

Interpretability of operative and pathological reports for radiotherapy planning of sinonasal carcinomas, an ancillary study of the GORTEC 2016-02 SANTAL trial

Short title: Sinonasal operative and pathological reports for poRT

Authors: Coline Labarre MD ¹, Florent Carsuzaa MD ^{1*}, Maxime Fieux MD PhD ², Benjamin Verillaud MD PhD ³, Antoine Moya Plana MD PhD ⁴, Ludovic de Gabory MD PhD ⁵, Vincent Patron MD ⁶ Francois-Régis Ferrand MD ⁷ and Juliette Thariat MD PhD ^{8*}

Affiliations :

¹: Centre Hospitalier Universitaire de Poitiers, Service d'ORL et chirurgie cervico-faciale, F-86000, Poitiers, France

²: Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Service d'ORL, d'otoneurochirurgie et de chirurgie cervico-faciale, France, Pierre Bénite cedex F-69495 ; Université de Lyon, Université Lyon 1, F-69003, Lyon, France

³: Hôpital Lariboisière, Service d'ORL et chirurgie cervico-faciale, Assistance Publique Hôpitaux de Paris, Inserm U1131, Université Paris Cité, Paris, France

⁴: Gustave Roussy, Département de Cancérologie et de chirurgie Cervico-Faciale, Université Paris-Saclay, Villejuif, France

⁵: Centre Hospitalier Universitaire de Bordeaux, Service d'ORL et chirurgie cervico-faciale, Bordeaux France

⁶: Centre Hospitalier Universitaire de Caen, Service d'ORL et chirurgie cervico-faciale, F-14000 Caen, France

⁷: Gustave Roussy Campus, Department of Medical Oncology, Villejuif, France. Institut de Recherche Biomédicale des Armées, Brétigny-sur-Orge, France

⁸: Comprehensive Cancer Center François Baclesse, Department of Radiotherapy, Caen, France. Université de Caen Normandie, ENSICAEN, CNRS/IN2P3, LPC Caen UMR6534, F-14000 Caen, France

*Equally contributed to the study

Corresponding author:

Pr Juliette Thariat

Department of radiation therapy. Comprehensive Cancer Center François Baclesse, Caen France.

Phone + 33 2 31 45 5050

Email : jthariat@gmail.com

Key points

- Interpretation of surgical mapping is essential for postoperative radiotherapy planning.
- Operative and pathological reports lack comprehensive information on margins quality and tissue block mapping.
- Standardizing reports is essential to reduce uncertainties, aiming for less morbid poRT.

Key words: sinonasal tumors; endoscopic endonasal surgery, surgical mapping; margins, radiotherapy

Introduction

The management of advanced sinonasal carcinomas relies on a multimodal approach, including surgery and postoperative radiotherapy (poRT) (1,2). Surgery, purely endoscopic or combined with an external approach, often implies tumor disassembling into small tissue fragments, i.e. multi-block surgery, intrinsically with tumor effraction (3). PoRT, such as intensity-modulated radiotherapy and proton therapy aim to reduce morbidity (4,5) but an accurate interpretation of surgical mapping to relocate tumor subvolumes into the three-dimensional space of multi-slice radiotherapy computed tomography (CT) is essential.

Therefore, comprehensive surgical reporting is crucial for precise RT planning and delivery. Inaccurate histosurgical mapping can lead to overestimated tumor volumes, increasing toxicity, or missed targets, the latter raising recurrence risk. Locating tissue blocks on CT slices is challenging due to modified postoperative anatomy and requires interdisciplinary collaboration.

We assessed whether operative and pathological reports clearly identified tumor pedicles involved resected tissue blocks and safe margins. We also evaluated the feasibility of transposing this information into radiotherapy CT space for accurate poRT planning.

Methods

This ancillary study involved sinonasal carcinoma patients from the GORTEC2016-02 trial (NCT02998385) assessing poRT +/- cisplatin after EESBS and/or open approach. Two surgeons (CL, FC) and one radiation oncologist (JT) reviewed operative and pathological reports for tumor pedicle presence, margins quality. Comprehensiveness of tissue block description and feasibility of tissue block location on postoperative CT was determined according to operative and pathological reports and postoperative CT. This study adhered the Declaration of Helsinki, with informed consent from all participants.

Reports were evaluated for identification of sinonasal tissue blocks per Bastier and de Gabory (38 structures) (6) and 10 additional tissue blocks from a Delphi consensus study. Endpoints included the presence of a tumor pedicle, margins quality, easiness of tissue block relocation on CT, and comprehensiveness of tissue block description.

Statistics: Numeric variables were expressed as median with interquartile ranges. Shapiro-Wilk test assessed data normality and heteroskedasticity. Wilcoxon test Fisher's exact test were used for continuous and discrete outcomes, respectively, with significance test at $p < 0.05$. Statistical analyses were performed using R software (v. 4.3.3 (<https://r-project.org>)).

Results

Clinicopathologic characteristics

The operative and pathological reports of 21 randomly selected patients (of 100 sinonasal carcinoma patients included in the GORTEC2016-02 study) were analyzed. Table 1 provides patients' characteristics based on the epicenter. Most cases were carcinomas of the ethmoid sinus (66.7%; 14/21). The procedures were EESBS alone in 12 patients, open surgery or combined approach in 9 patients.

Description of resected tumor and margins

The tumor pedicle was identified in all but 3 patients who had undergone EESBS for ethmoidal epicenters: a pedicle was not present in one patient and not described in the other two patients with ethmoidal carcinomas.

Surgical margins were considered safe by the surgeons in 85.7% (12/14) of ethmoidal and 85.7% (6/7) of non-ethmoidal epicenters. Although clearly identified on pathological reports, the quality of (macroscopic) margins was not assessed in the operative reports for 21.4% (3/14) of patients with ethmoidal epicenters and 57% (4/7) of other epicenters.

Of 48 potential tissue blocks, significantly more structures were described in the operative reports for ethmoidal epicenters than non-ethmoidal ones (14.0 [11.0-29.0] vs 11 [4.0-17.0], respectively; $p=0.046$) (Table 1). In pathological reports, 12 structures were described for ethmoidal epicenters and 10 for non-ethmoidal ones. Nine structures were identified in more than 50% of the operative and pathological reports (Table 2).

Ethmoidal, frontal, sphenoidal and brain structures were more frequently reported in ethmoidal epicenters' reports compared to others, although this difference was not statistically significant. Conversely, for structures related to the middle and inferior turbinates or nasal floor, tumor invasion was more commonly specified in non-ethmoidal epicenters (Table 2).

Tissue blocks relocation on multiplanar CT

Some tissue blocks structures (12/48, 25.0%) were well transposable in more than 20% of cases. There were significantly more structures that could not be transposed for non-ethmoidal epicenters with 33 structures [28–41] than for ethmoidal epicenter with 28 structures [16–33] ($p=0.022$). The structures could not be transposed on imaging due to a heavily modified anatomy or material interfering with visualization (implant or flap) (Table 2).

Discussion

Accurately defining volumes at risk for tumor relapse is crucial, given that radiotherapy toxicities are correlated with irradiated volumes. Documenting tumor pedicle can guide more precise irradiation, focusing on tumor implantation sites rather than including all sinonasal walls. In this study, tumor pedicles were identified in over 85% of operative reports.

Margins quality is a major prognostic factor (7). Multi-block resection create small tissues fragments, complicating the assessment of resection margins (8). Surgeons' perception of margins quality often appeared optimistic compared to pathological reports. Ensuring safe margins through biopsies around the tumor is essential for considering lower poRT doses (9).

Few anatomic structures were identified in the operative and pathological reports. The later varied in comprehensiveness, depending on whether the tumor epicenter was in the ethmoid or elsewhere in the paranasal regions. This suggests a need for standardized operative reports tailored to the tumor's location (10).

The study's limitations include its small sample size with higher proportions of ethmoid tumors. Some subjectivity could not be excluded when estimating the feasibility of relocating structures from the descriptive reports onto multiplanar images.

Conclusion

Operative and pathological reports often lack comprehensive and clear information on margins quality and tissue block mapping necessary for poRT planning. Standardizing these reports is essential to reduce uncertainties about tumor epicenters location and margins quality, aiming for less morbid poRT.

Declarations

Author contributions: CL was contributed to data collection. All authors contributed to the study conception and design as well as the drafting of the article. MF was responsible for statistical analysis of data. JT, FC, AMP, LDG RFR and BV revised it critically for important intellectual content, and all authors (CL, FC, MF, BV, AMP, LDG, VP, FRF, and JT) gave final approval of the version to be submitted.

Acknowledgments: MF is supported by the Foundation of the Hospices Civil de Lyon fellowship and wish to acknowledge the support of the Fondation Edmond Roudnitska (grant awarded), the Philippe Foundation (grant awarded), the France Stanford Centre (grant awarded) and the Association Française de Rhinologie (grant awarded).

Competing interests: All authors declare no competing interests in relation to this work.

Funding: This work as partly supported by grants allocated to one of the author (MF).

References

1. Orlandi E, Cavalieri S, Granata R, Nicolai P, Castelnuovo P, Piazza C, et al. Locally advanced epithelial sinonasal tumors: The impact of multimodal approach. *The Laryngoscope*. avr 2020;130(4):857- 65.
2. Thariat J, Carsuzaa F, Marcy PY, Verillaud B, de Gabory L, Ferrand FR. Precision Postoperative Radiotherapy in Sinonasal Carcinomas after Endonasal Endoscopic Surgery. *Cancers*. 25 sept 2021;13(19):4802.
3. Kuan EC, Wang EW, Adappa ND, Beswick DM, London NR, Su SY, et al. International consensus statement on allergy and rhinology: Sinonasal tumors. *Int Forum Allergy Rhinol*. 2 sept 2023;alr.23262.
4. Ferrari M, Orlandi E, Bossi P. Sinonasal cancers treatments: state of the art. *Curr Opin Oncol*. 1 mai 2021;33(3):196- 205.
5. Maggiore G, Fancello G, Gasparini A, Locatello LG, Orlando P, Chieca M, et al. Temporal evolution of quality of life in patients endoscopically treated for sinonasal malignant tumors. *Rhinology*. 1 juin 2023;61(3):231- 45.
6. Bastier PL, de Gabory L. Design and assessment of an anatomical diagram for sinonasal malignant tumour resection. *Rhinology*. 1 déc 2016;54(4):361- 7.
7. Baddour HM, Magliocca KR, Chen AY. The importance of margins in head and neck cancer. *J Surg Oncol*. mars 2016;113(3):248- 55.
8. Woolgar JA, Triantafyllou A. A histopathological appraisal of surgical margins in oral and oropharyngeal cancer resection specimens. *Oral Oncol*. nov 2005;41(10):1034- 43.
9. Jang JW, Chan AW. Prevention and Management of Complications after Radiotherapy for Skull Base Tumors: A Multidisciplinary Approach. In: Bleier BS, éditeur. *Advances in Oto-Rhino-Laryngology* [Internet]. S. Karger AG; 2013 [cité 25 juill 2024]. p. 163- 73. Disponible sur: <https://www.karger.com/Article/FullText/342293>
10. Carsuzaa F, Favier V, Ferrari M, Turri-Zanoni M, Ingargiola R, Camarda AM, et al. Need for close interdisciplinary communication after endoscopic endonasal surgery to further personalize postoperative radiotherapy in sinonasal malignancies. *Front Oncol*. 28 févr 2023;13:1130040.

Tables and Figures

Table 1: Patients' characteristics depending on the epicenter

Tumor epicenter	Ethmoidal epicenter n=14	Non-ethmoidal epicenter (maxillary, nasal fossa, frontal, or sphenoid) n=7	p-value
Age (median, [min-max])	62.0 [44.0-69.0]	56.0 [36.0 - 70.0]	0.124
Gender, n (%)			0.001*
Male	13 (92.9)	1 (14.3)	
Female	1 (7.1)	6 (85.7)	
Surgical approach, n (%)			0.686
Endonasal endoscopy	9 (64.3)	3 (42.9)	
Combined	2 (14.3)	1 (14.3)	
Open surgery	3 (21.4)	3 (42.9)	
Structures identified on operative report, (median, [min - max])	14.0 [11.0-29.0]	11.0 [4.0-17.0]	0.046*
Structures identified on pathological report, (median, [min-max])	12.0 [5.0-26.0]	10.0 [4.0-22.0]	0.331
Tumor laterality, n (%)			0.096
Left-sided tumor	3 (21.4)	4 (57.1)	
Right-sided tumor	9 (64.3)	1 (14.3)	
Median or bilateral tumor	2 (14.3)	2 (28.6)	
Tumor pedicle identified perioperatively, n (%)			0.521
No	3 (21.4)	0	
Yes	11 (78.6)	7 (100.0)	
Quality of margins according to surgeon? n (%)			0.407
Safe margins	12 (85.7)	6 (85.7)	
Close margins	2 (14.3)	0	
Involved margins	0	1 (14.3)	
Explicit reporting of areas at risk of relapse? n (%)			0.397
No	5 (35.7)	4 (57.1)	
Yes	9 (64.3)	3 (42.9)	
Histopathology n (%)			<0.001
Cystic adenoid carcinoma	0	6 (85.7)	
Intestinal-type adenocarcinoma	12 (85.7)	0	
Muco-epidermoid carcinoma	0	1 (14.3)	
Olfactory neuroblastoma	2 (14.3)	0	
pT, n (%)			>0.99
T1 and T2	3 (21.4)	2 (28.6)	
T3 and T4	11 (78.6)	5 (71.4)	

Legend: *: p < 0.05, pT: pathological tumor, pN : pathological nodes

Table 2: Presence of each structure in the operative or pathological reports by epicenter

Tumor epicenter	Ethmoidal epicenter			Non-ethmoidal epicenter (maxillary, nasal fossa, frontal, sphenoid)		
	n=14			n=7		
Analysed structures <i>n=48</i>	Presence or absence of the tumor on operative report <i>n (%)</i>	Presence or absence of the tumor specified by pathological report <i>n (%)</i>	Quality of margin assessable on pathological report <i>n (%)</i>	Presence or absence of the tumor on operative report <i>n (%)</i>	Presence or absence of the tumor specified by pathological report <i>n (%)</i>	Quality of margin assessable on pathological report <i>n (%)</i>
Nasal septum mucosa	12 (85.7)	10 (71.4)	9 (64.3)	5 (71.4)	5 (71.4)	4 (57.1)
Nasal septum cartilage	11 (78.6)	7 (50.0)	7 (50.0)	6 (85.7)	6 (85.7)	4 (57.1)
Nasal floor mucosa	11 (78.6)	7 (50.0)	7 (50.0)	6 (85.7)	6 (85.7)	4 (57.1)
Nasal bone	6 (42.9)	3 (21.4)	3 (21.4)	1 (14.3)	0	NA
Lateral nasal wall	6 (42.9)	5 (35.7)	2 (14.3)	6 (85.7)	5 (71.4)	4 (57.1)
Inferior turbinate	5 (35.7)	3 (21.4)	3 (21.4)	3 (42.9)	4 (57.1)	4 (57.1)
Head of middle turbinate	6 (42.9)	8 (57.1)	7 (50.0)	3 (42.9)	2 (28.6)	2 (28.6)
Tail of middle turbinate	8 (57.1)	10 (71.4)	9 (64.3)	3 (42.9)	3 (42.9)	2 (28.6)
Superior turbinate	1 (7.1)	2 (14.3)	1 (7.1)	0	1 (14.3)	1 (14.3)
Anterior ethmoidal cells	12 (85.7)	14 (100.0)	5 (35.7)	1 (14.3)	2 (28.6)	1 (14.3)
Posterior ethmoidal cells	13 (92.9)	13 (92.9)	5 (35.7)	1 (14.3)	2 (28.6)	1 (14.3)
Ethmoidal roof	11 (78.6)	7 (50.0)	3 (21.4)	1 (14.3)	0 (0.0)	NA
Uncinate process	3 (21.4)	2 (14.3)	2 (14.3)	1 (14.3)	2 (28.6)	1 (14.3)
Olfactory cleft mucosa	7 (50.0)*	6 (42.9)	3 (21.4)	0 *	0	NA
Cribriform plate	7 (50.0)*	7 (50.0)	4 (28.6)	0 *	0	NA
Dura	6 (42.9)*	6 (42.9)	2 (14.3)	0 *	0	NA
Crista galli	3 (21.4)*	4 (28.6)	2 (14.3)	0 *	0	NA
Falx cerebri	0	0	NA	0	0	NA
Olfactory bulb	3 (21.4)*	4 (28.6)	3 (21.4)	0 *	0	NA
Brain	3 (21.4)*	2 (14.3)	0	0 *	0	NA
Sphenoid sinus mucosa	9 (64.3)	12 (85.7)	7 (50.0)	1 (14.3)	1 (14.3)	0
Sphenoid intersinus septum	5 (35.7)*	4 (28.6)	1 (7.1)	0 *	0	NA
Anterior wall of sphenoid sinus	8 (57.1)	8 (57.1)	4 (28.6)	1 (14.3)	0	NA
Choanal mucosa	3 (21.4)	4 (28.6)	2 (14.3)	4 (57.1)	3 (42.9)	2 (28.6)
Sphenoid rostrum	2 (14.3)*	3 (21.4)	2 (14.3)	0 *	0	NA
Frontal sinus mucosa	5 (35.7)*	6 (42.9)	2 (14.3)	0 *	0	NA

Floor of the frontal sinus	7 (50.0)*	4 (28.6)	1 (7.1)	0 *	0	NA
Frontal sinus drainage pathway	1 (7.1)*	2 (14.3)	1 (7.1)	0 *	0	NA
Mucosa of the anterior wall of maxillary sinus	6 (42.9)	8 (57.1)	3 (21.4)	5 (71.4)	5 (71.4)	4 (57.1)
Mucosa of the medial wall of maxillary sinus	6 (42.9)	9 (64.3)	4 (28.6)	6 (85.7)	6 (85.7)	4 (57.1)
Mucosa of the postero-lateral wall of maxillary sinus	3 (21.4)	6 (42.9)	3 (21.4)	4 (57.1)	4 (57.1)	3 (42.9)
Lateral nasopharyngeal wall	0	0	NA	1 (14.3)	1 (14.3)	1 (14.3)
Superior nasopharyngeal wall	0	0	NA	1 (14.3)	1 (14.3)	0
Posterior nasopharyngeal wall	1 (7.1)	0	NA	1 (14.3)	2 (28.6)	1 (14.3)
Opening of pharyngotympanic tube	0	0	NA	1 (14.3)	2 (28.6)	1 (14.3)
Orbital floor	4 (28.6)	2 (14.3)	1 (7.1)	2 (28.6)	1 (14.3)	0
Lamina papyracea	7 (50.0)*	7 (50.0)	5 (35.7)	0*	0	NA
Orbital fat	3 (21.4)	4 (28.6)	3 (21.4)	1 (14.3)	0	NA
Eyeball	1 (7.1)*	1 (7.1)	1 (7.1)	0 *	0	NA
Inferior rectus	1 (7.1)*	0	NA	0 *	0	NA
Medial rectus	1 (7.1)*	0	NA	0*	0	NA
Infra-orbital nerve	2 (14.3)	1 (7.1)	1 (7.1)	2 (28.6)	2 (28.6)	1 (14.3)
Lacrymonasal duct	1 (7.1)	1 (7.1)	1 (7.1)	1 (14.3)	1 (14.3)	1 (14.3)
Lachrymal eminence	2 (14.3)	1 (7.1)	1 (7.1)	1 (14.3)	2 (28.6)	2 (28.6)
Clivus	2 (14.3)*	1 (7.1)	0	0*	0	NA
Infratemporal fossa	0	0	NA	1 (14.3)	1 (14.3)	0
Pterygopalatin fossa	1 (7.1)	1 (7.1)	0	3 (42.9)	2 (28.6)	1 (14.3)
Pterygoid process	0	0	NA	5 (71.4)	4 (57.1)	1 (14.3)

Legend:

* not reported in non-ethmoid tumors,

bold: discrepancy between pathological and operative reports with more comprehensive data in pathological reports than surgical reports (suggesting than operative reports do not perfectly recapitulate the resection process)

NA: quality of margins not assessable (as structure was not reported on the pathological report)