



## Utility of Intraoperative Margin Assessment by Frozen Section in Gastric Cancer

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Dear Editors,

We read with interest the recent publication by Nakanishi et al. regarding the accuracy and “usefulness” of frozen section (FS) margin analysis at the time of gastrectomy for gastric adenocarcinoma (GAC).<sup>1</sup> The authors reported that positive FS was associated with T4 tumors and tumor diameter  $\geq 5$  cm, and advocated FS, particularly for patients with these tumor characteristics.

Their results and the accuracy of the pathologists and surgeons at their institution are commendable, and the comprehensive nature of their study is excellent; arguably the more relevant clinical question, however, is the oncologic utility of the frozen section (FS) results and its implications. While we applaud the authors on their publication, we would caution that the utility of FS analysis for GAC remains unclear, particularly for locally advanced tumors.

The critical oncologic outcomes (recurrence-free and overall survival) were not reported and would be of considerable interest. In particular, what were the RFS and OS for the 87 patients who underwent additional resection and were converted from microscopically positive (R1) on FS to negative (R0) on permanent section (FS-R1-to-PS-R0), and how did these outcomes compare with those of the FS-R0 cohort?

Our group has examined the role of proximal margin FS analysis during gastrectomy for GAC among 520 patients of the US Gastric Collaborative, a seven-institution consortium of academic referral centers across the USA.<sup>2</sup> We found that a positive FS was more commonly observed among patients with larger tumors, T4 tumors, and node-positive tumors, similar to Nakanishi et al., but that margin re-resection after positive FS was not associated with any clear oncologic benefit. After accounting for additional adverse pathologic factors on multivariable regression analysis, worse OS and RFS were significantly associated with increasing T-stage and N-stage, but not proximal margin status.

As the authors acknowledge, no data exist to suggest that repeat gastric resection for an R1 margin in the setting of a T4 tumor or extensive lymphadenopathy confers any oncologic benefit. In fact, these patients with locally advanced disease tend to develop distant metastases and die due to progression of distant disease, not local recurrence.<sup>2–4</sup> The recurrence data by Nakanishi et al. highlight this fact, as the distant recurrence rate was significantly greater ( $p < 0.001$ ) in the PS1 cohort (37/87, 42.5%) versus the PS0 cohort (211/1146; 18.4%), but no significant difference in local recurrence rates was observed ( $p = 0.15$ ).<sup>1</sup> The authors report that, of six patients with FS-R1 who did not undergo additional resection, all six died of distant metastases without developing local recurrence.

In the current study, a positive FS was associated with T4 tumors and tumor size  $\geq 5$  cm, and it is exactly this patient population in whom distant recurrence, not local recurrence, remains the primary cause of cancer-related mortality. Resection to a grossly negative-appearing margin is standard of care, but the utility of additional resection

in order to achieve an R0 resection after an R1-FS, particularly in the setting of a T4 primary GAC tumor or N2–3 disease, remains questionable.

## REFERENCES

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