Acupuncture in Integrated Cancer Therapy: Scientific Evidence, Clinical Appropriateness and Care Model of the Tuscan Health Service

Franco Cracolici*

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* Vicepresidente WFAS (World Federation Acupuncture Society).
Vice-President of FISA (Italian Federation of Acupuncture Societies).
Scientific Director of Integrated Oncology Activities AUSL Toscana Sud Est.
President of FISTQ (Italian Federation of Tuina Qigong Schools).
Director of the School of Traditional Acupuncture of the City of Florence.
francocracolici@yahoo.it

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Abstract. *Integrated oncology represents a care model oriented towards combining conventional oncological treatments with complementary interventions selected on the basis of available evidence, safety and individual patient needs. In this context, acupuncture is one of the most studied methods for the management of neoplasia-related symptoms and adverse effects associated with surgery, chemotherapy, radiotherapy and endocrine therapies. The main areas of interest include pain, cancer-related fatigue, nausea and vomiting, chemotherapy-induced peripheral neuropathy, arthralgias associated with aromatase inhibitors, hot flashes, xerostomia, sleep disturbances and psychoemotional symptoms. Its role must be defined within supportive care and not as an alternative antineoplastic treatment. In parallel, experimental research has proposed mechanisms including neuromodulation, neurovegetative regulation, purinergic signaling, modulation of inflammatory mediators and neuro-immuno-endocrine interactions. Traditional Chinese Medicine offers a further interpretative paradigm based on the concepts of Zheng Qi, Yuan Qi and Fu Zheng; the comparison with biomedicine can generate research hypotheses, as long as unproven equivalences are avoided. Of particular interest is the experience of the Tuscan Health Service and the USL Toscana Sud Est, where integrated oncology has been progressively*

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structured through multi-professional pathways, acupuncture programs and research projects. The observational data collected in the services represent a real-world heritage of potential interest, although they require a reading consistent with the limits of uncontrolled studies.

Keywords: *Acupuncture, oncology, Health Authority, Safety, Protocols, Tuscany.*

Introduction: From Cancer Treatment to Personal Care

Advances in oncology have changed the prognosis of numerous neoplasms and at the same time have placed the management of the overall impact of the disease and treatments on the person at the forefront. The cancer patient not only experiences the biological consequences of the neoplasm: pain, nausea and vomiting, fatigue, peripheral neuropathies, sleep disorders, xerostomia, functional alterations, vasomotor symptoms and psychological distress can significantly interfere with the quality of life. In the paradigm of care, the therapeutic principles are traced back to six principles: evidence, appropriateness, humanity, global vision, personalization and safety [1].

Integrated oncology finds its place in this clinical space. The concept does not imply the replacement of conventional oncological treatments with complementary methods, but the inclusion of additional interventions within a coordinated therapeutic project. It is therefore essential to distinguish integrated medicine from alternative medicine: in the integrated model, interventions are selected on the basis of defined indications, evidence, safety, individual conditions and compatibility with oncological therapies. The goal is to intervene on the symptomatic burden and quality of life, not to replace antineoplastic therapy.

Acupuncture as Supportive Care in Oncology

The use of acupuncture in oncology has progressively shifted from a mainly empirical location to a structured clinical research field. The original data to be adopted in hospital use describes the diffusion of acupuncture in integrated oncology programs and identifies numerous conditions of interest: chemotherapy-induced nausea and vomiting, oncological and postoperative pain, fatigue, arthralgias associated with aromatase inhibitors, hot flashes, chemotherapy-induced peripheral neuropathy, xerostomia, anxiety, insomnia and other supportive and palliative care symptoms [1].

The Society for Integrative Oncology guidelines, including those developed with ASCO, address the use of integrative interventions in cancer pain, anxiety and depression, and fatigue [2-5]. This framework suggests that the methodologically

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correct question is not whether acupuncture is generically "effective in oncology", but for which outcomes, in which populations and under what conditions it can produce a clinically relevant benefit.

Clinical Evidence in the Main Indications

Cancer-Related Fatigue

Cancer-related fatigue (CRF) is a multidimensional condition that can persist during and after treatments, with consequences on physical activity, cognitive abilities, autonomy and quality of life. The 2024 ASCO-SIO guidelines on fatigue in cancer survivors examined 113 RCTs; for CRF management interventions, the overall certainty of evidence is variable and, for many strategies, low or moderate [5].

In the panorama of adoptable treatments, fatigue is one of the main indications considered in the Tuscan experience. Particularly relevant is the FAIR-AC project, a prospective randomized multicenter study on the association between radiotherapy and acupuncture in patients with breast and prostate cancer. The document reports 220 patients recruited and 183 subjects analyzed; in the breast cancer group, benefits are described on some items of the Brief Fatigue Inventory and on the overall index, while in prostate cancer the lower number of participants makes interpretation more difficult [1]. These data underline the usefulness of integrating validated tools and controlled designs into the evaluation of acupuncture.

Chemotherapy-Induced Peripheral Neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) is a clinically relevant complication of cancer therapies. The body of established evidence recalls systematic reviews and recent meta-analyses dedicated to acupuncture-related interventions. Among the most effective studies is the 2024 network meta-analysis by Yeh *et al.*, as well as a 2025 meta-analysis on breast cancer patients [1,6].

The literature suggests beneficial signals on neuropathic symptoms and pain, but problems of heterogeneity of protocols, populations, outcomes and controls remain. Future research should therefore focus not only on statistical significance, but on clinical relevance, duration of effect and identification of patients with the highest likelihood of response.

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Nausea and Vomiting

Nausea and vomiting associated with chemotherapy represent a further area of interest. In the wide use of this problem, the somatic protocol includes PC6, CV12, ST36, LR3, SP10 and SP6 [1]. In terms of care, acupuncture should be understood as a complementary intervention to the appropriate pharmacological antiemetic prophylaxis, not as a replacement for it. This principle can be generalized to the entire field of integrated oncology: the possible additional effect of a complementary treatment must be evaluated against the standard of care received by the patient.

Cancer Pain and Treatment-Related Pain

Pain is one of the main targets of acupuncture in oncology. The target use considers pain associated with the disease and pain resulting from therapeutic interventions, including postoperative pain, pain after thoracotomy, and endocrine treatment arthralgias [1]. The SIO-ASCO guidelines on pain in oncology place acupuncture among the integrative interventions evaluated in specific clinical conditions [3].

On a physiological level, analgesic effects are interpreted through the integration of peripheral, spinal and supraspinal modulation. The scientific rationale describes the involvement of dorsal root ganglia, neurotransmitter systems and inflammatory mediators [1]. However, it is sometimes essential to distinguish biological plausibility and clinical efficacy: the presence of a potential mechanism is not equivalent to the demonstration of a therapeutic benefit.

Arthralgias, Vasomotor Symptoms, Xerostomia and Sleep

Arthralgias associated with aromatase inhibitors can compromise the quality of life and, in some cases, the tolerability of endocrine therapy. Very frequently, this condition is included among the main indications for acupuncture, together with hot flashes [1]. Similarly, xerostomia, especially after radiotherapy of the head and neck area, is indicated as an area of application; the standard protocol reports LI2, LU7, CV24, KI6 and ST4 among the points used [1].

Anxiety, stress and insomnia are further targets of supportive care. In a multidisciplinary model, acupuncture does not replace psycho-oncological treatment when indicated, but can be placed within a broader symptom control strategy. The value of the integrated approach also lies in the ability to avoid the fragmentation of the patient into independent clinical manifestations.

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Biological Mechanisms: Neuromodulation and Systemic Regulation

Research into the mechanisms of acupuncture has identified several processes potentially involved, including neuromodulation, purinergic signaling, neuroimmune activity, and regulation of inflammatory mediators. The result is due to the role of dorsal root ganglia, spinal and supraspinal circuits, and neurotransmitter systems including GABA, glutamate, and serotonin [1].

Purinergic signaling is of particular interest. Goldman *et al.* experimentally demonstrated a local increase in adenosine during acupuncture and an antinociceptive effect dependent on A1 receptors, providing a possible molecular link between peripheral stimulation and analgesic response [7]. The scientific rationale also highlights mediators such as TNF-alpha, IL-1beta, IL-6 and IL-10 and intracellular pathways related to neuroinflammation [1].

These data require rigorous reading: experimental modulation of a cytokine or cell population does not demonstrate a clinical antitumor effect. Mechanistic studies provide biological plausibility and generate hypotheses, but should not be used to attribute unproven direct oncological efficacy to acupuncture.

Mitochondria, Energy Metabolism and Oxidative Stress

The current framework of studies proposes a comparison between the traditional concept of functional energy and cellular bioenergetics. Mitochondria are involved in ATP production, metabolism, oxidative stress and regulation of apoptosis; experimental studies are also mentioned in which electroacupuncture is associated with changes in mitochondrial function and oxidative stress [1].

Such a comparison may be heuristically interesting, but it requires a clear epistemological demarcation. Identifying Qi with ATP does not constitute a proven biological equivalence. Qi and ATP belong to different descriptive systems: the former derives from a complex traditional medical paradigm, the latter is a biochemically defined molecule. The relationship between the two can therefore be discussed as a conceptual analogy and not as a scientific identity.

Zheng Qi, Fu Zheng and Customization

One of the central concepts of the Chinese medical tradition developed in the material is that of Zheng Qi, interpreted as the overall ability of the body to maintain balance and resist pathogenic factors. The principle of Fu Zheng, "upholding

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the correct", takes on particular importance in the traditional reading of the person undergoing cancer treatments [1].

In the model presented, Yuan Qi, Zong Qi and Zheng Qi contribute to the description of individual constitution and functional capacity. These categories can be put in dialogue with modern attention to interindividual variability, but they do not have to be directly identified with the immune system, genetic heritage or individual biomarkers. A scientifically fruitful dialogue between TCM and biomedicine presupposes the recognition of the different levels of description.

Genetics, Epigenetics and Telomeres

The cultural syncretism of contemporary scholars proposes an interpretative link between Yuan Qi, constitutional heritage, genetics and telomere biology, also reporting preliminary experiences on acupuncture and telomerase activity [1 Telomere length must be considered a biomarker and not a substitute clinical outcome.

For this reason, it is not scientifically correct to formulate the equation "Yuan Qi = telomeres". It is more appropriate to consider the traditional attention to individual constitution as a stimulus to modern research on interindividual differences, adaptive capacity and factors that influence response to treatments.

Stress, Psychosocial Dimension and Oncology

PNEI devotes ample space to the relationships between chronic stress, hypothalamic-pituitary-adrenal axis, sympathetic system, glucocorticoids and catecholamines and recalls studies relating to social support, loneliness, childhood experiences and emotional regulation [1]. These issues are clinically relevant, but require extremely precise communication.

Psychological stress should not be proposed as a simplistic explanation of the genesis of the tumor, nor as an element that implicitly transfers responsibility for the disease to the patient. Instead, it is appropriate to study how stress, social isolation, sleep disorders and depressive symptoms influence quality of life, adaptation to diagnosis and physiological systems. A principle of integrated oncology derives from this: the psychological dimension is not an alternative to the biological dimension, but belongs to the multidimensional evaluation of the person.

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Security and Appropriateness

The application of acupuncture in oncology requires special attention to safety. The patient may have hematological, immune, dermatological, or anatomical alterations related to the disease and treatments. Recommendations for the safe practice of acupuncture in oncology emphasize the need to tailor the intervention to specific clinical conditions and oncological treatments [8].

A systematic review on the safety of acupuncture in oncology evaluated adverse events in randomized trials, also highlighting the need for better quality reporting [9]. In this context, appropriateness precedes efficacy: a potentially useful procedure can become inappropriate if applied without adequate clinical evaluation or coordination with the oncology team. Based on our experience in the public sphere, we propose the use of tools such as SF-12 and the Edmonton Symptom Assessment System (ESAS) to follow outcomes [1]. Integration therefore also means measuring.

The Tuscan Model of Integrated Oncology

One of the most characterizing aspects of the material is the experience developed in Tuscany. The current reality describes a progressive integration of complementary medicines into the regional health system, supported by organizational acts and paths dedicated to cancer patients. Among the measures referred to is Resolution 418/2015 on the integration of complementary medicines into the Tuscan oncology network, in addition to the subsequent PDTAs and dedicated regional initiatives [1].

This approach has at least three important elements: it reduces the separation between oncology and complementary treatments; it makes it possible to select indications more appropriately; it creates the conditions for a systematic collection of outcomes. The value of the model therefore lies not only in the offer of acupuncture, but in the clinical governance of its integration.

The Multi-Professional Network

In the model described, the global approach involves oncologist, doctor expert in rehabilitation, acupuncturist expert in TCM, psychologist or psychotherapist, rehabilitation therapist, nursing staff, general practitioner, home care, family and voluntary associations [1]. Integration therefore does not coincide with a simple sum of therapies, but with an organizational mode of care.

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The construction of connections between professionals makes it possible to orient interventions to the same care objectives, to promptly recognize the patient's needs and to reduce the risk that complementary therapies are used in isolation from the oncological pathway.

The Experience of the USL Toscana Sud Est

The creation of the Integrated Oncology network in 2020 within the Department of Oncology and the approval, on 14 August 2020, of the company procedure "Integrated Oncology Pathway" [1] was a pioneer in ITALY. I was personally involved in a first-level training project in integrated medicine in oncology, "Acupuncture in support of cancer patients" at the Valdarno Oncology, the regional project developed in Campostaggia and initiatives dedicated to well-being and lifestyles at the Misericordia Hospital in Grosseto, as well as a project currently underway in Campostaggia PSYCO-AGO, which involves cancer patients who are victims of ANXIETY AND DEPRESSION and the use of Acupuncture in this regard [1].

This network is a care laboratory of particular interest because it allows integration to be studied not only in an experimental environment, but in daily clinical practice.

Pitigliano, Grosseto and Campostaggia-SOUTH-EAST TUSCANY HEALTH AUTHORITY

In Pitigliano, we have an integrated hospital service in which the declared strategy consists of combining complementary medicine with conventional medicine without replacing oncological treatment [1]. In the Grosseto project, a structure aimed at improving the quality of life is proposed, with the involvement of nursing and collaboration in acupuncture, nutrition and psychology. Campostaggia represents the experience most characterized by the integration of acupuncture in the hospital oncology context [1].

The regional project developed in Campostaggia is described as aimed at improving the quality of life of cancer patients through complementary and integrated medicine techniques. The value of these experiences also lies in the possibility of experimenting with a model of integration within the public health service, directly in the ONCOLOGY department.

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Real-World Results of Clinical Experience

Observational data on clinical activity that should be discussed separately from RCTs and systematic reviews. In the general pain analysis, 292 patients and a mean reduction in intensity from 5.16 to 1.92 on the NRS scale, with $p<0.001$, are reported. In the subgroup of 231 patients with pain at baseline, the score is described as reduced from 6.53 to 2.43, with a change of 4.10 points [1]. High ratings of perceived efficacy and well-being are also reported.

These results are clinically interesting because they derive from daily practice, but must be interpreted according to the observational design. In the absence of randomization and an appropriate control group, it is not possible to causally attribute the entire observed variation to acupuncture or other integrated interventions. However, real-world data retain an important function: they describe the functioning of services, generate hypotheses, and can guide the design of prospective controlled trials.

Narrative Medicine and Patient-Reported Outcomes

Our thinking attributes importance to narrative medicine in the activity of the integrated oncology clinic [1]. This dimension is consistent with the use of patient-reported outcomes. Pain, fatigue, anxiety, sleep, general well-being and the ability to perform daily activities cannot be fully understood through isolated biological parameters.

Integrating quantitative outcomes and narrative of experience can therefore contribute to a more complete assessment of supportive care. This does not mean replacing quantitative evidence with narrative, but recognizing that the two dimensions answer different questions and can contribute together to the definition of the clinical value of the intervention.

Discussion

The overall analysis suggests that acupuncture can find a rational place in contemporary oncology especially as a supportive care tool. Three elements appear fundamental. The first is the specificity of the indication: there is no single efficacy of acupuncture "in oncology", but possible different effects on fatigue, pain, nausea, neuropathy, vasomotor disorders and other symptoms. The second concerns the level of evidence: results from randomized trials, systematic reviews, observational studies, preclinical research and clinical experience cannot be placed on the same level but undoubtedly acupuncture now has a large amount of studies and

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evidence of far-reaching scope. The third is the care context: a complementary method inserted in a governed health pathway, with defined indications, communication with the oncologist and monitoring of outcomes, is different from the same method used in isolation.

The Tuscan experience is particularly interesting for this third dimension. It shifts the question from "which complementary treatment to use?" to "how to build a system in which a complementary treatment can be used in an appropriate, safe, assessable and coordinated way?". In this perspective, the scientific value of the organizational model becomes an integral part of the evaluation of the intervention.

Limits of Evidence

The literature on acupuncture presents significant methodological difficulties. Number and frequency of sessions, points used, duration of stimulation, manual acupuncture and electroacupuncture can differ considerably between studies. A second problem concerns the choice of control: sham acupuncture is not necessarily biologically inert, while full blinding of the operator is not achievable in the same way as a pharmacological study.

Further limitations concern sample size, multiplicity of outcomes and risk of bias. It is also essential to separate preclinical evidence from clinical evidence. The modification of a cytokine, neurotransmitter or mitochondrial parameter in an experimental model does not allow the conclusion that there is a direct oncological benefit for the patient.

For the future, multicenter studies, better described protocols, clinically relevant outcomes, adequate follow-ups and integration of patient-reported outcomes with objective clinical indicators are therefore priorities.

Future Prospects

The future of acupuncture in oncology should develop along three converging lines: research, personalization and organizational integration. On the research level, it is necessary to identify responders more precisely, define the dose and characteristics of the intervention and evaluate the persistence of the effects. Personalization constitutes a possible meeting ground between TCM's traditional attention to individual constitution and modern research on clinical phenotypes, provided that the comparison is conducted through verifiable hypotheses and not symbolic equivalences.

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The third dimension is organizational. The Tuscan experience indicates a possible direction: integrating complementary interventions into oncology pathways rather than leaving them in a separate care space. In this scenario, the acupuncturist operates within a network oriented towards the same patient and the same general objectives of care.

Conclusions

Acupuncture is one of the most interesting complementary methods in integrated oncology. Its most scientifically appropriate location is not that of an alternative treatment of neoplasia, but of a complementary intervention aimed at managing specific symptoms of the disease and the adverse effects of oncological therapies.

The transition from complementary medicine to truly integrated medicine requires more than the demonstration of the effectiveness of a single technique. It requires selection of indications, safety, appropriateness, evaluation of outcomes, communication between professionals and inclusion of the intervention in the care pathway. The experience of the Tuscan health system and the USL Toscana Sud Est shows how these principles can be translated into clinical-organizational paths [1].

The real-world results described in the paper, including those related to pain, are clinically interesting signals worthy of further evaluation by prospective and controlled studies. In parallel, research on biological mechanisms broadens the understanding of the neurophysiological consequences of acupuncture stimulation. The dialogue with TCM can represent a field for reflection, provided that conceptual analogy, biological plausibility and experimental evidence are kept distinct.

Appropriateness, evidence and humanity can therefore be considered complementary components of a person-centered oncology. The value of acupuncture should not be measured on the ability to represent a "different" medicine, but on the possibility of becoming, when indicated and supported by evidence, an appropriate component of a multidisciplinary and quality-of-life-oriented oncological medicine.

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