

## RESEARCH ARTICLE

# Effectiveness of Aromatherapy with Light Thai Massage for Cellular Immunity Improvement in Colorectal Cancer Patients Receiving Chemotherapy

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### Abstract

**Background:** Patients with colorectal cancer are usually treated with chemotherapy, which reduces the number of blood cells, especially white blood cells, and consequently increases the risk of infections. Some research studies have reported that aromatherapy massage affects the immune system and improves immune function by, for example, increasing the numbers of natural killer cells and peripheral blood lymphocytes. However, there has been no report of any study which provided good evidence as to whether aromatherapy with Thai massage could improve the immune system in patients with colorectal cancer. The objectives of this study were to determine whether the use of aromatherapy with light Thai massage in patients with colorectal cancer, who have received chemotherapy, can result in improvement of the cellular immunity and reduce the severity of the common symptoms of side effects. **Materials and Methods:** Sixty-six patients with colorectal cancer in Phichit Hospital, Thailand, were enrolled in a single-blind, randomised-controlled trial. The intervention consisted of three massage sessions with ginger and coconut oil over a 1-week period. The control group received standard supportive care only. Assessments were conducted at pre-assessment and at the end of one week of massage or standard care. Changes from pre-assessment to the end of treatment were measured in terms of white blood cells, neutrophils, lymphocytes, CD4 and CD8 cells and the CD4/CD8 ratio and also the severity of self-rated symptom scores. **Results:** The main finding was that after adjusting for pre-assessment values the mean lymphocyte count at the post-assessment was significantly higher ( $P=0.04$ ) in the treatment group than in the controls. The size of this difference suggested that aromatherapy with Thai massage could boost lymphocyte numbers by 11%. The secondary outcomes were that at the post assessment the symptom severity scores for fatigue, presenting symptom, pain and stress were significantly lower in the massage group than in the standard care controls. **Conclusions:** Aromatherapy with light Thai massage can be beneficial for the immune systems of cancer patients who are undergoing chemotherapy by increasing the number of lymphocytes and can help to reduce the severity of common symptoms.

**Keywords:** Colorectal cancer - aromatherapy - light Thai massage - chemotherapy - cellular immunity

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### Introduction

Chemotherapy is one of the most common forms of treatment for cancer, but it usually involves unpleasant side effects, such as fatigue, nausea and depression, and some form of adverse health impact, especially a reduction in white blood cells, which are important for preventing and fighting infections. Cancer patients receiving chemotherapy can therefore have a high risk of infection.

Patients with cancer are increasingly using complementary therapies for reducing the symptoms of treatment side effects (Rees et al., 2000; Bernstein and Grasso, 2001; Molassiotis et al., 2005). Aromatherapy massage has been reported as the most commonly used

complementary therapy in the United Kingdom's National Health Service (Lundie, 1994). There are many anecdotal and case reports (Wright, 1999; Buckle, 2001) supporting the use of massage and aromatherapy massage as safe and claiming beneficial effects in cancer patients, including reduced anxiety, stress, pain, muscular tension, and fatigue (Corbin, 2005; Wilkinson et al., 2008; Imanishi et al., 2009) and an associated enhancement of immune system functioning (Ironson et al., 1996; Imanishi et al., 2009).

There have been three previous studies of the use of massage to reduce symptom scores in cancer patients. The first was a non-randomized controlled trial with 1,290 in- and outpatients by Cassileth and Vickers (2004), which found that Swedish massage improved the severity scores

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of the presenting symptom by approximately 58%. The second was a randomized controlled trial with 39 breast cancer women reported by Billhult et al. (2007), which showed that, while massage significantly reduced nausea compared with a no-treatment control condition when improvement was measured as a percentage of the five treatment periods, the reductions in anxiety and depression were not statistically significant. The last study was a non-equivalent control group pretest-posttest design with 58 hospice patients with terminal cancer (Chang, 2008) which found that patients receiving aroma hand massage showed significantly greater improvements in pain and depression scores than a control group receiving general oil hand massage.

Seven previous studies have indicated that massage may improve immune function. The first was a randomized controlled trial by Field et al. (2001), which compared massage therapy with standard medical care in 20 acute lymphoblastic leukemia patients and found that massage therapy resulted in a statistically significant increase in WBCs and neutrophils. The second study was a small randomized controlled trial with 24 HIV positive adolescents (Diego et al., 2001) which compared massage therapy and progressive muscle relaxation and found that CD4 cells and the CD4/CD8 ratio increased only in massage therapy group. The third study (Hernandez-Rief et al., 2004) compared massage therapy and standard medical care alone in a randomized controlled trial with 34 breast cancer patients and found a statistically significant 10% increase in lymphocytes in the massage group. There was no change in the control group. The fourth (Kuriyama et al., 2005) was a Japanese preliminary cross-over trial with 11 healthy volunteers to compare aromatherapy massage with massage using only a carrier oil. The results showed statistically significant increases in lymphocytes, CD8, and CD16 after aromatherapy massage, but not after massage with only the carrier oil. In the fifth study (Hernandez-Reif et al., 2005) 58 women with early stage breast cancer were assigned to massage, relaxation or standard treatment control groups. As in their previous study, the results showed a statistically significant increase in lymphocytes in the massage group, and the size of the increase (9%) in this group was also similar. Again, there was no increase of lymphocytes in the control group and only a 2% non-significant increase in the relaxation group. The sixth study was a randomized controlled clinical trial (Billhult et al., 2008) in which 22 breast cancer patients were allocated either to a group receiving massage with a cold-pressed vegetable oil or to a visit-only control group. No significant differences in CD4 or CD8 cells were found. The last study (Imanishi et al., 2009) was a non-randomized controlled trial with 12 women with breast cancer and found statistically significant increases in WBCs and lymphocytes following aromatherapy massage twice a week for four weeks.

However, there is no specific evidence that aromatherapy massage or Thai massage improves immune system functioning in colorectal cancer patients receiving chemotherapy. The aim of the present study was to determine whether the use of aromatherapy with light Thai massage in chemotherapy patients with colorectal

cancer can result in improvements in cellular immunity and reduce the severity of the common symptoms.

## Materials and Methods

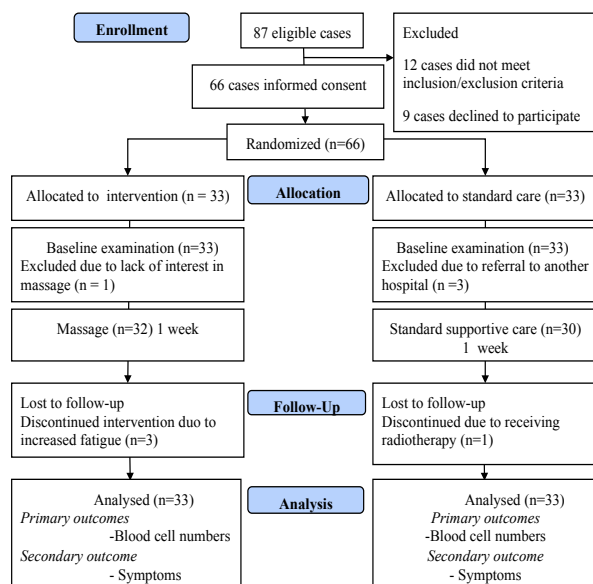
A single centre, single-blinded, randomized controlled trial was used to evaluate the effectiveness of aromatherapy with light Thai massage in colorectal cancer patients receiving chemotherapy at Phichit Hospital in Northern Thailand. During the 15 month period of data collection which ran from April 2011 to the end of July 2012, 94 patients with colorectal cancer in the chemotherapy unit were potential participants, and 87 (92.55%) responded to a recruitment advertisement. During screening, 12 of the respondents were found to be ineligible, and a further nine declined to sign the consent forms.

The inclusion criteria were: i) patients with early stage (stage 2 or stage 3) colorectal cancer, ii) patients receiving adjuvant chemotherapy (post surgery >1 month), iii) patients aged 30-70 years, and iv) patients with an anticipated life expectancy of at least one year. The exclusion criteria were: i) patients who received professional massage within one month before the beginning of this trial, ii) patients with marked oedema, iii) patients with physiological and/or psychological problems which were likely to affect their ability to participate in the intervention, iv) patients with platelet counts less than 100,000 cells/ml, v) patients for whom essential oil was an irritant, and vi) patients who were receiving medication to stimulate white blood cell production.

The remaining 66 patients were assigned in equal numbers into either the treatment or control group by block randomization with a block size of four. Three patients in the treatment group discontinued massage after the second session due to fatigue, but they were able to complete the post-assessment. Another patient declined to continue the massage sessions due to lack of interest. In the control group, four patients ceased participating: three decided to receive treatment at another hospital, and one received radiotherapy (Figure 1).

All subjects in the treatment group received the same aromatherapy with light Thai massage. This involved a standardized massage of the head, neck, face, back, shoulders, arms, hands, lower legs and feet with coconut oil containing 0.05 ml of ginger oil for 45 minutes by the same skilled therapist on three occasions over one week. Before beginning the first treatment session, a 15 minute closed skin patch test with blended oil was used on the forearm of each subject to confirm that there was no acute reaction to the oil. For the controls, only standard supportive care was used. For all subjects, the trial was conducted over a 1-week period following one of their 7-10 day cycles of chemotherapy.

For measurement of the primary outcomes variables (immunological changes), 2 cc. samples of blood were collected at pre-assessment (5-15 minutes before first massage in treatment group) and at post-assessment one week later (1-2 days after last massage in treatment group). Counts of WBCs, lymphocytes, and CD4 and CD8 cells were performed by PCT Laboratory Services Ltd., Bangkok, Thailand. The validity of the cell counts



**Figure 1. Flow Diagram of Progress Through the Trial**

was confirmed by haematocrits performed before and after transport to the Bangkok laboratory and by testing for haemodilution using red blood cell counts before and after the massage treatment.

The secondary outcome variables were the changes in the severity of the symptoms of common side effects of chemotherapy. At the pre- and post-assessment, patients were given a card with numerical rating scales for common symptoms (pain, fatigue, stress or anxiety, nausea, and depression) and were asked to rate the severity of each symptom on a 0 ('not at all bothersome') to 10 ('extremely bothersome') scale. The presenting symptom was defined as that with the highest pre-assessment score. If more than one symptom was scored equally high, the presenting symptom was chosen in the following order of priority: fatigue, pain, stress/anxiety, depression, nausea and other.

All statistical analyses were performed on an 'intention-to-treat basis' using Khon Kaen University SPSS software Model 17. Mean differences between treatment and control groups were tested using ANCOVA with pre-assessment values as the covariate, and 95% confidence intervals were used as indications of effect sizes. A P-value  $\leq 0.05$  was considered significant.

The study was conducted after obtaining approval from the Ethics Committee on Human Rights Related to Research Involving Human Subjects at the Faculty of Medicine, Khon Kaen University, Thailand (reference no. HE 532328).

## Results

### Demographic data

The average age of the study participants was  $59 \pm SD$  9 years (range: 32-70 years old), and the majority (59%) were men. The two groups were about equally balanced on the demographic and health status indicators (Table 1).

### Validity of the blood sample measurements

It was important to ensure that blood changes pre- and post-massage were due to the independent variable (treatment vs. control condition). The following steps were

**Table 1. Demographic Data for Massage Intervention Group and Control Group**

Variables		Massage Control	
		No.	%
Gender	Male	21	64
	Female	12	36
Age	Mean (SD)	59	1.5
	Status	58	1.6
Stage of disease	Single	1	3
	Married	26	79
	Separated and others	6	18
BMI	2	9	27
	3	24	73
Sleep Quality	<20	7	21
	21-23	14	43
	>23	12	36
Exercise	Not good	21	64
	Good	12	36
Alternative care	Never	15	46
	1-3 times/week	16	48
	>3 times/week	2	6
Type of chemotherapy	None used	29	88
	Used	4	12
Cycle of chemotherapy	Folfox-4	17	52
	Mayo	16	48
Underlying diseases	1	9	28
	2	12	36
	3	3	9
	4	3	9
	5	2	6
	6	3	9
	7	0	0
	12	1	3
	None	23	70
	Diabetes (DM)	3	9
	Hypertention (HT)	4	12
	DM and HT	2	6
Others	1	3	

taken to reduce the possibility that changes occurred due to some extraneous factor: i) haematocrits (Hcts) and red blood cell counts were done at pre- and post-assessment so that WBC counts could be adjusted if either haemodilution or haemoconcentration was found to have occurred; ii) all blood samples were collected between 8.00 am and midday to control for blood constituents, such as CD4, which vary with time of day; and iii) a complete blood count (CBC) was done on all the blood samples before they were sent to the P.C.T. Laboratory Service Co., Ltd., Bangkok. The CBCs were repeated after arrival by the P.C.T. Laboratory Service Co., Ltd., before WBCs, CD4s, and CD8s were measured. This was done to confirm that the quality of the samples and the blood constituents had not been affected in transit. The P.C.T. Laboratory Service Co., Ltd. reported that the CBC results were comparable in both tests.

Since blood cell counts may change due to haemodilution or haemoconcentration caused by massage, the cell counts measured after the massage therapy session were calibrated as if Hct values after massage were the same as those before the massage. Differences in Hct and RBC counts between pre- and post-massage sessions were analyzed by using paired t-tests, and no statistically significant differences were found. These results are shown in Table 2.

**Primary outcomes: cellular immunological changes**

For lymphocytes, the post-assessment counts adjusted for pre-assessment values were significantly higher in the aromatherapy with light Thai massage group than in the control group (mean difference=218 cells/ $\mu$ l, 95% CI: 20-575, P=0.04). None of the differences between the two groups in overall WBCs or in other specific types of WBCs were statistically significant. These results are shown in Table 3.

**Secondary outcomes: changes in symptom severity**

The most common presenting symptom was fatigue (n=36, 55%), followed by pain (n=20, 30%) and nausea (n=8, 12%). Fewer than 5% of patients reported stress/anxiety or depression as a presenting symptom. The post-assessment ratings adjusted for pre-assessment ratings were significantly lower in the intervention group than in the control group for fatigue (mean difference=-1.3, 95% CI:-1.9, -0.8, P=0.001), presenting symptom (mean difference=-1.3, 95% CI:-1.8, -0.8, P=0.001), pain (mean difference=-1.2, 95% CI:-1.8, -0.89, P=0.001) and stress/anxiety (mean difference=-0.4, 95% CI:-1.2, -0.1, P=0.03). However, there was no significant difference between two

groups for nausea (mean difference=-0.3, 95% CI:-0.5, 0.3, P=0.61) or depression (mean difference=-0.2, 95% CI:-0.9, 0.3, P=0.27). These results are shown in Table 4.

**Discussion**

With regard to immunological benefits, the present trial demonstrated that aromatherapy with light Thai massage can increase the lymphocyte count in colorectal cancer patients undergoing chemotherapy and that the effect size of this benefit can be large. Using the adjusted post-assessment values, the lymphocyte count was 11.4% higher in the treatment group than in the controls. This outcome is consistent with the findings reported by Hernandez-Rief et al. (2004; 2005), Kuriyama et al. (2005) and Imanishi et al. (2009) that massage (and, in particular, aromatherapy massage) can boost lymphocyte numbers. It is potentially very important, especially in terms of the apparent effect size, to cancer patients if an improvement in their immune system functioning can help to protect them from infections during the course of their chemotherapy. However, in contrast to other studies, no significant differences were found for WBCs in general or in the other measures of immune system functioning involving various specific different types of WBCs: for example, Field et al. (2001) found that massage increased WBCs and neutrophils, Diego et al. (2001) reported that it increased CD4 cells and the CD4/CD8 ratio, and Kuriyama et al. (2005) found that it increased the CD8 cell count. Differences between the results of the present and other studies may be explained in terms of differences in the populations studied, in the frequency, length, spacing and number of massage sessions, and in the massage procedure itself.

In respect of the secondary outcomes and the finding that aromatherapy with light Thai massage could reduce the severity score of four of the six common symptoms, including the presenting symptom, in colorectal cancer patients undergoing chemotherapy, it is notable that very similar effects were reported in prior studies with cancer patients: for example, Cassileth and Vickers (2004) found that massage therapy was associated with statistically significant reductions in pain, fatigue, anxiety and severity of presenting symptoms. However, the trial did not achieve reductions in nausea or depression. One explanation for this might be the ineffectiveness of ginger oil when a lower than normal dose is used to protect patients from allergic reactions or other side effects. This result was different from that found in other studies which reported that massage reduced nausea and depression: for example, Cassileth et al. (2004) and Chang (2008). It is possible that, while the essential oil was too diluted to have a therapeutic effect, the reductions in pain, stress and fatigue nevertheless occurred because of the light Thai massage, which is commonly thought to have these effects on its own.

An important limitation of the present study was the lack of any follow-up assessment to investigate the persistence of treatment effects after the end of the one-week trial. A further larger and more extensive study is required to determine longer term outcomes and also

**Table 2. Changes in RBCs and Hematocrit in Pre- and Post- Blood Assessments**

Group	Pre-massage		Post-massage		95% CI	P-value
	mean	SD	mean	SD		
<b>Massage Group</b>						
RBC (cells/ $\mu$ l)	4.2*	0.37	4.1*	0.36	(-0.14,0.14)*	0.1
Hct (%)	33.9	2.82	34.1	33.3	(-0.74,0.40)	0.55
<b>Control group</b>						
RBC (cells/ $\mu$ l)	4.2*	0.44	4.1*	0.42	(-0.74,0.06)*	0.91
Hct (%)	33.5	3.06	32.9	3.08	(-0.05,1.11)	0.07

\*Cellx1,000, RBC: Red blood cells, Hct: haematocrit

**Table 3. Comparison of the Adjusted Means and 95% CIs of WBC Counts at Post-Assessment, WBC Counts Adjusted for Pre-Assessment Values Using ANCOVA**

Blood cells (cell/ $\mu$ l)	Post-assessment*				
	Message (mean)	Control (mean)	Difference (mean)	95% CI	P-value
WBCs	4,969	5,321	-352	(-740, 1,133)	0.68
Neutrophils	2,481	2,647	-193	(-482, 450)	0.94
Lymphocytes	2,132	1,914	218	(20, 575)	0.04
CD4	650	698	-48	(-105, 96)	0.93
CD8	495	497	-2	(-109, 80)	0.76
CD4/CD8	1.7	1.8	-0.1	(-0.1, 0.3)	0.34

\*Adjusted values using pre-assessment values as the covariate

**Table 4. Comparison of the Adjusted Means and 95% CIs of the Common Symptom Scores at Post-Assessment**

Symptoms (scores 0-10)	Post-assessment*				
	Message (mean)	Control (mean)	Difference (mean)	95% CI	P-value
Presenting symptom	2.9	4.2	-1.3	(-1.8, -0.8)	0.001
Pain	1.2	2.4	-1.2	(-1.8, -0.9)	0.001
Fatigue	2.8	4.1	-1.3	(-1.9, -0.8)	0.001
Nausea	2.4	2.7	-0.3	(-0.5, 0.3)	0.61
Stress/Anxiety	2.4	2.8	-0.4	(-1.2, -0.1)	0.03
Depression	2.2	2.4	-0.2	(-0.9, 0.3)	0.27

\*Adjusted values using pre-assessment values as the covariate

the effects of different masseurs (only one was used), treatment periods longer than one week, and different concentrations of essential oils.

In conclusion, aromatherapy with light Thai massage can be beneficial for the immune systems of cancer patients, who are undergoing chemotherapy by increasing the number of lymphocytes and can help to reduce the severity of common symptoms. A further larger scale trial is recommended to confirm and extend the findings of the present study.

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