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# Computed Tomographic (CT) Guided Percutaneous Fine-Needle Aspiration Biopsy: The Yale Experience

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Fifty-one CT-guided percutaneous fine-needle aspiration biopsies (PFNAB) were performed on 46 consecutive patients over 15 months. Cytologies were obtained to identify primary or secondary malignancy in the abdomen, pelvis, retroperitoneum, bone, and paraspinal region. Adequate cytologic material was obtained in 50 of 51 biopsies. There were 29 true-positive, 0 false-positive, 12 true-negative, and two false-negative cases with an overall accuracy rate of 95 percent. There was one minor complication, mesenteric hemorrhage, which did not require transfusion. Fifteen of the 51 biopsies were performed on outpatients. The procedure is an accurate, safe, and cost-effective nonsurgical means of diagnosing primary or secondary malignancy.

## INTRODUCTION

Percutaneous fine-needle aspiration biopsy (PFNAB) under computed tomographic (CT) guidance has proved to be a widely accepted method of documenting malignancy [1–21]. Refinements in technique, experience with the procedure, and improvements in CT scanners have permitted a high degree of accuracy [1–3,8,9,16,18,21]. We present our experience over a 15-month period with this technique.

## MATERIALS AND METHODS

Between January 1984 and March 1985, 46 consecutive patients had PFNAB at Yale–New Haven Hospital. Lesions biopsied were initially detected by CT or referred to CT after prior clinical or radiologic examinations demonstrated an abnormality. Lesions ranged in size from 1–10 cm. Biopsies were performed to rule out malignancy. Lung biopsies and abscess aspirations were excluded from this series. The patient population consisted of 28 males and 18 females with a mean age of 62 years and an age range of 23–85 years. Thirty-six biopsies were performed on inpatients and 15 on outpatients. Twenty-eight patients had a known primary prior to the biopsy. These were as follows: colon carcinoma, seven; lymphoma, six; ovarian carcinoma, three; carcinoma of the cervix, three; renal cell carcinoma, two; breast carcinoma, two;



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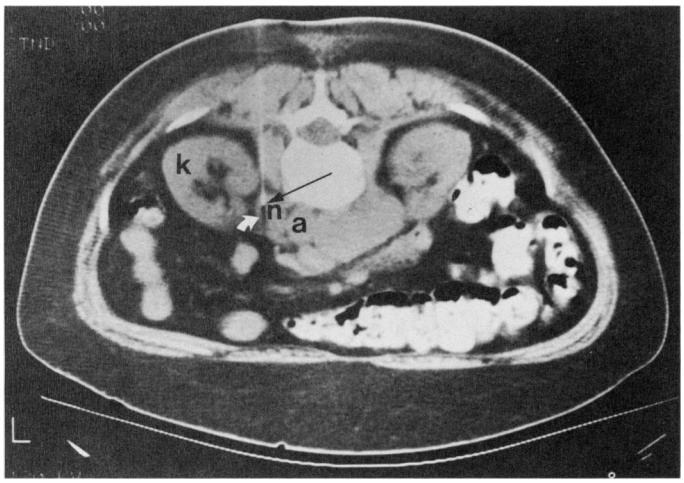


FIG. 1. Metastatic cervical carcinoma. CT scan demonstrating needle tip *(black arrow)* in para-aortic lymph node (**n**). Note that in this prone patient the access route avoids the kidney (**k**) and aorta (**a**). Curved white arrow shows a needle-tip artifact.

hepatoma, one; prostatic carcinoma, one; endometrial carcinoma, one; vulvar carcinoma, one; and leukemia, one. Sites biopsied were: intraperitoneal, ten; retroperitoneal, seven; presacral space, seven; liver, six; pancreas, six; bone/paraspinal, six; kidney, three; and adrenal, one.

The biopsy was performed on either the GE 9800 or 8800 CT scanner. Prior to biopsy, informed consent, a normal prothrombin time, partial thromboplastin time, and platelet count were obtained for all patients. In some cases, intramuscular meperidine hydrochloride 50–75 mg was given before the biopsy.

CT was used to determine the depth of the mass, internal relation of the mass to other structures, and the safest needle path. After sterile preparation and local anesthesia, the needle was placed within the lesion and the exact site of the needle tip was documented by a CT scan before any aspiration took place (Fig. 1). Twenty-two- or 20-gauge Franseen needles were used in all cases. Bowel was freely traversed but major vessels were avoided (Figs. 4,5). Within our cytology laboratory, smear preparations are stained immediately with Papanicolaou's stain and interpreted while a patient is undergoing the aspiration biopsy. Excessive material and fluid from a saline washout or purge of the needle is collected and centrifuged into an aggregate of cells or cell block. Cell blocks are processed by formalin fixation and paraffin embedding overnight and are stained with hematoxylin and eosin the following day (Fig. 3). Cytology results from the slides were obtained in 30 minutes; cell block slides were available within 24 hours.

The cytology aspirates were retrospectively reviewed by a single pathologist (KB) without knowledge of clinical outcome. Each case was assigned to one of the following five categories: *(1)* inadequate material; *(2)* no evidence of tumor; *(3)* atypical cells, probably reactive (non-neoplastic); *(4)* atypical cells, suspicious for malignant tumor (probably neoplastic); and *(5)* malignant cells present. All diagnoses which had originally been rendered as negative or positive diagnosis were confirmed (category *2* or category *5* ). Cases originally interpreted as indefinite were assigned to categories *3* or *4*. Standard cytologic criteria were employed to diagnose malignant cells as illustrated in selected cases (Fig. 2). A biopsy was considered positive for tumor if the cytology report was atypical cells, suspicious for malignant tumor (category *4* ) or malignant cells present (category *5* ).

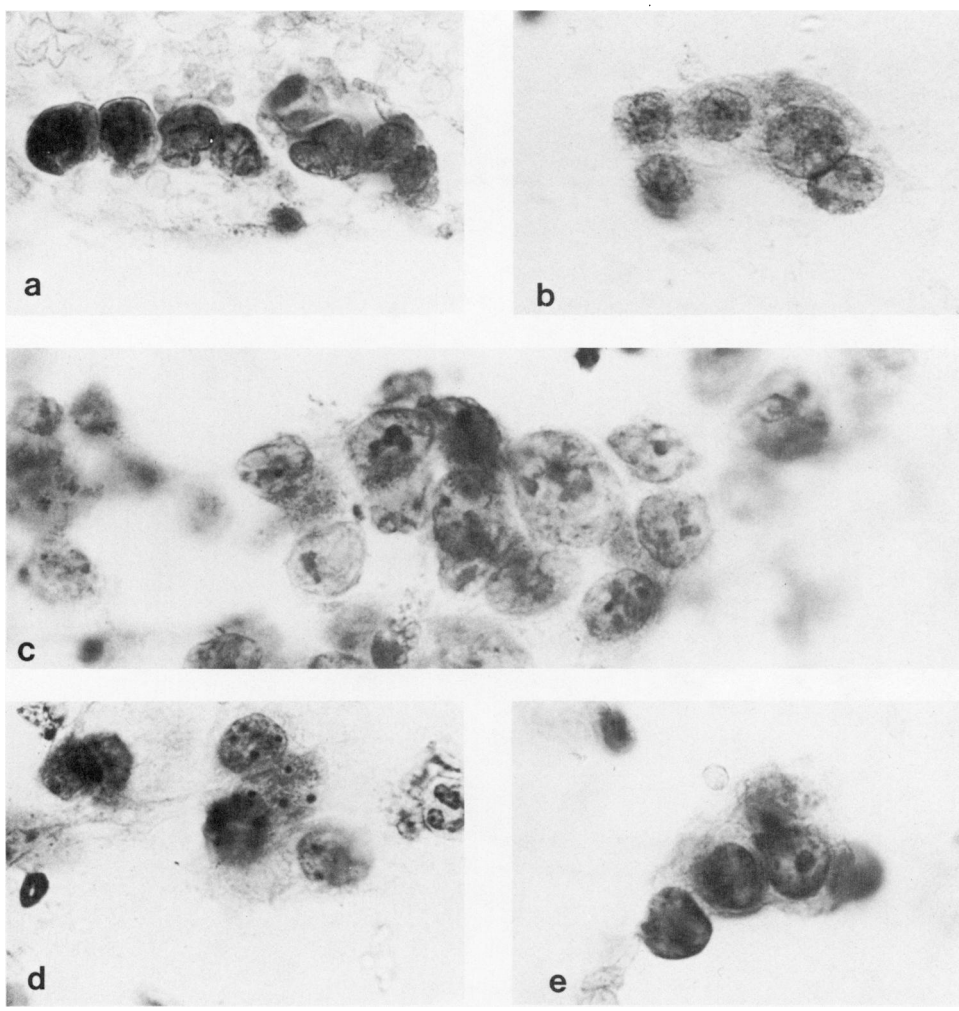


FIG. 2. Representative pathologic specimens. **A** Small cell carcinoma originating from uterine cervix (see Fig. 1). Nuclei demonstrate irregular shapes with polyploidy and molding. Chromatin distribution is coarse and relatively uniform. **B** High grade transitional cell carcinoma aspirated from retroperitoneal lymph nodes (see Fig. 7). The nuclei show minimal differentiation with coarse clumping of chromatin, irregular thickness and contour of the nuclear envelope, and variation in size. Moderate amounts of finely granular cytoplasm surround the nuclei. **C** Adenocarcinoma, poorly differentiated, of pancreatic origin (see Fig. 5). Nuclei show marked variation in size and shape, molding irregular prominent nucleoli, and abnormal chromatin dispersal. **D** Adenocarcinoma of pulmonary origin (see Fig. 6). Nuclei are characterized by multiple discrete nucleoli, variation in size, and coarse chromatin dispersal. **E** Papillary adenocarcinoma of ovarian origin (see Fig. 4). Cohesive cluster of cells with moderate vascular cytoplasm and crowded irregular nuclei with prominent nucleoli and peripheral clumping of chromatin (all preparations × 1,000, Papanicolaou stain).

A negative biopsy was considered a true-negative if: *(a)* surgery revealed no evidence of tumor; *(b)* one-year clinical follow-up was negative for evidence of tumor; or *(c)* one-year CT follow-up showed no change in the biopsy mass. A negative biopsy was considered false-negative if: *(a)* surgery proved there was a tumor at the biopsy site; or *(b)* a follow-up CT scan showed enlargement of the biopsy lesion and/or evidence of

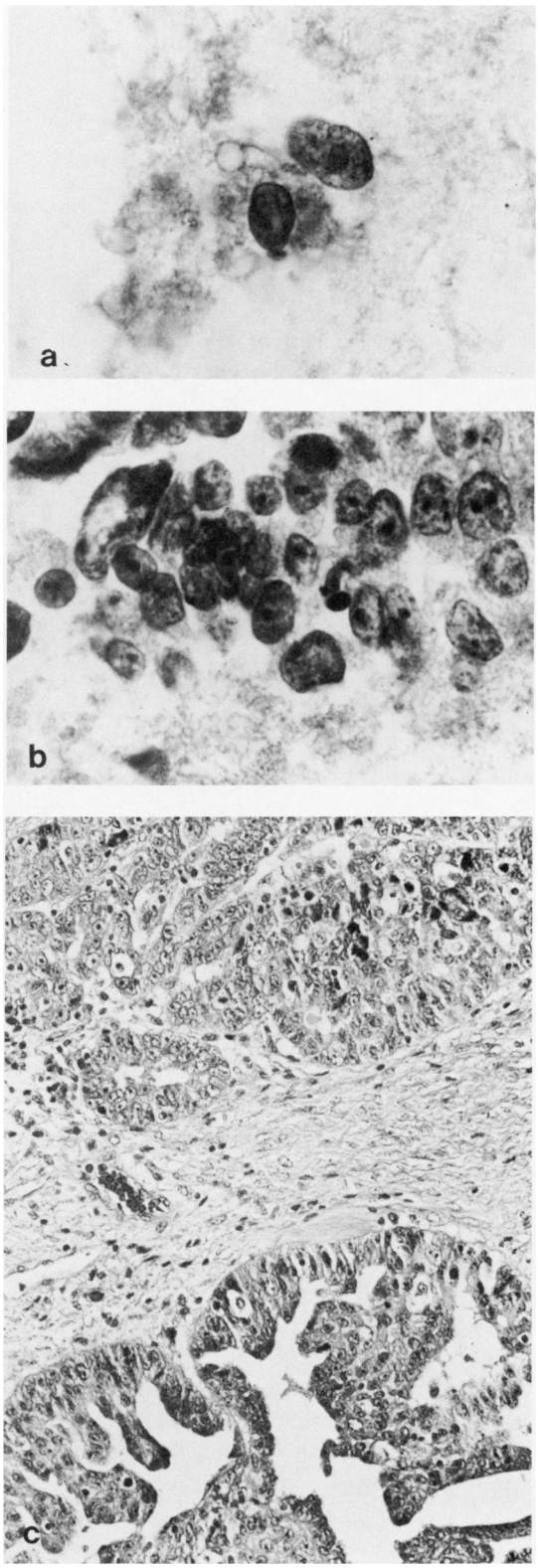


FIG. 3. Smears, cell block, and histologic preparation of high-grade papillary serous carcinoma of ovarian origin (see Fig. 4). **A** Smear demonstrating two malignant cells characterized by large irregular nuclei, prominent nucleoli, and clumped chromatin (Papanicolaou stain, × 1,000). **B** Centrifuged cell block of excess material which has been paraffin-embedded. This allows concentration of cells that may be difficult to evaluate in quantity on the smears (H&E, × 1,000). **C** Histologic preparation showing papillary serous carcinoma in the lower field, and solid, poorly differentiated carcinoma in the upper field (HxE, × 200).

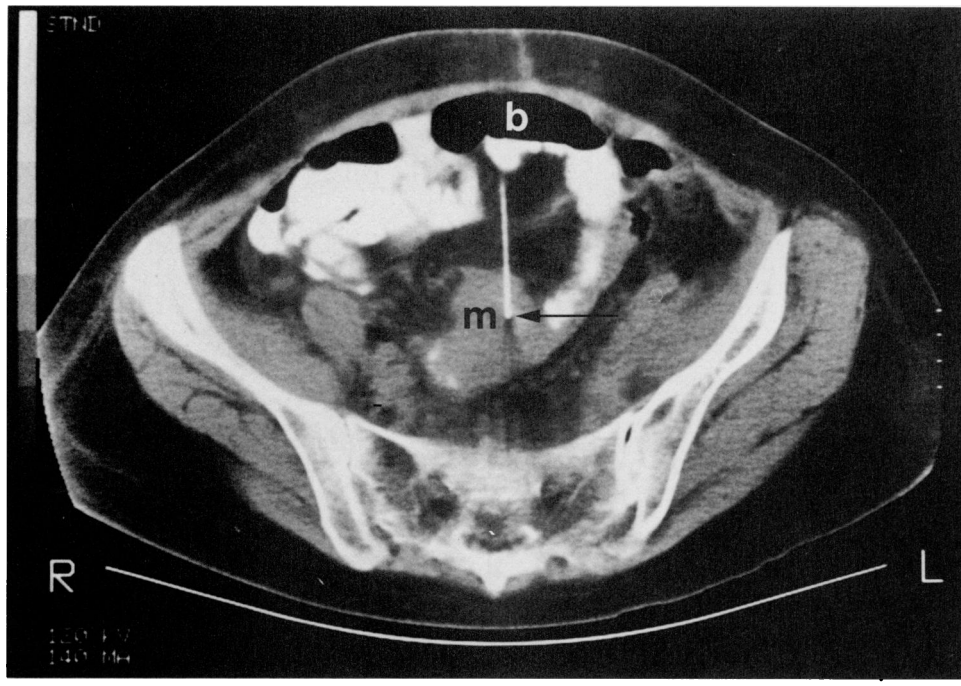


FIG. 4. CT scan of PFNAB of bowel mass (**m**) in patient with known ovarian primary revealing metastatic disease. Note that bowel (**b**) is freely transgressed. Arrow indicates needle tip.

metastasis. A category listed as "inadequate study" was used for: *(a)* patients who did not meet the biopsy criteria of three needle passes into an identifiable lesion on CT scan; or *(b)* patients who have not had at least one-year clinical, surgical, or CT follow-up.

Outpatients were instructed to arrange an escort home. The outpatients were monitored in the department for three hours post-biopsy. The patient and escort were instructed about possible complications.

## RESULTS

Fifty of 51 biopsies (98 percent) in 46 patients had sufficient cytologic material. There were 29 true-positives (TP), 12 true-negatives (TN), two false-negatives (FN), no false-positives (FP), and three inadequate study (see later). Sensitivity was 94 percent. Specificity was 100 percent. Overall accuracy was 95 percent. Predictive value of a positive biopsy was 100 percent, while predictive value of a negative biopsy was 85 percent. The initial biopsy was correct in 40 of 43 patients (93 percent) with adequate follow-up. Five patients had second biopsies. One initial biopsy that was atypical and not diagnostic of tumor was positive for tumor on the second biopsy. Three patients had two negative biopsies that were later proven to be true-negative. One person with two negative biopsies by CT guidance was later positive for tumor by ultrasound-guided biopsy. Of the 28 patients with a known primary, 17 were true-positives, nine true-negatives, one false-negative, and one inadequate study.

Seventeen of the 29 patients with true-positive results had known primary lesions with biopsies that were consistent with metastasis from the primary (Fig. 4). The remaining 12 true-positive biopsies were new diagnoses of cancer: pancreatic carcinoma, four (Fig. 5) (one had the liver biopsied, demonstrating adenocarcinoma in a

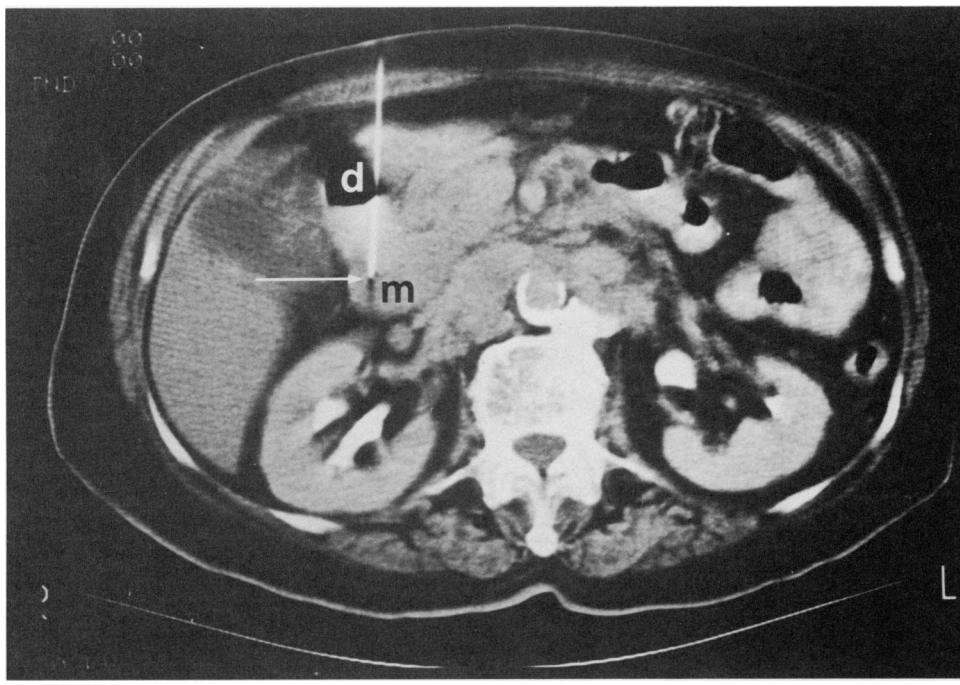


FIG. 5. CT scan demonstrating needle passing through duodenum (**d**) into pancreatic head mass (**m**). The biopsy revealed adenocarcinoma in the pancreas. The needle tip within the mass is demonstrated by the arrow.

patient with a large pancreatic mass); renal carcinoma, two; lymphoma, two; hepatoma, one; transitional cell carcinoma, one; lung carcinoma (bone was biopsied), one (Fig. 6); and colonic carcinoma, one. Nine of the 12 true-negatives had a known primary but negative biopsies, which were later confirmed by surgery, one; CT follow-up four; or clinical follow-up, seven.

Two patients had false-negative biopsies. One patient had a pancreatic mass and retroperitoneal adenopathy seen on CT; three needle passes were performed, and cytology was negative for tumor. Another biopsy was scheduled but not performed, due to the patient's clinical status. Radiation therapy was initiated. A follow-up CT scan has revealed an increase in the size of the pancreatic mass with new multiple lesions in the liver. The second false-negative biopsy occurred in a patient with known endometrial cancer who had a non-uterine pelvic mass that was negative for tumor on two separate CT-guided biopsies. Due to time constraints, a scheduled third CT-guided biopsy was transferred to ultrasound. The ultrasound-guided biopsy was positive for metastastic endometrial carcinoma.

Three patients were listed in the inadequate study category. Two patients did not meet the criteria for adequate biopsies while the third patient has not had a one-year clinical or CT follow-up. One patient with a pancreatic mass permitted only one needle pass, which was negative. Although a tissue diagnosis of cancer has not been made, a recent CT scan showed an increase in the size of the pancreatic mass and development of liver lesions during the interval. The second patient had abdominal pain with a negative CT examination. Since there was a strong clinical suspicion of a pancreatic abnormality, an ERCP and angiogram were performed which were abnormal. Two

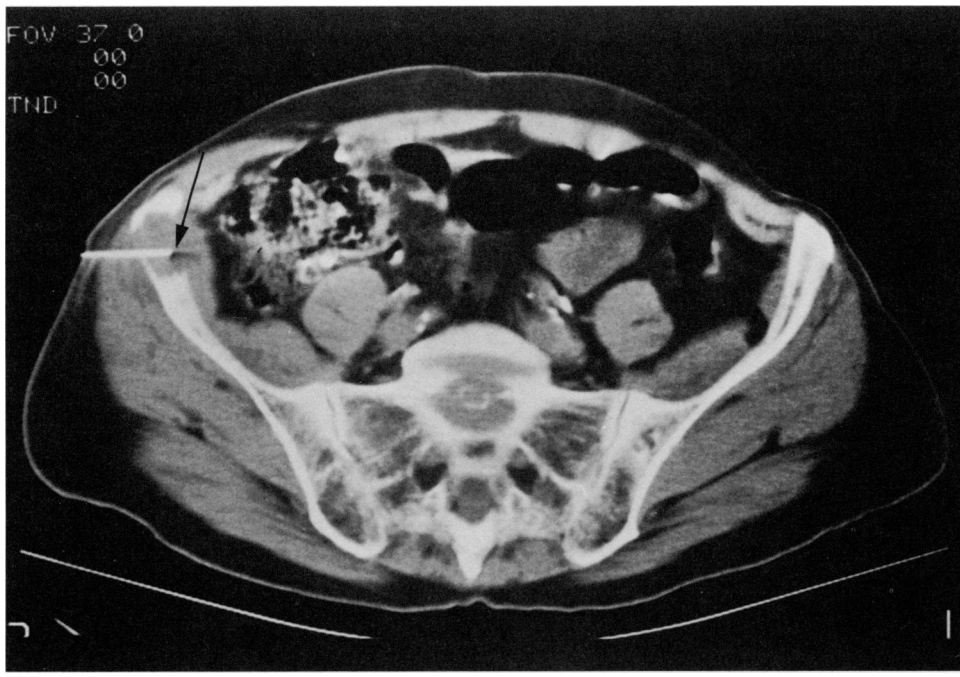


FIG. 6. CT scan showing needle tip *(arrow)* in destructive right ileum lesion of patient with an unknown primary. Cytology revealed poorly differentiated adenocarcinoma from a lung primary.

months later, another CT scan demonstrated no pancreatic mass. At the clinician's request, three CT-guided needle passes in the region of the pancreatic head were obtained and were negative for tumor. At surgery, a tumor was found in the liver, which was consistent with a pancreatic or biliary carcinoma. Unfortunately, the pancreas was not biopsied. The third patient with previous colon carcinoma presented with a large pelvic mass that was negative for tumor on CT-guided, ultrasound-guided, and surgical biopsy. Radiation therapy was initiated. One year follow-up is unavailable.

The only biopsy complication followed a pancreatic aspiration. After three passes with a 22-gauge Franseen needle, mesenteric hemorrhage was noted on the CT scans. The patient was admitted overnight for observation, and his course was uneventful. The patient's blood pressure remained stable, and no transfusions were required.

Patient management was definitely affected by the biopsy results (Table 1). Of the 29 TP, only five, thus far, have had surgery. The two new cases of lymphoma needed larger amounts of tissue for more specific histologic classification. The other three patients underwent debulking surgery. Nineteen of the 29 TP did not have any surgery but instead were treated with radiation and/or chemotherapy. The effect of five recent TP biopsies on patient care is indeterminate at this time.

Twelve patients had TN biopsies for malignant tumor. One patient had surgery after two negative biopsies; surgical pathology was also negative. Three patients with vertebral body destruction had biopsies negative for tumor; hence, they were treated with antibiotics and clinically improved. Four patients continued their prior chemotherapy regimen without the need for surgical intervention. Clinical follow-up at one year was negative for metastases. Four patients had follow-up CT scans showing no change in the previously biopsied mass and no evidence of new metastases.

TABLE 1
Biopsy Results

| Sites of Lesions Biopsied | TP | TN | FP | FN | IF | Total |
|---|---|---|---|---|---|---|
| Presacral | 4 | 3 | 0 | 0 | 0 | 7 |
| Abdominal/pelvic | 8 | 0 | 0 | 1 | 1 | 10 |
| Retroperitoneum | 6 | 1 | 0 | 0 | 0 | 7 |
| Liver | 2 | 4 | 0 | 0 | 0 | 6 |
| Pancreas | 3 | 0 | 0 | 1 | 2 | 6 |
| Renal | 3 | 0 | 0 | 0 | 0 | 3 |
| Bone | 3 | 3 | 0 | 0 | 0 | 6 |
| Adrenal | 0 | 1 | 0 | 0 | 0 | 1 |
| Total | 29 | 12 | 0 | 2 | 3 | 46 |

TP, true-positive TN, true-negative FP, false-positive FN, false-negative IF, inadequate follow-up

## DISCUSSION

CT-guided PFNAB is the most accurate method of performing biopsies [2,7,8]. Because of increased contrast and spatial resolution, modern scanners can accurately guide needle placement for biopsy of extremely small lesions (as small as 1 cm; see Fig. 7). CT has become the preferred method of PFNAB for lesions less than 3 cm in size and deep lesions [1,2,4] not readily accessible to sonography. The advantages of CT not only include clear definition of the lesion, access route, and needle-tip location, but also the capability of identifying highly vascular lesions via the use of intravenous

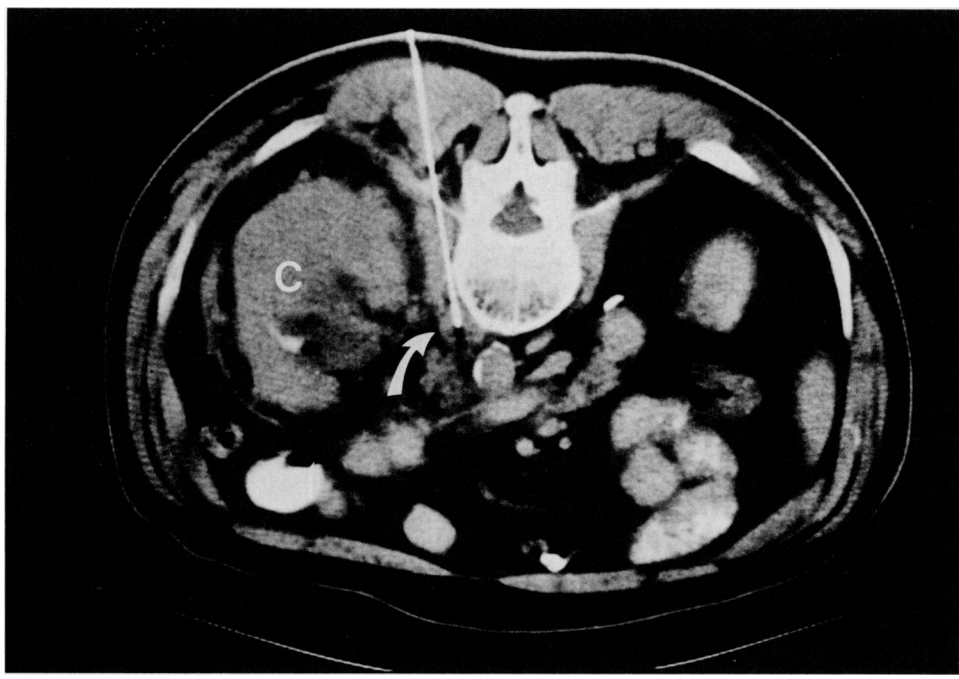


FIG. 7. CT scan of patient in prone position to enable needle access to a 1 cm retroperitoneal lymph node *(curved white arrow)* (non-pathologically enlarged by standard CT size criteria). Biopsy demonstrated metastatic disease in this patient with transitional cell carcinoma (**c**).

TABLE 2
Accuracy of PFNAB

| Organ | % Literature [References] | % Yale |
|---|---|---|
| Liver | 83–99 [4–8, 18, 19] | 100 |
| Retroperitoneum (including renal) | 78–100 [1–4, 7] | 100 |
| Presacral | Not available | 100 |
| Bone, paraspinal | 80–100 [1, 2, 10] | 100 |
| Abdomen/pelvic | 75–100 [4, 5, 7, 9] | 88 |
| Pancreas | 60–90 [1, 2, 4, 5, 7, 9] | 75 |

contrast medium [4,7,16,18]. Our accuracy was 100 percent for presacral, renal, liver, retroperitoneal, paraspinal, bone, and adrenal lesions, 88 percent for abdominal pelvic lesions, and 75 percent for pancreatic lesions. As can be seen from Table 2, our overall accuracy compares favorably with those in the literature.

The relatively lower accuracy of PFNAB of pancreatic masses is similar to results obtained at surgery [2]. The difficulty in obtaining a positive tumor diagnosis is due to the known inflammatory response which occurs with these tumors. Thus, despite exact localization of the needle tip within the lesion, tissue must be obtained from various areas to reduce sampling error. A biopsy of associated abdominal masses (e.g., liver metastases) may yield a positive tumor diagnosis rather than a sole biopsy of the primary pancreatic mass.

Reports of accuracy for the diagnosis of lymphoma range from 40 percent [7] to 75 percent [1]. Our accuracy was 100 percent (eight of eight patients). Recurrence was documented in six patients with known lymphoma. Two new cases that were not suspected prior to biopsy were diagnosed. Surgery was necessary to sub-type histologically these two patients. Our high accuracy may be attributable to utilization of 20-gauge needles in addition to the smaller 22-gauge needle, a state-of-the-art CT scanner, and the expertise of the pathologist.

Both cytologic and histologic cores of tissue are sought when biopsies are performed. We believe that needle selection depends on the clinical suspicion, safety, depth of the access route, the lesion vascularity, amount of tissue needed, and expertise of the pathologist. We routinely prepare smears stained by the Papanicolaou technique and slides from centrifuged cell blocks in our laboratory. The former preparation allows rapid interpretation during the procedure and may indicate a need for needle reposition. The latter technique allows concentration of the material and more ready application of histochemical and immunohistochemical techniques for tumor subclassification. This is an overnight preparation which usually confirms the diagnosis established based upon the smears. In our laboratory, however, about 1–2 percent of cell blocks reveal diagnostic material following an acellular or negative smear the preceding day. This finding requires deferment of all negative smears until completion of the cell block.

Clearly, PFNAB is an integral part of the diagnostic work-up of a patient with a suspected mass. In an era of cost-effective medical care, there is considerable incentive for rapid diagnosis without hospitalization. To date, no method of *in vivo* tissue characterization of masses has proved accurate enough to replace pathologic diagnosis; therefore, biopsy should be performed when a mass is identified. CT-guided biopsy is a safe, fast, and accurate means to obtain pathological tissue for the diagnosis of disease.

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