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ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Histopathology of thermal effects in endoscopic ear surgery: An experimental animal study

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Abstract

Objective: The potential risk of thermal damage in the transcanal endoscopic ear surgery has been a concerning issue. This study aimed to investigate the histopathological effects of heat exposure of different durations in external auditory canal (EAC) skin and facial nerve tissues.

Methods: This study was conducted on 20 rabbits assigned equally to five groups according to the endoscope-transmitted heat exposure duration: Control group (no exposure), 2, 10, 15, and 30 min. At the end of the procedure, EAC skin and the tympanic segment of facial nerve tissue samples were taken surgically and histopathologically examined.

Results: Significant histopathological thermal damage findings in external auditory canal skin and facial nerve tissues were observed under endoscope-transmitted heat exposure longer than 15 and 10 min, respectively.

Conclusion: This study demonstrated that prolonged exposure of the endoscope-transmitted heat can cause histopathological thermal damage in EAC skin and facial nerve on rabbit subjects.

KEYWORDS
ear surgery, endoscope, thermal damage

1 | INTRODUCTION

The use of endoscopes in middle ear surgery has become increasingly popular in the last two decades. Endoscopic transcanal approach to the middle ear is also performed in mastoidectomy, stapes surgery, glomus tumor surgery, and tympanoplasty.[1] Numerous comprehensive studies have affirmed the advantages of transcanal endoscopic approach to the middle ear.[2–4] In addition to the advantage of an incisionless procedure, a transcanal endoscopic approach to the middle ear cavity, either with straight or angled telescopes, offers a magnified and detailed view of the facial recess, hypotympanum, and sinus tympani, which are difficult to visualize with an operating microscope.[5] On the other hand, the disadvantages of endoscope use in otologic surgery include the need for one-handed surgery and the risk of thermal damage to the surrounding tissues.[6]

Given the increasing trend toward endoscope use in middle ear surgery, it is important to investigate the potential thermal damage to surrounding tissues caused by the endoscope light. In recent decades, several animal and ex-vivo studies have investigated the temperature changes caused by thermal radiation from the tip of 0-degree endoscopes.[7–9] Previous studies have primarily focused on measuring the temperature of the endoscope tip and within different middle ear

cavity structures, such as the round window, using various endoscope diameters and light sources. However, these studies have not provided histopathological information on the thermal effects of endoscope heat. In an experimental animal study with guinea pigs, a significant temperature rise was reported in the middle ear cavity, especially when xenon and halogen light sources were used, regardless of endoscope diameter.[9] Based on the knowledge provided by previous studies, we hypothesized that histopathological examinations could reveal reversible or irreversible thermal damage to the external auditory canal (EAC) skin or neural tissues, depending on the duration of exposure.

In this experimental animal study, we aimed to analyze histopathological alterations in the EAC skin and facial nerve samples due to thermal exposure caused by endoscope light at different exposure durations.

2 | MATERIALS AND METHODS

This study was conducted with the approval of the Institutional Animal Experiments Ethics Committee (Approval number: 2017-056) between September 2020 and June 2021 in concordance with international ethical standards and the World Health Organisation Helsinki Declaration.

2.1 | Experimental animals and study design

A total of 20 healthy New Zealand rabbits, at least 2 years of age and 3–4 kg of weight, were used in this study. Animals were randomly divided into five groups, each containing four rabbits (eight ears), according to the endoscope heat exposure time:

Group 1: control group, no exposure (*n*:8).

Group 2: 2 min (*n*:8).

Group 3: 10 min (*n*:8).

Group 4: 15 min (*n*:8).

Group 5: 30 min (*n*:8).

Following the surgical procedures and harvesting samples, the EAC skin and facial nerve tissues underwent detailed histopathological examination.

2.2 | Procedure

The animals were anesthetized with ketamine (80 mg/kg, intraperitoneal) and xylazine (10 mg/kg, intraperitoneal). The anesthetized animals were placed in a lateral decubitus position. Xenon light source operating at 100% power (Karl Storz® Xenon Nova 300®, Tuttlingen, Germany), and a 4-mm 0-degree rigid endoscope (Karl Storz® Endoscopes, Tuttlingen, Germany) were used during the procedures. Initially, the tympanic membrane was removed by using pick in order to simulate tympanomeatal flap elevation and to achieve heat exposure to the middle ear cavity with a transcanal approach. In each animal, the tip of the endoscope was placed on the level of isthmus of the EAC, approximately 3–4 mm lateral to annulus. An endoscope holder was utilized to make the scope stable during the procedure in the study groups (groups 2–5) except the control group. Following the planned exposure time, EAC skin samples, nearby endoscope tip, were taken by using a rosen circular knife from the posterior wall of the EAC. Then, the scutum and posterosuperior bony EAC were removed with a micro bone-curette, afterward the ossicular chain was removed by using a pick and forceps to gain access to the facial nerve course above the oval window. The bony wall over the nerve tract was not removed before the exposure, therefore it was removed to sample the neural tissue. Tympanic segment of the facial nerve samples were taken with a transcanal endoscopic approach by using pick, micro-curette, microscissors, and forceps. In total, eight EAC skin and eight facial nerve samples were taken for histopathological examination in each group. Finally, the animals were sacrificed with a high dose of ketamine and xylazine combination because of possible postoperative psychological adverse effects due to bilateral facial paralysis.

2.3 | Histological evaluation

All samples were evaluated blindly by two histologists. EAC samples were examined for inflammatory and ischemic changes, and facial nerve samples were examined for edema, sheath thickening, myelin degeneration, and S100 immunopositivity, without knowing which group the samples belonged to. The histopathological evaluations of both the EAC skin and the facial nerve samples were made by examining five serial sections taken from the middle part of the specimen, away from the ends that were thought to be damaged during collecting specimens.

External auditory canal skin tissue preparation: EAC skin biopsies for histological examination were fixed in 10% buffered formalin, processed routinely, embedded in paraffin, and sectioned at 5 μm. Five serial sections from each sample per group ($n = 40$/group) were stained with hematoxylin–eosin and Mallory's Azan. Light microscopic evaluation (Olympus BX51 microscope, Olympus DP71 camera) was performed to assess histopathological changes in the EAC. Scoring followed a pre-defined criteria table (Table 1) at 40× magnification in five areas per specimen. Scores for pyknotic cells, degeneration (including loss of keratinized layer, vacuolization, loose connective tissue, and sebaceous gland damage), and inflammation ranged from 0 to 3 (details in Table 1). The mean score from the five areas was used for statistical analysis.

Facial nerve tissue preparation: Samples were fixed in 2.5% glutaraldehyde followed by 1–2 h in OsO4. After a 15-min buffer wash (Millonig's), samples were dehydrated through a graded alcohol series, infiltrated with a 1:1 ethanol-propylene oxide solution for 30 min, and transitioned to pure propylene oxide. Following incubation in propylene oxide-epon mixtures (2:1 and 1:2 ratios), samples were embedded in pure epon containing DMT 30 and polymerized at 37, 45, and 60°C for 24 h each. Semi-thin sections were obtained using an ultramicrotome and stained with Toluidine Blue. For immunohistochemistry, sections were deparaffinized and subjected to antigen retrieval (citrate buffer, pH 6.0) and blocking with normal horse serum. After

TABLE 1 Scoring of histopathological changes in the external auditory canal.

Feature	0	1	2	3
Presence of pyknotic cells	No pyknotic cells	Few pyknotic cells (1–5)	Moderate number of pyknotic cells (5–10)	High number of pyknotic cells (>10)
Degeneration	No degeneration	Mild degeneration	Moderate degeneration	Severe degeneration
Presence of inflammation	No inflammation	Mild inflammation	Moderate inflammation	Severe inflammation

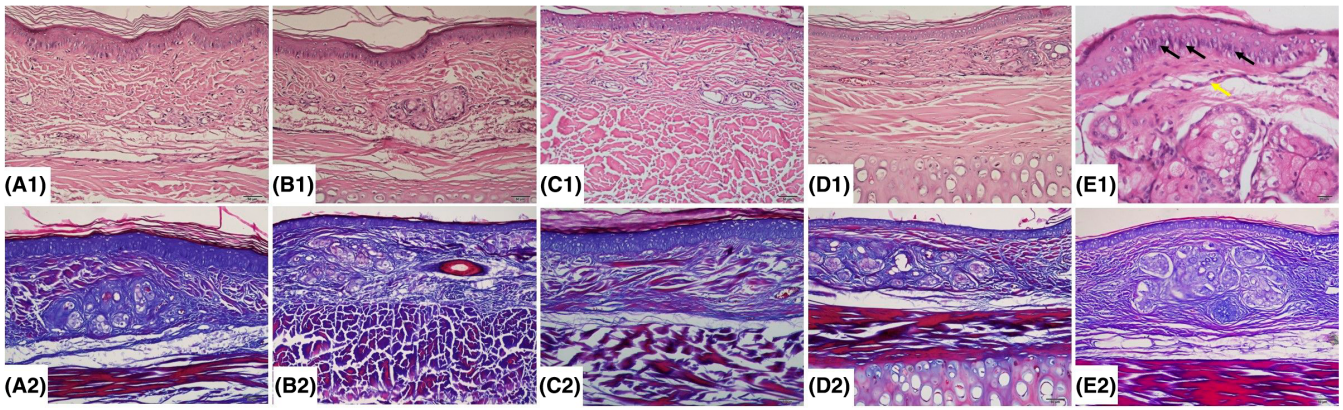

FIGURE 1 Histological appearance of the external auditory canal specimens. (A) Control (0 min) group. (B) 2 min exposure group. (C) 10 min exposure group. (D) 15 min exposure group. (E) 30 min exposure group. Hematoxylin&Eosin Staining (A1–E1). Mallory Azan Painting (A2–E2).

overnight incubation with the primary antibody (Anti-S100, 1:100 dilution), sections were washed and incubated with a secondary antibody followed by DAB chromogenic substrate. Finally, sections were mounted and photographed.

2.4 | Statistical analysis

For statistical analysis, the Statistical Package for Social Sciences (SPSS) was used (version 22.0; SPSS Inc., Chicago, IL, USA). Levene test was used to evaluate whether the data had homogeneous variance, and Kolmogorov–Smirnov test was used to analyze whether the variables with homogeneous variance showed normal distribution. Anti-S100 positive cells were counted in 10 different fields in 8 preparations for each group. For facial nerve histopathological findings, a post hoc analysis was performed using the Mann Whitney *U* test to compare two separate groups. Dunn's post hoc analysis using the Kruskal-Wallis test was used for the pairwise comparisons of EAC skin tissue histopathological scores. $p < .05$ was considered statistically significant. For post hoc analysis, $p < .005$ was considered to be statistically significant due to Bonferroni correction.

3 | RESULTS

3.1 | External auditory canal histopathological findings

Evaluation of EAC skin samples revealed that normal histological appearances were dominant in groups 1–3 (Figure 1A1-2,B1-2,C1-2).

TABLE 2 The pairwise comparisons of external auditory canal skin histopathological scores for each group.

Pairwise comparisons	*p*-Value (adjusted significance)
Control versus 2 min.	1
Control versus 10 min.	1
Control versus 15 min.	**.004**
Control versus 30 min.	**.001**
2 min. versus 10 min.	1
2 min. versus 15 min.	**.004**
2 min. versus 30 min.	**.001**
10 min. versus 15 min.	**.005**
10 min. versus 30 min.	**.002**
15 min. versus 30 min.	.077

Note: $p < .005$ was considered to be statistically significant due to Bonferroni correction. Bold values indicate statistical significance.
Abbreviation: min, minute.

Group 4 exhibited stratum corneum loss in the epidermis and a moderate number of pyknotic nuclei within the granulosum and spinosum layers. Notably, the lamina propria and submucosa remained unaffected, with no histopathological changes observed (Figure 1D1-2).

Light exposure time correlated with an increase in acute inflammatory reactions and ischemic changes. Notably, group 5 displayed degeneration of the stratum corneum's keratinized layer and pyknotic nuclei in the granulosum and spinosum layers. The lamina propria exhibited collagen discoloration. Heat exposure also affected the submucosal layer, with ceruminous gland cells showing disruption (vacuolization) and altered dye uptake patterns, likely due to changes in

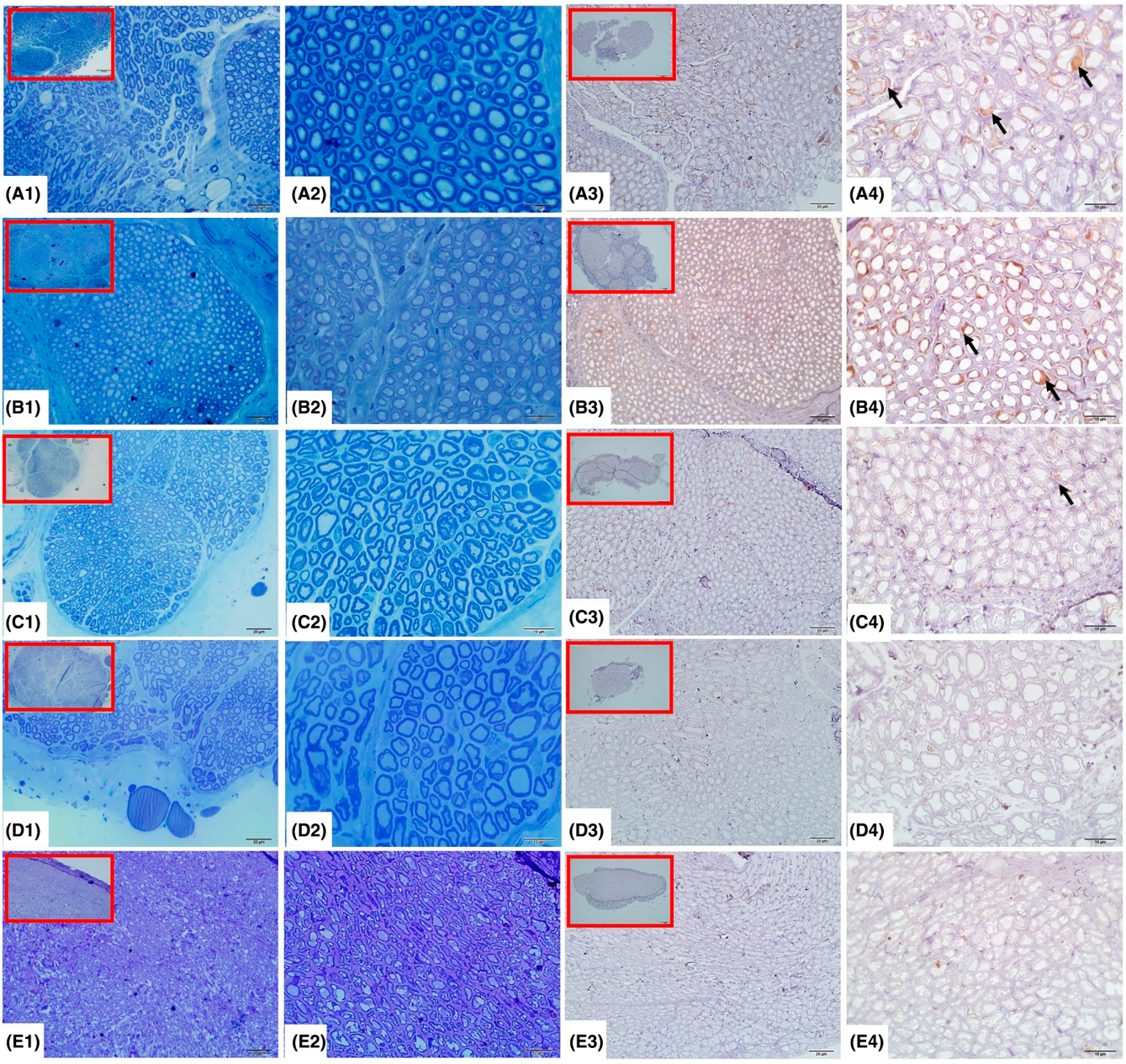

FIGURE 2 Histological view of semi-thin sections of facial nerve specimens. (A) Control (0 min) group. (B) 2 min exposure group. (C) 10 min exposure group. (D) 15 min exposure group. (E) 30 min exposure group. Toluidine Blue (A1-2, B1-2, C1-2, D1-2, E1-2) and Anti-S100 (A3-4, B3-4, C3-4, D3-4, E3-4) immunohistochemical staining.

secretory content. Additionally, the loose connective tissue surrounding these glands displayed degenerative changes (Figure 1E1-2). Table 2 shows the pairwise comparisons of external auditory canal skin histopathological scores for each group.

3.2 | Facial nerve histopathological findings

The control group displayed normal histological features. The epineurium, perineurium surrounding nerve fascicles, and endoneurial sheaths around individual axons all exhibited normal architecture. Myelinated axons (large, medium, small) and unmyelinated axons were unremarkable, with Schwann cells appearing normal as well. Notably, sections passing through Schwann cell nuclei revealed generally smooth profiles of small diameter myelinated axons. Additionally, blood vessels within the section plane appeared normal. Anti-S100 staining demonstrated strong immunoreactivity in Schwann cell processes and large-diameter axons within paranodal regions (Figure 2A1–4).

Group 2 resembled group 1 histologically, but with minimal edema evident in medium and small diameter axons. The perineurium surrounding nerve fascicles displayed mild thickening. Anti-S100 staining revealed significant immunoreactivity in Schwann cell

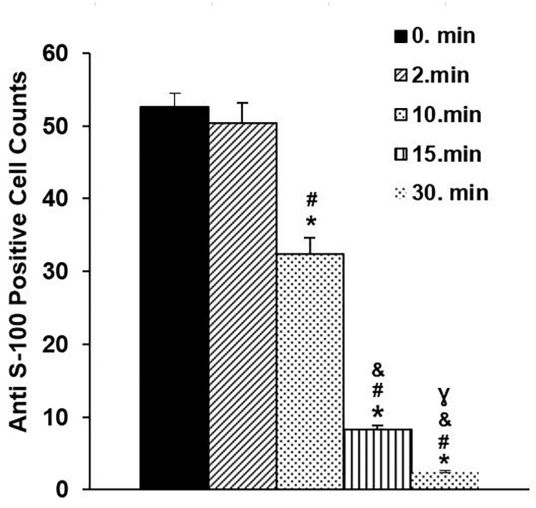

FIGURE 3 Statistical analysis of the number of anti-S100 positive cells. *Significant compared to the group 1. #Significant compared to the group 2. &Significant compared to the group 3. YSignificant compared to the group 4.

processes (Smith-Lanterman clefts) and medium/small diameter axons within paranodal regions (Figure 2B1–4).

Group 3 exhibited moderate thickening in the epineurium and perineurium, the connective tissue sheaths surrounding nerve fascicles. Large-diameter myelinated axons displayed significant edema, accompanied by mild degeneration and vacuolation of myelin rings. Anti-S100 staining revealed low immunoreactivity in the Schwann cell processes (Smith-Lanterman clefts) of these large axons (Figure 2C1–4).

Group 4 showed worsened epineurium and perineurium thickening. Edema involved endoneurial tissue and large/medium axons, with severe damage including myelin degeneration, vacuolation, and axonal discharge. Lamellar detachment and disintegration disrupted myelin sheaths. Most myelinated fibers displayed degeneration. Anti-S100 staining showed no immunoreactivity (Figure 2D1–4).

Group 5 resembled group 4 histologically, but with less prominent corrugated lamellar myelin detachments, possibly due to myelin sheath thinning, increased axonal edema, and occasional axonal loss. Significant edema affected most medium and small diameter axons. Edema extended to the epineurium and perineurium, with thickening of these connective tissue sheaths. As in group 4, anti-S100 staining showed no immunoreactivity (Figure 2E1–4).

Statistical analysis of the cell count performed to show the variation of anti-S100 (+) cell count according to the groups is shown in Figure 3. Especially in groups 4 and 5, the decrease in the number of immunopositive cells was evident and statistically significant ($p < .001$).

4 | DISCUSSION

Our study investigated the impact of endoscope-induced heat exposure on surrounding tissues during otological surgery. Endoscopes offer superior illumination and visualization within the operative field, but concerns regarding thermal injury remain. Here, we demonstrate that endoscope heat exposure for 15 min or longer causes significant thermal injury to the EAC skin near the endoscope tip compared to control tissue. Notably, facial nerve tissue also exhibits thermal damage after just 10 min of exposure. The severity of both skin and neural tissue damage progressively worsens with longer exposure times, potentially reaching irreversible levels at 30 min.

Endoscope diameter and light source selection are critical factors influencing thermal output. Larger diameter endoscopes (e.g., 4 mm) transmit more light and consequently, heat, to the surgical field compared to smaller ones (e.g., 2.7 mm).[7] Similarly, xenon light sources generate significantly more heat than light-emitting diode (LED) or halogen sources.[10,11] A study employing a 0-degree, 4-mm rigid endoscope with a xenon light source reported maximal tip temperatures ranging from 32.3 to 104.6°C.[10,12,13] Conversely, LED and halogen sources result in considerably lower peak temperatures, reaching up to 44.6 and 38°C, respectively.[14] These temperature elevations raise concerns for potential thermal injury to external, middle, and inner ear structures. Supporting this notion, Botrill et al. demonstrated a significant temperature rise in the lateral semicircular canal following endoscope heat exposure, exceeding that achieved with a standard 44°C water caloric test and even inducing a caloric effect.[7]

Despite concerns about the potential functional consequences of elevated temperatures in endoscopic ear surgery, no complications related to endoscope-induced heat exposure have been reported in the literature. Nevertheless, it is important to determine the temperature and duration of heat exposure that can cause thermal injury. In an experimental study on rabbits, Lin et al. reported that thermal damage to the skin tissue begins at 45°C, and collagen fiber structures denature as the temperature increases.[15] They also reported that severe thermal injury of the skin and severe deterioration of the collagen fibers alignment occur above 60°C. It is also known that temperatures above 50°C can cause tissue damage,[16] and such temperatures can be reached during endoscopic ear surgery with the use of a xenon light source. James et al. reported that a temperature rise of 9°C above normal body temperature resulted in facial nerve damage during an ultrasonic labyrinth irradiation procedure for Meniere's disease.[17]

The literature on the exposure time required to cause thermal damage is limited. Thermal injury is considered a progressive phenomenon, with its evolution unfolding over 24–48 h following initial heat exposure. However, some prior studies have demonstrated histopathological and inflammatory response evidence of thermal damage in various tissues, including skin and neural tissue, following immediate post-exposure sampling or sampling within few hours.[18–21] This suggests the possibility of significant acute injury upon endoscope-transmitted heat exposure. Aksoy et al. reported that vestibular function decreased in guinea pigs following intermittent 5-min periods of endoscope illumination with 15-s breaks over a total duration of 45 min in the middle ear cavity.[10] The time reported for endoscopes to reach maximum tip temperature varied in previous studies. A 0-degree 4-mm endoscope connected to a xenon light source set at

100% power has been reported to reach maximum tip temperature in 10–30 min following a significant rise within 60 s in room air.[12,22] Our study revealed that endoscope heat exposure for up to 10 min did not induce thermal damage to the EAC skin. However, 15 min or more of endoscope heat exposure caused histopathologically significant thermal damage to the canal skin. Additionally, the tympanic segment of the facial nerve susceptibility to heat exposure displayed a temporal pattern, with earlier (10 min) injury primarily affecting epineurium and perineurium, while prolonged exposure (≥15 min) triggered significant endoneurial damage. Moreover, no anti-S100 immunoreactivity was observed in the 15- and 30-min exposure groups. Since S100 is a Schwann cell marker and is frequently used in studies related to nerve damage, the decrease in S100 immunoreactivity was considered to be associated with Schwann cell damage.[23,24] Using anti-S100 immunoreaction analysis, this study demonstrated that prolonged exposure to endoscope-transmitted heat can damage neural tissues under direct irradiation.

Our findings of significant thermal damage in skin and nerve tissues are consistent with previous reports of thermal injury from various heat sources. Güzey et al. demonstrated full-thickness skin burns in rats exposed to an infrared heater for 10 min at 50 cm distance. Histopathological examination revealed denatured collagen bands and injury to skin appendages, including disruption in ceruminous gland cells.[25] Similarly, Nassar et al. observed extensive necrosis, degeneration, and inflammatory cell infiltrate in rat skin 24 h after thermal injury.[26] Notably, the literature on thermal injury in neural tissue due to light-transmitted heat exposure is scarce. Carlander et al. investigated morphological evidence of thermal injury in neural tissues following close electrocautery dissection in rats. Their study reported myelin degeneration, vacuolation, and coagulated fibers with myelin sheaths when using monopolar or bipolar cautery near the nerve.[20] However, their investigation did not utilize anti-S100 staining, which we employed to assess Schwann cell integrity in our study.

In this study, we did not measure the real-time temperature, but the maximum temperature in the middle ear cavity may have reached critical levels based on the data from previous studies.[8,13] Pan et al. observed that the temperature around the round window increased to 59.3°C with a 0-degree endoscope under 100% xenon power.[27] However, it is important to note that the dimensions of a rabbit ear are smaller than a human ear, therefore, the risk of such complications due to heat exposure may be lower in transcanal endoscopic ear surgery performed on human cases.

Ozturan et al. used an endoscope holder during transcanal ear surgery on human subjects and recorded a temperature of 48.4°C 5 mm beyond the tip of the endoscope with the use of a xenon light source and a 0-degree 4-mm endoscope.[28] They reported that utilization of the endoscope holder is safe with intermittent suction or irrigation. Nevertheless, we emphasize that utmost caution should be taken when using an endoscope holder in transcanal ear surgery.

Since our aim was to investigate the duration of continuous endoscope-transmitted heat exposure required to cause thermal damage, no cooling methods, such as suction or endoscope removal, were applied in this study. Previous studies have reported that cooling mechanisms such as saline irrigation, suction, or regular breaks are effective in preventing high temperature levels in the operative cavity. Kozin et al. demonstrated a 10°C decrease in temperature within 20 s using suction placed at the endoscope tip.[6] They also observed a rapid decrease in temperature following endoscope removal. In addition to these methods, in vivo studies have suggested that blood circulation can prevent the temperature from increasing to much higher levels.[7,14] However, in this study, although we studied live rabbit subjects and thus the maximal temperature may have been limited, we observed thermal damage in both skin and neural tissues following a long period (especially for at least 15 min of exposure) of high heat exposure.

This study has several limitations. First, simultaneous temperature measurement in the EAC and the middle ear cavity was not performed during the procedures. Therefore, a causal link between the histopathological findings of thermal injury and the temperature level could not be established. Second, only xenon light sources were used. This study could have had more comprehensive results by using different light sources such as LED or halogen. Another limitation of this study is the absence of real-time electrophysiological assessment of facial nerve function. Electrophysiological evaluations could have determined the clinical relevance of thermal damage. Real-time measurements would capture immediate functional effects, while long-term follow-up could reveal potential delayed degeneration.

5 | CONCLUSION

In this experimental animal study, we histopathologically demonstrated that endoscope-induced heat exposure can cause thermal damage to the nearby EAC skin and facial nerve tissues when a 0-degree 4-mm endoscope with a xenon light source set at 100% power is used uninterruptedly without using any cooling method. These histopathological thermal damage findings were observed in the EAC skin beginning at the 15th min and in the tympanic segment of the facial nerve from the 10th min of endoscope-transmitted heat exposure. Therefore, we suggest that sustained presence of a 4-mm endoscope connected to a xenon light source should be avoided to prevent thermal injury during transcanal endoscopic ear surgery.

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CONFLICT OF INTEREST STATEMENT

The authors declare no competing interest.

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