1 INTRODUCTION

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Intraoperative consultation (IOC) refers to the pathologist's role as a consultant during surgical procedures. While making a diagnosis is the cornerstone of intraoperative consultation, the role of consultant goes beyond making a diagnosis, and includes discussions about the usefulness, appropriateness and limitations of intraoperative diagnosis, the best specimen to procure for diagnosis, recommendations for ancillary tests, and suggestions for management when the pathologist is unable to make a definite diagnosis. The tools for intraoperative diagnosis (IOD) include some combination of gross examination, frozen sections, and cytologic tests, and at some institutions, a limited number of rapid special stains are also employed.[1] However, the older term "frozen section diagnosis" is so entrenched in our lexicon that we sometimes use it when we mean "intraoperative consultation."

CHANGES IN INTRAOPERATIVE CONSULTATION

The types of specimens submitted for IOD, and the pathologist's role in intraoperative management, have changed significantly over the past two decades. Most of these changes are due to technical innovations in diagnostic imaging, advances in image-guided needle biopsies, changes in surgical management, and advances in medical treatment. The following examples will illustrate these points.

The widespread use of screening mammography, and the shift to tissue-conserving surgery for malignancies, have resulted in a dramatic change in the surgical approach to diseases of the breast. Fine-needle aspiration biopsy (FNA) of palpable lumps and image-directed needle core biopsies are now the favored ways to make an initial diagnosis, and as a result, non-guided open breast biopsies, once the most frequent specimen submitted for frozen section evaluation,[2–4] are now encountered only infrequently.

Similarly, the need for an initial diagnosis by frozen section (FS) has decreased with the widespread use of endoscopic biopsies and image-directed needle biopsies. These procedures frequently yield a tissue or cytologic diagnosis pre-operatively, allowing the surgeon to plan definitive surgery with a firm diagnosis in hand. The resected specimen may be sent for intraoperative evaluation of surgical margins, but not necessarily for diagnosis.

Newer approaches to surgical management, including tissue-conserving surgery, have changed the types of specimens submitted for intraoperative evaluation. Lumpectomies of the breast are now more common than mastectomies, and limb sparing surgical resections of bone and soft tissue malignancies are more common than amputations.

Advances in medical treatment have virtually eliminated some types of surgical procedures. As an example, vagotomy, pyloroplasty, and gastric resections are rarely used to treat peptic ulcers because of the efficacy of antimicrobials, H_2-receptor antagonists and proton pump inhibitors. Consequently, gastric resections for peptic ulcer disease are rarely encountered in modern-day practice.

The pathologist's role in intraoperative management will continue to change as newer approaches to diagnosis and treatment are developed, and it is inevitable that some of the statements made in this book will become dated with time.

DIFFERENCES IN THE USE OF INTRAOPERATIVE DIAGNOSIS

The Mayo Clinic has a unique approach to IOD.[5] Frozen sections are performed on the majority of surgical specimens, and a pathology report is usually available when

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the patient is in the recovery room. This allows for efficient triaging of patient care and is suited to the philosophy of the Mayo Clinic. At virtually all other institutions, IOCs are requested selectively, and they account for approximately 5%–6% of surgical pathology accessions.[6,7] There is a great deal of variation in the utilization of IOC but the common thread is that the test is ordered selectively. This book is written for pathologists who are called upon to render intraoperative diagnoses in selected situations.

INDICATIONS FOR INTRAOPERATIVE DIAGNOSIS

The purpose of IOD is to provide pathologic information that will help the surgeon perform the appropriate surgical procedure as efficiently as possible. The indications for IOD are thus driven by the surgeon's needs. Occasionally there is discordance between what the surgeon would *like* to know and what the surgeon *needs* to know to execute optimal surgical treatment, a situation that may be challenging or frustrating, but one that an experienced pathologist should be able to handle. When performed selectively, there are five main indications for IOD.

1. To establish or confirm a diagnosis that will influence the surgical procedure. Requests for this indication have diminished with the availability of endoscopic procedures and image-directed needle biopsies, but there are still situations when open biopsy or resection are required for initial diagnosis. These include failure to obtain a diagnosis with less invasive methods (e.g., a non-diagnostic FNA of a pulmonary nodule), or when percutaneous needle biopsy is contraindicated (e.g., evaluation of a potentially malignant ovarian mass).

In the College of American Pathologists (CAP) Q-probe study published in 1996,[8] IOD directly influenced the nature of the surgical procedure in approximately 30% of cases. However, IOD is of value even when it does not alter the surgical procedure because it allows the surgeon to undertake a planned surgical procedure with greater conviction.

2. To evaluate margins of resection. When malignant neoplasms are treated by surgical resection, the goal is to remove the neoplasm with adequate clear margins. Requests for evaluation of surgical margins are almost as frequent as requests for initial diagnosis in some series.[9] See "Evaluation of surgical margins" below.
3. To determine the adequacy of an incisional biopsy specimen when the only purpose of the surgical procedure is to obtain tissue for diagnosis, e.g., incisional biopsy of a suspected sarcoma of soft tissue or bone. There are two issues to keep in mind when handling these biopsies: First, if FS is the test of choice, should the entire specimen be submitted for FS or should part of the specimen be spared from potential freezing artifact? This decision depends on the size of the specimen and the surgeon's ability and willingness to obtain more tissue for permanent sections, a question that is easily settled by direct communication with the surgeon. The second issue is to distinguish between *abnormal* tissue and *lesional* tissue. The surgeon's initial biopsy may be from reactive tissue surrounding the target lesion, introducing a risk that the pathologist may interpret these secondary changes as the primary disease. Familiarity with the clinical and imaging data, and discussion with the surgeon, can help to avert this error.
4. To stage malignant neoplasms intraoperatively. Most neoplasms can be successfully staged with diagnostic imaging, but there are situations when surgical staging is necessary to deliver optimal care. There are two main clinical scenarios: In the first situation, FS diagnosis will invoke the "stopping rule," i.e., definitive surgical resection is abandoned because the neoplasm has extended beyond the boundaries of resection; for example, a Whipple's procedure for pancreatic carcinoma will be abandoned if FS confirms the presence of peritoneal metastases. The second is the "go ahead rule." In this situation, IOD gives the surgeon permission to proceed with more extensive surgery; as an example, the surgeon will proceed with surgical staging if a diagnosis of primary carcinoma is rendered on an ovarian mass.*

* To the best of my knowledge, the terms "stopping rule," "go ahead rule," and "good enough diagnosis" were coined by Dr. Michael Hendrickson, Department of Pathology, Stanford University School of Medicine.

5. To procure fresh tissue for ancillary studies, such as microbiology, flow cytometry, cytogenetics, molecular diagnostic tests, electron microscopy, and research protocols.

EVALUATION OF SURGICAL MARGINS

Surgical resection is the treatment of choice for many malignant neoplasms, and when the tumor is resectable, the goal is to remove the neoplasm with adequate clear margins. The definition of an adequate margin depends on a variety of factors, including type of neoplasm, stage of disease, anatomic location, and proximity of the tumor to vital structures. The definition of an adequate margin is based on empirical data but there is also an element of arbitrariness, so that an adequate margin may range from 1 mm to 2–3 cm. There is also an increasing realization that, for some malignancies, narrow margins of excision are as good as wide margins.

The only reliable way to evaluate the adequacy of resection is to ink the surgical margins of the specimen, and with more than one color if this will help to localize a positive margin. Inking is best done with a Q-tip, and when the surface area is large, with a cluster of Q-tips or with a small brush. The specimen should not be dipped into a container of ink because this will allow the ink to seep into crevices on the surface of the specimen. Metal staples should be removed before inking because they may be masked by the ink and interfere with sectioning the specimen. Inking is not always as straightforward as one would like to believe. Sometimes, the margins are irregular, making it difficult to decide where to apply the ink. Irregular surfaces occur either because of the nature of the surgical resection (e.g., blunt dissection in partial hepatectomy), the friable nature of the surface tissue (e.g., fatty lumpectomy specimens of the breast) or because the surgeon has created more than one plane of dissection, resulting in flaps of tissue at the margins of the specimen.

A variety of factors determine how well the ink will adhere to the tissue. Ink will not adhere well to desiccated tissue, and the effectiveness of inking will be reduced if the surface is not well dried prior to inking. Adhesion of ink to tissue can be improved by spraying the inked surface with a mordant such as Bouin's solution or dilute acetic acid (white vinegar), but this should be done only after the ink has dried.

There are two main approaches to evaluating surgical margins in complex resections. In the first approach, the pathologist selects tissue from the margins of the excised specimen, whereas in the second approach, the surgeon submits biopsies from the resection bed after definitive excision. The advantage of the latter approach is that the surgeon samples the margins of concern; when these biopsies are small, the entire specimen is embedded for FS so that tumor anywhere in the specimen is interpreted as a positive margin.

Sometimes, the orientation of a specimen is obvious and does not require any specific labeling, e.g., an esophagogastrectomy. However, when orientation is necessary, the surgeon should submit the specimen with a sketch and/or mark the specimen with sutures. If the orientation is ambiguous, clarification should be obtained before inking and dissecting/sectioning the specimen. If sutures are used for orientation, the surgeon should place them with a loose loop to facilitate easy removal (see Chapter 4, p. 53). Specimens that have been oriented should be marked with at least two colors of ink, and more than two if this will localize a positive margin more precisely (see Chapter 3, p. 27).

When the pathologist samples the margins on an excision specimen, sections can be taken perpendicular or parallel to the margins. The method chosen depends on the type of specimen, the size and shape of the specimen, the type of neoplasm, the distance of the neoplasm from the surgical margin as judged by gross examination, and whether the surgeon is interested in the distance of tumor from the margin. Sections taken parallel to the margin (*en face*) allow for more thorough evaluation, but if the margin is negative, it may not be possible to obtain an accurate measurement of the distance of the tumor from that margin. In contrast, the width of a clear margin can be measured when sections are taken perpendicular to that margin. The latter approach results in partial evaluation of the margin, but thorough sampling and cutting levels into the FS block/s can reduce the risk of false-negative results. As a general guide, sections taken parallel to the margin work well when the neoplasm appears distant from the margin by gross examination (>1–2 cm depending on the anatomic site), whereas sections taken vertical to the margin are preferable when the malignancy is close to the margin by gross examination, e.g., <1 cm from the margin.

When tissue is re-excised from a positive margin, the new margin should be carefully inked to retain orientation during handling. If the re-excised tissue is >5 mm wide,

my preference is to make serial sections perpendicular to the new margin, but if the re-excised tissue is a narrow strip <3 mm wide, the entire specimen should be embedded on edge, with the new margin deep in the block.* Sections are thus cut toward the new margin.

Most tissues, especially those that contain muscle, will contract after surgical removal, a phenomenon that is especially noticeable in hollow muscular organs such as esophagus and intestine. This contraction results in a discrepancy between the surgeon's impression of the length of the surgical margin and the pathologist's measurements. As shown by Goldstein *et al.*, the margin in colorectal specimens can shrink to 60% of its in vivo length within 20 minutes of devascularizing the colon.[10] This is important when there are constraints on removing additional normal tissue, as in resections of the esophagus and rectum. Similar discrepancies between in vivo and in vitro measurements have also been reported for excisions from the oral cavity.[11] There is no way to avoid this problem, but the surgeon's measurements naturally take precedence if this comes up for discussion.

Clear margins are not synonymous with adequate margins, and the pathologist should be prepared to report the distance of tumor from the margin if the surgeon is interested in the extent of margin clearance. The width of a margin can be estimated accurately enough by using the diameter of the objectives of a microscope; for example, the diameters of the 2× and 10× objectives of the Olympus BX41 microscope are 10 mm and 2 mm, respectively.

When margins are evaluated with parallel sections, care should be taken to line up all the tissue layers before sampling the margin because some layers retract more than others, leading to incomplete evaluation if the sample is not collected with care; as an example, the mucosa in the upper aerodigestive tract has a tendency to retract from the margin so the sample selected for FS may not include mucosa and lamina propria, tissue layers that are very important to evaluate in resection specimens.

The issue of adequate margins is more complex than is apparent at first glance. One puzzling finding is the absence of residual malignancy in re-excised tissue following a positive margin. When re-excision is delayed, the absence of residual tumor can be explained by tumor ablation as a result of wound healing,[12] but how is the absence of residual carcinoma explained when re-excision is immediate? The corollary is also true: local recurrences may occur after seemingly adequate excision. Some explanations for local recurrence after negative margins are: (a) the reported negative margin was an interpretative error, and the margin was in fact positive; (b) the tumor is multifocal but its multifocality was not appreciated at the time of resection; and (c) the "recurrence" is a new neoplasm that arose in tissue that was normal by conventional histologic examination but abnormal by molecular analysis, and therefore capable of spawning a new malignancy (see Fig. 4.3, p. 46).[12]

Part of the problem with conventional FS evaluation of margins is that histologic sections employ a two-dimensional approach to evaluate lesions that have three dimensions. False-negative margins are more likely when neoplasms have a highly infiltrating pattern of growth and if the leading edge of the tumor happens to be in a plane different from the plane of the histologic sections. Wider margins of resection are therefore necessary for malignancies with an infiltrative pattern of growth. One way to reduce false-negative diagnoses is to prepare more than one FS block when appropriate, and to cut multiple levels when evaluating a malignancy with an infiltrative pattern of growth.

Every attempt should be made to evaluate surgical margins thoroughly during surgery; this includes adequate sampling of the margins, and when appropriate, cutting multiple levels into the block(s). The findings in deeper levels of the same FS block can sometimes be startlingly different, especially for malignancies with an infiltrative pattern of growth. There is no rational argument for intentionally saving tissue for permanent sections if evaluation of the margins is critical to immediate surgical care. The surgeon is interested in having the correct information *during* surgery, not the following day. The reversal of a FS diagnosis from negative to positive margins may require a second surgical procedure, which is unfair to the patient if this could have been averted by more thorough examination intraoperatively.

Sometimes, it is difficult to distinguish a positive margin from a reactive process, particularly with mesenchymal neoplasms such as desmoid fibromatosis, paucicellular dermatofibrosarcoma protuberans and some low-grade

* Some pathologists prefer to embed the tissue with the new margin closest to the surface of the block, in which case, the first section represents the true surgical margin. I prefer to embed the tissue with the true margin deep in the FS block for the following reasons: (a) The true margin is still available for evaluation if technical problems are encountered when facing the block; and (b) cutting towards the true margin allows one to determine if any tumor is present in the 3mm thick sample selected for FS, information that may be useful to the surgeon.

sarcomas. This distinction is particularly difficult if the tissue at the margins includes a fibroblastic reaction to previous surgery, leaving the pathologist no option but to defer interpretation of the margins to permanent sections.

Mohs micrographic surgery makes an attempt to evaluate all the surgical margins in a specimen by using a different approach to embedding and sectioning tissue (see Fig. 3.7, p. 29). The Mohs technique is applied mainly to cutaneous malignancies and is especially useful for complex cutaneous malignancies, previously excised malignancies with positive margins, recurrent malignancies, and when tissue conservation is at a premium. Mohs surgery is not subject to the same time constraints as conventional FS; after the first stage has been performed, the patient may leave the surgical suite with an open wound, and because the procedure is performed under local anesthesia, the second stage can be performed later that day after FS results are available. The time between different stages of excision allows the Mohs surgeon to order rapid special stains, including rapid immunohistochemical stains, if needed.

UNNECESSARY AND INAPPROPRIATE REQUESTS FOR FROZEN SECTION DIAGNOSIS

Every pathologist encounters unnecessary and inappropriate requests for IOD. *Unnecessary requests* for IOD are those that have no bearing on immediate management. In the study by Weiss *et al.*,[9] 5% of IODs were considered unnecessary or ambiguous, and this number is probably higher in most hospitals. Sometimes, FS is requested for reasons other than immediate surgical management, and what may appear to be an unnecessary FS can be justified on *non-surgical* grounds. For example, a FS may be ordered to expedite post-operative care, or facilitate post-operative discussion with an anxious patient or family.[8] Sometimes, however, a FS is requested to satisfy the surgeon's curiosity or for reasons that are not clear.[13] We probably all perform unnecessary FSs on occasion but four criteria should be met: (a) There is no risk of compromising the specimen; (b) the specimen has to be sufficient for routine examination as well as all possible ancillary studies; (c) there is a reasonable chance of making a meaningful diagnosis; and (d) there is little risk of providing misleading information. The pathologist should not hesitate to advise the surgeon against intraoperative evaluation if the test has nothing to offer. There is no reason, for example, to perform random FSs on a diagnostic J-wire directed breast biopsy that lacks a focal lesion. One way to handle requests for unnecessary FS is to re-formulate the request: the surgeon who asks for a FS diagnosis may not want or need the specificity of a FS diagnosis, and gross examination alone may suffice. For example, if FS is requested on a radical orchiectomy specimen, gross examination is usually sufficient to confirm the presence of a malignant neoplasm.

Requests for FS are *inappropriate* when IOD will have no influence on surgical management *and* there is a significant risk of compromising the specimen because of its small size. In this situation, the pathologist should convince the surgeon that nothing will be gained and much may be lost by subjecting the specimen to the artifacts of freezing. If the surgeon is unyielding in her demand, touch or squash cytology preparations may be prepared, as these could yield a good enough diagnosis, thus achieving the dual goals of appeasing the surgeon and preserving the specimen for permanent sections.

THE IMPORTANCE OF CLINICO-PATHOLOGIC CORRELATION

Every surgical pathologist understands the importance of clinico-pathologic correlation. One of the challenges of IOD is the frequent lack of adequate clinical information, a situation that can lead to serious errors. The best approach is to gather relevant clinical information by whatever means necessary, and to be adequately armed before the specimen is submitted for IOD. Failure to do this places the patient at risk and contributes towards tarnishing the pathologist's reputation. In a multi-institutional study by Zarbo *et al.*,[7] nearly 15% of diagnostic errors were due to lack of familiarity with the clinical history. Both surgeons and pathologists contribute to this unfortunate situation.

Surgeons order clinical laboratory tests without providing clinical information, and it is wrongly assumed that tissue submitted for IOD can be handled in the same way. Sometimes surgeons innocently withhold clinical information, not realizing that this may be crucial for pathologic interpretation. At other times, the surgeon may be focused on the technical challenges of the case and not be fully informed of clinical details that are of interest to the pathologist. Good communication between pathologist and surgeon will limit the impact of these lapses.

A detailed clinical history is not always necessary to render an accurate IOD, and this very fact may lull the pathologist into complacency about the value of clinical data. At many teaching institutions, pathologists or pathologists-in-training routinely pick up specimens from the operating room, allowing familiarity with all aspects of the case before handling the specimen. In the majority of non-teaching hospitals however, specimens are delivered to the laboratory by courier or a mechanical delivery system, and clinical information is limited to what is provided on the pathology requisition form. Pathologists who work under these conditions recognize the fallibility of the system and develop alternative avenues for obtaining clinical information. A quick check of the hospital's electronic information system, and a search for prior pathology reports are helpful first steps. In complex cases, or when the electronic record is deficient, the clinical history should be solicited directly from the surgeon as this may bring about perspectives on the case that cannot be acquired in any other way.

Some types of lesions require correlation with imaging studies. Reading the radiologist's report is often sufficient, but there are situations when it is preferable to review the imaging studies with a radiologist or the surgeon, especially in anatomic locations such as bone, central nervous system and mediastinum. There are situations where serious errors can be made if imaging studies are ignored (see Chapters 6, 17 and 19, on pp. 78, 266, and 306).

There are occasions when it is essential for the pathologist to check on the real-time surgical findings because the surgeon may not volunteer crucial information at the time that the first specimen is submitted for IOD. For example, a mucinous carcinoma of the ovary is more likely to be a metastasis if the malignancy involves both ovaries and other intra-abdominal sites; similarly, carcinoid tumor of the ovary is much more likely to be metastatic if both ovaries are involved. In these two situations, knowledge of the surgical findings should prompt the pathologist to recommend a search for a non-ovarian primary.

Many medical centers require institutional review of outside pathology slides prior to a major surgical procedure. Unfortunately, this practice is not universal so pathologists have to sometimes handle major resection specimens without the benefit of reviewing prior biopsy material. This lack of information places an added burden on the pathologist on FS duty.

It is important to know what is at stake in a particular case, and special attention should be given to high stake cases. This requires full awareness of the clinical issues, familiarity with relevant imaging and laboratory data, and familiarity with the surgeon's algorithm. When a definitive diagnosis is not possible in a high stake situation, the pathologist should visit the operating room, apprise the surgeon of the problem, and participate in making the best decision for immediate patient care.

LIMITATIONS OF INTRAOPERATIVE DIAGNOSIS

Intraoperative diagnosis often has the specificity of permanent sections, but a definite diagnosis cannot be made in every case. There are good reasons for these limitations:

- Problems may occur when an incisional biopsy is not representative of the lesion. As an example, we encountered an incisional biopsy of an anterior mediastinal mass that showed benign thymic cysts on FS. The pathologist was about to render a diagnosis of benign thymic cyst but was encouraged to first review the chest CT in the operating room, at which time it became clear that the surgeon had sampled the cystic component of a malignant neoplasm. A second biopsy was requested and this showed Hodgkin's lymphoma (Fig. 1.1). It is unlikely that the surgeon would have accepted a diagnosis of benign thymic cyst in this particular case, but failure to review the images, and rendering a diagnosis of benign thymic cyst, may have led the surgeon to conclude that the pathologist did not know how to recognize an obvious malignancy.
- Only a limited number of FS blocks can be prepared on large mass lesions so there is a risk of sampling an area that provides misleading or incomplete information. For example, primary mucinous carcinoma of the ovary may contain a spectrum of changes, including benign-appearing areas, and sampling the wrong area may lead to an incorrect diagnosis. Sampling errors can be minimized by careful gross examination, use of cytoscrape preparations to sample a larger surface area, and careful selection of tissue for FS. This situation underscores the reason why skilled gross examination is so important in the intraoperative arena.
- Some lesions are not amenable to IOD because the diagnosis hinges on focal changes that are identified only after thorough sampling. Minimally invasive follicular carcinoma of the thyroid gland is a case in

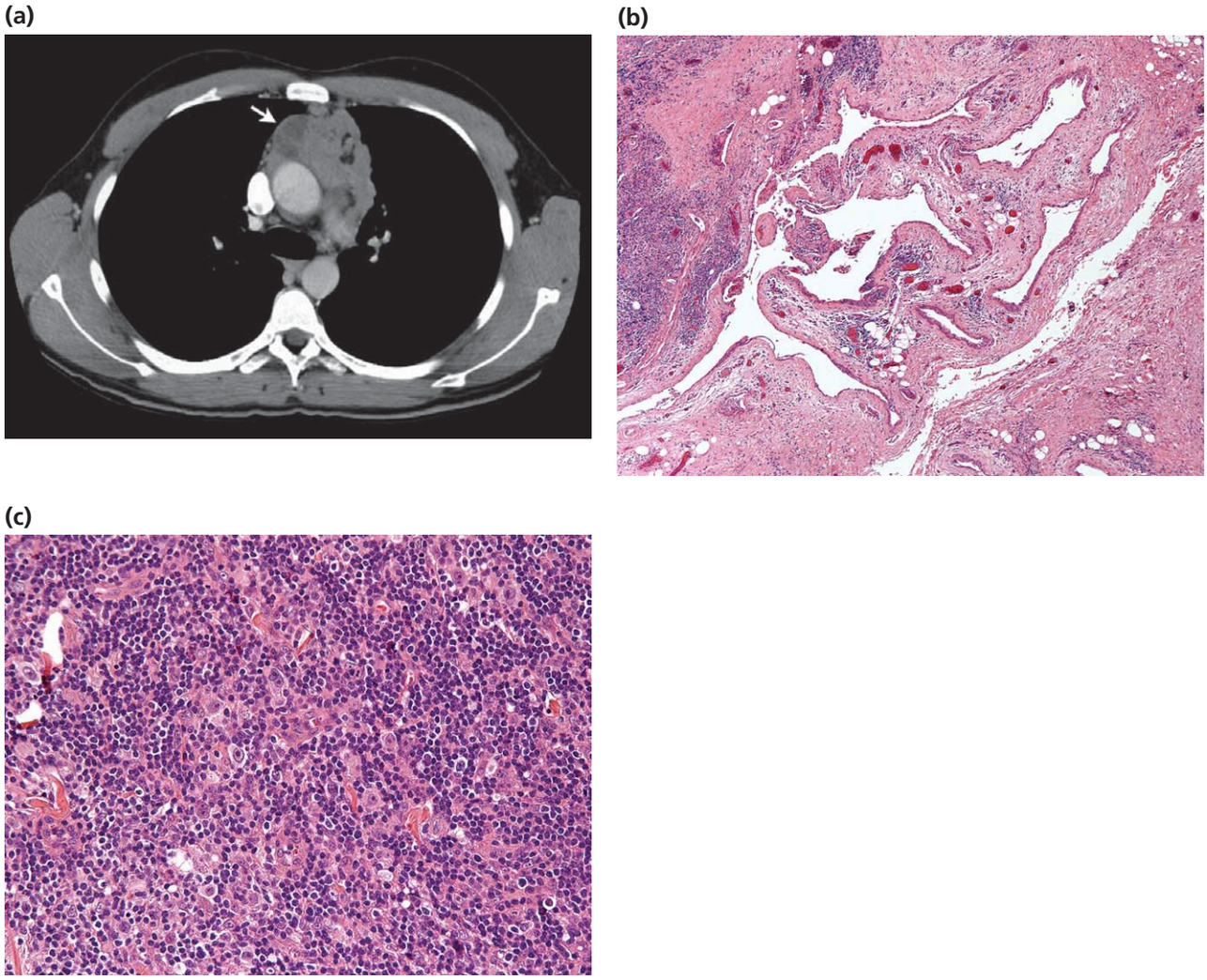

Fig. 1.1. (a) A 33-year-old man with a large anterior mediastinal mass. The surgeon performed an incisional biopsy of the most accessible portion of the lesion, and this happened to be cystic (arrow). (b) The initial FS showed benign thymic cysts. (c) Because the findings on CT scan are those of a malignant neoplasm, a second biopsy was requested and this showed Hodgkin's lymphoma. It is well known that malignancies such as Hodgkin's lymphoma and seminoma evoke the formation of epithelial lined cysts when they involve the thymus gland.

point; capsular and/or vascular invasion are required to make this diagnosis, and it is unlikely that a single FS will detect these changes. Because of the low diagnostic yield, it has been proposed that microscopic examination of an encapsulated solitary thyroid nodule should be deferred to permanent sections (see Chapter 11, p. 168).

- Some neoplasms, including lymphomas, small round cell malignancies of soft tissue and bone, and a variety of neoplasms in other anatomic sites, require ancillary studies for a specific diagnosis, and as a result, only a limited diagnosis can be offered intraoperatively. The pathologist's task is simplified if this limitation is accepted, and if it is understood that all the surgeon needs is a "good enough diagnosis" to facilitate immediate surgical management (see "Good enough diagnosis" below).

THE CONCEPT OF A "GOOD ENOUGH DIAGNOSIS"

Pathologists are programmed to make specific diagnoses, but this is not always possible, nor is it always necessary in the intraoperative setting. Surgical pathologists function on two planes, the scientific and the managerial,[14]

and this concept can be modified for the intraoperative setting by positing that a specific diagnosis should be rendered whenever possible, but what the surgeon needs is a "good enough" diagnosis in order to perform the appropriate surgical procedure. For example, when a diagnostic wedge biopsy is performed for a solitary pulmonary nodule, the surgeon's main question is whether the lesion is benign or malignant, and if malignant, if it should resected by lobectomy. If the FS shows a primary, poorly differentiated non-small cell carcinoma, there is no reason to spend an undue amount of time searching for squamous or glandular differentiation, because lobectomy is appropriate regardless of the tumor's differentiation. A diagnosis of "poorly differentiated non-small cell carcinoma, consistent with primary lung carcinoma" is good enough for the purpose of immediate surgical management.

COMMUNICATION DURING INTRAOPERATIVE CONSULTATION

Clear, concise, and skillful communication is essential in the intraoperative setting. Communication is simple when the diagnosis is straightforward, but more challenging when the case is complicated, or when the pathologist is unable to make a definite diagnosis. Pathologists vary in their ability to communicate effectively, but everyone can learn the principles of good communication. The following guidelines should be kept in mind.

- The surgeon is interested in information that will influence immediate surgical management, and she is unlikely to be impressed by histologic details that are of interest to the pathologist, but have no bearing on surgical management. Pathologic information should therefore, be distilled into clinically meaningful information.
- When a firm diagnosis cannot be made, the pathologist should be prepared to discuss management options with the surgeon, because the pathologist is the only person on the management team who understands why a specific diagnosis cannot be made, and who is able to offer a managerial diagnosis. For example, if a thyroid lobectomy specimen contains a neoplasm of uncertain nature, a recommendation could be made to perform no more than a lobectomy, and to wait for permanent sections.
- The way in which the communication is made will naturally depend on a variety of factors, including the complexity of the case, proximity of the frozen section suite to the operating room, communication facilities available, and traditions of the institution. Straightforward diagnoses can be transmitted by telephone or intercom, but there is no substitute for a visit to the operating room when that becomes necessary. Here are a few reasons to visit to the operating room: (a) It allows the pathologist to gather clinical information that may not have been forthcoming prior to surgery; (b) It allows review of diagnostic images that were not available pre-operatively, e.g., images of a bone lesion from another facility; (c) The pathologist can receive an update on the surgical findings when these are different from the surgeon's pre-operative assessment; (d) It allows face-to-face conversation with the surgeon when the diagnosis has to be deferred; (e) Sometimes a visit to the operating room is the only way to obtain a full grasp of the case, and errors are more likely if the pathologist chooses a less direct form of communication. There is one other point: failure to visit the operating room may be interpreted by the surgeon as unwillingness on the part of the pathologist to fully engage in the care of the patient. In my opinion, a pathologist who is unfamiliar with the clinical aspects of a case, and who is reluctant to visit the operating room when the situation calls for direct communication with the surgeon, has failed to discharge his duties as a consultant.

TURN-AROUND TIME OF INTRAOPERATIVE DIAGNOSES

The turn-around time (TAT) for intraoperative diagnosis depends on the test that is performed, the amount of dissection and preparation required, the complexity of the case, and the experience of the pathologist. In a CAP Q-Probe study, the result of a single frozen section was reported within 20 minutes in 90% of cases,[15] and when multiple FSs are performed on a single specimen, each of the additional FSs should take less than 20 minutes. Cytologic preparations (touch, cytoscrape and squash) often take less than 20 minutes, and gross examination can usually be completed within 10–15 minutes of receiving the specimen in the laboratory.

The turn-around time will be longer when there are multiple simultaneous requests for IOD that exceed the laboratory's capacity, or when there are technical problems in obtaining good-quality frozen sections. Delays will also occur in complicated cases that require additional study or when prior biopsy slides have to be reviewed at short notice. I think it is courteous to call the surgeon on the telephone or intercom when there is going to be a delay, with a brief explanation for the delay. Keep in mind that the surgeon is not privy to the goings-on in the frozen section laboratory, and the simple act of making a telephone call may forestall anxiety and irritation that may come from unexplained delays.

Many pathology departments record the arrival of the specimen in the laboratory and the time that the diagnosis is reported to the surgeon. Turn around time for IOD should be recorded if it is required by the institution, and these data should be included in the department's QA report.

DOCUMENTING INTRAOPERATIVE ACTIVITIES

The pathologist who initially handles a fresh specimen for IOD should accurately document the characteristics of the specimen, as well as record the way the specimen was handled, because some gross characteristics are markedly altered after dissection or sectioning, and cannot be reconstructed later. This documentation should be more detailed if the specimen will be "grossed in" by someone else. The following points should be recorded routinely:

- A note should be made if the specimen was received and handled differently from the usual, e.g., if the specimen was received in a sterile container and was initially handled in a sterile fashion.
- The specimen should be weighed when appropriate, and measurements should be recorded in three dimensions. The size and weight of some specimens can change dramatically, e.g., a cystic ovarian neoplasm, so size and weight should be documented before the specimen is sectioned. The weight and/or volume should be recorded for specimens that are received in multiple small pieces.
- It is helpful, and sometimes necessary, to draw a sketch of specimens such as skin and resections of the upper aerodigestive tract submitted for evaluation of margins, as this may be the simplest way to record the way a specimen was inked and sectioned.
- A note should be made if tissue was procured for ancillary studies such as culture, chromosome analysis, flow cytometry, electron microscopy, research etc. and this should include the volume or size of that sample.
- A note should be made of the intraoperative procedures that were performed, e.g., gross examination only, FS, cytologic examination or some combination of these.
- The written version of the IOD should faithfully reflect the verbal communication with the surgeon, and should include any recommendations that were made.
- A note should be made if photographs of the specimen were taken in the fresh state.

There are two main ways to document the real-time intraoperative diagnosis. The first is to have a separate "Intraoperative Diagnosis Requisition/Report Form" that is completed at the time of IOD. This written report is delivered to the operating room immediately after the verbal report has been transmitted, and becomes part of the patient's medical record.[16] This report can be delivered by courier or fax, and, in the future, will no doubt be transmitted electronically. In the second approach, the gross findings and diagnosis are recorded on the pathology requisition form or a separate "Intraoperative Diagnosis Report Form" that is for internal use in the pathology department. The advantage of the first approach is that the surgeon receives a real-time written report, minimizing potential misunderstanding of the pathologist's verbal communication.

ACCURACY OF INTRAOPERATIVE DIAGNOSIS

Intraoperative diagnoses cannot always be as accurate as final diagnoses given the limitations of sampling, time constraints, technical challenges, inability to perform ancillary tests, and restricted access to other opinions. As a result, the diagnosis has to be deferred in a proportion of cases (<5% in most studies).[4,7,13,17,18] When deferred diagnoses are excluded, intraoperative diagnosis is surprisingly accurate, no doubt because most diagnoses in surgical pathology can be made on H&E stained preparations. Interestingly, the accuracy rates are similar for small hospitals and large hospitals.[7,17] However, errors do occur, and the error rate is <2% in most

series.[4,6,7,13,17,18] Approximately one-third of the discrepancies between IOD and final diagnoses are due to errors in sampling the tissue specimen, one-third to inadequate sectioning of the tissue in the FS block/s, and the remaining one-third are interpretive errors.[6,17] The following guidelines can reduce sampling errors:

- Not enough can be said about the importance of careful gross examination and judicious selection of tissue for IOD. Skilled intraoperative gross examination requires an understanding of the histologic correlates of gross pathology, as well as insight of their significance for immediate surgical management.
- The tissue in the FS block should be adequately sampled. The pathologist who interprets frozen sections should be aware of the amount of tissue in the FS block, and check that the volume of tissue on the slide matches the tissue in the block. This is particularly important when the pathologist who interprets FS slides is different from the person who prepares the FS block, a situation that is common when pathology assistants and histotechnologists assist in the frozen section suite.
- Seasoned pathologists are familiar with the power of examining multiple levels. Multiple levels should be prepared when evaluating high stake biopsies, when the diagnosis is not evident on the first section, when the initial FS slide is suboptimal, when there are disparities between the FS and gross findings, and when evaluating surgical margins in malignancies with an infiltrative pattern of growth.

Approximately 30% of the errors in the 1996 CAP Q-probe studies were interpretive errors.[6,17] For neoplastic disease, false-negative errors (malignancies interpreted as benign) are more frequent than false-positive diagnoses; false-positive diagnoses (benign lesions interpreted as malignant) constitute <1% of the errors.[7] Interpretive errors can be reduced by careful clinico-pathologic correlation and by seeking other opinions when there is uncertainty.

The accuracy rate of IOD has been relatively constant over the past few decades in spite of significant changes in the types of specimens submitted for IOD. This relatively steady rate however, masks the fact that deferral rates are much higher for some types of specimens, but they go unnoticed if they constitute a minority of the cases accessioned (e.g., small volume of pediatric cases in a general hospital). This higher deferral rate however, becomes apparent in selected series, and as pointed out by Coffin *et al.*, error rates (4%) and deferral rates (25%) are higher in pediatric and adolescent populations because of the nature of the specimens encountered in a Children's Hospital.[19]

Two guidelines should be used when evaluating the accuracy of IOD in departmental QA programs: (a) A "good enough diagnosis" should be considered a correct diagnosis when a limited interpretation is all that can be reasonably offered; and (b) the intraoperative diagnosis should be compared to the most specific diagnosis that can be made on H&E stained, paraffin-embedded tissue sections, and not with the final diagnosis, whose specificity relies on ancillary studies such as immunohistochemistry or flow cytometry. When these criteria are applied to the data of Coffin *et al.*, approximately 95% of the deferred diagnoses were appropriate.

QUALITY CONTROL AND QUALITY ASSURANCE

Quality control refers to a process that ensures the highest degree of accuracy and efficiency in the real-time delivery of intraoperative diagnoses, whereas quality assurance refers to a retrospective review of the accuracy of IOD. The two processes are closely related.

Quality control

There are multiple steps between procuring a specimen for intraoperative evaluation and reporting the results to the surgeon. Some of these steps are within the immediate control of the pathologist and others are not, but the pathologist is ultimately responsible for ensuring that the entire process functions smoothly. Pathologists are dependent on the co-operation of the staff in the operating room and the laboratory, and it pays to have periodic educational meetings to reinforce the principles and fine points of specimen handling. Every step is important for a satisfactory outcome, and each participant should understand the importance of her role.

Quality assurance

Intraoperative consultation should be included in every department's quality assurance program. This review can be done monthly or quarterly, depending on the