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3D/4D breast ultrasound: diagnostic and intervention

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Background. *Three-dimensional (3D) and four-dimensional(4D) mammasonography is the most recent development in breast ultrasound imaging providing additional aspects to conventional two-dimensional (2D) sonography.*

Conclusions. *The new technique of mammasonography enable completely new superior diagnostic information such as the ability to study a breast mass and the surrounding tissue in 3 orthogonal planes, or to obtain new information about the mean blood flow intensity or vascularisation of breast lesions by evaluation of the 3D colour histogram. 4D ultrasound offers almost real time 3D rendered image information and is taken as a basis of multidimensional imaging of the breast.*

Key words: breast, ultrasound, mammasonography, three-dimensional, four-dimensional

Introduction

Three-dimensional (3D) and four-dimensional (4D) mammasonography is the most recent development in breast ultrasound imaging providing additional aspects to conventional two-dimensional (2D) sonography: completely new superior diagnostic information such as the ability to study a breast mass and the surrounding tissue in 3 orthogonal planes, or to obtain new information about the mean blood flow intensity or vascularisation of breast lesions by evaluation of the 3D colour histogram. 4D ultrasound offers almost real time 3D rendered image information and is taken as a basis of multidimensional imaging of the breast. In the following section about 3D and 4D breast ultrasound (US), after a short introduction to technical considerations, multidimensional imaging of solid benign and malignant breast lesions will be discussed. Display options, virtual computer-aided lesion analysis (VoCal), Shell™imaging, 3D-targeting and real-4D breast biopsy technique will be discussed.

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3D ultrasound technique and display options

Two principle techniques and the combination of both exist to obtain a 3D US information: manually or automatically scanner movement with echo-data processing along the US-

beam. All demonstrated cases were investigated with a linear array 2D and 3D US volume transducer, 5-13 MHz, with a 30° volume sector angle combined with the Voluson 730 (GE Medical Systems-Kretztechnik Ultrasound, Zipf, Austria). The Voluson™ technique offers the option to acquire a 3D US volume data set automatically with one and the same transducer without freehand movement of the probe. In about 2-3 seconds the system obtains the entire 3D data volume set (about 10 MByte) and displays the information in a multiplanar image display mode.

Multiplanar display mode

The multiplanar representation uses the 3D US information from the three planes (A-, B- and C-plane) that cut the voxel and which are orthogonal to each other. The A-plane shows the original scan plane during typical 2D US investigation and volume acquisition. The B-plane is orthogonal to A and C and offers the typical rectangular US information of two-dimensional scanning, for example, the sagittal or transversal plane. The completely new diagnostic information is obtained by the coronal plane (C-plane), which is orthogonal to A and B. Furthermore, the system allows navigation through the entire acquired volume conducting parallel interactive movement through the image slices. In all 3 planes a coloured dot (A: yellow, B: orange, C: blue) indicating an identical voxel can be directed in every activated plane into the volume of interest (VOI). Synchronous parallel image movement in the corresponding orthogonal planes can be observed and shows the VOI rectangular reformatted. A dynamic analysis of the 3D acquired US information of an anatomical detail is available and is easier to understand, e.g., complex collecting duct branching.

Niche mode view

The 3D US data are represented as a "cut-open" view of, e.g., the interior view of a tumorous breast lesion and its surrounding tissue. This mode also demonstrates the relationship of the converging subareolar collecting ductal system impressively. After 3D US data acquisition the volume offers the entire nipple area and the retromamillary region in one volume. An optimal time-gain adjustment is necessary to reduce shadowing behind the nipple area for full diagnostic information of the ductal system.

Surface mode

The surface mode provides the assessment of rendering surface structures. A good result of surface rendering can be obtained by studying the inner structures of a cyst or an intraductal papilloma outlined by echpoor fluid. The grey values of the surface are identical with the grey values of the original scan. An impressive surface information of a more complex three-dimensional lesion morphology can be acquired.

Transparency mode

The acquired US volume data allow a three-dimensional rendering using transparency mode and fading, e.g., between a maximum or minimum mode adjustment. This mode gives reliable information of ductal anatomy and pathology, e.g., intraductal papilloma. Additionally, an animated study distinctly illustrates ductal branching or intraductal pathological structures and gives information of their spatial relationships.

3D US characterization of solid breast lesions

All 2D and 3D US investigations were performed with the patients in supine position with elevated arms. The typical 2D US analysis of breast lesion shape, width and depth ratio,

margin characterization, lesion compressibility, lesion echogenicity and echo texture followed. The additional 3D/4D US information first displayed in the multiplanar mode offers the new coronal plane lesion aspect and allows a categorization into different breast masses by retracting and compressing lesion patterns as described by Rotten and colleagues.[1,2]

Fibroadenoma

The typical two-dimensional US appearance of a fibroadenoma is characterized by a well-defined ovoid or round (70%), partly lobulated, homogenous hyporeflexive mass (76%), with a sometimes thin hyperechogenous boundary to the surrounding tissue forming a pseudo capsule. Lateral shadowing (65%) and hyperreflexivity behind the fibroadenoma (in 25% to 38%) may be visible. Ten % show dorsal hyporeflexivity.[3] The typical 2-dimensional cross-sectional ovoid shape with the long axis diameter parallel to the skin and a transversal width-to-sagittal depth ratio of >1, can be found in about 70%. In 30% a lobulated polycyclic fibroadenoma with slightly inhomogenous internal echogenicity may occur. Mostly the short axis depth diameter can be compressed in about 20%. As described by Rahbar[4] the most reliable 2D US features characterizing a benign lesion are a round or oval shape (94% benign), circumscribed margins (91% benign) and a width-to-depth (anteroposterior dimension) ratio greater than 1.4 (89% benign).

3D US gives reliable information of the lesion shape. Fibroadenomas often show a round base, like a coin positioned parallel to the skin, embedded by breast tissue. Due to their transversal width-to-sagittal depth ratio of >1 on 2D cross-sectional images, they have a more cylindrical morphology than assumed by 2D US. Also real-time 2D US most of the time is not enough to give a clear understanding of the three-dimensional lesion aspect in cases of the more complex bases of fibroadenomas with lobulation of their surfaces and dumbbell-like or irregular aspects. In about 2-3 seconds the Voluson technique offers a 3D multiplanary image of the fibroadenoma without any dependence on long or short axis lesion diameter or angulation. Different measurements of width and depth distances can be accurately obtained, guided by all three planes.

3D US volume datasets show more objective fibroadenoma compressibility than 2D US, because during echo palpation a well-defined embedded lesion is movable and the probability increases that 2D US causes depth-axis diameter measurement in different positions, with the consequence of measuring incorrect distances. Comparing the three-dimensional morphology of the lesion before and after compression with 3D US datasets provide correct measurements of comparable slices.

Rotten and colleagues[1,2] investigated 186 solid breast lesions and described 2 predominant tissue patterns surrounding the breast lesion and visible in the coronal plane: the compressive pattern associated with benign lesions such as fibroadenomas and the retraction pattern, which was highly suggestive for malignancy. The 3D statistical performance to differentiate malignant from benign by the criteria of compressive and retraction pattern showed in the study of Rotten et al. a high specificity (0.938), high sensitivity (0.914) and high predictive values (positive pv: 0.869, negative pv: 0.960).

In my own studies of 254 solid breast lesions I found 86 (34%) lesions with a compressive pattern and 107 (42%) lesions with a retraction (star like) pattern sign. In the compressive pattern group 85 (99%) lesions were benign and 1 invasive lobular carcinoma of 5 mm long axis diameter imitated benign breast disease. The retraction pattern group of 107 lesions included 89 (83%) malignant lesions and 18 benign lesions mimicking malignancy. In 61 (24%) lesions criteria of compression as well as retraction were visible.

Therefore a third so called "indeterminate group" was necessary to establish. In this indeterminate group 48 (79%) lesions were benign and 13 (21%) lesions malignant.

The statistical analysis of my study group showed for the compression pattern (indicating benignancy) and retraction pattern (indicating malignancy) a sensitivity of 99.4%, a specificity of 82.5%, a positive predictive value of 0.9, a negative predictive value of 0.99.

The compressive pattern of a fibroadenoma shows a thin or different wide hyperechogenous boundary to the surrounding tissue caused by a space-occupying lesion. Sometimes forming a pseudo capsule, developed by distortion and compression of the surrounding structures, a fibroadenoma does not infiltrate the neighbouring tissue.

Invasive breast carcinoma

The macromorphological growth pattern of breast cancer is heterogenous. Invasive breast cancer can show a stellate and/or nodulary aspect, a circumscribed mass, a diffuse infiltrating growth pattern, or can be developed as a papillary carcinoma or a rare intracystic carcinoma.

Seventy-five % of invasive breast cancers are invasive ductal carcinomas frequently arising in the extralobular portion of the terminal duct. Macropathologically, they usually appear as a solid nodulary mass with stellate margins due to the tumorous infiltration into the surrounding tissue followed by fibroplastic reaction with architectural distortion. Additional intraductal tumorous spread combined with intraductal microcalcifications often can be found. In 10 to 15% invasive lobular carcinomas are arising of the epithelial layer of the lobule. They tend to grow diffuse along ducts, vessels and Cooper ligaments like wallpaper combined with architectural distortion, and frequently form diffuse palpable lesions, skin thickening (15%) and skin retraction (21%) In contrast the invasive mucous carcinoma and the invasive medullary carcinoma (5-7% of all invasive breast cancers) show smooth marginated borders with a pseudocapsule and imitate benign lesions like a fibroadenoma.

According to the study of Rahbar[4] 2D US features that characterize lesions as malignant are irregular shape (61% malignant), microlobulated (67% malignant), spiculated (67% malignant) and a width-to-depth (anteroposterior dimension) ratio of 1.4 or less (40% malignant). Most of the time the tumour centre is characterized by a homogenous echo-poor fibrohyalinosis followed by a dorsal shadowing due to ultrasound energy absorption. The echo-rich margins are the expression of many different tissue components of tumour cells, fibrous strands, fatty tissue and surrounding glandular parenchyma indicating the tumorous growth and infiltration zone. Mammography clearly shows this stellate infiltration pattern with the architectural distortion of the neighbouring structures.

3D US is the first ultrasound imaging modality which offers simultaneously the coronal, transversal and sagittal plane for eliminating the architectural distortion as in mammography. Although 2D US shows signs of disrupted connective tissue layers and changes of the shape and disruption of the superficial fascia in the transversal and sagittal planes, these signs are less impressive compared with the tissue distortion presented in the coronal plane. Even in stellate carcinomas smaller than 1 cm in diameter, the retraction pattern is visible in the coronal plane.

Multifocal breast cancer results from different invasive cancer origins of the ductal system of one glandular lobe and is a common finding. Translating and rotating the entire acquired 3D volume data of a breast cancer and the surrounding tissue in the multiplanar display mode, gives the opportunity easier to understand the underlying process of multifocal breast cancer disease.[5]

In particular, invasive lobular carcinomas

sometimes develop without mammographically and sonographically visible dominating mass. In such a situation the coronal plane helps to visualize the architectural distortion and enables understanding of the underlying pathology. Therefore dense, palpable, especially asymmetrical breast tissue should be investigated by 3D US to detect architectural distortion. When invasive lobular carcinoma forms a more circumscribed mass or tends to produce multifocal lesions, these tumorous lesions have a similar ultrasound aspect like an invasive ductal carcinoma. Although the retraction pattern is highly characteristic for malignant masses, we have to consider benign differential diagnoses such as the radial scar, the sclerosing adenosis or postoperative scarring.

Volume CONTRAST IMAGING (VCI)

Volume Contrast Imaging is a real-time 4D ultrasound technique which offers thick- slice rendering (4 mm slice thickness) or thin-slice rendering (2 mm slice thickness). The render algorithm is a combination of surface- and transparency mode. The most modern Voluson 730 technology offers VCI in the typical 2D ultrasound accessible planes as well as in the coronal plane. The advantage of the VCI technique compared with conventional 2D ultrasound is the contrast enhanced representation of almost isoechogenic lesions compared to the background. As a consequence VCI provides an accurate measurement and safe needle guidance into, e.g., an echo-poor fibroadenoma surrounded by echo-poor fatty tissue.

Volume calculation (VoCal)

The "3DVIEW™" is a workstation-like integrated computer program that offers volume calculations (VoCal). The basic principle of VoCal is to combine geometric surface information with the volume dataset of a lesion.[5,6] On the condition that the lesion is circumscribed with clear contours, the VoCal software enables automated or manual volume calculation. The surface geometry is defined by rotation of an image plane around a fixed axis. The surface geometry can be visualized as a coloured surface, a wire mesh model or a rendered greyscale surface. Well-defined lesions including fibroadenomas, papillomas or rare, well-defined breast cancers such as medullary or mucous carcinomas can be evaluated by VoCal.

3D power-Doppler combined with Shell™ imaging

The vascularisation of a breast lesion can be investigated using 3D technique with power-Doppler (amplitude-based colour-Doppler sonography) and frequency-based color-Doppler sonography. The neovascularisation of a carcinoma with an irregular vascular pattern, arterio-venous shunts and missing vessel-autoregulation in contrast to normal breast tissue vessels, is the background for many studies with two-dimensional ultrasound and computer-assisted quantitative colour Doppler analysis aiming at a differentiation between malignant and benign breast lesions.[7-9] The morphological pattern of tumour vessels and tumour feeding vessels is an approach for 3D power-Doppler studies. 3D power-Doppler imaging provides the analysis of blood flow and three-dimensional vascularisation patterns of the entire tumorous lesion without the limitation of scanning only two-dimensional planes, including the potential problem that the most representative slice might not be scanned.

3D power-Doppler volume information offers, combined with the "3DVIEW" software an effective tool to evaluate the colour histogram and the spatial distribution of the vessels inside and outside of the malignant or be-

nign tumour. 3D reconstructions of the colour volume data are an effective tool for studying the three-dimensional vessel distribution and the potential irregularities in vessel shape.[5,6] The colour histogram gives information about the vascularisation index (VI), the flow index (FI) and the vascularisation-flow index (VFI) inside a user-defined volume of interest (VOI). The vascularisation index (VI) gives information in percent [%] about the amount of colour values (vessels) in that volume of interest. The VI is calculated by dividing the figure of colour values by the figure of total voxels minus the background voxels of selected VOI. The dimensionless flow index (FI) measures the mean blood flow intensity. The figure ranges from 0 to 100. FI is calculated as the ratio of weighted colour values (weighted by their amplitudes) to the number of the colour values. The vascularisation-flow index (VFI) gives combined information of vascularisation and mean blood flow intensity. The figure of the VFI is also dimensionless and ranges from 0 to 100. It is calculated by dividing the weighted colour values (weighted by their amplitudes) by the total voxels minus the background voxels.

After defining a volume of interest (VOI)[5,6] either with manual contour tracing of a well-circumscribed lesion or with a spherical contour of an ill-defined mass, we can create different shells with varying shell thicknesses. The shell is defined by "parallel" contours and shell geometry consists of an outside and inside surface with a calculated volume in between. The 3D US information inside the defined shell like the colour histogram parameters or gray scale parameters are immediately available. Additionally the "3DVIEW" software allows to vary the shell position in relation to the defined VOI: inside, outside or symmetrical. This software feature enables the comparison of a significant amount of colour histogram information from different areas of a lesion, for example the marginal lesion zone with the entire lesion or a combination of the surrounding tissue zone and the neighbouring tumorous zone.

These correlations can be obtained and compared with each acquired 3D power-Doppler dataset from datasets at different times of the same lesion. For example, before and after the application of echo-enhancing contrast agents. In 1997 Madjar and Jellins[10] described the contrast enhancement flow from the periphery to the centre of malignant as well as benign tumors by 2D US studies. In that study the carcinomas showed this pattern more pronounced, with the malignant neovascularisation revealed as having a distinct radiating pattern and a vascular corona, equivalent to the growth zone of the tumour, visible in the echo-dense rim seen on B-mode US. 3D power-Doppler combined with the representation of three-dimensional vessel architecture, VoCal, Shell imaging, colour histogram and the additional option of intravenous application of microbubble contrast agents are important for further studies of tumour neoangiogenesis to determine their diagnostic efficacy for differentiation of benign and malignant lesions.

3D-targeting technique

The sonographic visibility of a suspicious lesion is the basis for an ultrasound-guided biopsy. 3D breast US offers a correlation of typical "freehand" 2D US guided core- or fine needle biopsy and hook wire localization of palpable and non palpable lesions in order to optimise tissue sampling and to reduce the miss rate.[11,12] The consequence of 3D-targeting should be a reduction of needle passes without increase of miss rate due to objective 3 dimensional demonstration of correct or incorrect core- or fine needle position.[13] First a 3D US volume dataset is acquired to study the morphology of the lesion. The multiplanar scan plane analysis offers comprehensive information of the lesion and the surroun-

ding structures. For large-core needle biopsy (14-gauge) with local anaesthesia a 2-3 mm skin incision is performed. In typical freehand 2D US guidance[14] the needle path should be as horizontal as possible to optimise visualization of the needle length and needle tip. Via the 13-gauge coaxial cannula a 14-gauge core-needle is positioned in front of the lesion. After a 22 mm core-needle stroke using a BIP (High Speed-Multi) biopsy gun (Biomed Instrumente und Produkte GesmbH, TŁrkenfeld, Germany) the Voluson technique offers the option to acquire a 3D US volume data set with one and the same transducer without freehand movement of the probe. In about 4 seconds the system acquires the entire 3D data volume and displays the information of the needle position in relation to the lesion accurately in a multiplanar imaging mode. This needle position check in all 3 planes is called 3D-targeting.[15]

Real-4D US breast biopsy

The Voluson 730 allows real-4D US needle guidance during breast biopsy. The acquired real-4D US volume data are displayed in a multiplanar scan plane analysis mode. Compared to conventional freehand 2D US needle guidance, real-4D offers additionally permanent information of all three planes in the multiplanary display mode, a rendered image of the breast lesion and needle position. The real-time three-dimensional analysis of lesion position as well as needle position in all three planes allows to navigate the core-needle in an optimal prefer position. After core-needle stroke, 3D-targeting follows unveiling the correct or incorrect needle position.

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