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Resection Margin Involvement after Endoscopic Excision of Malignant Colorectal Polyps : Definition of Margin Involvement and it's impact on Tumour Recurrence.

Running Title: Definition of Margin Involvement in Malignant Polyps

Keywords : Colon ; Polyp ; Carcinoma ; pT1

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Abstract.

Aims.

Malignant polyps are examined to assess histological features which predict residual tumour in the unresected bowel and guide surgical decision making. One of the most important of these features is resection margin involvement, however the best definition of margin involvement is unknown. In this study we aimed to investigate 3 different definitions and determine their impact on clinical outcomes.

Methods.

165 malignant polyps removed endoscopically were identified and histological features correlated with either residual tumour in subsequent surgical resections or tumour recurrence following a period of clinical follow-up. Involvement of the polyp margin by cancer was defined in 3 different ways and outcomes compared.

Results.

Tumour recurrence was associated with tumour grade, mucinous histology and resection margin involvement. All 3 definitions of margin involvement separated

polyps into clinically significant categories however, a margin less than or equal to 1mm identified 73% of polyps as “high risk” compared with 59.1% when involvement was defined as tumour within the zone of coagulation artefact at the polyp base or 50% when tumour was present at the margin. All 3 “low risk” groups had a loco-regional recurrence rate < 6.5%.

Conclusions.

Definitions of margin involvement for endoscopically removed malignant polyps in the colon and rectum vary between healthcare systems but a 1 mm clearance is widely used in Europe and North America. Our results suggest a 1mm margin is unnecessary and should be replaced by a definition based on tumour at the margin or within coagulation artefact at the polyp base.

Introduction.

Colorectal cancer is a major cause of mortality and morbidity in Europe and North America. While most tumours are diagnosed when they are at an advanced stage and causing symptoms, 10% to 20% are discovered when they are relatively small and still confined to the bowel wall. This is particularly true of carcinomas identified in national bowel cancer screening programmes (BCSP) where as many as 30.1 % of lesions are staged pT1 and 16.7% pT2[1,2]. Malignant polyps represent a subset of pT1 cancers (16 % of all tumours of all stages diagnosed in the UK BCSP) which in many cases are only diagnosed on histology after endoscopic resection and macroscopically resemble adenomas. Prognosis is excellent when pT1 tumours are treated with surgical resection encompassing the regional lymph nodes, however this entails significant morbidity and mortality. Post-operative death rates ranging from 1.7% to 3.5%, and severe complications in 8.3% of patients, have been reported while rectal cancer surgery in particular carries the risk of permanent colostomy, sexual and urinary dysfunction[3]. It is also widely recognised that a majority of these lesions, particularly malignant polyps, could be safely managed by local excision alone since extramural satellite tumour deposits and lymph node metastases occur in only 10-20% of cases[4,5]. Despite this the appropriate management of any individual patient with pT1 carcinoma is often uncertain and has to be discussed carefully at a multi-disciplinary team meeting. Identification of tumours which can be treated conservatively and those which require surgery has been intensively investigated for over 40 years. A large number of single centre studies (mostly retrospective) and meta-analyses have identified significant risk factors for lymph node metastasis including tumour site, tumour differentiation, lymphatic or venous channel invasion, depth of submucosal invasion, resection margin involvement and tumour budding[4,5]. Recent research has also suggested that tumour stroma ratio and area of submucosal invasion may give further prognostic information, though these

are not routinely assessed[6]. Histopathological factors have subsequently been incorporated into national and international guidelines to help identify “low risk” and “high risk” malignant polyps and guide surgical decision making[7,8]. Most guidelines focus on the core features of tumour grade, lymphatic channel invasion, venous invasion, depth of submucosal invasion (qualitative or quantitative assessments) and resection margin status to define clinical risk. While tumour budding is included in the Japanese national guidelines it is not yet a core data item in either the UK or North American datasets and is therefore not routinely reported in many pathology departments[7,8,9,10,11,12].

Ever since 1977 when Morson et al described the policy of local excision for early colorectal cancer at St Marks Hospital in London, resection margin status has been identified as one of the most important histopathological factors influencing the risk of recurrent or residual disease[13]. In their seminal 1984 paper on the endoscopic treatment of malignant polyps, Morson classified endoscopic resections as either “complete”, “doubtfully complete” or “incomplete”[14]. Doubtfully complete excisions were described as “carcinoma present within tissues of the diathermy burn at the margin of excision” while “incomplete” corresponded to “endoscopic and/or histological evidence which suggested that carcinoma was left behind at the site of polypectomy”. Since then the definition of a positive resection margin has been variously defined as tumour within 0 mm, 1 mm or 2 mm of the deep margin. Most European and North American guidelines use a cut-off of 1 mm or less, although the evidence for this is poor. More recently Brown et al and Richards et al have questioned whether a 1 mm clearance is needed and shown in two independent studies that where the resection margin can be adequately examined, it is probably tumour at the margin ie. 0 mm clearance, which is most predictive of residual disease[15,16]. Other authors have come to the same conclusion[11,17].

In this study of malignant polyps removed endoscopically from the rectum and colon we aimed to investigate the impact of different definitions of margin involvement on finding residual tumour in the surgical specimen when polypectomy was followed by surgery, or alternatively, how margin status affects the loco-regional and distant recurrence of carcinoma when local excision is the only treatment.

Materials & Methods.

Consecutive “malignant polyps” removed from the colon and rectum were identified from a pathology database of pT1 colorectal cancers during the periods 1998 – 2007 at St James University Hospital, Leeds and 2008 – 2020 at the Leeds Teaching Hospitals NHS Trust. Inclusion criteria included : pT1 on histology and cT1 on CT/MRI scan when available ; local excision as the primary procedure (eg. snare polypectomy, endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), trans-anal excision (TART), trans-anal endoscopic microsurgery (TEMS) or trans-anal endoscopic operation (TEO)) ; “complete” macroscopic excision recorded by the endoscopist. Malignant polyp was defined as a circumscribed flat, sessile or pedunculated tumour endoscopically similar to an adenoma with invasive carcinoma extending completely through the muscularis

mucosae into submucosa. Exclusion criteria included a history of chronic inflammatory bowel disease, Familial Adenomatous Polyposis, previous radiotherapy or chemotherapy to the lesion and suspected incomplete excision of the lesion endoscopically.

Endoscopy reports, histopathology reports, clinical notes and MDT (multi-disciplinary team) records were reviewed to extract demographic and clinico-pathological data. Particular attention was paid to any salvage surgery following local excision, the development of loco-regional recurrence of tumour or distant metastasis, and the occurrence of synchronous or metachronous carcinoma. When possible the MDT records were interrogated to try and determine the reasons for performing or not performing salvage surgery. Salvage surgery was defined as elective surgical excision of colon containing the polypectomy site and draining lymph nodes due to identification of high risk features at MDT review.

The original H&E stained slides from 159 out of 165 cases (96.4%) were reviewed by NS to confirm the diagnosis of a malignant polyp and review pathological features including tumour type, tumour grade, presence of lymphatic (LVI) or blood vessel invasion (BVI), maximum tumour diameter, polyp morphology and resection margin status. Mucinous carcinoma was diagnosed when 50% or more of the tumour volume consisted of extracellular mucin. Tumour grade was based on the least differentiated area of the carcinoma as recommended in the Royal College of Pathologists and UK Bowel Cancer Screening Programme guidelines. Poor differentiation was defined as complete absence of gland formation or small, poorly formed irregular glands in at least 10% of the tumour volume.

To investigate the definition of resection margin positivity further, when possible the distance from carcinoma to the deep tissue margin was measured using the vernier scale on the microscope stage in millimetres. In addition it was recorded whether tumour cells extended into the zone of coagulated tissue at the polyp base irrespective of whether the margin was directly involved or not (see figure 1a & 1b).

To investigate the relationship between clinico-pathological features and outcomes following endoscopic excision the following definitions were used. Salvage surgery was defined as above. Surgery for recurrence was defined as bowel resection following endoscopic and/or radiological evidence of recurrent disease. Loco-regional recurrence was defined as EITHER residual carcinoma in the bowel wall, adjacent mesocolon or regional lymph nodes following salvage surgery OR recurrence in one or more of these sites in the same location as the polypectomy following a period of surveillance. Distant recurrence was defined as metastatic disease involving non-regional lymph nodes, peritoneal cavity, liver, lung or other organs. Finally “Adverse Outcome” was defined according to Williams et al as EITHER loco-regional recurrence OR distant recurrence OR both[10].

Values for tumour grade, LVI, BVI and resection margin status used in the correlation with tumour recurrence were taken from the original report where possible. In a number of cases this was supplemented by histological review (NS) where these values were missing from the original report. Where the original report

referred to features “suspicious” of LVI or BVI this was counted as positive for these features.

To investigate whether the presence of 2 or more commonly used histopathological risk factors conveyed a higher risk of adverse outcome than demonstration of a single factor, carcinomas were classified according to the number of high risk features they possessed. These included poor tumour differentiation, LVI, BVI and positive resection margin . Since one of the main aims of this study was to examine different definitions of margin involvement, this analysis was repeated using three different definitions of a positive margin ie. 0 mm clearance, tumour 1 mm or less from the margin and tumour cells within the area of coagulation artefact at the polyp base.

Differences in outcome between groups were tested using Fisher's Exact Test. All analyses were two tailed. Statistical significance was defined as $p < 0.05$.

Results.

Out of 460 pT1 cancers in the database, 165 malignant polyps were identified from 165 individuals. 112 were male (67.9%) and 53 female. Median age was 68. 111 patients (67.3%) presented with symptoms while 54 (32.7%) were discovered by the Bowel Cancer Screening Programme. 56 tumours were located in the rectum (33.9%), 72 in the sigmoid colon (43.6%) and 22.5% proximal to the splenic flexure. The index procedure was snare polypectomy in 54 cases, EMR in 93 cases and ESD in 10 cases. 8 polyps were removed by TART, TEMs or TEO. Endoscopic Paris classification was available in 154 polyps. In 11 cases no Paris classification was recorded. 108 out of 165 lesions were removed en-bloc as a single fragment. The polyp was removed as 2 pieces in 21 cases; 3 pieces in 9 and as 4 or more pieces in 27 cases. Table 1 describes the clinico-pathological features of 159 polyps with clinical follow-up.

In 5 cases the size of the polyp was not recorded by the endoscopist. Of the remainder most lesions (91%) measured 10 mm or more endoscopically. Only 2 measured 5mm or less and 13 between 5 and 10mm. 48% measured 10-20mm and 43% >20mm.

The diagnosis of malignancy was confirmed by a second consultant pathologist at the original time of reporting in 116 specimens. In addition 159 out of 165 polyps were reviewed by NS during the study and all were confirmed to be pT1 adenocarcinomas.

Salvage surgery was undertaken in 54 cases, between 1 and 8 months after polypectomy. Most patients were operated on within 3 months of polypectomy. Two waited 5 months and one waited 8 months due to logistical issues. Lymph node metastases were found in 8 resections (14.8%) and residual tumour in the bowel wall or adjacent fat in 14.8%. 3 (5.6%) resections contained both lymph node metastases and residual extra-nodal carcinoma. In total 24.1% of surgical specimens contained

residual tumour. The relationship between the decision to perform salvage surgery and number of pathological risk factors in the local excision specimen is shown in Table 2.

Clinical follow-up was available in 159 patients (96.4%). Median follow-up after local excision (all cases) was 37 months (range 2 to 133 months). Median follow-up after polypectomy only (without salvage surgery) was 33 months (range 2 to 119 months). Loco-regional recurrence occurred in 20 cases overall (12.6%) and distant metastasis in 5%. Eight patients underwent colorectal resection after local tumour recurrence.

In total 23 out of 159 patients with follow-up (14.5%) experienced an “adverse outcome” i.e. either residual carcinoma at salvage surgery or disease recurrence after polypectomy alone.

Table 1 shows the principal clinico-pathological features studied in this investigation and their association with loco-regional recurrence, distant metastasis and “adverse outcome”. In the original reports tumour differentiation was unrecorded in 16 cases (9.7%), lymphatic channel and blood vessel invasion were missing in 3 cases and mucinous histology was rarely if ever described. Distance to deep margin was absent in 11% of reports. All results for tumour invasion into the zone of coagulation artefact were provided by histology review (NS) since this is not routinely reported in our laboratory.

Statistically significant differences in locoregional recurrence were seen for tumour type (mucinous carcinoma versus adenocarcinoma NOS; $p=0.048$), tumour differentiation ($p=0.013$) and resection margin involvement using all 3 histological definitions (0 mm margin $p=0.0002$, coagulation zone involvement $p<0.001$ and 1mm margin $p=0.02$). A trend was seen towards more recurrence for lymphatic channel and blood vessel invasion but this was not statistically significant. Only poor tumour differentiation demonstrated a significant association with distant metastasis ($p=0.048$).

As follow-up and pathological data were incomplete, the analysis was repeated for 145 out of 165 polyps (87.9%) where all 4 principal histological risk factors (tumour grade, lymphatic/venous invasion and resection margin status) were known and clinical follow-up was available. This confirmed a statistically significant association between loco-regional recurrence and tumour grade ($p=0.03$). Similarly, recurrence was more likely if tumour cells were found within the zone of coagulation artefact (26.3% versus 3.4%; $p=0.0001$) or directly at the margin (33.3% versus 6.3%; $p=0.0001$). Using the conventional definition of tumour 1 mm or less from the deep edge the local recurrence rates were 17.4% versus 5.1% respectively ($p=0.04$).

Finally compared with a local recurrence rate of 32.3% for carcinoma directly at the margin and 4.8% for tumour >1mm from the margin, when carcinoma invaded to between 0.1 mm and 1 mm of the deep edge, the loco-regional recurrence rate was 7.4%. In a further analysis of this group 1 mm or less from the margin but not at the margin, tumours within the zone of coagulation artefact showed a local recurrence

rate of 18.2% compared to 0% for tumours unaffected by diathermy artefact (p=0.025).

Table 3 shows the relationship between absolute distance of recognisable tumour from the deep resection margin and the presence or absence of tumour cells within the zone of diathermy coagulation artefact. Out of 159 polyps that were available for review, 58 contained carcinoma affected by diathermy, 90 showed tumour cells outside the area of coagulation and in 11 cases interpretation was impossible due to specimen fragmentation. In no cases where tumour was located > 1mm from the margin was carcinoma affected by diathermy. Of tumours between 0.1 and 1mm from the margin, approximately half showed coagulation artefact and half did not, whereas all tumour cells present at the margin were affected by diathermy.

Table 4 shows how often tumour recurrence occurred in patients with 0,1,2 ,3 or 4 pathological risk factors. This includes all cases where salvage surgery was performed or clinical follow-up was available. Results are given using three different definitions of resection margin involvement ie. tumour at the margin, tumour at or within 1 mm of the margin and tumour within the zone of diathermy artefact.

No carcinoma showed all 4 high risk features. The proportion of cases in the “low risk category” with no risk factors ie. patients who would normally be managed conservatively, ranged from 26.6% to 50% according to the definition of resection margin involvement. Using the most restrictive definition of margin involvement (0 mm clearance), 5 out of 79 (6.3%) “low risk” patients experienced an adverse outcome, whereas using the 1mm criterion only 1 out of 42 (2.4%) patients developed recurrence. A similar result was obtained using diathermy zone as a criterion where only 1 out of 61 patients (1.6%) had an adverse outcome.

Defining a high risk polyp as a tumour with any of the four pathological features, recurrence varied from 19% to 22.8% depending on definition of a positive margin. Interestingly however, this risk was increased significantly when 2 or more features were present in the same lesion.

Conclusions.

Submucosa invasive cancer is seen in 0.75% to 5.6% of all endoscopically excised colorectal polyps and represents as many as 10-15% of cancers diagnosed in the UK Bowel Cancer Screening Programme[10,18]. While new techniques such as chromoendoscopy and narrow band imaging have improved the endoscopic recognition of malignant polyps, the majority are still only diagnosed after histological examination. The subsequent management of these patients requires the clinician to balance the risk of leaving residual disease behind in the bowel wall or regional lymph nodes against the morbidity and mortality associated with surgical resection. As the overall risk of lymph node metastasis in pT1 colorectal cancer is only 10 – 15 %, routinely offering surgery to this population would entail overtreatment of > 80% of patients. Unfortunately current imaging techniques are relatively poor at detecting lymph node metastasis, particularly in early cancers, where involved nodes are likely to be smaller and less numerous[9,10]. Consequently pathological examination of the

local excision specimen provides the best guide to risk of residual tumour in the bowel and the likelihood of tumour recurrence if salvage surgery is not performed.

In this study of 165 malignant polyps undergoing “endoscopically complete” local excision, we aimed to investigate a range of histological features which are routinely used to guide clinical management and determine their predictive value for the presence of residual tumour following surgical resection of the polypectomy site. In those patients not undergoing surgery we interrogated the patient’s medical records to see how often loco-regional or distant recurrence occurred during clinical follow-up. We found that persistent local tumour was predicted by tumour grade, mucinous histology and margin involvement. While a trend was seen towards more frequent loco-regional recurrence in those tumours with lympho-vascular invasion this did not reach statistical significance in our study. This may be due to an inadequate sample size. The only factor which showed a significant correlation with distant metastasis was tumour grade.

A particular focus of this study was the relationship between resection margin involvement and tumour recurrence. Over the years multiple studies have described positive margins following endoscopic removal of malignant polyps in 11% to 41% of cases. Hassan et al described a positive margin in 33.2% of a pooled study of 980 polyps[19]. In the majority of these reports, margin positivity has been identified as a strong risk factor for residual tumour/tumour recurrence. More variability is seen however, in whether margin status predicts recurrence in the bowel wall, lymph node metastasis or both. Butte et al (2012) and Brown et al (2016) in their studies of 143 and 140 cases respectively, found no association between margin positivity and lymph node disease but described a significant association with persistent tumour in the bowel wall at the polypectomy site[15,20]. Hassan et al (2005) described similar findings in their pooled data analysis of 980 polyps[19]. In contrast Berg et al and Boenicke et al (2010) showed a significantly increased rate of lymph node metastasis in polyps with tumour at the margin[17,21]. In the current study we confirm that margin involvement is a significant risk factor for loco-regional tumour recurrence but not distant metastasis.

There is considerable variation in the literature as to how a positive margin is defined. This ranges from tumour cells at the margin (0 mm clearance) to any tumour within 1 mm of the margin, while in yet other studies a 2 mm cut-off is proposed. Several authors take into account the difficulties posed by polyp fragmentation (piecemeal excision) and coagulation of tissue at the diathermied polyp base. Brown et al (2016) define an involved margin as “carcinoma reaching the submucosal margin or obscured by diathermy artefact such that the completeness of excision cannot be determined”[15]. A similar approach was taken by the Scottish Screen-Detected Polyp Cancer Study in which 485 polyp cancers were reported as margin positive “if the margin could not be assessed or there was evidence of tumour extending to the diathermy edge”[22]. UK BCSP reporting guidelines currently state that “a distance of 1 mm or less from tumour to margin is considered margin involvement (R1 resection status)” and that “ if there is infiltration by malignant glands into the diathermy zone and this is associated with morphological distortion of tissue to the extent that it is not possible to confidently identify tumour clearance

from the outer margin , then this should be regarded as margin involvement and a distance of 0 mm of clearance recorded"[23]. In our experience reviewing the polyps in this series, all carcinomas identifiable within the zone of coagulation artefact also lay within 1 mm of the deep margin and would therefore be regarded as margin involvement using current BCSP criteria. Thirty one out of 89 tumours within 1 mm of the margin however, were not affected by diathermy artefact and using a definition based on the zone of coagulation at the polyp base would not be scored as margin positive.

Interpretation of the margin in polyps which are not removed en-bloc is more difficult. In many studies piecemeal excision of the polyp is regarded as a potential indication for surgery. This is the recommendation of the US Multi-Society Task Force on Colorectal Cancer in their 2020 guideline[8]. It is certainly the easiest and most reproducible solution to the problem of polyp fragmentation, however despite the best intentions of the endoscopist a substantial number of malignant polyps are still resected in two or more pieces (22% in this study) and arguably, to categorise all of these as potential margin involvement, may lead to significant overtreatment. In some of these cases the number of fragments is relatively few ie. 2-3 pieces, and malignant foci may be limited to one fragment only. In our experience it is possible to suggest that the margin is unlikely to be involved in a proportion of these cases, especially where the carcinoma is confined to one of the larger fragments and is clear of the coagulation zone at the fragment edge. We believe these patients may be managed conservatively provided no other risk factors are present. In 2017 Backe et al found that piecemeal excision was a clinical risk factor for incomplete endoscopic resection, however in our series while univariate analysis showed a trend towards more loco-regional recurrence following piecemeal excision this failed to reach statistical significance[24]. Undoubtedly this is an area of concern to pathologists and clinicians. We suggest that where en-bloc excision has not been achieved but no other risk factors are present, careful discussion at the colorectal MDT meeting is needed to balance the risks and benefits of any additional treatment.

In the current study we defined margin involvement in 3 different ways and found that while all three definitions showed a statistically significant relationship to residual loco-regional disease, the association was most powerful when positivity was defined as tumour at the margin (0 mm) or carcinoma extending into the zone of coagulation artefact at the polyp base. In this situation persistent local tumour was subsequently diagnosed in 20.3% and 19.3 % of "high risk" cases compared to 16.4% when the 1mm cut-off was used. Conversely when the margin was reported as negative, in the absence of poor tumour differentiation or lympho-vascular invasion the loco-regional recurrence rate was 5.9%, 3.3% and 4.8% for 0 mm, coagulation zone positive and 1 mm definitions respectively. We therefore conclude that in our study the 1mm margin which is currently widely used to signal an involved margin, is inferior to a definition based on tumour at the margin or extending into the diathermy coagulation zone. Using these definitions the proportion of cases that could potentially be managed conservatively increased from 26.6% based on a 1 mm clearance to 40.9 % and 50%. This finding is similar to studies reported in the past 10 years by Gill et al (2013), Brown et al (2016) and Richards et al (2019)[15,16,25].

In a separate analysis of tumours within 1 mm but not at the margin, we found that the presence of cancer within the zone of diathermy coagulation at the polyp base identified a subgroup with a higher rate of loco-regional recurrence (18.2%) compared to those unaffected by diathermy artefact (0%). We acknowledge the number of polyps in this group is small and the number with recurrence even smaller and that these results are therefore prone to statistical error. On this basis nevertheless we suggest that tumour within the zone of coagulation artefact at the polyp base should be taken into account as a potential “high risk” feature.

In 2004 Ueno et al showed that the risk of lymph node metastasis in pT1 cancer increased as the number of pathological risk factors increased[26]. In their study this included tumour grade, cribriform pattern, vascular invasion and tumour budding. We describe a similar effect in our series. The presence of 2 or more factors significantly increased the rate of distant metastasis compared with one risk factor ($p = 0.03$). The observed increase in loco-regional recurrence from 12.7% to 24.3% failed to reach significance however. Interestingly we also found that the likelihood that any individual subsequently underwent salvage surgery after polypectomy was strongly associated with the number of risk factors identified by the pathologist in the specimen (Table 2). It may be that in addition to patient age, co-morbidity etc. the presence of multiple histological risk factors also influenced surgeon and patient decision making.

Some investigators have found that the maximum width of invasive component in a pT1 cancer correlates with the presence of lymph node metastasis and suggest that this quantitative parameter may be useful in selecting patients for surgery following endoscopic removal. Thresholds identified as important however have ranged widely from 4mm to 11.5mm[26,27]. While this measurement was only available in 87% of our cases neither a 4 mm nor an 11 mm cut off showed a statistically significant association with loco-regional recurrence or distant metastasis.

Our study has a number of weaknesses. Since the investigation is retrospective some of the pathological and clinical data were missing, however it was possible to review over 96% of the cases and supplement many of the incomplete pathology reports. Histological review also allowed us to confirm the diagnosis of a malignant polyp. Overdiagnosis of malignancy is a significant problem in polyp cancers due to misinterpretation of epithelial misplacement in adenomas and could potentially impact on the results of other studies where expert review was not undertaken[28]. Unfortunately a small number of cases were not available for review due to slides missing from file etc. When we compared results using only those cases in which a complete dataset was available (87.9%) with analysis utilising all cases, there was no significant difference in the findings however. A second weakness is the length of follow-up, median duration 33 months after polypectomy alone. Previous series of pT1 cancer describe local and distant recurrences occurring as late as 68 months after polyp removal[24,29]. Longer follow-up is therefore required to fully document the true rate of tumour recurrence which we may have underestimated. Finally we have not included features such as tumour budding and depth of tumour invasion (from the muscularis mucosa) in our analysis. Most studies conducted in pT1 cancers have documented a significant association between budding cells at the invasive tumour

margin and the presence of lymph node metastasis (Odds Ratio 6.44) but the exact contribution of a budding score to decision making in the absence of other high risk factors remains unclear[7,30,31].Therefore while budding and depth of invasion in millimetres are included in Japanese national guidelines and are the subject of continuing research, they are not widely used in Europe or North America to determine management. Margin involvement, tumour grade and lympho-vascular invasion are still the principal risk factors currently used by most UK pathologists to define a “high risk” malignant polyp and like many other laboratories we do not routinely report tumour budding.

In conclusion this is the first study of malignant polyps to our knowledge which directly compares the impact of margin definition on classification as a “high” or “low” risk pT1 cancer and the first to test it’s relationship with loco-regional and distant tumour recurrence. The results suggest that the widely used 1 mm definition should probably be replaced by either tumour present at the margin ie. 0 mm, or tumour within the zone of coagulation artefact at the polyp base.

All authors were involved in data collection and manuscript preparation. Study design, histology review and data analysis were performed by Dr N Scott.

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Figure 1A. Adenocarcinoma present in zone of coagulation artefact but not identifiable at the deep margin. H&E x100.

Figure 1B. Adenocarcinoma present at the deep margin (clearance 0 mm). H&E x100.