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Efficacy and Safety of Superficial Radiotherapy in Treatment of Cutaneous Warts: A Meta-Analysis

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Corresponding author:
Xiao-Hua Tao

taoxiaohua@126.com

Author Affiliation:
Dermatology Hospital of Jiangxi Province.

Deng, YY; Li, CX; Li, GL; Tao, XH.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 May 2026 and was last updated on 18 May 2026.

INTRODUCTION

Review question / Objective The primary objective of this meta-analysis is to systematically evaluate the clinical evidence concerning the efficacy and safety of superficial radiotherapy (SRT) in the treatment of cutaneous warts.
Specifically, the study aims to:
Evaluate Efficacy: Determine the overall cure rate of SRT for cutaneous warts.
Assess Safety: Analyze the recurrence rate and adverse reactions associated with SRT.
Compare Therapies: Investigate the differences between SRT monotherapy and combination therapy (SRT used with other treatments like topical medications or cryotherapy).

Condition being studied Condition: Cutaneous Warts
1. Definition & Cause
Cutaneous warts are common benign disorders characterized by the hyper-proliferation of epidermal cells. They are caused by infection with the Human Papillomavirus (HPV). While these lesions are non-cancerous, they can cause significant physical discomfort and psychological distress.
2. Clinical Manifestations
The infection presents with diverse clinical forms, including:
Common warts (Verruca vulgaris): Often found on fingers, hands, or elbows.
Plantar warts: Located on the soles of the feet, often characterized by thick hyperkeratosis (hard skin) and can be painful due to pressure.
Periungual warts: Found around the nails, which are challenging to treat due to the risk of damaging the nail matrix.
Flat warts: Typically numerous and found on the face (especially in adolescents) or other body parts.

Condylomata acuminata (Genital warts): Affecting the anogenital region.
3. Impact on Patients
Although benign, these lesions are often visible and can:
Cause friction-related discomfort or pain (especially plantar warts).
Impair limb function or appearance.
Impose a substantial psychological burden, reducing the patient's quality of life and motivating them to seek treatment.
4. Context for SRT Treatment
The study focuses on using Superficial Radiotherapy (SRT) for these warts, particularly in cases where conventional treatments (like cryotherapy or laser) have failed, or for warts located in anatomically sensitive regions (e.g., periungual areas, face, soles). SRT is highlighted as a non-invasive option that minimizes damage to deep tissues.

METHODS

Participant or population Wart Type Participant Characteristics Study Examples
Periungual Warts Patients with warts around the nails. Xu et al. (2021)
Plantar Warts Patients with warts on the soles; often refractory to previous treatment. Song et al. (2023), Fang et al. (2023)
Common Warts Patients with multiple lesions; often resistant to cryotherapy. Lin et al. (2023), Shan et al. (2023)
Condylomata Acuminata Patients with anogenital warts (Perianal/Genital). Zheng et al. (2017), Lu et al. (2019).

Intervention The intervention of interest in this review is Superficial Radiotherapy (SRT), a non-invasive treatment modality utilizing low-energy X-rays (50–100 kV) to precisely irradiate target skin lesions. Due to its limited tissue penetration, SRT concentrates energy on the epidermis and superficial dermis, thereby minimizing damage to deeper tissues while disrupting HPV-infected keratinocytes, inhibiting viral DNA replication, and modulating the local immune microenvironment. The review evaluates SRT both as a monotherapy and as part of combination therapies, specifically assessing its efficacy when paired with other treatments such as topical retinoic acid cream, liquid nitrogen cryotherapy, CO_2 laser, or traditional Chinese medicine (e.g., Xiaoyou decoction). The primary focus of the evaluation is to determine the clinical efficacy (cure rates), safety profile (recurrence rates and adverse reactions like erythema or pigmentation), and the comparative effectiveness between SRT monotherapy and various combination regimens in the management of cutaneous warts.

Comparator The comparative interventions in this review primarily consist of SRT monotherapy, which serves as the baseline control to evaluate the incremental efficacy of various combination regimens (such as SRT combined with topical retinoic acid, cryotherapy, or CO_2 laser). Additionally, the review includes comparisons against conventional standard therapies, specifically liquid nitrogen cryotherapy and topical medications, as well as placebo or no-treatment controls in certain study designs. These comparators are utilized to benchmark the relative clinical effectiveness, cure rates, and safety profiles of Superficial Radiotherapy within the current therapeutic landscape for cutaneous warts.

Study designs to be included This review will exclusively include **Randomized Controlled Trials (RCTs)** to address its objective of evaluating the efficacy and safety of Superficial Radiotherapy (SRT). The selection criteria strictly adhere to this design to ensure the highest level of clinical evidence, while excluding non-randomized studies, case reports, case series, reviews, animal experiments, and trials with incomplete data or unavailable full texts.

Eligibility criteria Additional Inclusion Criteria
Language: Only studies published in English or Chinese were eligible for inclusion.
Additional Exclusion Criteria
Data Availability: Studies with incomplete data where key outcomes could not be extracted, or trials where the full text was unavailable, were excluded.
Study Type: Non-clinical research, specifically animal experiments, as well as reviews, case reports, and case series, were excluded.

Information sources To ensure a comprehensive and unbiased retrieval of relevant studies, this review will systematically search multiple electronic databases, including PubMed, Embase, Cochrane Library, CNKI, Wanfang Data, VIP Database, and SinoMed. Furthermore, to identify any additional eligible trials and minimize publication bias, the reference lists of all selected articles and pertinent review papers will be manually screened.

Main outcome(s) The **primary outcome** is the **cure rate**, while the **secondary outcome** is the **incidence of adverse events**. The timing for evaluating these outcomes is set at **3 months after the completion of treatment**. For statistical analysis, the review will use **Risk Ratios (RR) with

95% Confidence Intervals (CIs)** for dichotomous data and **Mean Differences (MD) with 95% CIs** for continuous data.

Quality assessment / Risk of bias analysis For the quality assessment of the included Randomized Controlled Trials (RCTs), this review will utilize the **Cochrane Risk of Bias (RoB) 2.0 tool**. The evaluation will systematically cover five specific domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in the measurement of the outcome, and bias in the selection of the reported result. Two independent reviewers will assess each study, and the final judgment for the overall risk of bias will be categorized as **low**, **some concerns**, or **high**.

Strategy of data synthesis This review will employ **RevMan 5.4 software** for statistical analysis. For dichotomous data, such as cure rates and adverse event incidence, the analysis will use **Risk Ratios (RR)** with **95% Confidence Intervals (CIs)**, while continuous data will be analyzed using **Mean Differences (MD)** with **95% CIs**. To account for potential clinical or methodological heterogeneity, a **random-effects model** will be utilized for meta-analysis. The assessment of statistical heterogeneity will be based on the **I^2 statistic**, where an I^2 value greater than 50% indicates significant heterogeneity. In the case of substantial heterogeneity, **sensitivity analysis** will be conducted to examine the stability and robustness of the results. Furthermore, **subgroup analysis** will be performed to explore potential sources of heterogeneity. If the number of included studies is sufficient, **meta-regression** will be applied to investigate the influence of specific variables on the outcomes. Finally, **publication bias** will be evaluated using **funnel plots**.

Subgroup analysis Subgroup analysis will be conducted to explore the heterogeneity of the treatment effect across different subpopulations and to identify specific factors that may influence the outcomes. This analysis aims to determine whether the observed effects vary significantly among predefined subgroups, such as those based on demographic characteristics, baseline severity, or specific treatment protocols. By partitioning the data into clinically homogeneous categories, this method allows for a more detailed examination of the intervention's efficacy and safety within distinct patient populations.

Sensitivity analysis Sensitivity analysis will be performed to assess the robustness and stability of the pooled results and to identify potential sources of heterogeneity. This will involve systematically removing studies with high risk of bias or specific characteristics to evaluate the influence of individual studies on the overall effect estimate. Additionally, the analysis will examine the impact of methodological choices, such as the statistical model (e.g., comparing random-effects vs. fixed-effects models) and the imputation of missing data, to ensure that the conclusions of the review remain consistent under different assumptions.

Country(ies) involved the authors/affiliations involved in the *included primary studies* are predominantly **Chinese**.

Keywords warts; superficial radiotherapy; meta-analysis.

Contributions of each author

Author 1 - Yu-Yu Deng.
Email: 15250955959@163.com
Author 2 - Chang-Xia Li.
Email: 873044739@qq.com
Author 3 - Guo-Lan Li.
Email: guolanli1009@163.com
Author 4 - Xiao-Hua Tao.
Email: taoxiaohua@126.com