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Kai Kanemoto

kakanemo@east.ncc.go.jp

National Cancer Center-Hospital East: Kokuritsu Gan Center Higashi Byoin https://orcid.org/0009-0009-7648-341X

Takeshi Shinozaki

National Cancer Center-Hospital East: Kokuritsu Gan Center Higashi Byoin

Manabu Hashimoto

National Cancer Center-Hospital East: Kokuritsu Gan Center Higashi Byoin

Hirofumi Kuno

National Cancer Center-Hospital East: Kokuritsu Gan Center Higashi Byoin

Masashi Wakabayashi

National Cancer Center-Hospital East: Kokuritsu Gan Center Higashi Byoin

Wataru Okano

National Cancer Center-Hospital East: Kokuritsu Gan Center Higashi Byoin

Toshifumi Tomioka

National Cancer Center-Hospital East: Kokuritsu Gan Center Higashi Byoin

Kazuto Matsuura

National Cancer Center-Hospital East: Kokuritsu Gan Center Higashi Byoin

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Original Article

Risk Factors and Analgesic Strategies for Postoperative Pain after Photoimmunotherapy for Head and Neck Cancer

Kai Kanemoto[1], Takeshi Shinozaki[1], Manabu Hashimoto[2], Hirofumi Kuno[3], Masashi Wakabayashi[4], Wataru Okano[1], Toshifumi Tomioka[1], Kazuto Matsuura[1]

・Authors' affiliations:

1 Department of Head and Neck Surgery, National Cancer Center Hospital East, Kashiwa, Japan

2 Department of Anesthesiology, National Cancer Center Hospital East, Kashiwa, Japan

3 Department of Diagnostic Radiology, National Cancer Center Hospital East, Kashiwa, Japan

4 Biostatistics Division, Center for Research Administration and Support, National Cancer Center Hospital East, Kashiwa, Japan

・Corresponding author:

Takeshi Shinozaki

Department of Head and Neck Surgery, National Cancer Center Hospital East, Kashiwa, Japan, 6-5-1,

Kashiwanoha, Kashiwa-shi, Chiba, 277-8577, Japan.

E-mail: tashinoz@east.ncc.go.jp

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Abstract (250/250 words)

Background: Photoimmunotherapy is a novel treatment for recurrent/unresectable head and neck cancer. Postoperative pain is a major adverse event; however, its risk factors and effective analgesic interventions remain unclear. This study aimed to identify risk factors for postoperative pain and evaluate analgesic strategies.

Methods: We retrospectively analyzed 48 photoimmunotherapy procedures performed in 19 patients with head and neck squamous cell carcinoma between January 2021 and July 2025. Postoperative pain was assessed using the Numerical Rating Scale (0–10). Associations with postoperative pain were examined using univariable and multivariable analyses, including linear mixed-effects models, accounting for repeated procedures.

Results: Postoperative pain increased in 46 of 48 procedures, with a median maximum Numerical Rating Scale score of 6. Pain peaked immediately after surgery, improved by 24 h, increased again on postoperative day 2, and persisted until day 7. The number of illuminations, tumor volume, and tumor thickness were significantly associated with higher Numerical Rating Scale scores in univariable analyses and univariable mixed-effects models. In multivariable linear regression, only tumor thickness remained significant; however, none remained significant in the multivariable mixed-effects model. Local ropivacaine infiltration

was associated with lower Numerical Rating Scale scores within 6–71 h but higher scores after 72 h.

Conclusion: Tumor burden and illumination parameters were associated with postoperative pain, although no independent associations were identified in multivariable mixed-effects analysis. These findings suggest a potential role for local ropivacaine infiltration in postoperative pain control within 6–71 h. Further studies are warranted to optimize perioperative pain management after photoimmunotherapy.

Keywords: PIT, photoimmunotherapy, pain, head and neck cancer

(2970/3000 words)

Introduction

Photoimmunotherapy (PIT) is a novel cancer treatment that uses tumor-targeting monoclonal antibodies conjugated to a light-activatable dye, IRDye700DX [1]. After binding to epidermal growth factor receptor-expressing tumor cells, near-infrared illumination at 690 nm induces a photochemical reaction that disrupts the cell membrane, ultimately leading to necrotic cell death [1, 2]. In Japan, PIT using cetuximab sarotalocan sodium (Alluminox™), an IRDye700DX-conjugated form of cetuximab, received conditional approval from the Ministry of Health, Labour and Welfare in September 2020 for the treatment of

unresectable locally advanced or locoregionally recurrent head and neck squamous cell carcinoma (HNSCC) [3–6].

Postoperative pain is a severe adverse effect of PIT. In clinical trials, 78.0% of patients experienced pain at the application site, with grade ≥3 pain reported in 29.3% of cases [2, 5]. Patients with poorly controlled pain after PIT may experience significant difficulty managing secretions, poor oral intake, dehydration, malnutrition, aspiration pneumonia, and prolonged hospitalization. Thus, effective perioperative pain management after PIT is essential to prevent complications and optimize recovery. Matsumoto et al. reported that patients with a history of reconstructive surgery may have a lower incidence of postoperative pain [7]. However, other risk factors for postoperative pain after PIT remain poorly understood. Furthermore, no studies have statistically evaluated the effectiveness of analgesic interventions for postoperative pain after PIT.

Therefore, the present study retrospectively analyzed 48 PIT procedures performed in 19 patients at our institution to identify risk factors for postoperative pain and evaluate the effectiveness of analgesic strategies.

Patients and Methods

Patients

We conducted a retrospective study of patients with HNSCC who underwent PIT at the National Cancer

Center Hospital Easr (NCCHE) between January 2021 and July 2025. During this period, 48 PIT procedures were performed in 19 patients. The following clinical data were collected.

- Patient characteristics: age at surgery, sex, and prior treatment history (history of radiotherapy and reconstructive surgery).
- Surgical information: illumination site, number of illumination sites, number of illuminations, tumor volume, and thickness.
- Anesthetic information: type of maintenance anesthetic (sevoflurane, desflurane, or total intravenous anesthesia), intraoperative fentanyl and remifentanil dosages, use of postoperative intravenous patient-controlled analgesia (iv-PCA), and intraoperative local infiltration with ropivacaine.

Reconstructive surgery was considered positive if free or pedicled flap reconstruction was performed. For tumor illumination, cylindrical diffusers inserted through needle catheters were used for interstitial tumors, whereas frontal diffusers were used for superficial tumors. The number of illuminations was defined as the total number of frontal and cylindrical diffusers used intraoperatively. Tumor volume and thickness were measured on pre-PIT computed tomography or magnetic resonance imaging scans using OsiriX software by a radiologist specializing in head and neck imaging.

The iv-PCA regimen consisted of 1 mg of fentanyl diluted in 20 mL of solution and combined with 80 mL of normal saline (total volume, 100 mL). The infusion was initiated immediately before the end of

surgery. A basal infusion rate of 2.0–2.5 mL/h was administered, with patient-controlled bolus doses of 2.0–2.5 mL per demand (fentanyl 20–25 μg per dose) available for breakthrough pain. For local anesthesia, 10 mL of ropivacaine (100 mg) mixed with 10 mL of normal saline (total volume, 20 mL) was injected into the illuminated site using a 23-gauge needle under direct visual or endoscopic guidance immediately before the end of surgery.

This study was approved by the Institutional Review Board of the National Cancer Center Hospital East (approval number: 2022-071) and conducted in accordance with the Declaration of Helsinki.

Outcomes

The primary outcome was postoperative pain intensity, assessed using the Numerical Rating Scale (NRS). The NRS is a unidimensional measure of pain intensity that is widely used in clinical practice and research owing to its simplicity and validity. Patients rate their pain on an 11-point scale ranging from 0 (“no pain”) to 10 (“the worst pain imaginable”). For each procedure, the maximum NRS score recorded between immediately after surgery and postoperative day (POD) 7 was extracted. In addition, to evaluate the effects of intraoperative administration of fentanyl and remifentanil, postoperative iv-PCA, and local infiltration with ropivacaine, the maximum NRS score was assessed separately for three postoperative intervals: 0–5 h, 6–71 h, and 71 h–7 days.

Statistical Analyses

Univariable analyses were first performed to evaluate associations between patient characteristics, surgical variables, anesthetic variables, and postoperative NRS scores. For categorical variables, the Mann–Whitney U test was used for comparisons between two groups, whereas the Kruskal–Wallis test was used for comparisons among three or more groups. Spearman's rank correlation coefficient was used for continuous variables.

As several patients underwent multiple PIT procedures, observations from procedures in the same patient were not statistically independent. Therefore, factors showing statistical significance or a trend toward significance in the univariable analyses were further evaluated using univariable linear mixed-effects models, with patient included as a random effect to account for within-patient correlation.

Multivariable analyses were performed using two approaches. First, conventional multiple linear regression analysis was performed, with each PIT procedure treated as an independent observation. Second, a multivariable linear mixed-effects model was fitted using the same variables, with patient included as a random effect to account for repeated procedures within the same patient. Conventional multiple linear regression was used to evaluate associations after adjusting for potential confounding factors, whereas the multivariable linear mixed-effects model additionally accounted for within-patient correlation.

Considering the limited sample size and exploratory nature of this study, the two-sided threshold for statistical significance was set at $p < 0.10$. All statistical analyses were performed using EZR (version 1.51;

Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria; version 4.1.1).

Results

Patient, surgical, and anesthetic characteristics

A total of 48 PIT procedures were performed in 19 patients (Table 1). The median patient age was 65 years, and 58% of the patients were men. All patients had a history of radiotherapy, and 47% had a history of reconstructive surgery. The most common illumination site was the oropharynx (39.5%), followed by the nasopharynx (33.3%). The median number of illuminations was three. To exclude cases in which preoperative imaging was unavailable or lesions were too small to be detected radiologically, tumor volume and thickness were assessed in 25 procedures, with median values of 0.93 cm^3 and 1.0 cm, respectively. Iv-PCA was used in 41 procedures (85%), and in all 41 cases, the initial 100-mL infusion was fully administered; however, no additional opioids were required. Local infiltration with ropivacaine was administered in five procedures (10%) performed after September 2024.

Postoperative pain

In 46 of the 48 PIT procedures, the NRS score ranged from 2 to 10, with a median of 6. The time course of the mean postoperative NRS scores across all 48 procedures is shown in Figure 1. The mean NRS score

151 increased to 4–5 immediately after surgery, began to decline after 3 h, and decreased to approximately 1 by
152 24 h postoperatively. Thereafter, the NRS score increased again on POD 2, and pain levels of approximately
153 2–3 on the NRS persisted until POD 7.
154
155 ***Risk factors for postoperative pain***
156 In the Mann–Whitney U test, neither sex nor a history of reconstructive surgery was significantly associated
157 with postoperative NRS scores ($p = 0.84$ and 0.65, respectively) (Supplementary Table S1).
158 In the Kruskal–Wallis test, postoperative NRS scores differed significantly among illumination sites ($p =$
159 0.081) (Table 2). Steel–Dwass post hoc analysis showed significantly higher postoperative NRS scores for
160 illumination of the posterior wall of the oropharynx than for illumination of the nasopharynx ($p = 0.061$).
161 Overall, postoperative NRS scores were higher for illumination of the anterior and posterior walls of the
162 oropharynx and the cervical skin, whereas lower scores were observed for the oral cavity and nasopharynx
163 (Supplementary Fig. S1).
164 Spearman's rank correlation analysis showed significant positive correlations of postoperative NRS scores
165 with the number of illuminations, tumor volume, and tumor thickness (Table 3, Supplementary Fig. S2).
166 Among these factors, tumor thickness showed a moderate positive correlation with postoperative NRS
167 scores (Spearman's $\rho = 0.60$, $p = 0.001$).
168 In univariable linear mixed-effects models accounting for repeated procedures within the same patient, the

number of illuminations, tumor volume, and tumor thickness remained significantly associated with postoperative NRS scores, whereas illumination site was not significantly associated with these scores (Table 4).

In multiple linear regression analysis including the number of illuminations, tumor volume, and tumor thickness, only tumor thickness remained significantly associated with postoperative NRS scores ($\beta = 0.88$; 95% CI, 0.06–1.70; $p = 0.037$) (Table 5). However, in a multivariable linear mixed-effects model accounting for repeated procedures within the same patient, none of these variables showed a statistically significant independent association with postoperative NRS scores (Table 6).

Analgesic strategies for postoperative pain

In the Mann–Whitney U test, iv-PCA was significantly associated with higher NRS scores after 72 h (Supplementary Table S2). However, this association was not statistically significant in the linear mixed-effects model, which accounted for repeated procedures within the same patient (Table 7).

For local ropivacaine infiltration, the Mann–Whitney U test showed significantly higher NRS scores after 72 h in procedures involving ropivacaine infiltration (Supplementary Table S2). However, in the linear mixed-effects model, local ropivacaine infiltration was significantly associated with lower NRS scores at 6–71 h postoperatively ($p = 0.026$) and with higher NRS scores after 72 h ($p = 0.056$) (Table 7).

Figure 2 shows the time course of the mean postoperative NRS scores according to whether local

187 ropivacaine infiltration. During the first 71 h after surgery, NRS scores tended to be higher in procedures
188 without ropivacaine infiltration, whereas after 72 h, NRS scores were higher in those who received
189 ropivacaine infiltration.
190 Neither the intraoperative fentanyl nor remifentanil dose was significantly correlated with postoperative
191 NRS scores.
192

193 **Discussion**

194 This study systematically analyzed postoperative pain following 48 PIT procedures for HNSCC, identifying
195 risk factors and evaluating pain management strategies. Greater tumor burden (volume and thickness) and
196 an increased number of illuminations were associated with higher postoperative pain following PIT. Local
197 ropivacaine infiltration was associated with lower NRS scores at 6–71 h postoperatively.
198 Shibutani et al. previously reported the characteristics of postoperative pain in five PIT cases, demonstrating
199 that pain was most severe immediately after or within 1 h of illumination and subsequently decreased by
200 the following day [8]. The present study expands on these findings by statistically evaluating pain
201 trajectories and risk factors over the first 7 PODs in a cohort of 19 patients who underwent 48 procedures.
202 Consistent with previous findings [2, 5, 8], almost all procedures were associated with postoperative pain
203 exacerbation, with NRS scores peaking at 4–5 immediately after surgery and decreasing within 24 h.
204 However, a novel finding of this study was that the pain increased again on POD 2 and persisted through

POD 7, potentially reflecting PIT-specific necrotic processes and prolonged inflammatory responses. Matsumoto et al. analyzed postoperative pain after 48 PIT procedures in 25 patients and reported that pain may be less frequent in patients with a history of reconstructive surgery [7]. However, their sample size precluded multivariable analysis, repeated PIT procedures within patients were not statistically accounted for, and analgesic interventions were not evaluated. In the present study, we used linear mixed-effects models to account for repeated procedures and multivariable analysis to adjust for potential confounding factors. We also evaluated risk factors for postoperative pain and the associations between analgesic interventions and postoperative pain.

In this study, the number of illuminations, tumor volume, and tumor thickness were significantly associated with higher postoperative NRS scores in both univariable analyses and univariable linear mixed-effects models. IRDye700-bound tumor cells undergo rapid, irreversible morphological changes upon illumination, and the reactive oxygen species generated during illumination can induce edema and inflammation [9, 10]. In cases with larger tumor volumes and greater thickness, broader and more numerous illuminations are required, thereby amplifying necrosis, edema, and inflammatory signaling, which in turn may contribute to the increased postoperative pain. In multivariable linear regression analysis, only tumor thickness remained significantly associated with postoperative NRS scores, suggesting that tumor thickness may be an important contributor to postoperative pain. However, in multivariable linear mixed-effects models accounting for repeated procedures in the same patient, none of these variables showed a statistically

223 significant independent association with postoperative pain. This discrepancy may be attributable to limited
224 statistical power, as tumor volume and thickness could be assessed in only 25 procedures. Regarding the
225 illumination site, although the association was not statistically significant in the linear mixed-effects model,
226 univariable analysis suggested a tendency toward greater pain in lesions involving the anterior and posterior
227 walls of the oropharynx and the cervical skin. In such cases, particularly those with greater thickness,
228 reinforcement of postoperative analgesia should be considered. Although we anticipated that patients with
229 a history of reconstructive surgery would experience reduced postoperative pain owing to the absence of
230 sensation in the flap, no significant difference was observed in the analysis. This finding may be explained
231 by the fact that, even after flap reconstruction, recurrence did not occur within the flap, and the pain induced
232 by illumination was perceived in a manner comparable to that in patients without a history of reconstructive
233 surgery.
234 With respect to pain management, iv-PCA was associated with higher NRS scores beyond 72 h in
235 univariable analysis, although this association was not significant in the linear mixed-effects modeling.
236 This may reflect the perception of stronger pain after the discontinuation of iv-PCA. However, iv-PCA may
237 have been selectively introduced in patients at higher risk of pain, and the potential influence of selection
238 bias cannot be ruled out. In contrast, local infiltration with ropivacaine was associated with lower NRS
239 scores at 6–71 h postoperatively. Although the difference was not statistically significant, Figure 2 suggests
240 a trend toward lower postoperative NRS scores within 0–5 h in patients who received local infiltration with

ropivacaine. Ropivacaine infiltration has been widely used for postoperative analgesia in other surgical fields, including orthopedic and gastrointestinal surgery [11–13], and may be beneficial for postoperative pain control following PIT.

Although the elimination half-life of ropivacaine after local administration is approximately 4–6 h, two mechanisms may explain why the analgesic effect persisted for approximately 71 h in the present study. First, local infiltration anesthesia is thought to exert not only voltage-gated sodium channel blockade but also anti-inflammatory effects [14]. Second, suppression of sensitization may be involved. Sensitization, characterized by a lowered pain threshold and enhanced response to painful stimuli, contributes to postoperative pain and consists of both peripheral sensitization of nociceptors and central sensitization at the dorsal horn level. Previous studies have reported that local anesthetics can suppress both peripheral and central sensitization [15, 16]; therefore, these effects may have contributed to the prolonged analgesia observed after ropivacaine concentrations declined.

The reason for the apparent increase in pain beyond 72 h in the ropivacaine infiltration group remains unclear. However, one possible explanation is that, although the anti-inflammatory and anti-sensitization effects persist for several days, patients may perceive pain more strongly relative to the initially reduced pain levels once these effects subside. These findings suggest a potential role for local ropivacaine infiltration in early postoperative pain control; however, additional analgesic strategies are needed to address severe acute pain within the first 0–5 h and persistent pain after 72 h.

One potential strategy is additional or continuous administration of ropivacaine. In the orthopedic field, both additional local infiltration on POD 1 [11] and continuous infusion of ropivacaine to prolong analgesia [12] have been reported. Similarly, in the context of PIT, additional or continuous administration of ropivacaine may be considered, depending on the illumination site. The second strategy is to add corticosteroids, such as dexamethasone, to ropivacaine. These agents have been reported to exert anti-inflammatory effects and prolong the duration of local anesthesia [17]. Third, instead of local infiltration directly into the surgical wound, targeting proximal sensory nerves through regional nerve blocks may also be effective. Suprazygomatic maxillary nerve blocks have been reported to decrease postoperative opioid consumption and alleviate pain after pediatric adenotonsillectomy [18]. In the dental field, inferior alveolar nerve blocks have also demonstrated efficacy in pain control during tooth extraction [19], suggesting that combinations of nerve blocks tailored to the illumination site may represent another promising avenue for investigation. Finally, previous reports have demonstrated that perioperative intravenous corticosteroid administration reduces postoperative pain following pediatric tonsillectomy and transoral robotic surgery for oropharyngeal squamous cell carcinoma [20, 21], suggesting that intravenous corticosteroids may also be effective in managing PIT-related pain and should be evaluated in future studies.

The present study had some limitations. First, because this was a retrospective study, the influence of selection bias could not be excluded. Second, pain assessment relied solely on NRS scores, and uniform evaluation was not feasible because the types and dosages of analgesics (e.g., acetaminophen,

nonsteroidal anti-inflammatory drugs, and opioids) were not standardized. Third, local ropivacaine infiltration was evaluated in only five procedures, limiting the ability to draw definitive conclusions about its analgesic efficacy. Although local infiltration with ropivacaine was associated with a significant reduction in postoperative pain at 6–71 h, the NRS scores were 1–2 in the infiltration group and 2–3 in the non-infiltration group, both remaining below 3. Thus, whether this difference is clinically meaningful remains uncertain.

Future large-scale prospective studies are warranted to further elucidate the mechanisms underlying PIT-specific pain and establish optimal strategies for managing both acute and prolonged postoperative pain. In conclusion, larger tumor volume, greater tumor thickness, and a higher number of illuminations were associated with higher postoperative NRS scores in univariable analyses, although these associations were not independently significant in multivariable mixed-effects models. Local ropivacaine infiltration was associated with lower NRS scores at 6–71 h postoperatively; however, additional strategies are needed for the immediate (0–5 h) and late (>72 h) periods. Optimal multimodal analgesia, including the potential roles of perioperative corticosteroids and targeted nerve blocks, should be investigated in prospective studies.

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Not applicable

Ethics declarations

Conflict of interest

Takeshi Shinozaki has received lecturer fees from Rakuten Medical Japan. The remaining co-authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

Ethical Approval

This retrospective study was conducted in compliance with the ethical standards of the institutional and national research committees and the 1964 Helsinki Declaration and its subsequent amendments or comparable ethical guidelines. This study was approved by the Institutional Review Board of the National Cancer Center Hospital East (approval number: 2022-071). Informed consent was obtained from all individual participants included in this study. Consent for publication was also obtained from each participant.

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Author information

Author and Affiliations

Department of Head and Neck Surgery, National Cancer Center Hospital East, Kashiwa, Japan

Kai Kanemoto, Takeshi Shinozaki, Takashi Kitani, Wataru Okano, Toshifumi Tomioka, Kazuto Matsuura

Department of Anesthesiology, National Cancer Center Hospital East, Kashiwa, Japan

Manabu Hashimoto

Department of Diagnostic Radiology, National Cancer Center Hospital East, Kashiwa, Japan

Hirofumi Kuno

Biostatistics Division, Center for Research Administration and Support, National Cancer Center Hospital East, Kashiwa, Japan

Masashi Wakabayashi

Contributions

Kai Kanemoto and Takeshi Shinozaki and Manabu Hashimoto designed the study and drafted the article. Hirofumi Kuno contributed to radiologic data acquisition and critically revised the manuscript for intellectual content. Masashi Wakabayashi provided advice on statistical analysis and critically revised the manuscript for intellectual content. Wataru Okano and Toshifumi Tomioka and Kazuto Matsuura critically revised the manuscript for intellectual content. All authors read and approved the final version of the manuscript prior to submission.

Corresponding author

Correspondence to Takeshi Shinozaki

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406 **Figure captions**

407 **Fig. 1** Mean Numerical Rating Scale (NRS) score after photoimmunotherapy

408 Note: The NRS score increased to 4–5 immediately after surgery, began to decline after 3 h, and improved

409 to approximately 1 by 24 h postoperatively. Thereafter, the NRS score increased again on postoperative day

410 (POD) 2, and pain of approximately NRS 2–3 persisted until POD 7

411

412 **Fig. 2** Mean Numerical Rating Scale after photoimmunotherapy in patients with or without local

413 ropivacaine infiltration

414 Note: Pain intensity within the first 71 h after surgery tended to be more severe in the group that did not

415 receive ropivacaine, whereas after 72 h, pain was more severe in the group that received ropivacaine

416

417 **Supplementary Fig. S1** Numerical Rating Scale across tumor illumination sites

418 Note: Pain tended to be most severe in the anterior/posterior oropharyngeal walls and the cervical skin,

419 whereas the oral cavity and nasopharynx showed relatively lower scores

420

421 **Supplementary Fig. S2** Spearman's rank correlation coefficients for the number of illuminations, tumor

422 volume, and tumor thickness

423 Note: Spearman's rank correlation analysis showed that the number of illuminations, tumor volume, and

424 tumor thickness were significantly and positively correlated with the postoperative Numerical Rating Scale
425 scores

426 Table 1 Patient, surgical, and anesthetic characteristics (48 PIT procedures in 19 patients)

427

	Number of patients or procedures (%) / Median [range]
Age at first surgery (y)	65 [47-83]
Sex	
Male	11 (58%)
Female	8 (42%)
Prior treatment with radiotherapy	
Yes	19 (100%)
No	0 (0%)
Prior treatment with reconstructive surgery	
Yes	9 (47%)
No	10 (53%)

Illumination site	
Oral cavity	3 (5.3%)
Nasal cavity and paranasal sinus	2 (4.2%)
Nasopharynx	16 (33.3%)
Oropharynx	
anterior wall	5 (10.4%)
lateral wall	4 (8.3%)
posterior wall	10 (20.8%)
Larynx	1 (2.1%)
Cervical skin	7 (14.6%)
Number of illumination sites	1 [1-4]
Number of illuminations	3 [1-10]
(frontal + cylindrical)	
Tumor volume (cm^3)	0.93
	[0.049-17.33]
Tumor thickness (cm)	1.0 [0.1-4.8]
Type of maintenance anesthetic	

Sevoflurane	15 (31.3%)
Desflurane	31 (64.6%)
TIVA	2 (4.1%)
Intraoperative fentanyl dosage (mg)	200 [100-500]
Intraoperative remifentanil dosage (mg)	0.76 [0.17-2.20]
Iv-PCA	
Yes	41 (85%)
No	7 (15%)
Local infiltration with ropivacaine	
Yes	5 (10%)
No	43 (90%)

Abbreviations: PIT, photoimmunotherapy; TIVA, total intravenous anesthesia; iv-PCA, intravenous patient-controlled analgesia

Table 2 Factors associated with postoperative pain on univariate analysis (Kruskal-Wallis test)

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	median NRS	*p* value	Pairwise comparison (Steel-Dwass)
Illumination site		0.081*	
Oral cavity	4.0		
Nasal cavity and paranasal sinus	6.5		
Nasopharynx	3.5		vs. Oropharynx posterior wall: p = 0.061
Oropharynx	7.0		
anterior wall	5.0		
lateral wall	7.0		
posterior wall	6.0		vs. Nasopharynx: p = 0.061
Larynx	9.0		
Cervical skin			
Type of maintenance anesthetic		0.25	
Sevoflurane	6.0		
Desflurane	5.0		

TIVA	9.0

Abbreviations: NRS, Numerical Rating Scale; TIVA, total intravenous anesthesia

Table 3 Spearman's rank correlation coefficient of risk factors for postoperative pain

	ρ	*p* value
Age at surgery	-0.17	0.23
Number of illumination sites	-0.017	0.91
Number of illuminations (frontal + cylindrical)	0.38	0.008*
Tumor volume	0.39	0.050*
Tumor thickness	0.60	0.001*

Table 4 Linear mixed-effects modeling of risk factors for postoperative pain (univariable analysis)

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	Estimate	*p* value
Number of illuminations (frontal + cylindrical)	0.39	0.047*
Tumor volume	0.24	0.063*
Tumor thickness	0.66	0.096*
Illumination site		
Oral cavity	1.95	0.39
Nasal cavity and paranasal sinus	1.90	0.58
Nasopharynx	Ref	Ref
Oropharynx		
anterior wall	0.90	0.70
lateral wall	-0.10	0.98
posterior wall	2.74	0.30
Larynx	1.40	0.70
Cervical skin	2.56	0.23

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Table 5 Multivariable linear regression analysis of risk factors for postoperative pain

	Estimate	95% CI	*p* value
Number of illuminations (frontal + cylindrical)	0.27	-0.24 to 0.78	0.28
Tumor volume	0.12	-0.16 to 0.39	0.38
Tumor thickness	0.88	0.06 to 1.70	0.037*

Table 6 Linear mixed-effects modeling of risk factors for postoperative pain (multivariable analysis)

	Estimate	*p* value
Number of illuminations (frontal + cylindrical)	0.27	0.23
Tumor volume	0.13	0.34

Tumor thickness	0.51	0.22

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455 Table 7 Analgesic strategies associated with postoperative pain on linear mixed-effects modeling

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	Estimate	p value
iv-PCA		
Overall (0-7 days)	-0.76	0.57
0-5 h post-op	-0.79	0.62
6-71h post-op	+0.76	0.47
≧72h post-op	+1.28	0.20
Local infiltration with ropivacaine		
Overall (0-7 days)	-0.11	0.92
0-5 h post-op	-1.14	0.43
6-71h post-op	-2.06	0.026*
≧72h post-op	+1.67	0.056*

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458 Abbreviations: iv-PCA, intravenous patient-controlled analgesia

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Fig. 1 Mean Numerical Rating Scale (NRS) after Photoimmunotherapy (PIT)

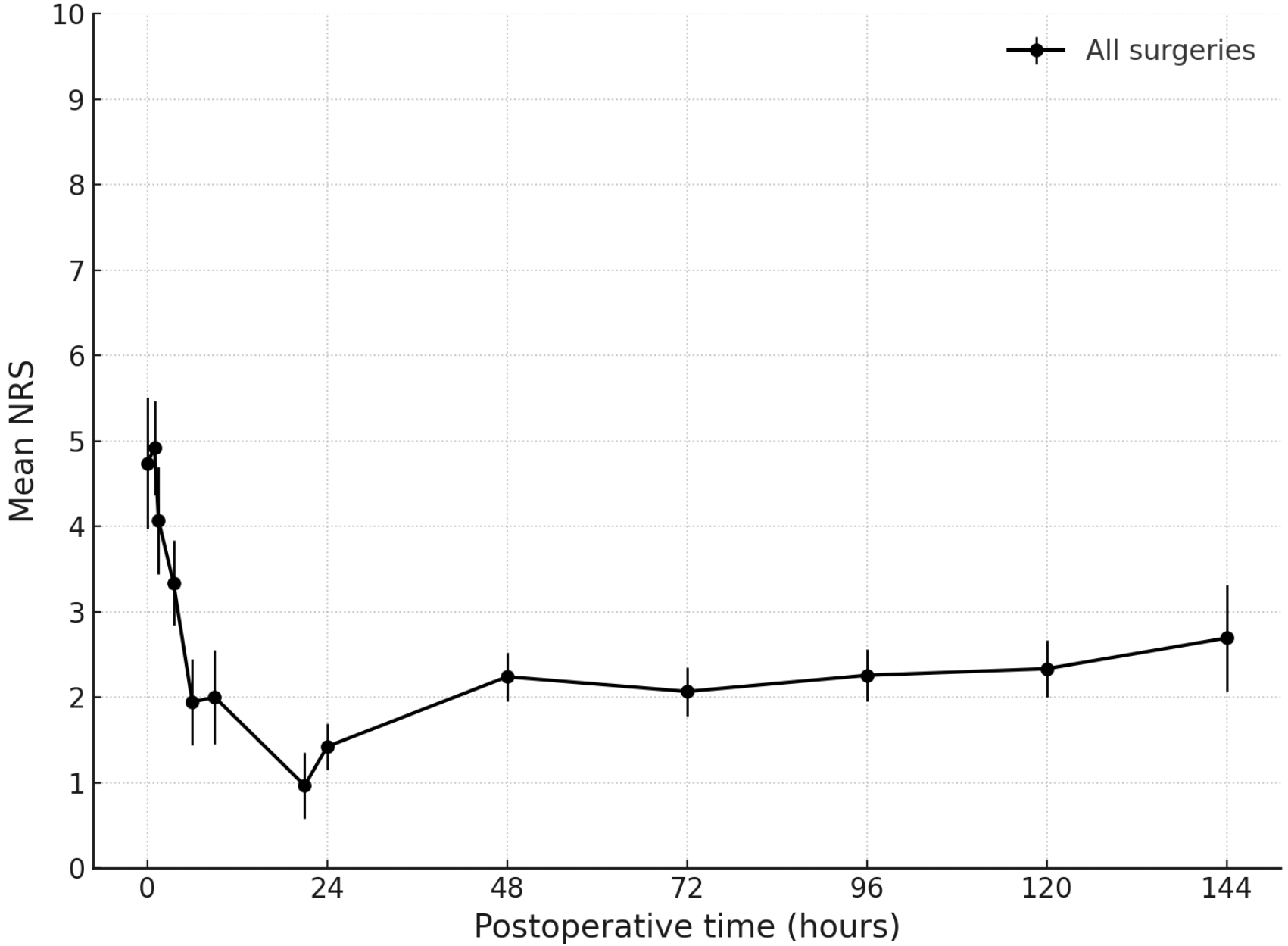

Fig. 2 Mean Numerical Rating Scale (NRS) after Photoimmunotherapy (PIT) in patients with or without local ropivacaine infiltration

