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Intraoperative surgical navigation as a precision medicine tool in sinonasal and craniofacial oncologic surgery

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ABSTRACT

Introduction: Recent evidence supports the efficacy of surgical navigation (SN) in improving outcomes of sinonasal and craniofacial oncologic surgery. This study aims to demonstrate the utility of SN as a tool for integrating

Abbreviations: RT, Radiation Therapy; SN, Surgical Navigation; ICA, Internal Carotid Artery; VR, Volume Resection; RPR, Reference Points Resection; MR, Magnetic Resonance; IMRT, Intensity-Modulated Radiation Therapy; CT, Computerized Tomography.

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surgical, radiologic, and pathologic information. Additionally, a system for recording and mapping biopsy samples has been devised to facilitate sharing of spatial information.
Materials and methods: SN was utilized for biopsy mapping in 10 sinonasal/craniofacial oncologic procedures. Twenty-five raters with experience in anterior skull base oncology were interviewed to identify 15 anatomical structures in preoperative imaging, relying on topographical descriptions and surgical video clips. The difference in the localization of anatomical structures by raters was analyzed, using the SN-mapped coordinates as a reference (this difference was defined as spatial error).
Results: The analysis revealed an average spatial error of 9.0 mm (95 % confidence interval: 8.3–9.6 mm), with significant differences between surgeons and radiation oncologists (7.9 mm vs 12.5 mm, respectively, $p < 0.0001$). The proposed model for transferring SN-mapped coordinates can serve as a tool for consultation in multidisciplinary discussions and radiotherapy planning.
Conclusions: The current standard method to evaluate disease extension and margin status is associated with a spatial error approaching 1 cm, which could affect treatment precision and outcomes. The study emphasizes the potential of SN in increasing spatial precision and information sharing. Further research is needed to incorporate this method into a multidisciplinary workflow and measure its impact on outcomes.

Introduction

Management of sinonasal and craniofacial tumors is a challenge since the balance between adequate resection and functional outcomes frequently represents a dilemma [1]. Surgery plays a pivotal role and often constitutes upfront treatment. Success of resection is primarily evaluated by status of surgical margins. Achieving negative margins is the main objective, as it ensures the highest chance of cure and represents the primary prognostic factor under surgeons' control [2,3]. Sinonasal and craniofacial tumor resections often require a multi-block approach [4,5]. Thus, evaluation of tumor extension and margin status relies on the ability to build a three-dimensional representation of the lesion based on imaging findings and analysis of the surgical specimen (s). This complex process, whether completely mental or supported by visual tools [6], is challenging and prone to spatial errors [7–9].

Management of sinonasal and craniofacial tumors requires a skilled multidisciplinary team for careful assessment of therapeutic options, with radiotherapy (RT) being of paramount importance in both the primary and adjuvant settings [10–12]. One of the main challenges for surgical and radiation treatment lies in the proximity of the lesion with numerous vital structures. The radiation oncologist must precisely delineate the radiation volumes to optimize oncologic outcomes and minimize the risk of toxicity [13]. Hence, the accurate definition of tumor extension and margin status necessitates a close interaction among surgeons, pathologists, radiologists, and radiation oncologists. This collaborative effort can be particularly demanding when adjuvant RT is administered in a center that is different from where the surgery was performed [12,14]. The conventional systems for documenting and naming intraoperative pathologic sampling and resection margins do not support a precise postoperative three-dimensional orientation. Therefore, planning adjuvant RT can be challenging since radiation oncologists may lack access to reliable information.

Among the strategies aimed at assisting the multidisciplinary team in evaluating tumor extension and surgical margins from a three-dimensional perspective, surgical navigation (SN) is particularly promising. Other methods of intraoperative marking have been described, including the use of surgical clips [15,16]. SN is widely used in operating rooms and is thus relatively accessible [17]. In recent years, SN has been hypothesized to provide therapeutic advantages by increasing the precision of oncologic resections and improving control of surgical margins

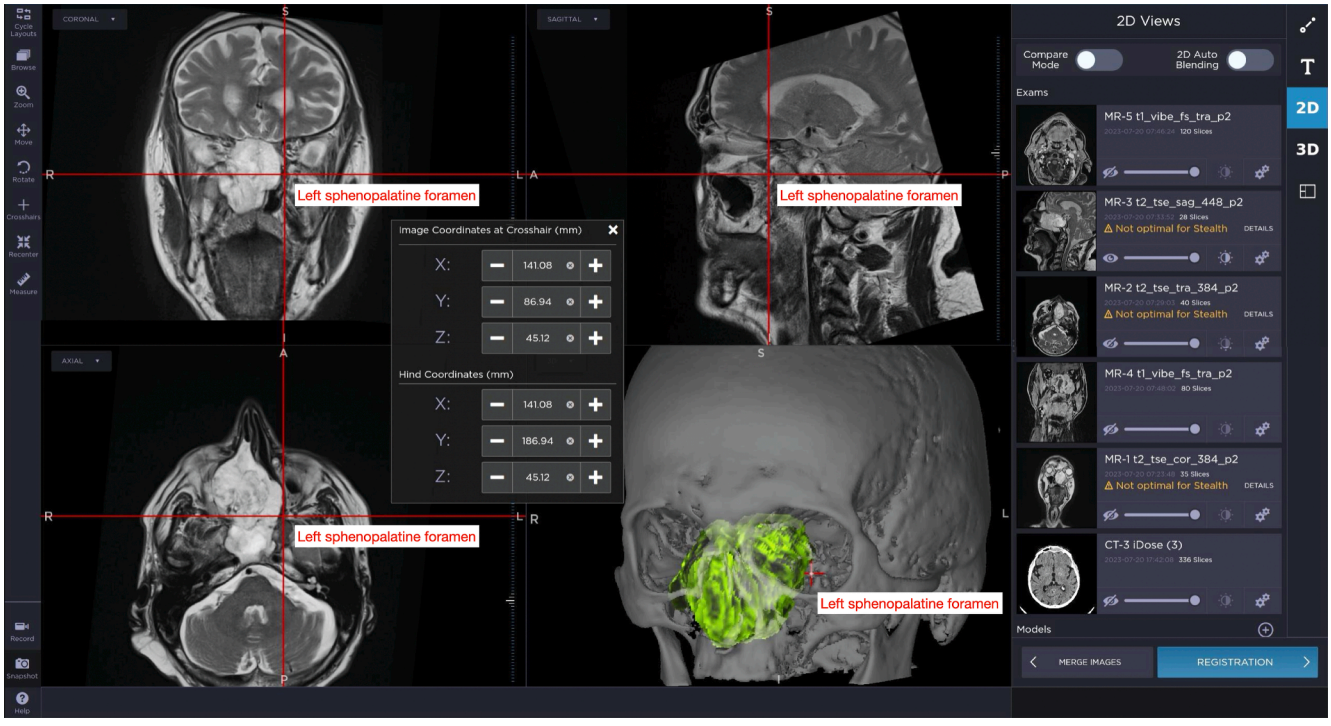

Figure 1. SN-guided intraoperative mapping, with the corresponding three-dimensional spatial coordinates.

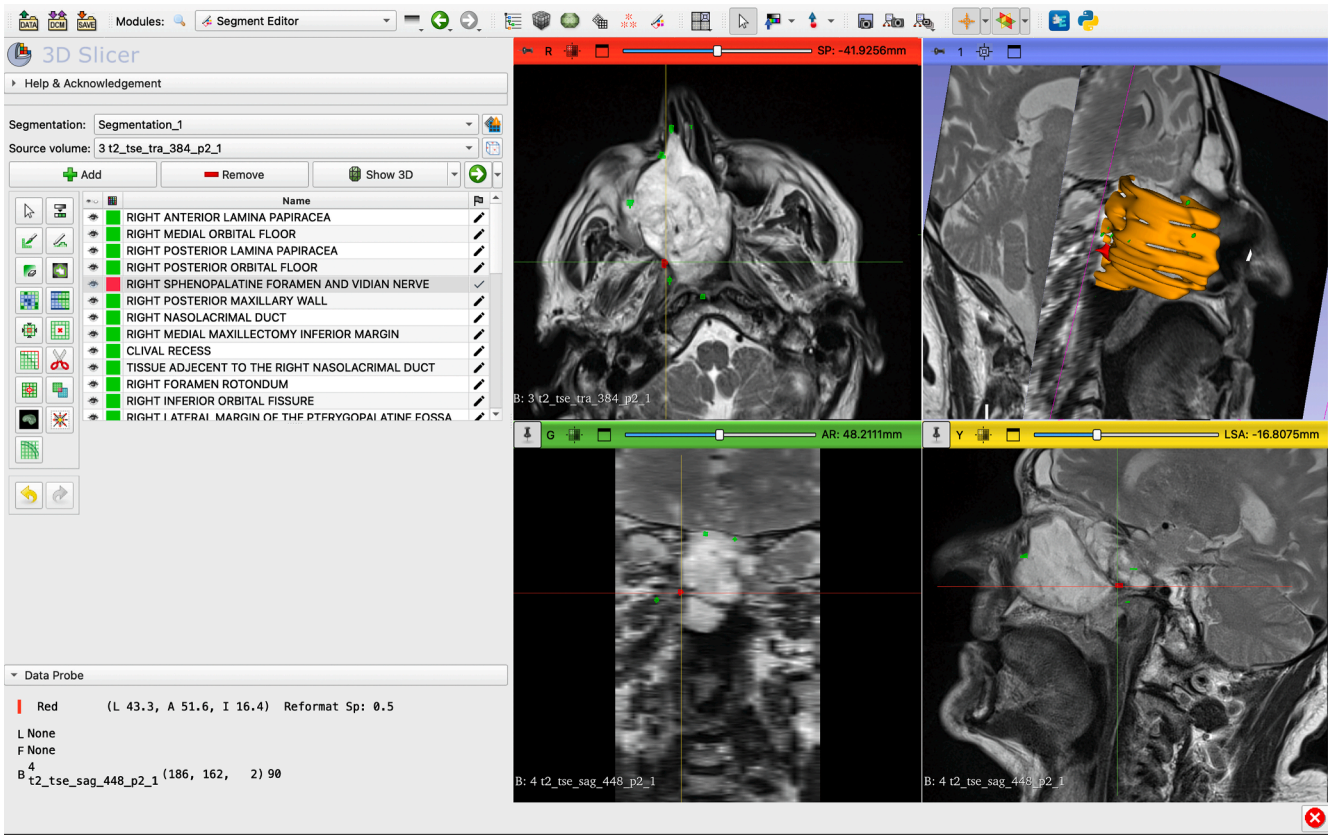

Figure 2. Transfer of SN-guided intraoperative mappings using the segmentation tool of the '3D Slicer' program.

[18–20]. Despite promising preclinical results, the application of SN in improving margin status remains limited, and there is a lack of data evaluating its actual benefits for patients.

The aim of this study is to use SN to improve precision of multidisciplinary communication and standardize the interpretation of tumor extension and margin status in sinonasal and craniofacial malignancies. The primary objective presented herein was to measure the spatial error that characterizes evaluation of tumor extension and margin status. The secondary aim was to develop a SN-based registration and mapping workflow for intraoperative biopsies, with the goal of having multidisciplinary information that can be shared and consulted.

Materials and methods

The present study prospectively included patients who underwent SN-guided surgery for sinonasal or craniofacial malignancies at the Section of Otorhinolaryngology – Head and Neck Surgery, Azienda Ospedale Università Padova (AOUP) from April 2021 to February 2024. Exclusion criteria were previous surgery in the craniofacial area and unwillingness to undergo additional imaging shortly before surgery.

In addition to (or as part of) the standard clinical practice for tumor staging, patients underwent a high-resolution (≤1 mm) non-contrast-enhanced craniofacial computed tomography (CT) scan, performed using an optimization protocol for SN (scan extended to include the head vertex and tip of the nose, gantry inclination at 0°, 1-mm-thick scans, and bone window). Subsequently, the Digital Imaging and Communication in Medicine (DICOM) files were imported into an electromagnetic SN system (Medtronic StealthStation S8; Medtronic®, Dublin, Ireland). The resection was planned using the segmentation system (Supplementary Figure 1) and the SN environment was registered before surgery, matching preoperative imaging with patient's anatomy. Registration was achieved by skin tracing and point matching, with a tolerated spatial error <1 mm in the entire region of interest, which included the gross tumor volume and neighboring tissues for at least 1 cm in all space directions (Supplementary Figure 2). To gain adequate precision also in the deep portion of the surgical field, both skin tracing and point matching included areas that were located posterior to the central midface and upper face, such as the temporoparietal skin, external ear, and posterior nasal spine. This technique of registration facilitated achieving a high-precision navigation environment that included also deep-seated areas such as the central skull base, nasopharynx, and infratemporal fossa. Precision of navigation environment was checked after registration by visually checking the accuracy of localization of anatomical landmarks that are easy to be identified both in the surgical field and at imaging (e.g., nasion, sphenoidal ostium, axilla of the middle turbinate, posterior nasal spine). The same technique (i.e., verification with easy-to-identify anatomical landmarks) was adopted periodically during surgery and every time a tissue was sampled and mapped as explained below.

During the surgical procedure, biopsies taken for frozen section analysis or definitive pathological examination were mapped using the SN system. This mapping allowed the accurate recording of the sampling locations on preoperative imaging (Figure 1). Subsequently, the recorded coordinates were transferred to the preoperative magnetic resonance (MR) through the freeware software 3D Slicer [21] (version 5.2.2, https://www.slicer.org). Transfer of the mark-ups was performed by inputting the 3D coordinates that were generated by the navigation system relative to the reference imaging that was selected at time of navigation (high-definition isotropic imaging packages were prioritized). Based on the definitive pathologic report, the recorded points corresponding to positive biopsy specimens were marked red, and those corresponding to negative biopsy specimens were marked green (Figure 2). A DICOM file including coordinates and pathologic status of intraoperative biopsies was generated to share information (Supplementary Figure 3).

Table 1
General characteristics of the cohort.

	N (% or IQ range)
Sex	
Male	8 (80 %)
Female	2 (20 %)
Median age (years)	61 (55.75–73.25)
Epicenter	
Nasoethmoid	7 (70 %)
Nasopharynx	2 (20 %)
Hard palate	1 (10 %)
Histology	
ITAC	5 (50 %)
Colic	1 (10 %)
Solid	1 (10 %)
Mucinous (alveolar goblet)	1 (10 %)
Mucinous (signet-ring)	2 (20 %)
SCC	2 (20 %)
Large cell NEC	1 (10 %)
SNUC	1 (10 %)
ACC	1 (10 %)
cT	
T1	1 (10 %)
T3	1 (10 %)
T4a	2 (20 %)
T4b	5 (50 %)
cN	
N0	9 (90 %)
N2b	1 (10 %)
cM	
M0	8 (80 %)
M1	2 (20 %)
Surgical approach	
Exclusively endoscopic	8 (80 %)
Combined	2 (20 %)
pT	
T1	2 (20 %)
T2	2 (20 %)
T4a	2 (20 %)
T4b	4 (40 %)
pN	
NX	8 (80 %)
N0	2 (20 %)
Surgical margin status (after multidisciplinary discussion)	
Uninvolved	6 (60 %)
Microscopically involved	4 (40 %)
Adjuvant treatment	
Yes	6 (60 %)
No	4 (40 %)
Median follow-up (months)	2 (0.25–3.75)

ACC, adenoid cystic carcinoma; ITAC, intestinal-type adenocarcinoma; NEC, neuroendocrine carcinoma; SCC, squamous cell carcinoma; SNUC, sinonasal undifferentiated carcinoma.

Spatial error assessment

Surgeons and radiation oncologists with expertise in anterior skull base oncology were asked to identify 15 anatomical structures mapped with SN. This assessment aimed to scrutinize and quantify the spatial error in the identification on preoperative imaging of anatomical areas that were sampled intraoperatively. The anatomical areas included the right vidian canal, left olfactory tract, left anterior dural margin of resection, falx cerebri, right nasolacrimal duct, right posterior orbital floor, right pterygopalatine fissure, left frontal mucosa, right posterior dural margin of resection, superior mucosa of the right maxillary sinus, sphenoid rostrum, mucosa of the floor of the right nasal fossa, right maxillary nerve, right tensor tympani muscle, and right medial pterygoid muscle insertion at the pterygomaxillary junction. Before the interviews, participants were provided with preoperative CT and MR images. During the interviews, raters could rate the position of points to be mapped by screen sharing and/or remote cursor control. Detailed spatial information regarding the precise location of the aforementioned anatomical structures was communicated verbally using the terms adopted by surgeons at the time of tissue sampling. Interviews were complemented with surgical video clips that showed the sampling procedure. For each anatomical structure evaluated, the distance between the coordinates identified by the physicians and those mapped intraoperatively, which were considered as reference, was analyzed. This distance was defined as "spatial error" (Supplementary Figure 4). Interview had a planned duration of roughly 1 h.

The software RStudio (version 4.3.1, https://www.rstudio.com/) was employed for statistical analysis. Mean, median, standard deviation, and interquartile range of spatial error were calculated. The calculation was made for the overall series of measurements and then clustered by anatomical area and specialty (surgeons vs radiation oncologists). The Mann-Whitney and Kruskal-Wallis tests were used to check for statistically significant differences, as appropriate. A significance level of 0.05 was adopted.

Table 2
Mean, median, standard deviation, and interquartile range of spatial error for each anatomical area.

ANATOMICAL AREA	MEAN (mm)	95 %-CI (mm)	MEDIAN (mm)	IQ RANGE (mm)
ANTERIOR DURAL MARGIN	9.9	7.3–12.6	8.7	7.0–10.7
FALX CEREBRI	10.4	6.6–14.2	7.3	5.4–12.8
FRONTAL MUCOSA	10.7	7.6–13.8	8.9	5.0–13.2
MEDIAL PTERYGOID MUSCLE	9.2	7.9–10.4	8.1	6.9–10.4
NASAL FOSSA FLOOR	7.7	5.6–9.7	5.5	4.0–12.4
NASOLACRIMAL DUCT	7.8	6.2–9.4	6.3	5.4–9.7
OLFACTORY TRACT	9.1	6.4–11.9	5.8	4.6–12.2
ORBITAL FLOOR	9.3	5.6–12.9	5.4	3.3–13.2
POSTERIOR DURAL MARGIN	7.9	6.4–9.5	7.8	4.4–11.1
SPHENOIDAL ROSTRUM	9.1	7.5–10.6	8.5	8.0–10.3
SPHENOPALATINE FORAMEN	6.4	4.8–8.1	5.2	3.5–9.4
SUPERIOR PART OF THE MAXILLARY OSTIUM	10.6	8.0–13.2	10.5	5.2–14.8
TENSOR TYMPANI MUSCLE	9.1	6.6–11.5	8.0	3.6–12.9
V2	10.6	7.7–13.4	10.5	5.3–12.8
VIDIAN CANAL	7.4	5.1–9.6	5.1	3.5–8.8
OVERALL	9.0	8.3–9.6	7.6	4.8–11.8

CI = confidence interval; IQ = interquartile.

Results

Ten patients were included. Table 1 summarizes the general characteristics of the cohort.

The primary tumor sites were localized in the craniofacial area, with the epicenter in the nasoethmoid, hard palate, or nasopharynx. After pathological examination, intestinal-type adenocarcinoma was detected in half of cases, with two exhibiting the mucinous subtype. The remaining half comprised squamous cell carcinoma, adenoid cystic carcinoma, large cell neuroendocrine carcinoma, and sinonasal

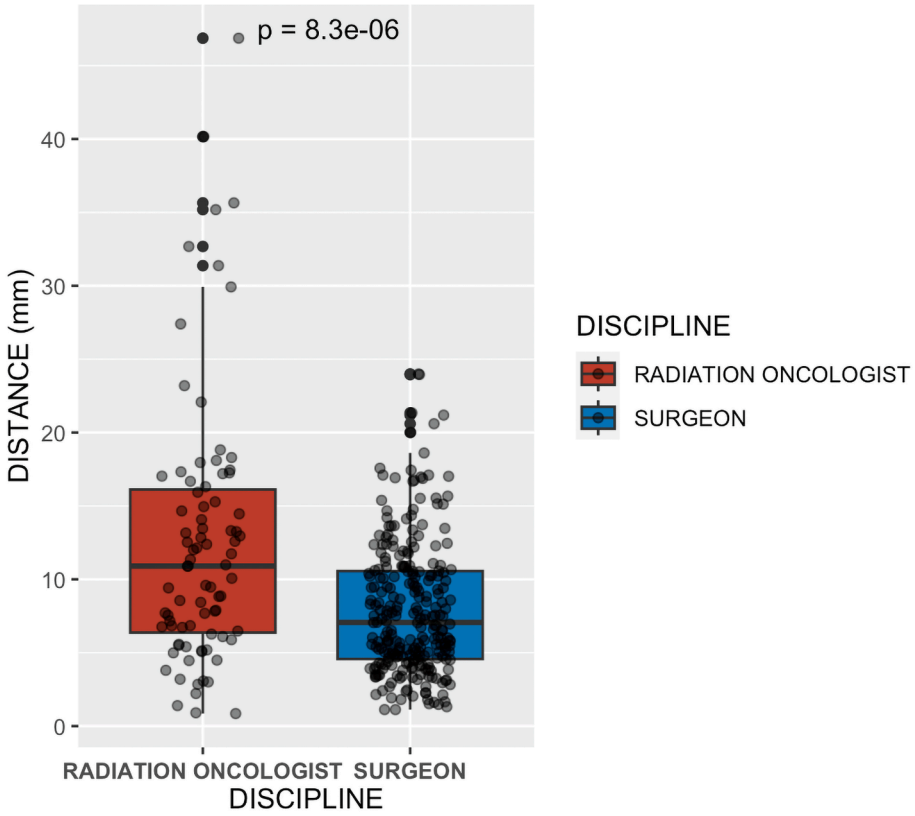

Figure 3. Box plot comparing the spatial error of surgeons and radiation oncologists.

undifferentiated carcinoma.

Twenty-five raters (19 surgeons and 6 radiation oncologists) participated in the interviews. Fifteen video clips were extracted from the surgical videos and examined during the interview. This process resulted in a comprehensive set of 375 rates. The overall mean spatial error was 9.0 mm (95 %-confidence interval (CI): 8.3–9.6). The spatial error did not vary significantly in relation to the different anatomical areas (Table 2, Supplementary Figure 5).

Subsequently, the spatial errors of the evaluations of surgeons and radiation oncologists were compared. The mean spatial error was 12.5 mm (95 %-CI 10.6–14.5) and 7.9 mm (95 %-CI 7.4–8.4) for radiation oncologists and surgeons, respectively. This difference was statistically significant ($p < 0.0001$) (Figure 3). The spatial errors of radiation oncologists and surgeons were compared for each anatomical structure. The results are reported in Table 3 and graphically represented in Figure 4. The difference between the evaluations of radiation oncologists and surgeons was statistically significant for the nasal floor, sphenoidal rostrum, maxillary nerve, and vidian nerve.

The spatial errors of involved and uninvolved structures were compared. The mean spatial error was 9.2 mm (95 %-CI 8.2–10.1) and 8.8 mm (95 %-CI 7.9–9.6) for uninvolved and involved anatomical structures, respectively. This difference was not statistically significant (Supplementary Figure 6).

Discussion

The scientific evidence published to date suggests that SN can contribute to improve oncologic outcomes in sinonasal and craniofacial surgery [18–20,22,23], and it does not have any relevant disadvantage that is directly associated with its application. Based on these considerations, the implementation of this technology in daily practice seems warranted. The present study analyzed the potential added value of SN as a tool to merge surgical, radiologic, and pathologic data with the intent to enable objective and reliable transmission of spatial information.

We collected surgical videos and preoperative imaging from 10 patients treated for sinonasal or craniofacial malignancies with SN-guided surgery. Twenty-five physicians with experience in anterior skull base oncology were interviewed and tasked to locate the position of 15 resected anatomical structures that were intraoperatively mapped with the SN system. The analysis of spatial error among raters revealed an inaccuracy approaching 1 cm, which is clinically relevant in terms of postoperative treatment. The spatial errors in the evaluation of surgeons and radiation oncologists were compared, revealing a significant difference, particularly for certain anatomical structures such as the nasal floor, sphenoidal rostrum, maxillary nerve, and vidian nerve. In our interpretation, this difference can be attributed to the greater familiarity of surgeons with the identification of anatomical structures based on intraoperative naming and endoscopic view. As an additional factor, surgeons routinely build a three-dimensional mental representation of sinonasal and craniofacial anatomy by comparing the intraoperative visualization (endoscopic or open) with imaging. Of note, radiation oncologists deal with the sinonasal tract anatomy less frequently than the surgeon, as postoperative treatment is reported for only 50–60 % of patients [4,24]. Moreover, radiation oncologists tend to predominantly use CT axial images to define clinical target volumes, which can be challenging for horizontally-oriented structures such as orbital floor, nasal cavity floor and maxillary nerve. The use of coronal images is generally a second step and is often supported by collaboration with a radiologist. Additionally, the contouring phase of volumes is usually long and suitable for adjustments. On the contrary, the present study involved a single session per physician with an average duration of 60 min. Overall, these results offer an additional example of how multidisciplinary collaboration and referral to centers with adequate patients volume and expertise is paramount in the management of sinonasal cancers [25,26].

The study is subject to some limitations that warrant mention. First, the navigation system could not directly export the mapped points,

Table 3
Mean, median, standard deviation, and interquartile range of spatial error, clustered by anatomical area and specialty.

ANATOMICAL AREA	DISCIPLINE	MEAN (mm)	95 %-CI (mm)	MEDIAN (mm)	IQ RANGE (mm)	p-value
ANTERIOR DURAL MARGIN	RADIATION ONCOLOGIST	12.4	2.5–22.2	9.6	5.5–13.1	0.8415
	SURGEON	9.1	7.5–10.8	8.7	7.2–10.6	
FALX	RADIATION ONCOLOGIST	15.4	0.5–31.4	6.8	6.1–15.3	0.6958
	SURGEON	9.1	6.5–11.7	7.8	5.2–11.8	
FRONTAL MUCOSA	RADIATION ONCOLOGIST	14.2	0.1–27.6	6.7	4.5–15.9	0.8035
	SURGEON	9.8	7.7–11.9	9.1	5.9–12.7	
MEDIAL PTERYGOID MUSCLE	RADIATION ONCOLOGIST	10.5	6.5–14.4	9.4	6.8–12.8	0.7761
	SURGEON	8.8	7.6–10.0	7.9	7.0–10.2	
NASAL FOSSA FLOOR	RADIATION ONCOLOGIST	12.8	9.4–16.2	13.3	12.4–14.1	**0.0125**
	SURGEON	6.2	4.2–8.2	4.7	3.8–7.3	
NASOLACRIMAL DUCT	RADIATION ONCOLOGIST	9.1	5.1–13.1	7.8	6.1–9.1	0.3861
	SURGEON	7.4	5.6–9.2	5.9	5.2–10.1	
OLFACTORY TRACT	RADIATION ONCOLOGIST	15.4	6.6–24.2	12.1	8.3–24.2	0.0857
	SURGEON	7.1	4.0–10.3	5.8	4.6–10.7	
ORBITAL FLOOR	RADIATION ONCOLOGIST	19.4	9.8–29.1	15.6	13.2–29.0	**0.0077**
	SURGEON	5.9	1.7–10.0	4.7	3.2–7.4	
POSTERIOR DURAL MARGIN	RADIATION ONCOLOGIST	7.7	5.0–10.3	7.6	5.7–10.1	0.8486
	SURGEON	8.0	6.1–10.0	8.6	4.2–11.5	
ROSTRUM	RADIATION ONCOLOGIST	13.2	10.1–16.4	12.7	10.7–16.2	**0.0041**
	SURGEON	7.6	6.4–8.8	8.3	5.3–8.6	
SPHENOPALATINE FORAMEN	RADIATION ONCOLOGIST	9.9	4.0–11.9	6.0	5.3–10.1	0.3087
	SURGEON	6.0	4.1–7.8	4.2	3.5–8.5	
SUPERIOR MAXILLARY OSTIUM	RADIATION ONCOLOGIST	9.5	3.7–15.3	8.9	5.1–14.9	0.7094
	SURGEON	10.9	7.9–13.8	10.9	5.4–14.3	
TENSOR TYMPANI MUSCLE	RADIATION ONCOLOGIST	11.8	5.6–10.8	10.9	8.5–14.5	0.2630
	SURGEON	8.2	5.6–10.8	6.5	3.5–10.9	
V2	RADIATION ONCOLOGIST	17.6	8.8–26.4	16.7	11.0–23.2	**0.0279**
	SURGEON	8.5	6.6–10.4	6.5	5.1–11.1	
VIDIAN CANAL	RADIATION ONCOLOGIST	11.6	6.6–16.7	12.3	9.6–16.1	0.0748
	SURGEON	6.0	3.4–8.6	4.7	3.4–5.7	
OVERALL	RADIATION ONCOLOGIST	12.5	10.6–14.5	10.9	6–7 – 16.1	**<0.0001**
	SURGEON	7.9	7.4–8.4	7.0	4.5–10.5	

CI = confidence interval; IQ = interquartile; NS = not significant.

requiring manual transfer of information to the imaging analysis software. This potential source of bias was controlled by relying on consistency of spatial coordinates provided by both the navigation system and the imaging analysis software. Second, the use of a video conferencing platform to interview experts posed some logistical challenges in the process of pointing out the position of samples on imaging. However, this system was deemed necessary to interview a selected cohort of experts on a worldwide scale. Moreover, for each biopsy to be rated, the raters' evaluation was optimized through a detailed description of the sampling procedure, as well as by sharing anonymized radiological images and surgical videos of the sampling about 1 week before the interview. This process might introduce a bias and thus overestimate the precision of judgement, since it deviates from the actual time and means that are routinely employed to delineate tumor extension and critical margins. Third, overall treatment planning routinely includes the comprehensive description of surgery alongside with information arising from post-surgery, pre-RT imaging, when available. This process might mitigate the spatial error through the combination of multiple topographic information, differently to the present experiment.

Despite the aforementioned limitations, our results highlight the ability of surgeons to achieve an acceptable mapping of tumor extension and margin status and the relevance of an interactive discussion on these findings within the tumor board. However, the error of surgeons' evaluation was still around 8 mm, a value that can be considered suboptimal in an area such as the craniofacial region which is dense in critical structures in view of the possible negative impact on oncologic and morbidity outcomes. Therefore, it appears logical to develop tools that can increase the precision of transmission of spatial information

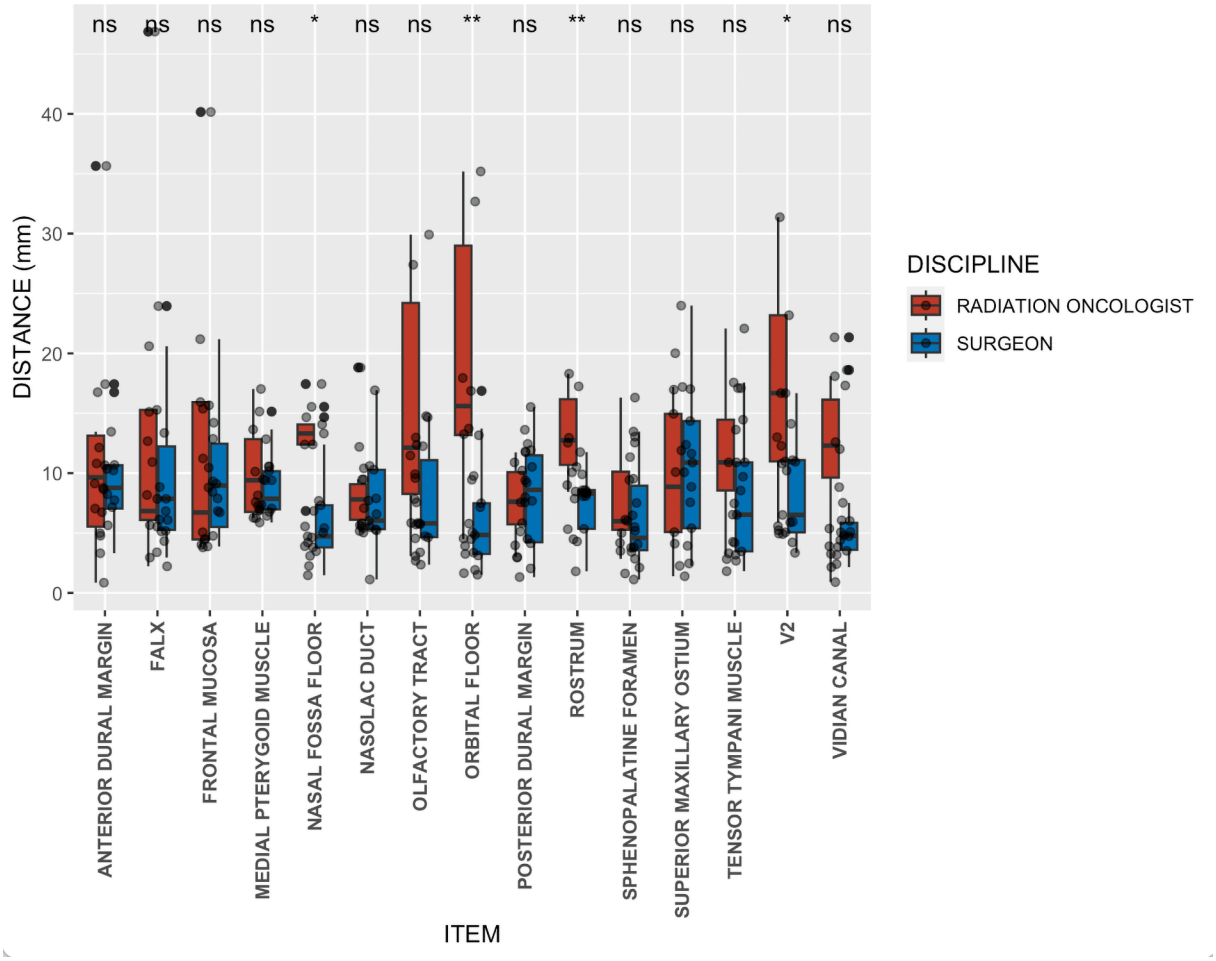

Figure 4. Box plot comparing the spatial error of surgeons and radiation oncologists, clustered by anatomical structure. *p < 0.05; **p < 0.01.

[18–20,22]. Indeed, SN has the necessary features to meet the need for spatial precision, allowing surgeons to intraoperatively map the relevant resected structures by imaging. Using dedicated computer programs, it is possible to transfer intraoperative SN-guided mappings into preoperative MR, exporting the result of this process as a DICOM file (Supplementary Figure 3). In the present case series, this model was tentatively incorporated into the multidisciplinary discussion to aid tumor delineation and localization of positive margins. From a radiation oncology standpoint, achieving high precision in identifying areas with the highest risk of microscopic residual disease via SN mapping may aid defining the clinical target volumes in the adjuvant setting. This has the potential to result in increased personalization of volumes receiving high dose (60–66 Gy). The main limitation of this workflow is represented by procedural complexity, since several informatic passages were needed to generate the final DICOM file. The automation of this process is a future crucial step to make this tool routinely applicable in cancer centers. Moreover, the future evolution of this research will aim to prospectively study whether SN-guided postoperative treatment could be associated with better local control and lower rates of toxicity.

Conclusions

The results of this study indicate that the implementation of SN in the management of sinonasal and craniofacial malignancies can significantly improve precision. The observed variability in spatial interpretation of resected structures between surgeons and radiation oncologists highlights the complexity of sinonasal and craniofacial anatomy, emphasizing the importance of close collaboration among professionals and the need to develop strategies that can improve the precision of multidisciplinary communication.

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CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.oraloncology.2024.106979.

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