

Frozen section in surgical treatment of non-melanoma skin cancer

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ABSTRACT

Background: Frozen section histology (FS) is often used when treating non-melanoma skin cancer (NMSC) with surgical excision and reconstruction. The aim of the study is to evaluate the efficiency of FS in the surgical treatment of NMSC.

Methods: A retrospective study was designed selecting all patients treated for NMSC from 1st of January to 31th of December 2015 at the Department of Plastic Surgery, Sygehus Lillebælt Vejle, Odense University Hospital, Denmark. Patients were identified by the WHO ICD-10 diagnosis codes for NMSC and the procedure code for FS. Data was retrieved from the Danish national pathology database Pato-Web and the patients' electronical journal.

Results: We identified 34 patients with NMSCs where peroperative FS was used. A total of 35 NMSCs were treated. Male-female ratio was 1.12. Mean age 71.5 years. Mean tumor size 12.5 mm (range 3-30 mm). BCC/SCC ratio was 4.8. Concerning stages, 86 % were T1 stage and 14.3 % T2 tumors. 44% of the operations were performed on high-risk areas of the head and neck area (ala nasi 29 %, medial canthus 6 %, lateral canthus 3 % and lip 6 %). Direct closure was performed in 12 %, skin transplants in 15 % and local flaps in 73 % of the patients. 76 % were hospitalized after surgery, mean time in hospital was one day. FS and paraffin section (PS) concurred in all but a single patient with a 15 mm T1 BCC of the temporal region, resulting in a 97 % concordance rate between FS and PS.

Conclusion: FS appears to be a valuable tool for the surgeon to control NMSC margins in selected cases with need for reconstruction. FS can minimize the extent of surgery as well as ensure a safe reconstruction for the patients.

INTRODUCTION

Background

The incidence of non-melanoma skin cancer (NMSC) is increasing.⁹ Surgery has several advantages over other treatments including histological examination of the margins as well as full tumor characterization. Excision with histological verified clear margins remains the golden standard for treating NMSCs. Surgical treatment of NMSCs in the head and neck area often include delicate areas (eyes, ears, nose and lips) and may result in the need of a reconstruction. Frozen section histology (FS) is commonly used to ensure tumor radicality prior

to flap/transplant reconstruction. It is of paramount importance to ensure tumor radicality before reconstruction, as reconstruction with a flap or skin transplant can cover residual tumor and mask a recurrence. The reconstruction may thus be discarded if margins are not clear. In areas involving important or delicate structures, this might result in a second complicated reconstruction and potentially leave the patient with a poor cosmetic and/or functional outcome.

FS is a fast peroperative technique of histologically assessing tumor radicality. However, FS is not as accurate as regular permanent section histology (PS) and no general consensus on the

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accuracy of FS compared to PS exists.

The aim of this study was to describe a single cancer center's treatment of NMSCs with peroperative FS over a time period of one calendar year (2015).

Methods

A retrospective study was designed identifying patients with NMSC and preoperative FS who had their assessment and treatment at the Department of Plastic Surgery, Sygehus Lillebælt Vejle Hospital, Odense University Hospital, Denmark.

Inclusion criteria were patients with BCC or SCC where peroperative FS was used. Patients were identified by the WHO ICD-10 codes DC44.0 to DC44.9 and procedure code for FS (KZXU00). The study design had no excluding criteria. Relevant data including patient demography, surgery and tumor characteristics was obtained through the journal notes in the Danish Electronic Patient Journal (EPJ) and histology was cross-checked with the Danish national histology database Pato-Web.

Excision margins were defined as the margins reported by the surgeon. High-risk areas were defined as tumors located on the nose, lips, periorbital area and ears.

Patients had clinical examination intervals ranging from 3 to 6 months. Follow up of this study was concluded in May 2017, resulting in a total recurrence follow-up time ranging from 17 months to 29 months. Data was achieved from the Danish Electronic Patient Journal.

The project was approved by the Danish National Health Authorities, The Danish Data Protection Agency and the local Ethics Committee. Data was organized using Microsoft Excel and

data examination was done using the statistical program STATA 11.1.

RESULTS

Characteristics

In 2015, a total of 34 patients were treated for 35 NMSCs with FS. Tumors excised without the use of FS were not included in the study. The male-female ratio was 1.12 and mean age was 72 years. No significant difference in age was found between patients treated for SCCs versus BCCs. Mean size of the tumors was 12.5 mm (range 3-30 mm). BCC/SCC ratio was 4.8. Concerning stages, 86% were T1 stage and 14 % T2 tumors.

Excisions

Excision margins were significantly different in BCCs compared to SCCs, with 4.0 mm (range 3-6 mm) in BCCs and 6.3 mm (range 3-10) in SCCs (Mann-Whitney test: p-value 0.04).

Following FS on primary excision, 51% of the patients had only one excision performed whereas 49% had two or more re-excisions performed to obtain clear margins. In 78% of the cases radical excision was achieved on first excision, though some with so close margins that re-excision was performed. Of the patients not radical on first excision, 71% were radical after re-excision. A few patients (n=3) did not have FS on re-excision despite non-radical first excision, but PS. The patients without clear margins on second re-excision were treated with re-excision (n=3) and radiotherapy (n=3).

44% of the operations were performed in high-risk areas (ala nasi 29%, medial canthus 6%, lateral canthus 3% and lip 6%). 76% of the patients were hospitalized after surgery with a median time in hospital of one day.

Frozen section

FS and PS concurred in all but a single patient with a T1 low-risk BCC of the temporal region, where PS revealed a narrower clear margin than FS resulting in a re-excision. This results in a 97% concordance rate between FS and PS in our study of non-selected patients. The high concordance rate demonstrates that FZ, at our department at least, is an accurate procedure.

Reconstruction

Regarding technique of reconstruction, direct suturing was possible in 12% of the patients. Skin transplants were used in 15% of the operations and local flaps in 73% of the patients.

No patients have relapsed or died during the follow up time of this study according to the patients' journals and Pato-Web.

Table 1 Demographics

Sex (n)	
Male	18
Female	16
Male/female-ratio	1.12
Patients (n)	34
Age (years)	
Mean _{total} (range)	72 (49-88)
Mean _{SCC}	74 (62-83)
Mean _{BCC}	71 (49-88)
Mean _{male}	70 (49-88)
Mean _{female}	74 (51-88)
Mean _{BCC}	12 (3-30)
Mean _{male}	14 (3-25)
Mean _{female}	11 (4-30)
Admittance, n (%)	
Admittance	25 (76)
Unknown	1 (3)
Median admittance-time (IQR)	1 (1-3)
Immunosuppression, n	1 (Imurel)
<i>IQR (abbrev.), interquartile range</i> <i>φ Mann Whitney Rank Sum Test</i> (range)	

Table 2 Tumor characteristics

T-stage, n (%)	
T1	30 (86)
T2	5 (14)
Tumor size millimeters (range)	
Mean _{total}	13 (3-30)
Mean _{SCC}	13 (5-25)
Tumor type, n (%)	
BCC	29 (83)
SCC	6 (17)
BCC/SCC-ratio	4.8
>1 NMSC	1 (3)
Biopsy at time of referral	33 (97)
Tumor localization, n (%)	
<i>High-risk areas</i>	
Ala nasi	10 (29)
Medial Canthus	2 (6)
Lateral Canthus	1 (3)
Lip	2 (6)
<i>Low-risk areas</i>	
Chin	6 (17)
Nose	4 (11)
Naso-labial	2 (6)
Palpebraum	2 (6)
Forehead	2 (6)
Temple	2 (6)
Cheek	1 (3)
Scalp	1 (3)

DISCUSSION

Several treatment options are available in the treatment of NMSC. These include radiotherapy, Mohs micrographic surgery (MMS), cryotherapy, imiquimod, curettage and 5-fluorouracil. Excision with histologically clear margins remains the preferred treatment¹ as full tumor characterization and histologically verified tumor radicality are obtained. BCCs and low-risk SCCs are generally slow-growing tumors that rarely metastasize.⁹

NMSC express a low rate of recurrence in case of non-radical excision.⁸ High-risk SCCs and BCCs have the potential to grow invasively. High-risk SCCs are capable of metastasizing to

regional lymph nodes or distant organs potentially resulting in a fatal outcome.⁹

No general guideline on the use of FS exists. FS is typically used when local flap or skin transplant is used for reconstruction or when aesthetically important or functionally critical structures like the nose, ears, eyelids etc. are at risk. NMSCs often occur in sun-exposed areas like the head and neck region and thus the face.⁹ Excision with standard excision margins in this area often involves fragile structures and potentially the need for a major or complex reconstruction. FS can in some cases be used to spare key structures by excising the tumor radically with narrower margins than the margins recommended by the guidelines. This may leave the patient with a better cosmetic and/or functional outcome.

Clear surgical margins prior to reconstruction are important as it reduces the risk of later having to discard the first choice reconstruction and thus lose the best reconstruction for the patient. Using a different type of reconstruction may result in both a functionally and aesthetically worse outcome. Furthermore, having clear margins at first excision spares the patient from additional surgery.

A previous study⁴ reported a significantly increased risk of incomplete excision of NMSCs in the absence of FS. Another study reported an increased risk of incomplete excision when the NMSCs are located in high-risk areas as well as an increased risk of positive margins in SCCs vs BCCs.³

Our study shows a high concordance rate of 97% in FS compared to PS. This result is comparable to other studies¹⁻⁶ that report a high concordance rate ranging from 81% to 98%. Previ-

ous studies,^{4,11} in general, reported that SCCs appear to have a higher risk of false negative FS compared to BCCs. Newer studies seem to report slightly higher concordance rates compared to older studies,^{1-6,10} indicating that FS may have become more accurate over time, perhaps due to optimized settings around FS. Several different types of FS exist. In our department the specimens are sent in toto to FS. In other departments, the perimeter of the specimen is sent to FS either in one or four parts and the main specimen to regular PS. Whether one or the other method is more accurate is unclear. The downsides of FS include the time and resource-demanding nature of the procedure and the general limitations in terms of limit of maximal size of specimen.¹⁰ An experienced pathologist as well as an optimized setup is needed for FS. This involves a close collaboration between the surgical department and the pathological department to avoid potential errors by both the surgeon, pathologists and in the preparation of the specimen. FS can be demanding for the patients. They may have a long waiting period of up to several hours before FS is complete and reconstruction is possible. In some cases this can lead to situations with extensive period in general anesthetics.

Additionally, the use of FS can in some cases lead to a suboptimal final PS assessment and thus a suboptimal histological examination of the specimen.

FS should therefore be limited to cases where the need of immediate knowledge of margin status is needed. Though rapid and relatively accurate, routine use of FS on all excisions of NMSCs is not cost-effective and should not be used. FS should be limited to selected cases.

These include complex subtypes of NMSC like morphea BCC or other invasive subtypes, tumors with poorly defined margins, recurrent tumors or tumors where the preservation of the surrounding skin or structures is important. In these cases, FS seems to be of high value to the surgeon and thus the patient.

MMS appears to be superior to FS in controlling tumor margins.¹¹ Important limitations to MMS, however, include heavy use of operator time in addition to the need of a highly skilled surgeon. These limitations significantly reduce the availability of MMS in large parts of health care systems. FS is far more accessible and as a result should remain a key supplement in surgical treatment of NMSC especially when MMS is not available.

CONCLUSION

With a 97% concordance rate between FS and PS this study concludes that in our setting, in selected cases, FS is a valuable and reliable tool for the surgeon in controlling tumor margins and thus ensuring a safe reconstruction for the patient. The study thereby adds data to the discussion about use of FS in excision of NMSCs.

ETHICAL STATEMENT

Funding: None

Conflict of interest: None

Ethical approval: Approved by the local Ethics Committee

Informed Consent: The project was approved by the Danish National Health Authorities and The Danish Data Protection Agency.

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