Integrative Oncology: An Evolving Discipline

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Leonard P. Zakim Center for Integrative Therapies
Dana-Farber Cancer Institute

November 13, 2015
University of Vermont Medical Center
1. Definitions and History
2. Cancer Challenges
3. Integrative Therapies
4. Research
5. Integrative Oncology - The Future
Evolution Of A Discipline

- Quackery, The Practice of
- Questionable Methods of Therapy
- Unproven Therapies
- Complementary and Alternative Methods of Therapy
- Integrative Medicine/Health
History

- October 1991 – 104th anniversary of the NCI
  a public law established an office and advisory
  panel to recommend a research program that would
  investigate promising unconventional medical
  practices
- June 1993 – the NIH revitalization Act established
  the Office of Alternative Medicine
- October 1998 – NCCAM and OCCAM were
  established per the “Omnibus Consolidated and
  Emergency Supplemental Appropriations Act”
HISTORY

• 2000 – The Leonard P Zakim Center for Integrative Therapies at the Dana-Farber Cancer Institute

• A bold initiative by the DFCI
The Leonard P. Zakim Center for Integrative Therapies at Dana-Farber Cancer Institute is dedicated to enhancing the quality of life for cancer patients and families by incorporating complementary medicine into traditional cancer care. The Center provides affordable clinical services for pediatric and adult patients and their families, educates and empowers patients about their use, and conducts peer-reviewed research.
Clinical Services Offered at Zakim Center

Individual:
- Acupuncture
- Massage
- Reiki
- Integrative Medicine Consults
- Integrative Nutritional Consults

Group:
- Music Therapy
- Expressive Arts Therapy
- QiGong
- Meditation
- yoga
Pain Severity And Interference

Mean

Pain Severity
Pain Interference

Week
HISTORY

• 2003 – The International Society of Integrative Oncology (SIO) was founded through a joint effort of the Dana-Farber Cancer Institute, The Memorial Sloan Kettering Cancer Center and the American Cancer Society
Integrative Oncology

We have come a long way

But

We still have a ways to go.
What Is CAM?

… medical and health care practices outside the realm of conventional medicine, which are yet to be validated using scientific methods

Complementary: together with conventional practices

Alternative: in place of conventional practices
The CAM Domains

- Biologically Based Systems
- Manipulative & Body-Based
- Common CAM Practices
- Yoga
- Prayer
- Meditation
- Homeopathy
- Naturopathy
- Energy Therapies
- Qi qong
- Magnets
- Reiki
- Diets
- Herbals
- Massage
- Chiropractic

NCCAM
Categories of Integrative Therapies

- Diet, OTC supplements, antioxidants, herbs
- MindBody Medicine
- Physical Activity and Modified Exercise Programs
- Massage and Touch Therapies
- Acupuncture
ACS Challenge Goals
1996-1998

• Reduce cancer mortality by 50% by 2015
• Reduce incidence of cancer by 25% by 2015
• Show measurable improvement in the quality of life; physical, psychological, social and spiritual
QOL Measures

- Assure appropriate care for cancer and treatment related symptom control
- Include palliative care, end of life care and survivorship issues
Cancer as a Chronic Disease

• With a decrease in cancer mortality and a steady incidence of cancer, there are more cancer survivors

• Result is that QOL issues become more important and Integrative Oncology becomes more significant
Integrative Oncology

- Combines the best of both conventional and evidence-based integrative therapies
- Emphasizes patient participation (e.g. exercise, diet, stress management) in maximizing health
- Emphasizes the primacy of the patient provider relationship and the importance of shared decision making
- Emphasizes the contribution of the therapeutic encounter itself
- Seeks to optimize and individuals’ innate healing capacity

Snyderman R, Weil AT, Arch Inter Med; 2002;162:395-397
Why an Oncology Center for Integrative Therapies?

- Cancer patients often have interest in or questions about Integrative Therapies, e.g., acupuncture, massage, herbs.
- Many patients benefit from Complementary Therapies in conjunction with conventional cancer care.
- Patients need advice from clinicians about contraindicated therapies, e.g., “alternative” medicine clinics, drug-herb interactions.
Cancer Patient Use of CAM

- 83% of patients across broad-spectrum of malignancies use CAM
- Highest use: vitamins/herbs, movement & physical therapies (excluding spiritual practices)
- Expectations were: improve QOL, alleviate symptoms, prolong life, cure their disease, boost their immune system
- Why did patients use CAM: hopefulness, lack of toxicity, and more control

Richardson et al, JCO 2000;18:2505-14
Who uses Integrative Therapies at Dana-Farber Cancer Institute?

- Patients with:
  - Pain
  - Fatigue
  - Anxiety
  - Other Symptoms (e.g., nausea; neuropathy)
  - Interest in nutrition counseling for special diets or supplements or other therapies
Clinical Services Offered at Zakim Center

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- Expressive Arts Therapy
- QiGong
- Meditation
- Yoga
Integrative Nutrition Consults

- Respond to pt inquiries re: diets, supplements, herbs
- Therapies with potential benefit:
  - Fish oil for cancer cachexia
  - Probiotics for bowel irregularities
  - Glutamine for chronic diarrhea
  - Various dietary manipulations for symptom control
    - Ex: a low fiber/residue diet for patients with acute or chronic diarrhea
Nutrition Guidelines

- Avoid being overweight, obesity
- Be physically active
- Avoid sugar
- Consume a phytonutrient rich diet
- Limit red meats, avoid processed foods
- Limit alcohol

ACS, AICR
Integrative Medicine Consults

Respond to questions about CAM:

• Safety
• Efficacy

Discuss role of integrative therapies alongside conventional therapy
"You've been fooling around with alternative medicines, haven't you?"
Guidelines For Advising Patients: Based on Evidence and Efficacy

<table>
<thead>
<tr>
<th>Therapies that may be <strong>recommended:</strong></th>
<th>Therapies that may be <strong>accepted:</strong></th>
<th>Therapies that should be <strong>Discouraged or unacceptable:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence supports efficacy</td>
<td>Evidence regarding efficacy is inconclusive</td>
<td>Evidence indicates inefficacy</td>
</tr>
<tr>
<td>and</td>
<td>but</td>
<td>or</td>
</tr>
<tr>
<td>Evidence supports safety</td>
<td>Evidence supports safety</td>
<td>Evidence indicates serious risk</td>
</tr>
</tbody>
</table>

Potential Concerns of Physicians – Herbs and Biologics use:

- Direct toxic effects
- Interactions with other medicine
- Reduced effectiveness of “standard therapy”
- Toxicity not related to cancer
- Impairment in overall “quality-of-life”
- Delay in obtaining known effective therapy
Direct Toxicity Of Cam

- **Laetrile** – cyanide toxicity of CAM
  - Moertel CG, et al. NEJM 1982;306:201

- **Shark cartilage** – nausea, vomiting, constipation, hepatitis

- **Hydrazine sulfate** – hepatorenal failure
Interactions With Other Medications

- Perioperative care –
  - Cardiovascular effects (ephedra)
  - Bleeding (garlic, ginkgo, ginseng)
  - Hypoglycemia (ginseng)
  - Sedative effects + anesthesia (kava)
  - Increased metabolism (St. John’s wort)

Ang-Lee MK, et al. JAMA 2001;286-208
Problems with Method of Administration

- Serious/life threatening infections (non-sterile inoculation), severe dehydration/electrolyte loss/hypotension (enemas)

Markman M. NEJM 1985;312:1640
Green S. JAMA 1992;268:3224
Green S. JAMA 1993; 270:1719
Ca Cancer J Clin 1993; 43:309
Drug-Herb Interactions

- Cytochrome P450 system can be stimulated or inhibited
- Anti-inflammatory effect usually implies antiplatelet effect
Reduced Effectiveness Of “Standard Therapy”

- **Irinotecan and St. John’s wort** (reduced systemic exposure to active metabolite)
  

- **Cyclosporin and St. John’s wort** (reduced cyclosporin plasma concentrations)
  
<table>
<thead>
<tr>
<th>Herb</th>
<th>Concurrent Chemotherapy/Condition (suspected effect)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garlic</td>
<td>Avoid with decarbazine (CYP2E1 inhibition); caution with other concurrent chemotherapy (inconclusive data)</td>
</tr>
<tr>
<td>Ginkgo</td>
<td>Caution with camptothecins, cyclophosphamide, EGFR-TK inhibitors, epipodophyllotoxins, taxanes, and vinca alkaloids (CYP3A4 and CYP2C19 inhibition); discourage with alkylating agents, antitumor antibiotics, and platinum analogues (free-radical scavenging)</td>
</tr>
<tr>
<td>Echinacea</td>
<td>Avoid with camptothecins, cyclophosphamide, EGFR-TK inhibitors, epipodophyllotoxins, taxanes, and vinca alkaloids (CYP3A4 induction)</td>
</tr>
<tr>
<td>Soy</td>
<td>Avoid with tamoxifen (antagonism of tumor growth inhibition), and treatment of patients with estrogen-receptor positive breast cancer and endometrial cancer (stimulation of tumor growth)</td>
</tr>
<tr>
<td>Ginseng</td>
<td>Caution with camptothecins, cyclophosphamide, EGFR-TK inhibitors, epipodophyllotoxins, taxanes, and Vinca alkaloids (CYP3A4 inhibition); discourage in patients with estrogen-receptor positive breast cancer and endometrial cancer (stimulation of tumor growth)</td>
</tr>
<tr>
<td>St. John's wort</td>
<td>Avoid with all concurrent chemotherapy (CYP2B6, CYP2C9, CYP2C19, CYP2E1, CYP3A4, and P-glycoprotein induction)</td>
</tr>
<tr>
<td>Valerian</td>
<td>Caution with tamoxifen (CYP2C9 inhibition), cyclophosphamide, and teniposide (CYP2C19 inhibition), cyclophosphamide, and teniposide (CYP2C19 inhibition)</td>
</tr>
</tbody>
</table>

Toxicity of CAM Use Not Specifically Related to Cancer

- Ginkgo – GI symptoms, headache, emesis
- Ginseng – diarrhea, headache, insomnia
- Saw palmetto – constipation, diarrhea
- Kava – liver damage, dizziness, stupor

Ernst E. Ann Intern Med 2002; 136:42
Delay In Obtaining Known Effective Therapy

- Delay seeking medical attending for symptoms suggestive of a serious illness
  
  Brienza RS, et al. J Women’s Health & Gender-Based Medicine 2002; 11:79

- Delay initiation of “standard effective treatment” for a malignancy
  
Reduced Effectiveness Of “Standard Therapy”

- **Irinotecan and St. John’s wort** (reduced systemic exposure to active metabolite)

- **Cyclosporin and St. John’s wort** (reduced cyclosporin plasma concentrations)
Websites

• Memorial Sloan-Kettering Cancer Center: http://www.mskcc.org/mskcc/html/5707.cfm?Criteria=about+herbs&x=13&y=

• The University of Texas MD Anderson Cancer Center: http://www.mdanderson.org/departments/CIMER

• American Cancer Society: http://www.cancer.org/docroot/ETO/ETO_5.asp

• National Center for Complementary and Alternative Medicine: http://nccam.hih.gov/


• Natural Medicines Comprehensive Database: http://www.naturaldatabase.com

• Natural Standard: http://www.naturalstandard.com
Mind Body Therapies

- Relaxation response and biofeedback
- Mindfulness meditation
- Guided imagery
- Self-hypnosis
- Self-expression in words
- Music therapy
- Expressive arts therapy
- Dance
- Yoga
- Tai chi
- Qi gong
- Support groups
Massage and Touch Therapies

- Swedish massage
- Aromatherapy massage
- Reflexology
- Acupressure
- Shiatsu
- Manual lymphatic drainage
- Reiki
- Deep tissue massage
Effect of Massage Therapy on Stress Levels and QoL in Brain Tumor Patients
by: Stephen T. Keir, DRPH, MPH
Duke University

- 25 Patients
- 45 minute massage sessions 2x/week for 4 weeks
  - Stress levels wk 2 through 4; 1 wk after showed increase but not same as baseline
  - QoL: emotional, social/family and physical well being and specific brain tumor concerns
Effects of complementary therapies on clinical outcomes in patients being treated with radiation therapy for prostate cancer.

By: Clair Beard, MD
DFCI Boston, MA

- 54 men with prostate cancer being treated with radiation
- Assigned to Reiki, Relaxation Therapy or wait list control to measure trends for effects on anxiety, depression and QoL
- 2 50 min sessions of Reiki, 2 60 min sessions of RRT/week for 8 weeks
- Trends: both Reiki and RRT showed \( \downarrow \) anxiety and depression and \( \uparrow \) QoL
Acupuncture

- Benefit in QOL of cancer patients
- May be recommended:
  - Chemotherapy-induced nausea and vomiting
  - Cancer pain
  - Post-chemotherapy fatigue
- May be acceptable:
  - Radiation-induced xerostomia
  - Insomnia
  - Anxiety
  - Hot flashes
Will patients accept acupuncture?
Acupuncture Safety

- Of 34,407 treatments:
  - 43 minor adverse events
  - 0 serious adverse events
  - MacPherson et al BMJ 2001;323:486-7
- At DFCI – No adverse events in over 10 years
What We Really Want To Know

MOTHER GOOSE & GRIMM by Mike Peters

TELL ME, DOES ACUPUNCTURE REALLY WORK?
Why Research

• Use of research studies & technology to better understand acupuncture & other integrative therapies

• Recognition that patients are continuing to use these therapies, so that questions of dose, synergy, and potential interactions can be investigated through established & refined research methods
Research Issues

- Do the same rules apply as studying a new chemotherapy agent?
- What is the best control for massage or a mind/body intervention?
- Sham acupuncture
- Whole systems vs reductionist research
DFCI Research

• Immunologic Activity, Physical Status, and QOL in Connection with Two Exercise Programs (Modified Exercise and Qigong)
  
  PI: Paul Richardson

• Acupuncture on Pain, Nausea and Quality of Life in Advanced Cancer
  
  PI: David S. Rosenthal, MD

• Acupuncture and Neutropenia in Ovarian Cancer
  

• QiGong on Mood and Cortisol in Breast Cancer
  
  PI: Ursula Matulonis, MD

• Use of Music Therapy with Metastatic Breast Cancer
  

• Reiki and Relaxation Response in Prostate Cancer Pts Receiving Radiation
  
  PI: Clair Beard, M.D.
Effect of Acupuncture on the Pain, Nausea, and Quality of Life for Patients with Advanced Cancer

R21, Feasibility Study - 40 patients

• Advanced ovarian or breast cancer receiving conventional palliative treatment
• 12 acupuncture sessions over 8 weeks
• Standardized Protocol
• Pre- and Post-Treatment symptom assessment at each acupuncture session
• QOL Questionnaires - 5 time points
Results/Conclusions

- 26 (65%) completed 8 wks of acupuncture
- 14 (35%) withdrew from study
- Feasible
- QOL results - Pts reported positive benefit from acupuncture treatments both for physical symptoms and measures of QOL
- No adverse events occurred
- Further analysis ongoing
## Symptom Response Rates

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Overall % with Symptom Pre-treatment</th>
<th>Response Rate</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>40%</td>
<td>60%</td>
<td>54 - 67%</td>
</tr>
<tr>
<td>Pain</td>
<td>32%</td>
<td>57%</td>
<td>50 - 64%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>24%</td>
<td>47%</td>
<td>40 - 58%</td>
</tr>
<tr>
<td>Depression</td>
<td>18%</td>
<td>49%</td>
<td>40 - 58%</td>
</tr>
<tr>
<td>Nausea</td>
<td>7%</td>
<td>35%</td>
<td>23 - 47%</td>
</tr>
</tbody>
</table>
Pain Severity And Interference

Mean

Week

Pain Severity

Pain Interference
Acupuncture for chemotherapy-induced neutropenia in patients with gynecologic malignancies, a pilot randomized, sham controlled clinical trial

Ursula A. Matulonis, M.D.

Anne Doherty-Gilman, MPH; Hang Lee, Ph.D.; Elizabeth Dean-Clower, M.D., MPH; Andrew Rosulek, B.S.; Carolyn Gibson; Roger B. Davis, Sc.D.;

Julie E. Buring, Sc.D.; Peter M. Wayne, Ph.D.; Anne Kathryn Goodman, M. D.; David S. Rosenthal, M.D.; Richard T. Penson, M.D.

Dana Farber Cancer Institute
Massachusetts General Hospital
Harvard Medical School
Specific Aims

• To test the hypothesis that acupuncture administered during chemotherapy can produce a higher WBC count and/or ANC at nadir of cycle 2 and 1st day of cycle 3 compared to sham acupuncture
• To determine whether acupuncture will increase G-CSF levels compared to sham
• To test the feasibility of conducting such a trial in 50 patients
• To test the effects of acupuncture on patients’ quality of life
Eligible patients identification

Consent, enrollment, baseline data collection

Randomization

Active acupuncture starts at day 15, 3/wk x 1 wk

Sham acupuncture starts at day 15, 3/wk x 1 wk

Cycle #1
Blinded

Active acupuncture
2-3/wk x 3 wk

Sham acupuncture
2-3/wk x 3 wk

Cycle #2
Blinded

Active acupuncture
2-3/wk x 3 wk

Sham acupuncture
2-3/wk x 3 wk

Cycle #3, 4
Unblinded

No acupuncture for 5 wk

Active acupuncture
2/wk x 5 wk, optional

Exit study at day 78
Change of Neutrophil and Acupuncture in a 21-day Chemo Protocol

1st recovery day = 2nd chemo
2nd recovery day = 3rd chemo

Acupuncture 10 sessions

1st nadir
2nd nadir

Day 1
Day 8
Day 15
Day 22
Day 29
Day 36
Day 43

Chemo cycle 1
Chemo cycle 2
Patient Eligibility (cont.)

- For newly diagnosed patients: standard DF/PCC carboplatin and paclitaxel (Taxol) chemotherapy, which is: paclitaxel 175 mg/m² IV over three hours, followed by carboplatin AUC 5 IV over 30-60 minutes
- Other myelosuppressive chemo in recurrent setting except liposomal doxorubicin
- No use of regular acupuncture in past 120 days
- Able to give informed consent, >18 yrs of age
Treatment Plan

- Enrolled patients are randomized to receive:
  1) Active acupuncture
     or
  2) Sham acupuncture/delayed active acupuncture

- Each arm will receive a total of 10 treatments during first and second cycles
Study Results
Screened for eligibility (n=587)

Excluded (n=565)
  Did not meet inclusion criteria (n=59)
  Competing protocols (n=117)
  Treating physician’s decision (n=310)
  Others and unknown (n=79)

Enrolled into study (n=22)

Withdrew consent (n=1)

Randomized (n=21)

Received active acupuncture (n=11)

Discontinued intervention (n=3)
  Disqualified for medical reasons: (n=0)
    Withdraw: 3
    1st week: 1
    2nd week: 1
    3rd week: 0
    4th week: 1

Observations available for Analysis (n=11)
  Baseline: 11
  Nadir: 8
  Recovery day: 9
  Analyzable set: 9

Received sham acupuncture (n=10)

Discontinued intervention (n=3)
  Disqualified for medical reasons: (n=1)
    Withdraw: 2
    1st week: 0
    2nd week: 1
    3rd week: 0
    4th week: 1

Observations available for Analysis (n=9)
  Baseline: 9
  Nadir: 7
  Recovery day: 8
  Analyzable set: 7
## Acupuncture effect on WBC between two groups during chemotherapy

### Median WBC changes between acupuncture and sham groups during chemotherapy

<table>
<thead>
<tr>
<th>Time points</th>
<th>Acupuncture group</th>
<th>Sham group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No of patients</td>
<td>No of patients</td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>11</td>
<td>9</td>
<td>2600 (1700-5200)</td>
</tr>
<tr>
<td>1st recovery</td>
<td>10</td>
<td>10</td>
<td>4400 (2000-10000)</td>
</tr>
<tr>
<td>Pre-nadir</td>
<td>8</td>
<td>7</td>
<td>2600 (1900-5200)</td>
</tr>
<tr>
<td>Nadir</td>
<td>8</td>
<td>7</td>
<td>2300 (1600-4600)</td>
</tr>
<tr>
<td>2nd recovery</td>
<td>9</td>
<td>8</td>
<td>4400 (2300-10000)</td>
</tr>
</tbody>
</table>

Note: All p values were measured after adjusting for baseline difference by ANCOVA.
Acupuncture effect on WBC between two groups during chemotherapy

![Graph showing WBC levels during different stages of chemotherapy for Active Sham and Active Sham groups. The graph indicates statistical significance with *p=0.046 and *p=0.16.]
### Acupuncture Effect on ANC changes between two groups during chemotherapy

<table>
<thead>
<tr>
<th>Time points</th>
<th>Acupuncture</th>
<th>Sham Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1640 (350-5250)</td>
<td>1610 (50-3870)</td>
<td>0.619</td>
</tr>
<tr>
<td>1st recovery</td>
<td>4110 (1470-8510)</td>
<td>3660 (760-8340)</td>
<td>0.619</td>
</tr>
<tr>
<td>Pre-nadir</td>
<td>3260 (990-3970)</td>
<td>1510 (980-3800)</td>
<td>0.11</td>
</tr>
<tr>
<td>Nadir</td>
<td>2080 (1050-4770)</td>
<td>1310 (160-2770)</td>
<td>0.115</td>
</tr>
<tr>
<td>2nd recovery</td>
<td>6670 (2630-10800)</td>
<td>3345 (1360-8200)</td>
<td>0.099</td>
</tr>
</tbody>
</table>

Note: All p values were measured after adjusting for baseline difference by ANCOVA.
Acupuncture Effect on ANC changes between two groups during chemotherapy
Limitations and Challenges of Study

• Recruitment is challenged by:
  - competing protocols
  - distance to travel the study sites
  - # of acupuncture sessions/week
  - use of myelosuppressive chemotherapy regimens (IV/IP combinations) that already incorporate neupogen/neulasta

• The small sample size limits a definitive conclusion

• Sham acupuncture may also elicit physiological responses
Conclusions

• Although a larger randomized trial is necessary to determine the effects of acupuncture on chemotherapy induced myelosuppression, there were consistent trends, and recovering WBC counts were significantly higher in patients receiving acupuncture. Formal evaluation of CAM is vital to confirm potentially clinically meaningful benefits.

• Acupuncture appears to be safe for this population

• Conducting rigorous and controlled acupuncture studies during a chemotherapy period is challenging, but important.
Acupuncture for Chemotherapy-Induced Peripheral Neuropathy: A Pilot Randomized Controlled Trial

Weidong Lu, MB, MPH, PHD
Jennifer Ligibel, MD
David S. Rosenthal, MD
Anita Giobbie-Hurder, MS
Laura Shockro & Kelly Stecker
Zakim Center & Breast Cancer Oncology
Dana-Farber Cancer Institute, Harvard Medical School
July 6, 2015
Chemotherapy-induced peripheral neuropathy (CIPN) is one of the most common side effects of taxane chemotherapy. Symptoms of CIPN: paresthesia and pain of extremities. Incidence rates of CIPN in breast cancer range from 30% to 97% with adjuvant taxanes. Results in loss of physical function, difficulty in ADL’s, decreased QOL, dose reductions and termination of treatment. No established therapy is currently available for this condition.
Prevalence of chemotherapy-induced peripheral neuropathy: A systematic review and meta-analysis

31 studies with 4179 patients

Paclitaxel

70.8%

(95% CI = 43.5–98.1)
Acupuncture

• A number of small studies have looked at acupuncture as a potential treatment of CIPN
  – A RCT (n=64) reported response rate of 88% for paclitaxel-specific CIPN
  – Studies to date not breast cancer specific.

• Potential mechanism of action for acupuncture and CIPN
  – Suppression of local and central inflammation
  – Opioid system activation
  – Nerve fiber regeneration
Research

Electroacupuncture for thalidomide/bortezomib-induced peripheral neuropathy in multiple myeloma: a feasibility study

M Kay Garcia¹, Lorenzo Cohen¹, Ying Guo², Yuhong Zhou³, Bing You⁴, Joseph Chiang⁵, Robert Z Orlowski⁶, Donna Weber⁶, Jatin Shah⁶, Raymond Alexanian⁶, Sheeba Thomas⁶, Jorge Romaguera⁶, Liang Zhang⁶, Maria Badillo⁶, Yiming Chen⁶, Qi Wei¹, Richard Lee¹, Kay Delasalle⁶, Vivian Green⁶ and Michael Wang⁶*
Case Report

- Joined the study from Nov. 25, 2014 to January 14, 2015
- Pain scores at the beginning: 9 out of 10 both hands and feet
- Acupuncture 18 sessions
- Pain scores at the end of the study: 3 out of 10 (hands); 5 out of 10 (feet)
- Continued acupuncture post study
- Pain scores: 2 out of 10 (hands); 4 out of 10 (feet) as of June 30, 2015
- The patient says: "I have tried everything and nothing works for my pain." "After acupuncture, I can feel my toes and fingers. It is wonderful!"
Previous Acupuncture Studies on CIPN

- A systematic review evaluated 7 acupuncture RCTs on CIPN
- One RCT from China (n = 64): 67% overall response rate; 88% response in paclitaxel specific CIPN using PNQ
  – Xu et al. Zhongguo Zhen Jiu 30:2010
- Another non-RCT trial (n=47), a significant increase of nerve amplitude in sural and tibial nerves measured by NCS test (response: 76% vs. 15%)
- However, poor quality design in general and non-breast cancer specific
Select Inclusion Criteria

1. Stage I-III Breast Cancer

2. Completion of adjuvant taxane-based chemotherapy (as single agents or in combination with platins or HER-2 directed therapy).

3. Presence of grade I or greater neuropathy

4. ECOG performance status of 0 or 1

5. Adequate hematological function: neutrophil count >1.0 x10^9/L, platelet count >50 x10^9/L

6. Patients who are on a stable dose of prescription medications or dietary supplements for CIPN and still symptomatic as defined above will be allowed to participate in the study.
Outcome Measures

- The Patient Neurotoxicity Questionnaire (PNQ)

- The Functional Assessment of Cancer Neurotoxicity (FACT/NTX) subscale

- The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Cancer (QLQ-C30) (version 3.0)

- The EORTC QLQ Chemotherapy-induced Peripheral Neuropathy 20 questionnaire (CIPN 20)

- Patient Medication Log.

- Blood draw
Primary Aim:
Evaluate the impact of acupuncture on PNQ score by comparing changes from baseline between acupuncture and usual care arms at the end of week 8.

The response rate is defined as the proportion of patients in whom there is a one unit or greater reduction in PNQ score between baseline and week 8.
Current Status of the Study

- IRB Approval received: April 14, 2014
- Study acupuncturists training: April 27, 2014
- Clinicaltrial.gov (NCT02129686): April 30, 2014
- IRB Activation: June 12, 2014
- Major Amendment No. 1 Approved: July 14, 2014
- DSMC approval: Feb. 24, 2015
- IRB continuing review approval: March 9, 2015
- The study is currently activated and ongoing
Study Recruitment Status

• The overall target goal: N = 40 (100%)
• First patient was registered in the study on Aug. 15, 2014
• 20 (50%) patients consented as of June 22, 2015
• 20 (50%) patients enrolled into the study:
  – 10 immediate, 10 delay
• 5 (12.5%) active patients: 3 delay, 2 immediate
• 12 (30%) patients completed the study
• 3 (7.5%) withdrawn from the study
• No serious acupuncture related complications
Financial Issues
### Funding Appropriations for IM

<table>
<thead>
<tr>
<th>National Center for Complementary and Alternative Medicine</th>
<th>NCI / OCCAM</th>
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</thead>
<tbody>
<tr>
<td><strong>FY 2011:</strong> $127.7 million</td>
<td>$122.5 (includes Recovery act)</td>
</tr>
<tr>
<td><strong>FY 2005:</strong> $123.1 million</td>
<td></td>
</tr>
<tr>
<td><strong>FY 2004:</strong> $117.7 million</td>
<td>$129 million</td>
</tr>
<tr>
<td><strong>FY 1998:</strong> $19.5 million (OAM)</td>
<td>$28 million</td>
</tr>
</tbody>
</table>
Integrative Oncology

The Future
Cancer is now defined more by a genetic defect and less by site of origin.
GENOMICS
Gene Profiling

• Individualizing cancer risk
• Individualizing cancer therapy
• Individualizing integrative therapies
Services Available To Cancer Patients And Their Primary Care Oncologists, Often Operating In Silos

- Physical Trainers
- Specialty Consultants
- Psychosocial Oncology
- Support Groups
- Patient & Family Care Services
- Nurse Specialists
- Social Workers
- Pain and Palliative Care
- CAM Practitioners
- Nutritionist
- Spiritual
- Ethicist
- Patient – Primary Care (Oncologist)
Coach/Navigator Assists Patient, Primary Care Oncologist In Individualizing Care.

Proposed Model

Patient – Primary Care Oncologist

Coach/Navigator
SIO Website

Society for Integrative Oncology

OUR MISSION:
TO ADVANCE EVIDENCE BASED, COMPREHENSIVE, INTEGRATIVE HEALTHCARE TO IMPROVE THE LIVES OF PEOPLE AFFECTED BY CANCER.

Events

Clinical Practice Guidelines

Conference

2 Day Integrative Medicine Program Workshop
Presented by The University of Texas Cancer Center

10.08.2015 - 10.09.2015
SIO 12th Conference 2015

SOCIETY FOR INTEGRATIVE ONCOLOGY
12TH INTERNATIONAL CONFERENCE

Program  Register  Support  Hotel/Travel

INTEGRATIVE INNOVATION
November 14-16, 2015 | Boston Park Plaza Hotel
Boston, Massachusetts
“It only takes one person to start a revolution of thought and spirit.”
Lenny Zakim