

Systematic Review and Meta-Analysis

Energy-Based and Ablative Destructive Therapies Versus Surgical Excision for Primary Basal Cell Carcinoma: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Surgical excision is the reference treatment for basal cell carcinoma (BCC), but energy-based and ablative therapies, including photodynamic therapy, radiotherapy and brachytherapy, laser ablation, electrochemotherapy and curettage-based destruction, are increasingly used.

Objective: To quantify the loss of tumour control and the cosmetic gain of these therapies relative to excision.

Methods: PubMed/MEDLINE, Scopus, Europe PMC and ClinicalTrials.gov were searched from inception for randomised and non-randomised controlled studies comparing these therapies with excision for primary BCC. The primary outcome was treatment failure. Risk ratios (RR) were pooled with Mantel–Haenszel random-effects models, and certainty was graded with GRADE.

Results: Fourteen studies (11 randomised) were included; 12 studies with 1,737 lesions or patients informed the primary outcome. In randomised trials, failure was more frequent after ablative therapy (RR 5.34, 95% CI 2.76 to 10.33; $I^2=23.3\%$; moderate certainty). Across all studies the RR was 3.26 (95% CI 1.47 to 7.23; prediction interval 0.27 to 40.00), an absolute excess of 7.6 failures per 100 tumours; heterogeneity ($I^2=60.3\%$) was explained by study design. Early failure and late recurrence also increased. Good or excellent cosmesis was more frequent after photodynamic therapy in two trials (RR 1.87, 95% CI 1.54 to 2.26; low certainty), but not after radiotherapy or cryosurgery.

Conclusion: Energy-based and ablative therapies increased the risk of treatment failure five-fold in randomised trials, while photodynamic therapy improved cosmesis. Excision should remain first-line when tumour control is the priority; non-surgical options suit selected thin, low-risk tumours or patients unfit for surgery, with imaging-supported selection and surveillance.

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1. Introduction

Basal cell carcinoma (BCC) is the most frequently diagnosed malignancy in fair-skinned populations, and registry studies published in the last five years showed that its incidence was still rising. A nationwide Swedish registry reported increasing incidence with a faster rise among women and among aggressive histological subtypes,¹ Norwegian pathology data showed that tumour-based incidence almost doubled between 2012 and 2022,² and a regional Spanish registry estimated a crude incidence of 410 tumours per 100,000 person-years with an annual increase of 3.91%.³ Comparable trends were documented in England, Wales and Asia. Incidence among Chinese Singaporeans rose 2.5-fold over five decades, and a quarter of Thai patients already had large tumours at first presentation.^{4–7} Global Burden of Disease modelling projected a further expansion of the burden among adults aged 55 years or older,⁸ and the Welsh cohort alone generated surgical costs of GBP 119–164 million over 18 years.⁵ Because most patients were elderly

and frequently multimorbid, treatment burden and quality of life have become central to management decisions.^{9–11}

Conventional surgical excision with predetermined margins remained the reference treatment, but it was not free of limitations. Contemporary surgical series reported incomplete excision in 16.9% of nasal tumours, with recurrence of 24.1% after non-radical versus 6.3% after radical excision,¹² and identified multifocality, depth of invasion and facial location as independent predictors of involved margins.^{13–15} Re-excision, frozen-section control or close surveillance were each proposed for compromised margins.^{16,17} In parallel, a broad group of non-surgical energy-based and physically ablative therapies expanded. Photodynamic therapy (PDT) with aminolevulinic acid (ALA) or methyl aminolevulinate (MAL) was refined through simplified, fractionated and new-formulation regimens tested in randomised trials,^{18–21} while superficial and image-guided radiotherapy and high-dose-rate surface-mould brachytherapy, including customised three-dimensional-printed applicators, reported high local control in patients unsuitable for

surgery.²²⁻²⁶ Ablative lasers, cryosurgery, curettage-based techniques and electrochemotherapy completed the non-surgical repertoire.²⁷⁻³¹

Imaging has become increasingly integrated into this therapeutic pathway. High-frequency ultrasound measured the deep margin of BCC with 91% accuracy and correlated closely with histological depth,^{32,33} discriminated invasive from non-invasive subtypes,^{34,35} and line-field confocal optical coherence tomography identified BCC subtypes with 90% agreement with histology.^{36,37} Such tools were used to select thin tumours for PDT, to monitor response and to guide laser ablation, which reported one recurrence per 100 person-years under combined reflectance confocal microscopy and optical coherence tomography guidance.^{38,39} The decisive clinical question, however, was how much tumour control was sacrificed when an energy-based or ablative option replaced excision. Previous evidence syntheses addressed single modalities, such as laser ablation,⁴⁰ or photodynamic therapy,⁴¹⁻⁴³ and none compared the energy-based and ablative class as a whole with excision. Since those syntheses, randomised trials with five-year and ten-year follow-up and a trial of curettage with electrocoagulation were published, but they had not been pooled with the earlier radiotherapy, cryosurgery, laser and electrochemotherapy trials, nor with contemporary comparative cohorts in which imaging informed the choice of treatment.

Radiology and imaging services now contribute to several steps of this pathway. Image-guided superficial radiotherapy uses high-resolution dermal ultrasound to visualise the tumour before and during treatment,²² brachytherapy increasingly relies on three-dimensional planning and printed surface applicators,^{26,44} and ultrasound or optical imaging is used to estimate depth before photodynamic or laser treatment and to follow response afterwards.^{33,38,45} Defining how much tumour control is exchanged for tissue preservation is therefore a question that is shared by dermatologists, surgeons, radiation oncologists and radiologists.

The novelty of this study lies in three features that previous syntheses did not combine: a single common comparator, surgical excision, applied to the whole class of energy-based and physically ablative therapies; explicit separation of randomised from non-randomised evidence; and the inclusion of trials and cohorts published between 2020 and 2025, among them the five-year curettage-imiquimod and ten-year photodynamic trials and imaging-selected laser ablation. The aim of this study was to estimate the relative and absolute risk of treatment failure (residual or recurrent tumour) of energy-based and ablative destructive therapies compared with surgical excision for primary BCC, to explore whether the effect differed by design, modality, subtype and follow-up, and to evaluate early clearance, late recurrence, cosmetic outcome and wound infection, grading the certainty of each finding.

2. Methods

Study design and registration. This systematic review and meta-analysis was conducted and reported in

accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.⁴⁶ The eligibility criteria, outcomes, effect measure and subgroup variables were specified before data extraction. Ethical approval was not required because only published aggregate data were analysed.

Search strategy. MEDLINE was searched through PubMed, Scopus was searched directly, non-MEDLINE journal content was searched through Europe PMC, and ClinicalTrials.gov was searched for registered trials, all from inception without language restriction. The PubMed strategy combined Medical Subject Headings and free-text terms for basal cell carcinoma, for each energy-based or ablative modality and for surgical excision, with a randomised-trial filter:

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("Carcinoma, Basal Cell"[Mesh] OR "basal cell carcinoma"[tiab] OR
"basal cell carcinomas"[tiab] OR basalioma*[tiab] OR "rodent
ulcer"[tiab]) AND ("Photochemotherapy"[Mesh] OR photodynamic[tiab]
OR aminolevulin*[tiab] OR aminolaevulin*[tiab] OR
"Radiotherapy"[Mesh] OR radiotherapy[tiab] OR "radiation
therapy"[tiab] OR brachytherapy[tiab] OR contacttherapy[tiab] OR
"Lasers"[Mesh] OR laser*[tiab] OR "Cryosurgery"[Mesh] OR
cryosurg*[tiab] OR cryotherap*[tiab] OR curettage[tiab] OR
electrodesiccation[tiab] OR electrocoagulation[tiab] OR
electrosurg*[tiab] OR ablation[tiab] OR ablative[tiab]) AND ("Surgical
Procedures, Operative"[Mesh] OR surgery[tiab] OR surgical[tiab] OR
excision*[tiab] OR excised[tiab]) AND (randomised controlled trial[pt]
OR controlled clinical trial[pt] OR random*[tiab] OR trial[ti])

("basal cell carcinoma"[tiab]) AND (photodynamic[tiab] OR
radiotherapy[tiab] OR "radiation therapy"[tiab] OR brachytherapy[tiab]
OR laser[tiab] OR cryosurg*[tiab] OR cryotherap*[tiab] OR
curettage[tiab] OR electrodesiccation[tiab] OR
electrochemotherapy[tiab]) AND (excision[tiab] OR "Mohs"[tiab] OR
surgery[tiab] OR surgical[tiab]) AND (recurrence[tiab] OR
recurrences[tiab] OR "local control"[tiab]) AND (compar*[tiab] OR
versus[tiab] OR "vs"[tiab] OR cohort[tiab] OR retrospective[tiab] OR
prospective[tiab]) NOT review[pt] NOT "case reports"[pt]
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Scopus was searched with the equivalent TITLE-ABS-KEY string. The strategy was translated for Europe PMC, restricted to records not indexed in MEDLINE, and for ClinicalTrials.gov (condition: basal cell carcinoma; interventional studies; intervention terms for each modality and for surgery or excision). The reference lists of included trials and of previous evidence syntheses were hand-searched.⁴⁰⁻⁴² Records were de-duplicated by digital object identifier and normalised title before screening.

Eligibility criteria. Eligibility followed the population, intervention, comparator, outcome and study design framework summarised in Table 1. Studies were eligible when adults with histologically confirmed primary BCC received an energy-based or physically ablative destructive therapy or conventional surgical excision within a randomised controlled trial or a non-randomised controlled comparative study with a concurrent excision group; randomised trials were analysed separately as the prespecified principal sensitivity analysis. Energy-based therapies comprised photodynamic therapy (light-activated photosensitiser), radiotherapy in any form (external beam, contact therapy or interstitial or surface brachytherapy) and laser ablation. Physically ablative therapies comprised cryosurgery and curettage with electrodesiccation or electrocoagulation. Combinations were eligible when the destructive component was the principal tumour-removing step (for example curettage followed by PDT, cryosurgery or a topical adjuvant). Trials comparing two non-surgical treatments, trials with a placebo or vehicle comparator, uncontrolled case series,

studies without BCC-specific event counts, and studies of recurrent, locally advanced or syndromic BCC were excluded.

Table 1. Eligibility criteria (population, intervention, comparator, outcome and design).

Element	Inclusion criteria	Exclusion criteria
Population	Adults with histologically confirmed, primary (previously untreated) BCC of any low-risk subtype and site	Recurrent, locally advanced, metastatic or syndromic (Gorlin) BCC; organ-transplant cohorts
Intervention	Energy-based therapy (photodynamic therapy, radiotherapy including brachytherapy, laser ablation, electrochemotherapy) or physical ablation (cryosurgery, curettage with electrodesiccation, electrocoagulation or a topical adjuvant)	Topical or systemic drug therapy without a destructive component
Comparator	Conventional surgical excision	Placebo, vehicle, sham, another non-surgical therapy, Mohs surgery alone
Outcomes	Treatment failure (residual or recurrent tumour); early failure; late recurrence; cosmetic outcome; wound infection	No BCC-specific event counts
Design	Randomised controlled trials; non-randomised controlled studies with a concurrent excision group	Case reports, uncontrolled series, reviews, conference abstracts

BCC, basal cell carcinoma.

Study selection and data extraction. Titles, abstracts and full texts were assessed against the eligibility criteria by one investigator, and all extracted numerical data were checked against the original reports.

All reports of the same trial were linked and treated as a single study; the report with the longest follow-up supplied the primary outcome and earlier reports supplied baseline, early clearance and cosmetic data. A standardised 23-item form captured trial identifiers, country, design, sample size, unit of randomisation, age, sex, subtype, anatomical site, intervention and comparator details, outcome definitions, numbers of events and participants per arm, reported effect estimates with 95% confidence intervals (CI), follow-up duration, funding and risk-of-bias judgements. Values not reported were recorded as not reported and no values were imputed.

The primary outcome was treatment failure, defined as clinically or histologically confirmed residual tumour after treatment or recurrence during follow-up, at the longest follow-up reported. When a trial reported failure only among lesions that had cleared initially, non-clearing lesions were added to the numerator and the randomised or treated lesions formed the denominator. Secondary outcomes were early treatment failure (absence of complete clearance within six months), late recurrence among lesions that had initially cleared, and good or excellent cosmetic outcome rated by investigators or independent observers and by patients. When one trial compared two eligible destructive arms with one surgical arm, the surgical arm was split evenly between the two comparisons to avoid double counting.

Trials with several reports were counted once, and no participant contributed to more than one comparison in any single analysis. A three-arm trial that reported outcomes only as percentages, without arm sizes, was included in a sensitivity analysis only.

Risk-of-bias assessment. Risk of bias for the primary outcome was assessed with the revised Cochrane risk-of-bias tool for randomised trials (RoB 2) across five domains: the randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome and selection of the reported result. Each domain and the overall judgement were rated

as low risk, some concerns or high risk. Non-randomised studies were assessed with the ROBINS-I framework across seven domains (confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes and selection of the reported result), rated as low, moderate, serious or critical; a serious overall rating was treated as high risk in the subgroup analysis. Because blinding of participants and surgeons was impossible, measurement of the outcome was judged by whether recurrence was confirmed histologically and whether the assessor was independent of the treating clinician.

Risk of bias was assessed for the primary outcome. Cosmetic outcomes, which were subjective and could not be assessed blind to treatment, were considered at higher risk of measurement bias when grading certainty. The certainty of evidence for each outcome was rated with the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach as high, moderate, low or very low, considering risk of bias, inconsistency, indirectness, imprecision and publication bias.

Statistical analysis. Risk ratios (RR) with 95% CI were calculated for each comparison and pooled with the Mantel-Haenszel method under a random-effects model, with the between-study variance (τ^2) estimated by the DerSimonian-Laird method; an RR above 1 indicated more treatment failures with the energy-based or ablative therapy. Risk differences were pooled in the same way to express absolute effects. Heterogeneity was quantified with Cochran's Q ($p < 0.10$ taken as evidence of heterogeneity), the I^2 statistic with its 95% CI and τ^2 , and a 95% prediction interval was calculated. To allow comparison with continuous-outcome syntheses, the pooled log odds ratio was also converted to a standardised mean difference (SMD) as $SMD = \ln(OR) \times \sqrt{3}/\pi$, where OR is the pooled odds ratio.

Prespecified subgroup analyses compared study design (randomised versus non-randomised), modality class (photodynamic therapy, radiotherapy, curettage-based physical ablation, electrochemotherapy and laser-based ablation), BCC subtype (superficial, nodular or mixed), length of follow-up (12 months or less, more than 12 to less than 36 months, 36 months or more) and overall risk

of bias, with a random-effects test for subgroup differences. Sensitivity analyses comprised restriction to randomised trials, leave-one-out re-estimation, inclusion of a three-arm trial that reported outcomes only as percentages, the Hartung–Knapp–Sidik–Jonkman adjustment of the confidence interval, the Paule–Mandel variance estimator, a common-effect Mantel–Haenszel model, the Peto odds ratio, exclusion of comparisons at high risk of bias, restriction to follow-up of at least 36 months and restriction to histologically confirmed failures. Small-study effects were examined with a funnel plot and, because at least ten comparisons were available, with Egger's regression test, Harbord's modified test for binary outcomes and trim-and-fill. Double-zero studies were retained in the systematic review and in the pooled risk difference but, as is standard for ratio measures, did not contribute to the pooled risk ratio. Analyses were run in R version 4.5.3 with the meta and metafor packages; figures were drawn at 300 dpi with R and Python. A two-sided $p < 0.05$ was considered statistically significant.

Because the DerSimonian–Laird estimator can underestimate between-study variance when studies are few and events sparse, the Hartung–Knapp–Sidik–Jonkman interval is reported alongside the primary estimate. Subgroup analyses were regarded as exploratory, and a p value below 0.05 was required for a

subgroup difference. Absolute effects were expressed as risk differences, as numbers needed to harm and, for the GRADE summary, as events per 1,000 patients at the pooled excision risk.

3. Results

Study selection. The database searches identified 1,391 records (PubMed/MEDLINE 282, Scopus 863, Europe PMC 246), and a further 69 registry records and 1 record from citation searching were retrieved. After removal of 279 duplicates, 1,182 records were screened and 1,135 were excluded on title and abstract. Of the 47 full-text reports assessed, 27 were excluded, most often because no surgical comparator was present, and 20 reports of 14 studies (11 randomised trials and 3 non-randomised controlled studies) were included, as illustrated in Figure 1. Twelve studies with 1,737 lesions or patients (13 comparisons) contributed to the primary outcome; one trial with no failures in either arm was retained in the systematic review and in the risk difference but was not estimable as a ratio, leaving 12 comparisons in the pooled risk ratio. Two further randomised trials contributed to secondary outcomes or sensitivity analyses only.^{47,48} In the three-arm trial with a single excision arm, the excision group was split between its two comparisons.⁴⁹

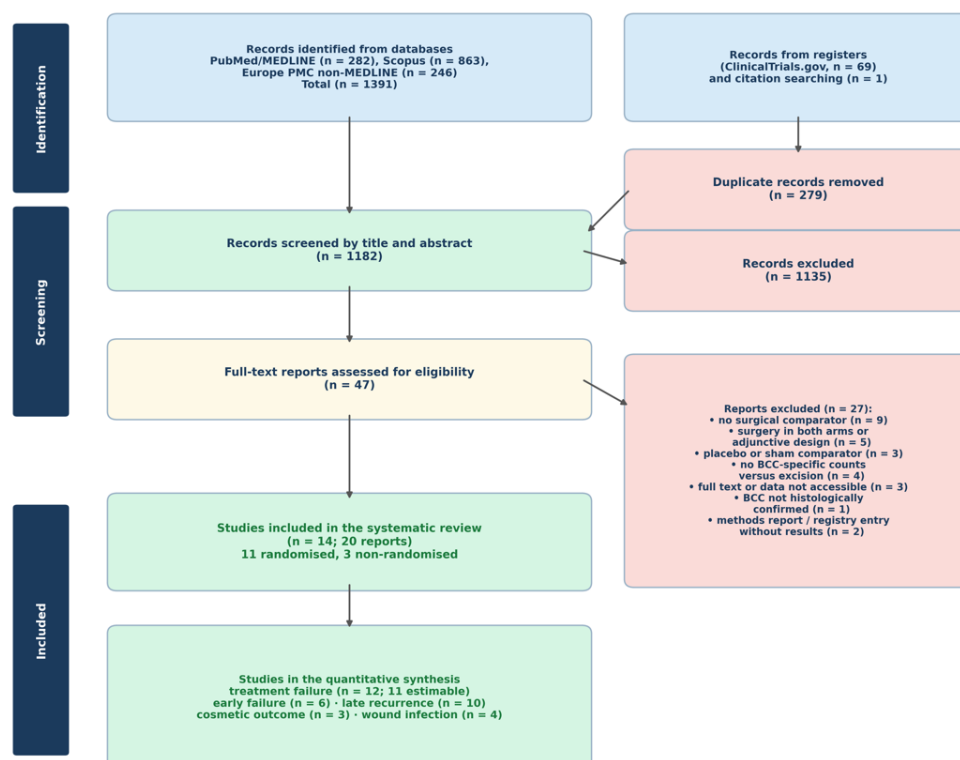


Figure 1. Flow of records through the review according to the PRISMA 2020 statement.

Study characteristics. The characteristics of the included studies are detailed in Table 2. Studies were conducted in France, the Netherlands, the United Kingdom and continental Europe, Ireland, Italy, Romania, Brazil, Iran and China and were published between 1997 and 2025.^{28,49–63} Photodynamic therapy and curettage-based ablation (curettage alone, or with cryosurgery, imiquimod, electrodesiccation or electrocoagulation) were the

commonest interventions (four studies each in the primary analysis), followed by laser-based ablation (two studies), and radiotherapy and electrochemotherapy (one trial each). The radiotherapy trial delivered interstitial iridium-192 brachytherapy to 55% of patients, contact therapy to 33% and conventional orthovoltage radiotherapy to 12%.⁵⁰ Four studies enrolled nodular BCC, one superficial BCC and seven mixed subtypes. Mean or

median age ranged from 57 to 72 years in the arms that reported it, and follow-up ranged from 12 to 60 months, with six comparisons followed for at least 36 months. The

unit of analysis was the lesion in eight studies and the patient in four.

Table 2. Characteristics of the included studies.

Study	Country	Design	n ablative / excision	Age, years (ablative / excision)	Energy-based or ablative therapy	Excision	Follow-up
Avril 1997 ^{50,64}	France	RCT (single centre, open)	173 / 174	66 (whole sample, SD 12) / 66 (whole sample)	Radiotherapy: interstitial Ir-192 brachytherapy 55%, contact therapy 33%, conventional 12%	Surgical excision, ≥2 mm margin, frozen section in 91%	48 months (mean 41)
Rhodes 2004 ^{51,52}	Multinational, Europe	RCT (multicentre, open)	52 / 49	69 / 67	MAL-PDT 160 mg/g, 3 h, red light 75 J/cm ² , two sessions 7 days apart, repeated if incomplete	Simple surgical excision	60 months
Kuijpers 2007 ^{53,65}	Netherlands	RCT (single centre, open)	51 / 49	67 (whole sample) / 67 (whole sample)	Curettage followed by cryosurgery, double freeze-thaw cycle	Surgical excision, 3 mm margin, delayed histology	60 months
Mosterd 2008 ^{54,55}	Netherlands	RCT (multicentre, open)	85 / 88	64.7 (whole sample, SD 13) / 64.7 (whole sample)	Partial debulking then fractionated 20% ALA-PDT (two illuminations, 1 h apart)	Surgical excision, 3 mm margin	60 months (median 67)
Szeimies 2008 ⁵⁶	Multinational (UK, Germany, Switzerland, Australia)	RCT (multicentre, open)	100 / 96	63.8 (whole sample) / 63.8 (whole sample)	MAL-PDT, two sessions 7 days apart, repeated at 3 months if incomplete	Simple surgical excision	12 months
Sinx 2020 ^{57,58}	Netherlands	RCT (two centres, non-inferiority)	73 / 72	68 (median, whole sample) / 68 (median, whole sample)	Superficial curettage followed by imiquimod 5% cream	Surgical excision	60 months
Clover 2020 ⁵⁹	Ireland	RCT (single centre, non-inferiority)	52 / 48	66.8 / 63.8	Electrochemotherapy (intratumoural bleomycin with pulsed electrical field), repeated once if incomplete	Surgical excision with histological margin control	60 months
Fonseca 2023 ^{60,61}	Brazil	RCT (single centre, open)	55 / 61	72 (median) / 71.5 (median)	Curettage and electrocoagulation, two cycles, 3 mm margin	Conventional excision, 3 mm margin, direct closure	24 months
Cosgarea 2013 ⁶²	Romania	Prospective controlled, non-randomised	32 / 40	NR / NR	Topical ALA-PDT, two sessions one month apart	Simple excision, 3 mm margin	16–37 months (mean 25)
Scurtu 2022 ⁶³	Romania	Quasi-experimental, non-randomised	129 / 50	67.78 / 61.64	Ablative CO ₂ laser plus two cryosurgery sessions with occlusive 5-fluorouracil and imiquimod	Standard elliptical surgical excision	Mean 21 months
Chen 2025 ²⁸	China	Retrospective comparative cohort	50 / 50	67.5 / 67.7	Ultra-pulsed CO ₂ laser ablation (selected for shallow invasion on preoperative ultrasound)	Traditional surgical excision	12 months
Zane 2017 ⁴⁸	Italy	RCT (three-arm, single centre)	240 patients in three arms / (arm sizes NR)	67.2 (whole sample) / 67.2 (whole sample)	Pulsed CO ₂ laser ablation; cryotherapy	Surgical excision	3 months
Salvio 2025 ⁴⁷	Brazil	RCT (three-arm)	189 ALA + 189 MAL / 189	64.2 (ALA); 65 (MAL) / 68.3	ALA-PDT or MAL-PDT with Brazilian photosensitisers	Surgical excision	120 months
Salmanpoor 2012 ⁴⁹	Iran	RCT (three-arm, single centre, letter)	20 curettage; 25 curettage + electrodesiccation / 24	57.3 (whole sample) / 57.3 (whole sample)	Curettage alone; curettage followed by electrodesiccation (two cycles, 1–2 mm margin)	Surgical excision, 4 mm margin	28 months

Numbers are lesions or patients according to the unit of randomisation or allocation. NR, not reported; RCT, randomised controlled trial; C&E, curettage and electrocoagulation; ECT, electrochemotherapy; PDT, photodynamic therapy; ALA, 5-aminolevulinic acid; MAL, methyl aminolevulinate.

Each study is listed under its first report, with all reports of the same trial cited. C&C, curettage and cryosurgery.

Risk of bias. Among the nine randomised trials contributing to the primary outcome, two were at low overall risk of bias, four raised some concerns and three were at high risk, as illustrated in Figure 2.^{49,54,57,59,60} Concerns arose mainly from per-protocol lesion analyses, attrition during long follow-up (28% of electrochemotherapy lesions were not assessed at five

years) and clinical rather than histological ascertainment of recurrence. All three non-randomised studies were at serious risk of bias under ROBINS-I, principally through confounding by indication, as shown in Figure 3; in the laser cohort, ablation was preferentially offered to tumours with shallow invasion on preoperative ultrasound.^{28,62,63}



Figure 2. Risk of bias of the randomised trials (Cochrane RoB 2). Green with a plus sign denotes low risk, amber with a question mark some concerns and red with a minus sign high risk.

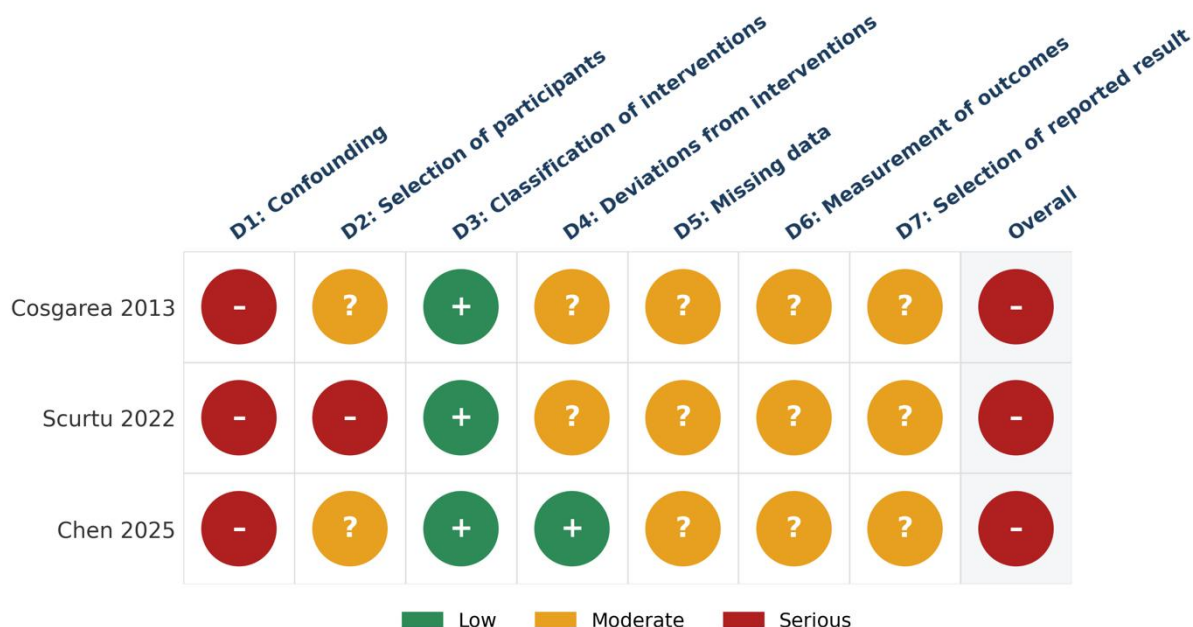


Figure 3. Risk of bias of the non-randomised controlled studies (ROBINS-I). Green denotes low, amber moderate and red serious risk of bias.

Primary outcome: treatment failure. Across 12 studies, treatment failure occurred in 109 of 917 lesions or patients (11.9%) after energy-based or ablative therapy and in 26 of 820 (3.2%) after surgical excision. The pooled

random-effects risk ratio was 3.26, 95% CI 1.47 to 7.23 ($p=0.004$), corresponding to an absolute excess of 7.6 percentage points (95% CI 2.3 to 13.0), as illustrated in Figure 4 and detailed in Table 3. Heterogeneity was

substantial ($I^2=60.3\%$, 95% CI 25.2% to 78.9%; $\tau^2=1.13$; $Q=27.69$, $df=11$, $p=0.004$), and the 95% prediction interval ranged from 0.27 to 40.00. The Hartung–Knapp–Sidik–Jonkman interval was wider but excluded unity (95% CI 1.39 to 7.64; $p=0.011$). The wide prediction interval reflected the divergence between randomised and non-randomised studies rather than uncertainty about the direction of effect in randomised trials. The common-effect estimate was similar (RR 3.83, 95% CI 2.54 to 5.78). The absolute excess corresponded to a number needed to harm of 13: one additional failure for every 13 tumours treated with an energy-based or ablative therapy instead of excision. Expressed on the standardised scale, the

pooled odds ratio of 3.67, 95% CI 1.57 to 8.62, corresponded to a standardised mean difference of 0.72, 95% CI 0.25 to 1.19, representing a moderate-to-large effect.

The excision arm of the retrospective laser cohort recorded 8 failures in 50 patients (16%), a rate several times higher than in any randomised excision arm (0% to 8.3%), and this cohort was the most influential study in the leave-one-out analysis; its omission reduced heterogeneity to $I^2=38.8\%$ and raised the pooled risk ratio to 4.19.²⁸

Table 3. Treatment failure by comparison and pooled estimate.

Comparison	Design	Modality	Subtype	Follow-up (months)	Failures, ablative	Failures, excision	Risk ratio (95% CI)	Weight
Avril 1997 (RT) ^{50,64}	RCT	Radiotherapy/brachytherapy	Mixed	48	11/173	1/174	11.06 (1.44 to 84.77)	7.5%
Rhodes 2004 (MAL-PDT) ^{51,52}	RCT	Photodynamic therapy	Nodular	60	11/53	2/52	5.40 (1.26 to 23.17)	9.8%
Kuijpers 2007 (C&C) ^{53,65}	RCT	Curettage-based ablation	Nodular	60	9/51	4/49	2.16 (0.71 to 6.56)	11.4%
Mosterd 2008 (ALA-PDT) ^{54,55}	RCT	Photodynamic therapy	Nodular	60	23/85	2/88	11.91 (2.90 to 48.95)	10.0%
Szeimies 2008 (MAL-PDT) ⁵⁶	RCT	Photodynamic therapy	Superficial	12	21/128	1/118	19.36 (2.65 to 141.69)	7.7%
Sinx 2020 (curettage + imiquimod) ^{57,58}	RCT	Curettage-based ablation	Nodular	60	15/73	1/72	14.79 (2.01 to 109.09)	7.6%
Clover 2020 (ECT) ⁵⁹	RCT	Electrochemotherapy	Mixed	60	5/47	1/40	4.26 (0.52 to 34.93)	7.2%
Fonseca 2023 (C&E) ^{60,61}	RCT	Curettage-based ablation	Mixed	24	0/51	0/57	Not estimable	0.0%
Cosgarea 2013 (ALA-PDT) ⁶²	Non-randomised	Photodynamic therapy	Mixed	25	4/48	4/46	0.96 (0.25 to 3.61)	10.4%
Scurtu 2022 (laser-cryo) ⁶³	Non-randomised	Laser-based ablation	Mixed	21	2/113	0/50	2.22 (0.11 to 45.50)	4.7%
Salmanpoor 2012 (curettage) ⁴⁹	RCT	Curettage-based ablation	Mixed	28	4/20	1/12	2.40 (0.30 to 19.04)	7.4%
Salmanpoor 2012 (C&E) ⁴⁹	RCT	Curettage-based ablation	Mixed	28	2/25	1/12	0.96 (0.10 to 9.57)	6.6%
Chen 2025 (CO ₂ laser) ²⁸	Non-randomised	Laser-based ablation	Mixed	12	2/50	8/50	0.25 (0.06 to 1.12)	9.6%
Pooled (random effects)					109/917	26/820	3.26 (1.47 to 7.23)	100.0%

Heterogeneity: $I^2=60.3\%$, $\tau^2=1.13$, $p=0.004$. Mantel–Haenszel random-effects model with DerSimonian–Laird variance.

Treatment failure: energy-based and ablative destructive therapies versus surgical excision

Risk ratio, Mantel–Haenszel random-effects model (DerSimonian–Laird); red bar = 95% prediction interval

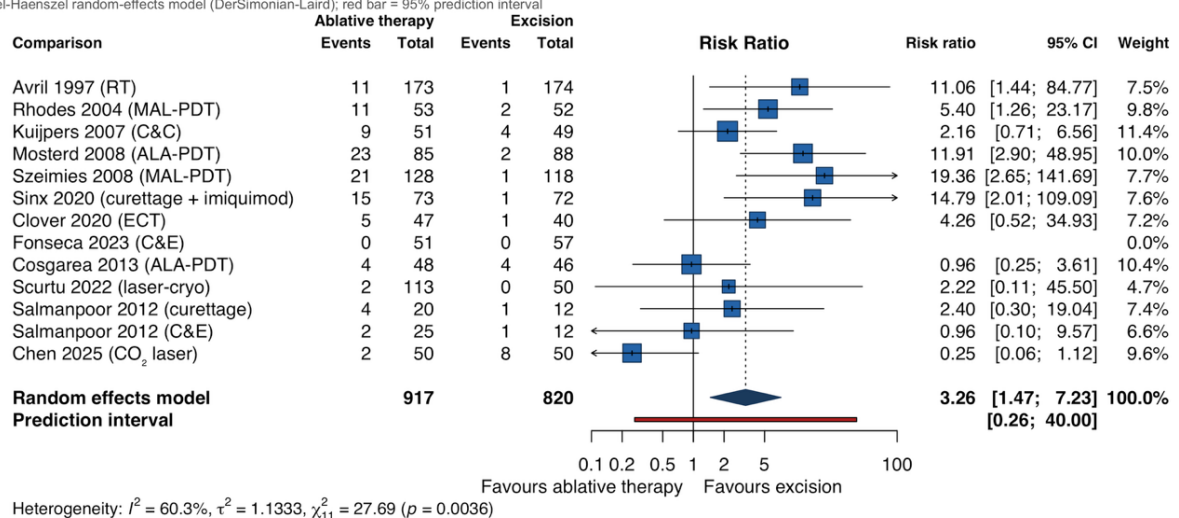


Figure 4. Treatment failure after energy-based or ablative therapy versus surgical excision. Squares are proportional to study weight, the diamond is the random-effects pooled risk ratio and the red bar is the 95% prediction interval. Values above 1 favour excision.

Subgroup analyses. Study design explained most of the heterogeneity, as shown in Figure 5 and Table 4. In randomised trials the excess risk was large and consistent (RR 5.34, 95% CI 2.76 to 10.33; $I^2=23.3\%$), whereas the non-randomised studies showed no difference (RR 0.62, 95% CI 0.21 to 1.87); the test for subgroup difference was significant ($p=0.001$).

By modality, as illustrated in Figure 6, the point estimates favoured excision for radiotherapy (RR 11.06), photodynamic therapy (RR 5.41), curettage-based ablation (RR 2.87) and electrochemotherapy (RR 4.26), whereas the two non-randomised laser studies did not (RR 0.50). Because each modality was represented by one to

four studies, the non-significant test for difference ($p=0.244$) does not establish that the modalities are equivalent.

The penalty was evident for nodular and superficial BCC but not for studies of mixed subtypes, a group that included all three non-randomised studies ($p=0.040$ for difference). It was consistent in comparisons followed for 36 months or longer (RR 5.65, 95% CI 2.85 to 11.21; $I^2=11.8\%$) and smaller or undetermined with shorter follow-up ($p=0.043$). The risk ratio was larger in studies at lower risk of bias ($p=0.001$). Follow-up, subtype and risk of bias were correlated with design, and these exploratory analyses cannot separate their effects.

Table 4. Subgroup analyses of treatment failure.

Variable	Subgroup	Comparisons	Risk ratio (95% CI)	I^2	p for difference
Study design	RCT	9	5.34 (2.76 to 10.33)	23.3%	$p=0.001$
Study design	Non-randomised	3	0.62 (0.21 to 1.87)	20.7%	$p=0.001$
Modality	Radiotherapy/brachytherapy	1	11.06 (1.44 to 84.77)	—	$p=0.244$
Modality	Photodynamic therapy	4	5.41 (1.36 to 21.46)	69.6%	$p=0.244$
Modality	Curettage-based ablation	4	2.87 (1.01 to 8.12)	28.3%	$p=0.244$
Modality	Electrochemotherapy	1	4.26 (0.52 to 34.93)	—	$p=0.244$
Modality	Laser-based ablation	2	0.50 (0.07 to 3.64)	38.4%	$p=0.244$
BCC subtype	Mixed	7	1.54 (0.57 to 4.19)	45.9%	$p=0.040$
BCC subtype	Nodular	4	5.77 (2.24 to 14.86)	41.6%	$p=0.040$
BCC subtype	Superficial	1	19.36 (2.65 to 141.69)	—	$p=0.040$
Follow-up	≥ 36 months	6	5.65 (2.85 to 11.21)	11.8%	$p=0.043$
Follow-up	≤ 12 months	2	2.10 (0.02 to 188.99)	92.3%	$p=0.043$
Follow-up	13–35 months	4	1.27 (0.49 to 3.28)	0.0%	$p=0.043$
Overall risk of bias	Some concerns	4	5.62 (2.01 to 15.73)	41.1%	$p=0.001$
Overall risk of bias	Low	2	12.80 (4.04 to 40.59)	0.0%	$p=0.001$
Overall risk of bias	High	6	1.04 (0.44 to 2.42)	17.5%	$p=0.001$

RCT, randomised controlled trial; CI, confidence interval. The p value tests for subgroup difference within each variable.

Treatment failure by study design

Risk ratio, Mantel-Haenszel random-effects model; test for subgroup differences shown below.

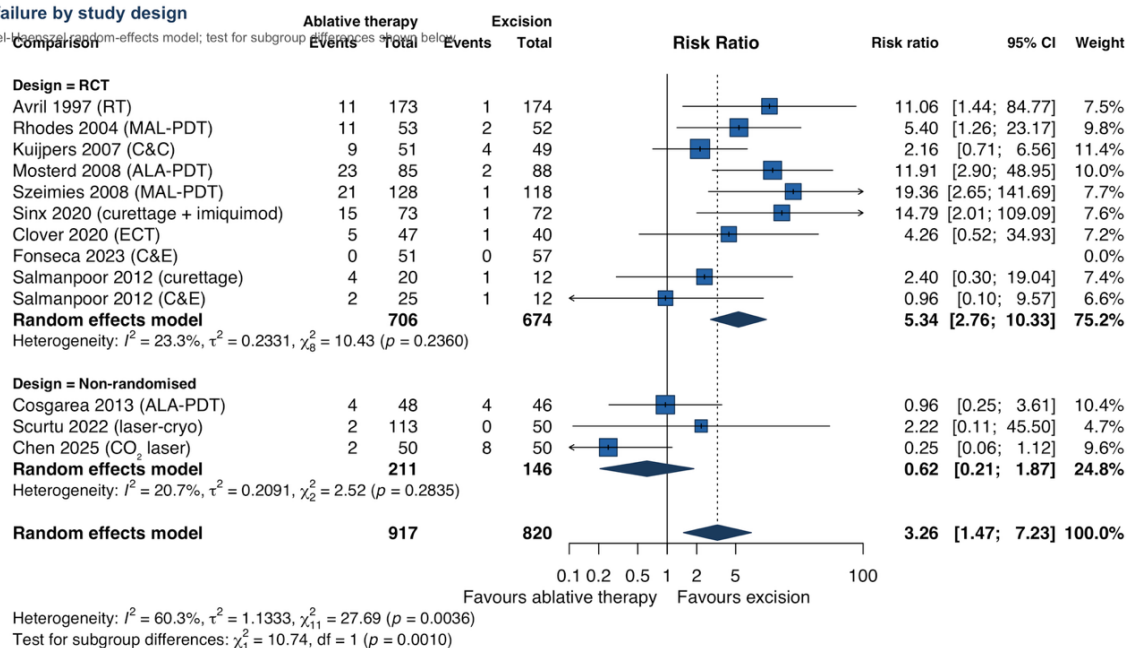


Figure 5. Treatment failure subgrouped by study design (randomised versus non-randomised).

Treatment failure by class of energy-based or ablative therapy

Risk ratio, Mantel-Haenszel random-effects model; test for subgroup differences shown below

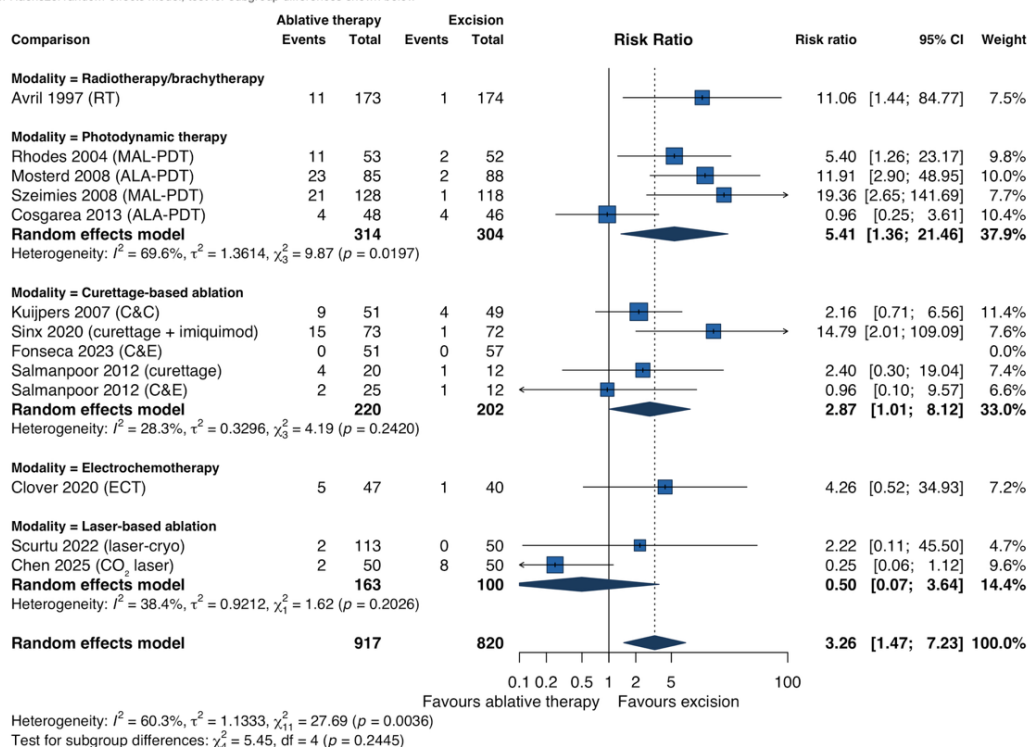


Figure 6. Treatment failure subgrouped by class of energy-based or ablative therapy.

Secondary outcomes. Early treatment failure, defined as absence of complete clearance within six months, was more frequent after energy-based or ablative therapy (67/743 versus 11/547; RR 3.74, 95% CI 1.95 to 7.18; 5 estimable comparisons; $I^2=0.0\%$), as illustrated in Figure 7. Among lesions that had initially cleared, late recurrence was also more frequent (68/755 versus 20/686; RR 2.51, 95% CI 1.09 to 5.80; 11 comparisons; $I^2=49.6\%$).

The cosmetic balance favoured the non-surgical options, as shown in Figure 8 and Table 5. Investigator-rated good or excellent cosmetic outcome was reported for 110/125 versus 61/131 (RR 1.87, 95% CI 1.54 to 2.26; $I^2=0.0\%$) in

the two photodynamic trials that reported this outcome, and patient-rated favourable cosmesis or satisfaction for 89/92 versus 74/93 (RR 1.21, 95% CI 1.08 to 1.34). The direction was reversed for radiotherapy and for cryosurgery: in the radiotherapy trial, 87% of surgically treated patients and 69% of irradiated patients rated their result as good at four years, and a slightly visible scar was recorded by the dermatologist in 79% versus 40%,^{50,64} while independent observers preferred excision to cryosurgery in the Maastricht trial.⁶⁵ Wound infection was infrequent and did not differ significantly (8/208 versus 14/202; RR 0.60, 95% CI 0.27 to 1.37).

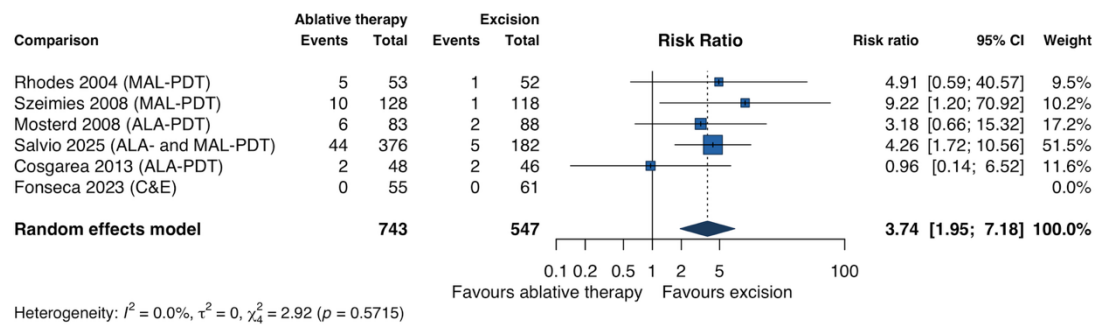
Table 5. Secondary outcomes.

Outcome	Estimable comparisons	Events, ablative	Events, excision	Risk ratio (95% CI)	p value	I ²
Early treatment failure (no complete clearance within 6 months)	5	67/743	11/547	3.74 (1.95 to 7.18)	p<0.001	0.0%
Late recurrence among initially cleared lesions	11	68/755	20/686	2.51 (1.09 to 5.80)	p=0.031	49.6%
Good/excellent cosmetic outcome (investigator-rated)	2	110/125	61/131	1.87 (1.54 to 2.26)	p<0.001	0.0%
Favourable patient-rated cosmetic outcome or satisfaction	2	89/92	74/93	1.21 (1.08 to 1.34)	p<0.001	0.0%
Wound infection	4	8/208	14/202	0.60 (0.27 to 1.37)	p=0.226	0.0%

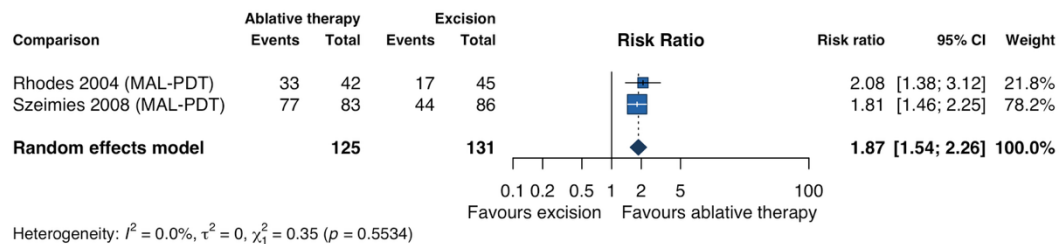
For cosmetic outcomes a risk ratio above 1 favours the energy-based or ablative therapy; for failure, recurrence and infection a risk ratio above 1 favours excision.

Early treatment failure (no complete clearance within 6 months)

Risk ratio, Mantel-Haenszel random-effects model

**Figure 7.** Early treatment failure (no complete clearance within six months).**Good or excellent cosmetic outcome (investigator or observer rated)**

Risk ratio, Mantel-Haenszel random-effects model; values above 1 favour the ablative therapy

**Figure 8.** Good or excellent investigator-rated cosmetic outcome in the two photodynamic trials that reported this outcome; values above 1 favour the ablative therapy.

Sensitivity analyses and small-study effects. The findings were robust to the analytical choices summarised in Table 6. The Hartung–Knapp–Sidik–Jonkman adjustment widened the interval but preserved significance (RR 3.26, 95% CI 1.39 to 7.64; $p=0.011$), and the Paule–Mandel estimator, the common-effect model and the Peto odds ratio gave concordant results. Restriction to randomised trials (RR 5.34, 95% CI 2.76 to 10.33; $I^2=23.3\%$), to studies not at high risk of bias (RR 7.08, 95% CI 3.26 to 15.39), to follow-up of at least 36 months and to histologically confirmed failures (RR 6.13, 95% CI 2.73 to 13.77) strengthened the association, and including a three-arm trial that reported outcomes only as percentages changed little (RR 3.59, 95% CI 1.77 to 7.30). In leave-one-out analyses the pooled risk ratio ranged

from 2.80 (omitting Szeimies 2008 (MAL-PDT)) to 4.19 (omitting Chen 2025 (CO₂ laser)) and remained statistically significant throughout; heterogeneity fell most, to $I^2=38.8\%$, when Chen 2025 (CO₂ laser) was omitted.

The funnel plot, shown in Figure 9, showed no clear asymmetry, although with twelve comparisons and marked between-design heterogeneity the tests had limited power and asymmetry could equally reflect design differences. Neither Egger's test ($p=0.467$) nor Harbord's test ($p=0.128$) was significant. Trim-and-fill imputed one comparison on the left of the funnel and attenuated the estimate to RR 2.78 (95% CI 1.28 to 6.06), which remained above unity.

Table 6. Sensitivity analyses for treatment failure.

Analysis	Comparisons	Estimate (95% CI)	I ²	p value
Primary: Mantel–Haenszel RR, random effects (DerSimonian–Laird)	12	3.26 (1.47 to 7.23)	60.3%	$p=0.004$
Hartung–Knapp–Sidik–Jonkman adjusted confidence interval	12	3.26 (1.39 to 7.64)	60.3%	$p=0.011$
Paule–Mandel estimator of between-study variance	12	3.24 (1.51 to 6.92)	58.5%	$p=0.002$
Mantel–Haenszel RR, common effect	12	3.83 (2.54 to 5.78)	60.3%	$p<0.001$
Peto odds ratio, common effect	12	3.66 (2.56 to 5.23)	60.0%	$p<0.001$
Excluding comparisons at high overall risk of bias	6	7.08 (3.26 to 15.39)	30.1%	$p<0.001$
Restricted to follow-up of 36 months or longer	6	5.65 (2.85 to 11.21)	11.8%	$p<0.001$
Restricted to histologically confirmed failure	5	6.13 (2.73 to 13.77)	28.8%	$p<0.001$
Restricted to randomised controlled trials	9	5.34 (2.76 to 10.33)	23.3%	$p<0.001$
Including a three-arm trial reporting outcomes only as percentages	14	3.59 (1.77 to 7.30)	55.3%	$p<0.001$
Pooled odds ratio, random effects (DerSimonian–Laird)	12	3.67 (1.57 to 8.62)	60.6%	—
Standardised mean difference equivalent, $SMD = \ln(OR) \times \sqrt{3/\pi}$	12	0.72 (0.25 to 1.19)	60.6%	—
Trim-and-fill adjusted risk ratio (one comparison imputed)	13	2.78 (1.28 to 6.06)	—	$p=0.010$
Leave-one-out (range)	11	2.80 to 4.19	38.8% to 63.8%	all $p<0.05$

CI, confidence interval; RR, risk ratio; OR, odds ratio; SMD, standardised mean difference.

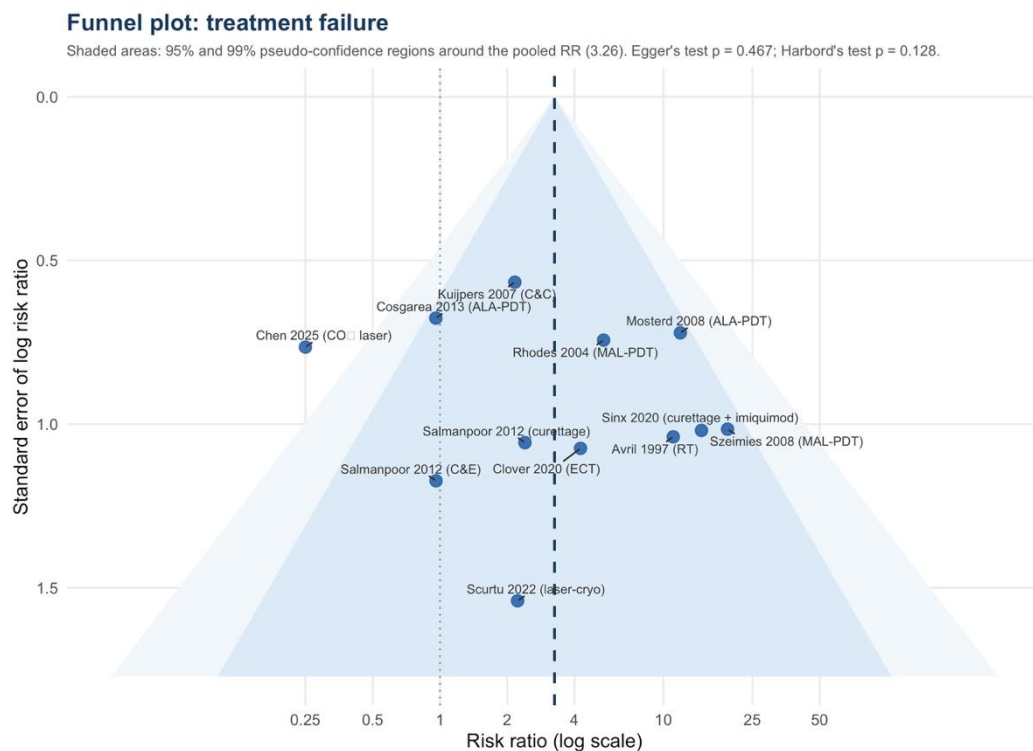


Figure 9. Funnel plot of the log risk ratio against its standard error for treatment failure, with 95% and 99% pseudo-confidence regions.

4. Discussion

Principal findings. This systematic review and meta-analysis found that replacing surgical excision with an energy-based or physically ablative destructive therapy increased the risk of treatment failure of primary BCC. In randomised trials the relative increase was large and consistent (RR 5.34, 95% CI 2.76 to 10.33; $I^2=23.3\%$), corresponding to approximately 111 rather than 21 failures per 1,000 tumours, and across all controlled studies the absolute excess was 7.6 failures per 100 tumours, a number needed to harm of 13. The penalty comprised both incomplete early clearance and late recurrence after initial clearance and was most evident with follow-up of three years or more. In exchange, photodynamic therapy increased the probability of a good or excellent investigator-rated cosmetic result (RR 1.87, 95% CI 1.54 to 2.26), whereas radiotherapy and cryosurgery did not confer a cosmetic advantage.^{50,64,65} The tumour-control finding was supported by moderate-certainty evidence and the cosmetic finding by low-certainty evidence, as summarised in Table 7.

Comparison with previous evidence. The results are consistent with, and extend, earlier evidence syntheses, each of which addressed a single modality. A review of 18 randomised photodynamic trials concluded that PDT was less effective than surgery but gave better cosmetic outcomes,⁴¹ and a meta-analysis of laser treatment reported recurrence of 3.1% after Nd:YAG and 9.4% after CO₂ laser ablation, derived largely from cohort studies, and did not recommend the CO₂ laser at the settings studied.⁴⁰ Two photodynamic syntheses found response rates comparable to surgery at 3 to 12 months but more recurrences with PDT at 24 to 60 months, and a pooled

recurrence of 13% to 15% across superficial and nodular BCC.^{42,43} The present analysis adds a single-comparator estimate for the whole energy-based and ablative class, separates randomised from non-randomised evidence and incorporates the five-year curettage-imiquimod analysis.⁵⁸ The ten-year photodynamic trial could contribute only early-failure data, because surgical-arm recurrence counts were not reported; its recurrence-free survival of 74.5% after ALA-PDT and 69% after MAL-PDT versus 92.8% after surgery is directionally concordant with the pooled estimate.⁴⁷ Danish registry data, which reported the lowest eight-year cumulative recurrence for nodular BCC after excision and higher recurrence hazards after photodynamic therapy, support the external validity of the randomised estimate.⁶⁶

Modality-specific considerations. Photodynamic therapy, with four studies, was one of the two most extensively studied modalities. The three randomised trials showed a consistent excess of failure, largest for nodular tumours and with long follow-up, whereas the non-randomised study showed no difference; cosmetic outcomes were superior. Recent randomised trials refined PDT regimens but did not remove this gap: a simplified single-session regimen was less effective than the standard double treatment,¹⁸ conventional two-stage MAL-PDT outperformed fractionated ALA-PDT in the long term,¹⁹ and 10% ALA gel was superior to vehicle but was not compared with surgery.²¹

The radiotherapy estimate rests on one trial that used brachytherapy, contact therapy and orthovoltage radiotherapy with dose schedules of the 1980s.⁵⁰ It may not transfer to contemporary practice. Image-guided superficial radiotherapy achieved freedom from recurrence above 99% at six years irrespective of

histology,²² and high-dose-rate surface-mould and interstitial brachytherapy achieved high local control with acceptable toxicity in elderly or periocular disease,^{23–25,67} but none of these series had a randomised excision control. Radiotherapy did not improve cosmesis in the only trial, in which radiodystrophy affected 41% of irradiated patients at four years.⁵⁰

Curettage-based techniques were heterogeneous. Curettage with cryosurgery and curettage followed by imiquimod both increased failure in nodular BCC,^{53,58} whereas curettage with electrocoagulation produced no recurrence in either arm over two years in a small trial of low-risk lesions,⁶⁰ a three-arm trial reported recurrence at 28 months of 20% after curettage alone and 8% after curettage with electrodesiccation, compared with 8.3% after excision,⁴⁹ and a randomised comparison of curettage with cryosurgery in superficial BCC found one-year clearance of 95.7% and 100%.²⁹ Because curettage-imiquimod and the laser-cryo-immunotherapy regimen combine a destructive step with a topical immune response modifier, they were classified with ablative therapies but represent hybrids; removing them would leave the direction of the pooled estimate unchanged, since the remaining randomised comparisons also favoured excision. Electrochemotherapy was compared with excision in one trial with substantial attrition,⁵⁹ and European registry data reported five-year disease-free survival of 92% in elderly patients.^{30,31} Laser ablation was represented only by non-randomised evidence, and the apparent absence of a penalty should not be taken as evidence of equivalence.^{28,63}

Several newer energy-based techniques have not yet been compared with excision. A 595-nm pulsed dye laser cleared 71.4% of low-risk truncal BCC versus 30.0% after sham treatment in a small randomised trial, and its authors did not recommend it at the settings tested,⁶⁸ although an uncontrolled series reported 90% clearance after two sessions.⁶⁹ High-intensity focused ultrasound was introduced in a pilot study,⁷⁰ calcium electroporation achieved complete response in only 32% of low-risk tumours,⁷¹ and immunocryosurgery for facial BCC relapsing after surgery achieved a five-year efficacy of 60.2%.⁷² These data reinforce the need for randomised comparisons with excision before new modalities are adopted for primary tumours.

Biological and technical explanations. Several mechanisms explain the excess failure. Destructive techniques, unlike excision, provide no histological confirmation of margin clearance, so subclinical extension beyond the treated field remains undetected. Photodynamic efficacy is limited by photosensitiser penetration and light attenuation: failure after fractionated ALA-PDT was concentrated in nodular tumours thicker than 0.7 mm,⁵⁵ nearly half of the treatment failures in a long-term trial of three photosensitisers were recorded only at the five-year visit,²⁰ clinical and histological assessments of subtype and thickness before PDT did not always agree,⁷³ and high-dose vitamin D accelerated clearance mainly in thin

tumours.⁷⁴ Laser ablation depends on the depth of vaporisation and curettage on the friability contrast between tumour and dermis, both less reliable in deeper or fibrotic tumours; contemporary laser series reported high clearance but with follow-up limited to about one year.^{27,75} Surgical excision, in contrast, fails mainly when margins are involved, which occurred in 16.9% of nasal excisions in one series and carried a four-fold higher recurrence.¹²

Role of imaging in selection, planning and follow-up.

Imaging offers a plausible route to narrowing this gap and is directly relevant to radiology practice, although it was not tested in any included randomised trial. High-frequency ultrasound measured the deep margin of BCC with 91% accuracy,³² correlated strongly with histological depth,³³ and discriminated invasive from non-invasive tumours with a validated prediction model;³⁴ optically guided ultrasound identified high-risk histological subtypes with a positive predictive value of 94.7%,³⁵ and ultrasound extension agreed with pathology in all BCC in a comparative series.⁷⁶ Line-field confocal optical coherence tomography matched histological subtype in 90% of tumours and outperformed dermoscopy in recognising superficial BCC,^{36,37} confocal microscopy was used to monitor photodynamic response,³⁸ and combined confocal microscopy and optical coherence tomography guidance of Er:YAG ablation reported one recurrence per 100 person-years.³⁹ After high-dose-rate brachytherapy, dermoscopy proved an adequate tool for monitoring tumour response.⁴⁵ These data support a hypothesis rather than a conclusion: that imaging-based selection of thin, low-risk tumours and imaging-based response assessment could reduce the failure penalty. Testing this in randomised trials is a research priority.

Heterogeneity and certainty of evidence. The heterogeneity of the combined analysis was largely explained by study design. Randomised trials yielded a homogeneous and larger penalty, whereas the three non-randomised studies, all at serious risk of bias, showed no difference. In these studies the less invasive option was preferentially offered to smaller, shallower or lower-risk tumours, and one cohort reported 16% recurrence after excision, which suggests that deeper tumours were channelled to surgery.²⁸ The prediction interval, which extended below unity, therefore reflects the divergence between designs rather than uncertainty about the direction of effect in randomised trials. Eight of the twelve studies analysed lesions rather than patients, and ignoring clustering overstates precision; the effect is probably modest because most patients contributed a single lesion, and the patient-level randomised trials showed the same direction.^{50,58} Time-to-event estimates reported by individual trials were concordant with the pooled risk ratios.^{50,53} Certainty was rated moderate for the randomised tumour-control estimate and for early failure, low for the combined estimate, late recurrence and investigator-rated cosmesis, and very low for patient-rated outcomes and wound infection, as detailed in Table 7.

Table 7. Summary of findings and certainty of evidence (GRADE).

Outcome	Studies	Risk ratio (95% CI)	Risk with excision	Risk with ablative therapy	Certainty	Main reasons for downgrading
Treatment failure — randomised trials	9 RCTs	5.34 (2.76 to 10.33)	21 per 1,000	111 per 1,000	Moderate	Risk of bias (per-protocol analyses, attrition, clinical ascertainment in some trials)
Treatment failure — all controlled studies	12 studies	3.26 (1.47 to 7.23)	32 per 1,000	103 per 1,000	Low	Risk of bias; inconsistency (I^2 60%, explained by design)
Early treatment failure (≤ 6 months)	5 studies	3.74 (1.95 to 7.18)	20 per 1,000	75 per 1,000	Moderate	Risk of bias
Late recurrence after initial clearance	11 studies	2.51 (1.09 to 5.80)	29 per 1,000	73 per 1,000	Low	Risk of bias; inconsistency
Good/excellent cosmesis, investigator-rated	2 RCTs	1.87 (1.54 to 2.26)	466 per 1,000	870 per 1,000	Low	Unblinded subjective outcome, industry sponsorship; indirectness (photodynamic therapy only)
Favourable patient-rated cosmesis or satisfaction	2 studies	1.21 (1.08 to 1.34)	796 per 1,000	959 per 1,000	Very low	Risk of bias; indirectness (mixed constructs); imprecision
Wound infection	4 studies	0.60 (0.27 to 1.37)	69 per 1,000	42 per 1,000	Very low	Risk of bias; serious imprecision (22 events)

Risk with excision is the pooled control-group risk of the contributing studies; risk with ablative therapy applies the pooled risk ratio to that baseline. For cosmetic outcomes the risks refer to a favourable result.

Strengths and limitations. This review had several strengths. It applied a single, clinically meaningful comparator across all energy-based and ablative modalities; searched four sources, including Scopus and a trial registry, without language restriction; linked all reports of each trial and used the longest follow-up; assessed randomised and non-randomised evidence with appropriate tools and analysed them separately; graded certainty; and tested robustness with ten sensitivity analyses, all of which preserved the direction and significance of the finding.

Several limitations must be acknowledged. First, the evidence base was small: individual modalities were represented by one to four studies, so modality-specific estimates were imprecise and the absence of a significant difference between modalities cannot be interpreted as equivalence. Second, three studies were non-randomised and at serious risk of confounding by indication; they were analysed separately, but their inclusion increased heterogeneity. Third, several trials were reported only briefly, as research letters or with limited methodological detail, which constrained the risk-of-bias assessment, and one trial reported outcomes only as percentages; including it in a sensitivity analysis did not alter the conclusions. Fourth, outcome definitions, time points, the unit of analysis and the method of ascertainment varied, and time-to-event data could not be pooled. Fifth, cosmetic outcomes were measured on heterogeneous scales, were available as counts for few studies and were at risk of measurement bias, while patient-reported quality of life, costs and treatment burden were rarely reported. Sixth, screening was performed by one investigator, and Embase and the Cochrane Central Register were not searched directly, although backward citation searching of previous evidence syntheses identified no additional eligible study. Finally, most trials enrolled low-risk tumours in European populations, limiting generalisability to high-risk subtypes, facial H-zone tumours and Asian populations, in whom nodular BCC predominates and incidence is rising.^{6,7}

Implications for practice and research. For fit patients with primary BCC in whom tumour control is the priority, surgical excision should remain the first choice. Energy-

based and ablative therapies are reasonable when surgery is contraindicated, when cosmetic or functional preservation outweighs a modest absolute increase in recurrence, or in older patients in whom the impact of BCC on quality of life is limited and treatment burden matters.^{9,11} Where photodynamic therapy is chosen, restriction to histologically confirmed superficial or thin nodular tumours is supported; where radiotherapy or brachytherapy is chosen, contemporary image-guided or individually planned techniques are preferable to historical approaches. In all cases, pre-treatment imaging of depth and subtype, shared decision-making that presents the absolute trade-off, and surveillance for at least five years are warranted. Future randomised trials should compare imaging-guided energy-based treatment with excision using histologically confirmed failure, patient-level analysis, time-to-event reporting and core cosmetic and patient-reported outcomes, and should include Asian and other under-represented populations.

Resource use also merits consideration. Surgically managed BCC generated substantial health-service costs in a national cohort,⁵ and a carbon dioxide laser-assisted photodynamic pathway reported a 43% saving per tumour compared with operative surgery, with five-year success comparable to excision in an uncontrolled series.⁷⁷ Any saving from a non-surgical first treatment must, however, be weighed against the cost of treating the additional failures identified in this analysis and of the longer surveillance they require. Formal cost-effectiveness analyses that incorporate the pooled failure penalty, imaging costs and patient preferences would help health systems, including those in Indonesia and other Asian countries where BCC incidence is rising, to allocate surgical, dermatological and radiological capacity.⁶

5. Conclusion

Energy-based and physically ablative destructive therapies for primary basal cell carcinoma were associated with a clinically important increase in treatment failure compared with surgical excision. The most credible evidence, from randomised trials, indicated an approximately five-fold relative increase (RR 5.34, 95% CI 2.76 to 10.33) with little heterogeneity, the absolute excess across studies was about eight failures per 100

tumours, and the difference became fully apparent only with follow-up of three years or longer. Photodynamic therapy delivered a better cosmetic result on low-certainty evidence, whereas radiotherapy and cryosurgery did not.

Surgical excision should remain the standard of care when tumour control is the principal goal. Photodynamic therapy, radiotherapy and brachytherapy, laser ablation, electrochemotherapy and curettage-based destruction remain valuable for selected patients who are unsuitable for or decline surgery, for thin low-risk tumours and for cosmetically sensitive sites, provided that selection is supported by imaging and histology and surveillance continues for at least five years. Randomised trials of imaging-guided selection are needed to determine whether the gap in tumour control can be narrowed while the cosmetic advantage is preserved.

Declarations

Ethical approval: Not applicable. This review analysed published aggregate data only, with no patient contact and no identifiable information.

Patient consent for publication: Not applicable.

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Author contributions (CRediT): NDASK: Conceptualisation, Methodology, Investigation, Data curation, Formal analysis, Visualisation, Writing – original draft. KKW: Conceptualisation, Validation, Supervision, Writing – review & editing. Both authors approved the final manuscript.

Data availability: All data analysed are contained in the published reports of the included studies. The data extraction workbook and analysis code are available from the corresponding author on reasonable request.

Declaration of AI use: None.

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References

- Kappelin J, Green AC, Ingvar Å, et al. Incidence and trends of basal cell carcinoma in Sweden: a population-based registry study. *Br J Dermatol*. 2022;186(6):963-969. doi:10.1111/bjd.20964
- Robsahm TE, Skog A, Veierød MB, et al. Nationwide study of cutaneous basal cell carcinoma incidence trends in Norway, 2012–2022. *Cancer Epidemiol*. 2026;105:103210. doi:10.1016/j.canep.2026.103210
- García Ruiz R, Mateu Puchades A, Alegre de Miquel V. Basal Cell Carcinoma: Incidence and Trends in Valencia, Spain. *Actas Dermosifiliogr*. 2024;115(10):T943-T947. doi:10.1016/j.ad.2024.09.010
- Mistry K, Levell NJ, Karponis D, et al. Trends in keratinocyte cancers in England, 2013–2022: basal cell carcinoma incidence, cutaneous squamous cell carcinoma incidence, and non-melanoma skin cancer mortality. *Br J Dermatol*. 2026. doi:10.1093/bjd/ljag315
- Ibrahim N, Jovic M, Ali S, et al. The epidemiology, healthcare and societal burden of basal cell carcinoma in Wales 2000–2018: a retrospective nationwide analysis. *Br J Dermatol*. 2023;188(3):380-389. doi:10.1093/bjd/ljac090
- Oh CC, Jin A, Koh WP. Trends of cutaneous basal cell carcinoma, squamous cell carcinoma, and melanoma among the Chinese, Malays, and Indians in Singapore from 1968–2016. *JAAD Int*. 2021;4:39-45. doi:10.1016/j.jdin.2021.05.006
- Tiyawatanaroj A, Sudtikoonaseth P, Chayangsu O. Basal cell carcinoma trends in Thailand: A 10-year retrospective study of demographic, clinical and histopathological features. *Dermatol Reports*. 2022;14(1):9413. doi:10.4081/dr.2022.9413
- Cai YX, Rong M. Global basal cell carcinoma in 55+ population: 1990–2021 burden, risk-factor trends and 2050 forecast. *Front Oncol*. 2025;15:1702129. doi:10.3389/fonc.2025.1702129
- van Winden MEC, Bronkhorst EM, Visch MB, et al. Predictors of surgical treatment burden, outcomes, and overall survival in older adults with basal cell carcinoma: Results from the prospective, multicenter BATOA cohort. *J Am Acad Dermatol*. 2022;86(5):1010-1019. doi:10.1016/j.jaad.2021.05.041
- Seretis K, Bounas N, Rapti E, et al. Basal Cell Carcinoma in Patients over 80 Years Presenting for Surgical Excision: Clinical Characteristics and Surgical Outcomes. *Curr Oncol*. 2025;32(3):120. doi:10.3390/curroncol32030120
- Van Coile L, Meertens A, Shen A, et al. The impact of basal cell carcinoma on the quality-of-life in older patients. *Sci Rep*. 2024;14(1):21739. doi:10.1038/s41598-024-67740-0
- Baltrušaitytė K, Zacharevskij E, Pilipaitytė L, et al. Assessment of Standard Surgical Excision Efficacy and Analysis of Recurrence-Associated Factors in 343 Cases of Nasal Basal Cell Carcinoma: A Single-Center Retrospective Study. *Healthcare (Basel)*. 2024;12(5):513. doi:10.3390/healthcare12050513
- Girardi FM, Wagner VP, Martins MD, et al. Factors associated with incomplete surgical margins in basal cell carcinoma of the head and neck. *Braz J Otorhinolaryngol*. 2021;87(6):695-701. doi:10.1016/j.bjorl.2020.02.007
- Di Maio P, Giudice M, Cavallero A, et al. Head and neck cutaneous basal cell carcinoma: a retrospective analysis of tumour features, surgical margins and recurrences. *Eur Arch Otorhinolaryngol*. 2025;282(6):3183-3191. doi:10.1007/s00405-025-09216-z
- Yildizdal S, Kucukguven A, Calis M, et al. Evaluation of histopathological margin and other recurrence parameters in basal cell carcinoma: A retrospective analysis of 8821 lesions. *J Plast Reconstr Aesthet Surg*. 2022;75(9):3390-3397. doi:10.1016/j.bjps.2022.06.013
- Stankovic P, Bock R, Rudhart SA, et al. Basal Cell Carcinoma of the Head and Neck—A Retrospective Single-Centre Comparison of the Recurrence Rate after R0 or R1 Resection. *Facial Plast Surg*. 2023;39(2):155-159. doi:10.1055/s-0042-1756466

17. Di Maria A, Barone G, Ferraro V, et al. Recurrence of Basal Cell Carcinoma Treated with Surgical Excision and Histopathological Analysis with Frozen Section Technique with Complete Margin Control (CMC-FS): A 15-Year Experience of a Reference Center. *Cancers (Basel)*. 2023;15(15):3840.
doi:10.3390/cancers15153840
18. Christensen E, Mørk E, Foss OA, et al. New, simplified versus standard photodynamic therapy (PDT) regimen for superficial and nodular basal cell carcinoma (BCC): A single-blind, non-inferiority, randomised controlled multicentre study. *PLoS One*. 2024;19(3):e0299718.
doi:10.1371/journal.pone.0299718
19. van Delft LCJ, Nelemans PJ, Kessels JPHM, et al. Long-Term Efficacy of Photodynamic Therapy with Fractionated 5-Aminolevulinic Acid 20% versus Conventional Two-Stage Topical Methyl Aminolevulinate for Superficial Basal-Cell Carcinoma. *Dermatology*. 2022;238(6):1044-1049.
doi:10.1159/000524745
20. Salmivuori M, Grönroos M, Tani T, et al. Long-term outcome of photodynamic therapy with hexyl aminolevulinate, 5-aminolevulinic acid nanoemulsion and methyl aminolevulinate for low-risk Basal Cell Carcinomas. *Photodiagnosis Photodyn Ther*. 2025;51:104432.
doi:10.1016/j.pdpdt.2024.104432
21. Schlesinger T, Chapman MS, Tu JH, et al. Red light photodynamic therapy with 10% aminolevulinic acid gel showed efficacy for treatment of superficial basal cell carcinoma in a randomized, vehicle controlled, double-blind, multicenter phase III study. *J Am Acad Dermatol*. 2025;93(6):1489-1498.
doi:10.1016/j.jaad.2025.08.031
22. McClure EM, Cockerell CJ, Hammond S, et al. Image-Guided Radiation Therapy Is Equally Effective for Basal and Squamous Cell Carcinoma. *Dermatopathology (Basel)*. 2024;11(4):315-329.
doi:10.3390/dermatopathology11040033
23. Chyrek AJ, Chicheł A, Burchardt WM, et al. Superficial high-dose-rate brachytherapy for primary tumors and relapses after surgery in patients with basal cell carcinoma of the head and neck region: results of a retrospective comparative cohort study. *J Contemp Brachytherapy*. 2022;14(5):438-445.
doi:10.5114/jcb.2022.121134
24. Laliscia C, Fuentes T, Coccia N, et al. High-dose-rate brachytherapy for non-melanoma skin cancer using tailored custom moulds – a single-centre experience. *Contemp Oncol (Pozn)*. 2021;25(1):12-16.
doi:10.5114/wo.2021.104688
25. Esmati E, Abyaneh R, Jaber R, et al. Surface mold brachytherapy for head and neck non-melanoma skin cancer – local control rates and survival: A retrospective analysis. *J Contemp Brachytherapy*. 2024;16(5):323-334.
doi:10.5114/jcb.2024.144703
26. Chatzikonstantinou G, Diefenhardt M, Fleischmann M, et al. Customized 3D-printed molds for high dose-rate brachytherapy in facial skin cancer: First clinical experience. *J Dtsch Dermatol Ges*. 2023;21(1):35-41.
doi:10.1111/ddg.14944
27. Ahluwalia J, Marsch AF, Zafar K, et al. Prospective Outcomes After 1064 nm Nd:YAG Laser Treatment of Basal Cell Carcinoma. *Lasers Surg Med*. 2026;58(4):290-293.
doi:10.1002/lsm.70106
28. Chen AC, Zheng C, Jian QC, et al. Comparison of clinical effects and patient satisfaction between ultra-pulsed CO₂ laser treatment and surgical excision in patients with facial basal cell carcinoma. *Front Surg*. 2025;12:1628257.
doi:10.3389/fsurg.2025.1628257
29. Backman EJ, Polesie S, Berglund S, et al. Curettage vs. cryosurgery for superficial basal cell carcinoma: a prospective, randomised and controlled trial. *J Eur Acad Dermatol Venereol*. 2022;36(10):1758-1765.
doi:10.1111/jdv.18209
30. Bertino G, Muir T, Odili J, et al. Treatment of Basal Cell Carcinoma with Electrochemotherapy: Insights from the InspECT Registry (2008–2019). *Curr Oncol*. 2022;29(8):5324-5337.
doi:10.3390/curroncol29080423
31. Groselj A, Bertino G, Minuti M, et al. Electrochemotherapy for basal cell carcinoma in the head and neck region: 5-year follow-up from the Insp-ECT registry. *Radiol Oncol*. 2025;59(2):233-243.
doi:10.2478/raon-2025-0040
32. Barcaui EO, Carvalho ACP, Valiante PM, et al. High-frequency (22-MHz) ultrasound for assessing the depth of basal cell carcinoma invasion. *Skin Res Technol*. 2021;27(5):676-681.
doi:10.1111/srt.12999
33. Bungărdean RM, Șerbănescu MS, Colosi HA, et al. High-frequency ultrasound: an essential non-invasive tool for the pre-therapeutic assessment of basal cell carcinoma. *Rom J Morphol Embryol*. 2021;62(2):545-551.
doi:10.47162/RJME.62.2.21
34. Wang LF, Zhu AQ, Wang Q, et al. Value of High-Frequency Ultrasound for Differentiating Invasive Basal Cell Carcinoma from Non-invasive Types. *Ultrasound Med Biol*. 2021;47(10):2910-2920.
doi:10.1016/j.ultrasmedbio.2021.06.006
35. Bozsányi S, Boostani M, Farkas K, et al. Optically Guided High-Frequency Ultrasound to Differentiate High-Risk Basal Cell Carcinoma Subtypes: A Single-Centre Prospective Study. *J Clin Med*. 2023;12(21):6910.
doi:10.3390/jcm12216910
36. Ruini C, Schuh S, Gust C, et al. Line-field optical coherence tomography: in vivo diagnosis of basal cell carcinoma subtypes compared with histopathology. *Clin Exp Dermatol*. 2021;46(8):1471-1481.
doi:10.1111/ced.14762
37. Orte Cano C, Sanak D, Lenoir C, et al. Diagnostic Performance of Line-Field Confocal Optical Coherence Tomography for Basal Cell Carcinoma: A Prospective Study. *Cancers (Basel)*. 2026;18(1):153.
doi:10.3390/cancers18010153
38. Tang Z, Lu T, Chen X, et al. Evaluation of confocal laser scanning microscopy in histological classification and photodynamic therapy of low-risk basal cell carcinoma. *Clin Exp Dermatol*. 2024;49(12):1601-1610.
doi:10.1093/ced/llae250
39. Kremer N, Cordova M, Sahu A, et al. Reflectance Confocal Microscopy-Optical Coherence Tomography-Guided Laser Ablation of Low-Risk Basal Cell Carcinoma: A Long-

- Term Prospective Follow-Up Study. *Lasers Surg Med*. 2026.
doi:10.1002/lsm.70201
40. Sharon E, Snast I, Lapidoth M, et al. Laser treatment for non-melanoma skin cancer: a systematic review and meta-analysis. *Am J Clin Dermatol*. 2021;22(1):25-38.
doi:10.1007/s40257-020-00562-8
 41. Koumprentziotis IA, Rompoti N, Liopyris K, et al. Photodynamic therapy for the treatment of basal cell carcinoma: a comprehensive review of randomized controlled trials. *Dermatol Pract Concept*. 2024;14(2):e2024105.
doi:10.5826/dpc.1402a105
 42. Ou-Yang Y, Zheng Y, Mills KE. Photodynamic therapy for skin carcinomas: a systematic review and meta-analysis. *Front Med (Lausanne)*. 2023;10:1089361.
doi:10.3389/fmed.2023.1089361
 43. Jiang M, Li D, Huang Y, et al. Efficacy and safety of ALA/MLA photodynamic therapy for superficial and nodular basal cell carcinoma: a systematic review and meta-analysis. *Front Oncol*. 2026;16:1802984.
doi:10.3389/fonc.2026.1802984
 44. Yadavalli P, Pareek V, Barthwal M, et al. Clinical and toxicity outcomes with 3D based-HDR surface mold brachytherapy in skin cancer. *J Cancer Res Ther*. 2024;20(3):930-934.
doi:10.4103/jcrt.jcrt_2641_22
 45. Krzysztofiak T, Suchorzepka M, Tukiendorf A, et al. Basal Cell Carcinoma After High Dose Rate Brachytherapy: Medium-term Dermoscopic Evaluation of Cancer's Response. *Dermatol Ther (Heidelb)*. 2023;13(9):2063-2078.
doi:10.1007/s13555-023-00981-5
 46. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
doi:10.1136/bmj.n71
 47. Salvio AG, Requena MB, Stringasci MD, et al. A 10-years follow-up of photodynamic therapy for nodular basal cell carcinoma: a randomized comparing the effectiveness of aminolevulinic acid-PDT, methyl aminolevulinic acid-PDT, and surgery. *Photodiagnosis Photodyn Ther*. 2025;54:104702.
doi:10.1016/j.pdpdt.2025.104702
 48. Zane C, Facchinetti E, Arisi M, et al. Pulsed CO₂ laser ablation of superficial basal cell of limbs and trunk: a comparative randomized clinical trial with cryotherapy and surgical ablation. *Dermatol Surg*. 2017;43(7):920-927.
doi:10.1097/DSS.0000000000001106
 49. Salmanpoor R, Motevalli D, Saki N, et al. Efficacy of excisional surgery, curettage and combined curettage and electrodesiccation in treatment of basal cell carcinoma. *Iran J Dermatol*. 2012;15(2):66-67. No DOI registered.
 50. Avril MF, Auperin A, Margulis A, et al. Basal cell carcinoma of the face: surgery or radiotherapy? Results of a randomized study. *Br J Cancer*. 1997;76(1):100-6.
doi:10.1038/bjc.1997.343
 51. Rhodes LE, de Rie M, Enström Y, et al. Photodynamic therapy using topical methyl aminolevulinate vs surgery for nodular basal cell carcinoma: results of a multicenter randomized prospective trial. *Arch Dermatol*. 2004;140(1):17-23.
doi:10.1001/archderm.140.1.17
 52. Rhodes LE, de Rie MA, Leifsdottir R, et al. Five-year follow-up of a randomized, prospective trial of topical methyl aminolevulinate photodynamic therapy vs surgery for nodular basal cell carcinoma. *Arch Dermatol*. 2007;143(9):1131-6.
doi:10.1001/archderm.143.9.1131
 53. Kuijpers DJ, Thissen MR, Berretty PJ, et al. Surgical excision versus curettage plus cryosurgery in the treatment of basal cell carcinoma. *Dermatol Surg*. 2007;33(5):579-87.
doi:10.1111/j.1524-4725.2007.33117.x
 54. Mosterd K, Thissen MR, Nelemans P, et al. Fractionated 5-aminolevulinic acid-photodynamic therapy vs. surgical excision in the treatment of nodular basal cell carcinoma: results of a randomized controlled trial. *Br J Dermatol*. 2008;159(4):864-70.
doi:10.1111/j.1365-2133.2008.08787.x
 55. Roozeboom MH, Aardoom MA, Nelemans PJ, et al. Fractionated 5-aminolevulinic acid photodynamic therapy after partial debulking versus surgical excision for nodular basal cell carcinoma: a randomized controlled trial with at least 5-year follow-up. *J Am Acad Dermatol*. 2013;69(2):280-7.
doi:10.1016/j.jaad.2013.02.014
 56. Szeimies RM, Ibbotson S, Murrell DF, et al. A clinical study comparing methyl aminolevulinate photodynamic therapy and surgery in small superficial basal cell carcinoma (8-20 mm), with a 12-month follow-up. *J Eur Acad Dermatol Venereol*. 2008;22(11):1302-11.
doi:10.1111/j.1468-3083.2008.02803.x
 57. Sinx KAE, Nelemans PJ, Kelleners-Smeets NWJ, et al. Surgery versus combined treatment with curettage and imiquimod for nodular basal cell carcinoma: one-year results of a noninferiority, randomized, controlled trial. *J Am Acad Dermatol*. 2020;83(2):469-476.
doi:10.1016/j.jaad.2020.04.053
 58. Verkouteren BJA, Nelemans PJ, Sinx KAE, et al. Imiquimod cream preceded by superficial curettage vs surgical excision for nodular basal cell carcinoma: a secondary analysis of a randomized clinical trial. *JAMA Dermatol*. 2025;161(3):299-304.
doi:10.1001/jamadermatol.2024.5572
 59. Clover AJP, Salwa SP, Bourke MG, et al. Electrochemotherapy for the treatment of primary basal cell carcinoma; a randomised control trial comparing electrochemotherapy and surgery with five year follow up. *Eur J Surg Oncol*. 2020;46(5):847-854.
doi:10.1016/j.ejso.2019.11.509
 60. Fonseca LPC, Haddad GR, Bastos LMH, et al. Curettage and electrocoagulation versus conventional surgery for treatment of low-risk basal cell carcinoma: a randomized study. *Int J Dermatol*. 2023;62(3):e128-e129.
doi:10.1111/ijd.16471
 61. Bastos LMH, Carvalho LP, Haddad GR, et al. Curettage and electrocoagulation versus surgical excision in the treatment of low-risk basal cell carcinoma – postoperative follow-up and satisfaction at three months: randomized clinical trial. *An Bras Dermatol*. 2022;97(3):384-386.
doi:10.1016/j.abd.2020.12.011

62. Cosgarea R, Susan M, Crisan M, et al. Photodynamic therapy using topical 5-aminolaevulinic acid vs. surgery for basal cell carcinoma. *J Eur Acad Dermatol Venereol*. 2013;27(8):980-4.
doi:10.1111/j.1468-3083.2012.04619.x
63. Scurtu LG, Petrica M, Grigore M, et al. A conservative combined laser cryoimmunotherapy treatment vs. surgical excision for basal cell carcinoma. *J Clin Med*. 2022;11(12):3439.
doi:10.3390/jcm11123439
64. Petit JY, Avril MF, Margulis A, et al. Evaluation of cosmetic results of a randomized trial comparing surgery and radiotherapy in the treatment of basal cell carcinoma of the face. *Plast Reconstr Surg*. 2000;105(7):2544-51.
doi:10.1097/00006534-200006000-00039
65. Thissen MR, Nieman FH, Ideler AH, et al. Cosmetic results of cryosurgery versus surgical excision for primary uncomplicated basal cell carcinomas of the head and neck. *Dermatol Surg*. 2000;26(8):759-64.
doi:10.1046/j.1524-4725.2000.ds00064.x
66. Sieborg J, Wenande E, Egeberg A, et al. Recurrence of basal cell carcinoma across different treatment modalities: a nationwide study with 8 years of follow-up and modelled prediction. *Acta Derm Venereol*. 2026;106:adv-2025-0064.
doi:10.2340/actadv.v106.adv-2025-0064
67. Cisek P, Kieszko D, Bilski M, et al. Interstitial HDR Brachytherapy in the Treatment of Non-Melanocytic Skin Cancers around the Eye. *Cancers (Basel)*. 2021;13(6):1425.
doi:10.3390/cancers13061425
68. Chow M, Eimpunth S, Hamman MS, et al. Effectiveness of a 595-nm Pulsed Dye Laser for the Treatment of Basal Cell Carcinoma Using One Double-Stacked Pulse Session: A Randomized, Double-Blinded Controlled Trial. *Dermatol Surg*. 2021;47(5):630-633.
doi:10.1097/DSS.0000000000002689
69. Baran KL, Cheung TC, Csank GA, et al. Pulsed Dye Laser for Treatment of Basal Cell Carcinoma. *Plast Reconstr Surg Glob Open*. 2023;11(3):e4850.
doi:10.1097/GOX.0000000000004850
70. Calik J, Sauer N, Woźniak B, et al. Pilot Study on High-Intensity Focused Ultrasound (HIFU) for Basal Cell Carcinoma: Effectiveness and Safety. *J Clin Med*. 2024;13(11):3277.
doi:10.3390/jcm13113277
71. Wiegell SR, Hendel K, Fuchs CSK, et al. An Explorative Study on Calcium Electroporation for Low-risk Basal Cell Carcinoma. *Acta Derm Venereol*. 2024;104:adv19678.
doi:10.2340/actadv.v104.19678
72. Gaitanis G, Zampeta A, Tsintzou P, et al. The Feasibility of Immunocryosurgery in the Treatment of Non-Superficial, Facial Basal Cell Carcinoma That Relapsed after Standard Surgical Excision: An Experience Report from Two Centers. *Curr Oncol*. 2022;29(11):8475-8482.
doi:10.3390/curroncol29110668
73. Mørk E, Mjones P, Foss OA, et al. Clinical versus Histological Assessment of Basal Cell Carcinoma Subtype and Thickness of Tumours Selected for Photodynamic Therapy. *Acta Derm Venereol*. 2024;104:adv18308.
doi:10.2340/actadv.v104.18308
74. Maytin EV, Zeitouni NC, Updyke A, et al. High-dose oral vitamin D in combination with photodynamic therapy can accelerate the clearance rate of basal cell carcinoma: A randomized clinical trial. *Photodiagnosis Photodyn Ther*. 2025;55:104704.
doi:10.1016/j.pdpdt.2025.104704
75. Nilsson PK, Knap U, Laurinaviciene R, et al. Comparative Study of CO₂ Laser and Curettage-Electrodesiccation for Superficial Basal Cell Carcinoma Treatment: A Focus on Cosmetic Results. *Dermatol Pract Concept*. 2025;15(3):5368.
doi:10.5826/dpc.1503a5368
76. Valian SK, Khorasanizadeh F, Kamyab K, et al. Basal cell carcinoma and squamous cell carcinoma: Comparison of high-frequency ultrasound and pathology. *Skin Res Technol*. 2024;30(8):e13897.
doi:10.1111/srt.13897
77. Azzopardi EA, Abdelrahman W, Azzopardi E, et al. Treatment of cutaneous basal cell carcinoma with combined laser extirpation and methyl aminolevulinic acid: five-year success rates. *Ann R Coll Surg Engl*. 2021;103(4):263-271.
doi:10.1308/rcsann.2020.7020