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Optical assessment of scars after endoscopic mucosal resection of large colorectal polyps in a multicenter, community hospital setting: is routine biopsy still necessary?

Lonne W Meulen, Roel M Bogie, Peter D Siersema, Bjorn Winkens, Marije S Vlug, Frank H Wolfhagen, Martine A Baven-Pronk, Michael P van der Voorn, M. P Schwartz, Lauran Vogelaar, Tom C Seerden, W.L. Hazen, R W Schrauwen, Lorenza Alvarez Herrero, Ramon Michel Schreuder, Annick B van Nunen, Gijs J de Bruin, Willem A Marsman, Marc de Bièvre, Robert Roomer, Rogier de Ridder, Maria Pellisé, Michael J. Bourke, Ad Masclee, Leon M Moons.

Affiliations below.

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Trial registration: NTR7477, Netherlands National Trial Register (http://www.trialregister.nl), Multicentre cluster randomised trial

Abstract:
Background and study aims: Piecemeal EMR of large (≥20mm) non-pedunculated colorectal polyps (LNPCPs) is succeeded by a 6-month surveillance endoscopy to evaluate the post-EMR scar for recurrence. Data from expert centers suggest that routine tattoo placement and scar biopsies can be omitted, but data from community hospitals are lacking.
Patients and methods: In a post-hoc analysis of the STAR-LNPCP study (NTR7477), containing prospective data on 6-month post-pEMR scar assessments in 30 Dutch community hospitals (October 2019 to May 2022), the agreement between optical assessment and histological confirmation by routine biopsies was evaluated. Documentation of optical characteristics, imaging, and biopsies of the post-EMR scar were performed according to a standardized protocol.
Results: In 1277 post-EMR scar assessments, identification of the scar was achieved in 1215/1277 (95%). Tattoo placement did not influence scar identification. Scar biopsy was performed in 1050/1215 cases (86%). Recurrences were seen in 200/1050 cases (19%). There was a good agreement between optical assessment of recurrence and histological confirmation (Cohen's kappa 0.78 [0.73-0.83]). The NPV was 98% [97-99%] and the PPV was 74% [68-80%]. Higher false positive rate was seen after prior

use of clips (11% vs. 5%, p=0.017). Dedicated endoscopists identified the scar more often (96% vs. 88%, p<0.001), and showed a lower optical recurrence miss rate (1%vs. 3%, p=0.111) compared to non-dedicated endoscopists.
Conclusion: Based on this multicenter community hospital study, routine tattoo placement and scar biopsies of the post-EMR scar can be omitted. Assessment of post-EMR scars by dedicated endoscopists is advised.

Corresponding Author:
Lonne W Meulen, Maastricht University Medical Centre+, Department of Gastroenterology and Hepatology, Maastricht, Netherlands, lonne.meulen@maastrichtuniversity.nl

Affiliations:
Lonne W Meulen, Maastricht University Medical Centre+, Department of Gastroenterology and Hepatology, Maastricht, Netherlands
Lonne W Meulen, Maastricht University, GROW School for Oncology and Reproduction, Maastricht, Netherlands
Roel M Bogie, Maastricht University Medical Centre+, Department of Gastroenterology and Hepatology, Maastricht, Netherlands
[...]
Leon M Moons, University Medical Centre Utrecht, Department of Gastroenterology and Hepatology, Utrecht, Netherlands

Thieme

Optical assessment of scars after endoscopic mucosal resection of large colorectal polyps in a multicenter, community hospital setting: is routine biopsy still necessary?

Lonne W.T. Meulen[1,2], Roel M.M Bogie[1,2], Peter D. Siersema[3], Bjorn Winkens[4,5], Marije S. Vlug[6], Frank H.J. Wolfhagen[7], Martine A.M.C. Baven-Pronk[8], Michael P.J.A. van der Voorn[9], Matthijs P. Schwartz[10], Lauran Vogelaar[11], Tom C.J. Seerden[12], Wouter L. Hazen[13], Ruud W.M. Schrauwen[14], Lorenza Alvarez Herrero[15], Ramon-Michel Schreuder[16], Annick B. van Nunen[17], Gijs J. de Bruin[18], Willem A. Marsman[19], Marc de Bièvre[20], Robert Roomer[21], R. de Ridder[1], Maria Pellisé[22], Michael J. Bourke[23], Ad A.M. Masclee[1], Leon M.G. Moons[24] (on behalf of the OPTICAL-STAR Working Group).

[1]Department of Internal Medicine, Division of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands

[2]GROW, School for Oncology and Reproduction, Maastricht University, Maastricht, The Netherlands

[3]Department of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

[4]Department of Methodology and Statistics, Maastricht University, Maastricht, The Netherlands

[5]CAPHRI, Care and Public Health Research Institute, Maastricht University, Maastricht, The Netherlands

[6]Department of Gastroenterology and Hepatology, Dijklander Hospital, Hoorn, The Netherlands.

[7]Department of Gastroenterology and Hepatology, Albert Schweitzer Hospital, Dordrecht, The Netherlands.

[8]Department of Gastroenterology and Hepatology, Groene Hart Hospital, Gouda, The Netherlands.

[9]Department of Gastroenterology and Hepatology, Haga Hospital, Den Haag, The Netherlands.

[10]Department of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, The Netherlands.

[11]Department of Gastroenterology and Hepatology, Diakonessenhuis, Utrecht, The Netherlands.

[12]Department of Gastroenterology and Hepatology, Amphia Hospital, Breda, The Netherlands.

[13]Department of Gastroenterology and Hepatology, Elisabeth-Tweesteden Hospital, Tilburg, The Netherlands.

[14]Department of Gastroenterology and Hepatology, Bernhoven, Uden, The Netherlands.

[15]Department of Gastroenterology and Hepatology, Sint Antonius Hospital, Nieuwegein, The Netherlands.

[16]Department of Gastroenterology and Hepatology, Catharina Hospital Eindhoven, Eindhoven, The Netherlands.

[17]Department of Gastroenterology and Hepatology, Zuyderland Medical Center, Sittard-Geleen, The Netherlands.

[18]Department of Gastroenterology and Hepatology, Tergooi Hospital, Hilversum, The Netherlands.

[19]Department of Gastroenterology and Hepatology, Spaarne Gasthuis, Haarlem, The Netherlands.

[20]Department of Gastroenterology and Hepatology, Viecuri Medical Center, Venlo, The Netherlands.

[21]Department of Gastroenterology and Hepatology, Franciscus Gasthuis & Vlietland, Rotterdam, The Netherlands

[22]Department of Gastroenterology, Hospital Clínic de Barcelona, Barcelona, Spain.

[23]Department of Gastroenterology and Hepatology, Westmead Hospital; Westmead Clinical School, University of Sydney, Sydney, New South Wales, Australia

[24]Department of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands.

OPTICAL-STAR Working Group

Yasser A. Alderlieste, Department of Gastroenterology and Hepatology, Rivas, Gorinchem, The Netherlands.
Alaa Alkhalaf, Department of Gastroenterology and Hepatology, Isala Clinics, Zwolle, The Netherlands.
Marloes Bigirwamungu-Bargeman, Department of Gastroenterology and Hepatology, Medical Spectrum Twente, Enschede, The Netherlands.
Femke Boersma, Department of Gastroenterology and Hepatology, Gelre Hospitals, Apeldoorn, The Netherlands.
Philip Bos, Department of Gastroenterology and Hepatology, Gelderse Vallei Hospital, Ede, The Netherlands.
John Groen, Department of Gastroenterology and Hepatology, Sint Jansdal Hospital, Harderwijk, The Netherlands.
Edith Kuiper, Department of Gastroenterology and Hepatology, Maasstad Hospital, Rotterdam, The Netherlands.
Monigue E. van Leerdam, Department of Gastroenterologic Oncology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands & Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands.

Jos M. Ramaker, Department of Gastroenterology and Hepatology, Elkerliek Hospital, Helmond, The Netherlands.
Linda B.J. Roberts-Bos, Department of Gastroenterology and Hepatology, Laurentius Hospital Roermond, Roermond, The Netherlands.
Esther Stoop, Department of Gastroenterology and Hepatology, Haaglanden Medical Center, Den Haag, The Netherlands.
Karsten Thurnau, Department of Gastroenterology and Hepatology, Hospital Group Twente, Almelo, The Netherlands.
Roland de Vries, Department of Gastroenterology and Hepatology, Deventer Hospital, Deventer, The Netherlands.

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Correspondence:
dr. Leon M.G. Moons
l.m.g.moons@umcutrecht.nl
Mob: +31-6-145 99 001 / Tel: +31-88-75 55 55
Heidelberglaan 100, 3508 GA Utrecht
The Netherlands

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Abbreviations: CI: confidence interval; EMR: endoscopic mucosal resection; ESCA: post-EMR scar clip artifact; ESD: endoscopic submucosal dissection; LNPCP: large non-pedunculated colorectal polyp; NPV: negative predictive value; OR: odds ratio; PPV: positive predictive value; SD: standard deviation.

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Abstract

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Introduction

The most commonly used treatment modality for non-invasive LNPCPs is endoscopic mucosal resection (EMR). A first surveillance after 6 months to check for local recurrence is advocated in several guidelines [1, 2, 3]. Until recently, guidelines recommended routine biopsies of the post-EMR scar to confirm the absence of recurrence, and to place a tattoo for post-EMR scar identification.[2, 4] The recently updated ESGE guideline stated that routine biopsies can be omitted if sufficiently trained endoscopists have evaluated the scar tissue with enhanced imaging[1], using a standardized imaging protocol.[5, 6] Importantly, detection of the post-EMR scar was possible with easy-to-use optical evaluation criteria, without the need for universal tattoo placement.[7]

However, it remains uncertain whether these results can be extrapolated to non-expert centers [8]. Therefore, in the setting of this prospective, multicenter study[9], we investigated whether the diagnostic accuracy of optical assessment of post-EMR scars for recurrence at a community level is high enough to refrain from standardized biopsies and the need for universal tattoo placement.

Methods

In this post-hoc analysis of the STAR-LNPCP study (NTR7477), follow-up colonoscopies after EMR of LNPCPs were included in 30 Dutch community hospitals from October 2019 to May 2022. The STAR-LNPCP study was a multicenter, cluster randomized trial, in which 59 endoscopists from 30 community hospitals included all consecutive LNPCPs. Participating hospitals were randomly chosen and were asked to nominate 1-2 candidates from their endoscopists dedicated to large EMR. Randomization in a training and control group was performed on cluster (center) level. Endoscopists from 15 centers were additionally trained in endoscopic mucosal resection of LNPCPs, while the endoscopists of the other 15 centers were not. Further study details are described in the original article by Meulen et al.[9] The study was approved by the Medical Ethical Review Committee of the Maastricht University Medical Center (MEC 2017-0017). All patients provided written informed consent prior to the study.

Patient selection

Consecutive patients undergoing follow-up colonoscopies after previous EMR of an LNPCP were included. Exclusion criteria were initially incomplete EMR, IBD, and poor bowel preparation (Boston Bowel Preparation Score <2 for the concerned segment). All patients that underwent a 6-months surveillance colonoscopy in the STAR-LNPCP study were included in this post-hoc analysis (Figure 1).

Baseline characteristics

Patient characteristics such as age, sex, ASA classification, medication use, and medical history were obtained from case record forms. Baseline lesion- and treatment characteristics were obtained from endoscopy- and histology reports. Baseline lesion characteristics consisted of size, morphology, location, accessibility, enhanced imaging, and initial histology. Baseline treatment characteristics consisted of EMR type (en bloc or piecemeal), use of

adjunctive treatment (e.g. hot avulsion, cold avulsion, snare tip soft coagulation, argon plasma coagulation), use of adjuvant thermal ablation, use of clips and tattoo placement. In case there was more than 1 LNPCP in a patient, only one LNPCP per patient was randomly included in the original study [9].

E-module assessment of post-EMR scar

Before starting the study, participating endoscopists had the opportunity to watch an e-module regarding the identification and assessment of post-EMR scars. In this e-module, criteria to identify the scar, the standardized scar assessment, and biopsy protocol were explained. Furthermore, the difference between recurrence and post-EMR scar clip artifact (ESCA) was demonstrated by discussing several examples. The e-module topics and order, as well as some example images, are presented in Supplementary Material 1.

Standardized assessment of the EMR-scar and biopsy protocol

A standardized protocol was followed during the assessment of the EMR-scar. This included in-vivo evaluation of the scar and potential recurrent neoplasia, with the combined use of white light, advanced imaging and zoom/near focus, and taking pictures for every imaging modality. The scar was carefully assessed for recurrent neoplasia and the following characteristics of the scar were documented: location of the scar, size of the scar, presence of recurrence, certainty (yes/no) about the presence/absence of recurrence, unifocal or multifocal recurrence, location of recurrence (at the edge, in the center, or both), and the morphology of recurrence. When recurrence was present, this was treated and documented in the endoscopy report. When there were no signs of recurrence, biopsies of the EMR-scar were taken according to a standardized biopsy protocol: depending on the size and shape (e.g., straight line or round) of the scar, 1-3 biopsies were taken from the center of the scar, and in the periphery of the scar at least one biopsy per quadrant was performed. Biopsies from the center and periphery of the EMR scar were separately presented for histological evaluation in the pathology lab.

Tattoo placement

Placement of a tattoo on the contralateral side of the post-EMR defect was left to the discretion of the endoscopist during the initial colonoscopy.

Outcomes

The primary outcome was optical assessment of recurrence. Furthermore, diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. The predictive value of tattoo placement for identification of the scar was also evaluated.

In addition, differences in post-EMR scar identification between dedicated and non-dedicated endoscopists were evaluated. Dedicated endoscopists were defined as endoscopists participating in the STAR-LNPCP study and performing large polypectomies in their center. Non-dedicated endoscopists were defined as the endoscopists not participating in the STAR-LNPCP study and not primarily performing large polypectomies in their center. At the start of the STAR-LNPCP study, participating centers were asked which doctors performed large EMRs in their centers. Furthermore, the effect of prior clipping on the optical assessment of post-EMR recurrence was evaluated, with the hypothesis that clipping leads to post-EMR scar clip artifacts (ESCA) which are wrongly mistaken as recurrence. To evaluate this hypothesis, PPV of clipped EMR defects was compared to PPV of non-clipped EMR defects. Optical recurrence miss rate was defined as all histologically confirmed recurrences that were optically assessed as negative for recurrence, calculated as a proportion of the total number of scar inspections performed. False positives were defined as all optically assessed recurrences, that were not confirmed as a recurrence by histology, calculated as a proportion of total scar assessments.

Statistical analysis

For descriptive statistics, categorical variables are presented as numbers and percentages, and numerical variables are presented as means with standard deviation or medians with interquartile range (25^{th} to 75^{th} percentile: p25-p75).

Pearson's Chi-squared or Fisher's exact test were used to compare groups regarding categorical variables.

Risk regression with correction for clustering of patients within endoscopists (generalizing estimation equations (GEE) with exchangeable covariance structure and probit link) was performed to evaluate which variables (dedicated or non-dedicated endoscopist, submucosal tattoo, size of initial LNPCP, location, accessibility, morphology) were independently related to the identification of the post-EMR scar. Furthermore, the same analysis was performed to evaluate the effect of clipping on optical recurrence assessment, with correction for dedicated vs. non-dedicated endoscopists. Next to the intra-class correlations (ICCs) obtained from these GEE analyses, we report the adjusted risk ratios with corresponding 95% confidence intervals (RR, 95%CI), and p-values for each risk factor, corrected for all other risk factors in the model.. As this included multiple testing, the Bonferroni corrected 95%CIs and p-values are provided as well.

Cohen's kappa was used to determine the agreement between the optical assessment of recurrence and histological evaluation of biopsies. According to the definition proposed by Landis and Koch, a kappa of 0.61-0.80 was considered "moderate to good" and a kappa of 0.81-1.00 was considered "(almost) perfect" [10]. Furthermore, we calculated NPV, PPV, sensitivity, specificity, and overall diagnostic accuracy with a 95% confidence interval.

Analyses were performed in a per-protocol manner, including only scars that were found, assessed, and biopsied. Additionally, intention-to-treat analysis was performed, assuming that scars that were not found and scars that were not biopsied, would not have shown any signs of recurrence when histological evaluation of biopsies would have occurred.

Furthermore, sensitivity analysis with cluster bootstrapping was performed, were correction for clustering of patients/scars within the same endoscopist was made. A two-sided p-value ≤0.05 (after Bonferroni correction) was considered statistically significant.

Statistical analysis was performed using IBM SPSS Statistics v27.0.0, except for cluster bootstrapping, which was performed using R (v4.3.1). Confidence intervals for proportions (with continuity correction) were computed using http://vassarstats.net/prop1.html.

Results

Baseline characteristics

A total of 1277 patients with 6-months surveillance colonoscopy after complete endoscopic resection of an LNPCP were included (Table 1). Mean age of patients was 68 (SD 9) years, 45% was female, median size of the LNPCPs was 30 mm (p25-p75: 25-40mm), and 64% were located in the proximal colon.

Surveillance colonoscopy and assessment of the post-EMR scars was performed by 161 endoscopists in 30 community hospitals, of whom 59 (37%) were dedicated endoscopists.

A total of 1215 scars were identified and assessed for the presence/absence of recurrence (Figure 1). In 1060/1215 cases (87%, 95%CI [85-89]), a dedicated large polypectomy endoscopist assessed the post-EMR scar, while in 155 cases (13%, 95%CI [11-15]), assessment of the post-EMR scar was performed by an endoscopist not specialized in large polypectomy (non-dedicated). The cohort of hospitals was representative for the Dutch community hospital population.

Post-EMR scar identification

A tattoo was placed in 488/1277 cases (38%, 95%CI [36-41]). In 1215 of 1277 cases (95%, 95%CI [94-96]), the post-EMR scar was identified and assessed during surveillance colonoscopy. The presence of a submucosal tattoo was not associated with higher identification rate of the post-EMR scar (95% vs. 95%, Bonferroni corrected p=1.000)(Table 2). Performing scar inspection by a dedicated endoscopist instead of non-dedicated endoscopist was independently associated with higher scar identification rate (96% vs. 88%, Bonferroni corrected p<0.001). Scar identification rate increased with increasing LNPCP size, from 92% (95%CI [89-95]) in 20-29mm lesions, to 95% (95%CI [92-97]) in 30-39mm lesions, and 98% (95%CI [96-99]) in ≥40mm lesions (overall Bonferroni corrected p=0.034). Other lesion characteristics (proximal location, difficult accessibility, and flat morphology) did not significantly influence scar identification rate.

Post-EMR scar assessment

All post-EMR scars were assessed by high-definition white light and advanced imaging, as validated by the presence of procedural images. In 1097/1215 (90%, 95%CI [88-92]) of the post-EMR scars, the use of zoom or near focus could be confirmed by inspection of procedural images. Histology of the post-EMR scar by biopsies or treatment of recurrence was obtained in 1050 cases. The median number of biopsies was 4 (p25-p75 3-5).

In Table 3, the outcomes of optical assessment compared with histological confirmation by biopsies are presented. The overall prevalence of recurrence in this prospective cohort was 200/1050 (19%, 95%CI [17-22]). The optical diagnosis of post-EMR recurrence showed a high diagnostic accuracy of 93% (95%CI [91-94]), with a sensitivity of 93% (95%CI [88-96]), a specificity of 92% (95%CI [90-94]), a PPV of 74% (95%CI [68-80]), and NPV of 98% (95%CI [97-99]). The agreement between the optical assessment of recurrence and histological evaluation of biopsies was good, with a Cohen's kappa (κ) of 0.78 (95%CI [0.73-0.83]). Intention-to-treat analysis, in which non-biopsied post-EMR scars were included, and the assumption was made that optical assessment and histology would both be negative for recurrence, showed similar results (Supplementary material 2, Table 1).

Sensitivity analysis, in which clustering of patients within endoscopists is taken into account, also showed similar results (sensitivity 93% (95%CI [90-96]), specificity 93% (95%CI [90-95]), PPV 74% (95%CI [68-81]), NPV 98% (95%CI [97-99]), diagnostic accuracy 93% (95%CI [91-95])).

The optical recurrence miss rate was 1% (11/960; 95%CI [0.6-2.0]) for dedicated endoscopists and 3% (3/90; 95%CI [1.1-9.3]) for non-dedicated endoscopists (p=0.111).

Influence of clip placement on post-EMR scar assessment

In 223 of 1050 histologically evaluated scars (21%), clips were used to close the initial EMR defect. PPV for optical diagnosis of recurrence in post-EMR scars decreased after clipping, from 78% (95%CI [72-84]) in the non-clipped group to 63% (95%CI [50-74]) in the clipped

group. Risk regression accounting for clustering of patients within endoscopist (GEE; ICC = 0.004) on accuracy of optical recurrence assessment with correction for dedicated vs. nondedicated endoscopists showed an RR for clipped vs. non-clipped of 0.73 (95%CI [0.58-0.90]; p=0.004). Furthermore, proportion of false positives out of total assessments was higher after clipping (11% vs. 5%; p=0.017).

Certainty of post-EMR scar assessment

There was high certainty about post-EMR scar assessment in 95% vs. 94% of cases performed by dedicated vs. non-dedicated endoscopists, respectively (p=0.709). In the post-EMR scars where endoscopists identified recurrence with certainty (n=187), the PPV was 86% (95%CI [80-90]), while this was only 41% (95%CI [29-54]) in the scars where endoscopists were uncertain about the presence of recurrence (n=63).

False positive cases in the uncertain group (n=37) were more often biopsied and less often endoscopically treated, compared to false positive cases in the certain group (n=27). Biopsies were performed in 20/37 (54%, 95%CI [37-70]) cases in the uncertain group, compared to 9/27 (33%, 95%CI [17-54]) cases in the certain group. Endoscopic treatment was performed in 17/37 (46%, 95%CI [30-63]) cases in the uncertain group, compared to 18/27 (67%, 95%CI [46-83]) in the certain group (p=0.090). Endoscopic treatment of false positive cases was performed with re-EMR, cold snare polypectomy, cold avulsion with snare tip soft coagulation, argon plasma coagulation, or hot snaring.

Discussion

In this post-hoc analysis of the STAR-LNPCP study[9], optical assessment of post-EMR scars for recurrence at 6 months was excellent, with a sensitivity of 93% (95%CI [88-96]), a specificity of 92% (95%CI [90-94]), a NPV of 98% (95%CI [97-99]), and a good agreement between optical assessment and histological confirmation, represented by a Cohen's kappa (κ) of 0.78 (95%CI [0.73-0.83]). Dedicated endoscopists were more likely to identify the post-EMR scar (96% vs. 88%). Tattoo placement was not significantly associated with scar identification. Clipping of the post-EMR defect significantly complicated the correct optical assessment of the scar, as demonstrated by a higher number of false positives after clipping (11% vs. 5%).

In this study, scar identification was associated with the experience of the endoscopist but not significantly with the placement of a tattoo, which argues against universal placement of a tattoo after pEMR. A recent Delphi agreement report stated that a tattoo should be placed for polyps larger than 20 mm resected piecemeal with additional predictors of recurrence [11]. There was an 84% level of consensus. The following additional predictors were suggested: a size larger than 40 mm, the use of adjunctive thermal techniques, SMSA score of 4, and a prior failed attempt. This advice is grounded on the assumption that it is difficult to identify the scar in a significant number of cases, although clear data on the magnitude are limited [12]. A submucosal marking would support correct identification of the scar. However, a more recent study showed that application of easy-to-use criteria such as a pale area, convergence of folds, and disruption of the normal colonic surface microvasculature showed a scar identification rate of 99.7% [5, 7]. Although these results were obtained in high volume, experienced centers, it shows that it is related to experience. Our study confirms these findings in a real-life practice setting. Scars of especially larger LNPCPs were more easily identified because of more clearly visible features. Altogether, these results provide an argument for a practice wherein performing EMR endoscopists will evaluate the post-EMR

scar themselves instead of universal tattoo placement. Tattoo placement has been shown to interfere with successful resection if the tattoo is aligning the scar or residual adenoma, might accidently be injected in the peritoneal cavity or mesorectum, and adds unnecessary costs. It should therefore be restricted to anticipated difficult to identify post-pEMR scars.

On a national level, outcomes are similar to outcomes reported in tertiary centers. This is demonstrated by a NPV of 98% and a PPV of 74% in this national cohort, which is in line with NPVs and PPVs in tertiary centers as reported by the Australian ACE cohort (NPV 99%, PPV 76%) and ESCAPE trial (NPV 97%, PPV 81%)[5, 6]. Clipping significantly complicated the optical assessment of post-EMR scars. With increasing use of clips to prevent post-polypectomy bleeding, ESCAs will be increasingly detected [13, 14]. The presence of ESCAs decreased the PPV and increased the rate of false positives, in which unnecessary endoscopic treatment was performed. However, careful inspection of the post-EMR scar with advanced imaging should lead to a correct differentiation between ESCA and neoplastic recurrence. Furthermore, the current study showed that uncertainty about the presence of recurrence led to more frequent biopsies instead of direct treatment. The latter, i.e., optical assessment and treatment of a suspected recurrence in the same session, is advised in current guidelines [2, 15]. Although recurrence was less often observed in uncertain cases, overtreatment of non-neoplastic tissue outweighs postponing treatment of the recurrence to obtain histological confirmation, as it results in unnecessary additional costs and burden for the patient. The most used treatment modalities for recurrence (CAST, hot avulsion, cold/hot snare polypectomy) are known to have only few complications. Furthermore, most recurrences have shown to be small, unifocal and easy to treat. While endoscopic overtreatment is not desirable, it should be noted that the risk of missing neoplastic recurrence is much more concerning than overtreatment of non-neoplastic tissue. Therefore, treatment of any inconclusive nodules or areas in a post-EMR scar should still be performed. Additionally, when there is absolute certainty about the absence of recurrence, biopsies can be omitted.

This study is important because it adds to growing evidence that optical diagnosis is highly accurate for the exclusion of post-EMR recurrence [16, 17]. Data are obtained from a structured multicenter trial, on community level, with a large number of post-EMR scars. Therefore, results are considered generalizable to everyday colonoscopy practice. Obtaining a NPV of 98% on community level, clearly surpassing the PIVI threshold of 90%, shows that with high certainty optical diagnosis, standard biopsies can be omitted and result in significant cost reductions.

Several limitations should also be emphasized. The first limitation concerns the observed protocol violations in 13.5% of cases in this study. According to the study protocol, all post-EMR scars should be biopsied in a standardized manner. However, in 165 out of 1215 this was not performed. This could have led to an overestimation of diagnostic accuracy and NPV of optical assessment of the post-EMR scar, because of possible false negative cases not being histologically confirmed in this cohort. However, given the large number of cases in this cohort and the high NPV with small confidence intervals obtained, it is unlikely that these protocol violations would have significantly changed outcomes.

A second limitation is that the follow-up is limited to the first surveillance at 6 months. As a result, it could be possible that late recurrences may have been missed. It is known that approximately 4% still develop a recurrence despite showing a scar without recurrence at 6 months [3, 18]. Routine biopsies are however unlikely to have a significant impact on this number of late recurrences. The biopsy protocol was extensive with biopsies at the center and at the periphery, with a median number of 4 biopsies. Sampling error could have occurred but would be inherent to implementation of routine scar biopsies, and therefore does not dismiss another follow-up endoscopy at 18 or 36 months after EMR.

A third limitation might be the effect of participating in a randomized controlled study on the performance of the endoscopist after training. An e-learning was offered at the beginning of the study. Although the e-learning on scar identification and recurrence detection was offered to all participants to increase the quality of the study, and by itself was not part of the study intervention, it may have caused a learning effect. This may limit the

generalizability of our results to an untrained group of community endoscopists. The uptake of the e-learning was 49%. The NPV in a group of trained dedicated endoscopists was similar compared to a group of untrained dedicated endoscopists (99% vs. 98%). The effect of training is therefore likely to be limited. Furthermore, participating in a study may have caused a Hawthorne effect, increasing the performance of the participants, which would also limit the generalizability to real-life practice.

A fourth limitation is a lack of power due to low numbers in the difference in optical recurrence miss rate between dedicated vs. non-dedicated endoscopists. Furthermore, the frequent use of zoom/near focus may limit the generalizability of our study, since this might not be available in every hospital. Previous studies have shown that the use of zoom/near focus increases the detection rate of recurrence[5, 6]. Lastly, post-EMR scar identification was performed by a dedicated endoscopists in the majority of cases in our study. This also might limit generalizability of our results to the population of endoscopists working in community practice settings. However, this further underlines the importance of dedicated endoscopists performing post-EMR scar assessment.

In conclusion, the quality of optical assessment for recurrence of the post-EMR scar at a community level was found to be high. Identification of the post-EMR scar is high and optical recurrence miss rate is low, especially in dedicated endoscopists. Therefore, routinely taking biopsies of the post-EMR scar could be omitted, as well as universal tattoo placement after pEMR.

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Tables and figures

Figure 1. Flowchart inclusion post-EMR scars.

Abbreviations:
LNPCP: large non-pedunculated colorectal polyp; EMR: endoscopic mucosal resection; eFTR: endoscopic full-thickness resection; ESD: endoscopic submucosal dissection

Table 1. Patient and index colonoscopy characteristics

	Prospectively included patients N=1277
Patient characteristics	
Age in years, mean (SD)	68 (9)
Female gender, n (%)	573 (45%)
ASA-classification, n (%) - ASA I - ASA II - ASA III - ASA IV	 238 (19%) 871 (68%) 167 (13%) 1 (0%)
Index colonoscopy and lesion characteristics	
Indication colonoscopy, n (%) - Bowel cancer screening program - Referred - Surveillance - Symptomatic -	 538 (42%) 199 (16%) 184 (14%) 356 (28%)
Boston Bowel Preparation Score ≥2 per inspected segment, n (%)	1253 (98%)
Location LNPCP, n (%) - Proximal - Distal	 820 (64%) 457 (36%)
Size LNPCP in mm, median (p25-p75)	30 (25-40)
Size groups, n (%) - 20-29mm - 30-39mm - ≥40mm	 399 (31%) 399 (31%) 479 (38%)
Morphology LNPCP, n (%) - Sessile - Flat	 789 (62%) 488 (38%)
Accessibility LNPCP, n (%) - Easy - Difficult	 1111 (87%) 166 (13%)
SMSA-score LNPCP, n (%) - SMSA II - SMSA III - SMSA IV	 64 (5%) 586 (46%) 627 (49%)
Clip placement, n (%)	258 (20%)
Submucosal tattoo, n (%)	488 (38%)

Abbreviations:
ASA: American Society of Anesthesiologists; LNPCP: large non-pedunculated colorectal polyp; SMSA: Size, Morphology, Site and Access

Table 2. Factors associated with post-EMR scar identification (multivariable GEE analysis with correction for clustering of patients within endoscopist; ICC = 0.014)

	Adjusted risk ratio	**95%-CI**	**p-value**	**Bonferroni corrected 95%CI**	**Bonferroni corrected p-value**
Dedicated endoscopist	1.82	1.35-2.47	*<0.001*	1.20-2.77	*<0.001*
Submucosal tattoo	1.04	0.82-1.32	0.719	0.75-1.45	1.000
Size					
- 20-29mm	Ref		*0.005*		*0.034*
- 30-39mm	1.19	0.91-1.54	0.201	0.83-1.69	1.000
- ≥40mm	1.68	1.23-2.29	*0.001*	1.09-2.57	*0.008*
Flat morphology initial LNPCP	0.88	0.68-1.13	0.310	0.62-1.25	1.000
Proximal location	0.84	0.65-1.09	0.187	0.59-1.20	1.000
Difficult accessibility	0.88	0.64-1.20	0.419	0.57-1.35	1.000

Abbreviations:
LNPCP: large non-pedunculated colorectal polyp
ICC: intra-class correlation

Table 3. Outcomes of optical assessment and biopsy of post-EMR scars

		Histology		
		Recurrence	**No recurrence**	
Optical assessment	**Recurrence**	186	64	250
	No recurrence	14	786	800
		200	850	1050

Prevalence	19% [17-22%]
Sensitivity	93% [88-96%]
Specificity	92% [90-94%]
Positive predictive value	74% [69-80%]
Negative predictive value	98% [97-99%]
Diagnostic accuracy	93% [91-94%]
Cohen’s kappa (κ)	0.78 [0.73-0.83]

SUPPLEMENTARY MATERIALS

Supplement to:

" Optical assessment of scars after endoscopic mucosal resection of large colorectal polyps in a multicenter, community hospital setting: is routine biopsy still necessary?"

Authors: Lonne W.T. Meulen[1,2], Roel M.M Bogie[1,2], Peter D. Siersema[3], Bjorn Winkens[4,5], Marije S. Vlug[6], Frank H.J. Wolfhagen[7], Martine A.M.C. Baven-Pronk[8], Michael P.J.A. van der Voorn[9], Matthijs P. Schwartz[10], Lauran Vogelaar[11], Alaa Alkhalaf[12], Tom C.J. Seerden[13], Wouter L. Hazen[14], Ruud W.M. Schrauwen[15], Lorenza Alvarez Herrero[16], Ramon-Michel Schreuder[17], Annick B. van Nunen[18], Esther Stoop[19], Gijs J. de Bruin[20], Philip Bos[21], Willem A. Marsman[22], Edith Kuiper[23], Marc de Bièvre[24], Yasser A. Alderlieste[25], Robert Roomer[26], John Groen[27], Marloes Bigirwamungu-Bargeman[28], Monique E. van Leerdam[29,30], Linda B.J. Roberts-Bos[31], Femke Boersma[32], Karsten Thürnau[33], Roland de Vries[34], Jos M. Ramaker[35], R. de Ridder[1], Maria Pellisé[36], Michael J. Bourke[37], Ad A.M. Masclee[1], Leon M.G. Moons[38] (on behalf of the OPTICAL-STAR study team)

TABLE OF CONTENTS:

SUPPLEMENTARY MATERIAL 1: BIOPSY E-MODULE

Duration e-module: 26 minutes
Topics:

- Prevalence of post-EMR recurrence
- Steps in optical assessment of the scar → size, margins, presence of nodules, number of sites of recurrence, location of recurrence
- Value of advanced imaging and near focus/zoom
- Examples of local recurrence and ESCAs
- Value of biopsies of the scar + standard biopsy protocol

Supplementary Figures S1 A-F: Examples of biopsy e-module

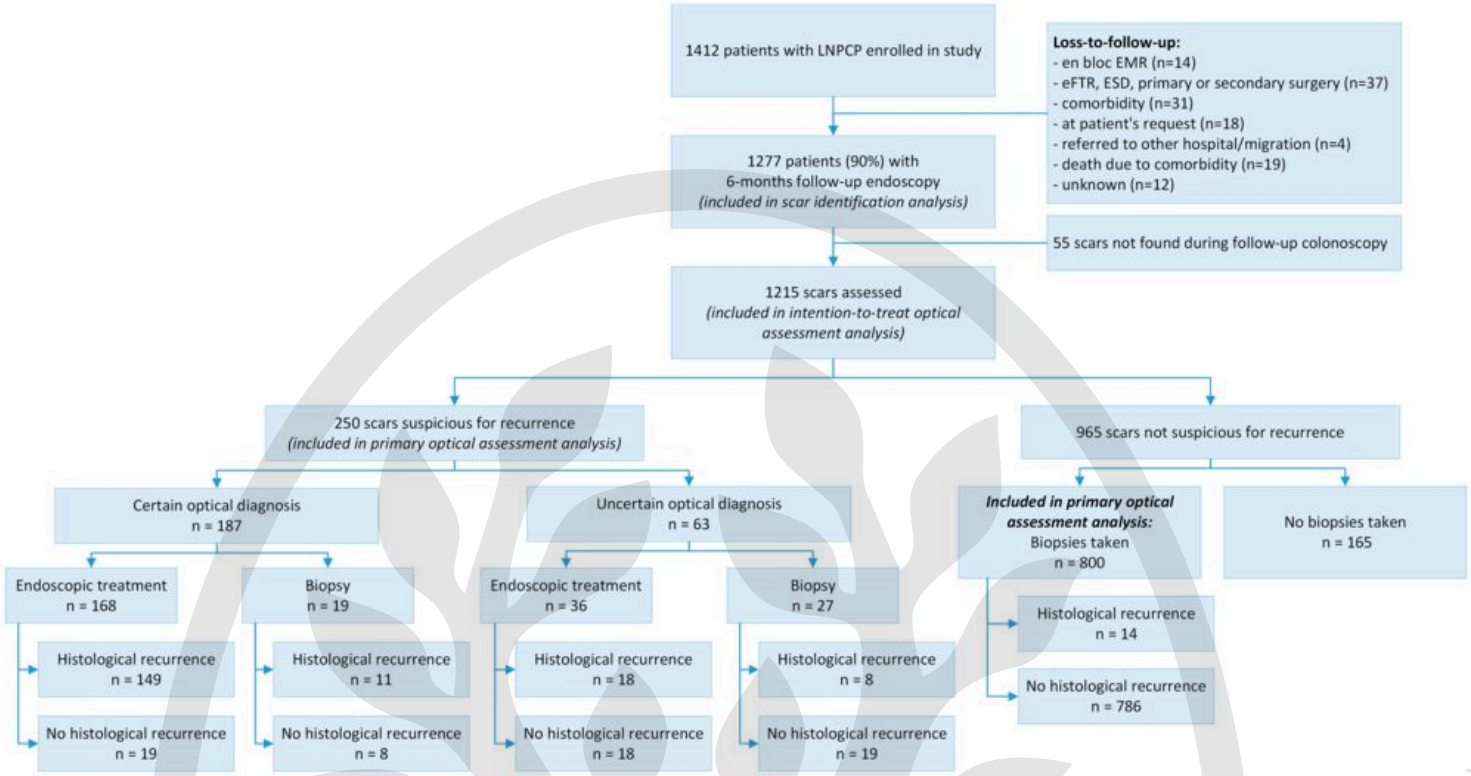
SUPPLEMENTARY MATERIAL 2

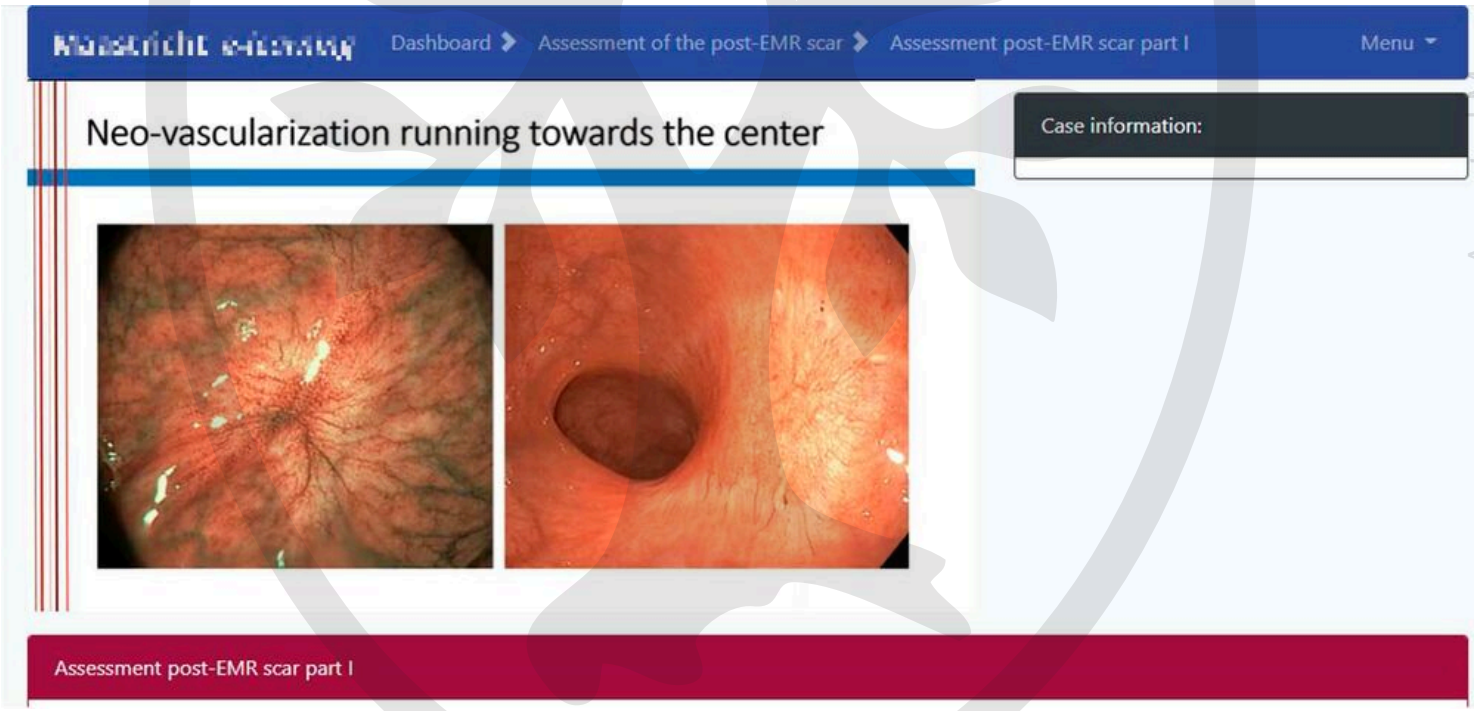
Supplementary table 1. Outcomes optical assessment and biopsy of post-EMR scars intention-to-treat*

		Biopsy		
		Recurrence	**No recurrence**	
Optical assessment	**Recurrence**	186	64	250
	No recurrence	14	951	965
		200	1015	1215

Prevalence	16% (14-19%)
Sensitivity	93% (88-96%)
Specificity	94% (92-95%)
Positive predictive value	74% (68-80%)
Negative predictive value	99% (98-99%)
Diagnostic accuracy	94% (92-95%)
Cohen's kappa (κ)	0.79 (0.74-0.83)

**Assuming that scars that were not found during colonoscopy did not reflect any signs of recurrence and non-biopsied scars would be confirmed histologically negative for recurrence if biopsy had taken place.*

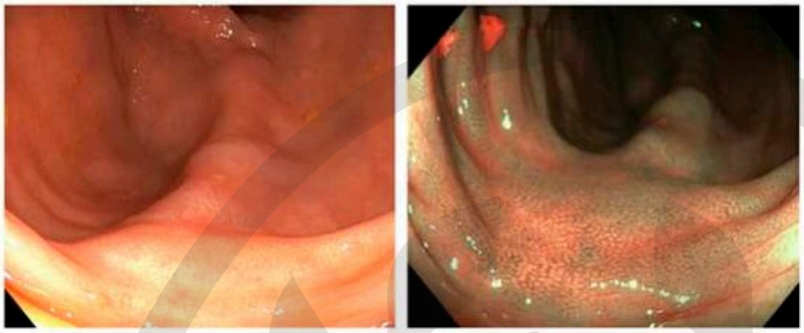




Dashboard > Assessment of the post-EMR scar > Assessment post-EMR scar part I Menu

Is this a scar?

Case information:



Assessment post-EMR scar part I

Question 1

Is this a scar?

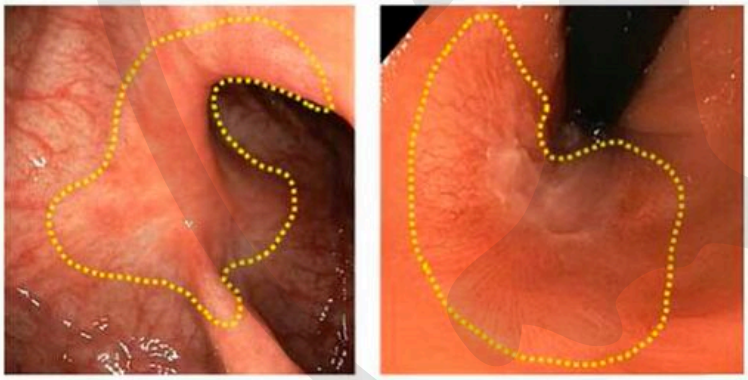
- Yes
- No

Stop Next case

Dashboard > Assessment of the post-EMR scar > Assessment post-EMR scar part II Menu

Size and margins of the scar

Case information:

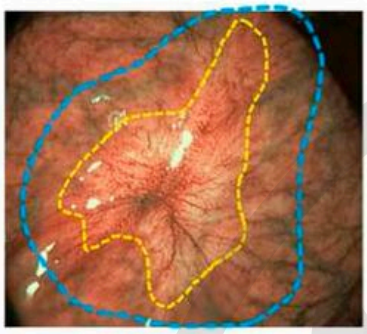


Assessment post-EMR scar part II

Dashboard > Assessment of the post-EMR scar > Assessment post-EMR scar part II Menu

Higaki criteria of local recurrence

Case information:



Higaki criteria

- All neoplasia within the scar (yellow line) as well as < 5 mm of the scar margin (blue line) is considered to be a local recurrence

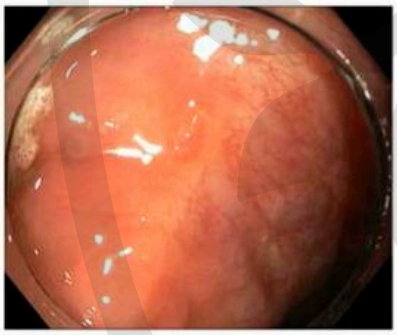
Higaki, Endoscopy 2003

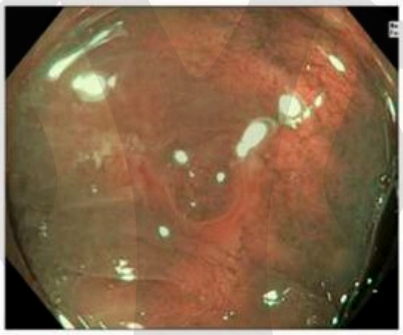
Assessment post-EMR scar part II

Dashboard > Assessment of the post-EMR scar > Assessment post-EMR scar part II Menu

Is this a local recurrence?

Case information:





Assessment post-EMR scar part II

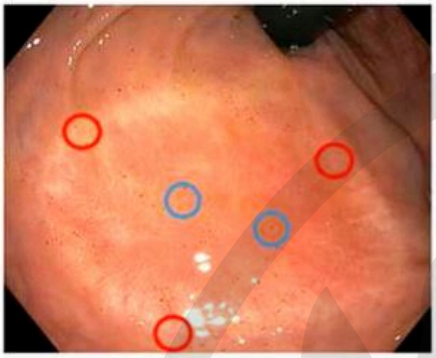
Question 1

Does this scar (or nodule) contain a recurrence?

- ○ Yes
- ○ No

Previous case | Next case

Standard Biopsy protocol



- Look for suspicious areas with advanced imaging with zoom (near focus)
- Remove or biopsy all suspicious areas
- In the absence of suspicious areas, dependent on the size
  - 1-2 biopsies from the center
  - 2-3 biopsies of the periphery

Case information:

Assessment post-EMR scar part IV