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Whole specimen intraoperative frozen section analysis. Experience with 1082 basal cell carcinomas

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Abstract

Background: Basal cell carcinomas (BCCs) excised leaving positive tumour margins, are at a higher risk of recurrence. Accordingly, complete tumour removal with preservation of healthy tissue, aiming for low recurrence rates, is the main goal in treating BCCs.
Objective: The present study aimed to identify the reliability of the Whole Specimen Intraoperative Frozen Section Analysis (WIFSA) technique by comparing intraoperative WIFSA and postoperative Formalin-Fixed Paraffin-Embedded section analysis (FFPE) results in 1082 basal cell carcinomas and by assessing the recurrence rates during a follow-up period up to 10 years.
Methods: A single-centre retrospective cohort of all patients with BCC of the face receiving surgical excision with the WIFSA method between January 2007 and December 2013 was evaluated. We compared the intraoperative frozen section results with postoperative FFPE in order to assess accuracy of the WIFSA. Recurrence rates were assessed among all BCCs with a tumour-free margin at final excision that had a minimum follow-up of 6 months.
Results: A total of 996 patients with 1082 BCCs were treated with the WIFSA. Overall agreement of WIFSA with conventional postoperative FFPE was 98·8%, sensitivity and specificity being 99·0% and 98·7% respectively. We excluded 23 BCCs that still had positive tumour margins at the end of the procedure and another 67 for the analysis of recurrence rate because follow-up was shorter than 6 months. A total of 992 BCCs with a tumour-free margin at final excision had a mean follow-up of 5·6 years (mean 67 ± 27·7 months (range 6–117 months)). The total recurrence rate was 2·1% (21 out of 992 BCCs). The recurrence rate among the primary tumours was 1·6% (13 out of 828 cases) and 4·9% among the recurring tumours (8 out of 164 cases).
Conclusion: This study indicates that, in patients with primary or recurring BCCs, WIFSA provides a high accuracy for intraoperative specimen analysis and has a low recurrence rate after a mean follow-up of 5·6 years.
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Keywords: Basal cell carcinoma; Whole specimen intraoperative frozen section analysis; Frozen section analysis; Recurrence rate

Introduction

Basal cell carcinoma (BCC) is the most frequently occurring type of skin cancer, with a prevalence up to 30% among adults [1]. The estimated incidence rates of BCC in the Netherlands and United States among men are respectively 122 and 247 per 100,000. Among women these incidence rates are respectively 119 and 150 per 100,000. Australia has the highest incidence rates with 2074 for men and 1579 for women per 100,000 [2,3]. This high incidence of BCCs consequently has a huge impact on patients' Quality of Life and creates an enormous burden on the health care system.

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BCC, a slowly growing and locally invasive tumour, is associated with high morbidity due to destruction of the skin and surrounding structures [4]. Up to 80% of BCCs are located in the area of the head and face [5,6]. The local damage is often greater in case of recurrence due to inadequate treatment of primary tumours [7]. Therefore, surgical techniques allowing margin control, such as standard surgical excision combined with intraoperative frozen section margin sampling (i.e. Mohs micrographic surgery (MMS), en face frozen section, bread loaf frozen section and cross sectional frozen section) forms the basis of an adequate treatment guideline [8]. After total tumour removal, recurrence rate is the most important clinical outcome in treatment of skin cancer in general.

At the Medical Centre Leeuwarden (MCL) in the Netherlands we use the Whole Specimen Intraoperative Frozen Section Analysis (WIFSA) technique. WIFSA is a fast bread-loaf intraoperative frozen section technique that aims to ensure complete removal of the whole tumour enabling safe direct reconstruction. Specimens are then postoperatively compared with the intraoperative outcomes to double check tumour-free margins. A previous study of surgical excision with the WIFSA technique showed low recurrence rates of BCCs after a mean follow-up of 4·9 years [9]. The present study aimed to identify the accuracy of the WIFSA technique by comparing WIFSA and postoperative formalin fixed paraffin embedded (FFPE) results and recurrence rates in a large cohort of BCC patients undergoing WIFSA with a follow-up period of up to 10 years.

Materials and methods

We performed a retrospective review of all electronic medical records. We included all patients diagnosed with BCC of the face who underwent surgical excision with the WIFSA technique at the Department of Plastic, Reconstructive and Hand Surgery between January 2007 and December 2013. All surgical excisions were performed by experienced plastic surgeons or by residents under their supervision.

Data gathered from medical records for analyses included patient demographics (i.e. age at time of surgery and gender), tumour characteristics (i.e. primary versus recurrent BCC, anatomical location and histopathological growth pattern), reason for referral, and duration of follow-up (i.e. recurrence rate). Primary lesions were defined as those that had not occurred previously, whereas recurrence was defined as reappearance of a histologically confirmed BCC in close relationship to or within the scar of the previous surgical excision.

For the WIFSA technique BCCs $\leq$ 10 mm were excised with a 3 mm clinically tumour free margin. A 5 mm margin was applied for BCCs $>$ 10 mm, BCCs with a morpheaform growth pattern and recurring BCCs. The tumour was marked in situ prior to complete excision with a suture at 12 o'clock after which it was processed and coloured by the analyst with red dye (12–6 o'clock) and blue dye on the left side to maintain orientation. After being cut in a bread-loaf fashion of 2 mm, the tissues were frozen in a gel-like compound (Tissue-Tek, Sakura Finetek USA Inc., Torrance, California) and cut with a cryostat microtome into sections of 10–30 μm. The coupes were then stained with hematoxylin and eosin and examined by an experienced pathologist. If necessary, this procedure was repeated after the residual tumour had been removed. The remaining specimen was then postoperatively analysed with traditional Formalin-Fixed Paraffin-Embedded section analysis (FFPE) as a final control. After consultation between the pathologist and surgeon, some patients with close tumour free margins received an additional excision without WIFSA but merely with postoperative FFPE.

Differences in patient or tumour characteristics between procedures with and without re-excision were assessed with Pearson's chi-squared tests for categorical variables and Mann-Whitney U test for continuous variables. Multivariate logistic regression analysis, including all variables with $p < 0{\cdot}05$ in univariate analyses, were used to asses associations of patient or tumour characteristics with re-excision. Considering FFPE as a gold standard for histological examination, a sensitivity and specificity analysis was performed with the intraoperative frozen section outcomes. Recurrence rates, with a minimum follow-up of 6 months, where assessed separately for BCCs with tumour free- and positive margins. Cox regression models were used to assess associations between patient or tumour characteristics and tumour recurrence of BCCs with tumour-free margins at initial excision. All statistical analyses were performed with the Statistical Package for Social Sciences, version 24·0 (SPSS Inc., Chicago, Illinois).

For this study, we did not engage in any direct physical contact with patients, and the required patient information was readily available and registered prior to this study. Therefore, in line with national guidelines permission from the institutional review board was not required to perform this study.

Results

Nine hundred sixty-six patients (478 male and 518 female) with 1082 BCCs were treated with WIFSA. There were 895 primary BCCs (82·7%) and 187 recurrent BBCs (17·3%). Patient mean age during WIFSA was 68·8 ± 13·3 years (range 19·4–97·7). Most patients were referred by a dermatologist, because of the location of the BCC in the high-risk zone of the face (H-zone). Other reasons for referral were recurring BCCs, and BCCs with a high-risk growth pattern (superficial, micronodular, morpheaform).

The majority of BCCs were located on the nose 557 (51·5%, Table 1). The detailed anatomical distribution of BCC is presented in Table 2. The histopathological growth pattern was nodular in 880 (81·3%), morpheaform in 31

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