Managing Radiation Therapy Side Effects with Complementary Medicine

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Over one-third of Americans use complementary and alternative medicine (CAM). The prevalence among cancer patients may even be higher. Complementary therapies may reduce possible symptom burdens caused by conventional cancer treatments. Integrating CAM therapies has become more common and more accepted in clinical oncology. However, little research is available on beneficial CAM therapies for radiation therapy patients. This article reviews potential CAM therapies that have been shown to be effective in decreasing the symptom burden related to radiation therapy treatments and includes clinical observations from CAM practitioners in a comprehensive cancer center.

Key words: *acupuncture, alternative medicine, cancer care, complementary therapies, fatigue, integrative oncology, massage, radiation side effects, radiation therapy, supportive care*

The prevalence of complementary and alternative medicine (CAM) use has increased both in the general population and among patients with cancer.[1,2] In 1990, an estimated 30% of Americans used some form of CAM, and this figure had increased to 40% by 1997.[3] A recent study indicated that approximately 67% of breast cancer survivors reported using CAM in 1998 and that by 2005, this figure had increased to 82%.[4] The prevalence of CAM use among patients with cancer ranges between 7 and 64%, with an average prevalence across adult studies of 31.4%.[5] One 2006 study showed that 54% of patients with cancer initiated at least one form of CAM therapy following their cancer diagnosis.[6] Another study done in 2005 indicated that 91% of patients with cancer reported using at least one form of CAM during their cancer treatment.[1]

Most patients with cancer hope that CAM therapies will alleviate or minimize the symptom burden of cancer and its treatments, as well as boost their immune systems.[7,8] Moreover, the incorporation of CAM therapies allows patients to become active participants in the management of their conditions, which gives them a sense of empowerment.[1,2] Toward this end, researchers and clinicians have begun to integrate CAMs into conventional treatment plans, a practice referred to as "integrative medicine." Integrative medicine is thus a collaborative approach used to treat conditions and promote wellness. Given that this article focuses on adjunct therapies that may be integrated with conventional oncology modalities, we refer to these adjunct therapies as complementary and integrative medicine (CIM) therapies.

Conventional cancer treatments in themselves may cause a variety of traumatic side effects with differing levels of severity and duration.[1] According to a recent national survey, the most common cancer treatment side effects are fatigue (80%), pain (48%), and nausea or vomiting (48%).[9] This article focuses on radiation therapy (RT), which is one of the main treatment options for cancer. More than half (approximately 60%) of patients with cancer will receive RT.[10] Even though integrating complementary therapies into cancer care has increased in use and acceptance, to date, there has been little research on CIM and RT, specifically in patients using CIM therapies during RT. A cross-sectional study found that 104 (68%) of 152 cancer patients were using some form of CIM while undergoing RT.[11] Such concurrent use may cause potential interaction and toxicity or, alternatively, may enhance the efficacy of conventional treatments.[12] Ionizing radiation may effectively kill cancer cells, but, unfortunately,

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it may also unavoidably change the surrounding normal tissues, compromising function and host defense.[13]

This article reviews potential CIM therapies that have been shown to be effective in decreasing the symptom burden related specifically to RT (Table 1 and Appendix) and includes clinical observations from CIM practitioners in a comprehensive cancer center.

Radiation-Induced Fatigue and Insomnia

Fatigue

Fatigue is the most common side effect experienced by cancer patients.[14–17] Eighty to 93% of patients undergoing RT report symptoms of fatigue.[18] Cancer-related fatigue (CRF), according to the National Comprehensive Cancer Network (NCCN), is defined as "a distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning."[14] CRF can be debilitating and can persist well after the completion of cancer treatment.[15,19] Nearly 81% of cancer survivors report pervasive fatigue.[19] Fatigue can affect physical functioning, activities of daily living, emotional well-being, and the ability to work and maintain financial stability; fatigue also may have a substantial impact on overall quality of life.[14,15,17] CRF is poorly understood, and the complexity of evaluating and effectively treating CRF has led to more research in nonpharmacologic approaches.[20,21]

Table 1. CIM Therapies for the Management of Radiation Therapy Side Effects

Symptoms	*CIM Therapy*	*Reference*
Fatigue	Exercise	14–16, 19, 22–27
	Energy conservation	14–16, 28–32
	Relaxation techniques (progressive muscle relaxation, yoga, breathing exercises)	33–35
	Energy therapies (polarity therapy, Reiki, healing touch)	36–39
Insomnia	Cognitive behavior therapy	14, 16, 44–47
	Melatonin	48
	Valerian	48–52
	Relaxation techniques (meditation, yoga, guided imagery)	53, 54, MDACC clinical observations
Dermatitis	Calendula ointment	56
	Honey	60
Psychological effects	Music therapy	64–68, MDACC clinical observations
	Relaxation techniques (progressive muscle relaxation, guided imagery, hypnosis)	33, 35, 69–78
	Massage	39, 54, 79–81, MDACC clinical observations
	Meditation	82–88
	Yoga	35, 92–95
	Healing touch	96
	Art therapy	97
	Laughter therapy	98, 99
	Acupuncture	100
	Supplements	61, 101–103
Oral mucositis	Glutamine	110–113
	Zinc	114, 115
	Traumeel S, homeopathic mouthrinse	105, 111, 113, 116, 117
	Proteolytic enzymes	118, 119
	Honey	109, 120–122
Xerostomia	Nutrition/diet modification	105, MDACC clinical guidelines
	Acupuncture	124–126
Radiation enteritis	Nutrition	128, MDACC clinical guidelines
	Probiotics	130–132

CIM = complementary and integrative medicine; MDACC = M. D. Anderson Cancer Center.

Activity enhancement is by far the most recommended nonpharmacologic strategy to manage CRF.[14,16,22] Physical activity has the potential to increase functional capacity and physical performance, thus reducing fatigue. Exercise is generally well tolerated among patients with cancer with various diagnoses throughout the continuum of care.[19] Several studies have demonstrated the efficacy of exercise in the management of CRF.[23–27] A variety of modalities from cardiovascular to resistance training have been implemented with various degrees of supervision.[27] Researchers advise that exercise programs begin at a low level of intensity, duration, and frequency. Gradual modification in these areas may be made in response to the patient's physical conditioning.[14,15,27] Programs should evaluate patients' comorbidities and modify the modalities employed accordingly. In addition to fatigue, researchers have shown that exercise may decrease emotional distress and enhance the quality of life in patients with cancer.[14,19,22]

Energy conservation is a widely advocated practice for managing cancer-related fatigue.[14,28,29] Conserving physical energy consists of advance planning and prioritizing activities. This type of activity management promotes a balance of rest and activity.[14–16] Although there are currently limited published studies on the efficacy of energy conservation among patients with cancer, this technique has produced significant improvement in fatigue levels among individuals with multiple sclerosis.[30–32] Given this effectiveness across health conditions, researchers believe that energy conservation is likely to benefit individuals suffering from radiation-induced fatigue.[14,16]

Relaxation techniques have been effective in reducing fatigue and improving sleep quality among cancer patients,[33] including those receiving radiation treatment.[34] Relaxation therapy refers to techniques that induce a state of physical and mental relaxation.[35] Decker and colleagues enrolled 63 patients undergoing RT in a randomized controlled trial to evaluate the use of relaxation therapy as an adjunct to cancer treatment.[34] The results indicated that patients in the treatment group experienced significantly less fatigue than those in the control group. Restorative yoga may also be a beneficial supportive therapy for patients with cancer. Restorative yoga or "active yoga, " as described by Danhauer and colleagues, is a form of yoga that uses props to provide a supportive environment with minimal physical effort.[36] It combines positioning, breathing, and deep-relaxation techniques and may significantly decrease CRF.

Energy therapy is a discipline of complementary medicine based on the theory that illness is a result of an energy imbalance. Veritable energy is measurable energy, and putative energy (biofields) is energy that is within and surrounds living organisms. The goal of energy therapies is to restore harmony to the individual and promote self-healing.[37] A variety of modalities exist, including polarity therapy, Reiki, and healing touch. These three therapies use gentle, nonmanipulative human touch, or placement of hands above the body, and have the fundamental goal of restoring harmony and balance by freeing the passage of "life energy" (also known as prana or qi) through the transference of energy by a trained practioner.[38–40] Although the following studies are limited by sample size, they report significant findings and should be seen as a catalyst for future research into energy therapy and CRF. A pilot study of 15 women with breast cancer suggested that polarity therapy may significantly improve radiation-induced fatigue, as well as health-related quality of life.[38] The findings indicated that 80% of the women who received treatment reported a decrease in CRF. In another study,16 patients with cancer found that Reiki reduced their levels of fatigue and improved their quality of life.[40] Healing touch may lower blood pressure, heart, and respiratory rates, thereby inducing a state of relaxation.[39] A randomized, crossover study of 230 chemotherapy patients showed that healing touch had a significant effect on CRF.[39] Additionally, participants described the treatment sessions as peaceful and energizing.

Insomnia

Quality of sleep is a major indicator of well-being. Sleep disturbances and lack of quality sleep occur in 30 to 75% of patients with cancer.[14,41,42] Patients receiving radiation tend to report sleep disturbances closer to the completion of their treatment.[43] Insomnia is the most prevalent type of sleep disturbance among cancer patients.[44] Insomnia refers to difficulty initiating or maintaining sleep and may or may not be associated with fatigue. Patients with cancer experiencing insomnia typically have a high metabolic rate, a high core temperature, and a heightened arousal (Mary Rose, The University of Texas M. D. Anderson Sleep Center, personal communication, 2008). Up to 50% of patients with cancer have reported experiencing insomnia.[45] It is important to note that the prevalence of fatigue and insomnia differs by cancer type. Patients with breast cancer, in particular, have a higher rate of insomnia, possibly owing to hot flashes induced by hormonal ablation therapy.[46]

Cognitive behavior therapy (CBT) has frequently been used to manage insomnia.[14,16,45,47–49] Savard and colleagues enrolled 57 women into an 8-week efficacy trial.[50] Patients receiving stimulus control, sleep restriction, cognitive therapy, sleep

hygiene, sleep journals, and fatigue management techniques reported significantly better subjective sleep indices, decreased use of sleep-related medications, lower levels of depression and anxiety, and a superior quality of life than those in the control arm. A similar study evaluated the efficacy of stimulus control, sleep restriction therapy, and sleep education and hygiene on fatigue, mood, and quality of life in 72 breast cancer survivors.[46] Those women who received CBT had significant improvements in fatigue, trait anxiety, depression, and quality of life. A larger trial of 150 cancer survivors reported parallel findings.[51] CBT was associated with mean reductions in wakefulness, increased sleep onset latency (amount of time to fall asleep), and decreased wake time after sleep onset. The results also indicated that CBT was associated with a significant effect on anxiety, depression, and daytime fatigue.

A number of natural products have been used to treat sleep disturbances, including valerian root.[52] Valerian root is commonly used to treat insomnia. The current literature reports mixed findings on valerian root's effectiveness on sleep quality and sleep latency.[52–57] Unlike most pharmaceutical-grade sedatives, valerian root seems to have no significant residual effects (fatigue, grogginess).[58]

Practitioners at The University of Texas M. D. Anderson Cancer Center have experienced similar success in managing fatigue and sleep disturbances with the above interventions. Based on their observations and research, effective interventions for fatigue and insomnia may be expanded to include Tibetan yoga,[59] meditation,[60] and expressive writing.[61] These practices typically focus on clearing the mind and creating a calm, relaxing environment. Mind-body therapies may be beneficial for patients experiencing poor sleep quality.[62,63]

Dermatitis

Approximately 80% of patients treated with RT experience some form of skin irritation, ranging from hyperpigmentation to ulceration.[64] These conditions may lead to pain, discomfort, itching, burning, or even permanent scarring, which all have the potential to affect a patient's daily activities and negatively affect quality of life.[64] Patients with radiation-induced dermatitis are typically instructed to keep the irradiated skin clean, dry, and free of skin irritants.[65,66] A moist wound-healing environment is encouraged through the application of moisturizing topical preparations.[66] A review of the literature indicated that the majority of the best supportive care treatments had conflicting outcomes. Aloe vera gel, sucralfate, and corticosteroid creams all had mixed reviews on their level of effectiveness.[64,66–68]

Calendula ointment is derived from *Calendula officinalis*, which is commonly referred to as the marigold and has historically been used as a wound-healing agent.[65] A randomized controlled trial of 254 patients with breast cancer found that calendula cream, when compared with trolamine cream, was highly effective in reducing the occurrence of acute dermatitis (grade 2 or higher) and provided relief from associated pain. Trolamine is a nonsteroidal topical agent commonly used for wound healing, first- and second-degree burns, and radiation dermatitis. Honey is another historical nutraceutical.[69] Honey's effectiveness on radiation-induced dermatitis has not been extensively researched. However, a small prospective randomized controlled trial of cancer patients with grade 3 RT-induced dermatitis reported that patients treated with a honey gauze/bandage (HoneySoft, 7 Seven's Ltd, Ilisia, Athens, Greece) had closure of skin toxicity and complete healing faster than the control group, which was treated with paraffin gauze.[70]

Psychological Effects

Psychological conditions affecting patients with cancer vary by patient, diagnosis, and treatment. These conditions may include anxiety, depression, mood disturbances, distress, and emotional challenges. Patients are likely to experience fear of death, pain, disability, and disruption of daily life.[71] Depressive and adjustment disorders may occur at any stage of the disease process (decision making, treatment, outcomes, and through survivorship).

Sehlen and colleagues investigated the psychosocial stress of 265 patients with cancer during and after RT.[72] Physical efficiency rated the highest stress factor subscale and remained constant throughout the assessment period. Pain and information scales significantly increased over the assessment points. Anxiety was also significant but was lower following treatment than before and 6 weeks after treatment. All patients reported high stress levels regarding (1) fear of disease progression, (2) not being able to care for their family in the future, (3) helplessness, and (4) frequent interruption of their activity.[72]

Karasawa and colleagues found that RT anxiety was related to the following concerns: acute adverse effects (60.6%), treatment outcome (41.3%), RT use indicating an incurable tumor (40.4%), radiation exposure (26.6%), excess irradiation (22%), equipment and treatment room (16.5%), isolation (11.9%), and late adverse effects (9.2%).[73]

Music therapy is an effective tool for coping.[74] It may be passive (listening, lyric discussion) or active (song writing, performing). Music therapy has the capacity to alleviate stress and anxiety, inducing a state of relaxation that leads to lower blood pressure, a reduced heart rate, and other therapeutic effects. Music therapy is also a great tool for distraction

and may also be recommended for socialization and self-expression.[75] Although, currently, research conferring the efficacy of music therapy for RT-induced anxiety is limited, music therapy has been shown to be beneficial for patients undergoing chemotherapy.[76] Additionally, Clark and colleagues found that patients undergoing RT with higher levels of anxiety respond more favorably than patients with lower baseline anxiety.[77] Smith and colleagues observed that music had a greater effect in the planning process and the early stage of radiation treatments as anxiety in both research arms declined with the familiarity of treatment.[78] Music therapists at M. D. Anderson believe that the vehicle in which the therapy is delivered is critical. Research should consider music selection in relation to patient mood (tempo, tone), cultural or personal preference, and listening equipment or environment (sound quality, loud medical devices, volume).

In addition to improving fatigue and sleep quality, relaxation techniques can effectively decrease a patient's anxiety levels.[34,36] Luebbert and colleagues conducted a meta-analysis of 15 studies and found that relaxation training significantly ($p < .05$) improved emotional adjustment—specifically depression, hostility, tension, anxiety, and mood.[79] Progressive muscle relaxation (PMR) is a process of deliberate concentration and sensory awareness to systematically relax individual muscle groups.[80,81] Decker and colleagues reported significant declines in tension ($p = .001$), depression ($p = .01$), and anger ($p = .01$) following PMR therapy.[34] Likewise, Bridge and colleagues indicated a similar relaxation technique that positively affected ($p < .05$) mood state among patients with breast cancer in an outpatient RT department.[80]

PMR is often coupled with guided imagery. Guided imagery may positively affect anxiety and depression among cancer patients.[82,83] Kolcaba and Fox found that guided imagery was significantly ($p < .05$) effective for enhancing comfort for women with early-stage breast cancer who were undergoing RT, and the intervention had a greater effect in the early stages of treatment.[84] Hypnosis induces a deep state of relaxation and heightened concentration. In this state of consciousness, the unconscious mind is more accessible, and the patient is more amenable to suggestions.[85,86] Although research on hypnotic interventions in oncology has recently increased, the research on hypnosis specific to RT-induced anxiety is limited.[87] However, one study found that although hypnosis had no significant effect on anxiety, the patients undergoing RT reported significant improvements in their mental and overall well-being.[86]

Massage may improve physical and psychological well-being in cancer patients.[88–91] Therapeutic massage increases circulation, decreases muscle tension, and stimulates venous and lymphatic drainage. Post-White and colleagues reported that therapeutic massage lowered blood pressure, respiratory rate, heart rate, and anxiety in their randomized, crossover trial of 230 patients with cancer.[39] In the largest massage study among patients with cancer to date, Cassileth and Vickers found that of the 1,290 patients, 400 (31%) presented with symptoms of anxiety, which was also the most common symptom.[89] After the patients received massage therapy, there was nearly a 60% improvement in anxiety and a 48.9% improvement in depression. Massage therapists at M. D. Anderson have observed similar symptom relief. Conventional cancer treatments may be invasive, isolating, and physically uncomfortable. Relaxation massages may provide an opportunity for "talk, time, and touch." Consequently, the therapists believe that the environment (level of comfort, tone of voice, softness of touch) in which the massage is given is noteworthy. Massage may also help ease pain caused by awkward positioning during radiation treatment, and the pain may be an adjunct or contributing factor to anxiety and/or depression. In addition to psychological and physical benefits, massage may influence treatment compliance, family interaction, and the patient's overall treatment experience.[91]

Meditation is a type of cognitive therapy involving the control or modification of thoughts and awareness, which can affect emotions and biologic processes.[74] Autogenic training is a type of meditation that consists of six mental exercises that evoke warmth, heaviness, and relaxation of the body. Autogenic training may improve anxiety and depression.[92] Ott described mindfulness meditation (also known as vipassana or insight meditation) as "a conscious discipline of intentional self-regulation."[93] The intent of mindfulness meditation is to redirect or focus your mind on the present moment and to experience each moment without judgment or critical thinking—to merely be present. Mindfulness-based stress reduction (MBSR) combines mindfulness meditation and hatha yoga. MBSR was developed in 1979 by Jon Kabat-Zinn and colleagues at the University of Massachusetts Medical Center. MBSR has been practiced in numerous clinical settings, including supportive cancer care.[93–98] Tai chi and qi gong, types of moving meditation, may also be beneficial for reducing psychological distress.[99–101]

Yoga is a type of mind-body practice that originated in India. Yoga is a gentle exercise, combining physical postures, breathing, and meditation. Therapeutic benefits include increased muscle strength, flexibility, range of motion, and energy. Yoga may also decrease pain and improve sleep quality, immune function, and other physiologic parameters (ie, blood pressure and heart rate).[102] Danhauer and colleagues

reported significant ($p \leq .05$) improvement in depression, negative affect, state anxiety, mental health, and overall quality of life following a restorative yoga intervention.[36] Likewise, yoga effectively reduced anxiety, depression, and perceived stress in a randomized trial of patients with breast cancer undergoing RT.[103] Similar studies have indicated that yoga may positively affect mood among patients with breast cancer.[104–107]

Healing touch,[108] art therapy,[109] laughter therapy,[110,111] and acupuncture[112] may also improve anxiety, depression, and other distress symptoms. Additionally, a number of medicinal herbs and supplements have been studied in patients with anxiety and depression. Kava and St. John's wort have been shown to be effective treatments for anxiety and depression, respectively, but owing to interactions and possible side effects, these supplements are cautiously recommended.[71,113] There are mixed findings on B vitamins, sage, SAM-e, tryptophan, and 5-hydroxytryptamine.[113–115]

The psychological side effects of RT are unique to the patient; therefore, treatments and/or interventions of those conditions must be adaptable to the patient's needs. CIM therapies are relatively inexpensive and cover a large spectrum of modalities, appealing to a wide range of personal interests. CIM interventions may effectively manage the psychological side effects associated with RT. Additionally, CIM programs present opportunities to connect with patients and enhance trust.[116]

Oral Complications

Radiation treatment in the head and neck region may lead to a dry mouth, painful swallowing, inflammation of the oral cavity, nausea, and pain.[117] Patients with reduced salvia production (xerostomia) should add sauces and oils to increase the moisture content of their food. Clinical dietitians at M. D. Anderson suggest blended and/or pureed foods, soups, and stews to ease swallowing. Thick, creamy, nutrient-rich (protein/calorie) liquids are recommended for patients with esophagitis. Foods rough in texture or eaten at extreme temperatures may exacerbate oral injury caused by radiation. Standard tips for controlling nausea include consuming frequent small meals and avoidance of food odors. According to the National Cancer Institute, capsaicin, the active ingredient in hot peppers (cayenne and red pepper), may help alleviate oral pain.[118] To minimize the risk of oral infection, patients should cleanse their palate by swishing with a water or baking soda rinse before and after eating. Adequate hydration (8 to 10 cups of clear fluids a day) and a stable weight should be maintained throughout the course of radiation treatment. Proper nutrition aids in the healing process[118] and constant body measurements are critical to the patient's treatments (radiation dosimetry and treatment positioning).

Oral Mucositis

Radiation-induced oral mucositis (OM) is a common side effect (average incidence of 80%) among patients with head and neck cancer.[119] OM or stomatitis is the inflammation and ulceration of the mucosal lining in the oral cavity, typically associated with pain and discomfort. Basic oral hygiene is critical.[118,120] OM may disrupt the function and integrity of the mouth,[121] impair the patient's ability to eat and swallow, interfere with the RT schedule, and increase the likelihood of hospitalization.[122] Unfortunately, to date, there is no standard effective treatment to prevent radiation-induced mucositis.[123] Many nonpharmacologic products have been investigated as treatment options for OM, from honey[124] and a simple baking soda wash[118] to intravenous glutamine.[125]

Glutamine may effectively minimize the severity and effects of OM.[125–128] A randomized trial of 17 patients with head and neck cancer evaluated the influence of glutamine using a 16 g wash solution. The results indicated a decreased duration of OM at all grades, as well as a decreased severity of the average maximum grade of objective OM ($p = .0058$).[127] Conversely, glutamine supplementation may potentially increase the risk of disease recurrence in bone marrow transplant (BMT) patients.[120] The NCCN recommends systematic glutamine not be used for the prevention of gastrointestinal mucositis.[120]

Zinc has also been used to treat and prevent OM. Studies found that zinc supplementation may delay the development and degree and severity of OM.[129,130] Zinc may also alleviate dermatitis.[129] Doses range from 25 mg given three times daily[129] to 50 mg three times daily.[130]

A homeopathic mouthrinse preparation, Traumeel S, also seems to effectively alleviate OM.[118,126,128,131] The mixture contains extracts from *Arnica montana* and other plants and minerals. Oberbaum and colleagues conducted a randomized controlled trial of 32 patients with BMT who were ages 3 to 25 years.[131] Whereas the overall incidence of OM was approximately 40% (80% for RT), the incidence among the BMT population reached 95%. Thirty-three percent of the treatment group did not developed OM compared with 7% of the placebo group, and the symptoms worsened in 93% of placebo group versus only 47% in the Traumeel group. Currently, there are no publications evaluating the efficacy of Traumeel S for radiation-induced mucositis, but an active phase I trial (NCT00584597) is under way at Oklahoma University Cancer Center.[132]

Honey is an ancient nutraceutical that may exhibit antiinflammatory and antibacterial properties.[133] Topical application of honey may positively affect radiation mucositis.[124,133–135] Biswal and colleagues assigned 20 patients ($n = 40$) to receive 20 mL of pure honey 15 minutes before, 15 minutes after, and 6 hours following RT.[124] There was a significant reduction in severe mucositis. Additionally, patients in the research arm showed no change or had a positive weight gain. This study was replicated by Motallebnejad and colleagues and Rashad and colleagues, who reported similar findings.[134,135]

Xerostomia

Xerostomia is dry mouth resulting from the reduction in or absence of salivary production and can result in difficulty eating, swallowing, and trouble speaking. Xerostomia may also increase susceptibility to infections, dental caries, gum disease, and tooth decay. Patients may experience changes in taste sensory (dysgeusia), increased thirst, and localized tongue pain (glossodynia). Salivary flow may decrease by approximately 50% during the first week of RT and upwards of 80% by the seventh week of treatment.[117] Acute radiation-induced xerostomia is associated with inflammatory reaction. Delayed or late radiation-induced xerostomia, which can occur up to 1 year after treatment, results from fibrosis of the salivary gland and is typically permanent.[136] Xerostomia is an expected complication of RT, affecting up to 100% of patients with head and neck cancer.[118,137]

Acupuncture has been readily cited as an effective treatment for radiation-induced xerostomia.[138] Currently, the recommended pharmacologic treatment is pilocarpine. As cited by Johnstone, the success rate from pilocarpine treatment ranges from 31 to 54%.[139] A small investigation offered acupuncture to patients with head and neck cancer who were experiencing xerostomia and could not find relief following pilocarpine therapy. The study results reported subjective improvement in salivation following acupuncture for all but two patients.[139] An additional study showed improvements in salivary flow rates for up to 6 months following a course of 24 acupuncture treatments.[140] Acupuncture and acupuncture-like stimulation[141] may induce saliva production[142] and improve the overall quality of life of patients with radiation-induced xerostomia.[143,144]

Gastrointestinal Complications

Acute radiation injury is a significant side effect of abdominal and pelvic irradiation. The intestinal mucosa, especially the small intestine, is extremely radiosensitive. Radiation enteritis (RE) and radiation-induced diarrhea (RID) are common side effects. Almost all patients receiving radiation to this region will experience some degree of RE.[145] RE is a functional disorder of the small intestine caused by radiation exposure. Diarrhea is described as an increase in stool liquidity and frequency (more than three unformed stools) during a 24-hour period.[145] RID can occur at any time in the treatment process. RID may lead to dehydration, electrolyte imbalance, and malabsorption of nutrients and may also interfere with treatment sequence and affect a patient's overall quality of life.[146] Anyone receiving radiation in the abdominal or pelvic regions is at risk. This risk may include patients receiving radiation for cancers of the prostate, bladder, testes, uterus, cervix, rectum, and anus.[146]

Dietary modifications are essential. Patients must rehydrate. The National Cancer Institute suggests 8 to 10 cups of clear fluids a day.[145] Likewise, foods high in sodium and potassium may be incorporated into a patient's nutritional plan to ensure replenishment of electrolytes if diarrhea or emeses are frequent. Foods to avoid include foods high in fiber, dairy products, caffeinated foods or drinks, spicy foods, and fried or greasy foods. Warm or hot fluids may also increase symptoms or exacerbate diarrhea. Gassy foods should be avoided as well. In addition to affecting bowel movements, gas may change the size of the colon, thereby repositioning the prostate and/or other organs of treatment interest. As previously mentioned, patients should be encouraged to maintain a stable weight throughout their radiation treatment period.

Radiation may disturb the colonization resistance of the indigenous flora; this disruption may lead to RE.[147] A probiotic is a symbiotic microorganism(s) that protects and contributes to the health and balance of its host, favorably altering the microflora of the intestinal tract. Delia and colleagues effectively used a probiotic preparation, VSL#3, to treat RE.[147] RT patients with sigmoid, rectal, or cervical cancer receiving the probiotic had diarrhea significantly less often, and the diarrhea was less severe; consequently, they waited longer to use the antidiarrhea medication.[147] Additional probiotic products have significantly improved fecal consistency.[148,149]

Discussion

Patients diagnosed with cancer are susceptible to the psychological and physiologic effects associated with their disease and its conventional treatments, namely RT. Many of these side effects pose a substantial threat to a patient's quality of life. Complementary therapies may decrease the symptom burden caused by RT while effectively treating the whole person. CIM therapies, as described in this article, are relatively inexpensive and convenient. Most programs offered at

M. D. Anderson are complementary for patients and caregivers. CIM therapies not only reduce the severity of radiation side effects but may also potentially lessen the need for palliative medication. CIM programs also provide an opportunity to empower patients by giving them a means to actively participate in their healing process.

Integrative oncology is an evolving field. It encompasses a multitude of therapeutic disciplines but also describes a philosophy of medical practice.[150] The field has substantially grown in the past decade.[151] In 1998, the National Cancer Institute created the Office of Cancer Complementary and Alternative Medicine (OCCAM) as a direct result of increased interest.[152] The Society for Integrative Oncology was established in 2003 as a scientific forum for complementary therapies in cancer care.[153] Additionally, medical schools have begun incorporating complementary medicine into their school curriculum, and the nation's leading cancer centers (the 2008 top 5 US cancer institutes as rated by *US News & World Report*: M. D. Anderson, Memorial Sloan–Kettering Cancer Centre, Johns Hopkins University, Mayo Clinic, and Dana–Farber Cancer Institute[154]) now have designated integrative oncology programs.

CIM treatments span the spectrum from biologic therapies to mind-body approaches. As with conventional medicine, what works for one patient may not be effective for another. CIM emphasizes individualized treatments. Clinical CIM research, as it applies to cancer, is still relatively in its infancy. Despite its historical use, only a small number of modalities have been evaluated using modern research techniques.[155] CIM models differ from the reductionist, mechanistic models of conventional medicine because they focus on whole systems and synergistic interactions—a holistic approach.[156] Challenges for integrative oncology include efficacy and safety, prioritizing research, medical pluralism, education, communication, and appropriate regulation and delivery.[155–157] Furthermore, additional research should evaluate the risks and benefits of CIM therapies at different stages of the cancer continuum (ie, supplements during RT versus after RT).

Complementary medicine is evidence based and seeks to enhance the effectiveness of conventional treatments. Patients should receive information and access to all health systems. As research in the field of integrative oncology continues to grow, the focus remains constant—to improve outcomes for patients with cancer.

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Appendix. Radiation-Induced Adverse Events: Evaluation of Evidence

FATIGUE

Exercise/activity enhancement

Exercise is recommended by the National Cancer Institute,[10] the National Comprehensive Cancer Network,[14] and the Oncology Nursing Society[16] as effective management for CRF. Numerous systematic reviews and meta-analyses support the benefits of moderate exercise at all phases of cancer treatment.[14–16,18,19,21–28]

Energy conservation

A large ($N = 296$) multisite, randomized clinical trial demonstrated that energy conservation and activity management have a significant effect on CRF.[29] A few studies evaluated the benefits of energy conservation among the MS population.[31,32] These studies, in addition to the large trial on CRF[29] and practice guidelines,[14] identify energy conservation as a likely effective intervention for patients with cancer. However, more clinical research needs to be conducted specific to CRF.

Relaxation

Two RCTs[33,34] and one comparative pilot study[36] indicated that muscle relaxation and modified breathing to induce a state of relaxation significantly reduce fatigue among patients with cancer. Relaxation therapies may be effective for CRF.

Energy therapies

Results from two small ($N = 15$, $N = 16$)[38,40] pilot studies and a larger ($N = 230$) randomized, crossover trial[39] suggest that energy therapies may likely be an effective intervention for CRF. More research needs to be conducted to better understand the underlying mechanisms.

INSOMNIA

Cognitive behavior therapy

A number of RCTs concluded that CBT is an effective intervention to optimize sleep quality for cancer patients.[46,48–51] CBT is identified as a standard of care in the clinical guideline for the evaluation and management of chronic insomnia in adults established by the American Academy of Sleep Medicine.[47]

Valerian root

Meta-analysis and systematic reviews indicate mixed findings concerning the effectiveness of valerian root to improve sleep quality.[54,56,57] The complexity of small sample sizes, various sources, and combinations of valerian investigated in clinical trials makes it difficult to adequately evaluate its effectiveness. More uniform research is needed to make a conclusive evaluation.

Relaxation

Many different techniques are used for relaxation.[59–61] Practices with the intent to clear a patient's mind may be effective interventions for patients experiencing insomnia. More research needs to be conducted specific to each technique.

DERMATITIS

Calendula ointment

A large ($N = 254$) phase III RCT of patients with breast cancer found calendula cream to be highly effective in reducing radiation-induced dermatitis.[65] However, no additional publications were found. More research needs to be conducted across cancer populations and levels of risk.[158] There is not enough evidence to make a conclusive evaluation.

Honey

Honey has been historically used for wound healing[69] and may be applicable to oncology patients.[69,133] A small ($N = 24$) RCT reported that honey helped alleviate radiation-induced dermatitis.[70] There is not enough evidence, specific to radiation-induced dermatitis, to make a conclusive evaluation; more research needs to be conducted.

PSYCHOLOGICAL EFFECTS

Music therapy

Music therapy may be effective as research shows that it may alleviate anxiety[76,78] and reduce emotional distress.[77] More research needs to be conducted specific to oncology and include diverse patient populations.

Relaxation techniques

Multiple clinical studies and meta-analyses suggest that relaxation techniques positively affect anxiety and other adverse psychological changes related to RT. Relaxation is likely effective for the psychological effects on patients undergoing RT.

Guided imagery and hypnosis

Four RCTs illustrate the efficacy of guided imagery and/or hypnosis for the reduction of anxiety among cancer patients. Guided imagery and hypnosis may be effective interventions for anxiety related to RT.

Massage

RCTs[39,88,89,159] and reviews[90,91] indicate that massage is likely effective on psychological effects associated with cancer treatment.

Meditation

Mindfulness mediation is commonly used in supportive care to manage psychological adjustments of patients with chronic illness.[94–98,160] Meditation and other mind-body therapies may be effective for the psychological effects associated with RT. More research is needed to better understand the benefits of the various forms of meditation.

Yoga

Six clinical trials reported that yoga positively affected psychological stress on patients with cancer.[36,103–107] Yoga is likely an effective therapy for managing the psychological changes associated with RT. Research was limited to the breast cancer population. Future research should include other cancer populations.

Supplements

Potential interactions, safety concerns, and mixed clinical results suggest that the incorporation of supplements should be personalized to the patient's specific treatment needs and include the close examination of concurrent use with other pharmaceutical and nonpharmaceutical medicine(s).[71,113–115] Supplements may be effective for the psychological effects associated with RT.

ORAL COMPLICATIONS

Glutamine

Two small ($N = 29$ and $N = 17$) RCTs found beneficial results from the use of glutamine on oral mucositis.[125,127] More research needs to be conducted specific to RT oral mucositis and the type of supplement administration. There is not enough specific evidence to make a conclusive evaluation.

Zinc

The positive results of two RCTs suggest that zinc may be an effective supplement for radiation-induced mucositis.[129,130] The National Cancer Institute references zinc as a helpful supplement for radiation-induced mucositis, dysgeusia, and dermatitis.[118]

Traumeel S (homeopathic mouthrinse)

At this time, there are no publications evaluating the efficacy of Traumeel S for radiation-induced mucositis. A small ($N = 22$) RCT of BMT patients resulted in a significant reduction in the development and mucositis symptoms.[131] There is not enough evidence to make a conclusive evaluation.

Honey

Honey has been historically used for wound healing[69] and may be applicable to oncology patients.[69,133] Three RCTs demonstrated that the prophylactic use of honey reduced the severity of mucositis among cancer patients.[124,134,135] Honey may be effective for treating radiation-induced mucositis.

Nutrition/diet modification

An RCT of 75 patients undergoing RT experienced better outcomes and fewer RT-related comorbidities following a nutritional intervention.[161] Nutrition counseling/modification is recommended by the National Cancer Institute to prevent and manage the oral side effects of radiation to the head and neck region.[118]

Acupuncture

Numerous clinical trials have identified acupuncture as a likely beneficial therapy for effectively treating radiation-induced xerostomia.[71,137,139–141,143,144] Larger clinical studies need to replicate the findings of these smaller referenced trials and identify standard treatment protocol.

GASTROINTESTINAL COMPLICATIONS

Nutrition

Nutrition counseling/modification is recommended by the National Cancer Institute to prevent and manage the gastrointestinal side effects of radiation to the abdominal and pelvic region.[10]

Probiotics

Three large ($N = 490$, 206, and 85, respectively) double-blinded, RCTs illustrated the effectiveness of probiotics for the treatment of radiation enteritis.[147–149] Probiotics are likely effective for the management of RT-related gastrointestinal side effects.

BMT = bone marrow transplant; CBT = cognitive behavior therapy; CRF = cancer-related fatigue; MS = multiple sclerosis; RCT = randomized controlled trial; RT = radiation therapy.