

# The Role of Integrative Medicine in Thoracic Cancer Treatment

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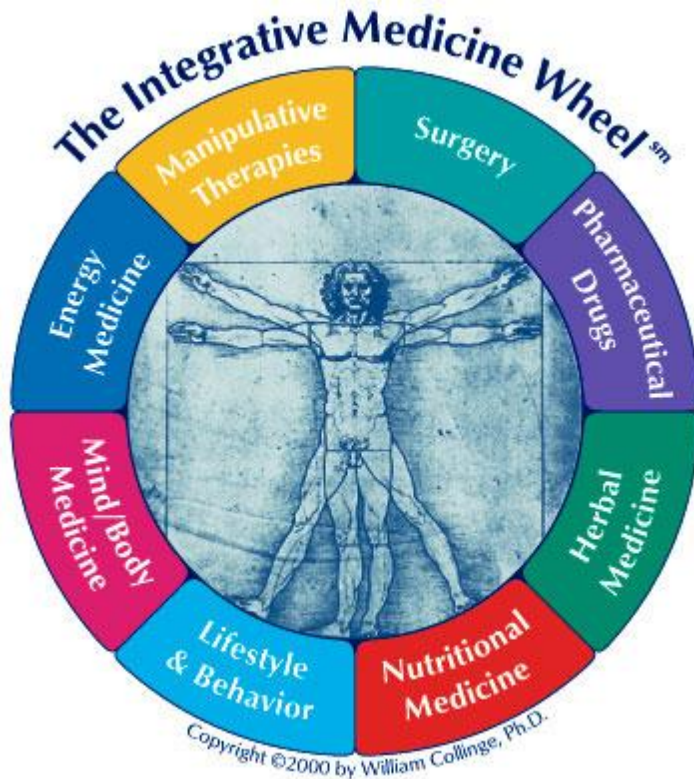
# Conflict of Interest Disclosure Statement

I have no conflicts of interest to report.

# Objectives

- Understand the definition of Integrative Medicine
- Define the landscape and breadth of resources related to Integrative Medicine at Aurora Health Care
- Understand the evidence for the use of Integrative Medicine and Therapies in the adjunct treatment of thoracic cancers, specifically lung and esophageal

# What is Integrative Medicine?



- **Integrative Medicine** is the evidence-informed combination of holistic and conventional medicine to assist each patient on their journey to health

# What Aurora Integrative Medicine Is NOT

- A substitute for the standard of care
- A grouping of voodoo practices without evidence or effectiveness
- A last resort



# Aurora Integrative Medicine (AIM)

## Integrative Medicine

- Fellowship-trained physicians and advanced practice providers
- Primary care, specialty and consultative practices
- 22 Aurora physicians and APPs

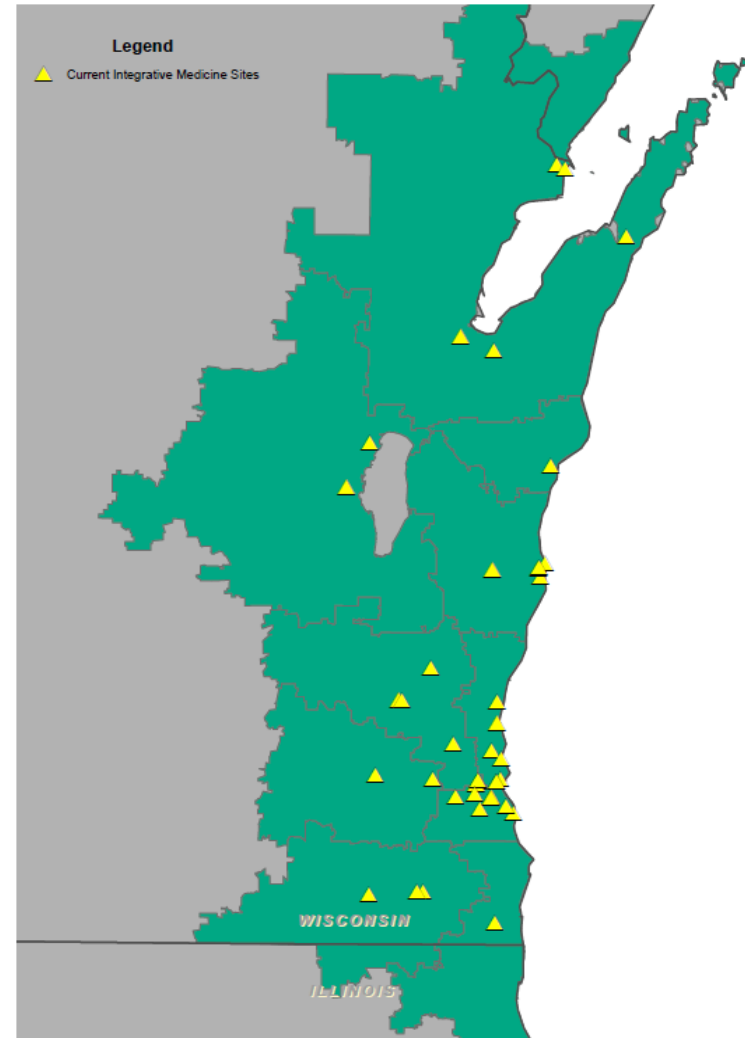
## Integrative Therapies

- Care provided by non-MD/DO/APP colleagues
  - Chiropractic
  - Massage Therapy
  - Acupuncture
  - Integrative Health Coaching
- Modalities outside of the traditional biomedical model
  - Aromatherapy/essential oils
  - Yoga
  - Tai Chi/Qi Gong
  - Craniosacral
  - Reiki
  - Guided imagery
- Competency-based training and quality standards in place

# Aurora Integrative Medicine Landscape

## Services Offered

- Physician/APP
- Acupuncture
- Massage Therapy
- Chiropractic
- Aromatherapy
- Craniosacral Therapy
- Health Coaching
- Guided Imagery
- Volunteer Reiki



# Integrative Medicine and Oncology

## Integrative Medicine Consults

Offered by some fellowship-trained physicians and APPs throughout the system

## Integrative Therapies Embedded In Oncology

### Acupuncture

Burlington, Grafton, Kenosha, St. Luke's, Racine, Germantown, Good Hope, Sinai

### Massage

Burlington, Grafton, Kenosha, St. Luke's, Racine, Summit, Germantown, Good Hope, Sinai, Sheboygan, Bay Care, Oshkosh, Two Rivers, Marinette

### Volunteer Reiki

Burlington, Grafton, Sinai, St. Luke's, Germantown, Sinai, West Allis, Bay Care, Summit





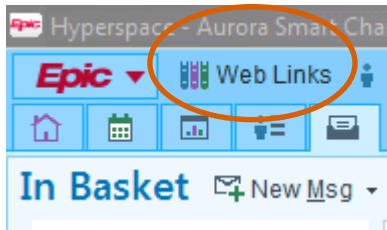
# 2017 Outcomes: Integrative Therapies at ACC

% reporting decreased symptoms after treatment

MODALITY	N	PAIN	NEUROPATHY	NAUSEA	STRESS
Acupuncture	3,175	87%	84%	91%	94%
Massage Therapy	3,800	86%	69%	68%	90%

- N=number of unique treatments, not unique patients
- Not all patients had all conditions

# Additional Resources: Chemo/Herbal Interaction Tool



## Oncology Websites

- |   |  |   |  |
|---|--|---|--|
| <ul style="list-style-type: none"><li>• <a href="#">Breast Cancer Clinical Guidelines</a></li><li>• <a href="#">Breast Complaints-Assessment and Management Pathway</a></li><li>• <a href="#">Colon Cancer Clinical Pathway</a></li><li>• <a href="#">Guidelines for Management of CNS Metastatic Disease</a></li><li>• <a href="#">Leptomeningeal Disease Pathway for Breast Cancer</a></li><li>• <a href="#">Intracranial Tumor-Lesion IP Pathway</a></li><li>• <a href="#">Intracranial Tumor-Lesion OP Pathway</a></li><li>• <a href="#">NSCLC Clinical Pathway Stage I-IIIa</a></li><li>• <a href="#">NSCLC Clinical Pathway Stage IIIB - IV</a></li><li>• <a href="#">Prostate Cancer Clinical Pathway</a></li><li>• <a href="#">Rectal Cancer Clinical Pathway</a></li></ul> | <ul style="list-style-type: none"><li>• <a href="#">Adjuvant!</a></li><li>• <a href="#">Research – Active Protocols – Aurora Cancer Care</a></li><li>• <a href="#">Aurora Pre-Printed Orders (PPO)</a></li><li>• <a href="#">Ambulatory Printed Orders</a></li><li>• <a href="#">Breast Cancer Best Practice Guidelines</a></li><li>• <a href="#">Colon Rectum Anus Cancer Best Practice Guidelines</a></li><li>• <a href="#">Foregut Cancer Best Practice Guidelines</a></li><li>• <a href="#">Pancreas Cancer Best Practice Guidelines</a></li></ul> | <ul style="list-style-type: none"><li>• <a href="#">Common Terminology Criteria for Adverse Events (CTCAE)</a></li><li>• <a href="#">CTCAE v4 Oncology Supplement Table</a></li><li>• <a href="#">Immunotherapy Adverse Event Treatment Guidelines</a></li><li>• <a href="#">My Cancer Genome</a></li><li>• <a href="#">Pneumococcal Vaccination Recommendations</a></li><li>• <a href="#">Vaccines for Adult Asplenic Patients</a></li><li>• <a href="#">Herbal/Supplements and Chemo/Biotherapy Reference</a></li></ul> | <ul style="list-style-type: none"><li>• <a href="#">Nat. Cancer Institute</a></li><li>• <a href="#">NCCN</a></li><li>• <a href="#">NCCN - Login Screen</a></li><li>• <a href="#">OA WEB</a></li><li>• <a href="#">Via Pathways</a></li></ul> |
|---|--|---|--|

## Ortho Websites

[Herbal/Supplements and Chemo/Biotherapy Reference](#)

# Integrative Medicine in Lung and Esophageal Cancer

- Nutritional supplements and herbal medicine
- Acupuncture & acupressure
- Mindfulness-based stress reduction (MBSR)



# Nutritional Supplements and Cancer

## General Considerations

- Expert guidelines from American Cancer Society, World Cancer Research Fund and American Institute for Cancer Research advise against supplements and advocate getting nutrients from food whenever possible<sup>1</sup>
- Use of self-prescribed supplements is widespread among patients with cancer (15-48%)<sup>2</sup>
- Most clinicians do not ask about specific supplement use<sup>2</sup>

<sup>1</sup>World Cancer Research Fund and American Institute for Cancer Research. Cancer survivors.  
[http://dietandcancerreport.org/cancer\\_prevention\\_recommendations/recommendation\\_cancer\\_survivors.php](http://dietandcancerreport.org/cancer_prevention_recommendations/recommendation_cancer_survivors.php). 2014

<sup>2</sup>Harvie, M. Nutritional Supplements and Cancer, ASCO Educational Book, 2014

# Antioxidants and Lung Cancer Risk

- Beta-carotene increases risk of lung cancer (RR 1.16[1.06 to 1.27])
- Selenium reduced lung cancer in populations with low selenium status (serum <106 ng/mL) but increased rates in those with higher selenium levels (serum > 125 ng/mL)
- Vitamin E increases risk of lung cancer (RR 1.03 [1.00-1.05])

Dolara P, Bigagli E, Collins A. Antioxidant vitamins and mineral supplementation, life span expansion and cancer incidence. Eur J Nutr, 2012; 51:769-781

# Omega-3 Fatty Acids in Lung Cancer

- Two-arm non-randomized phase II study
  - 46 patients with advanced NSCLC
  - 2.2 g EPA and 0.24-0.5 g DHA/day
  - Greater first-line chemo response 60% vs 35% ( $P = 0.08$ )
  - Ongoing NIH phase III trials for omega-3 use in lung cancer among other cancers (metastatic breast and childhood ALL)



Murphy RA, Mourtzakis M, Chu QS, et al. Supplementation with n-3 oil increases first-line chemotherapy efficacy in patients with advanced nonsmall cell lung cancer. *Cancer*, 2011; 117:3774-3780

# Omega-3 Fatty Acids in Esophageal Cancer

## Study Design

- 61 patients undergoing neoadjuvant chemotherapy (docetaxel, cisplatin, 5-FU) randomized to receive omega-3-rich enteral nutrition (EN) or omega-3-poor EN
- 900 mg EPA + DHA vs. 250 mg
- Primary endpoint—grade 3|4 neutropenia, secondary endpoints other chemo-related adverse events, body weight, inflammatory markers

Miyata H., Yano M, Yasuda T, Yamasaki M, Murakami K, Makino T, Nishiki K, Sugimura K, Motoori M, Shiraishi O, Mori M, Doki Y Randomized study of the clinical effects of omega-3 fatty acid-containing enteral nutrition support during neoadjuvant chemotherapy on chemotherapy-related toxicity in patients with esophageal cancer. *Nutrition* 33 (2017) 204-210

# Omega-3 Fatty Acids in Esophageal Cancer

## Outcomes

- No significant difference in incidence of leukopenia and neutropenia
- Stomatitis was significantly less frequent in omega-3-rich vs –poor group ( $P = 0.018$ )
- Diarrhea occurred relatively less frequently in omega-3-rich vs –poor group (16.1% vs 36.7%) but not significant ( $P = 0.068$ )
- Increase in ALT and AST seen significantly less frequently in the omega-3-rich vs –poor group ( $P = 0.012$  for ALT and  $P = 0.015$  for AST)

Miyata H., Yano M, Yasuda T, Yamasaki M, Murakami K, Makino T, Nishiki K, Sugimura K, Motoori M, Shiraishi O, Mori M, Doki Y  
Randomized study of the clinical effects of omega-3 fatty acid-containing enteral nutrition support during neoadjuvant chemotherapy on chemotherapy-related toxicity in patients with esophageal cancer. Nutrition 33 (2017) 204-210



# Glutamine (GLN) Supplementation for Esophagitis in Lung CA

## Study Design

- 32 patients
- 16 received prophylactic powdered GLN orally in doses of 10 g/8h (30 g/day) starting one week before radiation
- Treated with radiotherapy 2 Gy per fraction daily, 5 days per week
- Grading of esophagitis daily at end of each fraction of each treatment day until cumulative dose of 50 Gy was reached
- Acute esophageal toxicity was graded by Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer criteria
- No significant difference between GLN-supplemented and non-supplemented patients in esophageal dosimetric parameters

Gul K, Muge A, Taner A, Schri E. Oral Glutamine Supplementation Reduces Radiotherapy-induced Esophagitis in Lung Cancer Patients. *As Pac J of Ca Prev*; 16, 2015

# Glutamine (GLN) Supplementation for Esophagitis in Lung CA

## Outcomes

- Significantly more active esophagitis in the non-GLN treated group ( $P = 0.03$ )
- Cytokine levels (TNF-alpha, IL-1beta, IL-6, IL-8) measured at baseline and at 5 weeks showed significant decreases of IL-6 ( $P = 0.019$ ) and decreases in other cytokines but not statistically significant ( $P = 0.706, 0.651, 0.346$  respectively)

Gul K, Muge A, Taner A, Schri E. Oral Glutamine Supplementation Reduces Radiotherapy-induced Esophagitis in Lung Cancer Patients. *As Pac J of Ca Prev*; 16, 2015

# Wisconsin Ginseng (*Panax Quinquefolius*) for Cancer-Related Fatigue (CRF)

- Multisite, RDBPC study in cancer survivors
- 2000 mg American Ginseng daily vs placebo for 8 wks
- Primary endpoint Multidimensional Fatigue Symptom Inventory—Short Form (MFSI-SF)
- 364 participants from 40 institutions
- Statistically improved MFSI-SF score ( $P = .003$ ) at 8 weeks, but not at 4 weeks ( $P = 0.07$ )
- Greater benefit in those receiving active cancer treatment vs. those having completed treatment
- No statistically-significant toxicities reported

Barton DL, Liu H, Linquist B, Sloan JA, Nichols CR, McGinn TW, Stella PJ, Seeger GR, Sood A, Loprinzi CL. Wisconsin Ginseng (*Panax quinquefolius*) to improve cancer-related fatigue: a randomized, double-blind trial, N97C2. J Natl Cancer Inst 2013; Aug 21; 105(16):1230-8

# Acupuncture for Cancer-related Fatigue (CRF) in Lung Cancer

- 28 patients with NSCLC diagnosed with CRF
- Active acupuncture vs placebo acupuncture twice weekly for 4 weeks with 2 week follow-up
- Followed change of intensity of Brief Fatigue Inventory (BFI)

Week	Group 1 mean (SD)	Group 2 mean (SD)	P value
0	6.2 (0.2)	6.6 (0.4)	0.35
2	5.1 (0.3)	6.3 (0.2)	<0.01
4	5.2 (0.3)	6.6 (0.3)	0.005
6	4.5 (0.3)	7.1 (0.3)	<0.001

Cheng C, Chen L, Ning Z, Zhang C, Chen H, Chen Z, Zhu X, Xie J. Acupuncture for cancer-related fatigue in lung cancer patients: a randomized, double blind, placebo-controlled pilot trial. *Sup Care Ca* (2017) 25: 3801-3814

# Acupuncture for Constipation Following Lung Cancer Surgery

- Single-center RCT
- N=341 randomized to auricular acupuncture + usual vs usual care alone (psychological support, diet instruction and post-op activities guidance)
- Followed incidence of constipation and stool characteristics (Bristol Stool Scale)

Incidence of constipation **decreased** in acu group  
( $P < 0.001$ )

Stool characteristics **favorable** in acu group  
( $P = 0.047$ )



Li Y, Qi D, Gong L, Qu H, Xu B, Wen X, Li J, Xu J  
Effect of auricular point treatment combined with acupoint  
application in patients with constipation after lung cancer surgery.  
J Can Res Ther 2017; 13: 844-8

# Additional Symptoms Managed by Acupuncture in Lung Cancer

TABLE II Outcome of repeated measures presenting the effect of acupuncture on the Edmonton Symptom Assessment System score

	<i>Pre-acupuncture (mean±SD)</i>	<i>Post-acupuncture (mean±SD)</i>	<i>Z Statistic<sup>a</sup></i>	<i>p Value<sup>b</sup></i>
Pain	4.79±2.9	2.42±2.6	−3.74	<b>0.001</b>
Appetite	3.79±2.9	2.45±2.9	−2.84	<b>0.005</b>
Nausea	1.12±2.2	0.24±0.7	−2.37	<b>0.018</b>
Nervousness	3.06±2.9	2.15±2.2	−2.08	<b>0.038</b>
Well-being	3.76±2.6	2.70±2.2	−2.72	<b>0.007</b>
Shortness of breath	3.18±3.1	2.97±2.9	−0.95	0.341
Drowsiness	3.10±3.1	2.42±2.5	−1.41	0.160
Depression	2.03±2.7	1.88±2.0	−0.16	0.877
Strength	3.05±2.8	2.40±2.1	−2.01	0.064

<sup>a</sup> A negative value indicates an improvement in the symptom score.

<sup>b</sup> By a Wilcoxon signed-rank test based on positive ranks, two-tailed; bolding indicates significance (<0.05).

SD = standard deviation.

Kasymjanova G, Grossman M, Tran T, Jagoe R, Cohen V, Pepe C, Small D, Agulnik J.  
The potential role for acupuncture in treatment symptoms in patients with lung cancer: an  
Observational longitudinal study. Curr Oncol, 2013; 20: 152-57

# Mindfulness-Based Stress Reduction (MBSR)

## Lung Cancer: Study Design

- Multi-center, parallel-group, randomized controlled trial
- 8 week MBSR group-based intervention vs care as usual (CAU)
- Measured psychological distress (primary), QOL, caregiver burden, PTSD symptoms @ baseline, post-intervention, 3 month follow-up
- 31 patients and 21 partners CAU + MBSR
- 32 patients and 23 partners to CAU

Schellekens M, van den Hurk D, Prins J, Donders A, Molema J, Dekhuijzen R, van der Drift M, Speckens A. Mindfulness-based stress reduction added to care as usual for lung cancer patients and/or their partners: A multicentre randomized controlled trial. *Psycho-Onc*, 2017; 26:2118-2126

# Mindfulness-Based Stress Reduction (MBSR)

## Lung Cancer: Outcomes

- CAU + MBSR significantly less psychological distress ( $P = 0.008$ )
- Those who expressed more baseline distress benefited most from MBSR
- In patients, CAU + MBSR showed improved QOL, PTSD symptoms.
- In partners, no difference was seen in these secondary measurements between the two groups



# Complementary Therapies and Integrative Medicine in Lung Cancer

## Guidelines from ACCP (2013)

Recommendation	Integrative Modality	Strength of Recommendation
All patients should be asked about interest	General	2C
Reduce anxiety, improve mood, help sleep, improve QOL	Mind-body modalities Yoga Tai Chi	2B 2B 2B
Reduce acute or chronic pain Peripheral Neuropathy	Mind-body modalities Massage Therapy Acupuncture	2B 2B 2C
Reduce anticipatory chemo-induced N/V	Mind-body modalities Acupuncture	2B 2B
Use omega-3 fatty acids in sarcopenia	Supplement	2C

Deng G, Rausch S, Jones L, Gulati A, Kumar N, Greenlee H, Pietanza M, Cassileth B. Complementary Therapies and Integrative Medicine In Lung Cancer Diagnosis and Management of Lung Cancer, 3<sup>rd</sup> Ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. CHEST 2013; 143(5)(Suppl):e420S-e436S

# Summary

- Aurora has abundant integrative medicine and therapy resources to help with symptom management in lung and esophageal cancer patients
- Treatment modalities offered are evidence-based and well-tolerated



# Thanks!

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