

Integrative Medicine for Cancer Patients

Diagnostic and therapeutic care pathways

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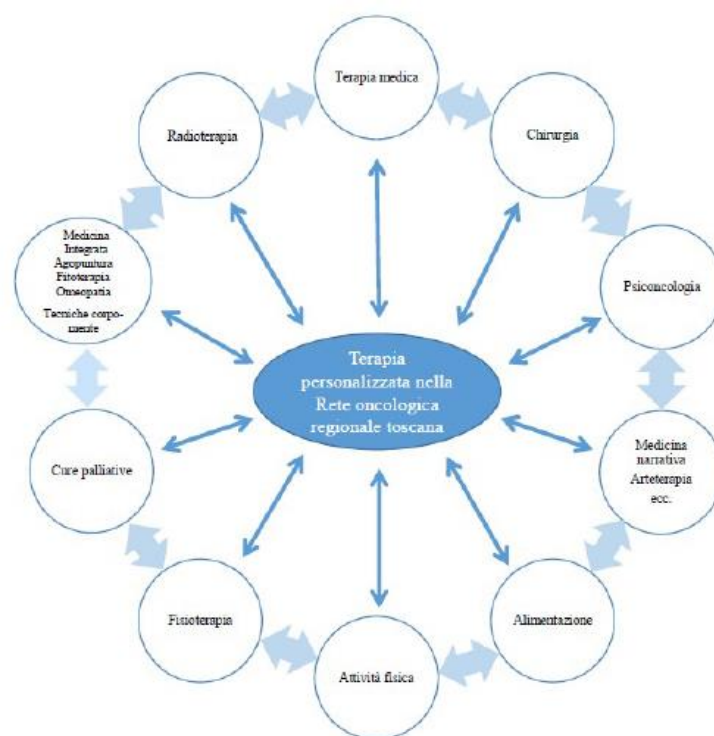
1. Integrative Medicine in the Tuscan Cancer Network

At the international level, the term “Integrative Oncology” refers to evidence-based cancer treatments that are implemented within a multidisciplinary and tailored framework, which, in turn, combines conventional cancer treatments with complementary treatments and healthy lifestyles. The main purpose is to strengthen patients’ empowerment and their proactive role, as well as to improve their health and quality of life while reducing the side effects of cancer therapy. The decision to combine the conventional therapies provided by Oncology Departments with Integrative Medicine is a significant element of innovation in healthcare systems. Such a holistic model has already been implemented at international-level cancer centers, such as the Memorial Sloan Kettering Cancer Center in New York. Noteworthy, it has also been implemented in the Tuscan Regional Cancer Network and its Coordinating Body. More in detail, the Integrative Medicine clinics located in the Tuscan territory refer to such organ with the purpose of ensuring proper quality and safety standards, alongside an interdisciplinary and multi-professional approach.

Since the late '90s, Integrative Medicine therapies (including acupuncture, phytotherapy and homeopathy) have been progressively implemented into the Tuscan Health Service (THS) by means of Regional Health Plans, since their inclusion in the Regional Law 40/2005.

Indeed, oncology has been identified as a priority field of intervention for Integrative Medicine (Regional Government Resolution n. 1224/2016, n. 642/2019). In line with the Tuscan Cancer Institute (ITT – now ISPRO) and with the Guidelines of the Italian Association of Medical Oncology, specific integrative therapies with documented efficacy and safety have been included within cancer care protocols, thus contributing to the multidisciplinary approach to cancer.

Figure 1. The inter-relations among healthcare professionals in the Tuscan Regional Cancer Network.



More in detail, the fundamental steps leading to a multidisciplinary patient-centered approach in the field of oncology are:

- Regional Government Resolution n.418/2015: "Integration of Complementary Medicines in the Oncology Network of the Tuscan Cancer Institute", which point at Integrative Medicine as a significant element of innovation within healthcare systems. In fact, integrative therapies are safe, effective, with few side effects and can help to improve the quality of life of people who use them. Furthermore, the Regional Government Resolution re-confirms the importance of a multidisciplinary approach to cancer including Integrative Medicine practices with sufficient levels of evidence, thus activating synergies between the Tuscan Network of Cancer Departments of ISPRO and public Integrative Medicine services.
- The Executive Decree n.3823/2019 approving the document: "Diagnostic, therapeutic and care paths" (DTCP) for breast cancer. In particular, Annex B highlights how Integrative Medicine helps to treat the side effects of conventional cancer therapies.
- The multi-year policy document of ISPRO (Regional Government Resolution n. 634/2019), which acknowledges the regional path for the implementation of specific Integrative therapies (i.e., acupuncture, phytotherapy and homeopathy) within the Network of Cancer Departments, in order to reduce the possible side effects of conventional cancer therapies. It is expected that CORD and A.I.U.T.O. Points will offer such activity, with a view to homogeneity and equality of access for all patients.
- The Working Group: "Integration of Complementary Medicines in the Cancer Network" (Decree n. 11285/2020; General Director Decree ISPRO 15.04.21) which ensures the monitoring, implementation and dissemination of Integrative Medicine in the field of oncology.

As far as the evaluation of the effectiveness of integrative therapies is concerned, Tuscany, as an associate partner of the Joint Action European Partnership Against Cancer - EPAAC (2011-2014) of the European Commission, has carried out a critical review of the literature; its purpose was to assess the effectiveness of acupuncture, traditional Chinese medicine, phytotherapy, homeopathy, homotoxicology and anthroposophic medicine in treating the side effects of conventional cancer therapies and improving quality of life. The results are reported on the EPAAC website (http://www.epaac.eu/images/END/Final_Deliverables/D5_Complementary_and_alternative_medicine_CAM_in_cancer_care_development_and_opportunities_of_integrative_oncology.pdf).

Given this scenario, a review was published in the book "Complementary Medicines for the cancer patient" (2015) and distributed to Tuscan healthcare professionals.

In order to improve communication and information on Integrative Oncology practices within the Tuscan Health Service, on behalf of ISPRO and the Tuscan Regional Centre for Integrative Medicine, Tuscany published the brochure: "Integrative Medicine for cancer patients" in 2018. The brochure, which has been distributed to all oncological facilities of the Tuscan Healthcare Service, provides information on the opportunities of Integrative Medicine application in oncology, on the possible interactions between conventional anticancer drugs, integrative therapies and correct lifestyles. Moreover, the brochure also invites patients to contact the Public Healthcare Service, warning them against resorting to unqualified personnel or to do-it-yourself approaches, thus avoiding therapies of proven effectiveness. The brochure, therefore, invites patients to turn to their General Practitioner, their reference Oncologist and/or the Integrative Medicine experts of the Tuscan Health

Service.

In June 2019, a Memorandum of Understanding was signed between the ISPRO, the Local Health Authority -Central Tuscany- and the Memorial Sloan Kettering Cancer Center New York (MSKCC) aiming at developing joint research and training programs on Integrative Medicine.

2. Epidemiological Data

In the United States, approximately 38% of adults and 12% of children use some form of Complementary and/or Integrative therapies (1). More in detail, a European multicenter study (2) reported that 32.2% of people are treated with complementary therapies, with percentages ranging from 5% to 74.8%. Furthermore, an estimated 40% of cancer patients in Europe use these therapies in addition to conventional cancer therapies. According to a study conducted on 4,349 French patients 2 years after cancer diagnosis, 16.4% used complementary medicine, and especially homeopathy (64.0%), acupuncture (22.1%), osteopathy (15.1%), phytotherapy (8.1%), and nutrition (7.3%). The choice of such treatments is associated with younger age, female sex, and a higher education level (3). The same predictive factors have been confirmed by a Swedish study (n. pts: 1297) according to which 26% cancer patients resorted to Integrative Medicine services after cancer diagnosis in order to improve their psychophysical well-being and their ability to fight the disease (4). A survey (5) on 633 patients treated at three Strasbourg cancer centers reported a complementary use of homeopathy of 30.7%, mainly to reduce the side effects of conventional cancer treatments (75%).

In Italy, the use of such therapies is widespread and consolidated, with rates recently estimated at 40% of cancer patients with sarcoma (6). According to a research (7) conducted in Tuscan Oncology Departments (Florence, Prato, Massa-Carrara), 37.9% of patients with cancer use one or more Integrative therapies, and especially diet and food supplements (27.5%), phytotherapy (10.8%), homeopathy (6.4%) and body/mind therapies (5.5%). Interestingly, 66.3% of patients informed their physicians and 89.6% experienced the benefits. A subsequent research by the same Author, aimed at highlighting the specific needs of cancer patients (8), showed that the use of Integrative Medicine was associated with the need to be more involved in the therapeutic choice (40% vs. 31.7%) and to have a greater dialogue with the therapists (44.4% vs. 37.2%). According to a multicenter survey (9) conducted in five Italian hospitals, 48.9% of cancer patients used Integrative Medicine, mainly women with a good level of education being treated in highly specialized facilities. According to a recent survey presented at the ASCO 2021 Congress and conducted by IQVIA, 73% of women with breast cancer report using at least one type of integrative therapy after diagnosis, and 43% of patients use these therapies during their cancer care.

Overall, the available data show an improvement in the quality of life of cancer patients who add their oncology pathway with integrative medicine treatments.

3. Adverse effects of Integrative Medicine

Integrative medicine has generally few side and adverse effects. For example, as far as acupuncture and homeopathy are concerned, they were highlighted by several studies. However, the issue of phytotherapy turned out to be more complex, since some medicinal plants and herbal preparations have specific contraindications and/or may result in interactions/interferences with anticancer drugs.

3.1 Acupuncture

Acupuncture is universally believed to constitute a technique with reduced side effects,

although increased hygiene precautions are required when treating immunocompromised patients undergoing chemo- and radiotherapy (10). Minor side effects, such as localized pain at the site of needle insertion, hematomas, and fatigue are possible (11). In addition, according to a recent review by the US National Cancer Institute, an important aspect in acupuncture treatments is the demonstrated rarity of serious side effects and the fact that incidental cases of infection are related to the violation of sterility procedures and negligence by providers (12). Therefore, acupuncture constitutes a relatively safe treatment, and informed consent could be helpful to both patients and physicians (13; 14).

3.2 Phytotherapy

The tolerability and safety properties of medicinal plant extracts are generally good; adverse effects seem to be mainly related to individual hypersensitivity, to the incorrect use or possible adulteration of free sale products, home preparations or herbs from spontaneous collection (15; 16; 17).

Regarding possible drug interactions, it is necessary to avoid resorting to *Hypericum*-based products while undergoing chemotherapy, as they tend to reduce chemo's effectiveness. Moreover, grapefruit-based drinks were found to maximize chemo's activity and toxicity. A cautious, individualized evaluation is required for other herbal preparations, such as *Echinacea*, *Ginseng* and *Curcuma*, since they could inhibit the Cytochrome P450. Specific cases include phytoestrogens, which are contraindicated in women with hormone-sensitive breast cancer, and green tea supplements, specifically contraindicated in patients with multiple myeloma undergoing bortezomib therapy (18; 19; 20; 21; 22).

3.3 Homeopathy

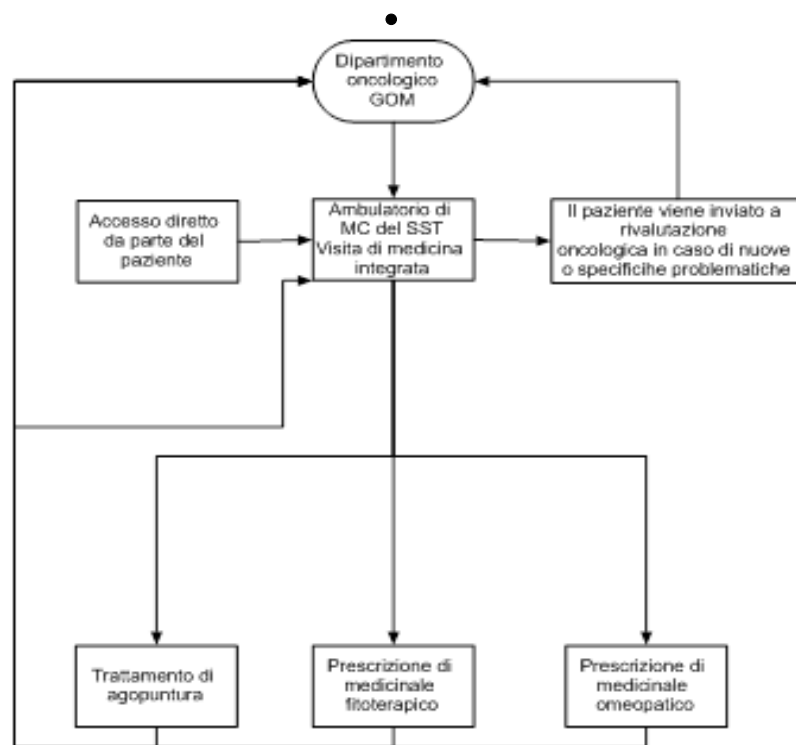
Generally, homeopathy is recognized as a safe therapy. Homeopathic medicines are non-toxic and show minimal adverse effects, which tend to disappear rapidly by discontinuing the medicine. Moreover, given the minimum doses administered, they are also suitable for pregnant women, infants and children (23; 24; 25). Patients who cannot take conventional drugs because of their side effects can refer to homeopathy. National Health Institutions guarantee the quality and the safety of homeopathic medicines, with a reference to EU legislation and the criteria of the European Pharmacopoeia.

4. Pathway of Integrative Oncology activities

A general description concerning the use of Integrative Medicine is reported in Chapter 2. Moreover, literature reviews allow to state that patients have the opportunity to be treated with Acupuncture and traditional Chinese medicine, phytotherapy and homeopathy at every stage of their oncological disease, from the diagnostic phase to that of recovery, remission and end of life, thus being able to mitigate the side effects of conventional therapies or symptoms related to the disease.

Patients can be referred to Integrative Medicine treatments (i.e., acupuncture, phytotherapy, and homeopathy), in line with their right to therapeutic choice and the international literature, since the initial evaluation of the Multidisciplinary Oncology Group (MOG). In any case, patients are referred to Integrative Medicine outpatient clinics by the CORD and the A.I.U.T.O. Points, or by single specialists within the oncological pathway. Direct access to Integrative clinics is allowed, even without the request from their physicians. The visit is carried out under exemption from the payment of the ticket according to the Regional Legislation in force (code 048).

Figure 2. Flow chart of the diagnostic and therapeutic care pathway



Cancer patients are guaranteed adequate information on Integrative Medicine therapies at every stage of the disease with special material, made available by the Cancer Service of reference and by the outpatient clinics of Complementary and Integrative Medicine. The material includes both the brochure published by Tuscany in collaboration with ISPRO and the CRMI, and information on the availability of Integrative Medicine therapies in cancer care and on how to access them.

Information can also be found on the ISPRO website:

http://www.ispo.toscana.it/rete_oncologica_toscana

Patients who directly access Integrative Medicine outpatient clinics and who are not followed by a reference oncologist of the Tuscan Healthcare Service are referred to the Department of Oncology of the reference Health Unit or University Hospital. In fact, the Integrative Medicine visit is usually performed after the patient's meeting with the oncologist of Tuscan Health Service or the GMO, who are responsible for the therapeutic prescriptions.

Integrative oncology facilities carry out the evaluation through specific indicators of outcome/process, and disseminate the results obtained.

In Tuscany, a model of implementation of Integrative Medicine in cancer care pathways has already been recognized in the Breast Unit network, where the modalities to implement both conventional and integrated therapies have been included in the latest regional Diagnostic, therapeutic and care pathways.

5. Diagnosis and staging

Distress in oncology "is a multifactorial, unpleasant experience of psychological (i.e., cognitive, emotional and behavioral), social, spiritual and/or physical nature that may interfere with the ability to cope with cancer disease, its physical symptoms and treatment. It extends along a continuum, ranging from normal feelings of vulnerability, sadness, and fear, to problems that can become disabling such as depression, anxiety, panic, social isolation, and existential and spiritual crisis" (NCCN Clinical Practice Guidelines in Oncology - Distress Management - version 2.2021 (26).

Cancer diagnosis and its consequences, according to Galway, can have a major negative impact on patients and their families (far beyond the wide range of physical symptoms on which caregivers generally focus). Approximately, 30% of newly diagnosed cancer patients experience clinically significant anxiety, whilst the prevalence of depression ranges from 20% to 35%. To end with, up to 75% of individuals develop psychological distress. Such symptoms can significantly limit patients in performing everyday life activities, even representing a social and economic problem and can hinder the ability to cope with the disease, reducing therapeutic compliance. At times, these aspects are so relevant that some Authors suggest considering cancer as a "biopsychosocial disease" (27).

Integrative Medicine is an important resource in the management of such symptoms.

	Acupuncture	Herbal medicine	Homeopathy
Anxiety, depression	X	X	X
Insomnia	X	X	X

Guidelines for the use of Integrative Medicine in Breast Cancer from the Society for Integrative Oncology-SIO (28), also endorsed by the American Society of Clinical Oncology-ASCO (29), suggest point at acupuncture as an option for treating anxiety, mood disorders, and improving quality of life in cancer patients.

Although there are no studies specifically conducted on cancer patients, a number of plant-based extracts can efficaciously treat insomnia, anxiety, and depression (30; 31). Excluding St. John's Wort, which can be used when the patient is free from the use of other drugs (32), Saffron shows good efficacy in treating mild to moderate anxiety and depression disorders (33), as well as Rhodiola for its adaptogenic and antidepressant properties (34).

Valerian (35), L-theanine (22), and Lavender essential oil (36) may be used primarily, alone or in combination, to treat anxiety and insomnia.

Some studies also documented the positive effects of homeopathy on symptoms anxiety and depression symptomatology (37; 38; 39; 40; 41; 42). However, no specific studies have been published concerning the Homeopathic treatment of insomnia in Oncology, whilst several studies positively evaluated its efficacy in insomnia in general (43; 44; 45; 46). In this field, studies include mostly small sample and non-randomized designs, but they generally demonstrate a high level of patient satisfaction in terms of outcomes.

6. Therapeutic plan

After diagnosis and staging processes, patients are referred to anticancer treatments. As far as immunotherapy and biologic drugs are concerned, at the moment there are not enough clinical experiences showing the effectiveness of Integrative Medicine.

6.1 Surgery

In recent years, several clinical studies described the effect/efficacy of Integrative Complementary Medicine on the most common surgery-related symptoms in cancer care.

Symptoms	Acupunct ure	Phytothera py	Homeopathy
Post-surgical nausea and vomiting	X	X	
Pre-, intra- and post-operative pain	X	X	
Prevention of hematomas and post-surgical edema		X	X
Lymphedema	X	X	
Scars	X		
Asthenia	X	X	
Anxiety, depression and insomnia	X	X	X

Post-surgical nausea and vomiting

The Guidelines concerning postoperative nausea and vomiting (PONV) of the Society for Ambulatory Anesthesia's (47) include acupuncture among possible non-pharmacological treatments for postsurgical nausea and vomiting, confirmed by the guideline update published in 2020 (48) and based on 59 trials with 7667 participants. Auriculotherapy has also shown to be effective with strong evidence (49).

Furthermore, acupuncture is indicated for the treatment and prevention of anticipatory nausea in the National Comprehensive Cancer Network (NCCN) Guidelines version 1.2021.

Ginger (*Zingiber off.*) may be used for the treatment of nausea and prevention of vomiting in cancer patients (50). Cannabis is a second-line therapeutic option (51; 52; 53) to control nausea, vomiting, and constipation in cancer patients, particularly from opioids.

Pre-, intra- and post-operative pain

According to the recent review and meta-analysis by Yihan et al. (54), acupuncture and acupressure result in significant improvement in cancer pain by reducing the need for analgesics including morphine (14 RCTs, 920 cases). Moreover, the review by Yuan et al. (55) also documented the role of acupuncture in promoting the rapid recovery of patients in the perioperative phase. Specifically, it seems to relieve patients' anxiety and distress during the preoperative phase, to reduce their analgesic use and stress response, and to maintain their respiratory stability and homeostasis during surgery. Hence, the

recommendation about the use of acupuncture, acupressure, and pharmacological interventions for multimodal pain management according to NCCN 2021 (56).

Boswellia was shown to control pain and reducing postoperative and aromatase inhibitor-induced edema (57). Cannabis may be another therapeutic option for the control of pain symptoms resistant to conventional therapy (58).

Prevention of hematomas and post-surgical edema

The use of Arnica Montana and other homeopathic medicines (e.g., Bellis perennis) to reduce the consequences of trauma, edema, seroma, and hematoma is well established (59; 60; 61; 62). Recent studies confirmed the efficacy of Arnica Montana (and to a lesser extent of other medicines such as Bellis perennis) in homeopathic dilutions in the prevention of post-surgical seroma and hematoma even after mastectomy (63; 64; 65).

Lymphedema

Acupuncture and moxibustion were found to be safe and to help improve lymphedema (66, 67). In detail, a meta-analysis by Jin et al. (20 RCTs, 778 participants) demonstrated that acupuncture and moxibustion-based treatment has a significantly higher efficacy rate than Western medicine-, physiotherapy-, and functional training-based treatments (RR 1.03; $p < 0.00001$) and is better than physiotherapy in reducing arm circumference ($p < 0.00001$).

Asthenia

Jang's 2020 review and meta-analysis (68) reported that acupuncture has a therapeutic potential in the management of cancer-related fatigue. Given this scenario, the ESO-ESMO Fifth Consensus on Advanced Breast Cancer Guidelines (69) and the NCCN Survivorship Guidelines (2021) indicate acupuncture as a treatment option for asthenia.

In addition, Guarana (70) extracts for its caffeine content and Ginseng extracts can be used to improve fatigue.

Anxiety, depression, insomnia

Refer to Chapter 5 Diagnosis and Staging for these symptoms.

6.2 Chemotherapy

Given the most frequent symptoms occurring because of chemotherapy treatment, Integrative Complementary Medicine can reduce their severity and improve patients' quality of life.

Symptoms	Acupuncture	Phytotherapy	Homeopathy
Post chemotherapy nausea and vomiting	X	X	
Asthenia	X	X	
Peripheral neuropathies	X	X	
Anxiety, depression and insomnia	X	X	X

Mucositis	X	X	X
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Post-chemotherapy nausea and vomiting

The use of acupuncture, acupressure, and auriculotherapy was positively evaluated by McDonald et al. (71). Auriculotherapy has also showed to be effective, with strong evidence (49).

The Guidelines from the Society for Integrative Oncology and the American Society of Clinical Oncology ASCO (28-29) recommend acupressure and electro-acupuncture, in addition to antiemetics, in order to reduce chemotherapy-related nausea and vomiting in patients suffering from breast cancer. The fifth ESO-ESMO Advanced Breast Cancer Guidelines Consensus (69) indicate the possible use of acupuncture for chemotherapy-related nausea and vomiting, and the National Comprehensive Cancer Network Guidelines (NCCN 2021) emphasizes the role of acupuncture for treatment and prevention of anticipatory nausea (72).

As far as phytotherapy is concerned, refer to Chapter 6.1 Surgery.

Asthenia

As far as acupuncture and phytotherapy are concerned, refer to Chapter 6.1 Surgery.

Peripheral Neuropathies

The NCCN Survivorship 2021 Guidelines (12) recognized acupuncture as a therapeutic option for neuropathic pain. A recent review by Jin et al. (19 RCTs, 1174 participants) showed that acupuncture significantly improves chemotherapy-induced neuropathy (73) and has a good outcome on nerve there has been a growing body of evidence highlighting the use of acupuncture in this field (74; 75; 76).

Anxiety, depression, insomnia

As far as these symptoms are concerned, refer to Chapter 5 Diagnosis and Staging.

Mucositis

Several studies confirmed the efficacy of specific herbal extracts, and especially Myrrh and Aloe, for the treatment of mucositis (77-79).

Homotoxicological mouthwash composed of Arnica, Calendula, Hamamelis, Bellis Perennis, and other substances in homeopathic dilution can significantly reduce the severity and duration of chemotherapy-induced stomatitis (80).

6.3 Hormonal therapy

Adverse effects of hormonal therapy for cancer may also benefit from some complementary medicine treatments.

Symptoms	Acupuncture	Phytotherapy	Homeopathy
Aromatase inhibitor-induced arthralgia	X	X	X

Hot flashes	X	X	X
Anxiety, depression and insomnia	X	X	X

Aromatase inhibitor-induced arthralgia

Acupuncture is also indicated for the treatment of aromatase inhibitor-induced arthralgias by the NCCN Survivorship Guidelines (2021) and the Italian Association of Medical Oncology Long-Term Care Guidelines, 2019 (81) (although, in this latter case, with lower recommendation power and quality of evidence).

In breast cancer patients, acupuncture is indicated in the treatment of arthralgia from aromatase inhibitors. Liu's meta-analysis showed that acupuncture constitutes a safe and effective treatment (82), and Hershman, as early as 2018, concluded that acupuncture provides satisfactory improvement in symptomatology (83). The most accredited international Oncology Guidelines have accepted this indication, after the Society of Integrative Oncology in 2017 first recommended electro-acupuncture for aromatase inhibitor-induced arthralgia, as reported in the most accredited international guidelines starting with the 2018 ASCO guidelines (12, 29, 81).

As far as phytotherapy is concerned, refer to Chapter 6.1. Surgery.

Homeopathy has a well-established use in relieving pain particularly musculoskeletal pain (84) and has positive effects in the treatment of joint pain and stiffness from anti-aromatase therapy (85).

Hot flashes

Garcia's review, which included eight studies, showed that acupuncture leads to more benefits with respect to sham stimulation, in line with, Chen's review, including 16 studies (86-87). In addition, several RCTs (88-90) demonstrated a significant reduction in hot flashes, and more than one paper has shown that this occurs with fewer side effects than gabapentin or venlafaxine. It is therefore not surprising that Acupuncture has been included in both international cancer and cancer survivorship guidelines (AIOM, ESMO, ASCO, NCCN) as a treatment option for vasomotor syndrome.

Isopropanolic extracts of *Cimicifuga* show an excellent tolerability and efficacy (91-93) even in cancer patients undergoing therapy with antiestrogens.

Several studies (94-100) reported the efficacy of homeopathy in the treatment of hot flashes (*Lachesis mutus*, *Sepia officinalis*, *Pulsatilla*, *Sulphur* and *Sanguinaria*).

Anxiety, depression, insomnia

Refer to Chapter 5 Diagnosis and Staging for these symptoms.

6.4 Radiotherapy

Individualized care plans will also take into account the use of Integrative Medicine to control the adverse effects of radiation therapy.

Symptoms	Acupuncture	Phytotherapy	Homeopathy
Asthenia	X	X	
Anxiety, depression and insomnia	X	X	X
Xerostomia	X		
Dysphagia	X		
Radiodermatitis		X	X

Asthenia

Refer to Chapter 6.1 Surgery for this symptom.

Anxiety, depression, insomnia

Refer to Chapter 5 Diagnosis and Staging for these symptoms.

Xerostomia

Acupuncture was effective in the management of radiation therapy-induced xerostomia (101). A recent review and meta-analysis (102), (8 RCTs, 725 participants), reports that acupuncture is effective without causing serious adverse effects. However, the quality of the studies here is low.

Dysphagia

A randomized pilot study (103) on acute dysphagia in patients with squamous cell carcinoma of the head and neck (SCCHN) during and after radio-therapy showed that acupuncture-related therapy was associated with improvement in quality of life 12 months after the end of radiotherapy, compared with no use of acupuncture.

Radiodermatitis

Boswellia cream preparations have been shown to be effective (104).

Homeopathy is effective in the prevention and therapy of radiodermatitis (Radium bromatum and Belladonna), in combination or in succession. Efficacy is confirmed by several studies (105-110).

6.5 Quality of life

The international literature reports a general improvement in the quality of life of cancer patients with integrative medicine treatments.

	Acupuncture	Phytotherapy	Homeopathy
Quality of Life	X	X	X

Acupuncture improves quality of life without significant adverse effects because it improves symptoms related to cancer and cancer therapies: in particular, it relieves fatigue, reduces diarrhea, pain, and flatulence after surgery (111). Shi's meta-analysis confirmed that TCM in support of chemotherapy reduces its side effects especially at the gastrointestinal level, thus improving quality of life (112).

Some herbal extracts (*Astragalus membranaceus*) maintain the efficiency of the immune system in cancer patients, reduce the side effects of chemotherapy, and improve the quality of life of patients, without risk of interactions with chemotherapy (87; 113-114).

Homeopathy has shown improvement in quality of life in women with breast cancer or multiple malignancies (115-116). Frass study also demonstrated significantly higher quality of life in patients with lung cancer (117).

7. Follow-up

Many symptoms present developed during anticancer treatment persist also in the follow-up (hot flashes, joint pain, anxiety, depression and insomnia mainly related to the evolution of the disease, lymphedema, asthenia and radiodermatitis).

Refer to Chapters 5 Diagnosis and staging and Chap. 6 Therapeutic plan for treatment of these symptoms.

8. Lifestyles

The WHO states that smoking, alcohol abuse, obesity, poor diet and little or no physical activity constitute major risk factors for chronic diseases, including cancer (118) and especially breast cancer (119-124). Other studies have documented a close relationship between colorectal cancer and diet (125-127), particularly, as noted by WHO itself and the International Agency for Research on Cancer - IARC), with excessive consumption of red meat and processed meats (128).

It is then emphasized that fruits and vegetables can play a role in protecting against the risk of gastric cancer (129). Regarding physical activity, integrative medicine recommends mind-body practices such as Qi Gong, Tai Chi, yoga, and mindfulness, in which movement is associated with breathing and mindfulness techniques.

Integrative Medicine, thus, may reinforce patients' motivation to maintain more "virtuous" lifestyles and health-enhancing behaviors (130). A survey by Tuscany and the Regional Tuscan Agency of Health (2014) on lifestyles of patients referred to Integrative Medicine outpatient clinics in the Tuscan Health Service reported that citizens who used complementary medicines had less sedentary lifestyle habits and healthier food consumption than the national population (131).

From a prevention perspective, Integrative Oncology suggests the adoption of healthy lifestyles and the reduction of the intake of refined carbohydrates (white sugar, white industrial flours "0" and "00"), red meat and sausages, favoring instead the consumption of small fish, whole foods, cruciferous vegetables (cabbage, broccoli, Brussels sprouts, etc.), fresh fruit and foods containing ellagic acid capable of inhibiting tumor angiogenesis (raspberries, blackberries, currants, blueberries and pomegranate). There are several ongoing studies on the cost-effectiveness of specific dietary regimens in patients with present or previous cancer. The complexity and duration of the same to date, however promising, has not yet reached universally agreed conclusions, but there is unanimous agreement on the value of a diet and lifestyle in line with the 10 rules of the WHO.

9. Palliative care and end of life

The symptoms treated for end-of-life management in Integrative Oncology are those already reported in the previous chapters (pain, neuropathic pain, anxiety/depression, etc.).

Acupuncture constitutes one of the most widely used complementary therapies in this phase, along with psycho-body techniques (massage with or without aromatherapy, Feldenkrais, Alexander Method, spinal manipulation, touch-massage, etc.). These techniques do not require physical effort, therefore finding application even in the presence of marked asthenia and at the end of life. Anxiety, insomnia, depression, fatigue and pain are the symptoms reported in clinical studies as an outcome. Other mind-body practices are also used (hypnosis, yoga, tai chi, qigong, meditation and mindfulness; expressive techniques such as music therapy, art therapy, dance movement therapy, etc.) that require the active participation of the patient, if his or her condition permits (132).

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