Usefulness of Core Roll Preparations in Immediate Assessment of Neoplastic Lung Lesions*

Comparison to Conventional CT Scan-Guided Lung Fine-Needle Aspiration Cytology

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Introduction: CT scan-guided fine-needle aspiration (FNA) of lung nodules is a well-established diagnostic technique. In our institution, both FNA and tissue core biopsy (using a 20-gauge needle) under CT scan guidance are routinely performed during the same procedure, and a preliminary diagnosis (an immediate assessment) is rendered. We compared core roll preparations (CRPs) with aspirate smears in the immediate assessment of pulmonary lesions and also assessed whether CRP resulted in the alteration of the histopathology of the core biopsy.

Study design: Twenty-five cases of neoplastic pulmonary lesions diagnosed in CT scan-guided lung FNA specimens, with core biopsies performed sequentially at the same visit for each patient, were evaluated. CRPs were made by lightly rolling the tissue core on a glass slide, followed by air-drying. Only stained slides (Diff-Quik; Mercedes Medical; Sarasota, FL) were reviewed, and were scored for cellularity and morphology.

Results: CRPs in seven cases (28%) scored more diagnostic points than FNA smears, and were found to be better for cellularity and morphology compared to the corresponding FNA smears. The FNA smears scored more than CRPs in 10 cases (40%), while in 8 cases (32%) both CRPs and FNA smears scored equal diagnostic points. Using both CRP and FNA smears in the immediate assessment of lung biopsy specimens, we could assign a specific malignant histologic cell type in 23 of 25 cases (92%). In comparison, if the FNA smears were evaluated alone, we could assign a specific malignant histologic cell type in only 16 of 25 cases (64%). The CRP did not alter the histopathology of the core biopsy specimens in any of the above cases.

Conclusion: The CRP complements the CT scan-guided lung FNA procedure in the immediate assessment of neoplastic lung lesions without altering the histopathology of core biopsy specimens.

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Key words: biopsy; core roll preparation; fine-needle aspiration; lung; neoplasm.

Abbreviations: CRP = core roll preparation; FNA = fine-needle aspiration

Transbronchoscopic fine-needle aspiration (FNA) biopsy is a well-established and safe diagnostic technique for the evaluation of thoracic lesions.\textsuperscript{1} Techniques that are commonly used for this imaging-guided percutaneous needle biopsy include fluoroscopy,\textsuperscript{2} conventional CT scanning,\textsuperscript{1,3} and helical CT scanning.\textsuperscript{3} The diagnostic sensitivity of transbronchoscopic FNA for malignant lesions has been shown to range from 76 to 97%, with specificity close to 99%.\textsuperscript{4–7} Automated cutting biopsy needles have been used for the diagnosis of lung lesions.\textsuperscript{8–10} The advantages of large-core biopsy specimens, compared with FNA biopsy specimens, are that it increases the diagnostic accuracy, improves the characterization of cell type in patients with carcinomas, and also increases the ability to diagnose carcinoma in the absence of a trained cytopathologist.\textsuperscript{11}
Imprint cytology of core needle biopsy specimens (called core roll preparations [CRPs]) has been shown to be accurate for the evaluation of surgical breast specimens and to be fairly accurate for the evaluation of abdominal masses when a touch preparation slide is made from a single core specimen. To our knowledge, there have been no such studies performed evaluating the usefulness of CRPs in the immediate assessment of neoplastic lung lesions in comparison with conventional CT scan-guided lung FNA cytology.

In our institution, both FNA and tissue core biopsy (using a 20-gauge needle) under CT scan guidance are routinely performed during the same procedure, and a preliminary diagnosis (called an immediate assessment) is rendered by the physician. The purpose of this study was to compare the value of CRPs with cytology smears in the immediate assessment of malignant pulmonary lesions and to determine whether CRP resulted in the alteration of the histopathology of the core biopsy.

Materials and Methods

We retrospectively reviewed malignant pulmonary lesions diagnosed on CT-guided lung FNA and core biopsies that had been performed sequentially at the same visit for each patient during the period from January 2001 to December 2002. Only cases with both FNA smears and corresponding CRPs were selected for this study. All patients in these cases had a final tissue histopathologic diagnosis that confirmed the diagnosis made using FNA. The study population included 25 patients (9 men and 16 women) with a mean age of 67 years (age range, 41 to 82 years).

Experienced chest radiologists performed all the biopsies after obtaining informed consent. FNA biopsies were performed with a coaxial technique using a 20-gauge or 22-gauge biopsy needle. The aspirates were expressed on a glass slide and immediately smeared against another glass slide using the pull-apart technique. One of the slides was air-dried and stained (Diff-Quik; Mercedes Medical, Sarasota, FL). The other slide was immersed in 95% ethanol for Papanicolaou staining. All the core biopsy specimens were obtained using a 20-gauge, coaxial, automated cutting needle biopsy system. For CRPs, each core was lightly rolled on a glass slide, and the slide was air-dried and stained (Diff-Quik). The core biopsy specimen was transferred into formalin for histopathologic analysis. The paraffin-embedded core biopsy tissue was cut into 5-μm sections and was stained by a standard hematoxylin-eosin stain. The “gold standard” in our study for comparing the cytologic and core biopsy diagnosis in each case was the final pathologic diagnosis rendered on formalin-fixed and hematoxylin-eosin-stained section of a resected tumor.

The stained (Diff-Quik) slides of the FNA biopsy and CRP samples made from the core biopsy specimens were examined under a light microscope. The FNA smears and CRPs were considered to be adequate for immediate assessment if cellularity and morphologic features were sufficient enough to make an impression (ie, benign or malignant). The FNA smears and CRPs were scored for diagnostic quality using a 4-point scale, as follows: 0, slides that showed only blood and no epithelial cells; 1, slides that showed either benign or atypical (ie, indeterminate for malignancy and could not be put in the category of malignant cells) cells; 2, slides that had malignant cells present but in which a cell type could not be recognized; and 3, slides revealing a malignant histologic cell type. The histopathology of the core biopsy sample in each case was also reviewed and was specifically evaluated for crush artifacts or an alteration in the tumor morphology and architecture that could be attributed to the making of CRPs.

Two observers (K.K.K. and V.S.C.) were involved in the retrospective review and scoring procedures on all samples in a blinded fashion. In 22 of the 25 cases (88%), the scores of both the observers matched, and the differences in the remaining 3 cases were resolved by consensus on reviewing the slides using a double-headed microscope. Both of the observers evaluated the FNA smears, CRPs, and tissue core biopsy samples for all of the patients in the study.

Results

Twenty-five cases with a cytologic diagnosis of non-small cell carcinoma (10 cases), adenocarcinoma (5 cases), small cell carcinoma (3 cases), squamous cell carcinoma (3 cases), metastasis (3 cases), and carcinoid tumor (1 case) were evaluated. The distribution of cases by the diagnostic scores for the CRP and FNA smears is shown in Figure 1. The average diagnostic scores were 2.48 for the FNA smears and 2.36 for CRPs. This difference between the means was not significant, as determined by the paired t test (p > 0.05).

Of the 25 cases, CRPs in 7 cases (28%) scored more diagnostic points than FNA smears, as they were more cellular, and contained cytologic and morphologic details that were more easily recognizable than those in the FNA smears. The FNA smears scored higher than the CRPs in 10 cases (40%), while in 8 cases (32%) both CRPs and FNA smears

Figure 1. Scatterplot showing the score distribution for 25 cases on CRP and FNA smears.
scored an equal number of diagnostic points. CRPs that were less than adequate compared to FNA smears in 10 of our cases were related to poor cell morphology (6 cases), poor cellularity (2 cases), excessive crush artifacts (1 case), and the absence of malignant cells (1 case). In contrast, FNA smears that were less than adequate compared to CRPs in seven of our cases were related to scant cellularity (five cases) and poor morphology (two cases).

Using both CRPs and FNA smears in the immediate assessment of lung biopsy specimens, we could assign a specific malignant histologic cell type (score, 3) in 23 of 25 cases (92%). However, if only FNA smears were used in the immediate assessment, we could have achieved a similar result in only 16 of 25 cases (64%).

Overall, CRPs permitted a diagnosis (score, 2 or 3) in 21 cases (sensitivity, 0.84 [21 of 25 cases]), and the FNA smears did so in 22 cases (sensitivity, 0.88 [22 of 25 cases]). The CRP established a rapid diagnosis of malignancy (score, 3) in one case for which the FNA smear was negative for malignancy and showed only RBCs. Conversely, the FNA smear was positive for malignancy in one case for which the corresponding CRP was negative for malignancy and showed only RBCs.

Of the four cases in which CRPs were not helpful, two showed only RBCs on the CRP slides, and the corresponding hematoxylin-eosin-stained histopathology sections in one of the cases was also negative for malignancy. However, the stained (Diff-Quik) FNA cytology smear showed an accurate diagnosis of malignancy (score, 3). The histopathology in the other case showed a small focus of malignant cells only when the deeper sections were cut into the block of the tissue core biopsy. The remaining two cases showed very few cells on the CRPs, rendering a diagnosis of atypical cells (score, 1).

In our study, there were no false-positive cases on CRPs (ie, there were no cases in which the CRPs were positive for malignancy and the corresponding FNA smear and/or histopathology of the core biopsy sample were negative). The CRPs did not alter the histopathology of the core biopsy sample in any of the above cases.

**DISCUSSION**

The role of percutaneous transthoracic needle biopsy in the evaluation of pulmonary lesions was first reported in 1883 by Leyden,17 and in 1927 Dudgeon and Patrick18 first introduced the concept of using cytology for the rapid diagnosis of tumors in the operating room. Since the early 1970s, imprint cytology has been shown to be a useful adjunct to frozen-section examination in the immediate assessment of biopsied tissue.19–21 With the emergence of better imaging techniques in the last 3 decades, transthoracic biopsy has become an integral part in the evaluation of pulmonary nodules and masses.22

Currently, preoperative CT scan-guided automated core needle biopsy combined with FNA biopsy is being routinely used to obtain diagnoses of pulmonary lesions. To our knowledge, studies to date have not evaluated the usefulness of CRPs combined with FNA smears in the immediate assessment of pulmonary lesions. The usefulness of cytopathologic touch preparations (ie, imprints) from core needle biopsy specimens combined with FNA smears in the immediate assessment of intra-abdominal masses has been previously reported.16 The value of intraoperative cytology in the diagnosis of tumors of the breast also has been studied by a number of authors.12–15,21,24 However, most of the studies have compared the usefulness of intraoperative cytology in conjunction with frozen-section examination. These studies have shown that imprint cytology produces a diagnosis that is as accurate as those arrived at from the histologic examination of frozen sections, with sensitivity and specificity rates approaching 97% and 99%, respectively.15,23,24

Using both the FNA smears and CRPs in the cytologic evaluation of the lung biopsy specimens, we could assign a specific malignant histologic cell type (eg, non-small cell carcinoma, adenocarcinoma, or squamous cell carcinoma) in 23 of 25 cases (92%). In comparison, if only the FNA smears were evaluated alone, we could assign a specific malignant histologic cell type (score, 3) in only 16 of 25 cases (64%). Although the diagnosis of non-small cell carcinoma does not refer to a specific cell type and encompasses a variety of tumors, like squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and other poorly differentiated carcinomas, therapeutically the management of lung carcinoma is based mainly on the distinction between small cell carcinoma and non-small cell carcinoma.25

The results of our study showed a higher rate of poor cell morphology in CRPs (six cases) compared with FNA smears (two cases). Also, poor cell morphology was the main reason why CRPs scored lower than FNA smears. Hence, while making CRPs the tissue core biopsy should be rolled very gently on the glass slide to minimize alterations in the cell morphology.

The results of our study are similar to those in the study by Hahn et al,16 who showed the usefulness of cytopathologic touch preparations (imprints) from core needle biopsy specimens combined with FNA smears in the immediate assessment of intra-abdominal masses. As seen in the above study, we
also usually found that while both the CRPs and FNA smears were cellular, the primary difference between them was in the smear pattern. In CRPs, the cells were arranged in cohesive groups and clusters illuminating the architectural details of the tumors, thus helping to assign a specific malignant histologic cell type. Individual single cells also were seen in the background on CRPs revealing the cytologic features.

A CRP is, in principle, similar to the intraoperative cytology of the excised tissue. CRP permits the rapid interpretation of the tissue core before fixation and staining. This immediate interpretation not only provides an assessment of whether the core biopsy sample contains representative material and the target lesion has been biopsied, but also reduces the number of passes a radiologist may have to perform on a particular patient. Correspondingly, it may also increase the number of passes performed if evidence of malignancy is not apparent on the slides examined and the sample is believed to be nonrepresentative of the lesion, thereby improving the overall diagnostic yield of the procedure and reducing the false-negative rate of FNA cytology for lung lesions. A more specific diagnosis regarding the histologic type of the tumor also can be provided during the immediate assessment of the lung biopsy specimens, which may play a role in the immediate patient care management. If on initial assessment of the CRP a hematologic malignancy is suspected, additional tissue can be collected for special studies like flow cytometry and cytogentic analysis.

We included only malignant pulmonary lesions in our study, as prior published studies have shown that FNA cytology for lung lesions has a seemingly high false-negative rate due to sampling error. Also, specific benign diagnoses are usually more difficult to render than specific malignant diagnoses on FNA cytology. Even a specific benign diagnosis does not completely exclude the possibility of cancer, especially in a patient population with a high prevalence of malignancy. Nonspecific negative diagnoses are less reliable, and clinical follow-up is particularly important.

The results of our study have shown that CRP complements and expands the diagnostic role of CT scan-guided lung FNA and core biopsies in the immediate assessment of neoplastic lung lesions without altering the histopathology of the core biopsy specimen.

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