Evaluating the Liver Tumors Using Three-Dimensional Ultrasonography. A Pictorial Essay

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Abstract

The liver tumors represent a major public health issue. Among the imaging techniques, ultrasonography remains an important diagnostic method, taking into consideration its large availability, the non-invasive and repetitive characteristics and the low cost. Its current limits can be surpassed, at least at some extent, by using some new techniques such as the 3D ultrasonography. 3D ultrasonography provides several advantages: increases the efficiency of the liver tumor screening by using the multislice function, allows a better time and human resource management, the precise location on three axes of the tumor and the exact assessment of the distances relative to the main vessel structures of the liver. It is also able to characterize the tumor texture and to sum up the total volume of liver masses, with applications in post-chemotherapy follow-up.

Key-words
Liver tumors – imaging techniques – three-dimensional ultrasonography

Introduction

The liver tumors represent a major pathology in the medical practice, considering their high incidence, the diagnostic difficulties and the high rate of morbidity and mortality. Other methods of imaging (CT, MRI) have a higher sensitivity than ultrasonography (US), but their use is limited by the high costs, lower accessibility, side effects (in the case of CT), problems with metallic prosthetics, stents, catheters (in the case of MRI) (1,2).

Ultrasoundography remains the main imaging method for diagnosing liver tumor masses. This position is sustained by the large addressability of the investigation, its non-invasive and, consecutively, repetitive character and the lower price. The specificity of the method for the diagnosis of hepatocellular carcinoma is 58.9% and the method’s sensitivity is 72-95% (1,3). Ultrasound and the dosing of α-fetoprotein repeated every 6, or even 4 months play an important role in early hepatocellular carcinoma detection in liver cirrhosis. In the case of small tumors (<1 cm), one recommends the ultrasound follow-up every 3 months for the early confirming or exclusion of hepatocellular carcinoma (4).

Doppler US identifies the neoangiogenesis in the liver tumors and plays an important role in the differential diagnosis of the well defined malignant tumors (high vascular signal) and the benign masses (weak or no vascular signal). In the staging of hepatocellular carcinoma, Doppler techniques are valuable regarding the proof of portal invasion (tumor “thrombus”). Doppler US is also used in echo-guided percutaneous cures of malignant liver tumors with ethanol instillation (5).

The sensitivity of US in the diagnosis of liver tumor masses is almost similar to CT or MRI, but the method is not equally suited for the staging of malignant tumors. The main limits of US are: operator-dependency, the limited reproducibility of images and the low specificity. In order to improve these limits (especially to raise the specificity), new techniques have been introduced: harmonics, contrast enhanced exploration, pulse-inversion and three-dimensional (3D) rendering.

The 3D evaluation of liver tumors

Three-dimensional ultrasonography (3D US) consists of the acquiring of a “virtual” volume by adding a large number of US planes. 3D US investigation is the result of a 2D US investigation more or less detailed, through collecting echoes which are afterwards spatially distributed, according to a specific algorithm. The quality of the 3D image is directly
linked to that of the originating 2D information. The more revealing and artifact-free the 2D image is, the better the 3D reconstruction.

**The 3D US image.** After the ultrasound acquisition, a set of 3D data is obtained, which sorts and aligns the echoes received from the examined volume of tissue. There are two classes of algorithms through which the 3D volume might be explored (6):

- **3D surface mode** relies on the identification of surfaces from the structures that have a strong enough contrast relative to the surrounding anatomical elements from the predefined volume. The advantage is a fast reconstruction, with less information available;

- **3D volume mode** (the “voxel” technique) consists of what we call today a conventional 3D US. It is based on the vectorial space representation of every reflective item within the explored structure, which leads to the creating of a sonographic “volume” called “voxel”. It is the most precise technique and a big advantage consists in the possibility of volume postprocessing. Every reflecting item has a well established position in the volume, according to reality, hereby the technique’s accuracy improves.

**Types of 3D information.** The 3D US dataset can be viewed using common techniques from other digital imaging methods (CT and MRI), such as reconstruction in arbitrary planes (intermediate to the anatomical ones), multiplanar reconstruction, nonplanar reconstruction, the reconstruction based on the surface analysis (3D “surface mode”) or the rendering based on volume analysis („transparent mode” or „ray tracing”) (7). With current equipments, the 3D US image can be viewed using a single mathematical processing model or a combination of algorithms (called „modes”):

- **multiplanar image** („quad mode”) is obtained right after the scanning and is composed of four images displayed on the equipment’s screen, out of which three are planar (reference images): the longitudinal, transverse and coronal sections, and the fourth is a 3D rendering. Every reference image is centered around the intersection of the three planes. The selected image might be rotated around this point in order to obtain the desired section. The rotation of one reference image is followed by the implicit rotations on the other planes, as well as the rotation of the rendered volume (Fig.1);

- **volume image** („transparent mode”). In this mode, the acquired volume is crossed by many parallel axes (from which the name of “ray tracing” or “ray casting”), along which the whole volume is projected on a plane and displayed as a 2D image. These axes (equal to the number of pixels from the final image) intersect on their trajectory a variable number of voxels. The computational algorithm is based on the summation of the voxels within the reconstructed volume, along each axis, displaying on the projection image either the maximum values („maximum mode”), the mean values („X-ray mode”), or the minimum values („minimum mode”) (Fig.2a);

- **surface image** („surface mode”). This mode reconstructs the surfaces of various organs and structures, which are afterwards better rendered with the help of some lightening and shadowing algorithms. The surface mode is ideally suited for organs or structures bordered by fluids (fetal face, liver from ascitis etc.) (Fig.2b).

The analysis and processing of the 3D image can be done on the reference images or on the upscaled sonographic volume, either on an external workstation, or directly on the US equipment and include the following functions:

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**Fig.1** Multiplanar image („quad mode”) of the gall-bladder.
- volume rotation. One can rotate the voxels on any axis with the help of the trackball in order to better view the interest area from different incidences;
- "cutting” in volume ("scalpel function"). It uses a "cutting" algorithm alongside a surface’s linear or irregular contour from a side of the volume. Holes might be cut inside the volume using a predefined "step" until the exit on the other side;
- the viewing in “transparency” and “inversion” modes. The “transparency mode” constitutes a reasonable ratio between echoes with different intensities, which allows the viewing of transonic tubulo-cavitary structures inside a solid mass (biliary ducts, vessels or cysts inside the liver). The “inversion mode” points out more convincingly the transonic structures, the color of which is reversed;
- the use of the "threshold" function for the selection of some interest areas is based on the selective rendering of the structures with an echodensity above a specified value, selected by the operator during postprocessing. With this function one can view tubulary structures inside parenchyma (vessels, bile ducts, cysts, collections) and one can calculate the oncologic volume and the vascularization index (8);
- "multislice” technique. Some US equipments have the ability to extract section planes from the total 3D volume and to show them in succession, as CT and MRI equipments do (9);
- angio 3D ultrasonography with and without contrast. 3D US allows a rather rough illustration of vessels inside large solid organs such as the liver. By combining it with the “power” mode, supplementary information concerning the spatial arrangement of vessels is acquired, valuable for the differentiation between the inflammatory vascularization (enhanced, but with preserved morphology) and the neoplastic one (enhanced, disorganized, with many vascular pedicles)(10,11).

The additive value of 3D ultrasonography to the diagnosis and the characterizing of the liver masses

During the diagnosis and US evaluation of the liver tumors, factors such as: the number of lesions, their exact location, dimensions, contour and delimitation, echogenicity, homogeneity, the evolutive changes (necrosis, calcifications, fibrosis and neoangiogenesis) and the extension and intimate relations with the surrounding vascular structures (invasion, imprinting, stenosis) have to be assessed. Some of these elements of tumor semiology might be better assessed through 3D US.

a. tumor topography and volume handling. A first step while evaluating a liver tumor consists of the precise assessment of the location. The 2D image offers data concerning the tumor position relative to various anatomical landmarks, such as: the skin, the liver borders, the portal system etc, but a precise location on three axes is very difficult to accomplish, due to the unlimited sections one can view by tilting the transducer (Fig.3a). The topographic landmarks become absolute while acquiring a 3D volume with the transducer sitting perpendicular in a fixed spot on the skin. The „quad mode” (multiplanar image) (Fig.3b) further allows the examination of the volume on all the three orthogonal axes (X,Y,Z), displaying the 3D rendered image in the fourth window. In order to see just the 3D rendering one can access the single window mode (Fig.3 c, d).

Then, the 3D acquired volume might be assessed through numerically measurable steps by setting the depth and rotation on each sectional plane. As the center of the windows is positioned in the anatomical center of the tumor on all three planes and knowing the size of the acquired volume, the exact position of the formation or of any of its elements might be measured. This method can be used for better guiding of the minimal invasive procedures that use orthogonal coordinates.

Another technique used for handling the 3D volumes is the “scalpel” (Fig.4). Removing layer after layer until the area of interest is reached, the regions situated at a certain depth might be extracted from the original volume. The “step” can be quantified. The final result of these transformations offers valuable, more eloquent visual relations.

b. the rotation of the acquired volume and of the selected area. One of the limits of 2D US is the limited spatial perspective over any explored structure. While the examiner succeeds in building the space image in his mind by scanning through many sections, there is much harder for a third person who sees just a few pictures to do the same. Also, frequently there are only a few ultrasound windows which might be used in one region, making the evaluation of all tumor relations virtually impossible. The 3D US eliminates
Fig. 3 Organized liver hydatid cyst. Methods of location. a) 2D image in B-mode; b) “Quad mode”. Volume examination on the three perpendicular axes (X, Y, Z), displaying the 3D rendered image in the fourth window; c) The “gray” “surface mode”; d) The “inversed” “surface mode”. The inhomogeneous texture due to the membranes and daughter vesicles (transparent on the image) and the less dense content of the cyst surrounding them (the solid areas) might be distinguished.

Fig. 4 3D Volume handling. The “scalpel” function. a) 3D rendered image in “transparency” and “inversion” modes at the level of the right kidney (rd); b) demonstration of kidney architecture by cutting in an angle using the “scalpel” function.

Fig. 5 Multiple liver metastases. A similar case with that from Fig.12, due to the hypoechogenic nature of the tumors (pancreatic carcinoma metastases). “Inversion” and “surface” modes are being used, allowing the representation of hypoechogenic metastases and vessel structures in a solid shape. Using the 3D volume rotation function, one can individually describe, count and characterize all the tumor formations and their relation with the surrounding vessels and even their own vascularization might be assessed.

all these limits and makes possible the examination of the masses from any angle and any distance. This way, the tumor might be assessed from several incidences (Fig.5).
c. multislice technique. Similarly with the homonymous technique used in CT and MRI investigations, the acquired 3D volume can subsequently be sliced in equally spread planes, on a predefined distance, perpendicularly on any axis (Fig.6). Doing so, one can easily see all the structures within the volume, without the risk of missing one, which is a very valuable asset in screening trials. The acquisition of 3D volumes can be done by semi-qualified personnel (technicians), leaving the physicians to analyze the slices. This way, one can improve a screening trial, by shortening the examination time (which also improves the patients’ compliance) and the human resources become better managed (leaving the specialist on the top of the pyramid). The acquired volume can be remotely transmitted for evaluation in an expert centre.

d. tumor – liver vessels, respectively tumor – biliary ducts relations using “inversion” plus “surface” rendering modes. By using the “inversion” mode the transonic structures within the liver (vessels, biliary ducts) become “lightened”, in contrast to the “darkened” surrounding liver tissue. The additive use of the “surface mode” and the rising of the “threshold” over the value of the liver parenchyma might isolate only the vascular structures together with the hypoechogenic tumors (Fig.7).

Fig.6 The representation of ultrasound information using the “multislice function”. The yellow contoured image represents the original volume, showing the orientation of the slices. Slices are created parallel, in spite of the curb nature of the volume.

Fig.7 Transonic liver metastases (primary tumor: the ovary). a) On the 2D image it is difficult to establish the type of relation with the surrounding vessels. b) On the 3D images using the transparency mode (“X-ray mode”) in “inversion” and, respectively, c) “grey” modes, one can better distinguish the main vascular branches in the close vicinity of the tumors. The transparency mode does not allow the correct assessment of the relation between the structures. d) On the 3D image using the “surface mode” the metastases are distinct and they do not invade the vessels. Also, on the obtained “cast” of the cysts the prints of the irregular tumor walls can be seen.
If the tumors are hyperechogenic, they appear “carved” in the solid liver tissue mass, leaving the vessels crossing through to be clearly seen (Fig. 8a, b).

The same principles involving the special relations of the tumors with the proximity transonic structures, seen in “inversion mode” apply in the assessment of the bile ducts tumors (Fig. 9).

**e. tumor characterization.** In the ultrasound assessment of the liver tumors, a vital role is played by the description of the tumor content: homogeneity, texture, evidence of necrosis, fibrosis, calcifications and neoangiogenesis. The 3D ultrasound could bring a few advantages in this situation. One can obtain valuable information regarding the evolving character of tumor masses, as well as the dominant anatomical items from that particular stage of their development (Figs. 10, 3c,d).

f. the use of “inversion mode” in the optimization of the US images of hypoechogenic and transonic tumors. As noted above, the best rendering mode for hypoechogenic and transonic structures is the “inversion mode”. Consecutively, “casts” of the hypoechogenic structure are obtained, sharply contoured within the surrounding liver tissue, which becomes transparent. Liver cysts are well outmarked, in a similar way to the intrinsic hepatic vessels and bile ducts, helping to the assessment of their spatial relations (Fig. 11).

**Fig. 8** Hyperechogenic liver metastases. a) 2D exploration in B-mode; b) 3D view in “inversion” plus “surface” mode: the 3D image shows the hepatic vessels passing through the metastases, in contrast with the 2D image.

**Fig. 9** Klatskin tumor (a cholangiocarcinoma developed in the liver hilum, between the right hepatic bile duct - hdr- and the left hepatic bile duct - hstg-). a) 2D image in color Doppler mode, revealing the bile ducts dilatation and the tumoral nature of the obstacle; b) the 3D image shows the same accuracy, but is more explicit for the surgeon, offering more visual landmarks regarding the way the tumor imprints and occludes the ducts.

**Fig. 10** a) Hepatocellular carcinoma (3D ultrasound exploration using the “surface” plus “inversion” mode). The tumor was hypoechogenic (appears solid in comparison with the transparent surrounding liver tissue), homogeneous and lacking feeding vessels. b) The same case (3D US exploration using the “surface” plus “inversion” mode), examined after 12 weeks. There was a strong increase in tumor volume (with a calculated volume doubling time of 24 days!), an increase in tumor density (becoming transparent compared with the surrounding less echogenic liver tissue, which appears now solid), becomes necrotic (in the upper-right area of the image, where the surface is more elevated) and presents its own feeding vessels (cylindrical shapes over the tumor’s “cast”.

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**Fig. 11** a) 2D us exploration in B-mode, b) 3D us exploration in “inversion” plus “surface” mode.
A practical use of “inversion mode” combined with the “threshold” function is the estimation of the total tumor volume in the case of hypoechogenic liver metastases, for better and dynamically assessment of the outcome of chemotherapy (Fig.12).

**Conclusions**

1. 3D ultrasonography, using the “multiplanary” and “quad mode”, allows the precise location on the three axes of the liver tumors and the accurate estimation of distances from the main vascular structures of the liver to the tumors (important for the surgeons!).
2. The rotation of the acquired volume and of the area of interest shows more efficiently the spatial relationships between the tumor masses and the surrounding structures.
3. The “multislice” technique can increase the efficiency of screening programs concerning liver tumors through a better management of time and human resources.
4. Using the “inversion” plus “surface” modes one can assess the relation between tumors and the liver vessels.
5. Using the “inversion mode” combined with either “
transparency” or “surface” mode, one can describe the tumor texture, necrosis areas, fibrosis, calcifications and tumor neoangiogenesis (improved with i.v. contrasting agents).

6. Combining the “inversion” function with an appropriate setting of the “threshold”, and later applying the “scalpel” utility, one can sum up the total volume of hypoechogenic and transonic metastases, with application in post-chemotherapy follow-up.

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