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Research Article

Frozen Section–Guided Resection Of Facial Basal Cell Carcinoma: Evaluating Intraoperative Margin Assessment And Preoperative Subtyping.

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Abstract

Background: Frozen section–guided excision and preoperative biopsy are widely used to control margins and to plan reconstruction in facial basal cell carcinoma (BCC), yet the accuracy of each step against definitive histology is rarely quantified in the same cohort.

Methods: Single-centre retrospective method-evaluation study of consecutive frozen section–guided facial BCC resections (January 2024–September 2025), reported per STARD 2015. The index test was the intraoperative frozen section margin (clear or involved); the reference standard was paraffin histology of the primary specimen. Sensitivity, specificity, predictive values and accuracy were calculated with Wilson 95% confidence intervals (CI). Biopsy–excision subtype concordance was assessed as exact and as dichotomised aggressive-versus-non-aggressive agreement.

Results: Of 280 consecutive BCC lesions (median patient age 77 years; 82.5% nasal), 278 had paired frozen and paraffin results. Frozen section sensitivity for an involved margin was 47.8% (95% CI 29.2–67.0), specificity 92.2% (88.2–94.9), positive predictive value 35.5% (21.1–53.1) and negative predictive value 95.1% (91.7–97.2). Among 269 lesions with paired subtypes, exact concordance was 72.1%; 11.9% were upgraded to an aggressive subtype at excision, and biopsy sensitivity for an aggressive subtype was 64.0% (53.7–73.2). In an exploratory analysis, upgrading increased with tumour size (>10 mm: odds ratio 2.49, 95% CI 1.18–5.25).

Conclusions: Both intraoperative frozen section and preoperative biopsy showed limitations in identifying involved margins and aggressive histological subtypes, a pattern compatible with limited tissue sampling, although the design cannot separate sampling from interpretation or from tumour exhaustion at frozen sectioning. Without follow-up data, these findings characterise diagnostic accuracy, not clinical consequences.

Keywords: Basal cell carcinoma · Frozen section · Surgical margins · Skin cancer · Diagnostic accuracy · Histological subtype.

INTRODUCTION

Basal cell carcinoma (BCC) is the most common malignancy in fair-skinned populations, and its incidence continues to rise across Europe and North America, driven by cumulative ultraviolet exposure and an ageing population [1,2]; registry data project a growing surgical burden over the coming decades [3]. Because most arise on the face, disproportionately on central, cosmetically sensitive regions such as the nose, much of the operative workload concerns anatomically constrained sites where complete tumour clearance must be balanced against the limited tissue available for reconstruction.

The World Health Organization classification distinguishes indolent growth patterns, principally nodular and superficial, from aggressive patterns (infiltrative, micronodular and morpheaform) that grow with irregular, finger-like projections and poorly defined borders [4–6]. Although these patterns do not necessarily signify aggressive behaviour of the tumour itself, the distinction is clinically consequential: aggressive subtypes show greater subclinical extension and carry a higher risk of incomplete resection and of surgically difficult recurrence, so identifying them before or during surgery can guide wider margins or intraoperative margin evaluation [6,7]. Complete removal is the standard of care for surgically treated BCC, and guidelines stratify treatment by the risk of residual disease [8–10]. For low-risk lesions, excision with a predefined clinical margin is adequate: a 4 mm margin clears more than 95%, and a 3 mm margin approximately 85%,

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of well-defined tumours smaller than 2 cm [11]. For high-risk facial BCC, guidelines favour complete circumferential peripheral and deep margin assessment: randomised trials of Mohs micrographic surgery versus standard excision reported fewer recurrences at five and ten years, significantly so for recurrent tumours [12–14], and registry and meta-analytic data confirm low recurrence across micrographic techniques [15,16]. Frozen section–guided excision is another approach to intraoperative margin control: specimen margins are examined by a histopathologist perioperatively, with protocols ranging from selected representative sections to complete en face evaluation [17], and further tissue is removed if a margin is reported as involved. Its accuracy, however, depends on sampling: conventional vertical ("bread-loaf") sectioning examines only a series of thin planes, so much of the true margin is never visualised and tumour between the planes may be missed [18].

Preoperative biopsy adds an earlier layer of information: beyond confirming the diagnosis, the subtype is routinely used to plan the resection margin and reconstruction. However, a small punch or curettage biopsy samples only a fraction of the lesion, and the literature consistently reports discordance between biopsy and excision subtype, usually with a more aggressive pattern revealed only at excision [19–21]. How often this "upgrading" occurs, and whether it varies with tumour size or biopsy technique, bears directly on how much weight the biopsy subtype should carry.

Few studies have examined both steps in the same anatomically homogeneous cohort. We therefore evaluated a consecutive series of frozen section–guided facial BCC resections, the vast majority involving the nose, with two aims: (1) to quantify the diagnostic performance of frozen section margin assessment against final paraffin histology, and (2) to assess the concordance of preoperative biopsy subtype with the excised tumour.

METHODS

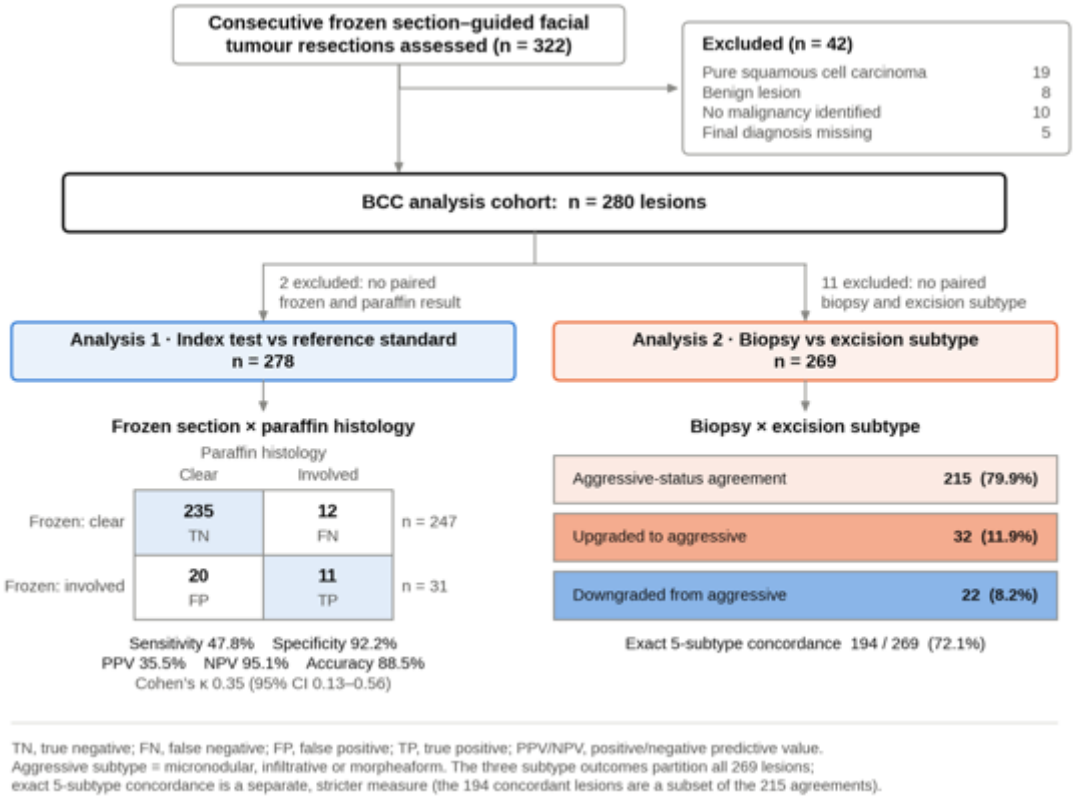
Study design and setting

This single-centre retrospective method evaluation compared an index test, intraoperative frozen section, with a reference standard, final paraffin histology, in patients undergoing frozen section–guided resection of facial BCC. Reporting follows STARD 2015 [22]; the completed checklist is provided as Online Resource 1. The final paraffin report was issued after a routine three- to five-week turnaround, so a discordant result was identified only after discharge. No frozen section result was recorded as indeterminate or deferred. No a priori sample size calculation was performed; the precision of the sensitivity estimate is limited by the number of margin-positive events. The study was not prospectively registered and was approved as a retrospective quality assurance project (EMN-2025-00153).

Participants

All consecutive patients who underwent frozen section–guided facial tumour resection between January 2024 and September 2025 were identified from the institutional registers. The surgeon decided the need for frozen section analysis. Of 322 consecutive resections, 42 were excluded because the final diagnosis was pure squamous cell carcinoma (19), a benign lesion (8), no malignancy (10) or a missing final diagnosis (5). The remaining 280 lesions formed the analysis cohort. The lesion was the unit of analysis for margin status and subtype, whereas age and sex are patient-level attributes. Of the 280 lesions, 278 had both a frozen and a paraffin margin result; the two without were excluded from the frozen-versus-paraffin comparison (**Fig. 1**).

Figure 1. STARD-based flow diagram of the cohort and analyses, from 322 assessed resections to the 280-lesion BCC cohort, and the two primary analyses (frozen vs paraffin, n = 278; biopsy vs excision subtype, n = 269).



Procedures, index test and reference standard

Lesions were excised with a clinical margin of 3 or 5 mm at the operating surgeon's discretion and assessed intraoperatively by frozen section. The index test was the frozen section assessment of the resection margin, recorded as clear or involved. Four frozen section samples were excised from the margins and one from the deep wound bed. The reference standard was the final margin status of the primary excision specimen on paraffin histology after formalin fixation and embedding; re-excision tissue did not contribute to this classification. Preoperative biopsy and final excision subtypes were each classified as nodular, superficial, micronodular, infiltrative or morpheaform; the micronodular, infiltrative and morpheaform subtypes were grouped as aggressive for analysis. Frozen and permanent sections were reported by the same departmental pathology service as part of routine care, not necessarily by the same pathologist, and without blinding, so review bias cannot be excluded. Tissue examined at frozen section was subsequently embedded and re-examined in paraffin, so the index-test material contributed to the reference standard (incorporation). Two operative variables were recorded and are reported separately: further tissue removed at the initial operation (same sitting), and a second or subsequent operation (return to theatre).

Variables and statistical analysis

Extracted variables included age, sex, anatomical location and nasal subsite, tumour diameter, excision margin, primary versus recurrent status, biopsy method, preoperative and final subtype, frozen and paraffin margin status, number of procedures, operative time per procedure, reconstruction and complications.

Continuous variables are summarised as median (interquartile range, IQR) and categorical variables as counts (%). Sensitivity, specificity, positive and negative predictive values and accuracy were calculated against the reference standard with 95% confidence intervals (CI) by the Wilson score method, and agreement was quantified with Cohen's κ. Biopsy–excision subtype concordance was assessed as exact agreement and for the dichotomised aggressive-versus-non-aggressive classification, with McNemar's test for asymmetry between up- and downgrading. Associations were assessed with Fisher's exact test, the chi-square test, the Mann–Whitney U test, univariable logistic regression (tumour diameter and upgrading) and the Cochran–Armitage test for trend across size quartiles. Two-sided $p < 0.05$ was considered significant. Analyses were performed in R version 4.6.1 (R Foundation for Statistical Computing). The two primary estimates were the diagnostic accuracy of frozen section and the biopsy–excision subtype concordance; all other comparisons, including the size analyses in **Table 3**, are exploratory, were not prespecified and are unadjusted for multiplicity.

RESULTS

Cohort characteristics

Median patient age was 77 years (IQR 68–82) and 149 (53.2%) were male (**Table 1**). Frozen section–guided excision was performed predominantly on the nose (231 lesions, 82.5%). The median tumour diameter was 9 mm (IQR 6–12), and 37 lesions (13.3%) were recurrent. A 3 mm clinical margin was used in 76.1% and 5 mm in 22.1%. At excision, 172 tumours (62.3%) were nodular and 92 (33.3%) aggressive (infiltrative 26.4%, micronodular 5.8%, morpheaform 1.1%). Further tissue was removed at the initial operation in 46 of 280 lesions (16.4%), and 18 (6.4%) required a second or subsequent operation. Among the 31 lesions with a positive frozen section, 24 (77.4%) had further tissue removed at the same sitting and 12 (38.7%) underwent a further operation, and in seven (22.6%) reconstruction with watchful waiting was chosen.

Table 1. Patient, tumour and treatment characteristics of the BCC cohort (N = 280 lesions).

Characteristic	n (%)	N with data
Age, years, median (IQR)	77 (68–82)	280
Age, years, mean (SD)	74.5 (10.4)	280
Male sex	149 (53.2)	280
Current smoker	25 (9.3)	268
Alcohol above limit	20 (7.5)	267
Location: nose	231 (82.5)	280
Location: periorbital	20 (7.1)	280
Location: buccal/cheek	13 (4.6)	280
Location: perioral	10 (3.6)	280
Location: other facial site	6 (2.1)	280
Nasal subsite: ala	135 (58.4)	231
Nasal subsite: apex	57 (24.7)	231
Tumour diameter, mm, median (IQR)	9 (6–12)	280
Recurrent tumour	37 (13.3)	279
Excision margin 3 mm	213 (76.1)	280
Excision margin 5 mm	62 (22.1)	280
Excision margin: other or not recorded	5 (1.8)	280
Biopsy: punch	176 (62.9)	280
Biopsy: curettage	33 (11.8)	280
Biopsy: other method	14 (5.0)	280
Biopsy: not recorded	57 (20.4)	280
Excision subtype: nodular	172 (62.3)	276
Excision subtype: infiltrative	73 (26.4)	276
Excision subtype: micronodular	16 (5.8)	276
Excision subtype: superficial	12 (4.3)	276
Excision subtype: morpheaform	3 (1.1)	276
Aggressive subtype (overall)	92 (33.3)	276
Reconstruction: local flap	226 (81.6)	277
Reconstruction: full-thickness graft	28 (10.1)	277
Reconstruction: other	23 (8.3)	277
Further tissue removed at the initial operation	46 (16.4)	280
Second or subsequent operation	18 (6.4)	280

Aggressive subtype = micronodular, infiltrative or morpheaform. IQR, interquartile range; SD, standard deviation. Biopsy categories sum to 280

Frozen section versus final paraffin histology

Among 278 lesions with both results, frozen section reported a clear margin in 12 whose paraffin result showed involvement, and an involved margin in 20 whose paraffin result was clear (**Table 2**). Against the reference standard, frozen section had a sensitivity of 47.8% (95% CI 29.2–67.0) and a specificity of 92.2% (88.2–94.9). The positive predictive value was 35.5% (21.1–53.1) and the negative predictive value 95.1% (91.7–97.2), with an overall accuracy of 88.5% (84.2–91.7). Agreement between the two methods was fair (Cohen's κ 0.35, 95% CI 0.13–0.56). The 12 false-negative lesions had a median diameter of 11 mm; ten were nasal, and seven were aggressive at excision.

Table 2. Diagnostic performance of frozen section against final paraffin histology (n = 278 lesions)

	Paraffin: clear	**Paraffin: involved**	**Total**
Frozen: clear	235 (TN)	12 (FN)	247
Frozen: involved	20 (FP)	11 (TP)	31
Total	255	23	278
Measure	**n/N**	**Estimate (%)**	**95% CI**
Sensitivity	11/23	47.8	29.2–67.0
Specificity	235/255	92.2	88.2–94.9
Positive predictive value	11/31	35.5	21.1–53.1
Negative predictive value	235/247	95.1	91.7–97.2
Overall accuracy	246/278	88.5	84.2–91.7
Positive likelihood ratio	—	6.1	3.3–11.1
Negative likelihood ratio	—	0.57	0.38–0.84
Cohen's κ	—	0.35	0.13–0.56

Reference standard is final paraffin histology of the primary excision specimen. 95% CIs by the Wilson score method; κ CI by Cohen's (1960) standard error; likelihood-ratio CIs by the log method. Margin-positive prevalence 23/278 (8.3%, 95% CI 5.6–12.1). TN, true negative; FN, false negative; FP, false positive; TP, true positive.

Preoperative biopsy versus final excision subtype

Paired subtypes were available for 269 lesions. Exact subtype concordance was 72.1% (95% CI 66.5–77.1). Thirty-two lesions (11.9%, 95% CI 8.6–16.3) were upgraded from a non-aggressive biopsy subtype to an aggressive excision subtype, and 22 (8.2%) were downgraded (McNemar p = 0.22; **Fig. 2**). For an aggressive subtype, biopsy had a sensitivity of 64.0% (95% CI 53.7–73.2), specificity 87.8% (82.2–91.8), positive predictive value 72.2% (61.4–80.8), negative predictive value 83.2% (77.2–87.8) and overall accuracy 79.9% (74.7–84.3), with moderate agreement (Cohen's κ 0.53, 95% CI 0.42–0.64). Biopsy correctly classified 86.3% of nodular tumours but only 52.8% of infiltrative and 28.6% of micronodular tumours. Concordance did not differ between punch biopsy and curettage (75.0% vs 72.7%; Fisher p = 0.83).

In an exploratory analysis, upgrading to an aggressive subtype was associated with tumour size, occurring in 8.6% of lesions ≤10 mm versus 19.0% of those >10 mm (odds ratio 2.49, 95% CI 1.18–5.25; p = 0.024; **Table 3**). The odds of upgrading rose by 8% per additional millimetre of diameter (odds ratio 1.08, 95% CI 1.01–1.14; p = 0.020), with a significant Cochran–Armitage trend across size quartiles (z = 2.81, p = 0.005), although the quartile proportions were not monotonic (5.0%, 5.1%, 22.9% and 15.0%; chi-square p = 0.002) and are reported descriptively.

Figure 2. Subtype migration from preoperative biopsy to final excision (n = 269), showing exact concordance of 72.1% and upgrading to an aggressive subtype in 11.9% (3.7% net of downgrading).

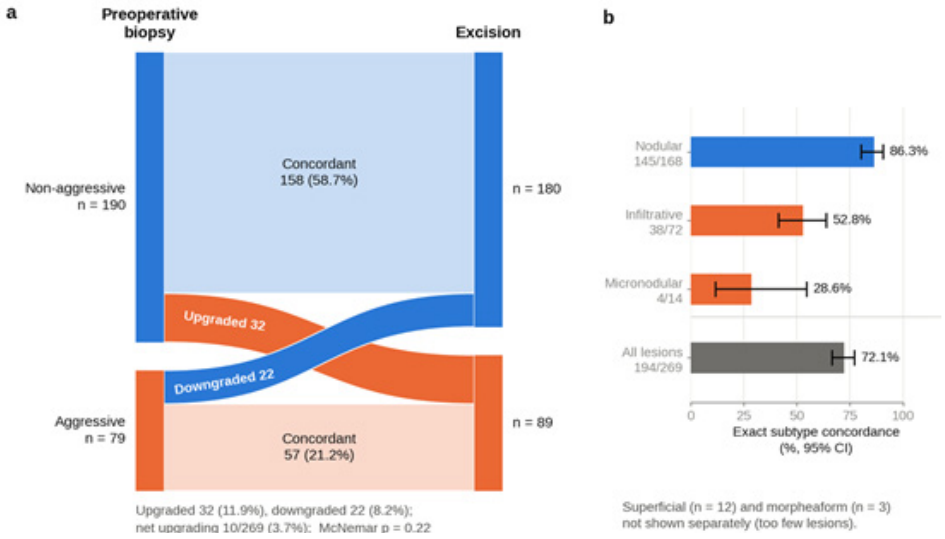


Table 3. Concordance between preoperative biopsy and final excision subtype (n = 269 lesions).

Measure	n/N (%)	95% CI
Exact subtype concordance	194/269 (72.1)	66.5–77.1
Upgraded to aggressive subtype	32/269 (11.9)	8.6–16.3
Downgraded from aggressive subtype	22/269 (8.2)	5.5–12.1
Biopsy sensitivity for aggressive subtype	57/89 (64.0)	53.7–73.2
Concordance: punch biopsy	129/172 (75.0)	68.0–80.9
Concordance: curettage	24/33 (72.7)	55.8–84.9
Correctly predicted: nodular	145/168 (86.3)	80.3–90.7
Correctly predicted: infiltrative	38/72 (52.8)	41.4–63.9
Correctly predicted: micronodular	4/14 (28.6)	11.7–54.6
Upgraded to aggressive subtype, tumour ≤10 mm[a]	16/185 (8.6)	5.4–13.6
Upgraded to aggressive subtype, tumour >10 mm[a]	16/84 (19.0)	12.1–28.7

Aggressive subtype = micronodular, infiltrative or morpheaform. 95% CIs by the Wilson score method. Punch vs curettage: Fisher p = 0.83. Upgrading by size quartile: chi-square p = 0.002. a Odds ratio for upgrading, >10 mm vs ≤10 mm: 2.49 (95% CI 1.18–5.25), Fisher p = 0.024.

Operative burden after a false-positive frozen section

To isolate the consequences of a false-positive result, false-positive lesions were compared with true negatives, which share the same true (clear) final margin status. False-positive lesions underwent a second or subsequent operation far more often than true negatives (7/20, 35.0%, vs 3/235, 1.3%; $p < 0.001$) and had longer operative times (median 150 vs 120 minutes; $p = 0.014$). Because a positive frozen result is, by protocol, the indication for further excision at the same sitting, both the higher procedure count and the longer operative time are partly protocol-driven rather than independent associations. Even so, seven false-positive lesions were re-operated without residual tumour having been identified on the permanent sections of the primary specimen.

DISCUSSION

In this predominantly nasal BCC cohort, two sequential assessments of disease extent fell short of the final histology in the same direction: intraoperative frozen section identified about half of truly involved margins (sensitivity 48%) and preoperative biopsy two-thirds of aggressive subtypes (sensitivity 64%), a pattern compatible with limited tissue sampling, although the design cannot separate sampling from interpretation.

Frozen section performance in context

The high specificity (92%) and negative predictive value (95%) resemble published frozen-section series [17], although at a margin-positive prevalence of 8.3% an uninformative test would already yield a negative predictive value of 91.7%. The limitation lies in sensitivity: at 48%, a truly positive margin was

as likely to be called clear as involved, with agreement only modestly better than chance (κ 0.35). This is the predictable signature of bread-loaf sampling, which examines only a small percentage of the true peripheral margin [18]; even the measurement of clearance margins varies between observers [23]. Micrographic techniques invert this geometry, examining the entire peripheral and deep margin en face, and achieve low recurrence [12–16], as do whole-specimen frozen protocols [15,17]. Our protocol samples the margin as a bread-loaf paraffin work-up does, so its sensitivity is bound by the same geometry: complete versus partial margin assessment matters more than frozen versus paraffin.

The low positive predictive value of 36% has a separate, practical cost. Two of every three positive frozen reports were not confirmed on paraffin, yet a positive result triggered further excision by protocol, and the false positives were re-operated more often and spent longer in theatre than true negatives with identical tumour-free margins. Part of this gap is definitional, but unnecessary tissue removal on the nasal ala or apex is not a trivial cost. Alongside sit the false negatives: in twelve lesions an involved margin was recorded only after paraffin, after the patient had been discharged; three were re-operated, and one patient received radiotherapy because comorbidity precluded surgery. The discordance therefore cuts both ways, over-treating some patients and under-treating others within the same protocol.

Biopsy subtyping and the size effect

The subtyping results tell a parallel story. Exact concordance of 72% is consistent with published ranges, and the predominance of upgrading over downgrading reproduces a well-documented feature of BCC biopsy sampling [19–21]. The most informative finding is the dependence on tumour size: the odds of upgrading were roughly two-and-a-half times higher in tumours larger than 10 mm, as a sampling model predicts, because a fixed-calibre punch removes a shrinking fraction of an enlarging lesion. Concordance was similar for punch biopsy and curettage, although with 33 curettage lesions this comparison is inconclusive; series documenting upgrading discovered only at micrographic surgery likewise implicate how much of the tumour is sampled [19,20]. A non-aggressive biopsy subtype is therefore a weaker reassurance in a larger tumour, a biopsy that samples more of the lesion should narrow the gap, and a nodular or superficial biopsy subtype should not justify the narrowest margins once diameter exceeds one centimetre, where incomplete excision is itself more frequent [24].

Two tools, one limitation

The two analyses describe one phenomenon at two moments in the pathway: a small biopsy under-samples the tumour and can miss an aggressive component; bread-loaf frozen sectioning under-samples the margin and can miss residual tumour. Partial sampling is a plausible common mechanism, but our data do not establish it: neither an aggressive excision subtype (false-negative frozen section in 7 of 13 involved margins with an aggressive subtype versus 5 of 10 without; p = 1.00) nor tumour diameter (median 11 versus 10 mm; p = 0.15) predicted a false-negative frozen section, although with 23 margin-positive events these comparisons are severely underpowered. The cohort does show that an aggressive subtype (p = 0.020) and a larger tumour diameter (p = 0.039) each predict a truly involved margin, so the tumours least likely to be cleared are those for which a clear frozen section offers least reassurance. The practical question is therefore not frozen versus paraffin but complete versus representative margin assessment, and not which biopsy instrument but how much of the lesion is sampled [17,18].

Strengths and limitations

Comparing the index test with paraffin histology of the same specimen minimises verification bias, and comparing false positives only with true negatives, lesions with the same true margin status, isolates the effect of a false-positive label from that of residual tumour. The cohort is consecutive, anatomically homogeneous and of reasonable size for a single centre. First and foremost, there was no follow-up: we cannot say whether the twelve lesions with involved margins identified only on paraffin recurred, nor whether the additional excisions in false-positive patients conferred benefit. The study therefore establishes that frozen section is discordant with paraffin and that biopsy under-recognises aggressive subtypes, but not that this discordance changed outcomes. The clinical significance of a missed margin must be imported from the recurrence literature, in which Mohs surgery lowered ten-year recurrence for recurrent but not significantly for primary facial tumours [14]. Second, because unblinded reading of the reference standard would inflate apparent agreement, and agreement was nonetheless only fair, the true concordance is plausibly worse than measured. Third, margin width was not compared, because 5 mm margins were chosen selectively for larger, recurrent and aggressive tumours. Fourth, biopsy method was unrecorded in a fifth of lesions, a group over-representing infiltrative tumours and therefore not missing at random; the method comparison was confined to lesions with a recorded technique. Fifth, frozen section was applied selectively rather than to all facial BCC, so the case mix is not representative and the predictive values apply only at the observed margin-positive prevalence of 8.3%; sensitivity and specificity are less prevalence-dependent, although spectrum effects, the single-centre design and the 23 margin-positive events limit their generalisability and precision. Sixth, the number of blocks and sections per specimen was not

recorded, so the proportion of the margin examined cannot be quantified. Finally, a positive frozen section not confirmed on permanent sections could reflect exhaustion of a small tumour focus in the tissue consumed at frozen sectioning rather than a diagnostic error; re-embedding recovers deeper levels but not the sections already cut, so this cannot be excluded, although the two specimens in which frozen-section BCC was not retrieved in the paraffin block were not among the discordant margin readings.

Implications

Of 100 such lesions, about eight have a truly involved margin; a clear frozen section lowers this to about five (negative likelihood ratio 0.57), so much of its reassurance reflects the low pre-test probability, whereas a positive result raises it to about 36 (positive likelihood ratio 6.1) and must be weighed against the cost of further excision on the central face. A non-aggressive biopsy subtype is informative but less dependable in larger tumours, where the threshold for wider margins or referral for complete margin control might reasonably be lower. Where recurrence risk is high, the evidence base favours complete circumferential margin assessment, and our results give a plausible mechanistic reason why partial-sampling alternatives may underperform [8–10,25]. Prospective work linking these discrepancies to recurrence, ideally with whole-specimen or en face sampling, would convert this accuracy estimate into the outcome estimate that clinical decisions require [15,17,18].

CONCLUSIONS

Frozen section–guided resection and preoperative biopsy each underestimated the extent of facial BCC, missing about half of involved margins and a third of aggressive subtypes respectively, with the subtyping gap larger in tumours over one centimetre in an exploratory analysis. This pattern is compatible with partial sampling as a common mechanism, which this design cannot confirm, and with complete margin and lesion assessment as the common remedy. Without follow-up, these results define diagnostic accuracy rather than clinical consequences, and are best read as a rationale for prospective, outcome-linked evaluation rather than as grounds for immediate changes in practice.

Statements and Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

Conceptualisation: A.N.M., L.K.R., M.K.H., I.S., F.P.W.M. and N.K.; methodology: L.K.R., M.K.H., I.S., F.P.W.M. and N.K.; validation: A.N.M., M.K.H., R.K., I.S. and F.P.W.M.; formal analysis: M.K.H. and L.K.R.; investigation: A.N.M., M.K.H., I.S., T.A., F.P.W.M. and N.K.; resources: I.S., T.A. and N.K.; data curation: L.K.R. and M.K.H.; writing—original draft: A.N.M. and F.P.W.M.; writing—review and editing: A.N.M., M.K.H., L.K.R., R.K., I.S., T.A., F.P.W.M. and N.K.; visualisation: M.K.H., L.K.R. and F.P.W.M.; supervision: I.S., T.A., F.P.W.M. and N.K.; project administration: A.N.M., M.K.H. and F.P.W.M. All authors read and approved the final manuscript.

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki. As a retrospective quality assurance study, it was approved by the hospital board of Zealand University Hospital (approval number EMN-2025-00153, 30 October 2025); formal research ethics committee approval was not required for this type of quality assurance project under national regulations.

Consent to participate

Patient consent was waived by the hospital board of Zealand University Hospital because this is a retrospective quality assurance study based on data recorded during routine clinical care. No identifiable patient information is reported, and all data were processed in compliance with the General Data Protection Regulation (GDPR).

Consent to publish

Not applicable; the manuscript contains no identifiable patient information.

Data availability

The data presented in this study are available on request from the corresponding author, subject to ethical and data-protection restrictions under the General Data Protection Regulation (GDPR) and the study's quality assurance approval (EMN-2025-00153).

Declaration of generative AI use

A large language model was used to assist with language editing and with organising the manuscript and reference list. All data, analyses, citations and interpretations were produced and verified by the authors, who take full responsibility for the content.

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