive response was defined as $\geq 30\%$ circumference reduction in affected vs. unaffected arms.	Acupuncture significantly reduced arm circumference in the affected arm ( $p < 0.0005$ ).
Hot flashes	72 women with breast cancer experiencing hot flashes	[38]	Patients were randomized to true or sham acupuncture twice weekly for 4 consecutive weeks. Hot flash frequency was evaluated at baseline, at 6 weeks, and at 6 months after treatment. Patients randomly assigned to the sham acupuncture group were crossed over to the true acupuncture group at Week 7.	Hot flash frequency reduction associated with true acupuncture treatment was not statistically significant compared with that of sham acupuncture ( $p > 0.05$ ).
Postoperative ileus (POI)	90 colon cancer patients undergoing elective colectomy	[47]	Patients were randomized to receive true or sham acupuncture for 30 minutes daily during their first three postoperative days. The following were determined: time patients first tolerated food, first passed flatus, and bowel movement.	True acupuncture did not reduce POI more significantly than sham acupuncture ( $p > 0.05$ ).
Pain and dysfunction after neck dissection	58 patients with chronic pain or dysfunction due to neck dissection	[56]	Patients were randomized to weekly acupuncture or usual care (e.g., physical therapy). The Constant-Murley score, a measure of pain and function was the primary outcome measure. Xerostomia also was assessed.	Patients receiving acupuncture experienced significant reductions in pain and dysfunction ( $p = 0.008$ ). Significant reductions in xerostomia ( $p = 0.02$ ) were observed.
Postthoracotomy pain	36 adult patients scheduled for unilateral thoracotomy with preoperative epidural catheter placement	[59]	Acupuncture was given immediately before surgery. 18 semipermanent intradermal needles were inserted on either side of the spine and four in the legs and auricles. Needles were removed after 4 weeks. Pain was measured with a numerical rating scale on the first postoperative days and assessed after discharge at 7 days, 30 days, 60 days, and 90 days.	Efficacy was not evaluated in this feasibility study. This novel intervention was found acceptable to patients undergoing thoracotomy and it did not interfere with standard preoperative care.

MSK = Memorial Sloan Kettering; POI = postoperative ileus.

symptom relief [55]. Acupuncture may be a potential treatment modality as it is well tolerated and has analgesic effects [2]. The primary objective of our MSK study was to assess whether acupuncture can reduce pain and dysfunction in cancer patients following neck dissection. A group of 58 patients were randomly assigned to weekly acupuncture versus usual care (e.g., physical therapy and/or inflammatory drugs) for 4 weeks. Pain and function were assessed as well as xerostomia. Results indicated that acupuncture produced significant reductions in pain and dysfunction and in xerostomia, suggesting that acupuncture could be a valuable treatment to alleviate postneck dissection pain and dysfunction, and to reduce xerostomia [56]. We found no other publications that assessed acupuncture for pain, dysfunction, or xerostomia after neck dissection in head and neck cancer patients. Additional research is warranted, and the use of acupuncture for these patients should be considered.

#### 4.3. Post-thoracotomy pain in lung cancer patients

Patients with primary lung cancer commonly are treated with thoracotomy, a surgical procedure in which an incision is made in the pleural region of the chest. After thoracotomy, patients typically report severe pain, which may limit respiratory function and impede postoperative recovery. Epidural catheters, local anesthetic infiltration, and nonsteroidal anti-inflammatory drugs (NSAIDs) are used to maximize analgesia [57,58]. Although acupuncture has been shown to reduce pain, acupuncture needles can potentially interfere with the surgical field and hamper epidural catheter placement, making acupuncture a poor choice for addressing post-thoracotomy pain. To address this possible concern, we investigated the feasibility of acupuncture in patients undergoing thoracotomy. A group of 36 patients scheduled for unilateral thoracotomy with preoperative epidural catheter placement received acupuncture treatment immediately before surgery. Eighteen semipermanent intradermal needles were placed on either side of the spine and four were placed in the legs and auricles. Needles were removed after 4 weeks. During the first 5 postoperative days and following discharge, pain was measured with a numerical rating scale.

Results showed that acupuncture was acceptable to patients undergoing thoracotomy and that it did not interfere with standard preoperative care. Although data from this single arm feasibility trial do not permit conclusions regarding the efficacy of acupuncture in managing post-thoracotomy pain, these data indicate decreasing severity of pain over time [59]. The study may demonstrate that this observed effect resulted from the acupuncture; additional research is warranted.

## 5. Conclusion

Acupuncture, assessed in multiple clinical trials conducted by MSK's Integrative Medicine Service, is a strong potential candidate for the treatment of cancer-related symptoms. Table 1 shows a summary of the research findings. Large clinical trials should be pursued to evaluate the potential of acupuncture to provide symptom relief as well as to

understand the mechanistic pathway by which it achieves its therapeutic effects. Additional acupuncture-related studies are underway at MSKCC, including a larger randomized trial of chronic lymphedema, a pilot trial in hematopoietic stem cell transplant patients, and a pilot study of chemotherapy-induced peripheral neuropathy in breast cancer patients.

## Disclosure statement

The authors declare that they have no conflicts of interest and no financial interests related to the material of this manuscript.

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