 Diagnosis and treatment of cancer are stressful and high levels of morbidity almost universally reported.
Of 269 women with early breast cancer, 49.6% were clinically anxious and 37.2% were clinically depressed in the first 3 months (PSE) (Hall et al, 1999)

Of 222 women with early breast cancer, 48% were clinically anxious and/or depressed in the first year (DSM IIIR) (Burgess et al, 2005)

Of 2,297 patients with cancer at OP clinics in 34 cancer centres in the UK, 36% were GHQ-12 positive (Fallowfield et al, 2001).

Of 987 patients with newly diagnosed inoperable lung cancer, 33% had clinically significant depression, which in many cases was persistent (Hopwood and Stephens, 2000).
Relaxation and Guided Imagery: Background

- Diagnosis and treatment stressful and high levels of morbidity reported.
- Stress can be immunosuppressive and immunosuppression may affect clinical outcome.
- Psychosocial interventions can offset stress-induced immunosuppression.
Relaxation and Guided Imagery: Background

Need to develop ways of reducing stress and enhancing coping following diagnosis.
The psychoimmunological effects of relaxation and guided imagery in women with locally advanced breast carcinoma: a randomised controlled trial.
Relaxation and Guided Imagery: Aims

To evaluate the effects of relaxation and guided imagery on:

- Quality of Life
- Mood
- Coping
- Host defences
- Response to chemotherapy
Trial Design

CVAP chemotherapy 6 cycles every 3 weeks  
Surgery  
RT  
FU

1 18 22 25 29 37
Psychological Intervention

Randomised to:

Control:
High level of support in the
Behavioural Oncology Unit
Aberdeen Behavioural Oncology Unit
Drop in Centre

- Professional but informal atmosphere.
- Welcome to telephone or visit at any time.
- Staff trained to elicit and respond quickly and appropriately to concerns.
- Customized information.
- Peer group and staff support.
- Chemotherapy given in the Centre.
- Co-ordination of investigations and treatments.
Psychological Intervention

Randomised to:

<table>
<thead>
<tr>
<th>Control:</th>
<th>High level of support in the Behavioural Oncology Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental:</td>
<td>Similar support plus relaxation and guided imagery</td>
</tr>
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</table>
Relaxation Response

- Integrated hypothalamic response.
- Opposite of the ‘fight-flight’ response.
- Increased parasympathetic a.n.s. tone.
- Associated with feelings of relaxation, calmness and confidence.
- Can be taught using live training or audio-cassette recordings.
Guided Imagery

- Visualise host defences destroying cancer cells
- Simontons claimed prolonged survival
- Biological and psychological effects previously unevaluated in a large, prospective, randomised, controlled trial
Aristotle (384–322 B.C.)

‘The soul never thinks without a picture.’
Images and Behavioural Change

Marlboro Lights

U.S. SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer. Heart Disease, Throat Cancer, And May Complicate Pregnancy.

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Images and Behavioural Change

I miss my lung, Bob.
‘Imagination is more important than education.’
Baseline Assessments

- Comprehensive assessment of personality, coping and quality of life.
- Structured clinical interviews.
- Immunological assays (NKCA, LAKCA, cytokines and CD profiles).
- Tumour size
Main Measures of Outcome

◆ Global Quality of Life
◆ Mood
◆ Coping
◆ Host defences
Patients

96 women with large (>4cms) or locally advanced (T_3, T_4, N_2 and M_0) breast carcinoma
Global Quality of Life

Group x Time Interaction p<0.02

Baseline
Post chemotherapy

Mean Scores

Control
Experimental

Group x Time Interaction p<0.02
Mood Rating Scale

Mean Total Scores

Pre Chemotherapy
After 5 cycles

Group x Time Interaction p<0.004
Emotional Suppression

Group x Time Interaction p<0.03

Pre Chemotherapy
After 5 cycles

Group x Time Interaction p<0.03

Control
Experimental
Social Conformity

Group x Time Interaction p<0.05

Mean Scores

Pre chemotherapy
After 5 cycles
End of study

Group x Time Interaction p<0.05
HADS Anxiety – All Women

Pre chemotherapy 21%
HADS Anxiety – All Women

Pre chemotherapy
21%

Pre surgery
5%

Significant
<table>
<thead>
<tr>
<th>Event</th>
<th>HADS Anxiety %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre chemotherapy</td>
<td>21%</td>
</tr>
<tr>
<td>Pre surgery</td>
<td>5%</td>
</tr>
<tr>
<td>12 weeks post DXT</td>
<td>2%</td>
</tr>
</tbody>
</table>

Significant
Other psychometric tests and Structured Clinical Interviews (DSM III\textsuperscript{R}) confirmed the low rate of psychiatric morbidity in both interventions.
Summary: Psychological Effects

The Intervention:

- Improved mood and quality of life.
- Enhanced coping.

- HADS D independently predicted clinical and pathological responses to chemotherapy.

Walker et al, Brit J Cancer, 1999, 80, 262-268
Activated T cells (CD25+)

Control

Experimental

RM ANCOVA Group X Time int. F=2.31, p=0.03
Summary: Immunological effects

The Intervention:

- Enhanced LAK cell activity.
- Increased number of various T lymphocyte subsets (CD2+, CD25+ and CD56+).
- Reduced TNF-α.

Imagery vividness correlated with changes in LAK and NK cell activity.
The incidence of clinically significant distress in both groups was only a quarter of the level expected.
Conclusions - 2

- Relaxation and guided imagery improve key aspects of quality of life.
- The clinical significance of the biological effects needs further study.
- Further research should develop and evaluate alternative ways to ‘switch on’ the relaxation response.
The psychoneuroimmunological effects of reflexology in women with early breast carcinoma: a randomised controlled trial

On behalf of
The Hull Breast Group
The Medical Laboratories
The Oncology Health Centres
20% of women do not practice relaxation and guided imagery regularly.

Reflexology may be an alternative way of ‘switching on’ the relaxation response.
Reflexology

- Popular in the UK
- Involves massage of ‘acupressure’ points (usually in the feet)
- Does not require home practice
- Has been shown to reduce radiotherapy-related fatigue (Smith, 2004)
- Has not been evaluated more generally within an adequately powered RCT
To evaluate the acceptability and biopsychosocial effects of reflexology in women with newly diagnosed early breast cancer.
Trial Design

- **Surgery Week 0**
- **Baseline Assessment Week 6 (plus or minus 7 days)**
- **Radiotherapy Commencing Week 12 (plus or minus 7 days) for 3 or 4 weeks**
- **Endpoint 1 Week 18**
- **Endpoint 2 Week 24**
- **Reflexology or Massage Weeks 7-14**
- **Blood Samples**
- **Psych & Physio Tests**

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Interventions

All patients received self-initiated support (SIS) according to local practice and they could access the full range of services in the Oncology Health Centres at PRH and CHH.

- **SIS**: as determined by the patients (records kept). Includes access to information, support, and self-help techniques. If required, treatment for clinically significant distress (comparator intervention).

- **SIS + Scalp Massage**: weekly for 8 weeks, commencing 2 weeks post surgery (control for physical and social contact – no acupressure points).

- **SIS + Reflexology**: weekly for 8 weeks, commencing 2 weeks post surgery.
Psychosocial Assessments

Quality of Life
- Functional Assessment of Cancer Therapy (FACT-B)
- Mood Rating Scale (MRS)

Mental Health
- Hospital Anxiety and Depression Scale (HADS)
- Structured Clinical Interview DSM IV (SCID)

Personality and Coping
- Courtauld Emotional Control Scale
- Multidimensional Locus of Control Scale
- Positive and Negative Affectivity Schedule (PANAS)
- Eysenck Personality Questionnaire

Other Questionnaires
- Patient Satisfaction Questionnaire (PSQ)
- Health Service Use (HSU)
- Complementary Medicine Questionnaire (CMQ)
- Social Support Questionnaire (SSQ)
Biological Outcomes

- Cortisol, Prolactin, Growth Hormone
- Th1/Th2 balance
- Lymphocyte phenotypes
- Pulse
- BP
Patients

- T1, T2 (<3cms), N0, N1a, M0.
- Fit to undergo surgery and, if necessary, radiotherapy and chemotherapy.
- Able to complete questionnaires
- Willing to give written, informed consent.
- No age restrictions.
- Female.
Randomisation stratified for radiotherapy and chemotherapy.

A difference of 5-6 points in the primary quality of life outcome measure (TOI FACT-B) judged to be clinically meaningful (MSD).

With 60 patients in each group, there is 85% power to detect an MSD in scores between two of the groups.

Repeated Measures ANCOVA followed if significant ($p<0.05$) by ANCOVA for EP1 and EP2 (covariates used were age, stage and baseline values).

Significance of paired comparisons adjusted with Bonferroni correction.
Patients Randomised

N = 223 patients referred, N = 222 eligible, N = 59 patients declined entry.

N = 183 entered trial

Participation Rate = 82.43%
183 patients randomised

- Median age 58 (range 32-99)
- 23% pre-menopausal
- $T_1 = 68\%$, $T_2 = 28\%$, $T_3 = 2\%$, DCIS = 2\%
- 80% - breast conservation, 14% - mast, 6% - mast + rec,
- 71%-adjuvant hormone therapy
- 84%-radiotherapy
- 17%-chemotherapy planned or given

No significant between-group differences at baseline.

Complete quality of life data available for all patients at baseline, 97.3% at EP1, and 95.6% at EP2.
Trial Outcome Index FACT-B

Mean (SE)

Baseline (Week 6)  EP 1 (Week 18)  EP 2 (Week 24)

M > SIS  R > SIS

SIS  SIS + Reflexology  SIS + Massage

R or M
MRS Easy-goingness

- M>SIS
- M>R

Mean (SE)

Baseline (Week 6) | EP 1 (Week 18) | EP 2 (Week 24)

R or M

- SIS
- SIS + Reflexology
- SIS + Massage

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MRS Relaxation

Mean (SE)

Baseline (Week 6)
EP 1 (Week 18)
EP 2 (Week 24)

R> SIS
M> SIS

R or M

SIS
SIS + Reflexology
SIS + Massage

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Cf. Of 269 women with early breast cancer, 49.6% were clinically anxious and 37.2% were clinically depressed in the first 3 months (Hall et al, 1999).
Immunology Analysis

- Immunological assays were carried out on the first 120 patients recruited.
- Neuroendocrine analyses were completed for all 183 patients.
Mean % Th Lymphocytes

T helper IL-4+ Lymphocytes

SIS > M

F = 3.90, df = 2, p = 0.02

Baseline (Week 6)  EP 1 (Week 18)  EP 2 (Week 24)

SIS  SIS + Reflexology  SIS + Massage

R or M
Mean % CD19+ Lymphocytes

- **SIS**
- **SIS + Reflexology**
- **SIS + Massage**

F=4.0, df=2, p=0.02
Summary of Neuroendocrinological and Immunological Results

Compared with SIS:

- Reflexology and Massage had:
  - no effect on any lymphocyte subset
  - no effect on cortisol, prolactin and growth hormone

- At EP2, Massage reduced IL-4

Compared with Reflexology:

- At EP2, Massage group had a significantly higher %CD19+ve cells
Massage, but not Reflexology, was significantly better statistically than Self-initiated Support at EP1 on TOI (not clinically significant).

Reflexology, but not Massage, was significantly better statistically than Self-initiated Support at EP2 on TOI (clinically significant).

Both Massage and Reflexology were significantly better than Self-initiated Support at EP1 for MRS Relaxation.
Conclusions

- Although Reflexology and Massage have measurable effects on various aspects of quality of life, they do not appear to affect the cancer-relevant neuroendocrine and immunological parameters evaluated in this study.
- Massage-induced reduction in IL-4 could mean alterations in antibody switching.
- The cancer relevance of the difference in B cells between Reflexology and Massage is also unclear.
- Reflexology and Massage can be recommended to patients for their psychological, but not, as yet, their biological effects.
- Rates of clinically significant distress were again very low in this study.
Conclusions

- Relaxation & guided imagery and reflexology have shown significant effects on quality of life in cancer patients.
- Some effects have also been found for immunological parameters, although the clinical significance of these is, as yet, unclear.
- Simple self-help psychological and complimentary interventions are likely also to be applicable in other areas of healthcare, where they may also improve the quality of life and psychological coping of patients.
- The provision of open access support and psychological intervention greatly reduces the incidence of clinically significant distress.