

THE LANCET Neurology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
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Supplement to: Kosugi Y, Hara N, Isobe A, Matsumoto F, Sasai K. Detection of ionising radiation by the CNS: a case report. *Lancet Neurol* 2022; **21**: 311–12.

The medical history of the patient in detail

Supplementary Figure 1 shows a schematic of the medical history of the patient.

A 34-year-old woman underwent transcranial resection of the Kadish stage C olfactory neuroblastoma (Supplementary Fig. 2A) at a national cancer centre in Japan in July. During the surgery, her olfactory bulbs, cribriform plate and epithelium were resected.

She was referred to us in April of the following year because the main head and neck surgeon (FM) moved to our hospital. Unfortunately, a recurrent tumour at the olfactory region was confirmed using nasal fiberscope, CT, and MRI (Supplementary Fig. 2B) in June. The second surgery, transnasal resection of recurrent tumour tissue, was performed in July.

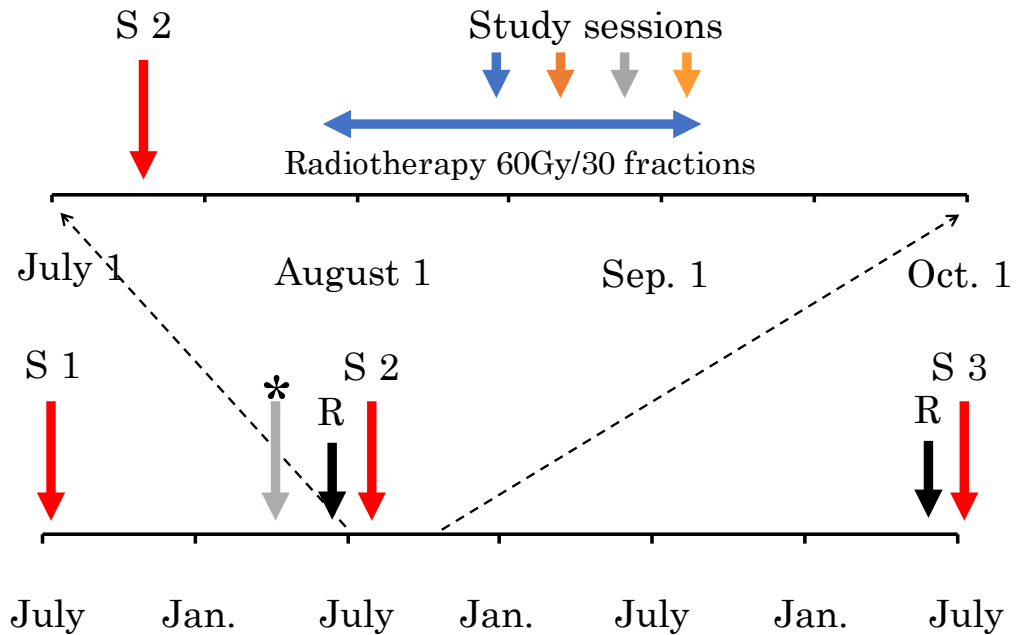
Twenty-one days after the second surgery, the patient received helical tomotherapy, a type of intensity-modulated radiotherapy, that was administered as 60 Gy in 30 fractions over 43 days, with one session per day and 5 sessions per week. Just before starting radiotherapy, she reported that she had no olfactory sensation at all after the first surgery, although it was not confirmed objectively. During radiotherapy sessions, the patient complained of a foul odour. Coincidentally, she joined a prospective observational study for unusual sensations during radiation sessions.³ In the study, after informed consent was obtained, she was asked to indicate using a button when a sensation commenced and ended. The data were recorded electronically by a device designed specifically for the study and collated with the treatment logs (Figure). This process was repeated 4 times, once a week.

The patient also complained of other adverse events such as mild nausea, dry sensation in the nasal cavity, mild oral mucositis, and dysgeusia.

Supplementary Figure 2C shows a coronal view of CT 3 months after the treatment.

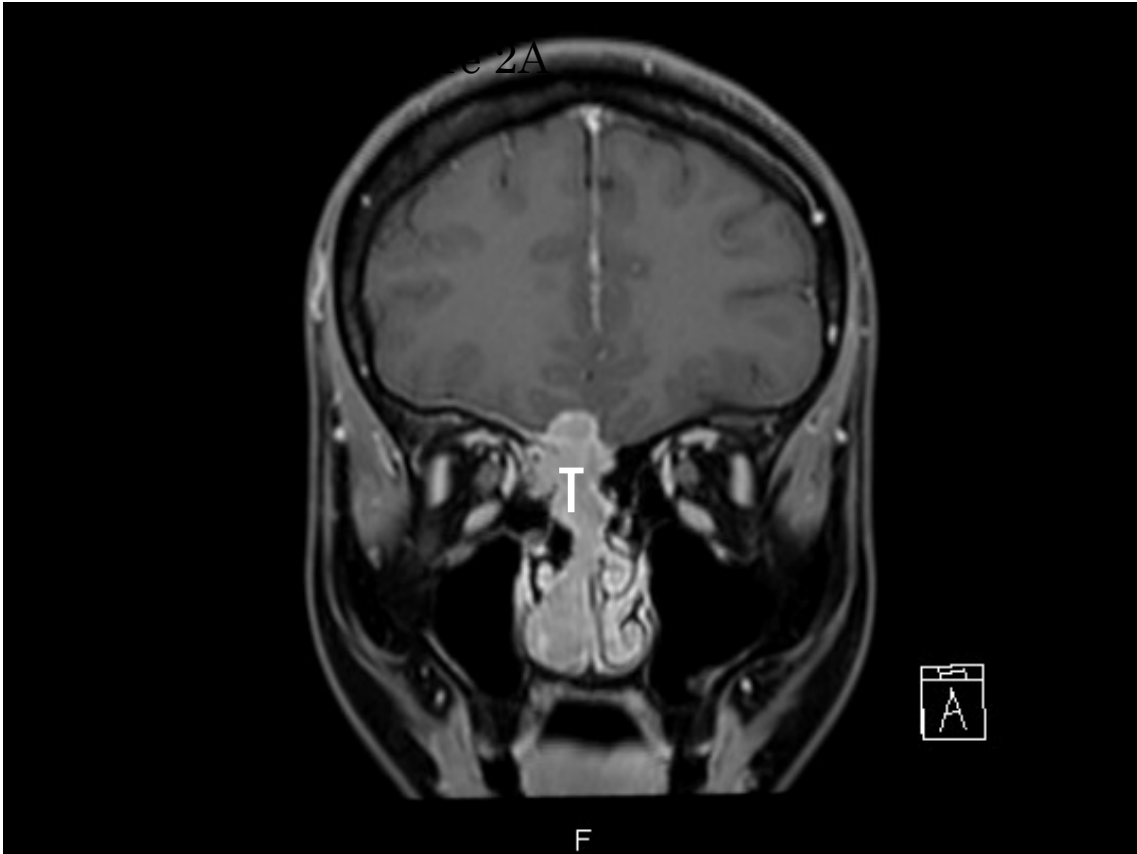
She was fine for approximately 2 years, except for anosmia. Supplementary Figure 2D shows a coronal view of MRI. However, follow-up nasal fiberscope examination and biopsy revealed another recurrence at the nasopharynx in June 2 years after the radiotherapy. The patient underwent transnasal resection of the tumour and received another round of radiotherapy with a total of 60 Gy in 30 fractions for the regions just caudal to the previous treatment. She did not report the pungent smell, which she perceived in the previous radiotherapy during the treatment sessions.

Supplementary Figure 1
Schematic of the medical history of the patient



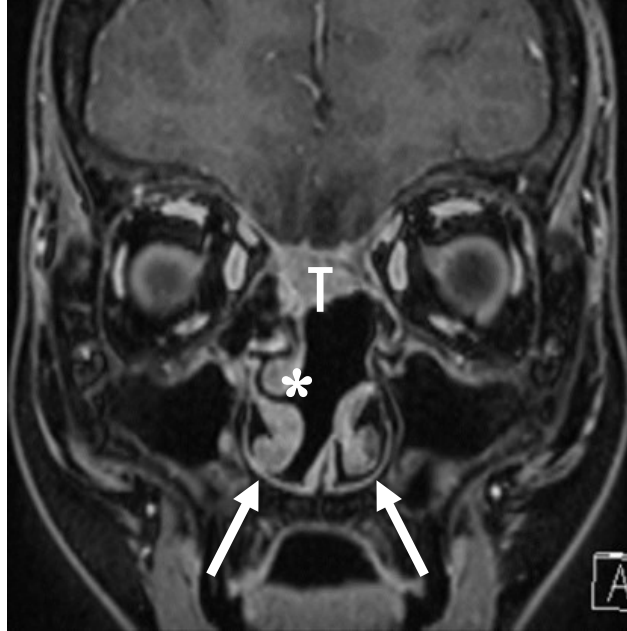
Lower column demonstrates the course of 3 years, and upper column shows the course from July 1 through October 1 of the second year.

S1: the first surgery, S2: the second surgery, S3: the third surgery, R: recurrence, * indicates the date on which the patient was referred to our institution.



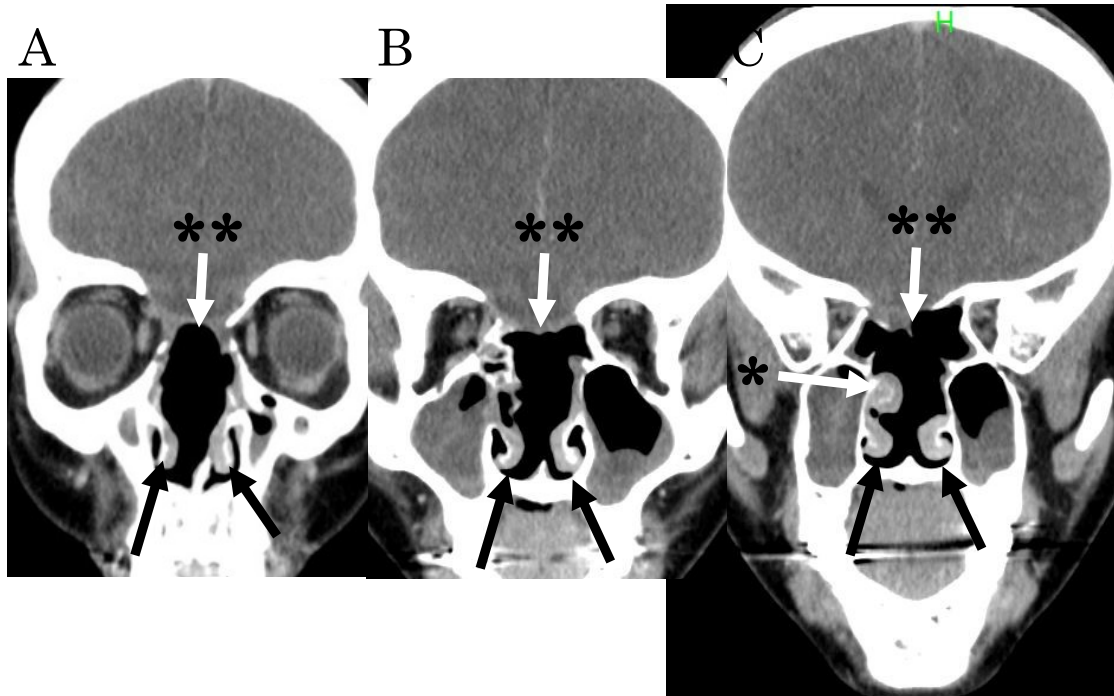
Coronal T1 weighted MRI just before the first surgery
T: tumour,

Supplementary Figure 2B



Coronal T1 weighted MRI just before the second surgery
T: tumour, Arrow: Inferior nasal concha, *: Middle nasal concha

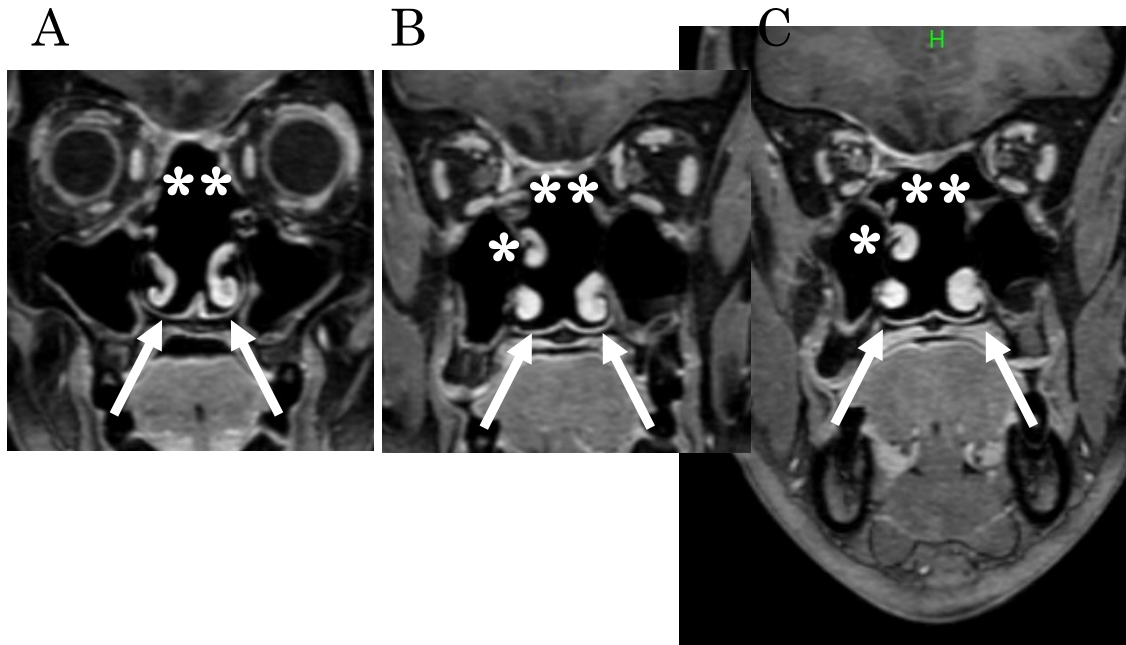
Supplementary Figure 2C



Coronal post radiation CT (3 months later) images of nasal cavity presented from anterior to posterior.

Arrow: Inferior nasal concha, *: Middle nasal concha, **: Resected area of upper part of nasal cavity and ethmoid

Supplementary Figure 2D



Coronal post radiation T1 weighted MRI (1 year and 9 months later, D) images of nasal cavity presented from anterior to posterior.

Arrow: Inferior nasal concha, *: Middle nasal concha, **: Resected area of upper part of nasal cavity and ethmoid

Supplementary table

Dosimetric analysis of olfactory tract and olfactory cortex

	D2% (Gy/fraction)	D50% (Gy/fraction)
Olfactory tract	1.98	1.69
Olfactory cortex	1.25	0.85
Olfactory epithelium	-	-

Dx% is the minimum absorbed dose in the hottest x% volume of the region of interest. Olfactory epithelium was not detected on CT. Therefore, its absorbed doses were not determined.

The dose distribution was heterogeneous during intensity-modulated radiation therapy. Therefore, it was hypothesized that higher doses might cause more unusual sensations. D2% and D50% (Gy)/fraction doses were used as representatives of that delivered to the organs. The olfactory tract was contoured as a virtual structure at the base of the olfactory sulcus using a 5-mm-circle brush in each coronal plane. The olfactory cortex is composed of several areas. Therefore, the prepiriform areas were contoured, located in the anterior part of the uncus and amygdala, to represent the olfactory cortex.³