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Dosimetric Predictors and Risk Factors for Vertebral Column Degeneration and Paraspinal Neuropathic Pain Following Radiotherapy in Breast Cancer Patients

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ABSTRACT

Introduction: Adjuvant breast radiotherapy frequently delivers off-target doses to the axial skeleton and paraspinal soft tissues, inducing insidious osteoskeletal degeneration and chronic neuropathic pain. Despite their clinical relevance, dosimetric thresholds governing these late sequelae remain poorly defined. This prospective study aimed to identify specific dosimetric predictors and independent clinical risk factors associated with vertebral degeneration and paraspinal neuropathic pain in breast cancer survivors.

Material and methods: This prospective observational cross-sectional study at Shahid Madani Hospital investigated 175 breast cancer survivors sampled via convenience methods, evaluating cervicothoracic musculoskeletal and neurological disorders through standardized clinical examinations, functional assessments, and dosimetric data analysis.

Results: This study revealed a high prevalence of cervicothoracic disorders in breast cancer survivors (myofascial pain: 50.3%; cervical ROM limitation: 43.4%), with supraclavicular irradiation (adjusted OR=2.87, P=0.003) and axillary dissection (adjusted OR=2.18, P=0.024) identified as significant independent risk factors.

Conclusion: Radiation therapy and surgical interventions for breast cancer significantly increase the burden of cervicothoracic musculoskeletal and neurological morbidities. Optimizing radiation field design and minimizing paraspinal exposure are crucial to improving long-term survivorship quality of life.

Introduction

Radiotherapy occupies an indispensable cornerstone position within the multidisciplinary management paradigm for modern breast carcinoma, providing marked reductions in locoregional recurrence alongside demonstrable survival advantages across early and locally advanced disease states. Modern oncologic standards integrate adjuvant tangential field irradiation directed to the whole breast or reconstructed chest wall, alongside comprehensive regional nodal irradiation encompassing supraclavicular, axillary, and internal mammary nodal stations for patients presenting with adverse clinicopathologic features or nodal dissemination.

Concurrently, profound advances in screening strategies, molecularly targeted agents, and systemic cytotoxic and endocrine therapies have prolonged post-treatment survival trajectories, creating an expanding demographic of long-term survivors vulnerable to insidious iatrogenic late effects. Among these delayed sequelae, non-target tissue injury represents an ongoing therapeutic paradox wherein critical curative ionizing dose delivery inadvertently causes cumulative biological, microvascular, and structural damage to contiguous anatomical structures.

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Consequently, characterization of durable treatment-related toxicities has shifted from broad categorical morbidity scores toward granular pathophysiological mapping of subclinical and overt functional tissue deterioration in anatomical territories contiguous with radiation treatment fields [1].

The axial skeleton, particularly the upper thoracic and lower cervical vertebral column, frequently resides in close anatomic proximity to regional nodal and tangential radiation fields, sustaining unintentional low-to-intermediate off-target dose exposure during treatment delivery. Despite refined field planning and computerized three-dimensional conformal radiotherapy or intensity-modulated delivery platforms, radiation beams traversing the supraclavicular fossa, axillary apex, and internal mammary chain inevitably deliver measurable exit, entry, and scatter radiation to adjacent vertebral bodies, costovertebral articulations, and paraspinal soft-tissue envelopes. Biological absorption of high-energy photons within bone and paraspinal tissues initiates a cascade of radiation-induced osteopenia, matrix protein cross-linking degradation, microvascular endarteritis, and osteocyte senescence. These microarchitectural derangements weaken trabecular integrity, blunt physiologic bone turnover, and impair reparative osteogenesis, establishing a primed substratum for accelerated osseous and articular deterioration. Although conventional radiotherapy planning historical guidelines have prioritized organ-at-risk dose constraints strictly for pulmonary parenchyma, cardiac chambers, and the brachial plexus, vertebral osseous sub volumes and adjacent paraspinal musculoligamentous complexes have historically received negligible formal dosimetric surveillance, leaving their physical tolerance margins poorly defined [2].

Radiation-induced skeletal injury operates through distinct biophysical pathways characterized by early endothelial injury, progressive obliterative endarteritis, and cellular depletion within the osteoblastic and osteoclastic lineages of irradiated cancellous bone. Endothelial swelling, microvascular occlusion, and resultant hypoperfusion generate persistent tissue hypoxia, which impairs the metabolic activity of alkaline phosphatase-producing osteoblasts while favoring localized osteoclastic matrix resorption. Over time, localized marrow conversion occurs, marked by progressive fatty substitution, hypocellularity, and progressive disruption of type I collagen organization within the vertebral cancellous matrix. These biological compromises yield diminished mechanical loading capacity, heightened susceptibility to subchondral microfractures, and premature degenerative changes in vertebral endplates and adjacent intervertebral disc spaces. Consequently, the affected axial segments undergo accelerated degenerative spondylotic changes, loss of intervertebral height, and irregular osteophytosis that parallel premature senescent degeneration but manifest with distinct anatomic boundaries corresponding precisely to radiation portal margins and dose-volume distributions [3].

Simultaneously, the paraspinal soft-tissue mantle, comprising paraspinal musculature, facet joint capsules, interspinous ligaments, and deep investing fascial layers, undergoes a stereotyped fibro-atrophic transformation driven by chronic radiation-induced myofibroblast activation. Radiation exposure stimulates sustained overexpression of pro-inflammatory and pro-fibrotic signaling cascades dominated by transforming growth factor-beta 1, tumor necrosis factor-alpha, and connective tissue growth factor. This perpetual molecular signaling promotes uninhibited extracellular matrix deposition, pathological collagen cross-linking, and vascular rarefaction, ultimately culminating in severe muscular hypoperfusion, ischemic contracture, and myocyte atrophy within the deep paraspinal compartments. As paraspinal extensor and stabilizer muscle mass diminishes and is replaced by unyielding fibrotic scar tissue, the functional muscular sleeve surrounding the spine loses its physiologic compliance and dynamic stabilizing capacity. This persistent biomechanical imbalance amplifies unphysiological stress concentrations on irradiated vertebral motion segments, establishing a destructive feedback loop wherein structural skeletal breakdown and myopathic contracture exacerbate mutual structural decay [4].

In parallel with skeletal and musculoligamentous deterioration, radiation delivery to the cervicothoracic junction and upper thoracic spinal corridor presents substantial neurotoxic hazards to neural architecture traversing the paraspinal space. While classical high-dose radiation myelopathy is exceptionally rare under modern fractionation schedules, low-to-intermediate dose spillover commonly incurs insidious, sub-threshold injury to dorsal root ganglia, spinal nerve roots, dorsal rami, and fine terminal nociceptive arborizations supplying paraspinal tissues. Pathologically, radiation induces perineural and epineural fibrosis, localized ischemia secondary to vasa nervorum microangiopathy, and focal demyelination within large- and small-diameter nerve fibers. Chronically compressed or ischemic neural elements develop sustained peripheral sensitization, characterized by lowered activation thresholds, spontaneous ectopic axonal firing, and abnormal neuroinflammatory mediator release into contiguous tissues. Furthermore, chronic myofascial contracture and degenerative disc disease mechanically irritate sensory nerve trunks within the neural foramina, fostering a complex neuropathic pain state marked by allodynia, lancinating paraspinal dysesthesias,

and progressive focal sensory deficits that resist standard non-steroidal anti-inflammatory analgesics [5].

Paraspinal neuropathic pain represents a severely debilitating yet clinically under-recognized late complication in breast cancer survivorship, frequently misdiagnosed as uncomplicated myofascial strain, skeletal metastatic progression, or systemic arthralgia related to adjuvant endocrine therapy. Patients afflicted by paraspinal neuropathic pain present with burning, stabbing, electrical-like paroxysms, and hyperpathia localized over the upper paraspinal and interscapular regions, often demonstrating dermatomal or regional somatic distributions concordant with irradiated margins. Unlike mechanical spinal pain that correlates predictably with postural loading and responds to rest, paraspinal neuropathic pain demonstrates prominent nocturnal exacerbation, mechanical and thermal allodynia, and variable refractoriness to conventional opioid analgesics. The diagnostic ambiguity surrounding this clinical syndrome often results in extensive non-targeted diagnostic workups, unwarranted spinal interventions, and persistent therapeutic delays. Diagnostic validated instruments such as the Douleur Neuropathies 4 and the Leeds Assessment of Neuropathic Symptoms and Signs facilitate systematic diagnostic discrimination; however, systematic correlation of neuropathic symptom scoring with formal volumetric radiation parameters remains scarce in existing clinical oncology literature [6].

Elucidating the dose-volume relationships governing non-target axial bone and paraspinal nerve injury is paramount for developing refined organ-at-risk definitions and meaningful radiation avoidance criteria. Classical normal tissue complication probability modeling relies heavily on empirical dose thresholds, yet contemporary understanding recognizes that vertebral spongiosa and paraspinal neural tracts are sensitive to complex spatial dose distributions, including cumulative mean dose, maximum local dose hotspots, and percentage volumes receiving incremental threshold doses, such as V10, V20, and V30. In contemporary multi-field planning, intensity-modulated techniques often disperse widespread low-dose radiation baths across vast tissue volumes, while three-dimensional conformal setups may deliver focal, higher-dose exit pathways directly through the cervicothoracic vertebral bodies. The lack of standard delineation for vertebral and paraspinal structures within clinical treatment planning systems hinders accurate dosimetric accountability, preventing radiation oncologists from establishing definitive dose-volume histogram cutoffs that could predict and avert long-term axial degeneration and chronic pain syndromes [7].

The vulnerability of the axial skeleton and paraspinal neural structures to radiation-induced injury is further modulated by a multifaceted spectrum of patient-specific and systemic oncologic risk factors that interact synergistically with physical dose deposition. Chief among these host factors is baseline bone mineral density; postmenopausal status, nutritional insufficiencies, and advanced chronological age deplete baseline skeletal reserves, markedly lowering the physical tolerance threshold of vertebral cancellous bone to ionizing radiation. Furthermore, adjuvant systemic treatments universally incorporated into modern breast cancer protocols actively amplify this susceptibility. The widespread use of third-generation aromatase inhibitors (such as letrozole, anastrozole, and exemestane) profoundly suppresses circulating estrogens, inducing rapid bone mineral loss, high bone turnover states, and systemic musculoskeletal arthralgia-myalgia syndromes that destabilize spinal motion segments. Similarly, historical exposure to taxane- and anthracycline-based chemotherapy regimens exerts both direct osteoclastic stimulation and systemic neurotoxicity, predisposing peripheral and paraspinal sensory nerve fibers to heightened vulnerability when subsequently subjected to localized radiation fields [8].

Surgical disruption of the surrounding neuromusculoskeletal architecture represents another crucial synergistic variable that fundamentally alters local biomechanics and neurovascular anatomy prior to radiation exposure. Extensive axillary lymph node dissection, chest wall resections, and reconstructive procedures disrupt superficial cutaneous nerves, fascial continuity, and localized muscular balance across the pectoral girdle and thoracic wall. Resulting imbalances, including chronic protective postural adjustments, altered scapulothoracic kinematics, and unilateral myofascial tension patterns, shift physiological weight-bearing forces toward the cervical and thoracic vertebral columns. When this biomechanically stressed, asymmetric axial segment subsequently receives adjuvant radiotherapy, the combined insults of localized muscular ischemia, radiation-induced soft-tissue fibrosis, and structural skeletal weakening accelerate degenerative remodeling far beyond what would be anticipated from surgical intervention or radiation exposure alone [9].

Despite increasing acknowledgment of treatment-associated survivorship morbidities, significant knowledge gaps persist regarding the quantitative threshold parameters that delineate safe vertebral and paraspinal radiation exposure. Existing studies examining post-radiation skeletal toxicity have predominantly focused on pelvic insufficiency fractures following gynecologic or anal canal radiotherapy, or localized rib fractures following stereotactic body radiation therapy for pulmonary malignancies, leaving the thoracic and cervical axial skeleton in breast cancer cohorts largely unmapped.

Contemporary cross-sectional imaging modalities, including modern computed tomography, magnetic resonance imaging, and quantitative dual-energy X-ray absorptiometry, allow precise anatomical phenotyping of vertebral height reduction, endplate sclerosis, facet degeneration, and paraspinal muscle fatty infiltration. Integrating these high-resolution imaging biomarkers with three-dimensional radiation dose distributions offers an unprecedented opportunity to discover robust dosimetric predictors and construct multivariable predictive risk models that bridge physical radiation physics with biological tissue outcomes [10].

Addressing these predictive gaps is critical for clinical oncology practice, as accurate risk prediction facilitates preemptive dosimetric optimization and individualized survivorship intervention protocols. Establishing validated dose-volume thresholds would allow radiation oncologists to implement proactive beam angle modulation, inverse optimization constraints, and avoidance sectors during treatment planning, mitigating accidental spinal and paraspinal dose burdens without compromising target volume coverage or locoregional tumor control. For patients whose anatomical geometry renders spinal dose exposure unavoidable, identifying independent patient-related and systemic risk factors provides a clinical rationale for initiating early targeted surveillance, bone-modifying therapies such as bisphosphonates or RANK-ligand inhibitors, specialized neuro-rehabilitative physical therapies, and early neuropathic-modulating pharmacological regimens before irreversible structural deformities and chronic neuropathic pain become established [11].

Notwithstanding these potential clinical applications, comprehensive prospective investigations that systematically correlate three-dimensional vertebral and paraspinal dose-volume metrics with validated longitudinal clinical and neuro-radiological endpoints in breast cancer populations remain exceptionally limited. Most available literature is constrained by retrospective designs, heterogeneous treatment planning modalities, short follow-up periods that precede late-onset radiation tissue remodeling, and a failure to differentiate mechanical nociceptive back pain from genuine, localized paraspinal neuropathic states. To overcome these fundamental limitations, well-characterized cohort studies combining rigorous dosimetric extraction, structured radiological spinal degeneration scoring, and standardized neuropathic pain phenotyping are required to delineate the pathophysiological underpinnings of axial radiation toxicity. Therefore, the primary objective of this prospective study was to identify specific dosimetric predictors and independent clinical risk factors associated with vertebral column degeneration and paraspinal neuropathic pain in breast cancer patients receiving adjuvant radiotherapy.

Material and methods

Study design:

This descriptive cross-sectional study was conducted in a prospective, clinic-based manner at Shahid Madani Hospital, Tabriz, Iran, a tertiary referral center providing multidisciplinary oncologic follow-up care. The study was designed to estimate the burden and clinical pattern of radiation-associated cervicothoracic musculoskeletal and neurological disorders among breast cancer survivors and to examine clinical and treatment-related correlates within a real-world survivorship setting. All assessments were performed using a standardized protocol by trained clinicians during routine follow-up visits within the study period.

Sampling and sample size:

Participants were recruited using convenience (available) sampling from eligible breast cancer survivors attending outpatient oncology and rehabilitation follow-up clinics at Shahid Madani Hospital. The required sample size was estimated using the Cochran sample size formula for proportions, $n = [Z^2 p(1-p)] / d^2$, assuming a 95% confidence level ($Z=1.96$), a conservative expected prevalence of 50% ($p=0.50$) to maximize sample size in the absence of definitive local estimates, and an absolute precision of 0.075 ($d=0.075$). Based on these assumptions, the minimum sample size was calculated as approximately 171, and was increased to 175 to account for incomplete data and to preserve statistical precision.

Inclusion and exclusion criteria:

Inclusion criteria were women with a confirmed diagnosis of breast cancer who had completed external beam radiotherapy to the breast/chest wall with or without regional nodal irradiation, had reached the post-treatment survivorship phase (at least 3 months after completion of radiotherapy), and were able to participate in clinical examination and structured symptom assessment at the time of enrollment; participants were required to have no evidence of active locoregional recurrence requiring urgent oncologic intervention at the study visit and to provide informed consent. Exclusion criteria included prior history of clinically significant cervical or thoracic spine disease before cancer treatment (e.g., known cervical myelopathy, severe degenerative disc disease with neurological deficit, inflammatory spondyloarthropathy, or prior vertebral fracture), documented metastatic disease to the spine or brachial plexus, prior radiotherapy to the neck or upper thorax for any reason, major trauma to the shoulder girdle or cervicothoracic region after cancer treatment, known peripheral neuropathy from non-cancer causes likely to confound neuropathic

phenotyping (e.g., uncontrolled diabetes with neuropathy, advanced hypothyroidism with neuropathy, or neurotoxic exposures unrelated to cancer care), active rheumatologic or neuromuscular disorders affecting the upper limb or neck function, current pregnancy, inability to cooperate with examination due to cognitive impairment or severe psychiatric illness, and incomplete medical records for key treatment variables required for the planned analyses.

Procedure:

After eligibility screening and consent, demographic and clinical data were obtained through interview and medical record review, including age, body mass index, menopausal status, dominant side, comorbidities, smoking status, and relevant medication history. Cancer- and treatment-related variables were extracted in a structured fashion, including laterality of breast cancer, type of breast surgery, axillary procedure (sentinel lymph node biopsy versus axillary lymph node dissection), receipt of chemotherapy, endocrine therapy (including aromatase inhibitor exposure), and radiotherapy characteristics with particular attention to exposure of supraclavicular regional nodal fields versus breast/chest wall irradiation alone. Time since completion of radiotherapy was recorded and categorized for survivorship analyses, and the clinically irradiated side was documented to enable laterality-based comparisons of symptoms and signs.

Clinical phenotyping focused on cervicothoracic musculoskeletal and neurological outcomes using standardized bedside assessment. Musculoskeletal variables included the presence of myofascial pain syndrome and active trigger points in periscapular muscles (with emphasis on upper trapezius and levator scapulae), objective limitation of cervical range of motion (flexion, extension, and rotation assessed by structured examination), postural alterations with emphasis on increased thoracic kyphosis assessed clinically, and scapular dyskinesis evaluated by observation of dynamic scapular motion during standardized upper-limb elevation tasks. Neurological variables included symptoms and signs consistent with cervical radiculopathy (dermatomal sensory disturbance, motor weakness patterns, and provocative clinical signs) and features suggestive of radiation-induced brachial plexopathy (motor deficits, sensory loss patterns, and clinical constellation consistent with plexus involvement). Neuropathic pain was assessed using the Douleur Neuropathies 4 (DN4) questionnaire, and neuropathic pain was defined using the established diagnostic threshold (DN4 score of 4 or higher). For each clinical condition, severity was categorized into mild, moderate, or severe based on participant-reported functional interference using a structured severity rubric, and laterality was recorded as ipsilateral, contralateral, or bilateral relative to the treated breast and radiotherapy field.

Statistical analysis:

Because the dataset was assumed to be normally distributed, continuous variables were summarized as mean ± standard deviation and compared using independent-samples t tests (or one-way analysis of variance when more than two groups were analyzed), while categorical variables were reported as frequency (percentage) and compared using the chi-square test (or Fisher's exact test when expected cell counts were small). Prevalence estimates were presented with 95% confidence intervals. Univariable logistic regression was used to evaluate associations between candidate predictors and the presence of cervicothoracic disorders, and variables with clinical relevance and/or a prespecified screening threshold were entered into multivariable logistic regression to estimate adjusted odds ratios with 95% confidence intervals. Model adequacy was evaluated using standard diagnostics (including assessment of multicollinearity and goodness-of-fit), and all tests were two-tailed with statistical significance set at $P<0.05$.

Ethical considerations:

The study protocol was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences (Approval code: IR.TBZMED.REC.1400.1157).

All participants provided written informed consent prior to enrollment. Data were collected confidentially, stored in a de-identified format, and used solely for research purposes in accordance with institutional and international principles for research involving human participants.

Results

As detailed in Table 1, the evaluated cohort comprised 175 female breast cancer survivors with a mean age of 52.8 plus minus 9.4 years and an average body mass index of 27.6 plus minus 4.2 kg/m^2. Surgical management predominantly involved modified radical mastectomy in 59.4% of patients, whereas axillary lymph node dissection was conducted in 47.4% of cases. The median post-radiotherapy survivorship duration reached 36.5 months (interquartile range: 24.0 to 54.0 months). Regarding therapeutic irradiation, the delivered mean cumulative dose was 50.4 plus minus 3.2 Gy, with 42.3% of the cohort receiving extended supraclavicular or axillary apex nodal irradiation in addition to breast or chest wall fields, and 64.0% undergoing supplementary tumor bed boost delivery.

Table 1. Demographic, clinicopathologic, and therapeutic profile of the cohort (N = 175)

Parameter	Summary Statistic
Chronological age (years), mean ± SD	52.8 ± 9.4
Body mass index (kg/m²), mean ± SD	27.6 ± 4.2
Primary tumor laterality, n (%)	-
Left hemisphere	94 (53.7%)
Right hemisphere	81 (46.3%)
Primary surgical management, n (%)	-
Modified radical mastectomy	104 (59.4%)
Breast-conserving procedure	71 (40.6%)
Axillary nodal intervention, n (%)	-
Sentinel lymph node sampling	92 (52.6%)
Complete axillary dissection	83 (47.4%)
Adjuvant systemic regimens, n (%)	-
Cytotoxic chemotherapy	142 (81.1%)
Endocrine intervention	131 (74.9%)
Molecular targeted therapy	24 (13.7%)
Post-irradiation interval (months), median (IQR)	36.5 (24.0–54.0)
Cumulative radiation dose (Gy), mean ± SD	50.4 ± 3.2
Target volume delineation, n (%)	-
Breast or chest wall exclusively	101 (57.7%)
Comprehensive nodal irradiation included	74 (42.3%)
Tumor bed boost administration, n (%)	112 (64.0%)

Abbreviations: SD, standard deviation; IQR, interquartile range; Gy, Gray.

As demonstrated in Table 2, clinical phenotyping revealed an extensive burden of both musculoskeletal and neurological sequelae in this survivorship cohort, with musculoskeletal derangements predominating in frequency. Specifically, myofascial pain syndrome characterized by active myofascial trigger points within the upper trapezius and levator scapulae musculature represented the most prevalent morbid manifestation, documented in 50.3% of participants (95% CI:42.9-57.7%), accompanied by objective limitations in cervical range of motion in 43.4% (95% CI:36.2-50.9%) and scapular dyskinesis in 39.4% (95% CI:32.4-46.9%). Among neurological complications, paraspinal neuropathic pain affected 28.0% of patients (95% CI:21.7-35.2%), whereas cervical radiculopathy and radiation-induced brachial plexopathy were observed in 18.9% (95% CI:13.7-25.3%) and 9.7% (95% CI:6.0-15.2%) of cases, respectively. Furthermore, severity grading indicated that moderate-to-severe impairment constituted the majority of symptomatic presentations across all categories, with morbidities predominantly localized ipsilateral to the irradiated breast or chest wall.

Table 2. Prevalence, Phenotypic Spectrum, Severity Grading, and Anatomical Distribution of Cervicothoracic Impairments in Breast Cancer Survivors

Clinical Entity / Phenotype	Overall, Burden, n (%, 95% CI)	Mild, n (%)	Moderate, n (%)	Severe, n (%)	Ipsilateral, n (%)	Bilateral, n (%)
Musculoskeletal dysfunctions	-	-	-	-	-	-
Myofascial pain syndrome	88 (50.3%, 42.9–57.7%)	26 (29.5%)	44 (50.0%)	18 (20.5%)	69 (78.4%)	19 (21.6%)
Scapulothoracic dyskinesis	69 (39.4%, 32.4–46.9%)	22 (31.9%)	35 (50.7%)	12 (17.4%)	58 (84.1%)	11 (15.9%)
Cervical motion restriction	76 (43.4%, 36.2–50.9%)	28 (36.8%)	36 (47.4%)	12 (15.8%)	54 (71.1%)	22 (28.9%)
Cervicothoracic postural deviation	61 (34.9%, 28.1-42.3%)	25 (41.0%)	27 (44.3%)	9 (14.8%)	18 (29.5%)	43 (70.5%)
Neurological dysfunctions	-	-	-	-	-	-
Cervical compressive radiculopathy	33 (18.9%, 13.7-25.3%)	11 (33.3%)	16 (48.5%)	6 (18.2%)	27 (81.8%)	6 (18.2%)

Radiation-induced brachial plexopathy	17 (9.7%, 6.0-15.2%)	4 (23.5%)	9 (52.9%)	4 (23.5%)	16 (94.1%)	1 (5.9%)
Paraspinal neuropathic symptom complex	49 (28.0%, 21.7–35.2%)	14 (28.6%)	23 (46.9%)	12 (24.5%)	38 (77.6%)	11 (22.4%)

Abbreviations: CI, confidence interval; ROM, range of motion.

Row percentages for severity and laterality subgroups are calculated based on the number of affected patients within each diagnostic category.
As detailed in Table 3, multivariable logistic regression analyses identified several independent risk factors significantly associated with an increased susceptibility to cervicothoracic musculoskeletal and neurological disorders among the evaluated breast cancer survivors. Specifically, the inclusion of supraclavicular nodal irradiation emerged as a prominent predictor, nearly tripling the adjusted odds of morbidity occurrence (adjusted odds ratio =2.87, 95% confidence interval: 1.44 to 5.72, P=0.003). Furthermore, undergoing axillary lymph node dissection compared to sentinel lymph node biopsy (adjusted odds ratio =2.18, 95% confidence interval: 1.11 to 4.29, P=0.024) and incremental increases in mean paraspinal or vertebral radiation dose (adjusted odds ratio =1.69 per 5 Gy increment, 95% confidence interval: 1.13 to 2.54, P=0.011) maintained independent statistical significance after controlling for potential confounders, whereas chronological age and body mass index exhibited no significant association.

Table 3. Univariable and Multivariable Binary Logistic Regression Analyses Identifying Determinants of Cervicothoracic Disorders

Covariate	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Chronological age (per 1-year increment)	1.02 (0.98-1.06)	0.312	1.01 (0.97-1.05)	0.654
Body mass index (per 1 kg/m² increment)	1.05 (0.96-1.15)	0.284	1.03 (0.93-1.14)	0.578
Axillary lymph node dissection (ref: SLNB)	2.41 (1.29-4.52)	0.006	2.18 (1.11-4.29)	0.024
Supraclavicular nodal irradiation (ref: localized)	3.25 (1.71-6.19)	0.001	2.87 (1.44-5.72)	0.003
Mean paraspinal/vertebral dose (per 5 Gy increment)	1.84 (1.26-2.69)	0.002	1.69 (1.13-2.54)	0.011
Interval since radiotherapy completion (per year)	1.14 (0.99-1.31)	0.068	1.09 (0.94-1.27)	0.256

Abbreviations: OR, odds ratio; CI, confidence interval; SLNB, sentinel lymph node biopsy; Gy, Gray; ref, reference category.

As illustrated in Figure 1, the comparative analysis across therapeutic radiation fields reveals a consistently elevated prevalence of both musculoskeletal and neurological disorders among breast cancer survivors whose treatment regimens included supraclavicular nodal irradiation compared to those receiving breast or chest wall radiotherapy alone. The greatest disparity was observed in myofascial pain syndrome, affecting 62.2% of individuals in the supraclavicular cohort versus 41.5% in the localized field group, followed by cervical range of motion limitation (55.4% versus 34.7%) and scapular dyskinesis (51.4% versus 30.7%). Similarly, neurological sequelae demonstrated substantial divergence, with paraspinal neuropathic pain reaching 37.8% and cervical radiculopathy manifesting in 27.0% of patients exposed to extended supraclavicular volumes, compared to 20.8% and 12.9% among patients treated with localized fields, respectively.

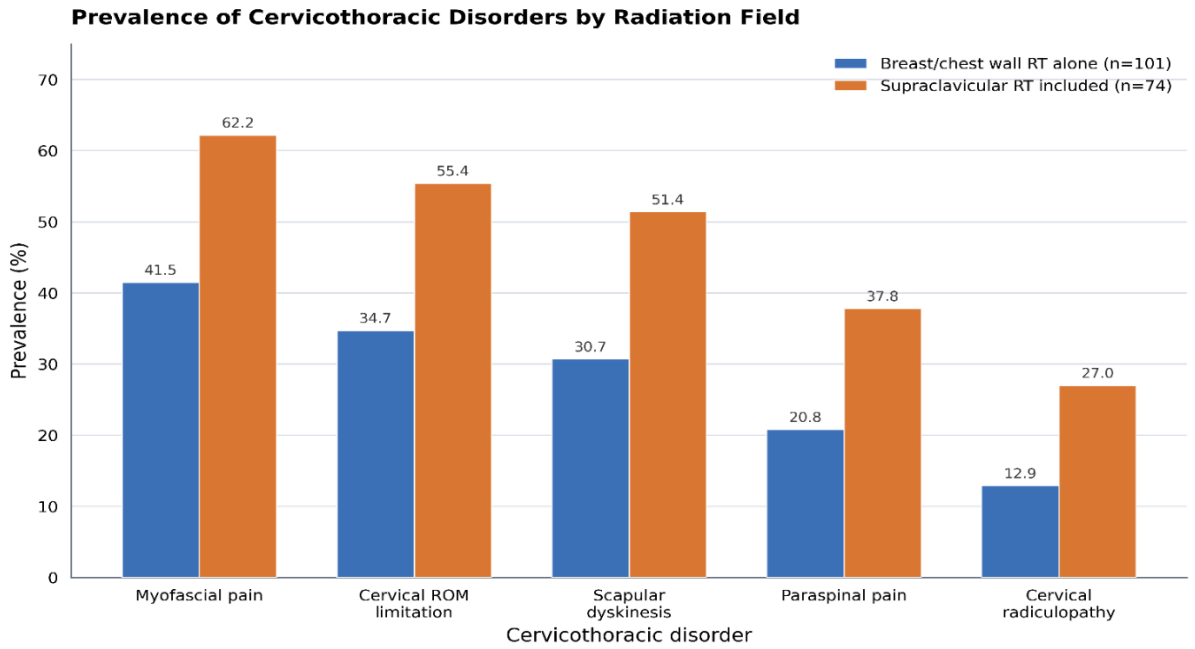


Figure 1. Comparative prevalence rates of cervicothoracic musculoskeletal and neurological disorders stratified by radiation treatment field design in breast cancer survivors

Discussion

In this cohort of 175 breast cancer survivors, cervicothoracic musculoskeletal complaints were more frequent than neurological disorders. Myofascial pain affected 50.3% of participants, cervical motion restriction 43.4%, and scapulothoracic dyskinesis 39.4%; paraspinal neuropathic symptoms affected 28.0%. Each of the five disorders compared in Figure 1 was more prevalent among patients who received supraclavicular irradiation than among those treated to the breast or chest wall alone. In the multivariable model, supraclavicular irradiation, axillary lymph node dissection, and higher mean paraspinal or vertebral dose remained associated with the modeled cervicothoracic outcome. These findings suggest that both treatment extent and local radiation exposure warrant attention during survivorship assessment, while leaving the direction of causation unresolved [10].

The predominance of myofascial pain is biologically plausible because breast cancer treatment can affect tissues that contribute to neck and shoulder movement. Surgery may alter muscle recruitment and shoulder mechanics, whereas irradiation can produce persistent changes in soft-tissue compliance. Protective movement in response to pain may further increase loading of the upper trapezius and levator scapulae. Over time, restricted movement, muscle guarding, and altered scapular control could reinforce one another, producing symptoms remote from the original treatment site. Nevertheless, the present examination cannot establish when myofascial symptoms began or determine the relative contributions of surgery, irradiation, pre-existing musculoskeletal disease, and subsequent changes in activity [11].

Cervical motion restriction and scapulothoracic dyskinesis were also common, affecting 43.4% and 39.4% of participants, respectively. These findings may reflect linked aspects of upper-quarter dysfunction rather than wholly separate complications. Shoulder discomfort can change scapular positioning during arm elevation, while reduced mobility of the shoulder girdle may prompt compensatory neck movement. Tissue tightness, pain-related avoidance, and deconditioning could contribute to both patterns. Their frequent ipsilateral presentation is consistent with a treatment-related contribution, although laterality alone does not establish its cause. The bilateral predominance of postural deviation further suggests that some findings may arise from whole-body adaptation rather than an isolated injury confined to the irradiated side [12].

Neurological findings require a more differentiated interpretation. Paraspinal neuropathic symptoms were reported in 28.0% of participants, cervical radiculopathy in 18.9%, and radiation-induced brachial plexopathy in 9.7%. Although these categories can share pain, sensory disturbance, or weakness, they do not necessarily have the same anatomical origin. Cervical nerve-root disease may result from degenerative or compressive processes, whereas plexopathy involves a different segment of the neural pathway. Myofascial pain may also mimic or coexist with neuropathic symptoms. Consequently, the observed frequencies should not be taken as evidence that every neurological presentation was caused by irradiation. Clear diagnostic criteria and, where clinically indicated,

electrodiagnostic or imaging evaluation are important for distinguishing these disorders [13].

Across all seven diagnostic categories, moderate or severe cases outnumbered mild cases among affected participants. This pattern indicates that the recorded impairments were not limited to minor examination findings and may have been relevant to everyday function. At the same time, the severity columns describe the distribution within each affected subgroup, not the proportion of the entire cohort with moderate-to-severe disease. Differences in the clinical meaning of severity across disorders also limit direct comparison: restricted motion, pain, and suspected plexopathy cannot be placed on a single scale merely by assigning the same labels. Future work should report the instruments and thresholds used for each diagnosis and relate severity to patient-reported disability [14].

The higher prevalence of each plotted disorder in the supraclavicular irradiation group is consistent with the broader anatomical exposure associated with regional nodal treatment. Compared with localized breast or chest wall irradiation, supraclavicular fields may bring additional cervical and shoulder-girdle tissues closer to treated volumes. This offers a plausible explanation for the observed differences in myofascial pain (62.2% versus 41.5%) and cervical motion restriction (55.4% versus 34.7%). However, treatment fields are selected according to clinical indications. Patients receiving regional nodal irradiation may therefore differ in disease extent, surgery, systemic therapy, or baseline vulnerability. The between-group differences should be interpreted as associations, not as an estimate of the causal effect of adding a supraclavicular field [15].

Supraclavicular irradiation retained the strongest reported association in the multivariable analysis (adjusted odds ratio, 2.87; 95% confidence interval, 1.44-5.72). This result supports the relevance of treatment-field design beyond the other covariates included in the model, but it does not establish a mechanism for any individual disorder. Nor does the odds ratio indicate that a patient's probability of impairment is nearly three times higher. Interpretation also depends on how the binary outcome, "cervicothoracic disorders," defined: a composite of heterogeneous conditions may conceal important differences in their relationships with radiation fields. Disorder-specific analyses, if adequately powered and specified in advance, would help determine whether the association is driven primarily by musculoskeletal symptoms, neurological findings, or both [16].

Axillary lymph node dissection was independently associated with the modeled outcome compared with sentinel lymph node biopsy (adjusted odds ratio, 2.18; 95% confidence interval, 1.11-4.29). More extensive axillary surgery may contribute to shoulder stiffness, altered movement, sensory disturbance, or pain, providing a plausible route to subsequent cervicothoracic complaints. It may also mark a different course of cancer treatment, including greater likelihood of regional irradiation. Although the regression model included both surgery and irradiation, adjustment for a limited set of measured variables cannot eliminate all differences between treatment groups. The finding is best understood as evidence that surgical history should be considered alongside radiation exposure when evaluating survivorship symptoms [17].

Mean paraspinal or vertebral dose was associated with higher adjusted odds of the modeled disorder outcome for each 5 Gy increment (adjusted odds ratio, 1.69; 95% confidence interval, 1.13-2.54). A dose-related association is of particular interest because it is more spatially specific than a comparison based solely on field designation. Nevertheless, mean dose is an incomplete description of exposure: it may obscure localized high-dose regions and does not identify which muscle, nerve, or bony structure is most relevant. Dose and supraclavicular field inclusion may also be closely related. Replication using clearly delineated anatomical structures, dose-volume measures, and an explicit assessment of correlation among predictors would strengthen interpretation of this result [18].

Age, body mass index, and time since radiotherapy completion were not statistically significant in the adjusted model. Their nonsignificant estimates should not be interpreted as proof that they have no clinical role. With 175 participants, the precision of multivariable estimates depends on the number of patients meeting the modeled outcome, which was not reported alongside the regression table. Convenience sampling may also limit how well this cohort represents the wider survivor population. Baseline symptoms, rehabilitation exposure, occupational demands, and comorbid spinal disease not accounted for in the presented model. These limitations leave room for residual confounding and restrict the extent to which the observed associations can be generalized [19].

The study's descriptive clinical assessment and treatment-dose analysis together identify a substantial burden of potentially actionable cervicothoracic symptoms. Its cross-sectional design, however, cannot determine whether the symptoms arose after treatment or progressed with increasing exposure. Importantly, the reported outcomes do not include imaging-confirmed vertebral column degeneration; the present findings therefore cannot substantiate that outcome in the proposed article title. A longitudinal study with pretreatment assessments, standardized neurological diagnoses, serial spinal imaging, and anatomically resolved dosimetry needed to examine degeneration and test temporal dose–response relationships. On the evidence presented here, the defensible

conclusion is that treatment extent and paraspinal dose are associated with cervicothoracic morbidity and merit further investigation [20].

Conclusion

Radiation therapy and surgical interventions for breast cancer significantly increase the burden of cervicothoracic musculoskeletal and neurological morbidities. Optimizing radiation field design and minimizing paraspinal exposure are crucial to improving long-term survivorship quality of life.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

References

[1] Amsterdam, E. A., Wenger, N. K., Brindis, R. G., et al. (**2014**). 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. *Circulation*, 130(25), e344-e426.

[2] Collet, J. P., Thiele, H., Barbato, E., et al. (**2021**). ESC Guidelines for acute coronary syndromes. *European Heart Journal*, 42(14), 1289-1367.

[3] Hosseinpoor, S., & Yousef, R. M. (**2027**). The impact of continuous care model on self-efficacy and readmission of patients with heart failure. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, 6(1), 1–14.

[4] Rahi, D., Ghotbi, N., Nosratabadi, R., Sayyari, M., & Sabzevari, B. (**2023**). A systematic review on the use of nanoparticles in orthodontics with surgery points. *The Seybold Report*, 18(6), 1542–1559.

[5] Rahi, D., Abbassi, S., & Tajbakhsh, N. (**2024**). Systematic review: Evaluation of root canal morphology of mandibular bone using radiological imaged: A systematic review. *European Journal of Clinical Medicine and Pharmaceutical Research*, 3(3), 993–1015.

[6] Rezai, M., Amiri, H., Delbari, D., Keshmiri, Y. S., Aghdam, H., Zohri, D., & Hesam, R. (**2019**). Comparison of intramuscular injection of ketorolac and conventional treatment in the field of cost-effectiveness, length of stay and pain relief in patients admitted to the emergency department with renal colic. *Bali Medical Journal*, 8(1), 83–87.

[7] Fard, M M , Kasnavieh, S M H , Hessam, R , Ghoddusi, M and Shokri, A . (**2025**). Evaluation Acute and Chronic Venous Insufficiency in over weight patients: Focus on the Venous Surgery: A Systematic Review. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *1*(12), 405-414.

[8] Hosseini Kasnavieh, S. M., Shaker, S. H., Milanifard, M., Hessam, R., & Ghadesi, M. (**2026**). Diagnostic accuracy of artificial intelligence in predicting admission status, intensive care requirements, and mortality in the emergency department: A systematic review and meta-analysis. *Medical Journal of the Islamic Republic of Iran.*

[9] Rezai, M., Javdani Esfehani, K., Valipour, A. M., Hessam, R., Soleymani, N., Zarei Jelyani, N., & Javan, A. (**2026**). Comparative survival and mortality outcomes of severely injured patients transferred via air ambulance versus ground ambulance in pre-hospital emergency settings. *European Journal of Scientific Research and Reviews*, 4(1), 95–111.

[10] Moghadam, A M. (**2026**). Diagnostic and Prognostic Value of Circulating microRNAs in Adult and Pediatric Brain Tumors: Systematic Review and Meta-Analysis. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(3), 156-167.

[11] Moghadam, A M. (**2025**). Comparative Outcomes of Preoperative and Postoperative Stereotactic Radiosurgery in Patients with Brain Metastases: Systematic Review and Meta-Analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *1*(11), 392-402.

[12] Moghadam, A M. (**2026**). Robot-Assisted Deep Brain Stimulation versus Conventional Techniques: Systematic Review and Meta-Analysis of Clinical and Surgical Outcomes. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(2), 147-155.

[13] Mehrasa, P and Eghdam Zamiri, R. (**2026**). Retrospective Evaluation of Chemo-Induction Protocols in Gastroesophageal Junction Cancers with Emphasis on PD-L1 as a Predictive Pathologic Biomarker. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(4), 276-284.

[14] Sadeghzadeh, A. (**2026**). Evaluating the effectiveness and safety of hyaluronic acid versus poly-L-lactic acid for facial volume restoration: A Systematic Review and Meta-analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *2*(2), 102-113.

[15] Hashemloo, A., Milanifard, M. (**2025**). Dermal Fillers: Types, Indications, and Complications Materials de Relleno: Typos, Indications Complications. Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research, 1(6), 161-170

[16] Motaqi, M, Afrand, M and Ghanjal, A. (**2022**). Care and Management of Pain in Patients with Musculoskeletal Pain during the Covid-19

Epidemic. *International Journal of Musculoskeletal Pain Prevention*, 7(1), 622-626.
[17] Motaqi, M , Ghanjal, A and Afrand, M . (**2022**). Treadmill Exercise and its Effect on Rehabilitation of Patients after Ischemic strok: A Narrative Study. *International Journal of Musculoskeletal Pain Prevention*, 7(3), 730-740.
[18] Motaqi, M , Samadi, M , Ghanjal, A and Afrand, M . (**2022**). A New Approach to Evaluate of Musculoskeletal Pain. *International Journal of Musculoskeletal Pain Prevention*, 7(4), 781-787.
[19] Samimi, A. (**2025**). Assessment of Risks Arising from Neuropsychological Crises in Cardiac Patients Using FMEA. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR), 1*(7), 196-203.
[20] Samimi, A. (**2025**). Risk Assessment in Hospitals Using the FMEA Method: A Data-Driven Analysis for Patient Safety Improvement. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR), 1*(6), 180-187.