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Preclinical Assessment of Tissue Effects by Gastrointestinal Endoscope Tip Temperature

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ABSTRACT

Background: Endoscope tips are heated by their electrical and illuminating components. During the procedure, they might get in close or even direct contact with intestinal tissues.
Objective: To assess endoscope tip and tissue temperature as well as histopathologic changes of gastrointestinal (GI) tissues when exposed to the heated tip of GI endoscopes.
Methods: The endoscope tip temperatures of four GI endoscopes were measured for 30 minutes in a temperature-controlled chamber. The temperature of ex vivo porcine GI tissues was measured for 5-, 15-, and 120-minute exposure to endoscope tips within a climate chamber to control environmental factors (simulation of fever as worst-case). Exposed tissues were histopathologically examined afterward. Control samples included untreated mucosa, tissue samples exposed to endoscope tips for 120 minutes, as well as tissue samples thermally coagulated with a bipolar high-frequency probe.
Results: Actual endoscope tip temperatures of 59 to 86°C, dependent on the endoscope type, were measured. After 10 to 15 minutes, the maximum temperatures were reached. Maximum tissue temperatures of 44 to 46°C for 5 and 15 minutes, as well as up to 50°C for 120 minutes, were recorded dependent on tissue and endoscope type. No direct heat-induced histopathologic tissue alterations were observed in the 5- and 15-minute samples.
Conclusions: Both clinically relevant and a worst-case control were tested. Even though elevated temperatures were recorded, no heat-related tissue alterations were detected. This overall supports the safety profile of GI endoscopy; however, the study findings are limited by the ex vivo setting (no metabolic tissue alterations accessible, no blood flow) and small sample number.

Introduction

Direct visualization and access of tools by minimally invasive techniques has boosted medical care during the past century. Starting with rigid fiberoptic endoscopes, the state-of-the-art is now flexible video endoscopes. The two fundamental functions are persistently providing an image (implemented by video camera) and sufficient illumination (implemented by so-called cold light sources such as xenon gas or light-emitting diode [LED]). Inherent to electric components is heat generation due to energy loss. Also, light emission results in heat.

The video function is implemented by chip-on-tip technology without major developments in the past years. On the other hand, to overcome the disadvantages of traditional illumination by a cold-light source at the processing unit and light-guiding cables along the endoscope (including low durability, high cost, and noisy fan cooling[1] due to extreme heat generation by the light to up to 750°C[2]), illumination can be achieved by LEDs at the tip. The newest technology, these LEDs create only a little heat contrary to past lightbulb[1] and standard xenon gas light sources[3] while providing sufficient illumination.[3]

For clinical areas such as otorhinolaryngology, endoscope tip temperatures and associated tissue effects have been studied, and a dependency on light source; endoscope dimensions; angulation; and most importantly, distance, was documented.[3–5] Reported temperatures range between 44°C to around 100°C. It has been long established that relatively low temperatures can lead to

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irreversible tissue damage given extended exposure times[6]; for example, complete epidermal necrosis after 3 hours at 45°C on human epidermis or 6 minutes at 50°C on porcine skin. Extent and timing of heat damage has been widely studied for tumor tissue with respect to thermal ablation treatment.[7,8] The commonly accepted threshold for irreversible and immediate cell damage is 60°C; that is, coagulation necrosis, whereas the extent of tissue damage at lower temperatures is a function of exposure time.[8]

Data on both gastrointestinal (GI) flexible endoscopes as well as GI mucosa damage with regard to temperatures are scarce. As outlined above, increased temperatures and/or tissue damage occur with minimal distance and prolonged exposure times. Thus, the clinical relevance for GI flexible endoscopy appears small because endoscopes are normally not in contact with the tissue surface and rarely hold still. Nevertheless, in some clinical procedures such as duodenoscopy, but also as use error, an endoscope tip can get in proximity or even make contact with GI mucosa for a certain duration. In conjunction with the relatively new illumination offered by LEDs, we report on the first assessment of heat damage to GI mucosa surfaces by flexible GI endoscope tips. An ex vivo porcine setting was chosen to create a controlled, easy-to-access setup in combination with simulation of worst-case conditions: feverish tissue baseline temperature, no blood flow, prolonged exposure times, direct contact, and simultaneous temperature measurement. As a first step in assessment, these advantages outweigh the shortcomings of an ex vivo setting such as the inability to access metabolic changes.

Materials and Methods

Endoscope tip temperatures

The surface temperature of the endoscope tips due to heat dissipation of the electronic components was measured on air to determine the heating curve of the distal tip. The measurements were done at 40 °C in a climate chamber. For the gastroscope (Ambu® aScope™ Gastro; Ambu A/S, Ballerup, Denmark) and colonoscope (prototype; Ambu, A/S), 3 temperature sensors were attached: 1 at one of the LEDs (ie, the hottest point), 1 at the border of the tip in between the two LEDs the second one (ie, the hottest point but without exposure to light), 1 opposite the second one (ie, heat dissipation across the tip). Two duodenoscopes were measured (a standard duodenoscope [prototype] and a modified duodenoscope based on Ambu® aScope™ Duodeno [Ambu A/S, Ballerup, Denmark], modified to 4-fold increase LED current input by an external power supply), with the 3 sensors attached to the LED, to the lateral side, and to the backside of the tip at the level of the objective.

The testing protocol was straightforward. After attaching all sensors, the endoscopes were acclimatized within a temperature-controlled cabinet (Universal Oven; Memmert GmbH + Co. KG, Schwabach, Germany) at 40°C. Then, the power of the operating unit was turned on (ie, camera and LEDs running) and temperatures were continuously measured for 30 minutes, followed by 10 minute cool-down (ie, camera and LEDs off).

Tissue exposure and temperatures

The porcine organs (esophagus, stomach fundus region, duodenum, and centripetal colon coils) of 3 animals each (German landrace swine, mean weight = 110.9 ± 23.7 kg) were collected from a slaughterhouse in the early morning stored and transported on ice trimmed for experiments at the study site. Tissue thickness was measured and images of the samples taken. The tissue samples were individually stored in plastic boxes to minimize mechanical influence on the mucosa during further handling as well as to avoid desiccation. All boxes were put into the climate chamber at once to allow for acclimatization and thereafter timely conduct of the experiments

All equipment for exposure of tissue to endoscope tips was arranged within a climate chamber (Konstant-Klimakammer; Memmert GmbH + Co. KG) with controlled temperature and relative humidity. Conditions inside were monitored by calibrated measuring equipment (Testo North America, West Chester, Pennsylvania).

The displaying unit Ambu® aBox™ 2 Ambu A/S, Ballerup, Denmark for all endoscopes except the modified duodenoscope that was used with Ambu® aBox™ Duodeno Ambu A/S, Ballerup, Denmark was switched on for at least 15 minutes to allow for equilibrium heating of the endoscope tip as defined in the first part of the study and in line with other studies.[2,9] The following endoscopes were tested on representative tissues: a gastroscope on stomach and esophagus Ambu® aScope™ Gastro a colonoscope on colon tissue (prototype), a duodenoscope on duodenal tissue (prototype), and a modified duodenoscope on duodenum (modified Ambu® aScope™ Duodeno).

One temperature sensor was guided alongside the endoscope to measure the temperature at the mucosal surface in a defined distance from the endoscope tip ($T_{tissue,1}$). A second sensor was guided through the agar-agar gel to measure the temperature at the lower side of the tissue, right underneath the endoscope tip ($T_{tissue,2}$). The 5% w/v agar-agar gel, mimicking the surrounding intestinal structures, was prepared following.[10] Reproducible endoscope and temperature sensor positions were achieved by a 3-dimensional-printed, multicomponent, customized fixation jig. The gastroscope and colonoscope were directed vertically toward the tissue surface (ie, touching with circular frontal plane of endoscope tip), whereas the duodenoscopes were oriented laterally (ie, touching the endoscope tube). The experimental setup is displayed in Supplemental Figure 1.

The tissue sample was placed onto the agar-agar gel to monitor $T_{tissue,2}$. When a baseline temperature of 40°C ±0.5°C was reached (simulation of fever), exposure to the endoscope tip was started manually via a screw mechanism that lowered the endoscope tip until it came into contact with the tissue sample. Temperatures and relative humidity were continuously measured.

Two different potentially clinically relevant exposure times were defined to account for time-dependency of possible tissue damages: 5 minutes (n = 2) and 15 minutes (n = 2). A 120-minute sample (n = 1) served as long-term exposure control. For each tissue sample, after the exposure time had elapsed, the endoscope was removed from the mucosa, and the tissue sample was immediately collected from the jig and chamber. The position of the contact area of the endoscope tip with the mucosa was indicated by incisions at the edges of the tissue sample. Subsequently, the tissue samples were pinned on cork plates with the mucosal side facing upward and submersed upside down in neutrally buffered 4% formaldehyde solution (Roti Histofix 4%; Carl Roth GmbH + Co. KG, Karlsruhe, Germany) for fixation for >24 hours at room temperature (see Supplemental Figure 2). The time span between end of exposure and submersion into formaldehyde solution was set to 15 minutes. Samples were sent in for histopathologic examination.

For additional negative and positive control samples, the tissue was acclimatized within the climate chamber as well, put into the jig, and baseline temperatures were recorded. For the negative control sample, no further treatment was done. The positive control sample tissue was created by 7 seconds' coagulation of the mucosal surface using a bipolar high-frequency probe (Injection GoldProbe; Boston Scientific, Marlborough, Massachusetts) with forcedCOAG, Effect 7, VIO3 (Erbe Elektromedizin GmbH, Baden-Württemberg, Germany). They were processed for pathologic examination as described above.

Histopathologic evaluation

Formalin-fixed tissue samples were trimmed to a size of approximately 2 cm × 2 cm, using the markings indicating the position of the contact area of the endoscope tip with the mucosa. To ensure that the contact area of the mucosa with the endoscope tip was represented in the subsequently prepared histology sections, the trimmed tissue sample was exhaustively serially cut into approximately 1-mm thick parallel tissue slabs, oriented vertically to the mucosal surface (see Supplemental Figure 2). Maintaining the orientation and sequence of their section surfaces, the tissue slabs were then routinely embedded in paraffin and the paraffin blocks were serially sectioned into approximately 3-µm thick sections. From each section stack, histological section pairs with a vertical distance of approximately 300 µm between the sections were selected, mounted on glass slides, and routinely stained with hematoxylin and eosin (HE), Giemsa, and Masson's trichrome stain, respectively (thus producing parallel, vertical histologic tissue section planes of 300–700 µm distance covering the complete tissue sample). Histopathologic evaluation was performed by a pathologist (A.Bl.) in a blinded fashion (ie, without knowledge of the treatment of the examined sample sections).

Statistical analysis

Mean (SD), maximum, and minimum temperatures were calculated. Due to the preliminary study character, no further statistical analysis was performed.

Results

Endoscope tip temperatures

The temperatures of 4 endoscopes per type without tissue contact were measured in a benchtop setting. In Figures 1 and 2, the absolute maximum and the course of the relative increase of temperatures are displayed at tissue-contacting locations for the gastroscope and colonoscope at the LED and for the duodenoscopes at the lateral side. The data of all 3 sensors per endoscope at distinct time points is provided in Supplemental Table 1, Supplemental Table 2, and Supplemental Table 3 for sensors 1, 2, and 3, respectively.

At the gastroscope's LED, an average maximum temperature of 78.8°C ±3.7°C was measured (range = 76.8–84.4°C). This reflects an increase of 39°C related to the ambient temperature of 40°C. Similar results were obtained for the colonoscope. At the colonoscope's LED, an average temperature of 81.2°C ±1.8°C was measured (range = 79.8–83.8°C). This reflects an increase of 41°C related to the ambient temperature of 40°C. For both endoscopes, the maximum temperatures were reached after around 10 minutes.

At the duodenoscope's lateral side, an average maximum temperature of 58.7°C ±4.3°C was measured (range = 54.9–64.8°C). This reflects an increase of 18°C related to the ambient temperature of 40°C. In contrast, at the same location but on the modified duodenoscope, an average maximum temperature of 86.2°C ±1.0°C was measured (range = 84.9–87.3°C). This reflects an increase of 46°C related to the ambient temperature of 40°C, hence a 2.5-fold increase compared with the normal duodenoscope. The maximum temperatures were reached after about 10 to 15 minutes for the duodenoscope and the modified duodenoscope, respectively.

Tissue temperatures and histologic examination

The tissue thickness varied across the different types of porcine GI tissue as shown in Table 1. Stomach was the thickest tissue with up to 4.8 mm and colon the thinnest. However, the thinnest sample was recorded in duodenum at just 1.5 mm.

The maximum temperatures at the tissue surface next to the endoscope tip reached between 43.2 and 49.1°C (Figure 3A). At the lower side of the tissue, the maximum temperatures ranged between 40.2 and 50.5°C (Figure 3B). Note that the measured temperatures depend on scope and tissue type (ie, thickness) as well as exposure time.

Because the start criterion for measurement was a baseline tissue temperature of 40°C ±0.5°C, the start temperature could differ up to 1°C among samples. To account for this potential difference, the relative change in temperature was investigated. For each measurement, the measured temperatures were normalized against the baseline tissue temperature at start of measurement, resulting in the relative temperature change (ΔT). For each tissue and endoscope, ΔT is shown in Figure 4.

The temperatures rose continuously over time, with a fast initial increase and a steadier state later. To better compare tissue temperatures across tissues, the mean temperatures (SD) were ex-

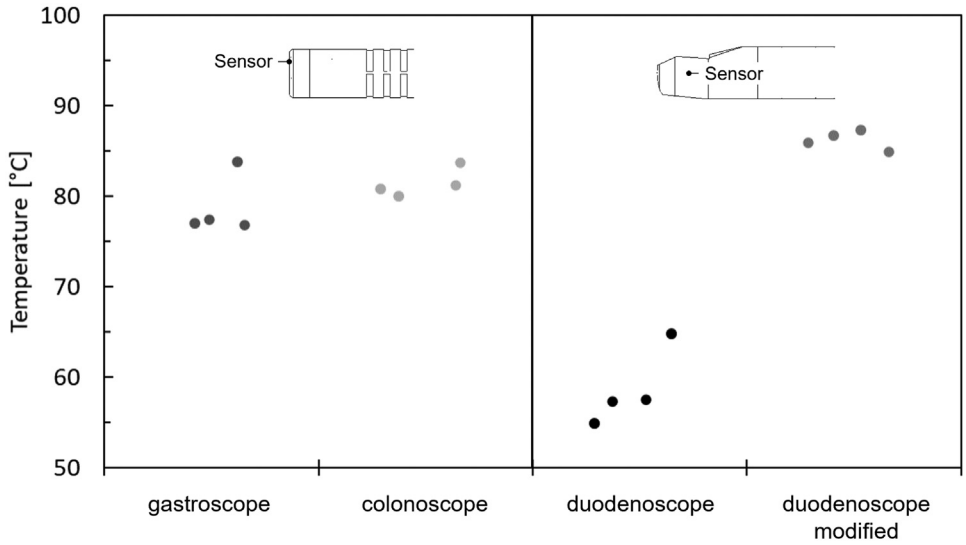

Figure 1. Absolute maximum temperatures at endoscope contact points. Four measurements per endoscope are individually shown. The sensors at the tissue-contacting area are shown for all endoscopes; that is, for gastroscope and colonoscope, the temperatures of the sensor at the light-emitting diode are shown, and for the duodenoscopes, the results of the sensor at the lateral side are shown.

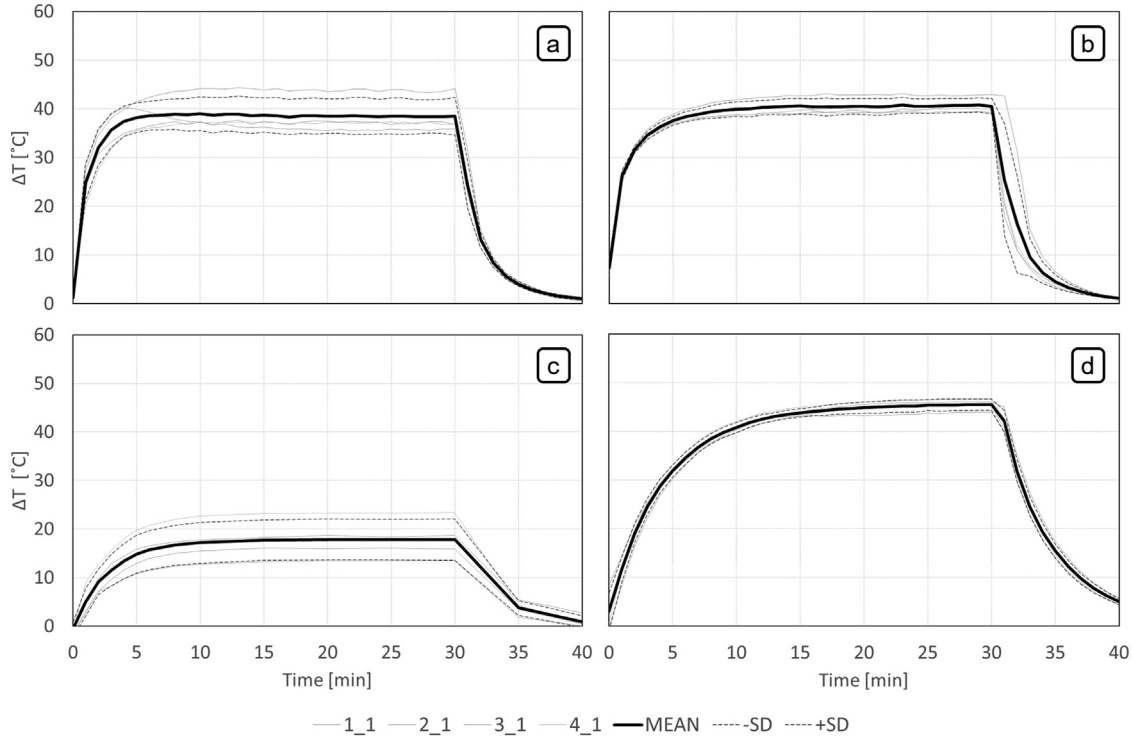

Figure 2. Endoscope tip temperature increase in a benchtop setting. Within the climate chamber, temperature change (ΔT) relative to chamber temperature. (A) Gastroscope, sensor at light-emitting diode (LED). (B) Colonoscope, sensor at LED. (C) Duodenoscope, sensor at lateral side (objective). (D) Modified duodenoscope, sensor at lateral side (objective). Mean (SD) is displayed as well as single experiments (n = 4).

Table 1
Tissue thickness across the different types of porcine gastrointestinal tissue. Each sample was measured when trimmed.

	Stomach (n = 5)	Esophagus (n = 5)	Colon (n = 5)	Duodenum (n = 10)
Mean (SD), mm	4.6 (0.3)	3.3 (0.4)	1.7 (0.2)	1.9 (0.2)
range, mm	4.1–4.8	2.8–3.8	1.6–2.0	1.5–2.1

tracted for 5, 30, and 60 seconds and 2, 3, 4, 5, 10, 15, and 120 minutes (see Supplemental Tables 4 and 5).

The temperature at the lower side of stomach tissue did not immediately increase as fast as in the other tissues, and the overall temperature increase was the lowest among all tissues. Because stomach was the thickest tissue in the study (4.1–4.9 mm; other tissues ~3 mm [esophagus] or 1–2 mm [colon and duodenum]), it took some time for heating to be recognized by the relatively farther sensor. One sample, 15_1, stands out and influences both mean and SD. Variability of (repeated) measurements is discussed further below.

The heating pattern by the tissue surface sensor was different for colon compared with the other tissues. That sensor was guided alongside the endoscopes and thus was heated during equilibrium heating of the endoscope before the start of measurements. Upon tissue contact, the intrinsic heat of the sensor was instantly removed as can be seen for all but the colon samples. Because colon was the thinnest tissue, "cooling" of the sensor by the tissue apparently took a bit more time, resulting in a decrease of $T_{tissue,1}$ during the first 20 seconds of measurement. Thereafter, the heating of the colon surface happened as for the other tissues.

Comparing the two duodenoscope settings, the more powerful light of the modified duodenoscope resulted in higher increase in mean temperature (for $T_{tissue,1}$, maximum ΔT was 5.0 vs 5.4°C, and for $T_{tissue,2}$, maximum ΔT was 3.3 vs 5.7°C, for the prototype normal duodenoscope and the modified duodenoscope, respectively). Overall, repeated measurements resulted in similar heating patterns across all tissues, endoscopes, and sensor positions.

Gross and histopathologic evaluation of untreated control sections of the esophagus, gastric fundus, duodenum, and colon revealed an overall well-preserved, regular mucosal histoarchitecture with mainly intact surface epithelium. Except for oligofocal lymphoplasmatic cell infiltrations present in the propria and the submucosa of gastric, duodenal, and colonic tissue samples in a few cases, there was no evidence of relevant pathological alterations.

Thermal coagulation of the mucosal surface of tissue samples with a bipolar HF probe for 7 seconds uniformly caused focal, well-demarcated, circular mucosal lesions that were approximately 2 mm in diameter and of white-greyish color with a central loss of mucosal tissue lined by a thin (0.5 mm wide), slightly elevated wall-like rim (Figure 5). Histopathologically, these lesions presented as focal, sharply demarcated thermal denaturations limited to the upper parts of the mucosal layer (ie, not reaching into the submucosa). The lesions showed thinning of the mucosa to approximatively 50% to 70% of its original height, complete loss of the surface epithelium in the center of the lesion, and marked heat denaturation of the adjacent and underlying mucosa. Direct heat-induced tissue alterations were characterized by an overall compaction of the tissue along with conformational changes of cells and nuclei, including loss of normal cytoarchitecture, cell shrinkage, marked cytoplasmic basophilia with loss of intracellular detail,

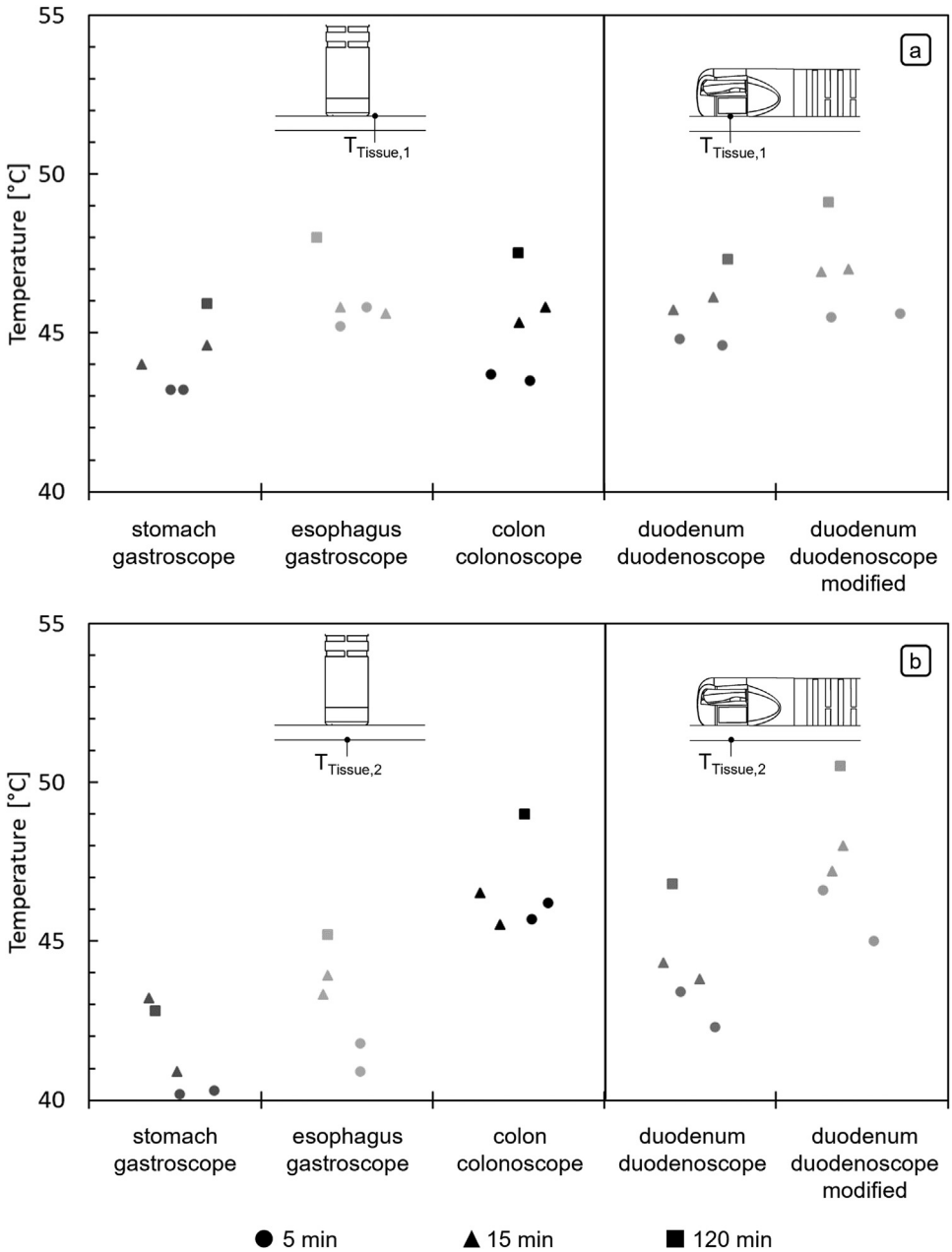

Figure 3. Maximum tissue temperatures measured. (A) Temperature at tissue surface next to the endoscope tip ($T_{tissue,1}$). (B) Temperature at the lower side of the tissue underneath the endoscope tip ($T_{tissue,2}$).

indistinct cell borders, loss of cell nuclei and of intranuclear structure, as well as compression and shrinkage of the interstitial space with occasional hyalinization of delicate connective tissue fibers (se Figures 6, 7, and 8).

Macroscopic and histopathologic findings in tissue samples exposed to a direct contact with the endoscope tip for 2 hours (120 minutes) varied in esophageal, gastric, duodenal, and colon tissue samples, as well as in different experimental settings (Figures 5, 6, 7, and 8). In esophageal tissue samples, a 120-minute exposure to the gastroscope caused only a moderate thinning of the height of the epithelium (particularly of the stratum corneum) of the esophageal mucosa compared with the adjacent tissue areas (likely due to mechanical compression), but no relevant histomorphological alterations indicative of direct thermal injury. In gastric, duodenal, and colon tissue samples, a 2-hour-contact of the mucosa with the gastroscope, duodenoscope, or colonoscope, respectively, caused a macroscopically apparent imprint of the mucosal surface (corresponding to the shape of the contact surface of the endoscope), due to the passing of mucosal folds and compression of the mucosa (Figures 5, 6, 7, 8). In corresponding histologic sections, the mucosa in these areas was thinned, with incomplete loss of the epithelium and variable degradation of the superficial mucosa characterized by an irregularly reduced interstitial, cellular, and nuclear stainability with a homogeneously pale-eosinophilic appearance and loss of structural details (Figures 7 and 8). Compared with the bipolar HF probe and the 120-minute exposure control tissue samples, a 5- or 15-minute exposure to the endoscope tips did not reproducibly induce similar; that is, relevant histomorphological alterations clearly attributable to isolated thermal effects in any of the examined tissues or experimental setups.

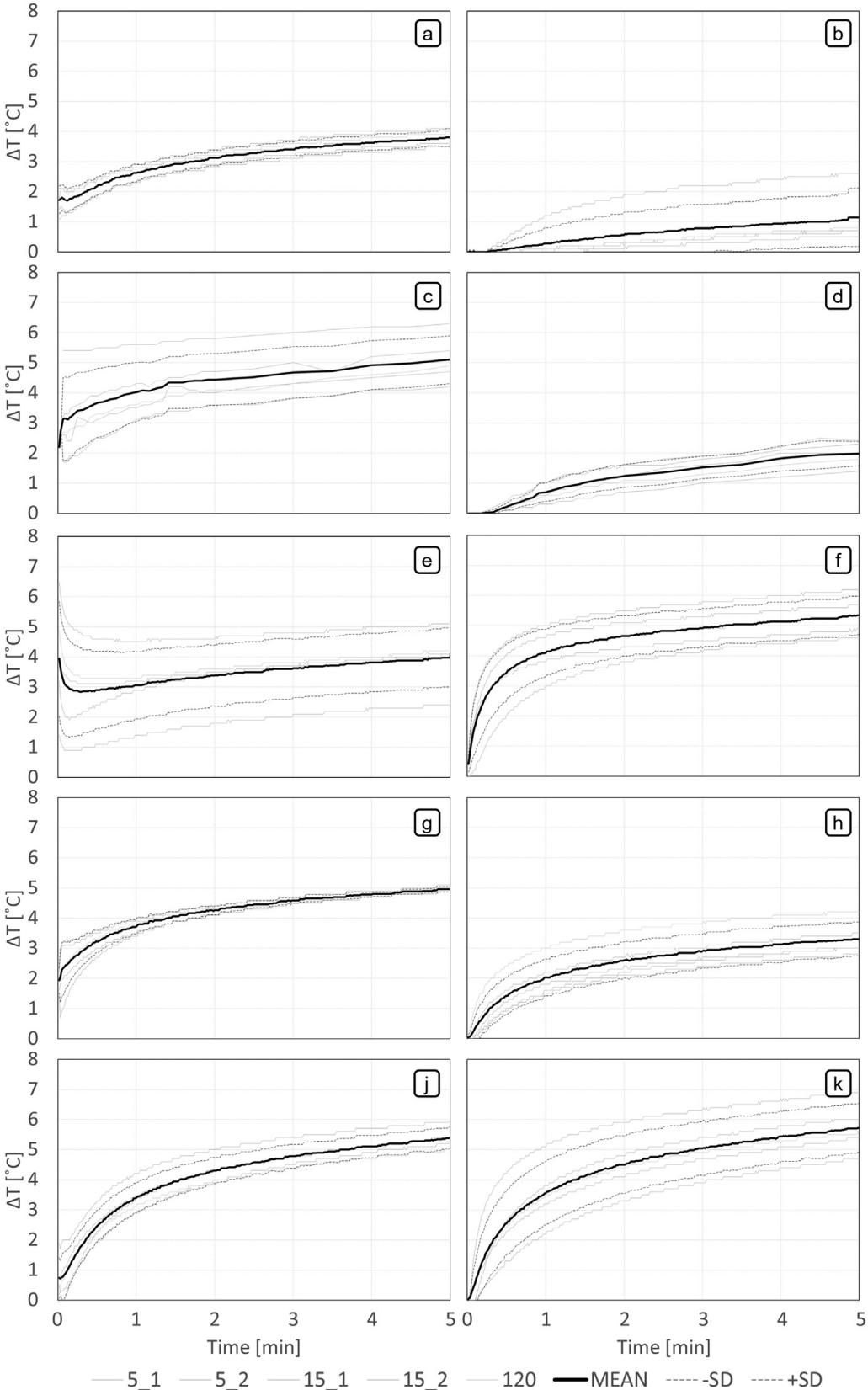

Figure 4. Tissue temperatures for 5-minute exposure. (A, C, E, G, J) Temperature at tissue surface ($T_{tissue,1}$) next to the endoscope tip. (B, D, F, H, K) Temperature at the lower side of the tissue underneath the endoscope tip ($T_{tissue,2}$). Stomach (A and B) and esophagus (C and D) were exposed to gastroscope (Ambu® aScope™ Gastro, Ambu A/S; Ballerup, Denmark). Colon (E and F) was exposed to colonoscope (prototype). Duodenum (G and H) was exposed to duodenoscope (prototype). Duodenum (J and K) was exposed to modified duodenoscope (based on Ambu® aScope™ Duodeno, Ambu A/S; Ballerup, Denmark, more powerful light). Mean (SD) is displayed as well as single experiments (5 minutes [n = 2], 15 minutes [n = 2], and 120 minutes [n = 1]). ΔT = Temperature change relative to start temperature per experiment.

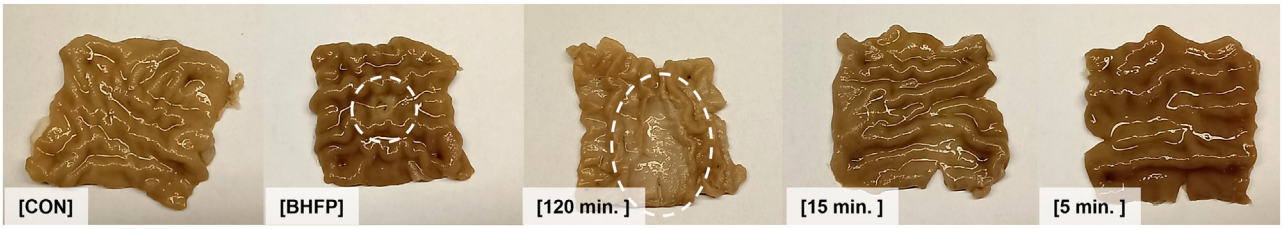

Figure 5. Representative images of the mucosal surface of formalin-fixed tissue samples of porcine duodenum. Duodenum without manipulation (control [CON]), after focal ex vivo thermal coagulation (7 seconds) with a bipolar high-frequency probe (BHFP) and following ex vivo exposure to the lateral side of a duodenoscope tip (modified duodenoscope based on Ambu® aScope™ Duodeno; Ambu A/S, Ballerup, Denmark,) for 120 minutes, 15 minutes, and 5 minutes. Note the circular, sharply demarcated loss of superficial tissue and the thermal coagulation of deeper mucosa layers (white-tan color) after BHFP-exposure (encircled by a dashed white line). After 120 minutes' exposure, the surface of the mucosa in the contact area to the endoscope tip was markedly compressed, whereas exposure for 15 or 5 minutes did not cause comparable alterations.

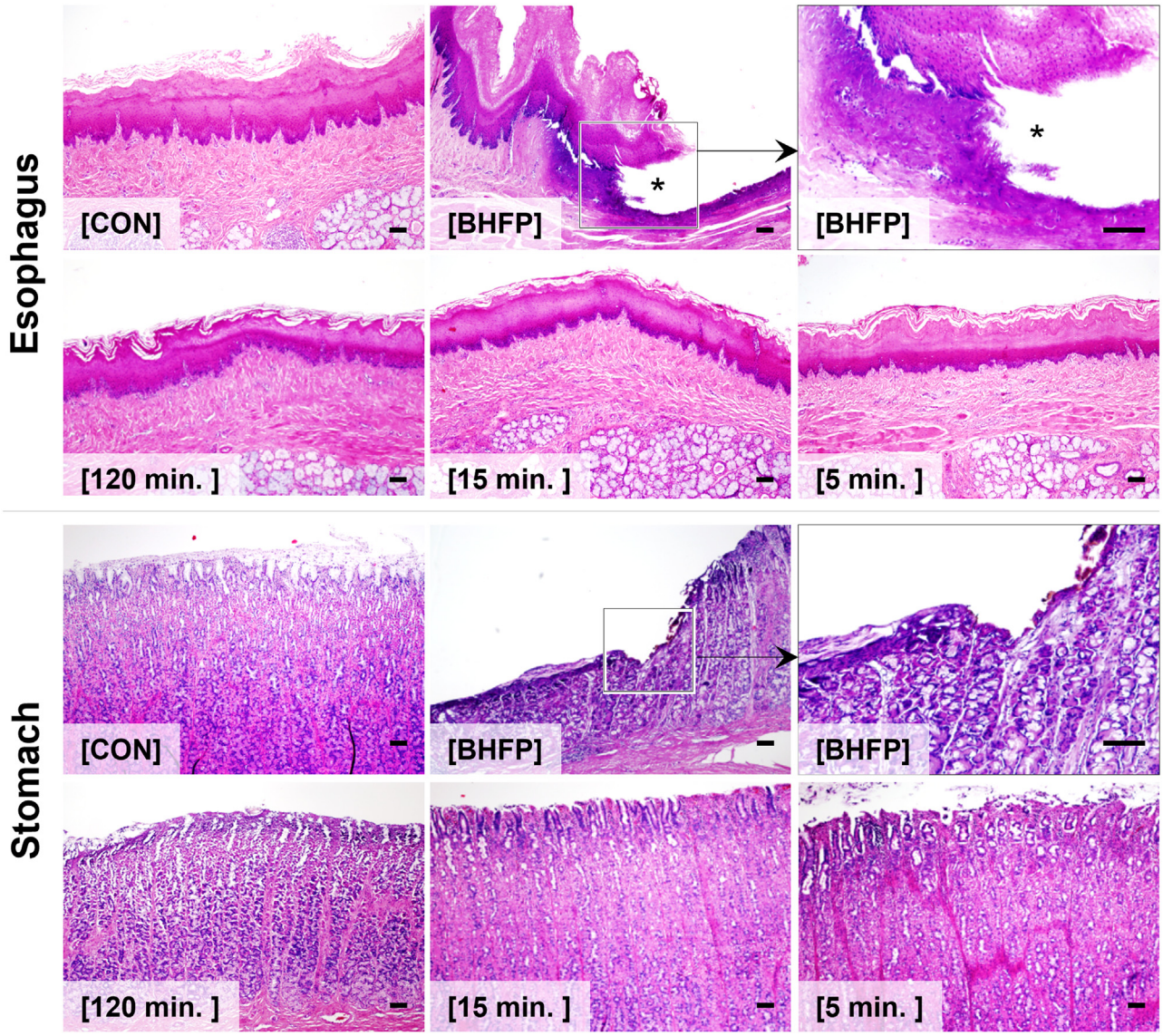

Figure 6. Histology of the mucosal surface of porcine tissue samples of the esophagus and the stomach (fundus region) (paraffin sections of formalin-fixed tissue). Esophagus and stomach without manipulation (control [CON]), after focal ex vivo thermal coagulation (7 seconds) with a bipolar high-frequency probe (BHFP), and following ex vivo exposure to the gastroscope tip (Ambu® aScope™ Gastro; Ambu A/S, Ballerup, Denmark) for 120 minutes, 15 minutes, and 5 minutes. *Note the loss of the superficial epithelial tissue and the thermal coagulation of the adjacent mucosa after BHFP exposure. hematoxylin and eosin (HE). Scale bar = 100 µm.

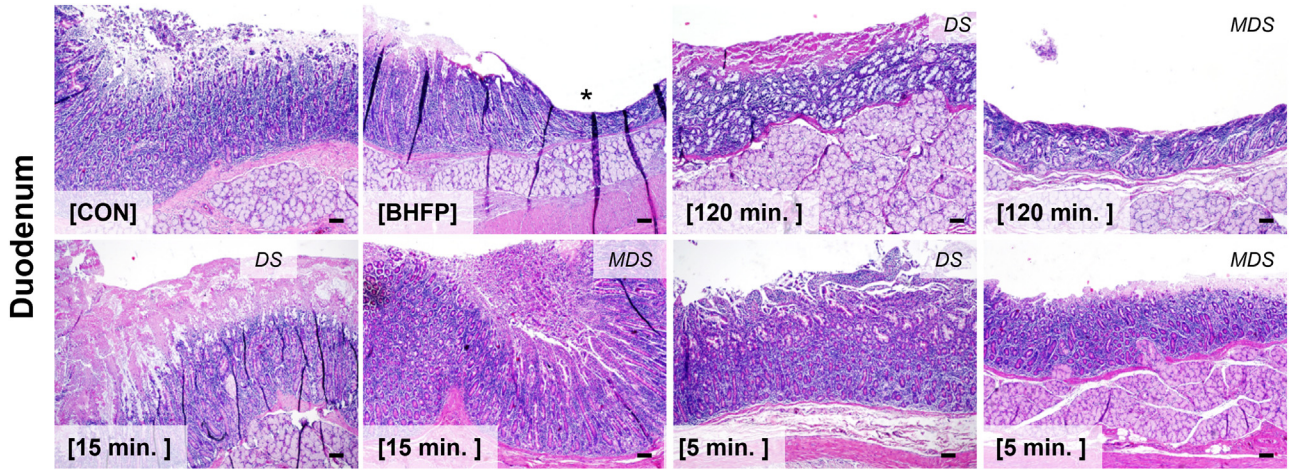

Figure 7. Histology of the mucosal surface of porcine duodenal tissue samples (paraffin sections of formalin-fixed tissue). Duodenum without manipulation (control [CON]), after focal ex vivo thermal coagulation (7 seconds) with a bipolar high-frequency probe (BHFP), and following ex vivo exposure to the lateral side of a duodenoscope tip for 120 minutes, 15 minutes, and 5 minutes. *Note the loss of the superficial tissue and the thermal coagulation of the adjacent mucosa after BHFP exposure. After 120 minutes of exposure to the duodenoscope tip, the vertical height of the colonic mucosa is reduced and there is variable degradation of the superficial mucosa. hematoxylin and eosin (HE). DS = duodenoscope (prototype, Ambu A/S); MDS = modified duodenoscope (based on Ambu® aScope™ Duodeno; Ambu A/S, Ballerup, Denmark). Scale bar = 100 µm.

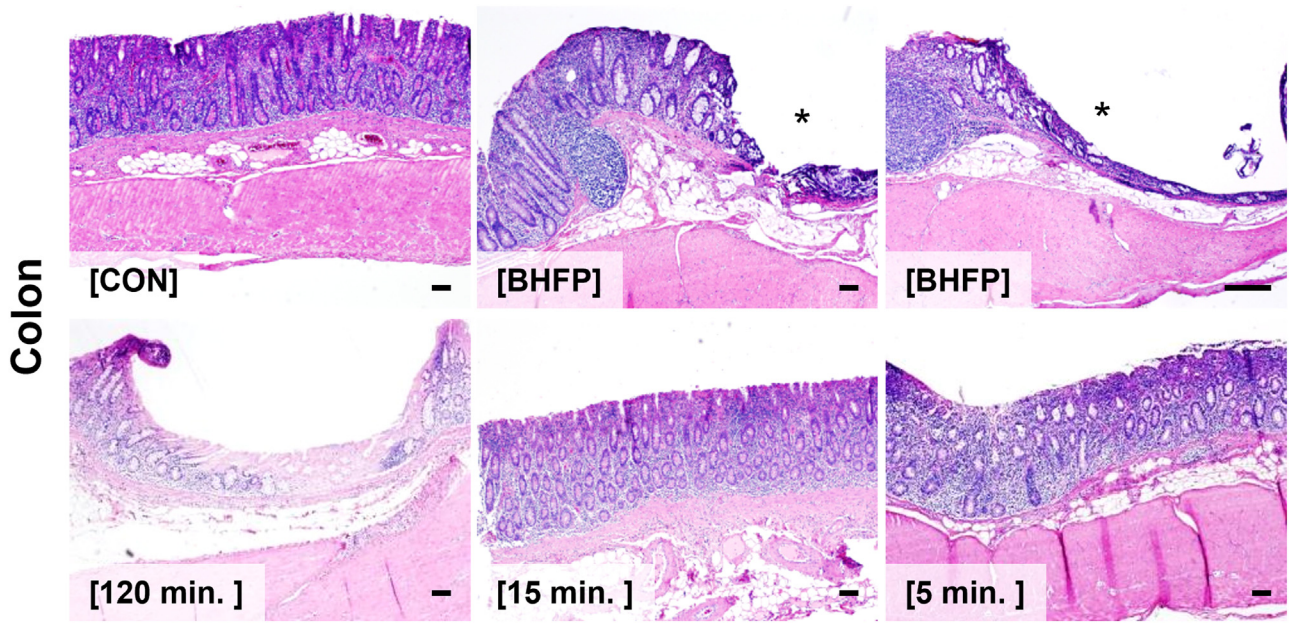

Figure 8. Histology of the mucosal surface of porcine colon tissue samples (paraffin sections of formalin-fixed tissue). Colon without manipulation (control [CON]), after focal ex vivo thermal coagulation (7 seconds) with a bipolar high-frequency probe (BHFP), and following ex vivo exposure to the tip of a colonoscope (prototype, Ambu A/S, Ballerup, Denmark) for 120 minutes, 15 minutes, and 5 minutes. *Note the loss of the superficial tissue and the thermal coagulation of the adjacent mucosa after BHFP exposure. After 120 minutes' exposure, the vertical height of the colonic mucosa is reduced and there is marked, focally extended degradation of the mucosa. hematoxylin and eosin (HE). Scale bar = 100 µm.

Discussion

The overall clinical safety of endoscopic procedures, irrespective of illumination concept, is generally accepted and further substantiated by this study. Following direct contact with endoscope tips, only minimal tissue alterations on cellular level were detected in clinically relevant samples (5- and 15-minute exposure). The temperature-over-time display shows that there is a fast initial increase that reaches a steady state after approximately 300 seconds as observed before.[3,4] The maximum recorded tissue temperatures are below the endoscope tip temperatures. This is in part due to the heat transfer from the endoscope to the tissue. In other words, when the endoscope makes contact with tissue, the same amount of heat is dissipated through a larger mass (ie, tissue sample and agar-agar phantom) reaching a lower equilibrium temperature. However, it must be noted that the hottest point of the endoscope; that is, directly at the LEDs, was not accessible to temperature sensors and consequently, tissue temperatures were measured at a certain distance from the hottest point ($T_{tissue,1}$ at the tissue surface next to the endoscope tip, $T_{tissue,2}$ at the lower side of the tissue underneath the tip and LEDs). The hottest points of the endoscopes were measured in a benchtop setting and revealed increases of 18°C for the duodenoscope up to around 40°C and hotter for the gastroscope, colonoscope, and modified duodenoscope. In contrast, much lower increases in tissue temperature were recorded (4.4–6.2°C, dependent on endoscope and tissue type). This difference can be attributed to heat distribution and location of the sensor. Heat distribution in biological tissue is a

complex topic that has been addressed in various models, starting with the basic work by Pennes[11] and further, more sophisticated developments.[12,13] However, there is consensus that the heat-transfer capability of biological tissue is low[13] and accordingly, temperature gradients are steep with increasing distance from the heat source. Thus, measuring temperatures only a few millimeters from the heating source will result in markedly reduced recorded temperatures. However, closer positioning of metal temperature probes could have interfered with the tissue heating by inherent heating of the sensor and heat dissipation along the metal wire. Because the hottest point was not accessible to the sensor, a computational model was developed to simulate the heat transfer from GI endoscopes to tissue (not shown). In the measurements, the temperature sensor $T_{tissue,1}$ was located approximately 3 mm from the hottest point of the tissue; that is, in front of the LEDs. The simulation pointed toward a steep gradient of temperature of about 4°C/mm between the sensor and the hottest point. Therefore, we estimate the single hottest point on the tissue surface to be up to 12°C higher than the values reported in Figure 3A.

In contrast, the whole exposure zone was accessible to histopathologic examination. And as mentioned above, no relevant direct heat-induced tissue alterations were observed. Also due to the fact that heat-transfer is low and accordingly slow, the 120-minute sample was included in this study as an additional control to allow for more heating and thus more damage. Besides a variable, focally extended degradation of the superficial mucosa in the area in contact with the endoscope tip, no histomorphologic lesions comparable to those observed in the bipolar high-frequency probe-positive control sample were detected. Because gastrointestinal mucosa heals rapidly following superficial injury,[14] it can be assumed that tissue alterations as observed in this study will have no persisting negative effect on patients.

Just recently, a study on thermal tissue damage by chromoendoscopy was published.[15] They report relatively low tissue temperatures (<40°C) for nonstained mucosa with the standard illumination source. However, the tissue baseline temperature was only at 24°C, thus neither representing physiologic (37°C) nor feverish conditions (40°C) as in our study. Also, the exposure times were much shorter than in this test (1–10 seconds) and the endoscopes used were different. Noticeably, much higher temperatures were recorded for stained mucosa, indicating that the light absorption of the tissue is an important factor in tissue heating and associated damage.

As mentioned, heat dissipation in biological tissue is a complex topic due to a variety of influencing factors; for example, heat removal by blood flow[12,13] also called heat sink effect.[16] In thermal tumor ablation, this causes a reduction in ablation zones.[16] However, thermal damage is an unwanted effect in endoscopy, hence cooling by blood circulation would be favorable. Because the tissue experiments were performed in a nonperfused ex vivo model, even lesser tissue effects are anticipated in vivo. Besides intrinsic cooling by the blood perfusion, in clinical application, there is also gas insufflation (air or carbon dioxide) and rinsing during endoscopy. The GI lumen has to be constantly insufflated to keep it expanded.[17] Rinsing of the lens and the area under treatment is also repeatedly performed to maintain best possible visualization throughout the procedure. Both insufflation and rinsing will have a cooling effect—and that was not present in the ex vivo setting of our study. This further contributes to the more serious scenario of the ex vivo experimental setting.

Variability in the single courses of temperature measurement might be due to sensor positioning issues and manual handling of the fixation jig. For the endoscope tip temperature measurements, the sensors were attached manually to the endoscopes, leaving room for slight variations in position. Similarly, the sensor for $T_{tissue,2}$ was manually guided through the agar-agar gel and because it was exchanged after 4 measurements, the sensor had to be newly positioned. It is possible that it stuck out a little, measuring closer to the heat source and accordingly measuring higher values, and being pushed back to its normal position throughout subsequent measurements. Minor differences in sensor position can result in marked differences in temperatures because the spatial gradient of temperature and heating is steep as outlined above.

Overall, the negative controls proved that no visible degradation occurred that could impede analysis of the test samples, whereas the 120-minute control samples displayed degradation of the superficial mucosa, corresponding to mechanical compression and heat transfer to the tissue occurring during the long exposure duration. Some artifacts were detected across most samples that were attributed to the direct contact; that is, mechanical pressure, of the endoscope tip to the mucosal surface. Contact was established manually while avoiding excessive pressure. However, secured contact was favored over sparing the mucosa because minimal distance of endoscope to tissue would have resulted in an insulating air layer and ultimately have disturbed the measurements.

Regarding the applied experimental setup in general, it has to be emphasized that histopathological examination of ex vivo tissue samples is suitable for detection of immediate, direct physical tissue damage due to exposure to mechanical and/or thermal insults (such as thermal denaturation of proteins or crushing of tissue),[18] whereas indirect and subsequent effects on cells in vivo, leading to cellular dysfunction with delayed cellular degeneration and/or cell death, cannot be unreservedly reliably captured.

Regarding the clinical relevance, in gastroscopy and colonoscopy, the endoscope tip would not be in frontal, full contact with the tissue if the endoscope is used according to normal clinical practice. The endoscope is supposed to provide live images of the GI tract but in frontal contact, nothing can be seen. Also, the clinical procedures require the endoscope to move around for inspection of the organs. Stable positioning is only required for very short periods of time during, for example, polyp resection. Thus, the conditions of this study represent worst-case scenarios such as a user error (eg, user leaves the endoscope in direct contact) or device failure situations (eg, the endoscope gets stuck, the angulation is blocked and therefore tissue contact cannot be resolved, or no image display due to a disrupted connection to the display unit and therefore the user does not notice that the endoscope is in direct tissue contact). Overall, these scenarios are very remote options, yet they need to be considered to ensure the safety and performance of the device during procedures.

In contrast, in duodenoscopy, the endoscope may be left in one position for an extended period of time compared with other GI procedures due to advanced interventions.[19,20] The duodenoscope provides access to the major papilla and thereby to the gall bladder and pancreas. Whereas interventions are performed inside these two organs, the duodenoscope “outside” them will stay still. As the camera is side-viewing, images can be obtained even when the lateral or the back side of the duodenoscope tip is in contact with the mucosa.

Testing an endoscope with enhanced power supply provides an estimate of effects by other sources of illumination as utilized in other endoscopes that were not part of this study. Clinical scenarios necessitating enhanced illumination encompass diagnostic procedures involving visual assessment and transillumination procedures.

Conclusions

In this study, it was established that heat transfer from the herein tested endoscope tips did not cause damage to ex vivo porcine GI tissues in clinically potentially relevant conditions. That

is despite the fact that the endoscope tips are heated up to 80°C at their hottest point. However, because assessment of metabolic effects at the cellular level was not possible further studies are needed. It is also important to consider possible heat-related risks of possible damage from the endoscope tip during actual clinical examinations.

Conflicts of Interest

L. Jäger, E. Morales-Orcajo, A. Bader, and A. Dillinger are employees of Ambu Innovation GmbH. A. Gager and A. Blutke performed the histopathologic examination of the tissue samples as part of the diagnostic service offered by the Institute of Veterinary Pathology of Ludwig-Maximilians Universitaet München, charging the regular price for samples submitted for histopathology. The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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L. Jäger was responsible for conceptualization, methodology, investigation, formal analysis, writing (original draft preparation), and project administration. E. Morales Orcajo was responsible for conceptualization, methodology, visualization, formal analysis, and writing (reviewing and editing). A. Gager was responsible for methodology, investigation, and writing (reviewing and editing). A. Bader was responsible for conceptualization, methodology, supervision, and writing (reviewing and editing). A. Dillinger was responsible for conceptualization, methodology, and writing (reviewing and editing). A. Blutke was responsible for methodology, investigation, supervision, and writing (reviewing and editing).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.curtheres.2023.100693.

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