The Use of Frozen Sections in Angiosarcoma Wider Excisions in NHS Greater Glasgow & Clyde

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Introduction

Frozen sections (FS) have been used for many years to provide rapid, real time histological evaluation of a tissue specimen with high diagnostic accuracy.[1, 2]

It has a wide number of clinical indications including preliminary diagnosis as well as assessing specimen adequacy, margin status and tumour extent; helping to guide intraoperative surgical decision-making.[1,3] Its use may decrease the need for further resection, potentially reducing subsequent risks to the patient.[3] The process however is not without its inherent errors (Table 1).

Type of error	Example
Technical	freezing artefact, poor staining, bloated cell morphology and poor quality sections e.g. folding of the tissue.
Sampling	inadequate sampling leads to a falsely reassuring result.
Interpretation	the potential for misinterpretation of a slide with the technical difficulties as mentioned compounded by the time pressure of the decision. [1,3,4]

Table 1: Potential errors associated with frozen section analysis.

FS has been used in our centre for intraoperative margin assessment during angiosarcoma resection. There is little literature on this topic and we believe there are no standard protocols for the use of FS in this setting. The literature reports contrasting data on the usefulness of FS in AS [1,4-7] giving little guidance on the best clinical practice in an ***NHS setting where time, cost and accuracy is pivotal***.

Current UK sarcoma guidelines state the FS technique is **not** encouraged for diagnostic purposes, but do not mention the use of intra-operative FS for margin assessment. The Royal College of Pathologists suggest FS diagnosis is rarely required due to the use of needle core biopsies and suggests it is **not** indicated for assessment of margins. [8-11]

In the ever busy and stretched pathology lab the time and costs of frozen section are increasingly difficult to meet. **The aim of this project is to audit the use of FS in angiosarcoma surgery in NHS Greater Glasgow and Clyde (GGC) from 2012 to present.**

Methods

Search of LIMS Telepath system from May 2012 to June 2019 using 'T' codes for skin, soft tissue, breast and free text search for '*angiosarcoma'* to capture all potential cases to include.

Cases were included when the diagnosis was angiosarcoma, and the wider excision or medical management was carried out in NHS GGC.

Patients were excluded when the definitive management was surgery in a different health board, oncological therapy or palliation.

Results (1)

AS data Total number of AS = 47.
- 41 cases met the inclusion criteria. 6 were excluded.
- 21 cases were skin/superficial soft tissue.
- 16 cases were breast.
- 4 cases were classified as 'other' masses – paracardiac, left posterior rib, left ureteric and right rib.

Results (2)

Management of Cases and FS Use
- 27 had surgical management.
- 2 had oncological management.
- 9 had palliation.
- 3 refused treatment.

- Of the 27 cases managed surgically, 14 had FS (51.8%).
- FS was used for margin assessment in 100% of cases. None were used solely for diagnostic purposes.
- The most frequently examined tissue was breast.
- FS analysis was done in 11 mastectomy and 3 skin cases.
- The range of FS performed in a case was between 4 and 22.
- On average there were 12 FS per case.

Results (3)

Macroscopic and Microscopic Clearance of Cases

- We reviewed the reported macroscopic abnormality and the pathological assessment of macroscopic and microscopic margins.

- This showed good correlation between what was judged with 'the naked eye' as a clear margin and what was considered adequate histological clearance.

Results (4)

FS Results and Impact on Operation
- In 86% of cases, the margin FS was negative.
- In two cases the FS result was reported as suspicious/not entirely negative (subsequently reported negative on paraffin assessment). This resulted in further margin sampling, both initial FS confirmed as negative on paraffin section. Both cases were cytological atypia related to radiotherapy change.
- In 71% of cases FS margin result had no impact on the surgical procedure.
- In the remaining cases (4 cases, including the 2 mentioned above); increased cellularity and cytological atypia reported on FS led to further margins.
- This FS reported atypia was frequently related to radiotherapy change.

Discussion

Pawlik et al.[7] looked at WLE resection margins and found 'false negative' FS margins in many cases, highlighting measurable differences between FS and paraffin. Our data suggests otherwise, this audit confirmed NHS GGC FS sampling is accurate and has excellent concordance between FS and paraffin sections.

Current RCPath guidelines state FS should ***not*** be used for margin purposes therefore our practice is not compliant with current standards. [12-15]
Furthermore, most cases involved multiple FS's at considerable time cost.
This highlights the need for a change in NHS GGC regarding use of FS in AS.
Support for this is further highlighted looking specifically at our FS margin data, as whilst we have excellent FS results, we also have excellent surgical margin clearance and when reviewing macroscopic and microscopic clearance there is good correlation.
This suggests macroscopic clearance (as judged intra-operatively by the surgeon) at the time of resection is giving good surgical clearance and histologically negative margins. Thus FS aren't 'missing' positive margins.

On a critical note of current FS practice;
- There is a risk of providing false reassurance with negative FS margins as they sample only tiny areas of what can be a large surgical margin.
- There can be an 'overcalling' of atypical features, a known difficult area.[8]
It could be argued these challenges in FS interpretation lead to a tendency to overcall malignancy and err on the side of caution.

Conclusions

• We show NHS GGC FS sampling is accurate and reliable, but also that macroscopic clearance correlates with microscopic margin status. As this is adequate, we feel the use of FS is not warranted and could be potentially falsely reassuring.
•The sole use of FS in sarcoma in this health board has been to date, for margin assessment; perhaps something that should be reviewed & discussed with the wider multi-disciplinary team given this is not recommended by the Royal College of Pathologists.

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