The Efficiency of Right Hemicolectomy Specimen Grossing and Blocking: A Quality Assurance Study

by

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Abstract

Pathologists' Assistants (PAs) are increasingly utilized in the pathology laboratory to perform grossing duties. With this increase in physician extenders performing gross dissections, steps should be taken to standardize grossing guidelines so that Pathologists are always given adequate and informative tissue sections. This study aims to analyze the impact of the introduction of a grossing manual on the grossing quality for malignant right hemicolectomy specimens in Manitoba, Canada. Five aspects of colorectal cancer grossing were analyzed in 88 pre-manual specimens and 92 post-manual specimens, including: total number of blocks submitted to histology, number of blocks containing tumour submitted, number of blocks containing margin submitted, lymph node submission, and the submission of non-informative tissue sections. After introduction of the manual, lymph node submission utilized significantly less blocks, and the submission of multiple types of non-informative tissue blocks (such as the sampling of anastomotic donuts when the margin is well-clear) significantly decreased. Additionally, the grossing manual recommends no more than five blocks of tissue including tumour should be submitted, however the submission of six or more tumour sections significantly increased and the total number of blocks submitted per case did not change after the manual's introduction. Based on this study's findings, two recommendations are made for future versions of the grossing manual: (1) sections of proximal and distal margin may not need to be submitted if the tumour is greater than 2cm from margin, and the tumour is not diffusely infiltrative or associated with inflammatory bowel disease; and (2) PAs should consult with a Senior PA or Pathologist when submitting six or more blocks. These recommendations will likely improve blocking efficiency and decrease costs associated with the processing of blocks, while providing patients with the same quality of care.

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Introduction

The Surgical Pathology Workflow

The practice of surgical pathology involves the macroscopic and microscopic examinations of tissues removed from a patient during surgical procedures. Specimens received in pathology laboratories can vary from simple skin biopsies to complex organ resections for invasive cancer, with the end goal of any specimen's examination being diagnosis and staging of the patient's disease. Generally, specimens are examined in their intact state, then dissected, and processed into microscope slides for the microscopic examination. This process typically involves three general steps: grossing, histology, and microscopic examination (Figure 1).

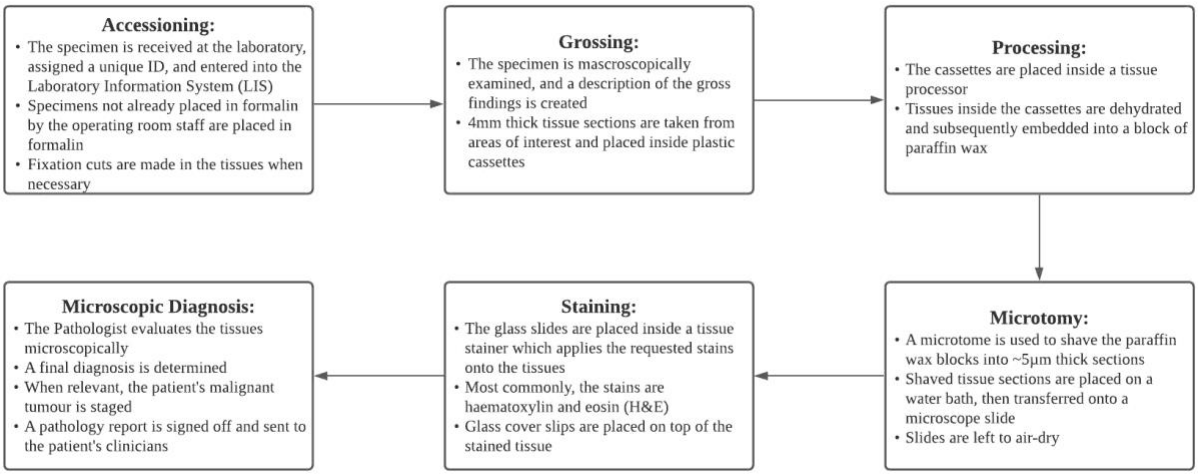

Figure 1. Pathology laboratory workflow and specimen processing steps.

Firstly, grossing is the macroscopic examination and documentation of the removed tissue. During grossing, a Pathologist or Pathologists' Assistant (PA) will examine the entire intact specimen while documenting important findings such as the size of a tumour, or how deeply a tumour invades through the surgically removed tissues. Once this documentation is complete, they must determine which portions of the specimen most appropriately demonstrate the greatest extent of the patient's disease. Once selected, the personnel will "block" (also known as "sectioning") the specimen by cutting out smaller pieces of these areas of interest at a thickness of approximately 3mm. Once sections are taken, they are placed in plastic cassettes and submitted to the histology laboratory.

In the second step at the histology laboratory, the tissue blocks are processed in a machine which dehydrates and embeds the tissues into a block of paraffin wax. The paraffin wax

blocks are then cut into 5µm thick slices with a microtome, mounted onto glass slides, and stained. Haematoxylin and eosin (H&E) staining is the most commonly used stain, but special stains and immunohistochemical stains may be performed as-needed. Lastly, a Pathologist reviews the sections microscopically with the end-goal of diagnosing a patient's disease, and in the case of malignant disease, determining the pathologic stage of a patient's cancer. The final diagnosis and stage of a patient's disease are made with information from both the gross and microscopic examination of the tissues.

Grossing and Pathology Personnel

In the past, Pathologists were responsible for all grossing duties in addition to their usual workload of reviewing microscope slides, teaching medical residents, and other duties as required[1]. As Pathologists began to receive increasingly large workloads, studies found that grossing errors increased as they became busier[2]. Grossing is a time-consuming process where accuracy cannot be sacrificed, which makes it difficult for Pathologists to gross while having a busy schedule. In response, hospitals throughout North America now utilize Pathologists' Assistants (PAs) who are mid-level professionals with specialized education and training in the grossing and blocking of surgical specimens, among other duties. By utilizing these employees who specialize in the meticulous and time-consuming grossing process, the grossing responsibilities of four full-time Pathologists can be delegated to one full-time PA[3]. This frees the Pathologist's schedule for their other duties, while also improving the quality of grossing and reducing labour-related costs[1,3].

Some studies find that the overall quality of grossing increases when PAs perform grossing duties[1,2]. In addition to improvement in overall quality, these studies also found quantifiable improvements in specific metrics such as the number of lymph nodes retrieved from specimens which required lymph node searches to be completed[2]. Grossing is a time- and labour-intensive process, thus grossing quality improves when pathology laboratories utilize employees who specialize in it and spend most of their working time grossing[1].

With the introduction of Pathologists' Assistants into the discipline of surgical pathology, there is a corresponding call for the standardization of grossing practices. One drawback to the use of PAs is that the person submitting tissue sections is not the person making a diagnosis with the sections, and sometimes the Pathologist may not receive all of the sections

they would expect to receive. When Pathologists gross surgical specimens, they personally see the specimen and are accountable for submitting their own tissue blocks, rather than having a PA submitting blocks for someone who is unlikely to the specimen grossly. Standardization will ensure consistency in gross evaluations and tissue blocking between PAs and ensure that informative blocks are always submitted for histology, thereby maintaining the accuracy and quality of a Pathologist's microscopic diagnosis without issue. If a comprehensive standard grossing procedure is in place at an institution, then the need for Pathologists to see non-complex specimens grossly should be lessened and the types of tissue sections submitted should stay consistent. This consistency created by the standardization of grossing ensures that Pathologists always receive the exact amount of information they need to make a microscopic diagnosis with minimal need to pull a case from storage for a second look.

Tissue Blocking and the Staging of Disease

It must be emphasized that the blocking of pathology specimens (i.e. the selection of tissue sections for submission to histology) has a direct impact on the Pathologist's ability to diagnose and stage malignant diseases. The selection of tissue blocks for submission to histology is a deliberate process and must be informed by evidence-based staging guidelines, such as the American Joint Committee on Cancer (AJCC) Cancer Staging Manual[4]. Cancers originating from different tissues each have unique staging parameters: for example, some cancers are staged by tumour size and others by the depth of invasion through tissue layers, and two different cancers both staged by tumour size may have different size cutoffs between stages.

Accurate cancer staging is a crucial component of quality patient care. Pathology reports provide clinicians with the pathologic stage of a surgically resected cancer[4], which is then integrated with other clinical factors to determine the patient's prognostic stage. This prognostic stage is the ultimate classification of "Stage I/II/III/IV" given by the patient's direct care providers[4]. As indicated by its name, the main difference between prognostic stages is a patient's prognosis – for example, a Stage I colorectal cancer patient has a statistically higher chance of survival than a Stage II colorectal cancer patient – and different patients may receive different treatment options based on stage. Thus, accuracy in the pathologic staging of cancers is vital to

patient care since it influences prognostic stage, and maintaining staging accuracy is of the utmost importance in pathology laboratories.

In North American pathology laboratories, malignant diseases are typically assigned pathologic stage using the AJCC's TNM staging criteria[4], which is an abbreviation for Tumour, Nodes, and Metastasis. In Tumour staging (T-staging), the characteristics of a patient's tumour are evaluated and assigned a T-stage based on severity; the characteristics to be evaluated vary between tissue types but typically include information such as tumour size, depth of invasion, or adjacent organs/structures involved by the tumour[4].

A common site of cancer metastasis is the lymphatic system, especially in lymph nodes. In lymph node staging (N-staging), the Pathologist evaluates all surgically removed lymph nodes histologically for signs of metastatic cancer. Criteria such as the size of a metastatic deposit or number of lymph nodes containing metastatic cancer will impact a patient's N-stage[4].

Lastly, distant metastasis staging (M-staging) is an evaluation of the presence of metastatic cancer in non-lymphoid areas distant to the primary tumour, such as metastatic deposits in the lungs of a patient. This is commonly determined clinically with radiology and is not pathologically M-staged. In some cases, distant metastasis can be determined pathologically if an area of distant metastasis is surgically removed or biopsied for histologic evaluation[4]. Once these are determined, all three of the T-stage, N-stage, and M-stage are reported together as a pTNM stage, in which 'p' denotes that this is a pathologic stage and not clinical. An example of a pTNM stage could be pT1N0M0, if a patient had a low T-stage (T1), no lymph node metastasis (N0), and no distant metastasis (M0).

This pTNM stage is determined by Pathologists when they evaluate tissues microscopically. If the Pathologist is given too few tissue blocks to evaluate, they may not be able to definitively stage the patient's disease and cannot sign off a final pathology report. This situation can occur if too few tissue blocks are submitted in total or if the selected tissue blocks are "non-informative" blocks which do not demonstrate essential information to the Pathologist. In these cases, the surgical specimen must be pulled from storage and re-blocked in order to provide the requested and required tissue block types on this second try. This is a time-consuming process for the PA who must divert their attention from grossing new cases and for the Pathologist who cannot yet sign out a pathology report. The submission of additional sections may sometimes be an inevitability in complex specimens or when there are unexpected

microscopic findings, but ought to be avoided in routine specimens because these delays impact the turnaround time for pathology reports and thus impact the timeliness of patient care.

Furthermore, the submission of non-informative blocks also has negative impacts on the laboratory. When a tissue section is submitted to histology, it is put through tissue processing which consumes non-reusable materials and has an associated labour cost for the Medical Laboratory Technologists who run these processes. Therefore, laboratories have an interest in reducing the submission of non-informative tissue sections because these have an associated cost without positively contributing to patient care. As a result, pathology personnel who perform grossing duties (most commonly PAs) must have the appropriate knowledge of staging guidelines and exhibit good judgement for the selection and submission of tissue blocks.

TNM Staging and Blocking of Colorectal Adenocarcinoma

To highlight the importance of tissue blocking and standard grossing practices, a study on colorectal cancer specimens found that PA sampling of tumors might impact T-staging[5]. For colorectal adenocarcinoma, the T-stage of a tumour is partly influenced by the involvement of tumour with peritoneum: pT3 is tumour invading "through the muscularis propria into pericolorectal tissues"[4] and pT4a is tumour invading "through the visceral peritoneum"[4] (see Tables 1a/b/c for full details). Klaver et. al. (2020) asked Pathologists to review previous colorectal cancer cases in which there was tumour grossly present at serosa, and provide the researchers with their opinion of whether a case is pT3 or pT4a. Cases containing an average of four tissue blocks of tumour with serosa tended to be staged as pT3, whereas cases with five sections on average were more likely to be called pT4a.

Therefore, adequate sampling of surgical specimens, with consideration for the cost efficiency of block submission when possible, is of utmost importance. Inadequate sampling may lead to the Pathologist not finding a microscopic feature which would up-stage a tumour. This issue is extremely important to patient care because the distinction between two stages, such as pT3 and pT4a, can influence whether a patient is given adjuvant chemotherapy/radiation (in the case of pT4a disease) or not (pT3). Therefore, a PA's gross dissection and section selection has a

considerable impact on patient care and needs to be actively evaluated and standardized in order to improve patient safety and quality of care.

In addition to the aforementioned distinction between pT3 and pT4a colorectal cancer, there are multiple other data points vital to the TNM staging of colorectal adenocarcinoma as outlined in Table 1. In the T-staging of this disease, it is vital for tissue sections to demonstrate the tumour's area of deepest invasion, which may be anywhere from submucosa to organs adjacent to the colon. While it is obvious that this deepest invasion must be demonstrated for staging purposes, there is a lack of evidence for the ideal overall number of tumour sections to submit. Some articles and institutional protocols indicate that a minimum of four to five blocks of tumour should be submitted for most cases[6,7], but do not provide data to support this recommendation. Additionally, the previously described study by Klaver et. al. suggests that five tumour blocks may be an ideal number, but is only applicable in cases of possible peritoneal involvement[5]. Every specimen is unique, and the nature of some specimens may require more blocks than normal. Many current grossing protocols are at or near this recommendation of four sections[6–8], but the current lack of data to support this number indicates a need for grossing-centered quality assurance studies.

Quality Assurance in Pathology

Quality assurance (QA) in the pathology laboratory traditionally involves histology and the Pathologist more often than the gross evaluation and the PA, and is concerned with measures such as turnaround time, staining quality, diagnostic accuracy, and clinician satisfaction with the pathology report[9]. Common QA procedures include performing controls on immunohistochemistry stains or double sign-outs where two Pathologists must agree upon the diagnosis before the pathology report is signed out[10]. Given that a PA's section selection can considerably impact patient care, it is important to also consider grossing in the development of QA protocols, one of which may be standardized grossing protocols. Many hospitals standardize grossing between PAs by providing a site-specific grossing manual, which is a detailed Standard Operating Procedure providing precise instructions on how each specimen type ought to be grossed and which types of tissue sections ought to be submitted.

Table 1a. Criteria for AJCC T-staging of colorectal adenocarcinoma[4].

T-stage	Criteria
Tis	Intraepithelial lesion, or invades lamina propria
T1	Invades submucosa
T2	Invades muscularis propria
T3	Invades beyond muscularis propria, into pericolonic soft tissues
T4a	Invades through the visceral peritoneum
T4b	Invades or adheres to adjacent organs or structures

Table 1b. Criteria for AJCC N-staging of colorectal adenocarcinoma[4].

N-stage	Criteria
N0	No metastasis to regional lymph nodes
N1a	Metastasis to 1 regional lymph node
N1b	Metastasis to 2-3 regional lymph nodes
N1c	Tumour deposits present in the subserosa, mesentery, or non-peritonealized pericolonic tissues without regional lymph node metastasis
N2a	Metastasis to 4-6 regional lymph nodes
N2b	Metastasis to 7 or more regional lymph nodes

Table 1c. Criteria for AJCC M-staging of colorectal adenocarcinoma[4].

M-stage	Criteria
M0	No distant metastases present
M1a	Distant metastasis to one organ/site
M1b	Distant metastasis to two or more organs/sites, or involvement of peritoneum

As mentioned earlier, pathology QA typically revolves around the processes occurring after grossing: staining quality, accuracy of the Pathologists' diagnosis, etc. There are minimal studies in the literature which approach QA at the level of the grossing bench, and this study aims to contribute to grossing quality for right hemicolectomy specimens containing a colorectal primary tumour. There are several papers in the literature which discuss grossing in the context of the College of American Pathologists (CAP) protocols and specific guidelines in place at different institutions[6,7,11–13], but few papers collect data related to grossing quality and explore the reasons behind why these guidelines are recommended.

The few papers which do explore these reasons cover a variety of topics, including: margins, lymph nodes, and serosal involvement. A study by Cross et. al.[14] found that proximal

and distal resection margins are rarely positive for carcinoma, and based on data collected at their institution, recommended that tissue sections of these margins do not need to be submitted if the tumour is greater than 2cm from both margins. In lymph node submission, there are multiple studies discussing techniques for improving the number of lymph nodes harvested from colon specimens[2,15,16], but little to no literature on techniques for the efficient blocking of lymph nodes exists. Lymph node counts are highly variable and often contribute to a large amount of blocks per case, so it is worthwhile to explore ways in which to submit more lymph nodes in fewer blocks without negatively impacting histology. Thirdly, the aforementioned study by Klaver et. al.[5] finds that the amount of tissue sections containing tumour with serosa initially submitted has an impact on the likelihood of colorectal cancer being staged as pT3 versus pT4a. This study aims to add to this growing body of knowledge on grossing quality in colorectal carcinoma specimens, with a focus on the institutional guidelines in Manitoba, Canada.

Grossing Practices in Manitoba, Canada and Study Aims

In the province of Manitoba, Canada, SharedHealth Manitoba oversees four pathology laboratory sites which all adhere to one standard grossing manual. This grossing manual was introduced in October 2019 with the goal of standardizing grossing and blocking performed by PAs in Manitoba. An initiative to make block selection more efficient had already taken place in 2017, and the manual served to create an easily accessible reference for PAs at the grossing bench. This initiative ensures that Pathologists are consistently given accurate information in the gross description, have access to specimen photographs as-needed, and are given adequate and informative tissue blocks.

For colorectal cancer specimens, the SharedHealth grossing manual indicates that 3-5 sections should be taken from the tumour, with additional sections from surgical margins, lymph nodes, or additional incidental findings. A detailed list of SharedHealth Manitoba guidelines are outlined in Table 2.

Most aspects of colorectal cancer blocking are easily kept to a minimum number of blocks, but lymph nodes are the most variable tissue sections which can greatly influence the total number of cassettes submitted to histology. A minimum of 12 lymph nodes should be found in order to accurately stage colorectal cancer[17], but the pericolonic fat must be entirely searched and *all* lymph nodes found must be submitted. Although 12 lymph nodes is the ideal number

cited in textbooks[4,17], studies found that patient survival increases as the total number of retrieved lymph nodes increases, even when the total number retrieved increases beyond the "ideal" number of 12 lymph nodes[16,18]. The total number of lymph nodes is highly variable due to several factors: the quality of the dissection plays an important role, but other factors such as neoadjuvant therapy, lymphatic invasion, and the patient's age can influence the average lymph node size and thus make them easier or more difficult to identify[12].

For the grossing manual to successfully achieve its goal of standardizing and improving the quality of grossing, the manual itself must be accurate and PAs must adhere to what is outlined in it. The aim of this study is to retrospectively analyze malignant right hemicolectomy specimens grossed in Winnipeg before and after the manual's introduction, with a goal of quantifying the manual's impact on efficiency and quality of colectomy grossing. Additionally, this data will be interpreted with the aim of finding areas of improvement in the manual. These aims will be achieved by collecting and analyzing data related to: (1) total number of blocks submitted per specimen, (2) total number of tumour blocks submitted per specimen, (3) total number of proximal/distal margin blocks submitted per specimen, (4) lymph node submission, and (5) the informative value of blocks submitted.

Methods

A retrospective database review was conducted with the database accessible from SharedHealth Manitoba's pathology laboratory information system (CoPath Plus; Cerner Corporation). Data was extracted by searching for colectomies performed in the first and second quarters of the years 2019 (pre-manual) and 2020 (post-manual). Multiple data points were collected for all colectomy procedures found during the specified time periods, as listed in Table 3. The data was further refined to only include right hemicolectomies performed for colorectal cancer and exclude all other non-cancer or non-right hemicolectomy specimens. Data points specific to the five quality assurance goals were further extracted from this raw data, as listed in Table 4.

Table 2. SharedHealth Manitoba grossing manual guidelines for block submission in colorectal cancer specimens[8].

Block Type	# of blocks submitted	Additional Criteria
Proximal and distal margins	1-2	- Tumour ≥5cm from margin: one proximal and one distal margin section submitted together in one block - Tumour <5cm, but >2cm: one proximal and one distal section, in two separate blocks - Tumour <2cm: perpendicular section from closest margin and en face section from farthest margin, submitted in two separate blocks
Tumour	3-5	These blocks must all demonstrate the tumour's deepest invasion, closest serosal surface, and closest radial margin.
Appendix (if present)	1	- If unremarkable: submit one block of tissues, including the distal tip. - If abnormal: submit the appendix entirely.
Additional abnormalities (if present)	Variable	Variable
Anastomotic rings (when applicable)	0-2	Only submitted when tumour is <2cm from proximal or distal margin.
Lymph nodes	Variable	- Submit grossly unremarkable nodes entirely. - Submit one cross-section from each grossly tumour-replaced node. - Up to five nodes can be placed in one block if they are <0.5cm in size and are intact. - Two bisected lymph nodes >0.5cm in size may be submitted together in one block if they are inked with different colours.

As previously mentioned, this study will be looking at data in relation to: (1) the total number of blocks submitted per specimen, (2) total number of tumour blocks submitted per specimen, (3) total number of proximal/distal margin blocks submitted per specimen, (4) lymph node submission, and (5) the informative value of blocks submitted. The data was tested for normality with Kolmogorov-Smirnov and Shapiro-Wilk tests, and all data was found to be normally distributed.

Table 3. Data elements collected from CoPath database for each case.

Data Element	Information Collected
Time	Whether a specimen was processed in: - Q1/Q2 2019 - Q1/Q2 2020
Specimen block total	Total # of tissue blocks submitted per specimen
Gross report	Full transcript of PA's gross description, including block descriptions
Synoptic report	Full transcript of Pathologist's final synoptic report

Table 4. Data elements extracted from the raw data.

Data Element	Information Collected	Unit
Lymph node count	Total number of lymph nodes harvested	#
Lymph node blocks	Total number of blocks containing lymph nodes submitted to histology	#
Lymph node inking	Whether the grossing PA differentially inked small bisected lymph nodes	Yes/No/Not Applicable
Margin blocks	Total number of blocks containing proximal and distal margins submitted to histology	#
Tumour blocks	Total number of blocks containing tumour submitted to histology	#
Shortest distance to margin	Closest distance of the tumour to intestinal margin	cm
Block deficiencies	Whether the grossing PA submitted non-informative blocks	Yes/No

Total Blocks Submitted

The average number of total blocks submitted in pre-manual and post-manual cases was calculated. Then an independent samples t-test was performed at a 95% confidence interval to determine if a significant difference in total block count exists between the two groups.

Tumour Blocks Submitted

The difference in number of tissue blocks containing tumour was analyzed by calculating the average number of tumour blocks submitted in pre-manual and post-manual cases. An independent samples t-test was performed at a 95% confidence interval to determine whether a significant difference between the two groups exists.

Proximal and Distal Margin Blocks Submitted

Similarly to the tumour blocks, the difference in number of margin blocks was analyzed by calculating the average number of margin blocks submitted per case in the pre-manual and post-manual groups. An independent samples t-test was performed at a 95% confidence interval to determine whether a significant difference exists.

Lymph Node Submission

Analysis of lymph node submission involved three data sets: the total number of lymph nodes found per specimen, total number of blocks containing lymph nodes submitted per specimen, and whether small bisected lymph nodes were differentially inked and submitted together in one block as per the grossing manual (Table 2). For each data set, an independent samples t-test was performed at a 95% confidence interval to look for significant differences between pre-manual and post-manual specimens.

Non-Informative Block Submission

Non-informative blocks were identified for the fifth aim by reviewing the grossing manual guidelines for block submission[8] and forming a list of "block deficiencies", as outlined in Table 5. A block deficiency was defined as the presence of any tissue block which is not required to be submitted according to the grossing manual, and thus is likely to be a non-informative block. The gross descriptions and block descriptions of each case were individually reviewed to look for block deficiencies, then the frequency of each deficiency type in pre-manual and post-manual cases were collected. Independent samples t-tests were then performed on each deficiency type to determine if there was a significant change in the submission of non-informative blocks between pre-manual and post-manual cases.

Table 5. Definitions of block deficiency types collected for analysis of non-informative block submission.

Deficiency Type	Criteria for a Deficiency
Anastomotic donuts	If any blocks of anastomotic donuts are submitted when the tumour is >5cm from proximal and distal margins
Proximal and distal margins	If 2+ blocks of margin are submitted when the tumour is >5cm from proximal and distal margins; or 3+ blocks of margin submitted when the tumour is 2-5cm from proximal and distal margins
Tumour	Six or more blocks of tumour
Ileocecal valve	Any blocks of grossly unremarkable ileocecal valve
Appendix	Two or more blocks of grossly unremarkable appendix
Polyps	Ten or more blocks of additional incidental polyps
Diverticula	Any blocks of uncomplicated diverticula not involved by tumour
Random mucosa	Any blocks of grossly unremarkable mucosa

Results

Overall, 180 right hemicolectomies performed for primary colorectal carcinoma resection were identified in the first and second quarters of the years 2019 ("pre-manual", n=88) and 2020 ("post-manual", n=92). All specimens reviewed had a grossly visible tumour and no specimens were in the post-neoadjuvant therapy setting.

Total Blocks Submitted

Pre-manual cases had an average of 23.30 tissue blocks submitted in total and post-manual cases an average of 21.50 blocks, however this decrease was not a statistically significant finding ($p>0.05$).

Tumour Blocks Submitted

Pre-manual cases had an average of 5.08 tissue blocks containing tumour submitted, and post-manual cases an average of 5.65 tumour blocks. This was a statistically significant increase in tumour block submission ($p=0.01$).

Proximal and Distal Margin Blocks Submitted

Pre-manual cases had an average of 1.49 margin blocks submitted and post-manual cases an average of 1.38 margin blocks. This was not a statistically significant difference ($p>0.05$). Additionally, in 2019 the average distance of tumour to the closest resection margin was 7.5cm and in 2020 the average distance was 8.4cm. This was not a statistically significant increase in the distance of tumour to margin ($p>0.05$), and zero cases had a positive proximal or distal margin.

Lymph Node Submission

Pre-manual cases had an average of 27.66 lymph nodes found per specimen and post-manual cases had an average lymph node count of 24.49, however this decrease was not statistically significant ($p>0.05$). Pre-manual cases submitted 12.45 tissue blocks containing lymph nodes on average and post-manual cases had an average of 10.02 lymph node blocks. This was a statistically significant decrease in the number of lymph node blocks submitted ($p=0.015$). Lymph nodes were differentially inked and submitted in the same tissue block in 43.5% of pre-manual cases and 68.0% of post-manual cases where differential inking could have been utilized; this was a statistically significant increase in the use of differential inking ($p=0.014$).

Non-Informative Block Submission

Overall, 52 pre-manual cases and 45 post-manual cases were identified in which there was at least one type of non-informative block submitted. This was not a statistically significant decrease ($p>0.05$). Analysis of each deficiency type indicates a statistically significant decrease in non-informative block submission for blocks containing anastomotic donuts ($p=0.001$), proximal/distal margins ($p=0.000$), grossly normal appendix ($p=0.000$), and random mucosa ($p=0.000$) (Figure 2). There was a significant increase in non-informative tumour block submission ($p=0.037$) (Figure 2).

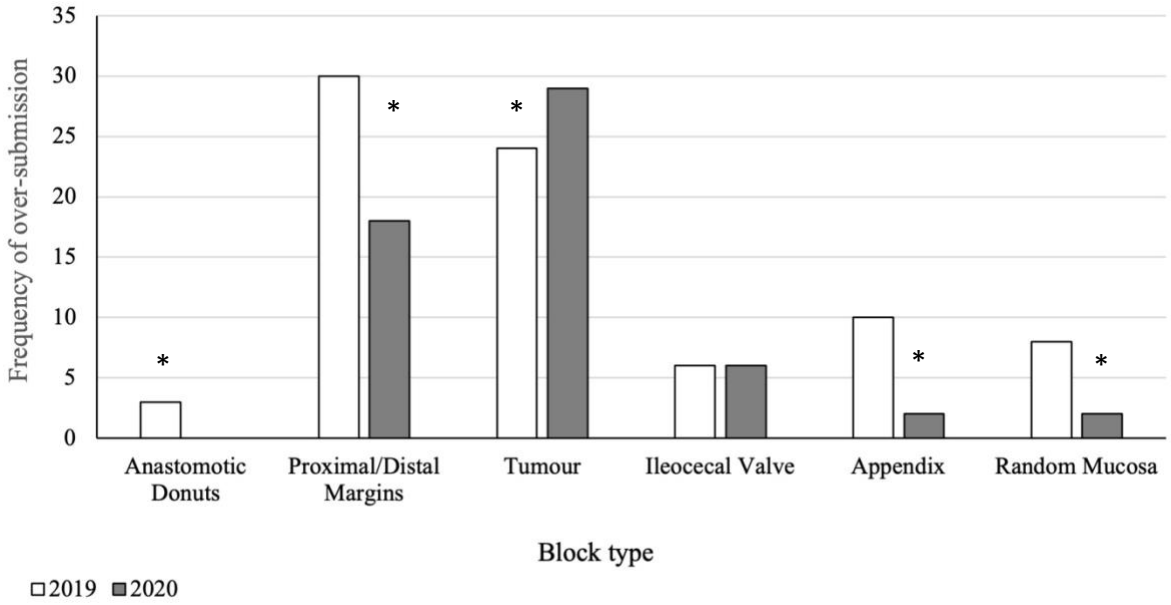

Figure 2. Frequency of block over-submission by block type and year. An asterisk denotes significantly significant changes in frequency between 2019 and 2020.

Discussion

In summary, the introduction of the grossing manual improved the efficiency of block selection in multiple categories: proximal/distal margins, lymph nodes, anastomotic donuts, normal appendix, and random mucosa. In all of these categories, less blocks were submitted per case after introduction of the manual but without compromising the informative value of the tissues selected for each block. Despite the improvements seen in individual categories of blocks, the overall total number of blocks submitted per case did not decrease in the post-manual cases. This may be in part due to the increase in tumour blocks submitted post-manual, and in part due to the inherent variability of lymph node counts between cases.

It is not clear why tumour block submission increased. One theory as to why this occurred is that there may have been an increased number of complex cases which required more extensive sampling. Very rarely, a PA might need to submit more than five blocks if the tumour is involving multiple structures, such as the ileocecal valve, appendix, or omentum. This occurred in some post-manual cases but more notably, many of the cases in which tumour was over-submitted went one to two blocks over the recommended limit if there was possible serosal involvement. Thirteen out of 24 (54%) pre-manual cases which were identified as having six or

more tumour blocks submitted had "puckered serosa" or "tumour abutting serosa" mentioned in the gross description, whereas 21 out of 29 (72%) of post-manual cases mentioned probable serosal involvement. Even though our study defined "six or more blocks of tumour submitted" as being "non-informative", these extra blocks may be informative in some cases since the increase in tumour blocks is simultaneous with an increase in cases containing probable serosal involvement.

Despite this increase in tumour block numbers technically being the submission of "non-informative" blocks as per the grossing manual, there is justification for increased block submission since serosal involvement is difficult to determine grossly and PAs need to ensure adequate sampling of possibly involved areas. As mentioned earlier, a recent study found that colorectal tumours were more likely to be staged at pT4a (i.e. serosal/peritoneal involvement), rather than pT3 (i.e. pericolonic fat involvement without serosal involvement), when more blocks containing possible serosal involvement were submitted[5]. This is a delicate balance between blocking efficiency and grossing quality, as it is justified in these cases to over-submit tumour blocks in order to ensure the accurate staging of a patient's tumour. With this balance in consideration, a recommendation we would make for improvement of the grossing manual is to suggest consultation with a Senior PA, or Pathologist when necessary, if a PA believes that they will need to submit more than five tumour blocks. Although most cases with tumour over-submission did have probable serosal involvement, there were several cases both pre- and post-manual which did not have gross involvement of serosa. By having an extra set of eyes examine the gross specimen, this will ensure that block over-submission is justified when necessary to maintain the quality of patient care, and ensure that blocks are not over-submitted when possible.

Aside from the Klaver et. al.[5] paper which focuses on cases with serosal involvement, there is not much literature providing evidence-based recommendations for the ideal amount of tumour blocks to submit in surgical specimens for colorectal carcinoma. Some articles containing other institutional guidelines do exist, such as The Royal College of Pathologists (UK) guidelines[7] which suggest a minimum of five blocks of tumour, in contrast to SharedHealth Manitoba's guideline of minimum three to a maximum of five[8]. Due to the lack of literature on overall tumour sampling in right hemicolectomies, the reason for this difference is not clear. Based on this information, a possible recommendation to add to the SharedHealth Manitoba manual would be for PAs to consult with their Senior PA, or a Pathologist in particularly

complex cases, if they believe that they need to submit more than five blocks. Due to the lack of literature on this topic, this recommendation simply keeps the manual's grossing guidelines the same while adding an extra layer of security for those cases which may require the PA to deviate from the guidelines.

Moving on to margins, the submission of proximal/distal margin blocks decreased with the introduction of the grossing manual. This indicates that in other cases, the manual did achieve its goal of standardizing grossing procedure between PAs while improving the efficiency of block submission. The current guideline for margin submission is to submit one block containing both margins when the tumour is >5cm away from margins, and two blocks of margin when the tumour is within 5cm of margin. The average distance to margin was 7.5cm in 2019 and 8.4cm in 2020, which indicates that the most common type of margin submission should consists of one block.

Of all the cases reviewed, the closest resection margin on a right hemicolectomy was 1.0cm from tumour, with 11 other cases ranging from 1.5 to 3.5cm in distance. Despite the closeness of tumour to margin in these cases, zero cases had positive margins. If all margins, even ones present within a couple centimetres of tumour, were negative then it may be unnecessary to submit blocks containing margin if the tumour is well-clear. The grossing manual currently requires a longitudinal section of tumour with margin when the distance is <2cm[8], so we recommend that margin submission may not be necessary if tumour is >2cm from margin. Longitudinal sections are ideal for any tumour within 2cm of margin, as the Pathologist will need to assess the tumour's microscopic approach towards margin[8,17]. A previous study recommends that margin submission is not needed with a distance of >3cm[14], and several other papers cite a 3cm cut-off as a reasonable guideline for margin submission[6,12].

Exceptions to the non-submission of margins exist and must be carefully considered. Margins should be adequately and extensively sampled in the case of diffusely infiltrative tumour or tumour arising from inflammatory bowel disease, since the presence of these conditions greatly increases the probability of a positive margin occurrence[11,19]. Lymph node presence should also be considered, since a positive lymph node present near the bowel wall at margin may influence margin status[14].

The routine submission of lymph nodes also proved to be successfully standardized and made more efficient after introduction of the grossing manual. The number of lymph nodes

found per case did not significantly differ between the years of 2019 and 2020, yet there was a significant reduction in lymph node blocks submitted by approximately two blocks per case. The practice of differentially inking bisected lymph nodes and placing them together inside one block increased, which is a very likely cause for the reduction in lymph node blocks. This proves that the inking of lymph nodes is a worthwhile guideline to implement: it only takes the PA an extra several minutes to do while it greatly reduces the cost of block submission.

All in all, the grossing manual did not reduce the overall numbers of blocks submitted per case, but did improve the informative value of blocks submitted. The small and insignificant changes in the total numbers of submitted blocks may be explained by three things: firstly, the previously mentioned block efficiency initiative in 2017 had already brought issues in blocking to the attention of PAs, therefore block counts would not have changed drastically between 2019 and 2020. However, other issues outlined in the manual (such as lymph node inking) did improve, which may be a direct result of PAs having easy access to grossing guidelines.

Secondly, right hemicolectomies for colorectal cancer are variable specimens, especially due to differences in lymph node counts between patients, so the reduction of overall block submission may be a difficult task to achieve. For example, one patient might have 15 small lymph nodes easily submitted in 3 blocks while another has 30 large lymph nodes which require 15 blocks; this sort of variation in block count is out of the PA's control as they cannot exclude lymph nodes from submission. Despite this, it is still worthwhile to implement grossing guidelines which can improve blocking efficiency in colorectal carcinoma cases, such as using the differential inking of smaller lymph nodes in order to submit more tissue in one block. These guidelines serve a purpose of creating standardization between PAs and reducing block count where possible.

Thirdly, a possible limitation to this study and explanation for the manual's small effect is the post-manual time interval. Post-manual cases were taken from Quarters 1 and 2 (i.e. January through June) in 2020, which is only 3-9 months after the manual's first implementation. There may be a learning curve for PAs after the manual's introduction, especially for experienced PAs who already developed their own grossing "style". Therefore, a greater effect of the manual on grossing quality might be observed if data from late 2020 and onwards is analyzed in the future.

There are two opposing factors which influence the submission of tissue sections to histology: the cost of processing a block, and the need to provide Pathologists with tissue sections which provide valuable information for the purposes of T-staging a patient's disease. This study found that block submission can be made more cost-efficient by inking small lymph nodes different colours then placing multiple nodes in the same cassette, and by providing PAs with an easily accessible manual which provides guidelines on which tissue sections are appropriate to take. These small changes provide Pathologists with the same amount of information needed to T-stage a disease, and therefore patients with the same quality of care, while reducing costs associated with tissue processing.

Despite the positive impact of these changes, some cases prove to be difficult for block efficiency and there are instances in which block submission justifiably tips in favour of "staging information" rather than "efficiency". Specifically, primary colorectal carcinoma specimens with possible serosal involvement (i.e. puckered or indurated serosa identified grossly) typically had more blocks submitted than what the manual recommended. Current literature supports the submission of multiple blocks of possible serosal involvement in these cases, since patients are more likely to be staged up to pT4a when the Pathologist is given multiple blocks of serosa and more likely to be staged down to pT3 when fewer tissue samples are provided[5].

Conclusion

In October 2019, a grossing manual was introduced in Pathology laboratories across the province of Manitoba after a blocking efficiency initiative took place in 2017, with the aim of standardizing grossing practices between PAs while ensuring that block selection is adequate and efficient. This study found that after the manual's introduction, the overall number of total blocks submitted, as well as number of tumour and proximal/distal margin blocks, did not decrease. However, the submission of non-informative margin, anastomotic donut, normal appendix, and random mucosa blocks did decrease and the efficiency of lymph node submission improved. Decreasing the total number of blocks submitted is difficult due to the inherent variability in colorectal cancer specimens and in pericolonic lymph nodes, but the amount of non-informative blocks submitted is worthwhile to address since the informative value of tissue sections impacts the Pathologist's ability to diagnose and stage disease. Based on our findings, we suggest two recommendations for future versions of the grossing manual: (1) consult with a Senior PA, or

Pathologist when necessary, if the submission of more than five tumour blocks may be necessary; and (2) do not submit any blocks of proximal or distal margins if the tumour is present >2cm from both margins.

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