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Digital image enhancement may improve sensitivity of cholesteatoma detection during endoscopic ear surgery

Talisa Ragonesi[1] | Laura Niederhauser[2] | Ignacio Javier Fernandez[3,4] | Giulia Molinari[3,4] | Marco Caversaccio[1] | Livio Presutti[3,4] | Lukas Anschuetz[1]

[1]Department of Otolaryngology – Head and Neck Surgery, Inselspital, University Hospital and University of Bern, Bern, Switzerland

[2]Department of Psychology, University of Bern, Bern, Switzerland

[3]Department of Otolaryngology – Head and Neck Surgery, IRCCS Azienda Ospedaliero – Universitaria di Bologna, Bologna, Italy

[4]Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

Correspondence
Ignacio Javier Fernandez, Department of Otolaryngology – Head and Neck Surgery, IRCCS Azienda Ospedaliero – Universitaria di Bologna, University of Bologna, Via Albertoni 15, 40138, Bologna, Italy.
Email: ignacio.fernandez@aosp.bo.it

Abstract

Objectives: This study investigates the possible benefits and limitations of the digital image enhancement systems provided by Storz Professional Image Enhancement System (SPIES) during endoscopic ear surgery (EES) for cholesteatoma. An increased detection of cholesteatoma residuals during the final steps of endoscopic surgery using DIE technology was hypothesized.

Design: Cross-sectional study.

Setting: Tertiary referral hospital.

Methods: A total of 10 questionnaires of 18 intraoperative pictures with equal numbers of cholesteatoma and non-cholesteatoma images, each presented in three different image-enhancing modalities (Clara, Spectra A, Spectra B), were generated. Fifty-one experienced ear surgeons participated to the survey and were randomly assigned to a questionnaire and completed it at two time points. The experts were asked to rate for each picture whether cholesteatoma was present or not. The answers were compared with the histopathological reports.

Results: Clara showed the highest accuracy in cholesteatoma detection, followed by Spectra A and lastly Spectra B. In contrast, Spectra B showed the highest sensitivity and Clara the highest specificity, while Spectra A was placed in the middle for both values. Using the Spectra B modality, most responses agreed across the two time points. Ear surgeons assessed the usefulness, as well as preference among image modalities for cholesteatoma surgery, in the following order: Clara, Spectra B, Spectra A.

Conclusion: Digital enhancement technologies are applicable to EES. After complete cholesteatoma removal, Spectra B showed the highest sensitivity in the detection of cholesteatoma residuals as compared with Clara and Spectra A. Thus, Spectra B may be recommended to avoid missing any cholesteatoma residuals during EES.

Talisa Ragonesi and Laura Niederhauser are equally contributing first authors.

KEYWORDS
cholesteatoma; Clara, Spectra A, Spectra B; endoscopic ear surgery; image enhancement; outcome; SPIES

1 | INTRODUCTION

Endoscopic ear surgery (EES) has become an internationally recognised surgical method to treat the whole variety of middle ear diseases. Due to its wide view and the possibility to use angled lenses to access hidden anatomical areas of the middle ear, it is a suitable minimal-invasive technique for the treatment of cholesteatoma.[1–6] Due to the locally invasive and destructive behaviour of middle ear cholesteatoma, detection and radical removal of even microscopic residuals is required to prevent re-growth and complications.[7]

Despite technical advancements regarding the visual control of the middle ear as offered by the endoscope, the complete eradication of the squamous cell matrix from the middle ear remains a surgical challenge. Especially in diffusely infiltrating cholesteatoma, it may be difficult to remove the cholesteatoma "en-bloc," and the quest for possible remnants may impact on surgical time.

To improve endoscopic visualisation and disease detection, digital technologies enhancing the signal visible on the screen have been developed.[8,9] As an example, narrow band imaging (NBI) technology by Olympus uses a filter enabling narrow band light to penetrate tissues at different depths, whereby the microvascular pattern can be recognised.[8,9] Several studies have shown a significant added value in detection of neoplasms in the larynx and oro-hypopharynx.[10,11] Similarly, the Storz Professional Image Enhancement System (SPIES), allows the surgeon to use several digital modifications in addition to traditional white light (WL) during endoscopic surgeries, to increase colour brightness and contrast, as well as to enhance the tissue vasculature.

The use of this digital image enhancement (DIE) technology has been also applied to endoscopic cholesteatoma surgery. So far, in a small case series on 45 patients reported by Lucidi et al., an added value in cholesteatoma detection by SPIES was supposed.[8] Under SPIES filters, cholesteatomatous tissue was clearly recognisable as a highly reflective and brilliant white material, distinctive from the surrounding tissues. In 11% of cases from this preliminary case series, cholesteatoma residuals, which had not been identified at white-light inspection at the end of surgery, were detected by combining Spectra A and B, with 97% sensitivity, 97% specificity, 95% positive predictive value and 95% negative predictive value.

Therefore, we aim to further investigate possible benefits and limitations of the SPIES during EES for cholesteatoma. We hypothesize increased detection of cholesteatoma during the final steps of endoscopic cholesteatoma surgery using DIE technology.

Key points

- Detection and radical removal of even microscopic residuals of middle ear cholesteatoma is required to prevent re-growth and complications from the disease.
- Despite technical advancements regarding the visual control of the middle ear as offered by the endoscope, the complete eradication of the squamous cell matrix from the middle ear remains a surgical challenge.
- Histological analysis is the gold standard to assess the presence of cholesteatoma residuals during the final check of the tympanic cavity. However, digital enhancement technologies are applicable to endoscopic ear surgery (EES) for supporting the detection of cholesteatoma residuals at the end of surgery.
- Spectra B showed the highest sensitivity, as compared with Clara and Spectra A, in cholesteatoma detection at the end of the surgery, while Clara showed the greatest specificity and was the preferred modality during all surgical steps of cholesteatoma surgery, according to surgeons' feedback.
- Spectra B may be recommended to avoid missing any cholesteatoma residuals during EES.

2 | MATERIALS AND METHODS

2.1 | Patients and images

A total of 12 patients undergoing endoscopic resection of middle ear cholesteatoma were prospectively enrolled in the present study. All patients provided informed consent and the study was approved by the local ethical committee (Kantonale Ethikkommission Bern KEK-BE 2019-00555). At the end of the cholesteatoma removal, a final endoscopic check of the tympanic cavity is routinely performed to detect any residual disease. During this check, zones with residual tissue (consisting either of cholesteatoma or granulation tissue) in areas previously involved by cholesteatoma were photographed by the same operating surgeon (LA), regardless of their appearance. Three DIE modalities (as illustrated in Figure 1) were applied with light intensity standardised to 50% for every imaging modality (PowerLED300, Karl Storz, Tuttlingen, Germany):

- Clara, a homogeneous enhancement of the lightness, that allows to maintain a low intensity of the light source, without modifying the standard image. This enhancement does not change information

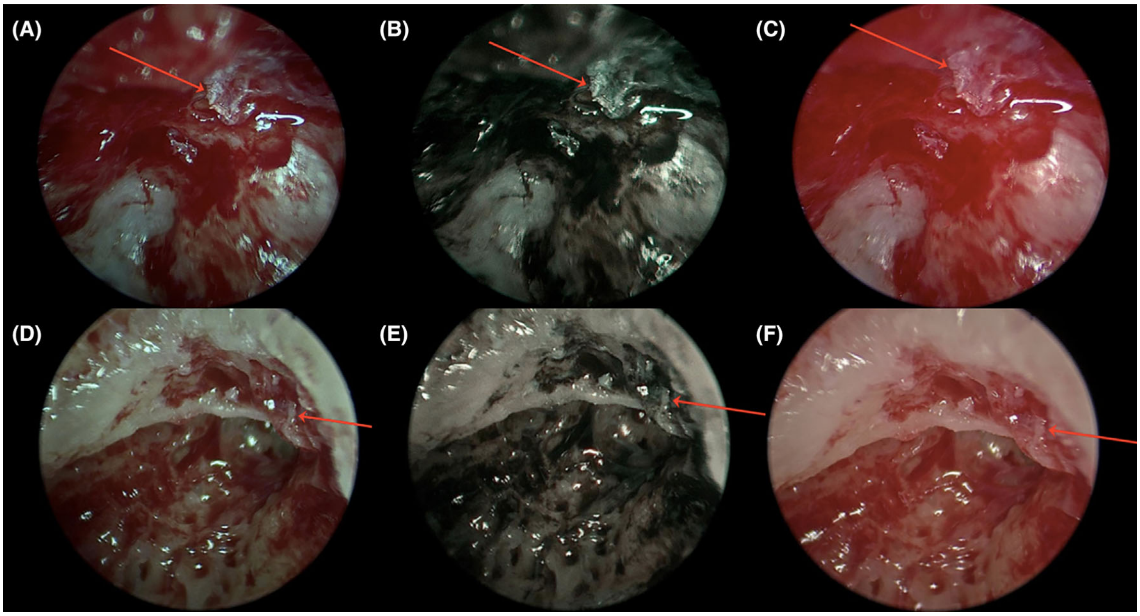

FIGURE 1 Illustration of residual cholesteatoma in the top row (A–C) and granulation tissue in the bottom row (D–F) in the three different image modalities: A/D = spectra B, B/E = spectra A, C/F = Clara.

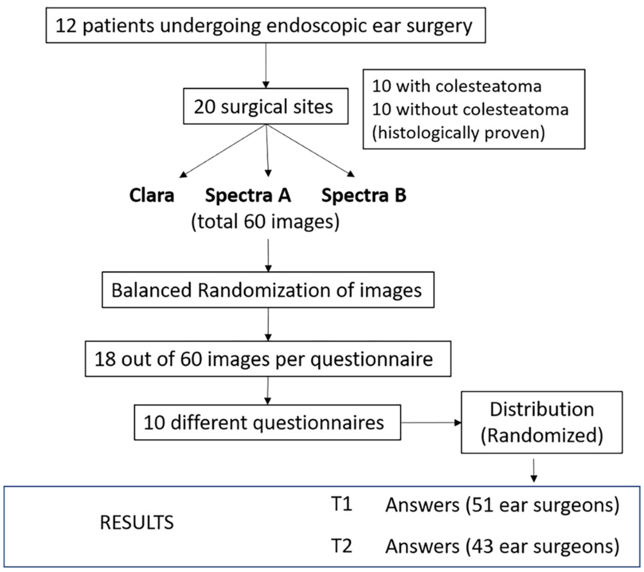

FIGURE 2 Flow chart describing the steps of the study design. T1 (time 1): first questionnaire administration an T2 (time 2): second administration of the questionnaire.

provided by standard WL, as it only increases the brightness of the image. Thus, Clara has been used as the reference standard.

- Spectra A, a digital enhancement of green and blue light signal that improves the contrast of vessels and capillaries in the superficial layers of the mucosa.
- Spectra B, a digital enhancement based on a colour tone shift algorithm, reducing the reflexion of the red signal, while maintaining the signal from deeper layers of the mucosal and submucosal lining. Both Spectra A and B theoretically help to differentiate normal mucosa and vascular granulation tissue from avascular cholesteatoma matrix.

Thereafter, the photographed tissue was removed and sent for separate histopathological evaluation, performed by the referral pathologist of the Otolaryngology Head and Neck Surgery Department of Bern University. A sample of 10 sites of residual cholesteatomatous tissue and 10 sites of non-cholesteatomatous tissue (e.g., granulation tissue, healthy mucosa) were randomly selected based on the histological analysis.

Accordingly, all-modalities images from the corresponding 20 selected surgical sites provided the final set of 60 images to be used in the following steps of the study. Study design is described in Figure 2. This allowed us to investigate the value of Clara and to compare Spectra A and Spectra B with Clara, as control.

2.2 | Questionnaires and participants

We generated 10 online questionnaires on Qualtrics (www.qualtrics.com), each containing 18 images out of the 60 images from the dataset, balanced regarding the three different imaging techniques and presence of cholesteatoma or not (Table 1). We chose 18 images per questionnaire to allow respondents to complete it in an acceptable time and therefore receive more responses, while still allowing a solid statistical analysis, as defined by a preliminary power analysis. All 60 images were used, and every image was present in three different questionnaires.

Thereafter, the questionnaires were randomly sent to ear surgeons with expertise in cholesteatoma surgery to assess the presence of cholesteatoma or not (time 1 – T1). The image enhancement

TABLE 1 Number of responses for each image divided by imaging technique.

Image number	Clara No. of responses	Spectra A No. of responses	Spectra B No. of responses	Total
1	12	16	18	46
2	21	18	8	47
3	18	8	20	46
4	8	20	18	46
5	15	18	14	47
6	18	14	14	46
7	14	14	15	43
8	14	15	18	47
9	15	18	12	45
10	18	12	16	46
11	12	16	18	46
12	21	18	8	47
13	18	8	20	46
14	8	20	18	46
15	15	18	14	47
16	18	14	14	46
17	14	14	15	43
18	14	15	18	47
19	15	18	12	45
20	18	12	16	46
Total	306	306	306	918

Note: Due to differences in surgeon response to the invitation to participate in the present study, not every image was equally rated.

technique was indicated on every image, but no additional details were provided. After a few weeks, the same participants were asked to complete the same questionnaire for a second time (T2). General information (age, gender), details regarding the microscopic and endoscopic surgical experience, as well as subjective preferences regarding the three different DIE to perform the whole surgical procedure were assessed (usefulness on a scale from 1—not useful at all to 5—extremely useful—and a single choice for one of the three techniques).

2.3 | Statistical analysis

Variables were described in terms of mean or median and standard deviation (SD).

Chi-square tests were applied to responses at T1 to analyse the differences between the three imaging techniques in terms of distribution of correct and incorrect responses (accuracy) as defined by histopathology.

For the overall inter-rater and the intra-rater reliability, we calculated the intra-class-correlation (ICC)[12] based on a method for data sets with missing values by Brueckl.[13]

To assess the overall intra-rater reliability we calculated the ICC with a mean rating, two-way random effect model with absolute agreement. For the single image enhancement techniques, the intra-rater reliability was calculated by comparing T1 and T2 answers—did the participant give the same answer?—followed by calculating a Pearson's χ^2 test to assess the difference in agreements between the techniques (same vs. not same).

For calculating the overall inter-rater reliability, the ICC estimate was based on a mean rating ($k = 51$), one-way random effect model.

We calculated sensitivity and specificity values (with 95% confidence intervals [CIs]) for all three imaging techniques. Sensitivity refers to the ability of an evaluator to correctly classify an image as "diseased" (cholesteatoma), while specificity as the ability to correctly classify as "disease-free" (non-cholesteatomatous tissue).[14] Positive predictive value (PPV) and negative predictive value (NPV) were measured for each DIE modality, as well.

3 | RESULTS

3.1 | Participants at T1

Fifty-one participants (7 female [13.73%]) with an average age of 44.80 years (SD 9.94 years; range 27–66) from nine different countries filled out the questionnaires at T1. They all had experience in cholesteatoma surgery and microscopic ear surgery in particular, with 72.55% ($n = 37$) of them having performed more than 200 mainly microscopic cholesteatoma surgeries including endoscopy as a visualisation tool. Around 41% ($n = 21$) had performed

TABLE 2 All responses for the three imaging techniques.

	Clara Cholesteatoma			Spectra A Cholesteatoma			Spectra B Cholesteatoma		
	Yes	No		Yes	No		Yes	No	
Yes	116 (70.7%) *TP*	48 (29.3%) *FP*	164	124 (67.8%) *TP*	59 (32.2%) *FP*	183	126 (65.9%) *TP*	65 (34.0%) *FP*	191
No	37 (26.1%) *FN*	105 (73.9%) *TN*	142	29 (23.6%) *FN*	94 (76.4%) *TN*	123	27 (23.5%) *FN*	88 (76.5%) *TN*	115
	153	153	306	153	152	306	153	153	306

Abbreviations: FN, false negatives; FP, false positives; TN, true negatives; TP, true positives.

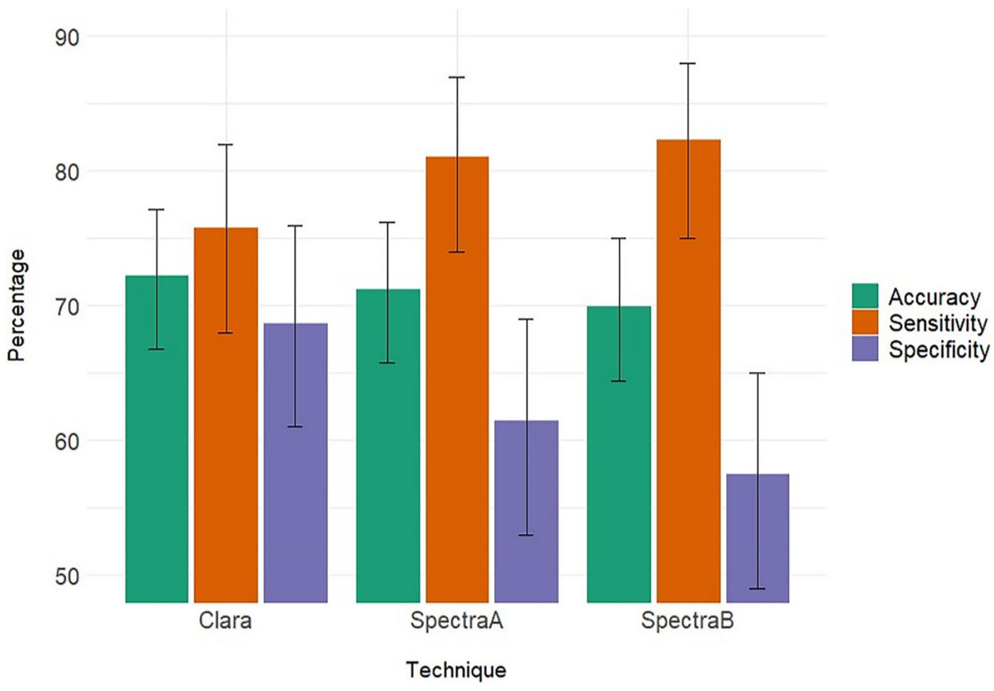

FIGURE 3 Accuracy, sensitivity and specificity (with the respective 95% CI) for the three imaging techniques.

more than 200 exclusive or mainly endoscopic cholesteatoma surgeries.

3.2 | Questionnaires and images at T1

Each questionnaire was answered by a minimum of 4 and a maximum of 8 participants. This resulted in an unbalanced response distribution for the 60 images (Table 1). Overall, when combining the number of responses for each of the selected 60 images, most of them were evaluated by a similar number of raters (mode = 46), with a range of 43–47.

3.3 | Responses at T1 and inter-rater reliability

Out of 918 responses overall, 653 (71.13%) were correct. Accuracy was highest with the Clara modality (221; 72.22%; 95% CI: 67%–77%) followed by the Spectra A (218; 71.24%; 95% CI: 66%–76%), and the Spectra B modality (214; 69.93%; 95% CI: 64%–75%). This difference was not statistically significant ($p = .7112$). Table 2 shows all responses across the three DIE techniques.

Sensitivity in cholesteatoma detection was higher for Spectra B (82.35%; 95% CI: 75%–88%), followed by Spectra A (81.05%; 95% CI: 74%–87%) and Clara (75.81%; 95% CI: 68%–82%). Specificity was higher for Clara (68.63%; 95% CI: 61%–76%), followed by Spectra A (61.44%; 95% CI: 53%–69%), and Spectra B (57.52%; 95% CI: 49%–65%), as shown in Figure 3.

PPV and NPV for each technique are included in Table 2. The highest PPV was reached by Clara (70.73%), followed by Spectra A (67.76%), and Spectra B (65.97%), while the highest NPV was reached by Spectra B (76.52%), followed by Spectra A (76.42%), and Clara (73.94%).

Figure 4 shows that certain images were very difficult to interpret, or information were interpreted wrongly with accuracy below 40% (image 4 and image 8). To illustrate this challenge, the most difficult images are presented in Figure 5.

Regarding inter-rater reliability we observed an overall agreement value of 0.8798 ($p < .001$, 95% CI: 0.8303–0.9200), indicating good reliability.[15]

3.4 | Responses at T2 and intra-rater reliability

Forty-three (84.31%) participants filled out the questionnaire at T2. Time between the two responses was a median of 45 days (mean 55.8 days, SD 27.8). The sample consisted of 38 male participants (88.37%) and had an average age of 44.7 years (SD 9.87). Out of 774 responses at T2, 609 (78.68%) were consistent with the responses from T1. The agreement was higher for images evaluated with the Spectra B modality (215, 83.34%) than with Clara and Spectra A (both 197, 76.36%). However, the difference was not statistically significant ($p = .082$). The overall agreement for intra-rater reliability was 0.7189 ($p < .05$, 95% CI: 0.6763–0.7559), indicating moderate reliability.[15]

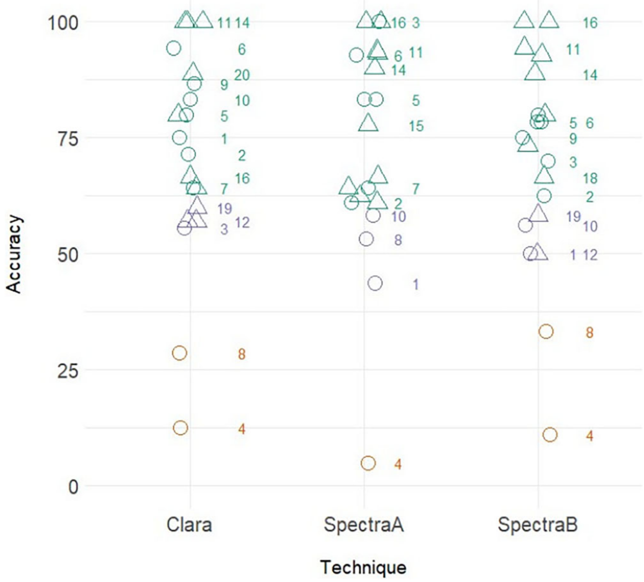

FIGURE 4 Accuracy for image number 1–10 (without cholesteatoma) and 11–20 (with cholesteatoma). Δ: Cholesteatoma, O: no cholesteatoma. Green: accuracy >60%, Purple: accuracy 40%–60%, Orange: accuracy: <40%.

3.5 | Subjective evaluation

Responses for subjective evaluation were collected from T1, or if missing, from T2. One participant failed to fill out the subjective evaluation questions; one participant had partial missing data. This resulted in 50 responses for the single choice and 49–50 responses for the usefulness rating. Participants' evaluation in terms of usefulness to perform an entire cholesteatoma surgery was highest for Clara (mean 3.32, SD 0.98). The overall DIE modality choice (one response only) was also in favour of Clara enhancement, with 29 votes for Clara, 11 votes for Spectra B and 10 votes for Spectra A.

4 | DISCUSSION

Residual cholesteatoma is the first cause of failure in cholesteatoma surgery, leading the surgeon to adopt sometimes demanding and invasive strategies, such as the "second look" tympanoplasty. DIE systems

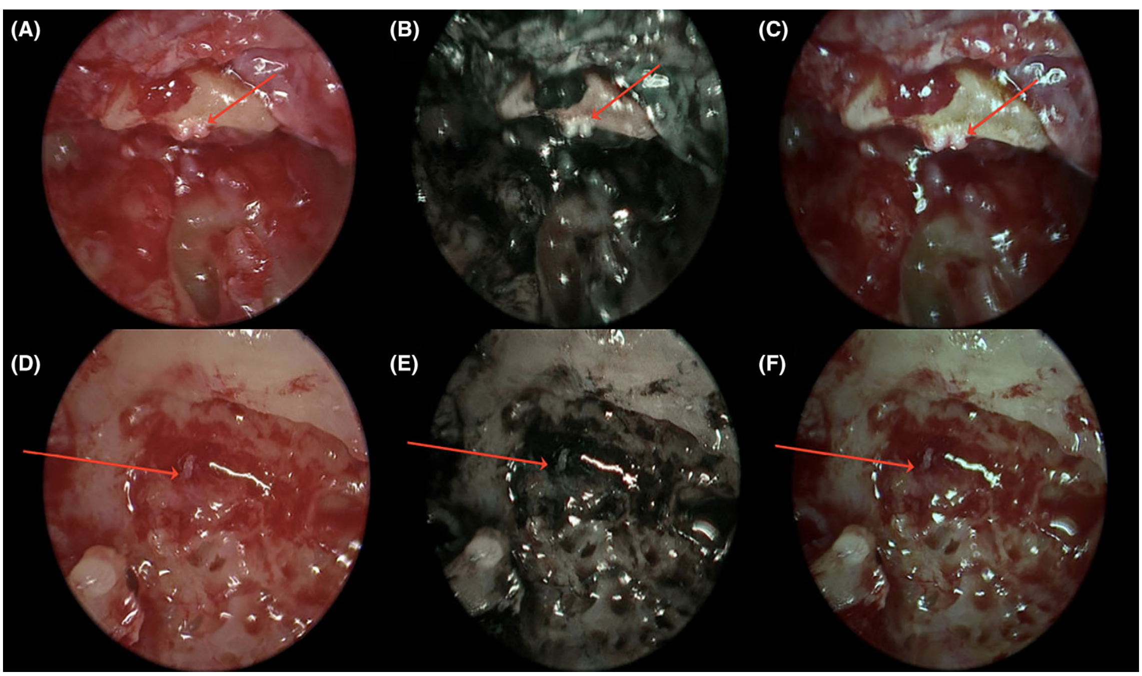

FIGURE 5 Examples of two special non-cholesteatoma situations leading to frequent false positive responses. Top row (A–C): tendon of the tensor tympany muscle mistaken for cholesteatoma. Bottom row (D–F): histologically proven granulation tissue and bonemeal from drilling, mimicking residual cholesteatoma. A/D = Clara, B/E = spectra A, C/F = spectra B.

have been developed to better identify and distinguish pathological from healthy tissue and may be a further advance in the intraoperative detection of residual cholesteatoma. The SPIES applies a visual–digital reprocessing of the endoscopic image, using a spectral separation algorithm of the record within a high-definition camera system. This system enhances the appearance of the mucosal surface, and the architecture of the vascular network within and under it, through five modalities (Clara, Chroma, Clara + Chroma, Spectra A and Spectra B).[10]

These DIE modalities have shown their value in two different settings:

a. Identification of abnormal vasculature (in terms of altered shape, number of vessels and branching vessels, presence of vessel loops or dot-like loops) in pathologic tissue, as compared with healthy tissue. The increased contrast of the vasculature, together with the surface mucosal changes and epithelial abnormalities, support the surgeon in the diagnostic endoscopy of epithelial cancer, distinguishing benign versus malignant lesions. Indeed, in several specialties such as ureteroscopy, pharyngo-laryngoscopy, sinonasal endoscopy and laparoscopy, SPIES has been applied for early tumour detection.[8–10,16,17]
b. Distinction between vascularized versus avascular tissue. Under Spectra filter, the former gets a more visible vascular pattern, while the latter appears more whitish and uniform. This tissue response to Spectra is the basis of the application of SPIES in cholesteatoma surgery to distinguish the cholesteatoma matrix from granulation tissue or normal mucosa. This allows the surgeon to better define the cholesteatoma extension and to remove the disease completely. To the best of authors' knowledge, the retrospective case series by Lucidi et al. was the first article to investigate the usefulness of the SPIES image enhancing system in ear surgery,[8] in facilitating the complete removal of the squamous epithelial, while sparing normal mucosa. According to the previously mentioned study, Spectra A and B filters in EES are deemed suitable to recognise cholesteatoma remnants.[8]

Another DIE system, the narrow band imaging (NBI) has been investigated in the otologic field. The NBI was suggested by Bruno C et al. in the differential diagnosis of middle ear masses, with paragangliomas and aural polyps showing a very peculiar NBI vascular texture.[18] Cordero Devesa et al. investigated the vasculatisation patterns of abnormal tympanic membrane areas with NBI, suggesting its role as supplementary diagnostic tool in the work-up of tympanic membrane perforations and surgical decision-making.[19] Nevertheless, it is in cholesteatoma surgery that the advantages of the DIE systems seem to provide the most interesting results.

In our study, the comparison of the three DIE techniques (Clara, Spectra A, Spectra B) of the SPIES makes clear that each of those modalities brings along its own advantages. When considering the surgeons' point of view on the suitability of the three image-improving modalities, a general attitude in favour of the use of Clara followed by Spectra B and lastly Spectra A was found. This is expected, as Clara is the "state-of-the-art" technique used to perform EES. The Spectra A and B techniques have recently been introduced to depict residual cholesteatoma after complete removal of the disease.

We investigated and quantified separately the added value of Clara, Spectra A and Spectra B for the first time. In all three imaging techniques, the presence of cholesteatoma is recognised more successfully than its absence, meaning a better sensitivity than specificity for all imaging modalities. This difference becomes very apparent with Spectra B, when comparing it with Clara used as a reference standard. With the highest sensitivity but the lowest specificity, a lot of tissue is misinterpreted as cholesteatoma but only few cholesteatomas are missed. In our opinion, this increase in sensitivity justifies its use at the end of every cholesteatoma surgery. Using the Spectra B technique most cholesteatoma-remnants may be detected and results regarding residual cholesteatoma may be improved. Moreover, a high intra-rater reliability was observed and was highest for Spectra B. In our opinion, this further indicates an additional value regarding the performance of spectra B. Clara in contrast has the highest accuracy overall. Its general image properties with high illumination and without modification of the information provided by white light, makes it most suitable to perform the surgery itself. Spectra A lies between Clara and Spectra B in terms of sensitivity–specificity-difference, as well as in terms of detection, missing, identification and misidentification of cholesteatoma. Therefore, we do not see any indication in the use of the Spectra A technique in cholesteatoma surgery.

Interestingly, some special situations require special considerations while using digital image enhancement in EES (Figure 5). For example, the tendon of the tensor tympani muscle appears bright at its insertion in the malleus and may be mistaken for squamous epithelium. Similarly, upon thorough review of the image set represented in Figure 5D–F and related histopathology, it appears that bone fragments produced during drilling may also be mistaken for cholesteatoma. In summary, Clara may be considered the most appropriate image modality for use during surgery. However, as the removal of small amounts of inflamed mucosa has few consequences for the patient, whereas cholesteatoma remnants can result in serious complications and require a second operation, we recommend the use of Spectra B as a final overview at the end of cholesteatoma surgery, in order to avoid missing any pathological finding. Indeed, the combined use of Clara and Spectra B, as proposed, permits to increase the overall accuracy of the endoscopic visualisation up to 75.4% in our study.

The interpretation of our results should consider that instead of p values, we used confidence intervals to show the difference between techniques. Almost all point estimates in the current article lie within the other techniques' confidence intervals, therefore we do not have any statistically significant differences on the 0.05% level. However, since the sample is small, statistically non-significant results are not surprising. Despite not significant, the increased sensitivity of Spectra B may have a clinically significant implication, as it indicates a tendency of Spectra B to a higher detection rate of residual cholesteatoma, as compared with Clara or Spectra A. Therefore, in our opinion, balancing the possible disadvantage of extended surgical time for additional check with SPIES with the advantage of a higher rate of radicality in cholesteatoma removal, a final check with Spectra B may be justified.

The present study includes responses from ear surgeons with different surgical background, different experience and from different countries. This is a strength of the study, as it explores the accuracy of the DIE technique in ear surgeons with variable experience in dealing with endoscopic images of the middle ear, eventually providing data which can be considered closer to real-life (high external validity).

Since not all surgeons who were invited to fill out the questionnaires responded, we eventually obtained an uneven distribution of responses across the questionnaires. As a result, not all images were presented with each technique the same number of times overall. This is certainly a limitation of the current study, as some responses therefore influenced the overall result heavier than others. Nonetheless, due to the high number of responses received, the limited availability of ear surgeons overall and also limited time resources, we decided to stop data collection with a slightly unbalanced distribution. The involvement of a high number of surgeons was considered in order to reduce the bias associated with an unbalanced distribution of expertise level of surgeons e.g. too many experienced surgeons or too many novice surgeons.

Another limitation is represented by the use of the same order of images in the questionnaire between T1 and T2, which could have influenced the intra-rater reliability measure. However, as the focus of the current study was on the results of the first time point, this limitation can be neglected.

Finally, another limitation can be the static nature of pictures, which is different from the dynamic visualisation, which occurs during EES along with the manipulation of the suspicious tissue. Indeed, accuracy in the detection of cholesteatoma could be affected by the dynamic movements of the endoscope, changes in the point of view, light reflexion, direct suction and information about previous surgical steps.

5 | CONCLUSIONS

Digital enhancement technologies are applicable to EES. Most otologic surgeons preferred Clara throughout cholesteatoma surgery. During the final check after complete cholesteatoma removal, Spectra B showed the highest sensitivity in the detection of cholesteatoma residuals as compared with Clara and Spectra A. Thus, Spectra B may be recommended to avoid missing any cholesteatoma residuals during EES.

AUTHOR CONTRIBUTIONS

Talisa Ragonesi and Laura Niederhauser study design, data analysis and drafting the article; Ignacio Javier Fernandez data collection, data interpretation, drafting the manuscript, final review; Giulia Molinari data collection and final critical review of the manuscript; Marco Caversaccio and Livio Presutti critical review of the manuscript; Lukas Anschuetz study design, drafing the manuscript, critical review of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

Data available on request from the authors.

ETHICS STATEMENT

The study was approved by the local ethical committee (Kantonale Ethikkommission Bern KEK2019-00555).

ORCID

Ignacio Javier Fernandez https://orcid.org/0000-0002-9120-6586
Giulia Molinari https://orcid.org/0000-0002-3402-4364

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