Tenth International Conference of the Society for Integrative Oncology

Translational Science in Integrative Oncology: From Bedside to Bench to Best Practices

Conference Chair: Lynda G. Balneaves, PhD, RN
Conference Co-Chairs: Emma S. Tomlinson Guns, PhD, Richard T. Lee, MD

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In October 2013, more than 300 researchers, clinicians, patient advocates, and patients joined together at the historic Fairmont Hotel Vancouver in Vancouver, British Columbia, Canada, for the 10th International Conference of the Society for Integrative Oncology (SIO). This conference was held to examine the growing evidence base for complementary therapies and practices currently being used in cancer care and the rapid translation of that literature into standard care and best practice guidelines. The conference theme, “Translational Science in Integrative Oncology: From Bedside to Bench to Best Practices,” encouraged conference attendees to consider how the growing evidence base on the efficacy of integrative therapies for cancer prevention and control can be effectively translated to clinical practice to improve the lives of people affected by cancer.

The conference focused on several plenary sessions. At the first plenary session on knowledge translation, several speakers addressed the need for strategies to support the transfer of research findings to both cancer patients and oncology health professionals. A presentation by Sunita Vohra, MD (University of Alberta) reported on a novel approach to monitoring natural health product–drug interactions using a population-based surveillance database that captured provider-reported information about natural health product–drug combination outcomes. Lynda Balneaves, PhD, RN (University of British Columbia) presented...
MyChoices Project, an intervention trial testing the effect of a decision aid on knowledge and decision-making outcomes among women with breast cancer who are seeking complementary therapies to manage their menopausal symptoms. Dugald Seely, ND, MSc (Ottawa Integrative Cancer Centre) reviewed the process of working through a series of systematic reviews, including the use of meta-analysis on specific therapies relevant to integrative oncology, and discussed the limitations and challenges of synthesizing, sharing, and using this type of evidence. Michelle Kohl, MBBS, BSc, FRCP (LOC: Leaders in Oncology Care) discussed barriers to knowledge uptake in integrative oncology using her professional experience in directing the Living Well Programme in London, United Kingdom.

A conference highlight was a joint plenary session presented by SIO and the American Society of Preventive Oncology (http://www.aspo.org), which was designed to foster collaborative bridges between research organizations. This session featured presentations on challenges and recruitment and retention strategies in behavior change research (Wendy Demark-Wahnefried, PhD, RD, University of Alabama at Birmingham); a review of mind–body interventions (Anita Kinney, PhD, University of New Mexico); a discussion of study design issues in diet and physical activity research (Karen Basen-Enquist, PhD, MPH, MD Anderson Cancer Center); and survivorship research resources, including the Women’s Health Initiative Cancer Survivor Cohort (Electra Paskett, PhD, Ohio State University Cancer Center).

A third plenary highlighted data on mind–body interventions designed to reduce stress and improve social support for cancer patients and survivors. In this symposium, Susan Lutgendorf, PhD (University of Iowa) provided an overview of recent advances in our ability to study and detect stress influences in cancer markers and disease progression. Linda Carlson, PhD, CPSych (University of Calgary and Tom Baker Cancer Centre) presented an example of clinical research on mindfulness-based and supportive interventions that affect a range of potentially important biomarkers in breast cancer survivors. Joanne Stephen, PhD (British Columbia Cancer Agency) discussed the potential of disseminating mind–body interventions through the Internet, with reference to research on an innovative pan-Canadian psychosocial intervention “CancerChatCanada.”

Other highlights from plenary sessions included presentation of data on the potential role of the microbiome and probiotics for chemoprevention and treatment of cancer, including clinical trial results describing the use of probiotics as a component of supportive care among children and adolescents (Paul Rogers, MD, University of British Columbia; Gregory Plotnikoff, MD, MTS, FACP, Penny George Institute for Health and Healing; David Mack, MD, University of Ottawa; Satya Prakah, PhD, McGill University; Elena Ladas, PhD, RD, Columbia University); a review of recently published guidelines on the use of integrative oncology for lung cancer in Chest along with a description of future SIO guidelines in development (Gary Deng, MD, PhD, Memorial Sloan Kettering Cancer Center; Heather Greenlee ND, PhD, Columbia University; and Suzanna Zick, ND, MPH, University of Michigan); and a description of the spectrum of basic, clinical and health services research that has been conducted on cannabis within the context of cancer care (Lynda Balneaves, PhD, RN, University of British Columbia; Donald Abrams, MD, University of California, San Francisco; and patient advocate David Hutchinson, British Columbia, Canada).

The SIO’s 11th International Conference will be held in Houston, Texas, on October 26-28, 2014. The conference theme will be “Personalized Integrative Oncology: Targeted Approaches for Optimal Outcomes.” The conference will be chaired by Richard T. Lee, MD and Peiying Yang, MS, PhD, both of the University of Texas MD Anderson Cancer Center, Houston, TX.

Authors’ Note
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Reference

Top 10 Scoring Conference Abstracts
Best of SIO Abstracts

Abstract 107: The Effect of Two Types of Self-Administered Acupressure Compared to Standard of Care on Depression and Anxiety in Fatigued Breast Cancer Survivors

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Abstract

Background: There are nearly 3 million breast cancer survivors (BCS) in the United States. Mood disorders in BCS are common, with 38% of women having moderate to high anxiety, and 22% having moderate to high depression. Depression may interfere with survivors’ quality of life, decreased adherence to adjuvant therapy and be associated with lower rates of survival. Current treatments for mood disorders can be difficult to implement and/or have unacceptable side effects; thus, there is a need for new treatments in this area. Methods: We compared the effect of 6 weeks of 2 types of self-administered acupressure (stimulating [SA] and relaxing [RA]) versus standard of care (SC) in 32 women for depression, and in 57 women with anxiety who reported ≥8 at baseline on the Hospital Anxiety Depression Scale (HADS) depression or anxiety subscales, as appropriate, and who were from an ongoing randomized clinical trial on acupressure for persistent cancer-related fatigue in BCS. Analyses of variance (ANOVA) were performed on mean differences of changes (baseline to week 6) in anxiety and depression subscales by group. Results: There was a significant decrease in depression (P = .02 vs SA; P = .06 vs SC) but not in anxiety (P = .36 vs SA; P = .46 vs SC) in the RA group compared with either SA or SC. This represents a ~47% mean decrease from baseline in depression in the RA group versus ~16% in the SA group and 22% in the SC group, and on average a movement from being borderline abnormal on the HADS depression subscale at baseline (9.2 ± 0.98, 0-21 point scale) to normal (4.9 ± 2.7) at 6 weeks. Conclusion: In this preliminary analysis, self-administered RA engenders a greater antidepressive response as compared with either SA or SC in fatigued BCS. These findings should be interpreted with caution given our small sample size. More rigorous studies are recommended.

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Abstract 67: Electro-Acupuncture for Aromatase Inhibitor–Related Arthralgia and Comorbid Symptoms in Breast Cancer Survivors: A Randomized Placebo-Controlled Trial

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Abstract 53: Association of Physical Activity and Telomere Length in Breast Cancer Survivors

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Abstract

Background: Cellular telomere length (TL) is a biomarker of accumulated cellular damage and human aging. Evidence suggests that TL may be affected by a host of psychosocial and lifestyle factors, including physical activity (PA). This is the first study to evaluate the relationship between PA and TL in breast cancer survivors.

Methods: A cross-sectional sample of 392 postmenopausal women with stage 0-III breast cancer at an outpatient breast oncology clinic of a large university hospital completed questionnaires and provided a blood sample. TL was determined using mean terminal restriction fragment length and isolated from peripheral blood mononuclear cells. PA was dichotomized into 2 groups (none vs moderate to vigorous) using the International Physical Activity Questionnaire. Multivariate logistic and linear regression analyses were performed to identify factors associated with TL and PA.

Results: Among participants, 66 (17\%) did not participate in any PA. In the adjusted model, older women (>65 years) has significantly shorter TL (coefficient = -0.27; \(P = .001\)) were both significantly more likely (AOR = 2.37; \(P = .001\)) or graduate education (AOR = 2.37; \(P = .001\)) were both significantly more likely to engage in PA. Women with a college (AOR = 2.37; \(P = .03\)) or graduate education (AOR = 2.37; \(P = .001\)) were both significantly more likely to engage in PA. Lack of PA is associated with shortened TL, warranting prospective investigation of the potential role of PA on cellular aging in breast cancer survivors. Future research is needed to address the barriers to PA in women with breast cancer, especially for those who are obese and with lower education.

Preclinical

Abstract 30: Pomegranate Extracts Impact Androgen Biosynthesis Pathways In Vitro and In Vivo

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Abstract

Background: Residual tissue androgens are consistently detected within prostate tumors from chemically castrated patients and are thought to facilitate androgen receptor (AR)–mediated disease progression to castration-resistant prostate cancer (CRPC). The source of these steroids has been attributed to the conversion of adrenally sourced precursor substrates. Testosterone and dihydrotestosterone (DHT) can be produced through
3 biosynthesis pathways: $\Delta^4$, $\Delta^5$, and backdoor pathways. Pomegranate extracts have been demonstrated to have anticancer activity, particularly in CRCP. This study examines the effects of pomegranate extracts (POMELLA) on steroid biosynthesis using PCA cell lines (22RV1 and LNCaP) in vitro as well as the conditional PTEN knockout prostate cancer model in vivo. **Methods:** Steroids produced by 22RV1 and LNCaP cells (treated by POMELLA) for 48 hours at 2, 4, 5, 8, 12 $\mu$g/mL, respectively, as well as mouse serum taken after treatment with PFEs in drinking water (0.17 g/L of POMELLA in 1% sucrose solution for 20 weeks) or control (1% sucrose water) were analyzed via UPLC/MS/MS. **Results:** In vitro experiments showed that POMELLA extracts significantly reduced testosterone, DHT, dehydroepiandrosterone (DHEA), androstenedione, androsterone, and pregnenolone production. Testosterone and DHT were significantly lower in cells treated with pomegranate extracts compared with controls, at 5 to 12 $\mu$g/mL concentrations (n = 6, P < .05). Our in vivo study also confirmed that testosterone and DHEA in the serum of the POMELLA-treated mice were significantly lower than control mice (n = 7, P < .05). **Conclusion:** Pomegranate extracts attenuate testosterone and DHT in vitro and lower serum androgen levels in vivo, in a conditional PTEN knockout prostate cancer model.

**Abstract 109: Drug–Micronutrient Interactions in Cancer: The Case of Vitamin D**

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**Abstract**

**Background:** The chemopreventive and therapeutic effects of vitamin D3 are exerted through 1α,25-(OH)₂D₃, the dihydroxy metabolite of vitamin D3. Inactivation of 1α,25-(OH)₂D₃ by cytochrome P450 3A (CYP3A) enzymes can be an important determinant of its serum and tissue levels. The purpose of the present study was to assess the potential of various medications, which are commonly used in the treatment regimens of patients with cancer (eg, abiraterone, ketoconazole, tamoxifen, taxanes) and as premedications (eg, dexamethasone, prednisone) to chemotherapy, on biotransformation of 1α,25-(OH)₂D₃ in human and mouse liver microsomes. **Methods:** Adult CD-1 mice were treated with vehicle (50% ethanol), dexamethasone (80 mg/kg/day) or prednisone (80 mg/kg/d) for 3 consecutive days by intraperitoneal injection. Mouse livers were used to prepare microsomes by differential ultracentrifugation. In vitro reaction mixtures contained potassium phosphate buffer, mouse or human hepatic microsomal protein (XenoTech LLC) or human recombinant CYP3A4 supersomes, NADPH, and a fixed concentration of 20 $\mu$M 1α,25-(OH)₂D₃. Reactions were initiated with NADPH after initial preincubation of microsomes with 1α,25-(OH)₂D₃ and various concentrations of abiraterone (0.2-100 $\mu$M), ketoconazole (0.05-10 $\mu$M), tamoxifen (1-100 $\mu$M), and docetaxel (0.1-1.24 $\mu$M) at 37°C. Formation of hydroxylated metabolites of 1α,25-(OH)₂D₃ were analyzed by liquid chromatography–mass spectrometry method. **Results:** The formation of hydroxy metabolites was significantly stimulated in hepatic microsomes from mice treated with dexamethasone compared with vehicle- and prednisone-treated group. Co-incubation of 1α,25-(OH)₂D₃ with various drugs led to up to ~85% to 99% inhibition of formation of hydroxylated metabolites of 1α,25-(OH)₂D₃ and therefore reduced inactivation of active vitamin D3. The IC50 values (GraphPad PrismTM v4.0 software) for individual metabolites of 1α,25-(OH)₂D₃ ranged from 0.012 to 2.20 $\mu$M in human liver microsomes. **Conclusions:** In summary, our results suggest that premedications and co-medications administered in cancer patients can either exacerbate or inhibit the CYP3A-mediated inactivation of active vitamin D3 leading to altered vitamin D homeostasis.

**Mind–Body**

**Abstract 71: Disturbed Sleep in Cancer Survivors: Is There a Place for Mindfulness-Based Interventions?**

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**Abstract**

**Background:** After completing treatment, cancer survivors often suffer from a multitude of physical and mental health impairments, resulting in compromised quality of life. This exploratory study investigated whether 2 mind–body interventions, Mind–Body Bridging (MBB) and Mindfulness Meditation (MM), could improve posttreatment cancer survivors’ self-reported sleep disturbance and comorbid symptoms, as compared to Sleep Hygiene Education (SHE) as an active control. **Methods:** This randomized controlled trial examined 57 cancer survivors with clinically significant self-reported sleep disturbance, randomly assigned to receive MBB, MM, or SHE. All interventions were conducted in three sessions, once per week. Patient-reported outcomes were assessed via the Medical Outcomes Study Sleep Scale and other indicators of psychosocial functioning relevant to quality of life, stress, depression, mindfulness, self-compassion, and well-being. **Results:** Mixed effects model analysis revealed that mean sleep disturbance symptoms in the MBB and MM groups
were lower than in the SHE group, indicating that both mind–body interventions improved sleep. Also, compared with the SHE group, the MBB group showed reductions in self-reported depression symptoms and improvements in overall levels of mindfulness, self-compassion, and well-being at postintervention. **Conclusions:** This study provides preliminary evidence that brief sleep-focused MBB and MM are promising interventions for sleep disturbance in cancer survivors. Integrating MBB or MM into posttreatment supportive plans should enhance care of cancer survivors with sleep disturbance. Because MBB produced additional secondary benefits, MBB may serve as a promising multipurpose intervention for posttreatment cancer survivors suffering from sleep disturbance and other comorbid symptoms. Management of sleep problems in survivors is a high priority issue that demands more attention in cancer survivorship.

**Abstract 133: EEG Imaging and Neuromodulation of Acute Pain in Head and Neck Cancer Patients Undergoing Radiotherapy**

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**Abstract**

**Background:** We investigated the effectiveness of a brain–computer interface (LORETA neurofeedback) to manage acute onset pain and examine the neurophysiological mechanisms and localization of pain as a result of head and neck radiation. **Methods:** Patients undergoing head and neck radiation (n = 4 of 10 to date; male; right-handed; mean age = 53.5 years) completed baseline questionnaires and underwent a baseline electroencephalography (EEG). A second EEG was done on the first written prescription for pain medications, but before the medications were started, and a final EEG was performed at the conclusion of radiotherapy. Patients had a total of 6 LORETA neurofeedback sessions after their pain became at least a 4 on a 0 to 10 scale for 3 consecutive days. Patients were asked to rate their pain on a scale of 0 to 10 before and after each neurofeedback session. The Brief Pain Inventory (BPI), the Multidimensional Pain Inventory (MPI), and the MD Anderson Symptom Inventory for Head and Neck Cancer (MDASI-HN) were completed at baseline and end of radiotherapy. **Results:** LORETA results demonstrated that (1) regions of the pain network increase in beta (13-21 Hz) activity relative to baseline (primary somatosensory cortex, dorsolateral prefrontal cortex), and other regions not associated with the pain network also increased in activity (precuneus). During LORETA neurofeedback sessions, patients could reduce activity in the pain network relative to their “painful” EEG map activity. Pain ratings also decreased from pre- to post-session (mean decrease = 2.14). Self-report data and the association between self-report and brain activity will be presented with the complete data set (n = 10). **Conclusions:** We were able to capture brain activity during acute pain onset and show that patients can change that brain activity to a less painful state with LORETA neurofeedback. Identification of these regions and successful EEG neurofeedback training will allow a targeted approach to acute pain management that is independent of medications.

**Abstract 136: Baseline Depression Levels Moderate the Effectiveness of Expressive Writing for Patients With Renal Cell Carcinoma**

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**Abstract**

**Background:** Expressive writing (EW) has been demonstrated to be an effective approach to improve quality of life in cancer patients. We previously reported that EW reduced intrusive thoughts and improved cancer-related symptoms (MD Anderson Symptom Inventory [MDASI]) in renal cell carcinoma (RCC) patients. Here we examined if depressive symptoms at study entry moderated the effectiveness of the EW program. **Methods:** Patients (n = 277) with RCC scheduled to receive surgical or systemic treatment were randomly assigned to write about either their deepest thoughts and feelings about their cancer (EW) or neutral topics (NW) on 4 separate occasions over 10 days. Patients completed measures of depressive symptoms (Center for Epidemiologic Studies–Depression [CES-D]), MDASI, fatigue (Brief Fatigue Inventory [BFI]), and sleep disturbances (Pittsburgh Sleep Quality Index [PSQI]) at baseline, and 1, 4, and 10 months after the writing sessions. **Results:** The mean age of participants was 58 years, and 41% were female. Participants had been diagnosed with stage I (38%), stage II (14%), stage III (18%), or stage IV (28%). After controlling for baseline levels of the outcome variables, multilevel modeling analyses revealed that participants in the EW group who had elevated depressive symptoms at baseline had worse outcomes than those in the NW group with elevated depressive symptoms at baseline. Specifically, at 1 month postintervention, participants in the EW
group reported more cancer-related symptoms (MADSI; \( P < .01 \)), sleep disturbances (PSQI; \( P < .01 \)), and fatigue (BFI; \( P < .01 \)) compared with those in the NW group. There were no group differences for those low in baseline depressive scores. **Conclusions:** These findings suggest that patient baseline characteristics may moderate the effectiveness of an EW program. Those with elevated depressive symptoms at study entry do not appear to benefit from an EW program and, in fact, EW may result in worse outcomes. Clinician-facilitated treatments providing more intense supportive care may be need to improve quality of life outcomes in patients with depressive symptoms.

**Traditional Chinese Medicine and Acupuncture**

**Abstract 127: Acupuncture for Dysphagia After Chemoradiation Therapy in Head And Neck Cancer: A Pilot Randomized Sham-Controlled Trial**

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**Abstract**

**Background:** Dysphagia is a common side effect following chemoradiation therapy (CRT) in patients with head and neck cancer (HNC). The purpose of this pilot trial was to assess the feasibility of recruiting HNC patients and to collect preliminary data on the efficacy and safety of acupuncture on dysphagia-related quality-of-life (QOL).

**Methods:** Patients were eligible if diagnosed with stage III-IV HNC, without evidence of distance metastasis, receiving curative-intent CRT. Patients were randomized to 12 sessions of either active or sham acupuncture, once every 2 weeks, over 24 weeks from during CRT to 20-week post-CRT. All study personnel and the patients were blinded; the treating acupuncturists were not. MD Anderson Dysphagia Inventory (MDADI) and other questionnaires were measured at baseline (end of CRT), end of acupuncture, and at 6 months follow-up (12-month post-CRT). Data were analyzed by repeated-measures analysis of variance (ANOVA) adjusting for baseline.

**Results:** Accrual was completed in December 2011. Among 42 patients enrolled, 35 (83%) received at least 8 sessions of acupuncture, and 28 (67%) received all 12. Six patients withdrew because of time constraints. No serious side effects were observed. The mean MDADI total scores improved from baseline in both treatment arms (64.5 [SE ±2.4] vs 71.4 [SE ±3.1], \( P = .048 \); 64.5 [SE ±2.4] vs 77.8 [SE ±3.0], \( P < .001 \)); the difference in improvement was not significant (\( P = .12 \)). The median feeding tube duration did not differ between active and sham treatments (n = 39, median 125 days vs 147 days, \( P = .93 \)). **Conclusions:** Acupuncture is a safe and feasible treatment for HNC patients. In the pilot trial, improvements in QOL parameters from end of CRT to the time points examined were observed but they did not differ between the 2 arms. Efficacy of acupuncture to improve swallowing-related QOL in HNC patients may require more frequent or longer duration of treatment.