

# Prognostic value of surgical margins during endoscopic resection of paranasal sinus malignancy

Lakshman Manjunath, BS<sup>1</sup>; Taylor Derrouseau, BS<sup>1</sup>; Pete Batra, MD<sup>2</sup>

<sup>1</sup>*Department of Otolaryngology, University of Texas Southwestern Medical Center, Dallas, Texas*

<sup>2</sup>*Department of Otolaryngology, Rush University Medical Center, Chicago, Illinois*

## ABSTRACT

**Background:** Complete tumor resection with intraoperative frozen section control remains a central tenet of head and neck surgical oncology. The purpose of the present study was evaluate the significance of margins in predicting local recurrence and disease status following endoscopic resection of sinonasal cancer.

**Methods:** This single-institution observational cohort study was performed on 68 patients over a 5-year period that underwent curative minimally invasive endoscopic resection (MIER) for sinonasal malignancies.

**Results:** The mean age was 58.8 years and 69.1% were male. The mean follow-up after definitive MIER was 15.9 months. A mean of 10.8 margins were taken per surgery (range 2 – 27). False negative frozen section analysis was 22.1% for the entire cohort, being slightly higher at 25.0% for T3 or T4 malignancies. At the last follow-up, no evidence of disease (NED) status was noted in 60.0% of those with positive margins versus 83.0% in those with negative margins, respectively ( $p = 0.0795$ ). Regional or distant recurrences were observed in 39.9% of patients with positive margins and 13.2% of those with negative margins, respectively. Disease free survival (DFS) was 9.7 months for patients with positive margins, whereas those with negative margins had a DFS of 15.9 months.

**Conclusion:** Statistical significance could not be achieved regarding the prognostic value of margin status on patient outcome. However, NED status as a function of residual microscopic disease proved to be marginally significant. These results suggest that complete resection with clear margins may reduce mortality in patients undergoing MIER for cancers of the paranasal sinuses.

## INTRODUCTION

One of the major tenets of surgical oncology of the head and neck is complete tumor resection, both at a macroscopic and microscopic level. When handling malignancies of the paranasal sinuses and anterior skull base, however, obtaining the desired negative margins can be difficult or even impossible given proximity to critical structures such as the carotid artery or the optic nerve. Consequently, patients may be left with tumor-positive surgical margins, indicative of residual microscopic disease.

Literature regarding the relationship between positive margins and patient survival remains somewhat equivocal. Several studies on sinonasal malignancies have shown evidence that positive margins are correlated with poorer survival, but others have not demonstrated such an association. The purpose of the present study therefore is to evaluate the significance of margin status in predicting recurrence and disease status in a cohort of 68 patients following curative endoscopic resection of sinonasal cancer.

## MATERIALS AND METHODS

A retrospective chart review was conducted on 68 patients undergoing minimally invasive endoscopic resection (MIER) for malignant sinonasal and/or anterior skull base (ASB) neoplasms by the senior author between August 2008 to June 2013 at the Comprehensive Skull Base Program of the University of Texas Southwestern Medical Center. In addition to margin status and patient outcomes, key data collected included patient demographics, past medical history, prior treatment, tumor characteristics (histopathology, TNM staging), surgical parameters (intraoperative details, skull base reconstruction, complications), and postoperative therapies. Institutional review board (IRB) approval was obtained prior to initiating the study.

Surgical margin status was assessed by verifying intraoperative frozen section diagnoses with the corresponding final pathology report. Patients with negative margins included those whose margins were reported free of tumor involvement by the pathologist both during surgery as well as on permanent pathology. Patients with positive margins were defined as those in whom cancer cells were found either in the tissue section when inspected under a microscope (residual microscopic disease) or visible to the unaided eye (residual gross disease). When tissue specimens revealed evidence of tumor cells but the anatomical area was ultimately further resected, these samples were not tallied as positive margins.

Data collected regarding patient outcome included recurrences, salvage surgery, and long term status (no evidence of disease [NED], alive with disease [AWD], died of disease [DOD], died of other causes [DOC]).

## CANCER HISTOPATHOLOGY

Histopathology	Count	Percent
SCC	17	25.0%
Olfactory Neuroblastoma	9	13.2%
Melanoma	9	13.2%
Adenocarcinoma	8	11.8%
Sarcoma	6	8.8%
SNUC	5	7.4%
Adenoid Cystic	4	5.9%
IP with Carcinoma in Situ	3	4.4%
Basal Cell Carcinoma	2	2.9%
Hemangiopericytoma	2	2.9%
Clear Cell Carcinoma	1	1.4%
Mucoepidermoid Carcinoma	1	1.4%
Lacrimal Sac Poorly Differentiated Carcinoma	1	1.4%

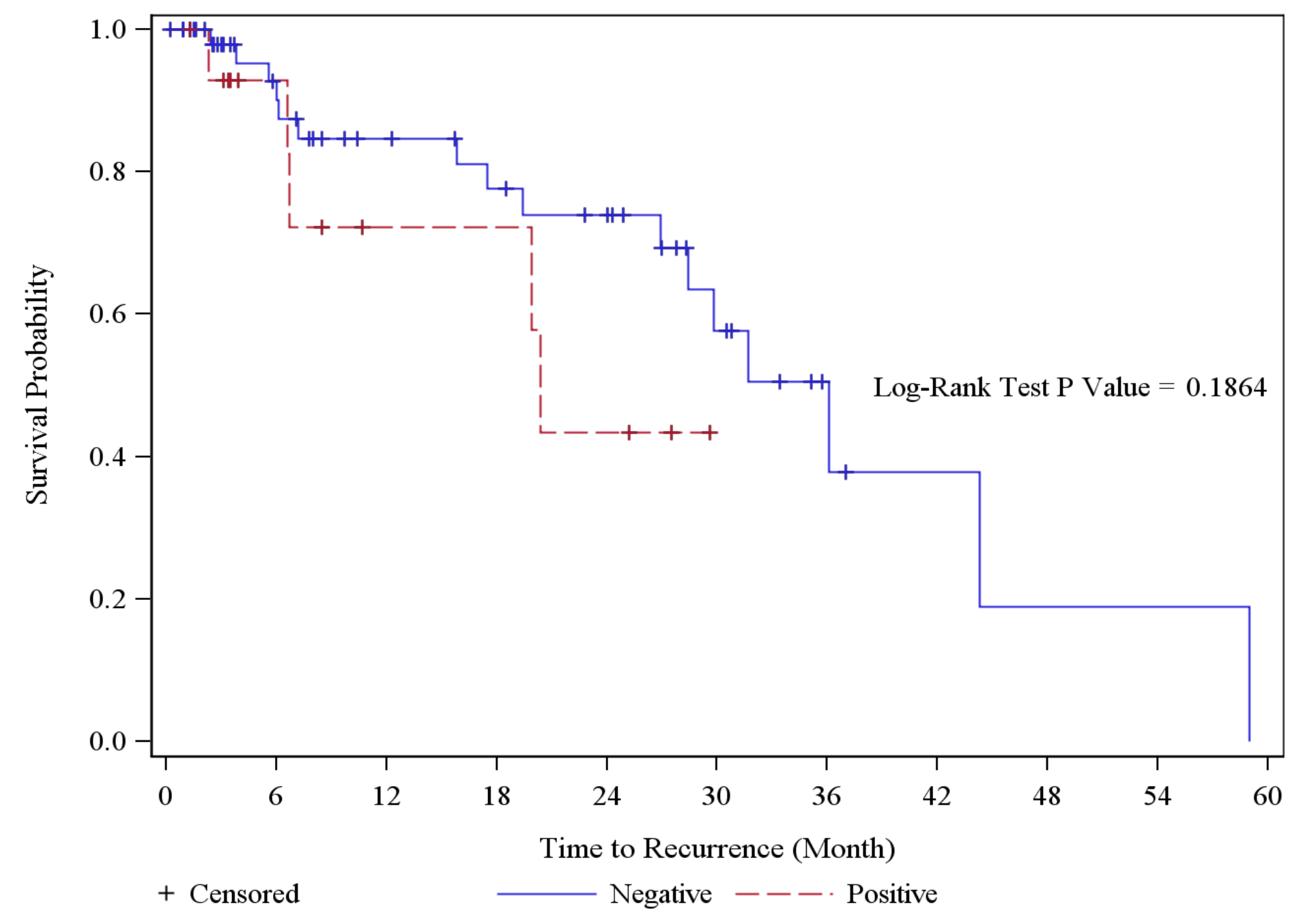
## RESULTS

A mean of 10.8 intra-operative margins were taken per procedure, with a range of 2 to 27. Fifteen patients (22.1%) were reported to have negative intraoperative margins but ended up with positive residual microscopic disease upon review of permanent pathology. Six of these patients had further resection and ultimately did not count towards those with true positive margins. At least one false negative reading was associated with 41.2% of squamous cell carcinomas, 33.3% of melanomas, 25.0% of adenoid cystic carcinomas, 16.7% of sarcomas and 11.1% of olfactory neuroblastomas. Furthermore, false negative readings were noted in 25.0% of malignancies that were staged T3 or T4. Ultimately, fifteen (22.1%) of the 68 patients had true intra-operative positive surgical margins.

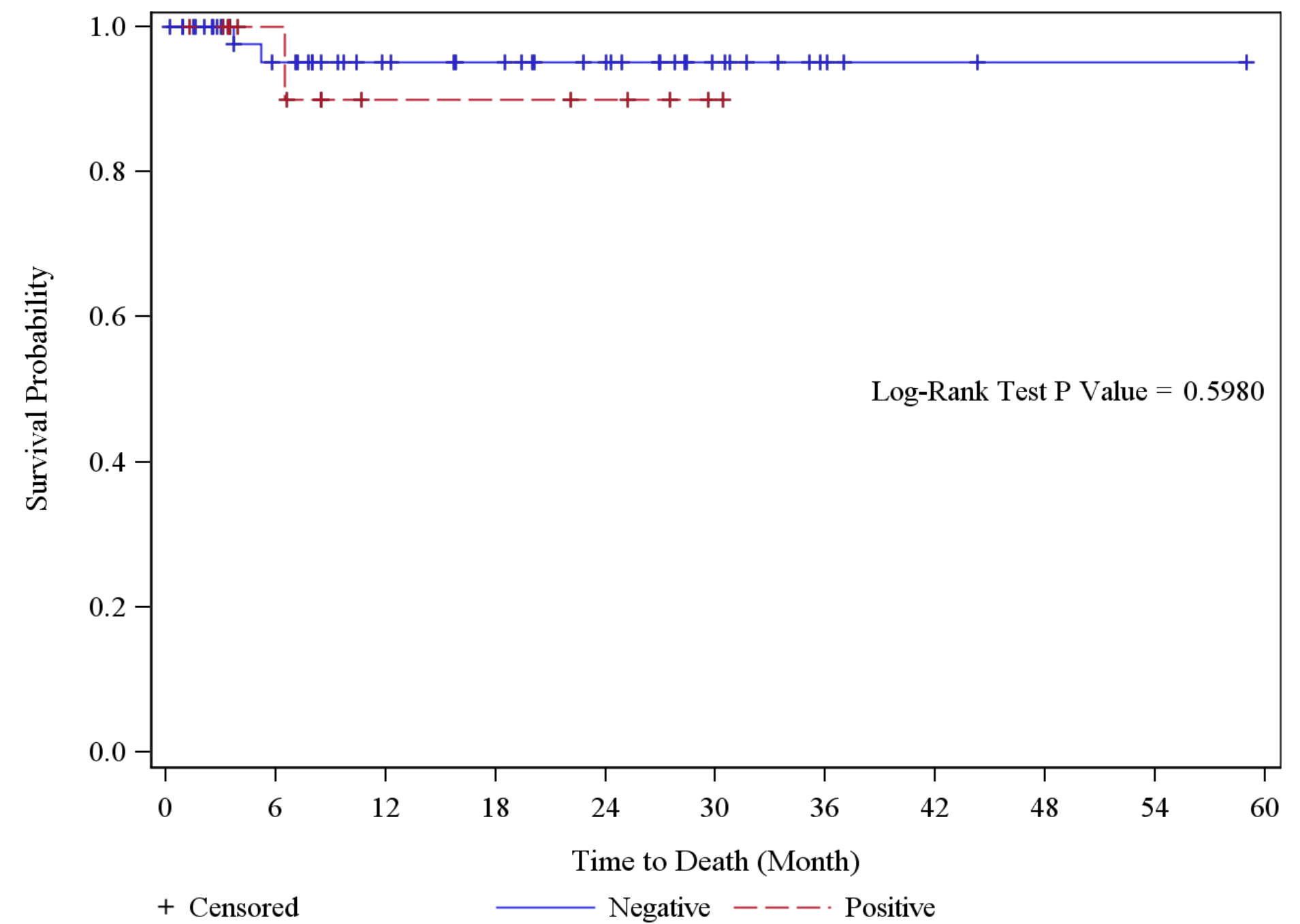
Locations of residual microscopic disease included the pterygomaxillary fossa (4 patients), sphenopalatine region (2), orbit (2), dura (2), sphenoid sinus (2), superior turbinate (2), nasopharynx (1), maxillary sinus (1), Eustachian tube (1), ethmoid roof (1), cavernous sinus (1), frontal sinus (1), anterior skull base (1). Due to small numbers, statistical significance for these findings was not achieved.

## KAPLAN-MIER CURVES

### Disease Free Survival (DFS)



### Overall Survival



## RESULTS

### Recurrence as a function of margin status

Reccurrence	Positive Margins	Negative Margins	P Value
Local	13.3%	24.5%	-
Regional	13.3%	5.7%	-
Distant	26.6%	7.5%	-
Combined	33.3%	30.2%	1.000

### Survival as a function of margin status

FOLLOW-UP	Positive Margins	Negative Margins	P Value
Average Overall Survival (months)	12.7	16.8	0.598
Average Disease Free Survival (months)	9.7	15.9	0.1864
NED	60.0%	83.0%	0.0795
AWD	33.3%	13.2%	-
DOD	6.6%	1.8%	-
DOC	0.0%	1.8%	-

## CONCLUSION

### Summary

- No statistical difference in mean post-operative survival time ( $p = 0.5980$ ) between those with positive margins and those with negative margins.
- Disease free survival Kaplan Meier comparisons between the two groups showed a reduced time to recurrence for patients with positive margins, but these results also did not achieve significance ( $p = 0.1864$ )
- Positive margins proved to be a marginally better indicator of disease status at the time of last follow-up ( $p = 0.0795$ );.

Traditionally, open craniofacial resection with minimal adjunctive therapy has been the mainstay of sinonasal cancer treatment. However, advances over the last several decades have introduced many additional options for adjunctive and even definitive management, including minimally invasive endoscopic resection (MIER), radiation, chemotherapy, and molecular targeted therapies. Although not all sinonasal malignancies can be handled by these alternative treatments, many patients with residual microscopic disease are no longer restricted to additional surgery with its accompanying morbidities. These novel management choices are particularly relevant when positive margins occur adjacent to vital anatomical structures (such as the carotid artery) or structures that play a large role in quality of life (such as the eye). Ultimately, residual microscopic disease may be a tolerable circumstance in patients who serve as eligible candidates for these alternative therapies.

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