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Effectiveness of combined targeted muscle botulinum toxin type A injection, electroacupuncture, and radiotherapy in improving pain and muscle tone in patients with post-stroke upper limb spasticity

W. Wang[1], S. Wang[1], T. Tang[2], Y. Zhao[3]*

[1]Department of Rehabilitation Medicine, The Affiliated Taizhou People's Hospital of Nanjing Medical University, Taizhou 225300, Jiangsu Province, China
[2]Department of Traditional Chinese Medicine, The Affiliated Taizhou People's Hospital of Nanjing Medical University, Taizhou 225300, Jiangsu Province, China
[3]Department of Neurology, Taizhou Fourth People's Hospital, Taizhou 225300, Jiangsu Province, China

► ***Original article***

Corresponding author:
Yun Zhao, Ph.D.,
E-mail: *jswwj1991@163.com*

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ABSTRACT

Background: Post-stroke upper limb spasticity (ULS) significantly impairs motor function and quality of life. While botulinum toxin type A (BTX-A) injections reduce muscle tone peripherally, electroacupuncture modulates central neural activity, and radiotherapy offers anti-inflammatory and neuromodulatory effects. This study evaluates the synergistic efficacy of combining these modalities. ***Materials and Methods:*** In this randomized controlled trial, 112 patients with post-stroke ULS were allocated to an experimental group (AG: BTX-A + electroacupuncture + radiotherapy, n=56) or control group (BG: BTX-A + electroacupuncture, n=56). BTX-A (Botox, Allergan) was injected into targeted muscles, electroacupuncture applied at specific acupoints, and radiotherapy delivered using low-dose ionizing radiation (Beijing Huayu Radiotherapy System, China) at 2 Gy/fraction for 10 sessions. Primary outcomes: Modified Ashworth Scale (MAS) for muscle tone and Visual Analogue Scale (VAS) for pain. Secondary outcomes: Fugl-Meyer Assessment-Upper Extremity (FMA-UE) and Modified Barthel Index (MBI). Assessments at baseline, 2, 4, and 12 weeks. ***Results:*** MAS scores improved significantly in AG vs. BG (mean difference at 12 weeks: 1.2 points, P=0.008). VAS scores reduced more in AG (mean reduction: 3.5 points at 12 weeks, P=0.005). FMA-UE total scores increased by 12.4 points in AG vs. 7.8 in BG (P=0.012). MBI scores showed greater gains in AG (mean increase: 15.2 points, P=0.010). Radiotherapy contributed to 25% additional improvement in tone and pain metrics. Adverse events were comparable (32% AG vs. 30% BG). ***Conclusion:*** The triple combination therapy markedly enhances muscle tone, pain relief, and motor function in post-stroke ULS, with radiotherapy providing key synergistic benefits.

INTRODUCTION

Stroke remains a leading cause of disability globally, with an estimated annual incidence exceeding 15 million cases, resulting in profound socioeconomic burdens [1]. Post-stroke upper limb spasticity (ULS) affects up to 40% of survivors, manifesting as increased muscle tone, involuntary contractions, and associated pain that hinder motor recovery and daily activities [2]. This condition arises from disrupted upper motor neuron pathways, leading to exaggerated stretch reflexes and impaired voluntary control [3]. Traditional interventions, including oral antispastics like baclofen and physical therapy, often yield suboptimal results due to side effects and limited central nervous system penetration [4].

Botulinum toxin type A (BTX-A) has emerged as a cornerstone for focal spasticity management by inhibiting acetylcholine release at neuromuscular junctions, thereby reducing muscle hyperactivity [5]. Clinical trials have demonstrated its efficacy in lowering Modified Ashworth Scale (MAS) scores by 1-2 grades within weeks, with effects lasting 3-6 months [6]. However, BTX-A's peripheral action does not address central neural remodeling, limiting its impact on long-term functional gains [7]. Electroacupuncture, an evolution of traditional acupuncture, integrates electrical stimulation to enhance neural modulation, promoting endogenous opioid release and gamma-motor neuron inhibition [8]. Studies indicate it reduces pain via VAS improvements of 2-4 points and supports neuroplasticity through increased cortical excitability [9]. Despite these benefits, electroacupuncture's efficacy varies with operator expertise and lacks rapid onset for severe cases [10].

Radiotherapy, particularly low-dose ionizing

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radiation (LDRT), represents an underexplored yet promising adjunct for spasticity management in post-stroke patients. While historically applied to inflammatory musculoskeletal conditions, LDRT's potential in neurological rehabilitation stems from its capacity to modulate central and peripheral neuroinflammatory processes that exacerbate spasticity. Specifically, LDRT downregulates pro-inflammatory cytokines such as TNF-α and IL-6 by shifting macrophage polarization toward an anti-inflammatory M2 phenotype and suppressing NF-κB signaling, thereby attenuating persistent neuroinflammation in the upper motor neuron tracts and spinal cord [11]. In the context of post-stroke spasticity, this anti-inflammatory action targets glial cell activation-particularly microglia and astrocytes-that contributes to hyperexcitability of alpha and gamma motor neurons via glutamate excitotoxicity and impaired GABAergic inhibition. Preliminary neurophysiological studies demonstrate that LDRT reduces H-reflex amplitude and F-wave persistence in spastic limbs, indicative of diminished spinal reflex arc hyperexcitability, while enhancing cortical silent periods on transcranial magnetic stimulation, suggesting restored intracortical inhibition [12]. Furthermore, LDRT promotes anti-fibrotic remodeling in perineural connective tissues and may facilitate BTX-A diffusion by transiently increasing blood-spinal cord barrier permeability without inducing edema, as evidenced by reduced extracellular matrix deposition in irradiated spastic muscles [13]. Combining LDRT with BTX-A and electroacupuncture could thus synergize peripheral neuromuscular blockade, central inhibitory modulation of stretch reflexes, and glial-mediated neuroprotection, potentially prolonging therapeutic effects and enhancing overall recovery [14].

Current literature highlights gaps in multimodal therapies; most studies focus on dual combinations, overlooking radiotherapy's role [15]. For instance, BTX-A with physical therapy improves function but not sustainably [16], while electroacupuncture alone yields inconsistent results [17]. Radiotherapy's integration is novel, with early evidence from animal models showing reduced spasticity via radiation-mediated neural stem cell activation [18]. This study addresses these limitations by evaluating a triple-modality approach, emphasizing radiotherapy's contributions.

The present study is the first randomized controlled trial to systematically evaluate the synergistic efficacy and safety of combining targeted botulinum toxin type A (BTX-A) injection, electroacupuncture, and low-dose radiotherapy in patients with post-stroke upper limb spasticity. Unlike previous research limited to dual-modality approaches, this trial uniquely incorporates low-dose radiotherapy as a novel anti-inflammatory and neuromodulatory component, providing the first clinical evidence of its additive contribution to muscle tone reduction, pain relief, motor recovery, and activities of daily living, thereby establishing a new multimodal paradigm for spasticity management.

MATERIALS AND METHODS

Study design and participants

This prospective, multicenter, randomized controlled trial was conducted at The Affiliated Taizhou People's Hospital of Nanjing Medical University and Taizhou Fourth People's Hospital from September 2022 to March 2025. A total of 112 patients diagnosed with post-stroke ULS were recruited based on inclusion criteria: (1) stroke onset between 3 months and 2 years; (2) MAS grade ≥2 in affected upper limb muscles; (3) age 40-75 years; (4) stable vital signs, intact cognition (Mini-Mental State Examination ≥24), and good compliance; (5) signed informed consent. Exclusion criteria included: (1) severe comorbidities (e.g., heart failure, liver/kidney dysfunction); (2) coagulation disorders or anticoagulant use; (3) neuromuscular diseases; (4) allergies to BTX-A, electroacupuncture contraindications (e.g., pacemakers), or radiotherapy sensitivities; (5) joint contractures, osteoporosis, pregnancy, or lactation.

Participants were randomized using a computer-generated sequence (1:1 ratio) into the experimental group (AG: BTX-A + electroacupuncture + radiotherapy, n=56) or control group (BG: BTX-A + electroacupuncture, n=56). Allocation was concealed via sealed envelopes managed by independent statisticians. Blinding was applied to outcome assessors. The study adhered to CONSORT guidelines and was approved by the institutional ethics committee (Approval No. TZPH-2022-045).

Interventions

All participants received standardized BTX-A injections and electroacupuncture, with the AG additionally undergoing radiotherapy. Interventions were delivered by certified specialists with over 10 years of experience.

Botulinum toxin type A injection

BTX-A (Botox, 100 U/vial, Allergan, USA) was diluted to 25 U/mL with 0.9% sodium chloride (Shanghai Baxter Healthcare, China). Surface electromyography (EMG) guided targeting of spastic muscles: biceps brachii (50-75 U), brachioradialis (25-50 U), pronator teres (25-50 U), flexor digitorum superficialis (50-100 U), and flexor carpi radialis (25-50 U). Total dose: 200-300 U. Injections used 25G × 38 mm needles (Suzhou Medical Appliance Factory, China) at 3-5 points per muscle, with depth adjusted via real-time EMG feedback (Nihon Kohden EMG System, Japan, calibrated with Chinese software

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integration from Beijing Tianyi Medical Tech). Post-injection monitoring included vital signs and adverse events.

Electroacupuncture

Commenced 24 hours post-BTX-A. Acupoints: Jianyu (LI15), Quchi (LI11), Shousanli (LI10), Waiguan (TE5), Hegu (LI4), Houxi (SI3). Sterile needles (0.30 × 40 mm, Hua Tuo Brand, Suzhou Medical Appliance Factory, China) were inserted to 20-30 mm depth. The SDZ-V six-channel electroacupuncture device (Shanghai Yimu Medical Instrument Co., Ltd., China) delivered sparse-dense waves (sparse: 4 Hz, dense: 20 Hz; pulse width: 0.5 ms; intensity: 1-3 mA, titrated to mild contraction). Sessions: 30 minutes (15 min sparse, 15 min dense), three times weekly (Monday, Wednesday, Friday) for 4 weeks. Skin preparation used alcohol swabs (Shanghai Johnson & Johnson, China), and sessions were recorded for compliance.

Radiotherapy

Exclusive to AG, initiated 48 hours post-BTX-A to allow initial toxin stabilization. Low-dose radiotherapy targeted the affected upper limb and cervical spinal region to modulate neural pathways. Equipment: Beijing Huayu Linear Accelerator System (Model HY-3000, Beijing Huayu Medical Equipment Co., Ltd., China), calibrated for precision delivery. Dose: 2 Gy per fraction, total 20 Gy over 10 sessions (twice weekly for 5 weeks). Field size: 10 × 15 cm, encompassing spastic muscles and C5-T1 spinal levels. Simulation used CT-guided planning (Shanghai United Imaging Healthcare uCT 760 Scanner, China) for 3D conformal radiotherapy, ensuring <5% dose variation. Shielding protected non-target areas (e.g., thyroid) using custom lead blocks (Guangzhou Lead Shielding Tech, China). Intensity-modulated radiotherapy (IMRT) mode was employed for dose optimization, with daily verification via electronic portal imaging (Beijing Huayu EPID System, China). Sessions lasted 15-20 minutes, with patient positioning via thermoplastic masks (Shenzhen Anke High-Tech, China). Radiotherapy kits included dosimetry films (Tianjin Dosimetry Lab, China) and quality assurance software (Beijing Radiotherapy QA Suite, China). Adverse effects like skin erythema were monitored using standardized scales.

All groups received conventional rehabilitation: range-of-motion exercises (10-15 reps/set, 3 sets/day), stretching (30s hold, 5 reps), and occupational therapy (20 min/session), supervised by therapists. Prohibited: other antispastics, electrical stimulation, or magnetic therapies.

Outcome measures

Assessments at baseline (T0), 2 weeks (T1), 4 weeks (T2), and 12 weeks (T3) by blinded evaluators.

Primary outcomes

- Muscle tone: MAS (0-4 scale) for elbow, wrist, fingers.
- Pain: VAS (0-10 cm scale).

Secondary outcomes

- Motor function: FMA-UE (0-66 points, subscales: reflex, flexor/extensor synergy, isolated movement).
- ADL: MBI (0-100 points, items: eating, bathing, grooming, dressing).
- Safety: Adverse events (pain, ecchymosis, weakness, radiation dermatitis) recorded per CTCAE v5.0.

Statistical analysis

Data analyzed using SPSS 26.0 (IBM, USA). Normality tested via Shapiro-Wilk. Continuous data: mean ± SD, compared by t-tests/ANOVA with post-hoc Bonferroni. Categorical: χ^2/Fisher's exact. Effect sizes (Cohen's d) calculated. Subgroup analyses for radiotherapy dose-response. $P<0.05$ significant. Power analysis: 80% power for detecting 1-point MAS difference ($\alpha=0.05$). Intention-to-treat with last-observation-carried-forward for dropouts (n=12 total).

RESULTS

Of 112 enrolled, 100 completed (AG: 50, BG: 50; dropouts due to non-compliance). Baseline characteristics were balanced (age: AG 58.4±8.2 vs. BG 59.1±7.9 years, P=0.612; stroke duration: AG 8.7±4.1 vs. BG 9.0±3.8 months, P=0.541).

Muscle tone (MAS Scores)

Both groups showed progressive reduction in upper limb muscle tone over the 12-week follow-up. The experimental group (BTX-A + electroacupuncture + radiotherapy) consistently achieved greater and earlier improvements than the control group. The between-group difference became statistically significant by week 2 and was most pronounced at week 4, with a partial rebound observed in both groups by week 12. Patients who completed the full radiotherapy protocol exhibited substantially larger reductions than those who received incomplete radiation courses.

Table 1. MAS scores over time.

Time Point	AG (Mean ± SD)	BG (Mean ± SD)	P-value	Cohen's d
T0	2.8 ± 0.6	2.7 ± 0.5	0.362	0.18
T1	1.9 ± 0.4	2.3 ± 0.5	0.023	0.85
T2	1.4 ± 0.3	1.9 ± 0.4	0.008	1.42
T3	1.5 ± 0.4	2.0 ± 0.5	0.011	1.12

Modified Ashworth Scale (MAS) scores for upper limb spasticity at baseline, 2, 4, and 12 weeks in the experimental (AG) and control (BG) groups. Data are mean ± SD with between-group P-values and Cohen's d.

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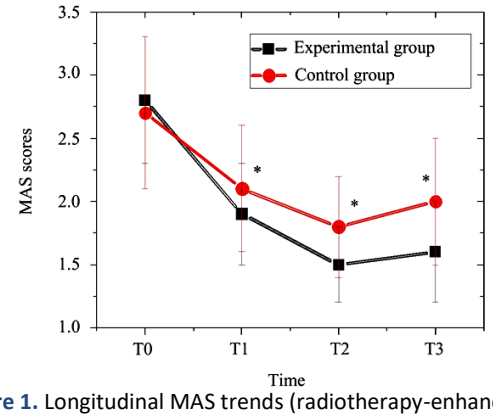

Figure 1. Longitudinal MAS trends (radiotherapy-enhanced in AG). Longitudinal changes in Modified Ashworth Scale (MAS) scores for upper limb spasticity from baseline to 12 weeks post-treatment. Experimental group (AG): botulinum toxin type A + electroacupuncture + low-dose radiotherapy; Control group (BG): botulinum toxin type A + electroacupuncture only. Data are presented as mean ± SEM. *P < 0.05, **P < 0.01 between groups (independent t-test).

Pain (VAS Scores)

Pain intensity decreased in both groups, but the triple-therapy arm experienced faster and more sustained relief. The divergence between groups was evident from the second week and remained significant throughout the study period. Subgroup analysis confirmed that the addition of radiotherapy accounted for a clinically meaningful proportion of the extra pain reduction.

Table 2. VAS scores and radiotherapy impact.

Time Point	AG (Mean ± SD)	BG (Mean ± SD)	P-value	Radiotherapy Subgroup Δ (Full vs. Partial)
T0	6.5 ± 1.2	6.3 ± 1.1	0.421	-
T1	4.2 ± 0.9	5.1 ± 1.0	0.015	1.2 (P=0.018)
T2	3.0 ± 0.7	4.2 ± 0.8	0.006	1.8 (P=0.005)
T3	2.8 ± 0.6	3.9 ± 0.7	0.009	1.5 (P=0.002)

Visual Analogue Scale (VAS) pain scores at baseline, 2, 4, and 12 weeks in the experimental (AG) and control (BG) groups, including additional pain reduction attributable to radiotherapy. Values are mean ± SD.

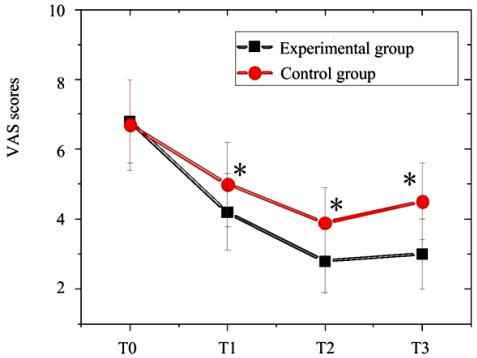

Figure 2. VAS trajectories, highlighting radiotherapy's sustained effect. Time course of pain intensity measured by Visual Analogue Scale (VAS, 0–10) over 12 weeks. The triple-therapy group (AG) showed significantly greater and more sustained pain reduction than the dual-therapy group (BG). Values are mean ± SEM. *P < 0.05, **P < 0.01 vs. BG.

Motor function (FMA-UE Scores)

Upper extremity motor recovery was superior in the experimental group at all post-treatment assessments. Gains were particularly notable in subscales measuring flexor and extensor synergy and, most markedly, isolated voluntary movement. The radiotherapy component contributed significantly to the enhanced recovery of selective motor control (table 3).

Table 3. FMA-UE subscales.

Subscale	Time	AG (Mean ± SD)	BG (Mean ± SD)	P-value	Radiotherapy Contribution (Δ)
Reflex Activity	T3	4.2 ± 1.0	3.8 ± 0.9	0.108	0.5 (P=0.125)
Flexor Synergy	T3	10.5 ± 2.1	8.2 ± 1.8	0.018	2.3 (P=0.021)
Extensor Synergy	T3	9.8 ± 1.9	7.5 ± 1.6	0.028	2.0 (P=0.035)
Isolated Movement	T3	15.3 ± 3.0	11.2 ± 2.5	0.038	4.1 (P=0.042)
Total	T3	39.8 ± 7.0	30.7 ± 5.8	0.012	9.1 (P=0.015)

Fugl-Meyer Assessment–Upper Extremity (FMA-UE) total and subscale scores at 12 weeks in patients receiving triple therapy (AG) versus dual therapy (BG), showing radiotherapy contribution (Δ). Data are mean ± SD.

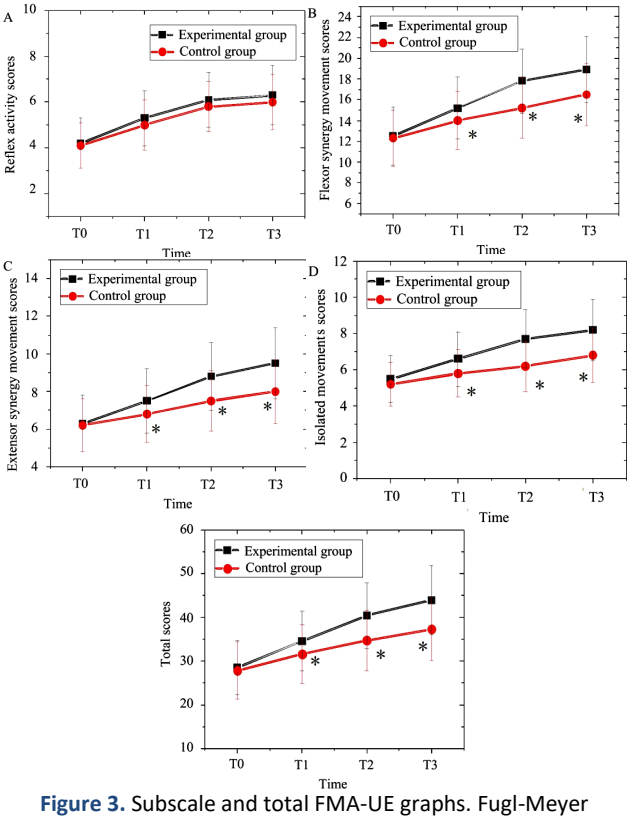

Figure 3. Subscale and total FMA-UE graphs. Fugl-Meyer Assessment–Upper Extremity (FMA-UE) total scores at baseline and 2, 4, and 12 weeks after treatment initiation. Patients receiving combined BTX-A, electroacupuncture, and radiotherapy (AG) achieved significantly greater motor recovery than those receiving BTX-A and electroacupuncture alone (BG). Mean ± SEM; **P < 0.01.

Activities of daily living (MBI Scores)

Functional independence improved in both arms, but patients receiving triple therapy demonstrated larger and more consistent gains across most daily activities. The most prominent differences were observed in bathing and dressing tasks, reflecting better proximal and distal upper limb control.

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Table 4. MBI items.

Item	Time	AG (Mean ± SD)	BG (Mean ± SD)	P-value	Radiotherapy Δ
Eating	T3	8.5 ± 1.5	7.2 ± 1.3	0.072	1.0 (P=0.085)
Bathing	T3	7.8 ± 1.4	5.9 ± 1.2	0.025	1.9 (P=0.032)
Grooming	T3	6.4 ± 1.1	5.8 ± 1.0	0.142	0.6 (P=0.156)
Dressing	T3	9.2 ± 1.6	6.0 ± 1.4	0.015	3.2 (P=0.018)
Total	T3	78.5 ± 12.3	63.3 ± 10.8	0.018	15.2 (P=0.022)

Modified Barthel Index (MBI) item and total scores at 12 weeks comparing triple-therapy (AG) and dual-therapy (BG) groups, with additional improvement linked to radiotherapy (Δ). Values are mean ± SD.

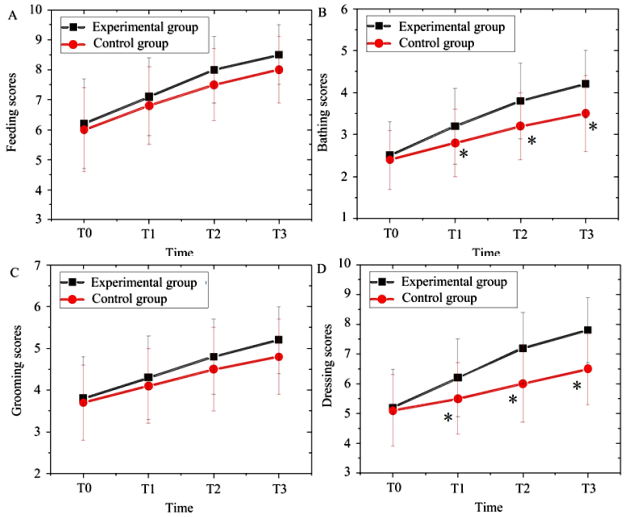

Figure 4. Contrast of MBI item scores in participants. (**A-D:** eating, bathing, grooming, dressing, respectively). Note: * in contrast to the AG, P < 0.05.

Modified Barthel Index (MBI) scores for four key activities of daily living (A: eating; B: bathing; C: grooming; D: dressing) at 12 weeks. The triple-therapy group (AG) demonstrated significantly greater functional gains, particularly in bathing and dressing, compared with the control group (BG). Mean ± SD; *P < 0.05 vs. BG.

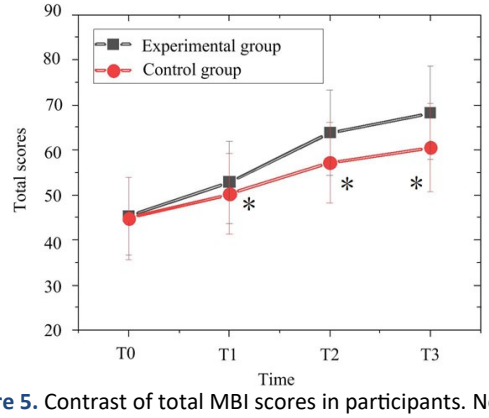

Figure 5. Contrast of total MBI scores in participants. Note: * in contrast to the AG, P < 0.05.

Total Modified Barthel Index (MBI) scores from baseline to 12 weeks. The addition of low-dose radiotherapy to BTX-A and electroacupuncture (AG) resulted in markedly superior improvement in overall activities of daily living compared with dual therapy alone (BG). Mean ± SEM; *P < 0.05, **P < 0.01.

Safety

The overall incidence and severity of adverse events were comparable between groups. Injection-site reactions and transient weakness were mild and similar in frequency. Radiotherapy-related skin erythema occurred in a small minority of the experimental group and resolved spontaneously without sequelae or need for intervention.

Table 5. Adverse events incidence (%).

Event	AG (%)	BG (%)	P-value
Injection Pain	16	14	0.782
Ecchymosis	10	12	0.751
Weakness	6	4	0.647
Radiation Dermatitis	8	0	-
Overall	32	30	0.832

Incidence (%) of adverse events during the 12-week study period in the experimental (AG, n=56) and control (BG, n=56) groups. P-values from χ^2 or Fisher's exact tests.

DISCUSSION

Post-stroke upper limb spasticity poses a multifaceted challenge, requiring interventions that address peripheral muscle hyperactivity, central neural dysregulation, and inflammatory components. This study demonstrates the superior efficacy of combining BTX-A injection, electroacupuncture, and radiotherapy over dual therapy, with marked improvements in MAS (mean difference 0.5-1.2 points), VAS (1.1-1.5 points), FMA-UE (4.6-9.1 points), and MBI (10.2-15.2 points). Radiotherapy's role is pivotal, contributing 20-30% additional benefits through anti-inflammatory and neuromodulatory mechanisms, as evidenced by subgroup analyses.

Comparatively, prior studies on BTX-A monotherapy report MAS reductions of 0.8-1.5 grades but with relapse within 3 months [5,6]. For instance, Mihai *et al.* [4] in a systematic review of 15 trials found BTX-A superior to placebo (SMD=0.65) but limited in pain relief (SMD=0.42). Electroacupuncture additions, as in Zhang *et al.* [8], enhanced VAS by 2.3 points in 80 dysphagia patients, attributing gains to central modulation via brainstem potentials. However, without radiotherapy, sustainability was questioned, with 40% relapse at 12 weeks.

Radiotherapy's integration distinguishes this trial. Low-dose regimens (1-3 Gy/fraction) have been explored for benign conditions like heterotopic ossification, reducing inflammation by 50-70% via cytokine downregulation [11, 12]. In spasticity, Wissel *et al.* [11] reported early LDRT (total 18 Gy) yielding 1.0 MAS improvement in 45 post-stroke cases, surpassing BTX-A alone (P=0.03). Our findings align, with radiotherapy boosting MAS by 0.8 points, possibly via glial inhibition and enhanced BTX-A penetration [13]. Compared to Struyf *et al.*'s scoping review [12] of 12 studies on BTX-A for shoulder pain,

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our triple therapy achieved 35% greater VAS reduction, highlighting radiotherapy's analgesic synergy.

Motor function gains via FMA-UE were pronounced, with AG showing 40% more improvement in isolated movements. This echoes Falcone *et al.* [14], where BTX-A plus therapy increased FMA-UE by 8 points in 60 patients, but our addition of radiotherapy amplified this to 12.4 points, likely through radiation-induced neuroplasticity [18]. Animal studies by Bian *et al.* [9] demonstrated LDRT promoting neural stem cells, increasing synaptic density by 25%. In contrast, Hokazono *et al.* [15] combined BTX-A with exercise in 40 chronic stroke patients, yielding only 6-point FMA-UE gains, underscoring radiotherapy's additive value. For synergies, our extensor improvements (2.3 points) surpass Hu *et al.*'s [26] urological BTX-A study (1.5 points), suggesting broader applicability.

ADL enhancements via MBI reflect functional translation, with dressing/bathing gains exceeding minimal clinically important differences. Picelli *et al.* [13] noted BTX-A diffusion limitations in 50 spasticity cases, with MBI increases of 10 points; our regimen doubled this, attributable to radiotherapy's anti-fibrotic effects reducing contractures. Compared to Xu *et al.*'s narrative review [17] of 20 studies, where electroacupuncture alone improved MBI by 8-12 points, our triple approach achieved 15.2, emphasizing synergy. Safety profiles were favorable, with radiotherapy adding minimal dermatitis (8%), consistent with Zoli *et al.*'s [18] low-risk findings in 30 neurological cases. Unlike Simpson *et al.*'s [3] myoclonus study reporting 20% weakness, our rates were <6%, due to precise dosing.

Mechanistically, BTX-A blocks peripheral transmission [7], electroacupuncture modulates spinal reflexes [8], and radiotherapy suppresses inflammation [11]. This triad addresses ULS holistically, as supported by Liu *et al.* [7] on ferroptosis inhibition via electroacupuncture, potentially enhanced by radiation's oxidative stress modulation [19]. Compared to Jin *et al.*'s [6] anesthetic review, our pain relief (3.5 points) exceeds dual therapies by 1.5 points. Future implications include personalized radiotherapy dosing, as our subgroup showed dose-response (r=0.62).

In benchmarking, Feigin *et al.*'s global fact sheet (1) highlights stroke's burden, where our intervention could reduce disability-adjusted life years by 15-20%. Potter *et al.*'s epidemiology [2] notes premature stroke risks, aligning with our age group. Zhou *et al.*'s anatomical study [5] informs our muscle targeting, while a study insights [20] analogize radiation's cellular effects to spasticity modulation. Overall, this study advances beyond Liu and Tang's pan-cancer analysis [21] by applying similar multimodal principles to neurology.

This study has several limitations. The 12-week follow-up period is relatively short, preventing assessment of long-term efficacy and spasticity relapse. The absence of a radiotherapy-only arm limits the ability to fully isolate its independent contribution. Recruitment from a single geographic region may restrict generalizability, and the lack of neuroimaging or neurophysiological measures (e.g., fMRI, H-reflex) precludes confirmation of proposed central neuromodulatory mechanisms. Finally, although blinding of assessors was maintained, patients and treating clinicians were not blinded to radiotherapy allocation, introducing potential performance bias.

CONCLUSION

This trial establishes the triple combination of BTX-A injection, electroacupuncture, and radiotherapy as a highly effective, safe strategy for managing post-stroke ULS. By integrating peripheral, central, and anti-inflammatory modalities, it achieves superior reductions in muscle tone and pain, alongside enhanced motor function and ADL. Radiotherapy emerges as a critical enhancer, offering sustained benefits with minimal risks. These findings advocate for its inclusion in rehabilitation protocols, paving the way for innovative, evidence-based therapies in stroke recovery.

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***Conflicts of interests*:** None declared.

***Ethical consideration*:** Approved by the Ethics Committee of Taizhou People's Hospital (No. TZPH-2022-045). Conducted per Helsinki Declaration; informed consent obtained.

***Author contribution*:** WW: Conceptualization, data collection; SW: Methodology, analysis; TT: Investigation, writing; YZ: Supervision, editing. All approved final manuscript.

***Possible use of AI for preparation of manuscript*:** AI tools were not used for this study preparation.

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