

The Use of Needling and Self- Needling for Treatment of Vasomotor Symptoms in Patients With Breast Cancer and Fatigue After Chemotherapy

Jacqueline Filshie

Consultant in Anaesthesia and Pain Management

Royal Marsden Hospital

London and Surrey

Vasomotor symptoms affect more than 50% of females at the natural menopause



HRT gives the best results but is contraindicated in patients with oestrogen sensitive cancers.

- In breast cancer an abrupt or early treatment-related menopause causes symptoms in up to 70% of patients.
- They are often related to treatment with anti-oestrogen drugs and patients with prostate cancer get similar distressing symptoms on anti-androgenic drugs.
- They are common following chemotherapy and therapeutic oophorectomy.
- The symptoms can persist for longer than five years.

Anti-Oestrogen and Anti-Androgen Drugs

Anti-Oestrogen

Aromatase inhibitors

GnRH analogues

Anti-androgens

Tamoxifen

Anastrozole

Letrozole

Exemestane

Leuporelin

Goserelin

Bicalutamide

Cyproterone

Flutamide

Two Recent Trials

aTTom and ATLAS have shown that ten years of tamoxifen significantly reduces the risk of recurrent cancer and mortality.

*Gray et al, 2013,
Davies et al, 2013*

Yet a number of studies show that over 50% of women do not adhere to even five years of endocrine treatment, and have an increased mortality.

Makubate et al, 2013

Whilst non-life threatening, they can cause a significant impact on quality of life

- Sleep deprivation and fatigue
- Irritability and mood reduction
- Embarrassing e.g. at work
- Affects personal relationships
- A significant unmet need for patients who need long term treatment

Patients increasingly access alternative treatments for these symptoms

Venlafaxine

Citalopram

Clonidine

Gabapentin

Cognitive Behavioral Therapy (CBT)

Acupuncture

Herbal treatments and Phyto-oestrogen –but there are safety concerns

Acupuncture for vasomotor symptoms in cancer patients

Rx-related hot flushes in women with ca breast

Towlerton et al, 1999

Tukmachi, 2000

Cumins & Brunt, 2000

Hervik & Mjåland, 2004

Filshie et al, 2005

de Valois, 2002, 2003, 2007

Deng, 2007

Lee et al, 2009

Walker et al, 2010

Bokmand and Flyger, 2013

Men with ca prostate

Hammar et al, 1999

Hayes et al, 2005

Frisk et al, 2008

Lee et al, 2009

Ashamalla et al, 2011



How We Approached Treatment

LR3 SP6 GB20 GB34 CV4

Then simplified



LR3 + SP6

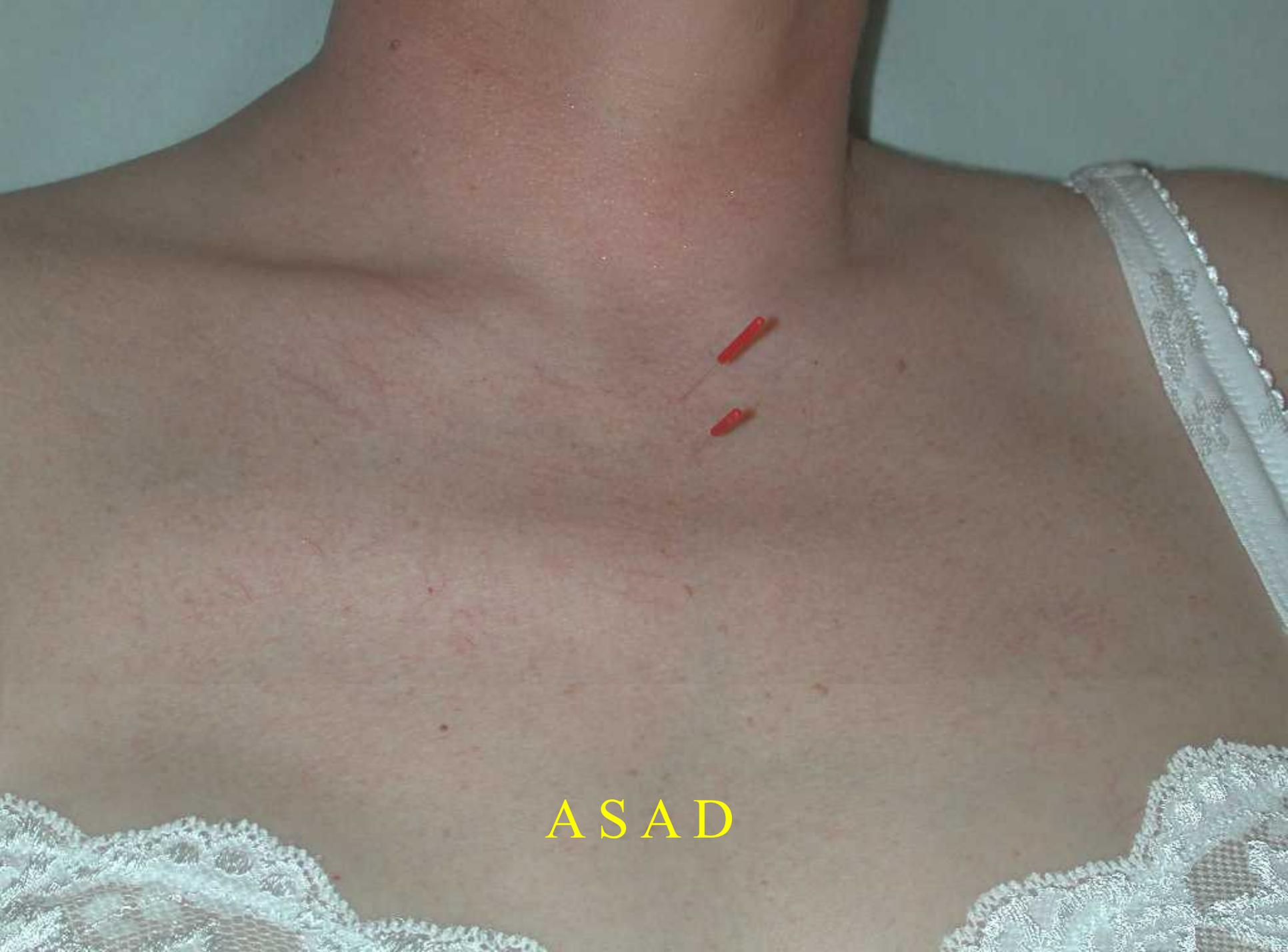


but ↑ dose with ↑ complex cases

SP6 LR3 LI4 TE5 ASAD







ASAD

Treatment Details

- LR3 SP6 *L14* TE5 ± ASAD
Avoid any lymphoedematous or lymphoedematous prone limb
- 6 weekly treatments then
- Teach self administered ‘one off’ needling weekly to SP6 +/- LR3
- Increase interval between treatments
 - 4 weeks
 - 6-8 weeks
 - 3 months etc
- Give careful instructions on how to save the used needles for safe disposal at a hospital, general practice or pharmacy.

If response slightly slow:

- Semipermanent needles inserted at 4 to 5 weeks at SP6 **only**
- Spirit swab to site pre-treatment
- Bio-occlusive dressing
- Massage tds
- Massage when prodromal symptoms
- Change studs weekly, slightly alternating site to avoid skin damage
- Patients taught self-needling/use of studs
- Universal container to store used needles

Contraindications for Use of Semi-permanent Needles

- Heart valve disease/replacement
- Post splenectomy
- Severe immunosuppression
- Strong reactors
- Known hepatitis B&C

Relative

- Current chemotherapy or DXT

Filshie et al, 2005

For further safety information and instructions
for patients

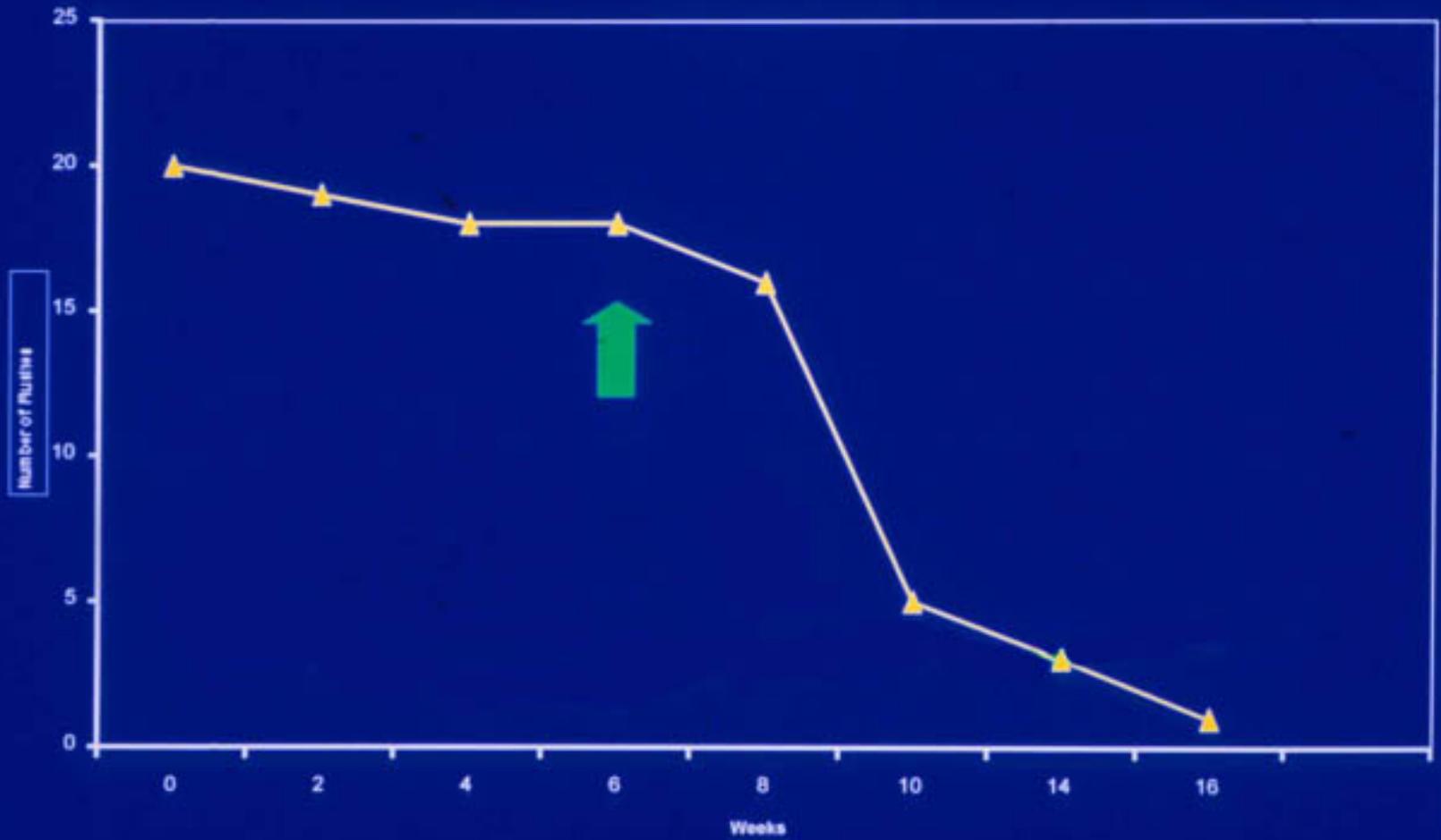
- Guidelines for providing acupuncture for cancer patients in primary and secondary care - a peer-reviewed sample policy document

Filshie J & Hester J, 2006



Number of Night time Flushes

patient 1



Retrospective Audit

194 Patients

182 Female 12 Male

- Average number of flushes 16 per day of 159
- Studs tried after a mean of 4.7 treatments

Filshie et al, 2005

Retrospective Audit 194 Patients

114/144 evaluable

50% or greater reduction in number 79.2%

Less than 50% reduction in number 20.8%

Duration of studs evaluable in 135 patients

< 1 month - 6 years

Median 9 months

Bolton & Filshie, 2003

Filshie et al, 2005

Side Effects of Studs 9%

- Red mark where stud had been 4
- Dressing allergy 3
- Rash/itch/inflammation 5
- Infected stud 1
- Bleeding 1
- Made leg cramps worse 1
- Legs swelling after insertion (but concurrent fracture) 1
- Pain 1

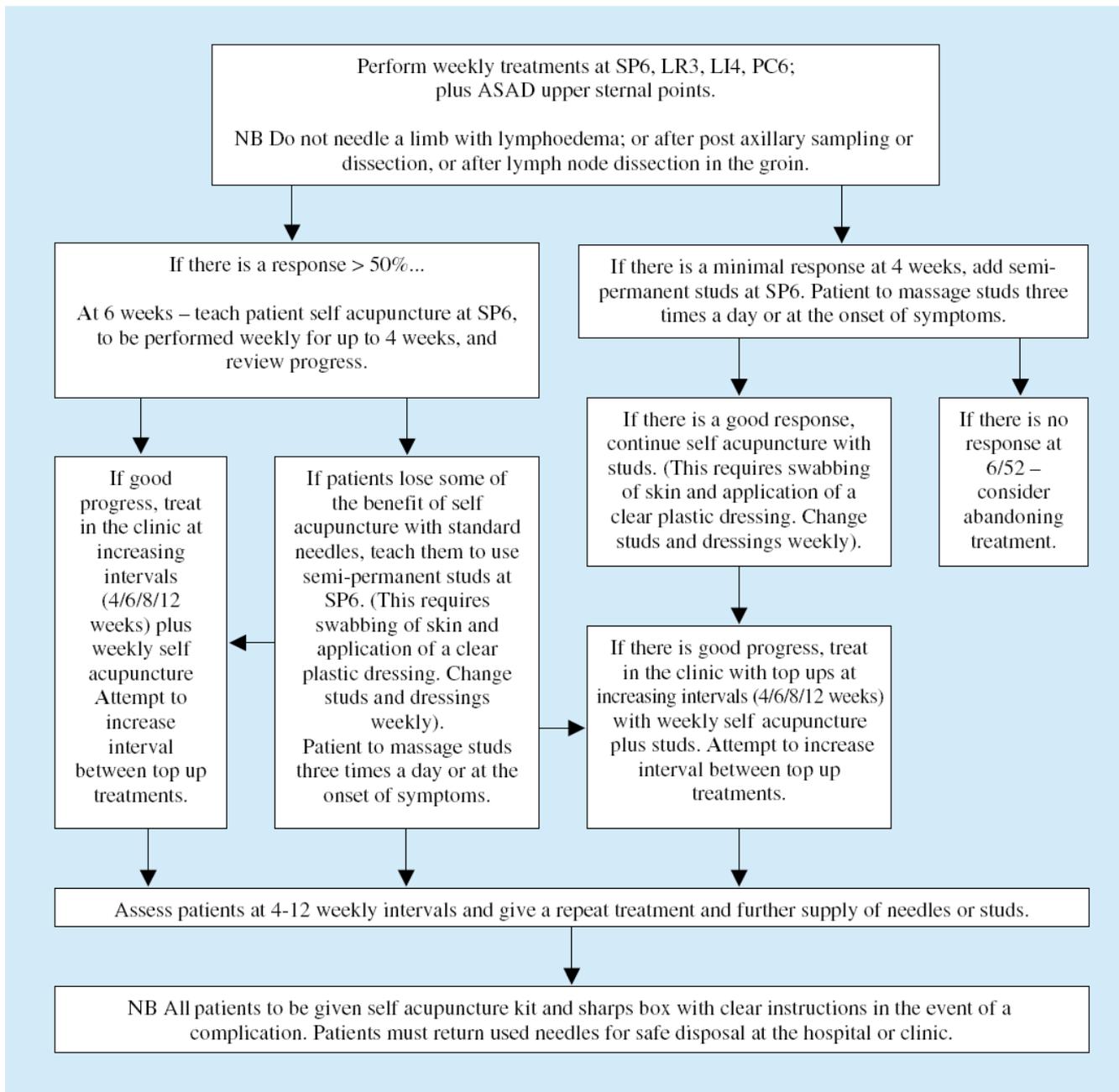


Figure 1 This is an algorithm for long term treatment with acupuncture and self acupuncture.



Filshie et al, 2005

We use a very flexible patient-centered approach

Some patients use self needling for 10 years or more

For example the patient who engages in a lot of sport we recommend using 'one-off' self-needling every 4-7 days +/- LR3

Use one-off needles when patients travel to avoid the need for unsightly dressings

Patients given an instruction leaflet

- Self needling is very cost effective after a ‘loading dose’ of practitioner-administered treatment.
- Patients told how to purchase 100 or 200 needles or semi-permanent studs for themselves.
- Patients told how to dispose of them safely in a pharmacy or general practice surgery or hospital.

Safety

- Good safety record of acupuncture in prospective studies (largest to date included 2.2 million treatments)

White, 2001; 2004

MacPherson, 2001

Witt, 2009

- Oncology patients – vulnerable with often rapidly changing clinical picture
- Orthodox diagnosis first and treat alongside conventional treatment
- Acupuncture treatment is more complex in cancer care
- Guidelines & safety aspects in palliative care

Filshie and Hester 2006

Acupuncture and self acupuncture for managing cancer related fatigue in breast cancer patients following chemotherapy : a randomized controlled study

Prof. Alex Molassiotis

Professor of Cancer & Supportive Care, University of Manchester

Prof. Alison Richardson, University of Southampton, **Prof. Emma Ream**, King's College London; **Dr Peter Mackereth**, Christie NHS Trust; **Dr Jacqueline Filshie**, Royal Marsden Hospital, **Jenny John**, KCL; **Joy Bardy**, University of Manchester

Definition

- Cancer-related fatigue (CRF) includes sensations of physical tiredness, mental slowness, and lack of emotional resilience. Although patients may experience muscle weakness, fatigue is not synonymous with weakness (Nail, 1997)
- Can be sudden and overwhelming
- It is one of the most common problems reported by patients after chemotherapy and radiotherapy (62-92% of patients)

Molassiotis et al, 2001; 2002;

2005

Fatigue is a major problem in patients with cancer

- Most frequently-reported and most troublesome symptom
- Affects almost all patients
- >70% during treatments
- 40% long-term symptoms in survivors
- Can be dose-limiting symptom e.g. after chemotherapy
- Limited strategies available to help
- Mechanisms ill understood

Impact of fatigue

- Too tired to do anything
- Unable to concentrate
- Frustrated by feeling that they are not themselves
- Concerns about disease progression or not doing well
- Depression because of constant tiredness
- Limitations in activities of daily living are dramatic

Chan & Molassiotis 2001

Interventions to manage fatigue

- Regular assessment
- Delivering preparatory information
- Managing treatable causes
- Controlling symptoms and side effects
- Providing instructions about energy conservation, prioritising activities and appropriate exercise
- Promoting sleep and rest
- Cognitive-behavioral therapy
- Supportive care
- Complementary therapies



Pilot study

- 47 patients after chemotherapy who are screened for fatigue and shown high levels (>5 on 0-10 scale) randomized to one of 3 groups, acupuncture, acupressure and sham acupressure.
- Acupuncture: 3 points bilaterally, 3 times/wk; for 2 weeks.
- Acupuncture improved fatigue by 36% and greater than 2 control groups

Molassiotis et al, 2007

Cancer Related Fatigue Post Chemotherapy

- Cohort study
37 patients 31 completed the study
- Mean improvement of fatigue scores 31.1%

Vickers et al, 2004

Aims of the trial

- To assess the effectiveness of a course of acupuncture in the management of cancer-related fatigue in a homogeneous sample of patients with breast cancer who have completed adjuvant chemotherapy
- To assess the effectiveness of self-acupuncture in comparison to therapist administered acupuncture in sustaining any longer term effects beyond the 6-week course of acupuncture.

75 Enhanced usual care

302 Patients

227 Patients given
6 weekly Acupuncture
treatments
Plus enhanced usual care

4 weekly treatments with
Therapist

4 weekly treatments
Self administered

No further treatment

Re-randomized

6 Weeks

4 Weeks

8 Weeks

Molassiotis et al, 2012 and 2013

Phase I: Randomised (3:1) to receive:

20 mnts acupuncture treatment at 3 points LI4, SP6 and ST36
bilaterally every once a week for 6 weeks plus fatigue booklet

Or

Usual care plus booklet on coping with fatigue - enhanced usual
care

Molassiotis et al, J Clin Oncol, 2012

(Phase II): Then Acupuncture group randomised to receive:

4 sessions over 4 weeks of continuation of acupuncture by
therapist

Or

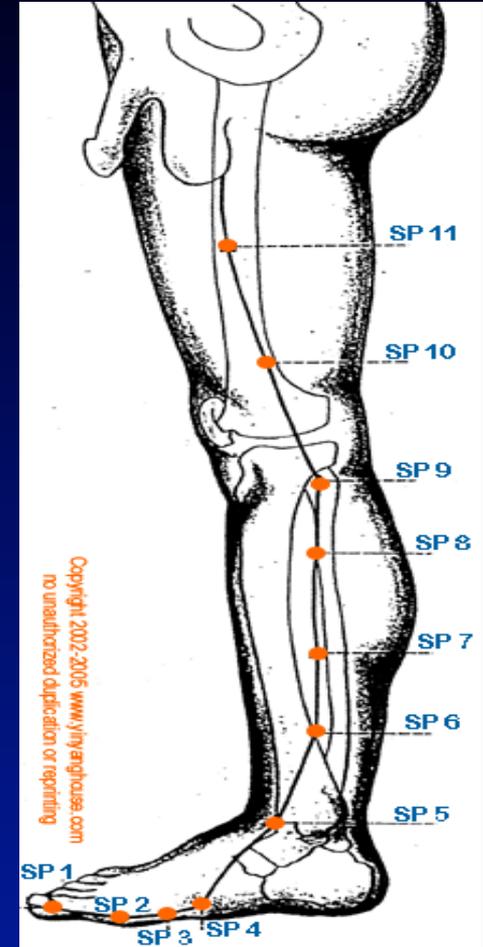
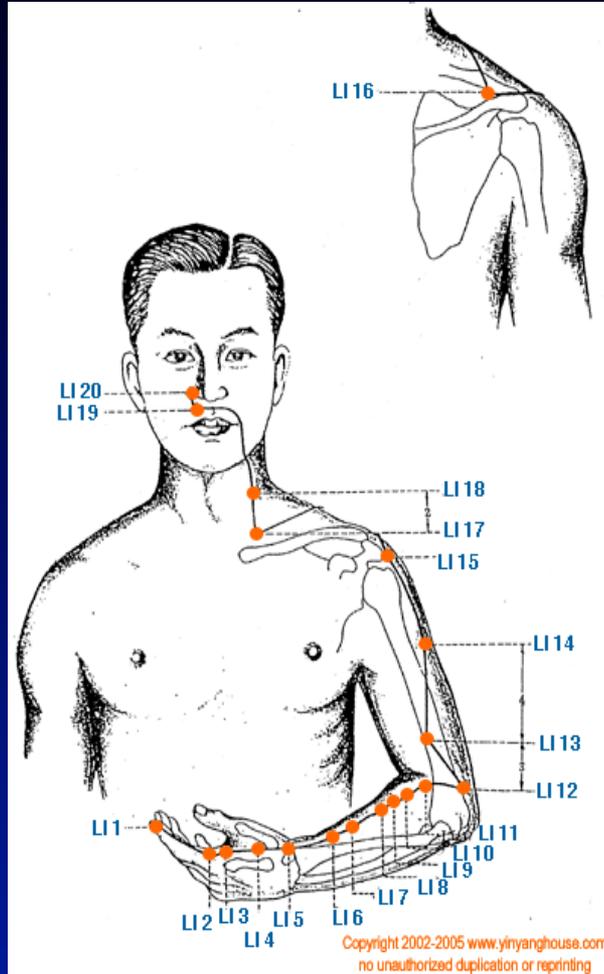
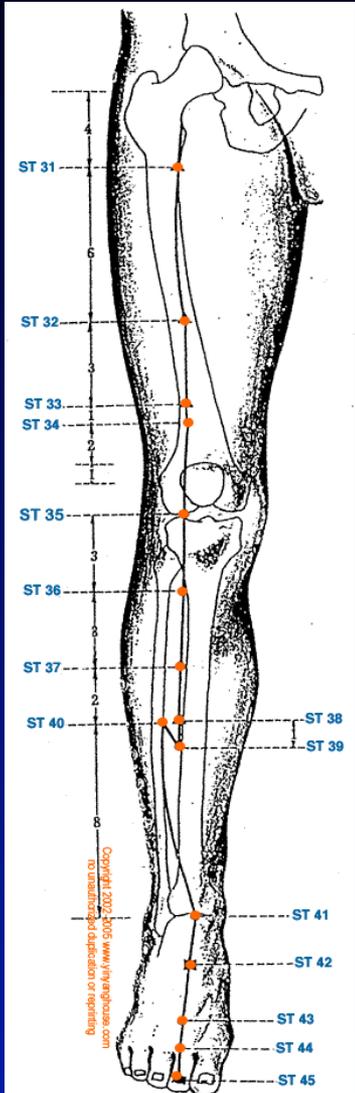
Self acupuncture weekly for 4 weeks

Or

No maintenance therapy

Molassiotis et al, Ann Oncol, 2013

Acupuncture points



Data Collection

- Multidimensional Fatigue Inventory (MFI) (Smets et al, 1995). This is a brief 20-item scale measuring general fatigue and the dimensions of physical and mental fatigue, activity and motivation.
- Hospital Anxiety & Depression Scale (Zigmond & Snaith, 1983). This is a 14-item scale assessing anxiety and depression.
- FACT-G & Breast cancer module. This is a well-validated quality of life scale focusing on functional assessment, supplemented with a breast-cancer specific module (Fairclough & Cella, 1996).
- Sociodemographic and treatment characteristics.
- Use of complementary therapies in the past and during the study participation.
- Patients were asked about their treatment expectations, how much they believe this method will help them alleviate fatigue and how much faith they have in acupuncture using three 10-point scales.

Duration & Sites

- Duration of trial: 3 years with patients recruited from:
 - Christie Hospital NHS Foundation Trust, Manchester (and its peripheral clinics)
 - Royal Marsden Hospital NHS Foundation Trust, London and Surrey sites
 - Royal Lancaster Infirmary
 - Breast Cancer Haven (London, Leeds, Hereford)
 - Guy's & St Thomas Trust, London

Study funded by Breakthrough breast cancer charity

Eligibility

Patients with breast cancer who had completed chemotherapy between 1 month and 5 years who scored greater than 5 on a 0-10 screening scale.

Exclusions

- Distant metastatic disease
- Platelets < 50,000
- Hb < 10g / DL
- Patients on steroids
- Pregnancy
- Life expectancy < 6 months
- Ipsilateral limb not needed after axillary dissection
- Lymphoedematous limbs not needed

Acupuncture Details

Serin 36 gauge needles 20 minutes
duration

SP6 ST36 LI4

Other points e.g. GB34 or SP9 were used if an arm was prone to lymphoedema or a patient had a lymphoedematous limb so that the overall 'dose' was 6 needles per treatment.

Needles were inserted 1-2 cms and not stimulated any further following insertion

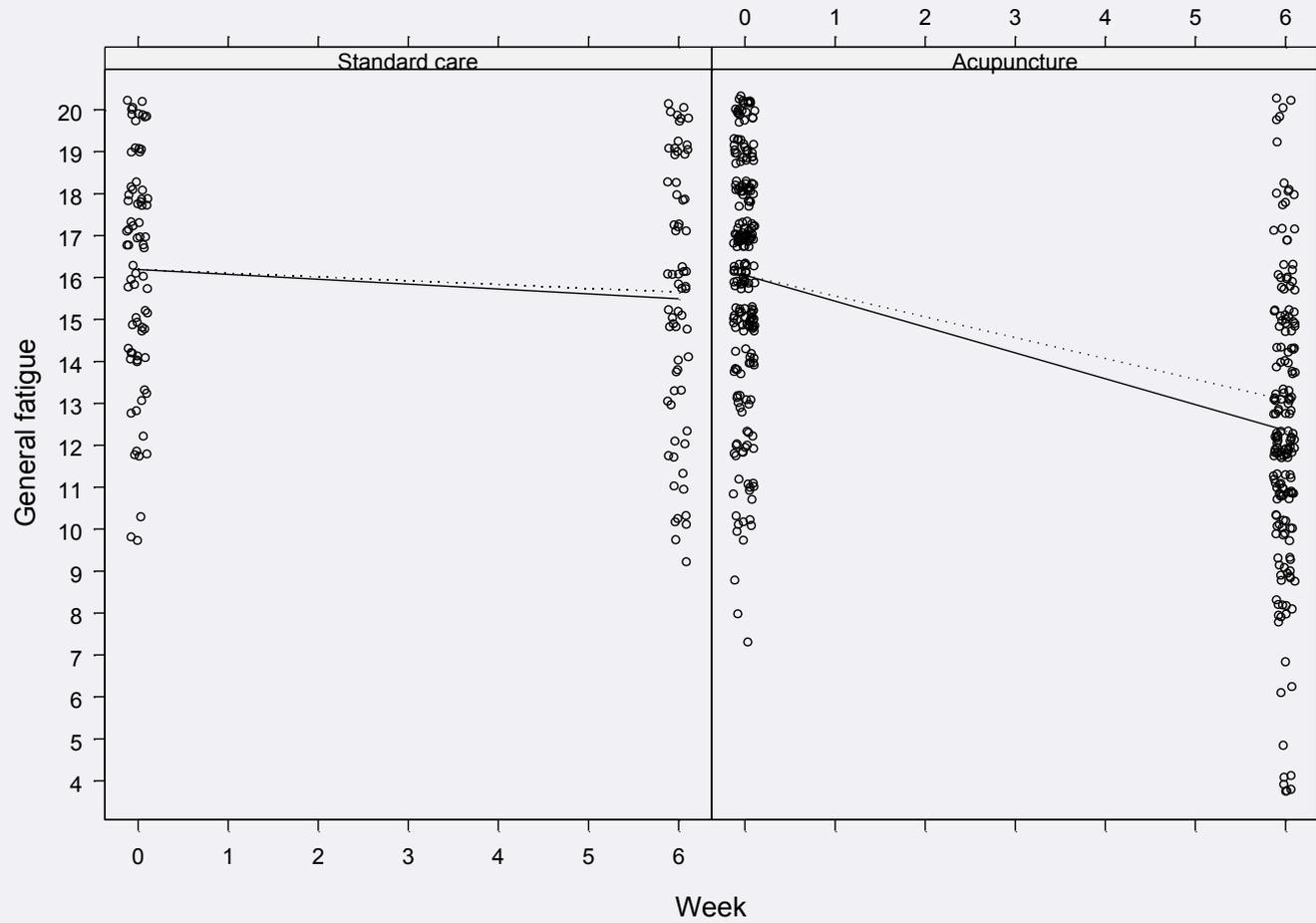
Sample size

- Phase 1: for power $>95\%$ and including attrition, based on pilot study findings, we need 320 patients randomised (3:1) 240 in experimental and 80 to control group. This part of study is over-powered to provide enough subjects for Phase II part.
- Then re-randomise remaining 192 (after attrition) equally to the 3 maintenance groups (64 per group), which provides 80% power at an $\alpha=0.05$.

Sample



Primary Outcome



Primary Outcome

	Complete case (n=246)	LVCF (n=302)
Mean [GF.6 – GF.0] (SC)	-0.62	-0.53
Mean [GF.6 – GF.0] (Acu)	-3.72	-2.96
Difference (Acupuncture – Standard Care) in mean change in GF (GF.6 – GF.0)	-3.10	-2.43
95% CI	(-3.98, -2.23)	(-3.19, -1.67)
p-value	< 0.001	<0.001

GF = General Fatigue, SC = Standard Care, LVCF = Last Value Carried Forward

Results

246 patients provided data at 6 weeks

The difference in mean general fatigue score between those who received the acupuncture vs those who did not was -3.11 (P>0.0001 95% CI -3.97 to 2.25)

All other aspects improved anxiety and depression, and quality of life

Difference in outcomes at week 6 for fatigue, quality of life, anxiety and depression

Scale	Trial arm p-value	Acupuncture Effect*	S.E.	95% CI
MFI				
General Fatigue	<0.0001	-3.11	0.44	(-3.97, -2.25)
Physical Fatigue	<0.0001	-2.36	0.45	(-3.25, -1.47)
Reduced Activity	<0.0001	-2.29	0.41	(-3.10, -1.48)
Reduced Motivation	<0.0001	-2.02	0.40	(-2.82, -1.22)
Mental Fatigue	<0.0001	-1.94	0.44	(-2.81, -1.07)
HADS				
Anxiety	<0.0001	-1.83	0.44	(-2.69, -0.97)
Depression	<0.0001	-2.13	0.36	(-2.85, -1.41)
FACT-B				
PWB	<0.0001	3.30	0.57	(2.17, 4.43)
SFWB	0.05	1.05	0.54	(-0.01, 2.11)
EWB	0.0001	1.93	0.49	(0.96, 2.90)
FWB	<0.0001	3.57	0.61	(2.38, 4.76)

Re-randomisation (maintenance treatment)

N=195

Acupuncture 65 (60 valid)	Self- Acupuncture 65 (51 valid)	No Maintenance 65 (56 valid)
General Fatigue 10 46	General Fatigue 10 56	General Fatigue 10 48

Maintenance therapy

	Complete case (n=150)	95% CI
Mean [GF.6 – GF.10] (SC)	-0.35	(-0.52, 1.21)
Mean [GF.6 – GF.10] (A)	0.57	-0.18, 0.04)
Mean [GF.6 – GF.10] (SA)	0.54	(-0.21, 0.13)
ANOVA: p-value	0.13	

Multicentre Randomized Controlled Study

Acupuncture significantly improved general fatigue compared with the control arm at 6 weeks

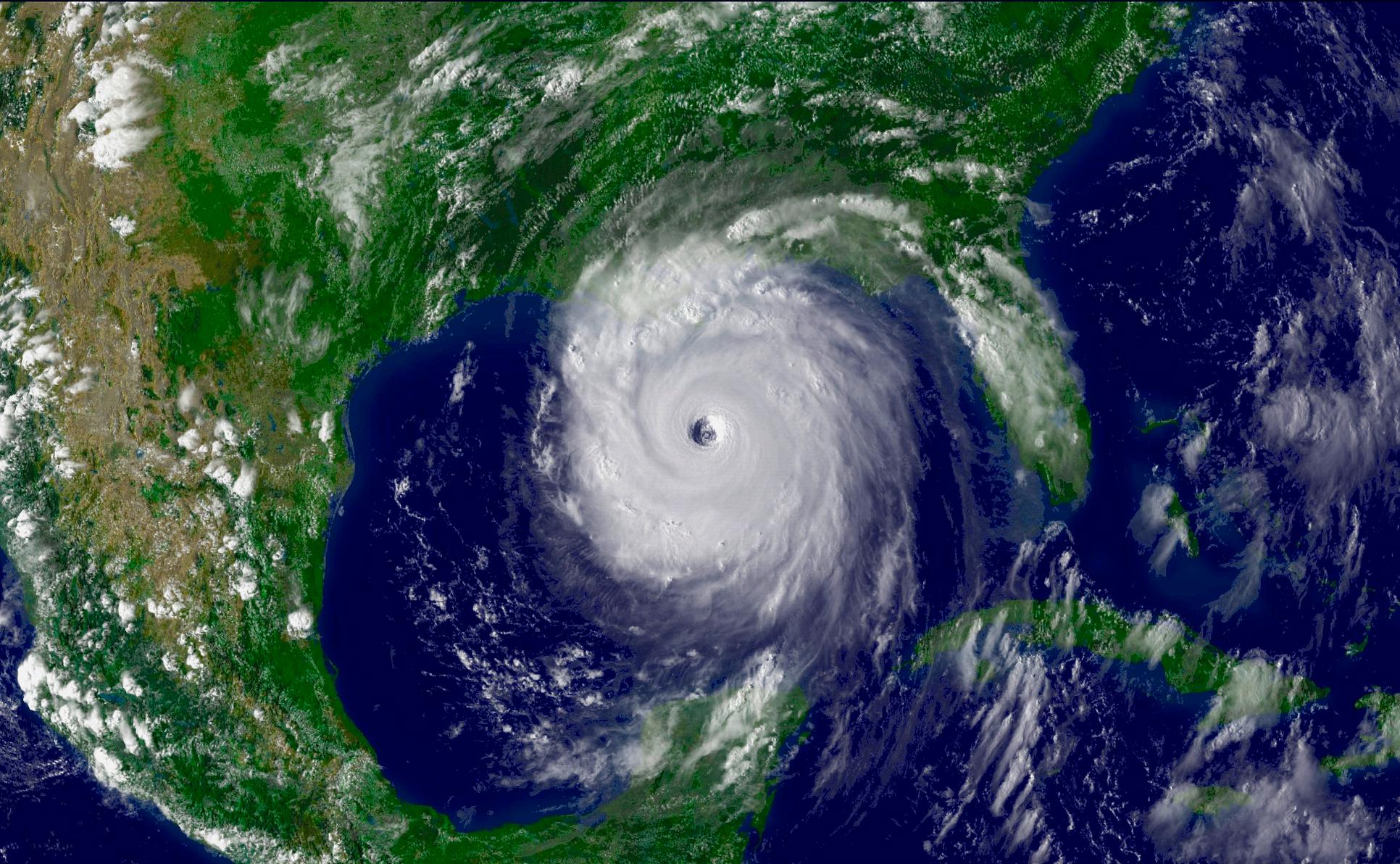
The results were sustained at 10 weeks with a trend towards significance in both acupuncture treatment groups vs no treatment

As survivorship increases with all the advances in oncology, we should plan to treat patients who respond well to acupuncture for symptom control long term or even indefinitely for their physical problems.

- A Utopian course of treatment



The real world!



Conclusion

- Acupuncture is an effective way to manage Cancer Related Fatigue
- Maintenance Therapy may not be needed as frequently as for patients with vasomotor symptoms but self needling can facilitate this well.
- Improvements in other symptoms reported by patients (particularly hot flushes & joint pains)- Many positive qualitative comments from 28 interviews
- Improve quality of life and activities of daily living
- Empowerment of patients for self care

Acknowledgements

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