Root Cause Analysis of Problems in the Frozen Section Diagnosis of In Situ, Minimally Invasive, and Invasive Adenocarcinoma of the Lung

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• ***Context.***—**Frozen sections can help determine the extent of surgery by distinguishing in situ, minimally invasive, and invasive adenocarcinoma of the lung.**

Objective.—**To evaluate our experience with the frozen section diagnosis of these lesions using root-cause analysis.**

Design.—**Frozen sections from 224 consecutive primary pulmonary adenocarcinomas (in situ, 27 [12.1%]; minimally invasive, 46 [20.5%]; invasive, 151 [67.4%]) were reviewed. Features that could have contributed to frozen section errors and deferrals were evaluated.**

Results.—**There were no false-positive diagnoses of malignancy. Frozen section errors and deferrals were identified in 12.1% (27 of 224) and 6.3% (14 of 224) of the cases, respectively. Significantly more errors occurred in the diagnosis of in situ and minimally invasive adenocarcinoma than in the diagnosis of invasive adenocarcinoma ($P < .001$). Frozen section errors and deferrals were twice as frequent in lesions smaller than 1.0 cm ($P = .09$). Features significantly associated with errors and deferrals included intraoperative consultation by more than one pathologist ($P = .003$) and more than one sample of frozen lung section ($P = .001$). Inflammation with reactive atypia, fibrosis/scar, sampling problems, and suboptimal quality sections were identified in 51.2% (21 of 41), 36.6% (15 of 41), 26.8% (11 of 41), and 9.8% (4 of 41) of the errors and deferrals, respectively (more than one of these factors was identified in some cases). Frozen section errors and deferrals had significant clinical impact in only 4 patients (1.8%); each had to undergo completion video-assisted thoracoscopic lobectomy less than 90 days after the initial surgery.**

Conclusions.—**The distinction of in situ from minimally invasive adenocarcinoma is difficult in both frozen and permanent sections. We identified several technical and interpretive features that likely contributed to frozen section errors and deferrals and suggest practice modifications that are likely to improve diagnostic accuracy.**

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A revised classification of *pulmonary adenocarcinoma* was proposed in early 2011 by the International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society.[1–3] This newly proposed classification is primarily based on histology but also considers recent advances in molecular biology, genetics, imaging, therapy, and treatment outcome. One of the most important changes in terminology is the designation of neoplasms previously classified as *bronchioloalveolar carcinoma* as *adenocarcinoma in situ* to emphasize that they tend not to spread to regional lymph nodes or to metastasize. In the proposed classification, invasive pulmonary adenocarcinomas are subclassified as either *minimally invasive adenocarcinoma,* when they exhibit 5 mm or less of stromal invasion, or as *invasive adenocarcinoma,* when they exhibit more than 5 mm of stromal invasion. Distinguishing between these types of pulmonary adenocarcinoma is important because the risk of metastatic disease or disease recurring at 5 years is minimal in patients with in situ and minimally invasive adenocarcinomas, whereas those with invasive adenocarcinoma characteristically have more aggressive disease.[4] Patients with in situ and minimally invasive adenocarcinoma in our population are often elderly, frequently have multifocal disease, and have a relatively high incidence of comorbidities, such as chronic obstructive pulmonary disease, cardiovascular disease, and others. Recognition that certain histologic types of pulmonary adenocarcinoma are associated with much better prognosis than are others has stimulated interest in using molecular methods to study these neoplasms and in evaluating the efficacy and/or benefits of wedge or segmental resection, compared with lobectomy, for patients with in situ and minimally invasive adenocarcinoma. Lobectomy is still considered the standard treatment for patients with invasive adenocarcinoma.

The new trend toward more conservative lung surgery can present pathologists with diagnostic dilemmas. In situ and minimally invasive adenocarcinoma are usually peripheral

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Table 1. Features Evaluated in Root-Cause Analysis of Frozen Section Errors and Deferrals

Size of lesion
Number of pieces of lung frozen
Number of frozen section levels examined at surgery
Number of pathologists who consulted on frozen section diagnosis at surgery
Quality of frozen section
Difficulty in estimating extent of invasion
Presence of prominent inflammation with associated pneumocyte atypia

lung lesions that cannot be accurately diagnosed by transbronchial biopsy and transthoracic fine-needle aspiration biopsy because of limitations in accurate localization and/or inadequate sampling and because the entire lesion needs to be examined for correct classification. Because these tumors are difficult to diagnose preoperatively, intraoperative consultation with frozen section often helps thoracic surgeons identify patients who would be better served by wedge or segmental resection than by lobectomy. Hence, in our hospital, pathologists are frequently asked not only to make the initial diagnosis of pulmonary malignancy at intraoperative frozen section but also to distinguish between in situ, minimally invasive, and invasive adenocarcinoma, a task that is difficult and fraught with potential errors.[5–7] As this classification is still in a period of validation, the role of frozen section in the diagnosis of in situ and minimally invasive adenocarcinoma remains investigational. To our knowledge, no root-cause analysis data on errors and deferrals in the frozen section diagnosis of these lesions, using the newly proposed classification, have appeared in the literature.

Originally developed for industry, root-cause analysis has also been applied to a wide variety of medical and health care issues during the past 20 years. Problem areas in pathology that have been investigated with root-cause analysis include specimen misidentification, patient misidentification, lost specimens, turnaround time, cytology-histology diagnostic discrepancies, and others.[8–12] Although several different analytical techniques are used, all root-cause analysis involves a structured approach to identifying the factors that contributed to one or more undesirable or harmful past events, the aim being to decrease the occurrence of those and similar events in the future. Characteristically, this entails identifying and defining a problem, gathering relevant data, investigating all possible factors that could have contributed to the harmful or undesirable event, categorizing these "causes," and identifying actions that are likely to prevent or decrease the incidence of future, similar events.[13] This study uses a root cause analysis approach to evaluate our experience with the frozen section diagnosis of in situ, minimally invasive, and invasive adenocarcinoma of the lung.

MATERIALS AND METHODS

After institutional review board approval, our pathology database was searched using one or more of the following diagnostic terms: *lung*, *frozen section*, *adenocarcinoma*, *bronchioloalveolar carcinoma*, *adenocarcinoma in situ*, *mostly bronchioloalveolar carcinoma*, *bronchioloalveolar carcinoma with focal invasion*, *minimally invasive adenocarcinoma*, and *mixed adenocarcinoma*. The pathology reports were reviewed from 224 consecutive cases from 2006 to 2009 of primary pulmonary adenocarcinoma and lung neoplasms, which had previously been diagnosed as any of the above and in which a frozen section of the lung was immediately followed by a wedge or more-extensive pulmonary resection. The frozen sections had been performed by a variety of pathologists; none employed inflation techniques. All frozen sections and the final diagnoses were recategorized using the proposed International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society terminology into *in situ*, *minimally invasive*, or *invasive adenocarcinoma*. Cases previously diagnosed as *bronchioloalveolar carcinoma* were tentatively categorized as *adenocarcinoma in situ*. Cases diagnosed as *mostly bronchioloalveolar carcinoma* or as *bronchioloalveolar carcinoma with focal invasion* were tentatively categorized as minimally invasive adenocarcinoma. All slides of all cases diagnosed as *in situ* and *minimally invasive adenocarcinoma* were reviewed and diagnoses were confirmed. Given that the term *mixed adenocarcinoma* has been used variably by our pathologists, cases diagnosed as *mixed adenocarcinoma* were categorized as *invasive adenocarcinoma*. After substituting *adenocarcinoma in situ*, *minimally invasive adenocarcinoma*, or *invasive adenocarcinoma* for the original terminology in the frozen section and the final diagnoses reported, the frozen section diagnosis rendered during surgery was compared with the final diagnosis in the pathology report, and the frozen section diagnosis was classified as *concordant*, *deferred*, or *discordant*. All available hematoxylin-eosin–stained slides from all frozen section deferrals and discordances were retrospectively reviewed by both authors) and subjected to comprehensive root-cause analysis. The slides reviewed for each case included the original frozen section slide or slides, the "permanent"/deeper level or levels from the frozen section block, and all additional slides of the case. For this study, no wet tissue was reviewed, and no additional sections were cut or stained with hematoxylin-eosin or immunostains.

The root-cause analysis process consisted of 5 steps:

1. Identification of discrepancies between frozen section and final diagnoses on pathology reports; categorization of correct, deferred, and erroneous frozen section diagnoses by diagnostic tumor category updated to the proposed International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society terminology; and comparison of the proportions of errors and deferrals using the Fisher exact test.
2. Further categorization of frozen section errors and deferrals by comparing the diagnoses rendered during intraoperative consultation with the final correct diagnoses on pathology reports to understand which differential diagnoses were more prone to cause frozen section errors and deferrals.
3. Evaluation of the features listed in Table 1, based on review of all available information from each case with a frozen section error or deferral.
4. Tabulation of the incidence of frozen section errors and deferrals by lesion size (<1 cm or ≥ 1 cm), by the number of pathologists consulted at frozen section (1 or ≥ 2), and by the number of pieces of lung frozen (1 or ≥ 2). The number of section levels examined at frozen section was also recorded (1 or ≥ 2) for each case with a frozen section error or deferral. The results were compared using the Fisher exact test.
5. Tabulation of the incidence of frozen section errors and deferrals by sampling adequacy, technical quality of frozen section slides, presence or absence of inflammation with reactive atypia, and presence or absence of scar hampering assessment of invasion. Two aspects of sampling were evaluated: presence of tumor or invasion only in a block that was not frozen, and presence of tumor or invasion in the frozen section block but only in a deeper level than had been examined at surgery. Frozen section slide quality was categorized as *adequate* or *suboptimal*.

To gauge the clinical impact of these frozen section errors and deferrals, our departmental files were searched for follow-up during the 90 days after frozen section.

Table 2. Comparison of Frozen Section and Final Diagnoses				
	All Cases, n = 224, No. (%)	AIS, n = 27, No. (%)	MIA, n = 46, No. (%)	IA, n = 151, No. (%)
Frozen section correct	183 (82)	16 (59)	21 (46)	146 (97)
Frozen section deferrals	14 (6)	7 (26)	4 (9)	3 (2)
Frozen section errors	27 (12)	4 (15)	21 (46)	2 (1)
Sum of frozen section errors and deferrals	**41 (18)**	**11 (41)**	**25 (54)**	**5 (3)**

Abbreviations: AIS, adenocarcinoma in situ; IA, invasive adenocarcinoma; MIA, minimally invasive adenocarcinoma.

RESULTS

The cases under study included 27 in situ adenocarcinomas (12.1%), 46 minimally invasive adenocarcinomas (20.5%), and 151 invasive adenocarcinomas (67.4%). The tumors ranged from 0.2 cm to 7.0 cm. Fifty-one discrepancies (22.8%) between frozen section and final diagnosis were identified. Unexpectedly, in 10 of the 51 cases with discrepancies (19.6%), the frozen section diagnosis of *invasive adenocarcinoma* was confirmed as correct on review by both authors. Those 10 cases (4.5% of all 224 cases in the study) had been diagnosed on the pathology reports as *minimally invasive adenocarcinoma*. In each case, the original frozen section slide or slides contained at least one area of more than 5-mm of invasion that was not present in any of the "permanent" or deeper levels prepared from the frozen section block or the additional slides of the case. Presumably, the final diagnosis in these cases was incorrect because the frozen section slide or slides were not reviewed during final sign-out. The remaining 41 discrepancies comprised 18.3% of all 224 cases in the study and included 27 frozen section errors (65.9% of discrepancies; 12.1% of all 224 cases) and 14 frozen section deferrals (34.1% of discrepancies; 6.3% of all 224 cases).

Table 2 shows the distribution of frozen section errors and deferrals by correct tumor category. There were significantly more frozen section errors and deferrals in the in situ and minimally invasive adenocarcinoma cases than there were in the invasive adenocarcinoma cases ($P < .001$ and $P < .001$, respectively). As shown in Table 3, of the 27 errors, 13 (48.1%) involved minimally invasive adenocarcinoma cases that were misdiagnosed as invasive adenocarcinoma at frozen section, 9 (33.3%) were false-negative frozen section diagnoses of malignancy, and 3 (11.1%) involved minimally invasive adenocarcinoma cases that were misdiagnosed as adenocarcinoma in situ at frozen section. Difficulty deciding whether the lesion was benign or malignant was the basis for the deferral in 12 of the 14 frozen section deferrals (85.7%). In the remaining 2 frozen section deferrals, the differential diagnosis involved the presence or absence of focal invasion. There were no false-positive diagnoses of malignancy.

Table 4 shows that frozen section errors and deferrals were almost twice as frequent in lesions smaller than 1 cm (32% versus 16.6%, respectively), but the difference was not statistically significant. In contrast, there were significantly more frozen section errors and deferrals in cases shown to more than one pathologist and in cases where more than one sample of lung tissue was evaluated at frozen section ($P = .003$ and $P = .001$, respectively). The latter findings suggest that certain cases were particularly difficult to accurately diagnose intraoperatively.

Table 5 provides further information about features that could have contributed to frozen section errors and deferrals. More than one of these features was present in several cases. Proportions of these features could not be estimated or analyzed with statistics because we were not able to evaluate those features in all slides from the 224 cases. Inflammation with reactive atypia was the most frequent confounding feature identified in 21 of the 41 frozen section errors and deferrals (51.2%). Difficulties in estimating the presence or extent of invasion in frozen sections showing fibrosis or scar were present in 15 of the 41 cases (36.6%), sampling problems were identified in 11 of the 41 frozen section errors and deferrals (26.8%), and suboptimal quality frozen section contributed to 4 of the frozen section errors and deferrals (9.8%). (There was more than 1 factor in some samples.) In 38 of the frozen section errors and deferrals (92.7%), at least 2 section levels had been examined intraoperatively. In 9 of the 41 cases (22%), tumor or invasion was present only in nonfrozen section blocks. Tumor or invasion was observed in the frozen section block but only in sections at deeper levels than had

Table 3. Errors and Deferrals in Frozen Section (FS) Diagnoses of Adenocarcinoma In Situ (AIS), Minimally Invasive Adenocarcinoma (MIA), and Invasive Adenocarcinoma (IA)		
FS Diagnosis	**Correct Diagnosis**	**Cases, No. (%)**
Errors, n = 27		
Benign	Malignant (AIS, 2 of 9 [22%]; MIA, 5 of 9 [56%]; IA 2 of 9 [22%])	9 (33)
Malignant	Benign	0 (0)
AIS	MIA	3 (11)
AIS	IA	0 (0)
MIA	AIS	1 (4)
MIA	IA	0 (0)
IA	AIS	1 (4)
IA	MIA	13 (48)
Deferrals, n = 14		
Benign versus Malignant	Malignant (AIS, 5 of 12 [42%]; MIA, 4 of 12 [33%]; IA, 3 of 12 [25%])	12 (86)
AIS versus MIA	MIA	2 (14)
AIS versus IA	NA	0 (0)
MIA versus IA	NA	0 (0)

Table 4. Root Cause Analysis of Frozen Section (FS) Errors and Deferrals				
	FS Diagnosis Correct, n = 183, No. (%)	FS Errors and Deferrals, n = 41, No. (% of Deferrals; % of Total Cases [n = 224])	FS Errors and Deferrals as Percentage of All Cases With That Characteristic, No. (%)	*P* Value
Size of lesion, cm				
<1.0	17 (9.3)	8 (19.5; 3.6)	8/25 (32)	.09
≥1.0	166 (90.7)	33 (80.5; 14.7)	33/199 (16.6)	
Pathologist consultants at FS				
1	155 (84.7)	26 (63.4; 11.6)	26/181 (14.4)	.003
≥2	28 (15.3)	15 (36.6; 6.7)	15/43 (34.9)	
Pieces of lung frozen				
1	155 (84.7)	25 (61.0; 11.2)	25/180 (13.9)	.001
≥2	28 (15.3)	16 (39.0; 7.1)	16/44 (36.4)	

been examined intraoperatively in only 2 of the 41 frozen section errors and deferrals (4.9%); in these 2 cases, 2 and 3 levels, respectively, of the frozen section blocks had been examined intraoperatively (Figures 1, A and B, and 2, A through D).

No apparent disproportionate clustering of frozen section errors was observed among pathologists. Pathologists with more experience in pulmonary pathology appeared to have fewer frozen section deferrals and fewer intraoperative consultants than those with less experience, but we did not evaluate this information in a rigorous manner because it was not feasible for us to accurately normalize frozen section results by pathologist while taking into consideration the frequency of pulmonary frozen sections each performed during a particular period, tumor size, diagnosis, and the various features described above.

Clinical Impact of Frozen Section Errors and Deferrals

For purposes of this study, a *significant clinical impact* was defined as leading to a second surgical procedure. Three of the frozen section deferrals (21.4% of deferrals) and one of the frozen section errors (3.7% of errors) had a significant clinical impact on patients in our study. These 4 patients (comprising 9.8% of the 41 frozen section errors and deferrals and 1.8% of all 224 patients in the study) underwent completion lobectomy within 90 days following the frozen section. These cases are detailed in Table 6. Completion lobectomy showed residual tumor with invasive adenocarcinoma (3 of 41 cases) and no residual tumor (1 of 41 cases). Each of the 10 patients (19.6% of 51 cases) who had been correctly diagnosed with invasive adenocarcinoma in frozen section, but misdiagnosed as having minimally invasive adenocarcinoma in the final report, had undergone lobectomy during frozen section, and none required a second operation.

COMMENT

Root-cause analysis of our experience with the frozen section diagnosis of in situ, minimally invasive, and invasive adenocarcinoma identified a variety of diagnostic problems that fortunately had a significant clinical impact in only 1.8% of the 224 patients (n = 4) in this study. One false-negative and 3 deferred frozen section diagnoses resulted in 4 patients undergoing a second video-assisted thoracotomy with residual invasive adenocarcinoma found in 3 of the completion lobectomy specimens. Interestingly, in 2 of these 3 cases (67%), tumor (invasive adenocarcinoma) in the completion lobectomy was more advanced than that in the wedge resection (minimally invasive adenocarcinoma), suggesting that wedge resection may not be adequately representative of a lung neoplasm in some cases.

Perhaps the most surprising finding in the root-cause analysis was that in 10 of the 224 cases (4.5%), the original frozen section slides provided more accurate information than the subsequent "permanent" sections of the frozen section block and other blocks processed from the neoplasm. In each of these 10 cases, invasion exceeded 5 mm in the original frozen section slide or slides but was almost or entirely cut through during frozen section, such that the "permanent" sections subsequently prepared from the frozen section remnant and additional blocks submitted from the area of the lesion showed only minimally invasive adenocarcinoma. This type of sampling issue could be important in an increasing proportion of lung lesions in the future as (1) the mean size of tumors operated on continues to decrease, (2) increased importance is placed on accurate

Table 5. Root Cause Analysis of Frozen Section (FS) Errors and Deferrals			
Contributing Features	FS Errors,[a] No.	FS Deferrals,[a] No.	Total,[b] No.
Sampling			
Tumor or invasion present only in non-FS block	8	1	**9**
Tumor or invasion in FS block but only in deeper level than examined intraoperatively	1	1	**2**
Suboptimal quality FS	3	1	**4**
Inflammation with reactive atypia	11	10	**21**
Presence of scar and/or fibrosis with difficulty interpreting presence or extent of invasion	11	4	**15**
Absence of prominent atypia	0	2	**2**

[a] In some cases, >1 feature contributed to FS error or deferral.
[b] Slides from 3 cases were not available for review.

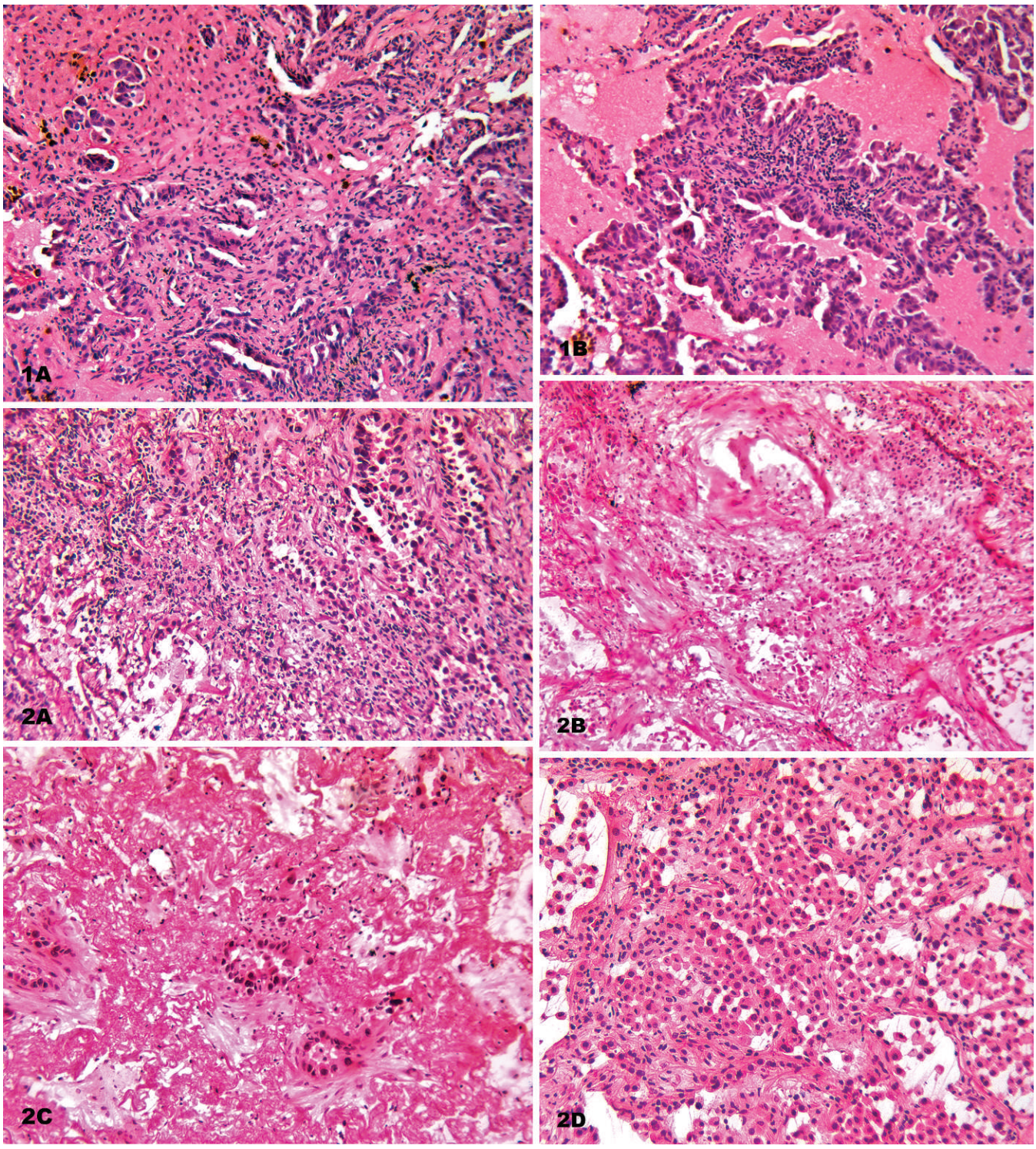

Figure 1. *Case illustrating the presence of invasion in original frozen section slide but not in permanent slides. A, Focus of invasion <5 mm in frozen section, diagnosed as minimally invasive adenocarcinoma. B, No residual invasion (only adenocarcinoma in situ) in permanent sections (hematoxylin-eosin, original magnifications ×100 [A and B]).*

Figure 2. *Frozen sections illustrating problems in the diagnosis of in situ, minimally invasive, and invasive adenocarcinoma. A, Inflammation and fibrosis hamper assessment for presence and extent of invasion. B, Suboptimal quality section with atypical cells. C, Fibroelastosis hampers assessment for presence/extent of invasion. D, False-negative diagnosis due to sampling error. Frozen section shows endogenous, lipoid pneumonia with increased alveolar macrophages. Mucinous adenocarcinoma was present in an adjacent block, (hematoxylin-eosin, original magnifications ×100 [A through D]).*

Table 6. Frozen Section (FS) Errors and Deferrals With Significant Clinical Impact,[a,b] n = 4			
Original FS Diagnosis	Final Diagnosis on Wedge Resection	Findings in Subsequent Lobectomy Specimen	Final Diagnosis
Benign, n = 1	MIA	Residual tumor	IA
Deferred (benign versus malignant), n = 1	AIS	No residual tumor	AIS
Deferred (difficulty estimating extent of invasion), n = 1	MIA	Residual tumor	IA
Deferred (benign versus malignant), n = 1	IA	Residual tumor	IA

Abbreviations: AIS, adenocarcinoma in situ; IA, invasive adenocarcinoma; MIA, minimally invasive adenocarcinoma.

[a] These 4 cases = 1.8% of all cases in the study.
[b] Significant clinical impact was defined as patient requiring a second surgical procedure.

assessment of focal invasion at frozen section, and (3) complex schedules necessitate that the frozen section and final reporting of lung neoplasms be performed by different pathologists. This finding underscores the importance of reviewing the original frozen section slides during the final sign-out of lung neoplasms.

Frozen section errors and deferrals occurred in 18.3% of the 224 cases because of a variety of technical and/or interpretive factors. More than one factor was present in most cases where there was difficulty distinguishing between benign processes, adenocarcinoma in situ, and minimally invasive adenocarcinoma. Significantly more errors and deferrals were found in cases with in situ and minimally invasive adenocarcinoma diagnoses and in difficult cases for which additional sampling and/or consultations had been obtained during frozen section. There were twice as many errors and deferrals in the frozen section diagnosis of lesions smaller than 1 cm, although this difference was not statistically significant. Factors that were present in most of the problematic cases and probably contributed to frozen section errors and deferrals involve the interpretation of atypical cells as reactive or malignant in frozen sections with extensive, chronic inflammation and the identification of invasion or the estimation of the extent/size of invasion in the presence of scar or fibrosis with architectural distortion and entrapped epithelial elements. Our findings suggest that pathologists performing frozen sections on lesions that exhibit any of these features need to be particularly careful during intraoperative consultation.

Sampling issues contributed to 26.8% (11 of 41) of the frozen section errors and deferrals. We recognize that retrospectively applying the new classification to frozen sections that were managed before the existence of this classification has some inherent limitations. Whereas a pathologist using the new classification would be particularly attentive to the extent and size of invasion and freeze additional sections before rendering a diagnosis of minimally invasive or invasive adenocarcinoma, the main concern of a pathologist faced with the same frozen section before the new classification would probably have been only whether or not there was any invasion present.

Based in part on this root-cause analysis, several changes have been made in our pathology practice. All original frozen section slides are now carefully tracked and always submitted to the pathologist with all other slides of each case for final sign-out. To improve the quality of frozen section slides, the preparation of frozen sections has been centralized and relocated within the pathology department (previously frozen sections were performed in a variety of surgical suites dispersed throughout the medical center) so that faculty, experienced histotechnologists, or pathology assistants are immediately available to assist when the initial frozen section slides are of suboptimal quality or there is difficulty in making a diagnosis, and all slides are fixed in methanol for at least 1 minute. Efforts to address difficulties in identifying the presence of, or estimating the extent of, invasion include (1) improved communication with surgeon and correlation with imaging because both can provide information regarding the presence (or absence) and size of a mass or solid component (often an indication of a focus of invasion) versus uniform ground-glass appearance, and (2) sampling more tissue blocks for frozen section. Although imaging information was not available for the cases in our study, radiologic-pathologic correlation has the potential to improve sampling during frozen section in cases where the lesion is small, not palpable, and/or not apparent on sectioning the fresh tissue. The use of embedding medium to inflate lung biopsies before sampling for frozen section, previously reported to improve the quality and diagnostic accuracy of frozen sections in small or nonpalpable lung lesions,[14] is also currently being performed in selected cases. We suspect that consulting more pathologists during frozen sectioning, beyond that which we already do, is unlikely to substantially reduce our frozen section errors and deferrals in the diagnosis of in situ, minimally invasive, and invasive adenocarcinoma. Because most of our frozen sections were examined at 2 or more levels and tumor was found at a deeper level of the frozen section block in only 2 of the 41 cases (4.9%), we also assign a low priority to initiating changes in these aspects of our frozen section practice. Future studies that address the clinical applicability of the newly proposed classification should also evaluate intraobserver and interobserver diagnostic agreement in frozen section diagnosis of in situ, minimally invasive, and invasive pulmonary adenocarcinoma.

Problems in the frozen section diagnosis of lung lesions have previously been investigated in our laboratory[5–7] and by others.[15] In a review of frozen sections performed on 183 small (<1.5 cm) lung nodules, Marchevsky et al[5] concluded that the distinction between bronchioloalveolar carcinoma (currently adenocarcinoma in situ) and atypical adenomatous hyperplasia was often problematic, and that the diagnostic accuracy was lowest for small (<1.1 cm) lesions. In a subsequent study, Gupta et al[6] used an evidence-based approach to identify 5 features (multiple growth patterns, anisocytosis, atypia involving >75% of the lesion, macronucleoli, and atypical mitoses) that were most useful in distinguishing *bronchioloalveolar carcinoma-well differentiated adenocarcinoma* from *reactive atypia* in frozen sections. In their study, *bronchioloalveolar carcinoma-well differentiated adenocarcinoma* was considered the same diagnosis, and the problem was to distinguish these lesions from *reactive atypia*. In accordance with the new proposed classification, our surgeons now request that a more-precise diagnosis (no

invasion versus ≤5 mm of invasion versus >5 mm of invasion) be made at frozen section. Borczuk[16] recently addressed the assessment of invasion in in situ and minimally invasive adenocarcinoma. Difficulties distinguishing malignant cells from atypical reactive cells based on cytomorphology have long been recognized in the cytology literature and remain as diagnostic problems.[17–20]

The importance of monitoring and sharing errors to improve the practice of pathology and the contribution that root-cause analysis can make in decreasing the incidence of future errors have been recognized by pathologists and endorsed by the Joint Commission and the Institute of Medicine.[21–24] The root-cause analysis process recognizes that diagnostic problems usually have multiple causes and helps to identify and delineate the components that contribute to medical errors. It also provides an analytic, rather than punitive, approach to decreasing future errors/deferrals, whereas, at the same time, it recognizes that elimination of some errors/deferrals will be very difficult or impossible within the constraints of current medical practice. More important, root-cause analysis provides a basis for the development of prioritized, cause-related practice modifications.

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