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

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

3
4 Short title: Sinonasal operative and pathological reports for poRT

5
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36

37 **Key points**

38

39 - Interpretation of surgical mapping is essential for postoperative radiotherapy planning.

40 - Operative and pathological reports lack comprehensive information on margins quality and
41 tissue block mapping.

42 - Standardizing reports is essential to reduce uncertainties, aiming for less morbid poRT.

43

44

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

46

47 **Introduction**

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

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

59 The main aim was to assess whether operative and pathological reports clearly identified
60 tumor pedicles involved resected tissue blocks and safe margins. We also evaluated the feasibility of
61 transposing this information into radiotherapy CT space for accurate poRT planning.

62

63 **Methods**

64 *Study design:* This ancillary study involved sinonasal carcinoma patients from the GORTEC2016-02
65 trial (NCT02998385) assessing poRT +/- cisplatin after surgery (purely endoscopic and/or open
66 approach) and was approved by an institutional review board. Two surgeons (CL, FC) and one
67 radiation oncologist (JT) reviewed operative and pathological reports as well as postoperative CT.
68 Reports were evaluated for identification of sinonasal tissue blocks per Bastier and de Gabory (38
69 structures) (6) and 10 additional tissue blocks from a Delphi consensus study. Endpoints included the
70 presence of a tumor pedicle, margins quality, easiness of tissue block relocation on CT, and
71 comprehensiveness of tissue block description.

72 *Statistics:* Numeric variables were expressed as median values with interquartile ranges. Shapiro-Wilk
73 test assessed data normality and heteroskedasticity. Two groups were made based on tumor epicenter
74 for statistical comparisons, ethmoidal epicenters versus non-ethmoidal epicenters. Wilcoxon test and

75 Fisher's exact test were used for continuous and discrete outcomes obtained from operative and
76 surgical reports, respectively, with significance test at $p < 0.05$. Statistical analyses were performed
77 using R software (v. 4.3.3 (<https://r-project.org>)).

78

79 **Results**

80 **Clinicopathologic characteristics**

81 The operative and pathological reports of 21 randomly selected patients (of 100 sinonasal
82 carcinoma patients included in the GORTEC2016-02 study) were analyzed. Table 1 provides patients'
83 characteristics based on the epicenter. Most cases were carcinomas of the ethmoid sinus (66.7%;
84 14/21). The procedures were endoscopic endonasal skull base surgery (EESBS) alone in 12 patients,
85 open surgery or combined approach in 9 patients.

86

87 **Description of resected tumor and margins**

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

91 Surgical margins were considered safe by the surgeons in 85.7% (12/14) of ethmoidal and
92 85.7% (6/7) of non-ethmoidal epicenters ($p=0.XXX$). Although clearly identified on pathological
93 reports, the quality of (macroscopic) margins was not assessed in the operative reports for 21.4%
94 (3/14) of patients with ethmoidal epicenters and 57% (4/7) of other epicenters ($p=0.XXX$).

95 Of 48 potential tissue blocks, significantly more structures were described in the operative
96 reports for ethmoidal epicenters than non-ethmoidal ones (14.0 [11.0-29.0] vs 11 [4.0-17.0],
97 respectively; $p=0.046$) (Table 1). In pathological reports, 12 structures were described for ethmoidal
98 epicenters and 10 for non-ethmoidal ones $5P+\grave{a};xxx^\circ$. Nine structures were identified in more than
99 50% of the operative and pathological reports (Table 2).

100 Ethmoidal, frontal, sphenoidal and brain structures were more frequently reported in
101 ethmoidal epicenters' reports compared to others (XX% vs XX%) although this difference was not
102 statistically significant ($p=0.XXX$). Conversely, for structures related to the middle and inferior

103 turbinates or nasal floor, tumor invasion was more commonly specified in non-ethmoidal epicenters
104 (XX% vs XX%; p=0.XXX; Table 2).

105

106 **Tissue blocks relocation on multiplanar CT**

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

112

113 **Discussion**

114

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

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

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

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

130

131 **Conclusion**

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

136 **Declarations**

137 **Author contributions:** CL was contributed to data collection. All authors contributed to the study
138 conception and design as well as the drafting of the article. MF was responsible for statistical analysis
139 of data. JT, FC, AMP, LDG RFR and BV revised it critically for important intellectual content, and all
140 authors (CL, FC, MF, BV, AMP, LDG, VP, FRF, and JT) gave final approval of the version to be
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142

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149

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180

181 **Tables and Figures**

182

183 **Table 1:** Patients' characteristics depending on the epicenter

184

| 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) | |

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

186

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

188

| Tumor epicenter | Ethmoidal epicenter | | | Non-ethmoidal epicenter (maxillary, nasal fossa, frontal, sphenoid) | | |
|---------------------------------|---|--|--|---|--|--|
| | n=14 | | | n=7 | | |
| Analysed structures n=48 | Presence or absence of the tumor on operative report n (%) | Presence or absence of the tumor specified by pathological report n (%) | Quality of margin assessable on pathological report n (%) | Presence or absence of the tumor on operative report n (%) | Presence or absence of the tumor specified by pathological report n (%) | Quality of margin assessable on pathological report n (%) |
| 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) |

189 Legend:

190 * not reported in non-ethmoid tumors,

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

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

195