Ultrasonography is a safe and noninvasive cross-sectional imaging modality that is used worldwide by a variety of medical practitioners for a broad range of applications. It allows excellent spatial and contrast resolution and as such is invaluable for the evaluation of any accessible solid organ. Ultrasound constitutes one of the most frequently performed examinations, and its popularity and applications continue to grow. Oncologic indications for sonography are many and varied and include the detection of tumors as well as their diagnosis on the basis of their morphology on a grayscale sonographic exam. Ultrasonography is used intraoperatively for tumor evaluation where the use of high-frequency probes placed intimate to the region of interest affords superb resolution and allows for the detection of tiny tumor deposits. In addition, the real-time multiplanar capability of ultrasonography makes it the modality of choice for both guidance of biopsy procedures and for therapeutic techniques such as mechanical tumor ablation with radiofrequency or alcohol injection.

Ultrasonography transducers include those of traditional design, which are placed on the skin surface, as well as those designed for intracavity work, including transvaginal and transrectal applications. There is a broad range of transducer frequencies available. Low-frequency transducers allow for sufficient penetration for evaluation of the entire abdominal cavity, whereas high-frequency high-resolution probes allow for study of small and superficial organs such as the testicles and the breast. Ultrahigh-frequency transducers can even be used to study the layers of the skin, for melanoma staging, and for study of structures such as the eye.

The incorporation of Doppler (both duplex and color) technology permits the noninvasive evaluation of organ and tumor vasculature. State-of-the-art Doppler is excellent for evaluation of blood vessels in the neck and the extremities as well as the major intraabdominal vasculature. Although conventional Doppler may show blood flow in hypervascular tumors such as hepatocellular carcinoma and carcinoma of the cervix, it is often limited in its ability to evaluate tumor blood flow in lesions deeply positioned in the body, in those where the inherent signal is weak, or if the tumor is in a location where either motion or blooming artifact limits interpretation.

RECENT ADVANCES

Oncologic sonography, however, may be dramatically altered in the future by significant recent advances in ultrasonographic technology including the introduction of ultrasonography-specific microbubble contrast agents, which have revolutionized the ability of ultrasonography to evaluate tumor vascularity. When used in conjunction with new imaging methods, they offer the potential to see tumor angiogenesis in real-time. Microbubble contrast agents are comprised of tiny bubbles of gas in a supporting shell. Injected intravenously, they enhance the Doppler signal from blood. Microbubble contrast agents are unique in that they interact with the scanning technique. When exposed to a low mechanical index (MI) field, the bubbles oscillate with the production of higher frequency signals including those at the second harmonic. When exposed to a high MI insonation, the microbubbles are disrupted with the production of a brief but transient echo as the bubbles are destroyed in a single pulse.

To satisfactorily image microbubble contrast agents, specialized imaging techniques are required which preferentially detect the signal from the microbubble with suppression of the linear signal from the background tissue. These advancements include harmonic imaging, pulse inversion imaging, and other pulse and phase modulation techniques. Although their descriptions are beyond the scope of this chapter, they can be found in several excellent publications.1,2 These techniques have dramatically improved the ability of ultrasonography to visualize the blood flow in major vessels, both in the organ and tumor of interest. Furthermore, enhancement of a tumor may be compared to the enhancement of the background tissue allowing for assessments of vascularity similar to those achieved on contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) scan (Figure 36g-1). This is a requisite component of tumor characterization. Other potential applications in oncology are promising as tumor blood flow is a critical element in many treatment regimes and may also offer prognostic information.

TUMOR DETECTION AND CHARACTERIZATION

Lung and bone are not suitable for sonographic study. Virtually all of the solid soft-tissue organs of the body, however, may be studied with ultrasonography. The small and superficial organs, including the thyroid, salivary glands, and the testicles, are ideal organs in that high-frequency transducers which afford superb resolution may be used for their evaluation. The solid organs of the abdomen and pelvis, by comparison, require an artful technique to optimize visualization of the viscera and minimize the interference that may occur from obesity and bowel gas.

SMALL PARTS SCANNING

THE SCROTUM In the oncologic setting, scrotal sonography is performed most often for the evaluation of a palpable scrotal mass and is aimed at detection and characterization of testicular pathology. In patients with a hydrocele, a sonogram may also be performed as clinical palpation may be limited by the presence of scrotal fluid. Any focal mass identified within the testicle must be presumed to be a testicular neoplasm until proven otherwise. By comparison, most nontesticular scrotal masses will be benign. The strong association of testicular cancer with retroperitoneal adenopathy would suggest that a thorough sonographic examination showing a testicular neoplasm should also include evaluation of the retroperitoneum for adenopathy. Conversely, a biopsy of either a mediastinal or retroperitoneal lymph node mass suggestive of a gonadal primary should lead to a scrotal ultrasonography in search of an occult primary malignancy.

THE NECK Sonographic evaluation of the patient with a palpable nodule in the thyroid constitutes one of the most common indications for sonographic study. Initially performed to differentiate a solid from a cystic nodule and to determine numerality, state-of-the-art imaging now allows for exquisite resolution and detail regarding the morphology of a thyroid lesion. Thyroid nodules are extremely common, especially in young women, and the overwhelming majority of them are benign. Malignant thyroid nodules do occur, however, and there are some sonographic features that raise the likelihood of malignancy. Because there is a recognized overlap in the morphology of benign and malignant lesions on sonography, percutaneous ultrasonography-guided biopsy is the mainstay of investigation and diagnosis of sonographically confirmed thyroid nodules.

Staging of head and neck malignancy is well performed with sonography, and the addition of
Doppler will reveal the involvement of the carotid arteries in patients with cervical adenopathy.\(^3\) Furthermore, the other solid organs in the neck, including the parotid glands and the parathyroid glands, are well assessed on sonography.

### THE BREAST

Mammography used in conjunction with breast ultrasonography is now the standard of care for the detection and characterization of breast nodules. Breast ultrasonography is not advocated as a routine screening modality, although in the young patient with very dense breasts, it may detect cancers that cannot be seen on a mammogram. Routinely, however, any indeterminate nodule or abnormality seen on a mammogram should undergo ultrasonography evaluation. Malignant sonographic features include a lesion that is taller than it is wide, has acoustic shadowing, and shows marginal angulations.\(^4\) Sonography may identify the lesion with a high probability of benignancy thereby reducing the number of breast lesions requiring biopsy. Ultrasonography is the guidance technique of choice for breast biopsy and for cyst aspiration. Another application of ultrasonography in breast cancer patients is the detection of adenopathy in the internal mammary lymph node chain.\(^5\) Future considerations for breast mass characterization with ultrasonography include evaluation with ultrasonography contrast agents using nonlinear imaging techniques. These are, however, still in their infancy and no conclusions can be drawn regarding accuracy at this time.

### THE ABDOMINAL ORGANS

Choice of a cross-sectional imaging modality for abdominal evaluation is motivated by many factors, including availability, local expertise, and cost of the procedure. Sonography has many advantages including noninvasiveness, broad availability, and low cost. Technically, sonography provides excellent spatial and contrast resolution such that even very small lesions may be detected in many organs. Its negative aspects include inconsistent results in the abdomen as body habitus, and bowel gas may interfere with the quality of a sonographic exam. This has led to a recognition of ultrasonography as a highly operator-dependent procedure and to the choice of CT scan, in particular, for abdominal imaging in many patients. Ultrasonography, however, is an excellent choice and unsuccessful examinations occur in only a small percentage of examinations. In women and young adults in whom radiation dose is a factor, ultrasonography should always be given serious consideration.

Identification of a tumor in an abdominal organ may occur as an incidental observation on a test performed for an unrelated reason or it may occur as a result of a dedicated search to find a tumor in a patient at risk for either primary or secondary malignancy. Tumors may also be found in symptomatic patients in which case certain symptom combinations may suggest the likelihood of a specific diagnosis. For example, in a patient with weight loss and epigastric pain, an astute clinician would consider pancreatic cancer or possibly gastric cancer as a diagnostic possibility and request an abdominal imaging study.

### LIVER TUMORS

Although the spatial resolution on a sonographic exam allows for the identification of very tiny lesions (2- to 3-mm in diameter), detection of a tumor on a liver examination may often be limited by an inherent lack of contrast between the tumor and the background liver such that the lesion is not appreciated or underestimated in terms of its extent and size.\(^6,7\) Detection of hepatocellular carcinoma (HCC) in the cirrhotic liver is particularly difficult.\(^6\) The addition of contrast agents to a liver examination alters lesional contrast such that smaller and more lesions may be detected than on baseline scan alone. This has now been successfully performed with both first- and second-generation contrast agents. Levovist (Schering, Berlin, Germany), a simple air-containing first-generation agent has a liver-specific postvascular phase where the microbubbles persist within the normal liver parenchyma following clearance of the microbubbles from the vascular pool. A high MI sweep through the liver, performed 3 to 4 min following intravenous injection, will produce bright enhancement of the normal liver as the persistent contrast agent is disrupted by the ultrasonography scan. Malignant lesions including all metastases and the majority of hepatocellular carcinomas will not enhance and thereby show increased conspicuity (Figure 36g-2). A multicenter trial evaluating 150 patients with liver metastases showed increased detection of liver metastases over baseline or unenhanced scan alone.\(^8\) Detection of metastases was equivalent to CT scan.

More recently, second-generation perfluoropropane agents such as Definity (Bristol-Myers Squibb, Bellerica, MA) are available for ultrasonography use and have further improved the ability to detect liver tumors with ultrasonography. In patients with metastases and, more importantly,
in patients screened for hepatocellular carcinoma, low MI nondestructive imaging allows for both arterial and portal venous phase evaluation of the liver. Hypervascular masses such as HCC will enhance brightly and show increased conspicuity in the arterial phase. HCC will show washout in the portal phase and will then show as a nonden-versed void within the enhanced liver. By comparison, hypovascular lesions, which include most metastases, will show as a negative void in both the arterial and the portal venous phases. The addition of these contrast agents for liver study holds great promise in the future and may ultimately play a role in the detection of HCC, in particular. In North America, where CT scan is so firmly established for the detection of metastatic liver disease, it is doubtful that routine sonographic study with contrast agents will ever be performed as a regular procedure for detection of metastases.

Characterization of a liver mass is another major role of liver imaging. Grayscale sonography alone may show many features that suggest the correct noninvasive diagnosis of a mass (Figure 36g-3). Lesional vascularity, however, has proven to be the mainstay of liver mass diagnosis and contrast-enhanced CT and/or MRI scan are performed routinely for characterization of liver lesions. From knowledge of tumor vascularity as seen on angiography and more recently on CT/MRI scans, algorithms can be developed for diagnosis of liver masses based on pattern recognition. Ultrasonography with conventional Doppler alone is unable to consistently provide this vascular information. The addition of microbubble contrast agents has totally changed this potential. We have shown lesional vascularity in patients with hilar cholangio-

The gallbladder and the improved detection of liver tumor with postvascular Levovist scanning in patient with hilar cholangiocarcinoma. Transverse sonogram shows a highly echogenic and shadowing mass (arrows) with a hypochoic rim, a classic appearance for a calcium-containing mucin-producing metastasis.

The Biliary Tract The gallbladder and the biliary ducts are both important sites of neoplasia and their evaluation is difficult on all imaging modalities. Jaundice, a frequent presenting symptom for patients with neoplastic disease in this area, is optimally studied with sonography. Objectives on the imaging study include the determination of the presence of biliary obstruction, and if present, the level of the obstruction and the cause. In patients with obstruction, ultrasonography is highly accurate at predicting the presence and level of obstruction, although there is variability regarding the ability of ultrasonography to determine the cause. It is our belief that meticulous ultrasonography technique allows for good determination of the cause as well.

In patients with hilar biliary obstruction, we have found that the addition of postvascular scans of the porta hepatis of the liver with Levovist greatly improves the ability of sonography to differentiate benign from malignant disease and see an obstructing mass and also to determine the extent of disease. Tumor both within the biliary ducts and invading into the liver is nonenhancing and hence shows increased conspicuity relative to the enhanced liver parenchyma. We have shown increased tumor conspicuity in 50 patients, and further extent of disease in the majority of patients (Figure 36g-4).

The Kidney Renal cell carcinoma (RCC) is a frequent incidental observation on a cross-sectional imaging study performed for an unrelated cause. The natural history of these tumors suggests that a solid renal mass that represents RCC may not grow significantly or metastasize over many years of observation. It is the demonstration of vascularity in a solid renal mass or within the
nодules or septations of a complex mass that is the basis for the recommendation for resection of a renal lesion. Because of the high likelihood that vascular lesions will be malignant, resection rather than biopsy is the management rule.

Although ultrasonography may and does detect many tumors in the kidney, contrast-enhanced CT scan is regarded by most as the essential element in the work-up of a patient with hematuria, symptoms referable to the kidney, or a known kidney mass. Currently under investigation is the potential role for ultrasonography with microbubble contrast agents in the characterization of indeterminate lesions on contrast-enhanced CT scan.

Ultrasonography is an excellent accompaniment to contrast-enhanced CT in the preoperative evaluation of the patient with a renal cell carcinoma. Invasion of the renal veins with tumor extension into the inferior vena cava and even into the right atrium may be well shown on sonogram. Furthermore, detection of arterial signals into the right atrium may be well shown on sonography.21

Lymphadenopathy is frequently associated and this organ, and may be primary in the spleen, or a known kidney mass. Currently under investigation is the potential role for ultrasonography with microbubble contrast agents in the characterization of indeterminate lesions on contrast-enhanced CT scan.

The Pancreas The pancreas may be involved with primary and secondary tumors of the exocrine and endocrine components of the gland, which creates a variety of sonographic appearances representative of the spectrum of neoplasia. Medical imaging studies are focused on lesion detection, diagnosis, and staging of disease. Sonography is an excellent modality for evaluation of all aspects of imaging of these tumors, and when used in conjunction with color and spectral Doppler, ultrasonography reliably predicts unresectability of pancreatic cancer on the basis of vascular involvement, lymphadenopathy, and liver metastases. As with other imaging modalities, prediction of resectability is less reliable predominantly regarding microscopic tumor deposits in normal-sized lymph nodes.

The Spleen The detection of focal splenic lesions and of splenomegaly may be a reflection of tumor involvement of the spleen. Lymphoma constitutes the most common neoplastic lesion in this organ, and may be primary in the spleen, or involve the spleen as part of multicentric disease. Lymphadenopathy is frequently associated and careful assessment of the retroperitoneum should be part of every imaging scan. Secondary tumors may also involve the spleen although with less frequency than involvement of the liver.

The Hollow Viscera Sonographic evaluation of the gut may be performed with the use of conventional transducers placed on the abdominal wall. Conversely, endoscopic sonography, performed with high-frequency ultrasonography transducers, coupled with an endoscope, provides high-resolution evaluation of both the stomach and gut wall, as well as adjacent structures such as the pancreas and distal bile duct. Esophageal and gastric cancer, in particular, are frequently staged with the use of endoscopic sonography to evaluate for the depth of penetration through the gut wall and the presence of lymphadenopathy. The gut wall layers are shown clearly with sonography; consequently, the depth of penetration of neoplastic lesions can be predicted with a high level of accuracy.22 Rectal cancer, by comparison, is optimally staged with the use of a rigid intracavitary probe placed in the rectum.23 Currently, transrectal ultrasonography is the modality of choice for accurate determination of tumor invasion and the presence of regional adenopathy. Several recent publications have found transrectal ultrasonography to be superior to CT and other imaging modalities, both for preoperative staging and for follow-up of rectal cancer, with accuracy of endorectal ultrasonography for predicting depth of invasion in the 81% to 92% range.24 The data derived bear directly on avoidance of abdominoperineal resection. Furthermore, it allows for the appropriate selection of patients with locally invasive disease who would benefit from adjuvant chemoradiation prior to surgery. Additionally, submucosal lesions and local adenopathy can be identified.

Conventional sonograms are not routinely performed for the detection of gut neoplasia although frequently a gut-related tumor may be detected on a sonographic study. In any situation where there is gross pathology, ultrasonography will usually detect the abnormality. Gut wall thickening and gut wall masses may be associated with primary and secondary tumors of the gut.

The Peritoneum The peritoneum is frequently a site of secondary malignancy and is less commonly involved as a site of primary neoplasia. Ovarian cancer and tumors of the gastrointestinal tract and pancreas are frequent primary sources in patients with disseminated peritoneal disease. The peritoneum and the peritoneal cavity may be well assessed with sonography, although more commonly, in clinical practice, patients will be referred for CT or MRI scan if peritoneal disease is present. We feel that this is related to lack of awareness of the familiar appearances of peritoneal disease on sonography.24 Furthermore, a sonographic study must be tailored to achieve a high accuracy in the detection of peritoneal disease. As many patients with ovarian cancer do have sonography, we recommend inclusion of the peritoneal cavity in the sonographic study.

Sonography is highly sensitive to the detection of even trace amounts of free intraperitoneal fluid. In addition to the quantitative assessment of ascites, sonography may provide a rough qualitative assessment as well. Particulate ascites has an association with blood, pus, and inflammatory cells in the peritoneal fluid and its discovery should be correlated with the clinical situation.

Peritoneal carcinomatosis shows omental caking, and tumor deposits involving any of the visceral or parietal peritoneal surfaces (Figure 36g-5). The dependent pelvic pouch is optimally studied in women with transvaginal sonography where high frequency probes may detect even tiny peritoneal seeds. Confirmation of blood flow in any tumor deposit supports an initial impression of neoplasia. All patients at risk for peritoneal malignancy should have a survey of the peritoneal cavity to include the region of the mesentery, the omentum, the diaphragmatic surfaces, both paracolic gutters, and the pelvic pouch.

Gynecologic Organs

Ultrasoundography is the most frequently used modality for first-line evaluation of patients thought to have gynecologic disease. Transvaginal ultrasonography probes, placed in close proximity to the organs of interest, allow for excellent accuracy in the detection of disease. Uterine tumors, including benign fibroids, sarcomas, and endometrial and cervical cancer are all visible on sonography. Measurement of endometrial thickness on transvaginal sonography is a frequently performed screening parameter for the detection of endometrial cancer with different threshold levels determined for specific clinical situations above which endometrial sampling is recommended (Figure 36g-6).

Ovarian cancer is most often first seen on sonography in symptomatic patients presenting with this disease. As well, sonography is a frequently performed screening test in patients with an identified genetic risk of ovarian cancer, including those patients with a first-degree relative with the disease. Sonography and CA125 levels are performed at 6 monthly intervals in the hope of detecting disease prior to its peritoneal dissemination. Ovarian cancer is most consistently differentiated from benign adnexal pathology on a sonogram on the basis of the morphology of the mass on grayscale evaluation.

The role of Doppler in diagnosis and in management decisions of malignant gynecologic tumors includes monitoring treatment response, as well as documenting tumor angiogenesis.
PROSTATIC AND TRANSRECTAL SONOGRAPHY

Prostate cancer diagnosis has been revolutionized by the development of suitable transrectal probes and the spring-loaded biopsy gun. Rigid intracavity probes placed in the rectum allow for evaluation of the prostate gland in addition to the rectum itself. Transducers with side-fire and end-fire designs are both suitable for prostatic study. Transrectal ultrasonography (TRUS) is frequently used as a screening procedure for the detection of prostate cancer, although the technique is nonspecific with regard to differentiating benign from malignant nodules. Ultrasonography-guided biopsy has replaced finger-guided biopsy and allowed for markedly increased accuracy with decreased complication rates. Approximately 70% of prostate cancer is visible by TRUS, the remainder are not visible because of variations in pattern of pathologic growth. As a result, cancer detection is improved if ultrasonography-guided biopsy is performed not only of visible lesions, but also from the remaining gland, by using a systematic pattern. Skilled operators with good ultrasonography equipment have better results. Screening for prostate cancer is most cost-effectively performed with prostate-specific antigen and digital rectal examination. When cancer is suspected, TRUS combined with biopsy is currently considered the diagnostic test.

TRUS is also used during brachytherapy to guide radioactive seed placement.

CENTRAL NERVOUS SYSTEM ULTRASONOGRAPHY

The brain and the spinal cord are totally protected by bone and are, therefore, not accessible to ultrasonography study. There is one notable exception in the central nervous system where ultrasonography can play a significant role in tumor imaging: during surgery, a sterile, sheathed ultrasonographic transducer can be placed directly on the exposed brain or spinal cord to locate or facilitate the approach to a known lesion and to minimize damage to adjacent neural tissue. In addition, ultrasonography can be used to help ensure that a tumor resection is complete. Intraoperative ultrasonography can also be used to assist in the resection of spinal masses, including tumors and arteriovenous malformations.

INTRAOPERATIVE ULTRASONOGRAPHY

The use of high-frequency transducers placed directly on a surgically opened organ allows for excellent detection and demonstration of neoplastic lesions in various organs. The liver, in particular, is optimally studied with this technique and in most tertiary centers, intraoperative ultrasonography (IOUS) is a part of every liver resection for either hepatoma or metastatic disease. In the liver, it is now generally accepted that IOUS is more accurate in identifying hepatic masses than any of the routinely used noninvasive techniques, including CT and MRI. Modification, or even cancellation, of planned surgical technique may be the result of IOUS if new or previously unsuspected lesions are identified or if lesions are identified in intimate juxtaposition to vital vascular structures. IOUS also lends itself well to the study of the pancreas, kidney, brain, and the spinal cord. In all areas, detection of previously unknown lesions is the major objective of IOUS, although vascular mapping for determination of the best surgical plane and guidance for biopsy are all aided by this technique.

CONCLUSION

Ultrasonography will continue to play a major role in the evaluation of symptomatic patients with both detection and characterization of tumors in a variety of locations. Microbubble contrast agents and new imaging techniques offer promise of an expanding role of ultrasonography for monitoring tumor response to therapy and for sophisticated evaluation of tumor blood flow.

REFERENCES

26. Cheng WF, Wei LH, Su YN, et al. The possible use of colour flow Doppler in planning treatment in early inva-


