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ULTRASONOGRAPHY IN ONCOLOGY

A review

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Abstract

The applications of ultrasonography (US) in oncology have rapidly increased during the past few years. Technical improvements, development of new technologies, easy availability, and non-invasiveness are some of the reasons for the rapid diffusion of US. Nowadays a large number of malignancies, both superficial and deep-seated, can be examined by US. In order to give an overview of the present role of US in oncology it is necessary to discuss many different topics including tissue characterization, diagnostic role, staging, follow-up and future developments.

Key words: Ultrasonography; oncology, review.

Tissue characterization

The first attempt to characterize normal or pathological biological tissues by means of US was made at the end of the 1950s (1), when good quality 2-dimensional ultrasonographic images became available.

However, whereas US imaging became widespread during the 1970s, mainly after the development of the 'gray scale', the application of tissue characterization developed much more slowly, due to intrinsic difficulties.

Tissue characterization can be classified as physical and clinical. 'Physical tissue characterization' is defined as an analytical tool based on measurement of physical parameters of interaction between US and biological tissues. It is developed in order to characterize the different tissue components.

As 'clinical tissue characterization' we define the attempt to identify morphological patterns of pathological entities, using current imaging techniques.

The physical tissue characterization has also been called tissue characterization 'tout court' or 'telehistology' (2). It is based on parameters other than reflection, like attenuation coefficient, backscattering coefficient, variation in transmission velocity, and the frequency shift of the acoustic signal (3). Some of these parameters may be measured with techniques like transmission tomography; other parameters by using some new technologies currently available (Doppler, FM module).

Furthermore, efforts have been made to obtain from conventional 2-dimensional images, statistical data (histograms) giving information about the intensity of the reflected signal in order to identify small intensity differences, not visible to the human eye.

The breast is one organ which has been especially subjected to research on tissue characterization. Studies with Doppler signal (4) have shown increased blood flow in the periphery of breast tumors compared with the center. However, analytical techniques of tissue characterization are limited by the requirement of more and more complex techniques which are only available in special research laboratories.

The clinical tissue characterization found its first application when the introduction of the 'gray scale' enabled identification of tumoral patterns more complex than the simple 'liquid' or 'solid' patterns. Efforts were made to correlate the grade of echogenicity of a lesion (compared with the surrounding tissues) with tissue in the lesion itself.

This simple parameter, together with morphology and criteria of site, extension and statistical data, points to a number of conditions in which US may accurately distinguish benign from malignant masses, often better than other diagnostic techniques. For instance, a hyperechoic, regularly shaped round hepatic lesion, less than 3 cm in diameter, located near the hepatic veins or the liver capsule, is very likely (95%) to be benign (capillary angioma),

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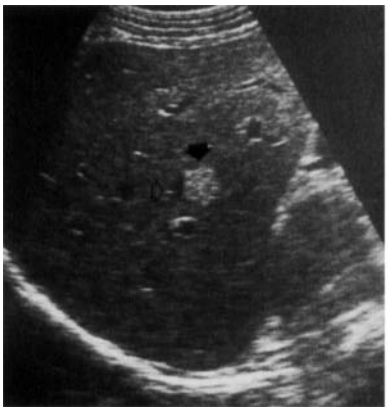

Fig. 1

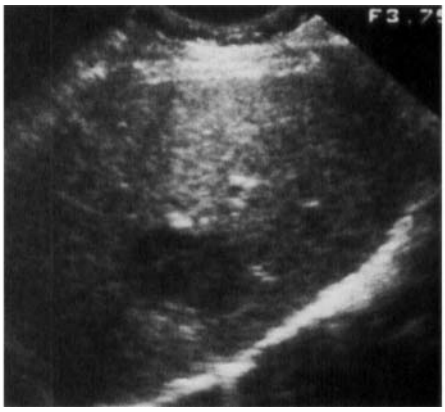

Fig. 2

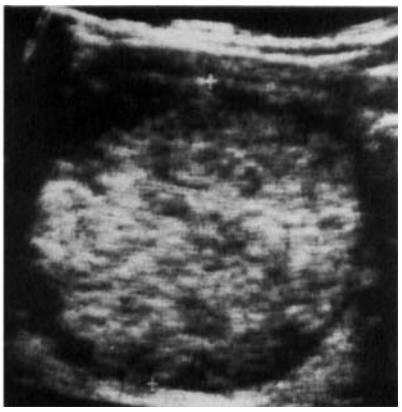

Fig. 3

Fig. 1. Angioma of the liver: round, hyperechoic lesion (black arrow), 1.5 cm in diameter, close to a hepatic vein (open arrow).

Fig. 2. Hepatocellular carcinoma: oval, hypoechoic lesion, 3 cm in diameter, in the right lobe of the liver.

Fig. 3. Adenoma of the thyroid gland: large hyperechoic lesion with hypoechoic halo.

also in patients with cancer (Fig. 1). Conversely a similar but hypoechoic lesion is very likely to be a small hepatocellular carcinoma or a metastasis even in patients with normal α-feto protein and CEA (Fig. 2).

A similar situation applies to lesions in the thyroid gland. A focal, single, hyperechoic (hypo- or non-functioning at scintigraphy) area is more likely to be benign (95–98% probability) (Fig. 3), while a hypoechoic round lesion represents a follicular or papillary carcinoma in about 40% of the cases (5) (Fig. 4).

Therefore, clinical tissue characterization, considering its simplicity, may often be very informative from a clinical point of view. However, it should be kept in mind that it can never give the histologic type of the tumor. Conventional 2-dimensional US, based on reflection, represents only the interfaces due to differences of acoustic impedance; therefore differences in histology which are the basis of the interfaces (connective tissue, fat, vessels, inflammatory infiltrates, etc.) cannot be distinguished and US cannot correctly characterize the neoplastic tissue with exception of organs where one histologic tissue predominates (prostate, kidney, biliary ducts). For the same reasons US cannot distinguish benign from malignant lesions with similar histologic structure (e.g. regenerative nodule versus well differentiated hepatocellular carcinoma). Despite these limitations, however, US has the advantage of giving a real time image that is of considerable help in performing percutaneous biopsy.

With percutaneous US guided biopsy the needle track can be defined with high precision, especially when the track is short and a probe with a biopsy channel is used. For deeply located lesions the US guidance is usually performed with the normal transducers allowing definition of the 3 coordinates.

US guided biopsy facilitates not only puncture of the lesion but also selection of a suitable part of the lesion (e.g. center or periphery). By using different needles cytological or histological specimens can be obtained depending upon the consistence of the tumor.

In general, the risk of dissemination introduced by fine needle biopsy is extremely low and can probably be considered as merely theoretical (6).

Table 1

Sensitivity of ultrasonography. Tumors in superficial organs

	Sensitivity		References
	Min (%)	Max (%)	
Parotid gland	78	98	(27, 28)
Breast	67*	95	(9, 29)
Lymph nodes	88	92	(30, 31)
Thyroid	90		(32)
Testis	90		(33)

* Tumors less than 2 cm (T1).

Diagnostic role

An evaluation of the diagnostic role of US should include 3 aspects: detection of the lesion, definition of the nature of the lesion and estimation of its extension. In this section, only the problems concerning the detection of the lesion will be considered. The other aspects are discussed in connection with tissue characterization and staging.

A large number of organs can be studied with US with good sensitivity (Tables 1–3). For various technical reasons we have separated tumors in superficial and deep-seated organs. Superficial organs can nowadays be examined with high frequency transducers (5–10 MHz) which give high spatial and contrast resolution. US is used mainly for the diagnosis of tumors of thyroid, parathyroids,

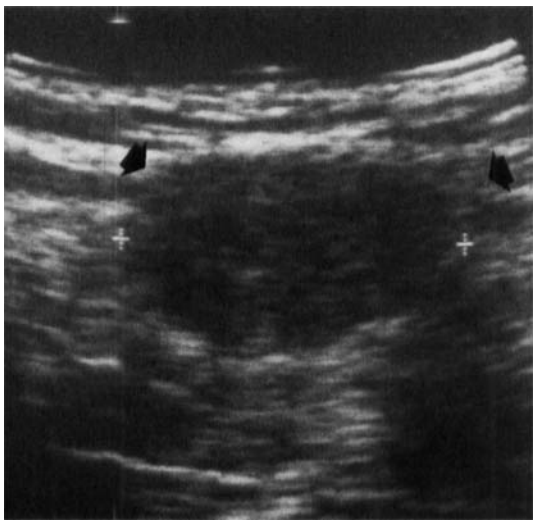

Fig. 4. Papillary carcinoma of the thyroid gland: oval hypoechoic lesion infiltrating the muscle (arrows).

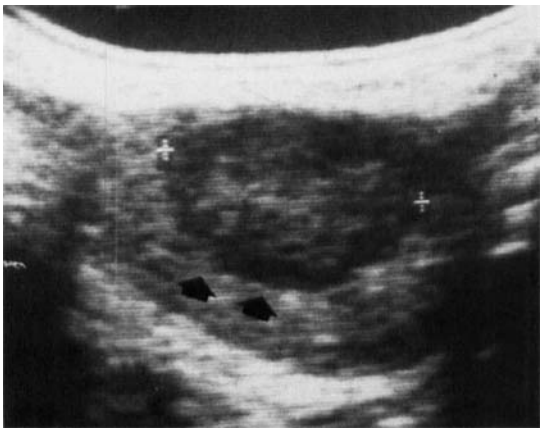

Fig. 5. Seminoma of the testicle: oval hypoechoic non-homogeneous lesion (arrows) surrounded by normal testicular parenchyma.

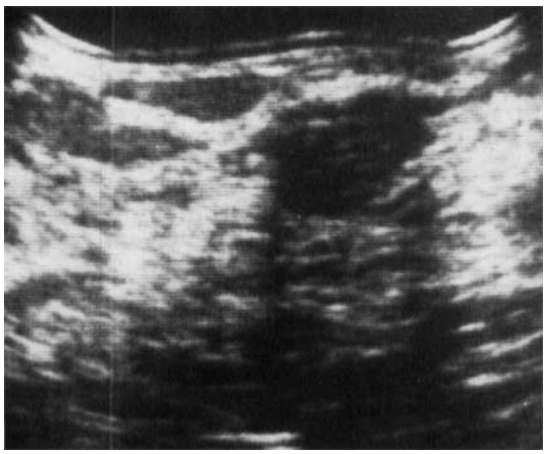

Fig. 6. Breast adenocarcinoma: irregularly shaped hypoechoic lesion with posterior absorption.

breasts, salivary glands and testicles (Table 1). For some of these organs, such as the testicles (Fig. 5) and the salivary glands, US is the examination of choice due to its ability to identify the lesion or confirm the clinical diagnosis. For the thyroid and the breast (Fig. 6) US may still play an important role, although complementary to other diagnostic modalities. For the breast US can supplement mammography, which has a sensitivity of more than 90% (7, 8), mainly in doubtful cases and in the diffusely dense breast. The 2 examinations considered together may reach a sensitivity of 96% (9).

For deep-seated organs, mainly in the abdomen, the results of US are not as good as for superficial organs. Nevertheless, tumors in the liver, pancreas, kidneys, gallbladder, biliary ducts, ovaries, prostate and bladder can be detected by US with quite good sensitivity (Tables 2, 3). Less favorable results are generally obtained in the retroperitoneum and the adrenals. For several organs US has a sensitivity close to CT. Therefore US is generally employed as first examination when hepatic, pancreatic and biliary tumors are suspected (10).

Staging

The possibilities of US in tumor staging also depends on the site of the organ.

In superficial organs the size of a primary tumor (T stage) can always be determined by US. Furthermore, the regional nodal status (N stage) may be defined better with US than with other diagnostic modalities, including clinical examination. This is the case with breast and thyroid tumors. Distant spread of these tumors (M stage) can as a rule be detected by US only when it concerns liver metastases.

Concerning deep-seated tumors, in general, US does not allow a detailed evaluation of tumor spread to surrounding tissues and lymph nodes, with the exception of lymph nodes in the hepatic hilum. US may give information about vascular involvement (e.g. portal vein thrombosis in hepatocellular carcinoma) (Fig. 7). US cannot be used for definite staging of renal and pancreatic neoplasms and for tumors located in retroperitoneum.

Tumor staging may sometimes be improved by intracavitary US, as in tumors of the esophagus and the stomach (4, 11). For staging small and superficially located tumors in the true pelvis, US today offers new possibilities due to improvements in probe technology. Using transrectal high resolution probes, the spread of a rectal carcinoma in the rectal wall can be assessed, and the intra- or extracapsular extension of a small prostatic tumor can be recognized (Fig. 8) (12–15). With small intraurethral and intravesical probes, the extension of a bladder tumor inside the wall can be well shown (16). However, the extension of these tumors in the surrounding tissues and organs is not readily shown by US and is better assessed by CT or MRI.

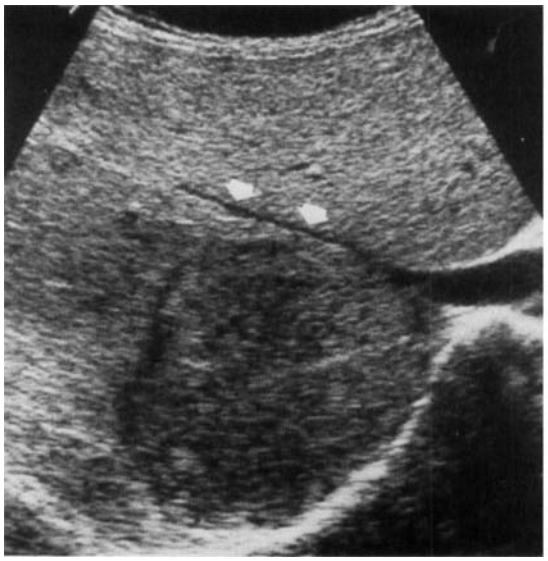

Fig. 7. Large hypoechoic non-homogeneous mass in the right lobe of the liver displacing and infiltrating the right hepatic vein (arrows).

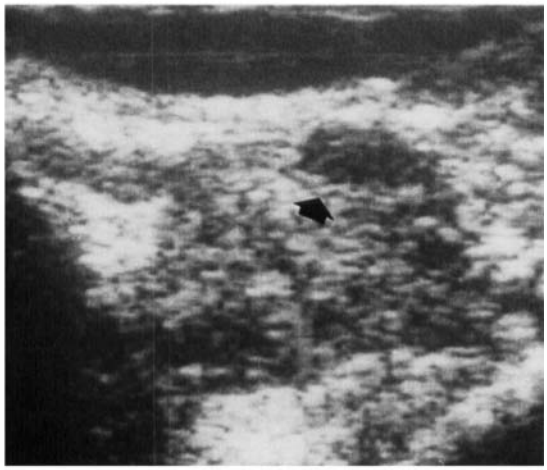

Fig. 8. Transrectal ultrasonography of the prostate: oval hypoechoic lesion (arrow) located in the posterior prostate.

Table 2

Sensitivity of ultrasonography and CT. Tumors in abdominal organs

	Ultrasonography		CT		References
	Min (%)	Max (%)	Min (%)	Max (%)	
Liver	75	94	82	96	(34–36)
Pancreas	56	94	83	96	(37–40)
Gallbladder	44*	89	–	–	(41, 42)
Kidney	94	98	97	100	(43, 44)
Lymph nodes	40	90	65	80	(18, 45, 46)
Spleen	35	77	31	64	(45, 47–49)

* Including asymptomatic patients with gallstones.

Follow-up

Theoretically US may be used for the detection of recurrence or distant metastases and for assessment of tumor size during follow-up.

Tumor recurrence after surgery is not generally well assessed with US due to interference by scar tissue which impairs visualization of the lesion and the differentiation between scar tissue and recurrent tumor.

Tumor size may be defined using US; however, CT is more accurate for assessment of the morphology and volume of the lesion and should therefore, if available, be preferred. The important role of US in the follow-up of oncologic patients is the search for and monitoring of liver metastases (17). US is for this purpose almost as valuable as CT and may be used for monitoring patients operated for gastrointestinal carcinomas and other malignancies (18). US may also be used for assessment of response in patients with primary or secondary malignant tumors treated by intraarterial infusion of cytotoxic drugs (19).

Table 3

Sensitivity of ultrasonography. Tumors in pelvic organs

	Ultrasonography		References
	Min (%)	Max (%)	
Prostate	80	94	(50, 51)
Rectum	80*	89*	(8, 14)
Bladder	33*	95*	(52)

* Values concerning staging.

Future developments

The first point to be mentioned is the continuous development of new probes. The evolution of transducers is directed towards increasing density and homogeneity of the crystals with the aim of obtaining more detailed images. Efforts are also made to improve the focalization of

the transducers, which will give good image quality at all levels.

Doppler US is a well established technique for the study of arterial and venous blood flow. A new field of application is related to its ability to give tissue characterization. The application of Doppler US to characterization of benign and malignant tumors is based on changes of flow in tumoral vessels due to loss of normal flow resistance. These changes are related to the absence of unstriated muscle in the tumoral vessels, which have walls formed by connective tissue and endothelium. Thin-walled vessels, large vascular spaces and arterial-venous anastomoses are commonly found in neoplastic tissue. Therefore, a high flow velocity may be expected in tumoral tissue. This has been confirmed by studies both in animals and in humans (1, 20, 21).

Enhancement of US with contrast media represents a further field of research (11, 22–24). Contrast media have been proposed for liver US in order to improve the detection of malignant tumors, mainly metastases. Perfluorochemical compounds (PFOB) and CO_2 microbubbles are examples of contrast media that have been studied for US liver imaging. PFOB is concentrated in macrophages (therefore mainly taken up in liver and spleen) and causes a diffuse increase of echogenicity throughout the liver, probably due to changes in acoustic impedance.

Finally, new possibilities may concern endoscopic US. We have already mentioned the value of intracavitary US, for instance in tumors of rectum, prostate and bladder. New applications are already available for the upper gastrointestinal tract based on the possibility of combining US with endoscopy. Recent reports show that details of esophagus, stomach and pancreas can be studied with high quality images (25, 26).

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