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ORIGINAL PAPERS: CLINICAL OR BASIC RESEARCH

Ultrasonographic features of cutaneous malignant melanoma – a preliminary study

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INTRODUCTION

Cutaneous malignant melanoma (CMM) represents about 4% of cutaneous tumors and about 2% of malignant tumors, determining lately a quick increase of incidence compared to other neoplasm. It is a tumor with an important aggressiveness and it accounts for approximately 77% of cutaneous tumor deaths [1].

There are 4 subtypes of primary cutaneous melanoma: the superficial spreading melanoma, the nodular melanoma, lentigo maligna melanoma and the acral lentiginous melanoma. There are clinical, prognosis and biomolecular differences between these types [1]. The CMM evolution is characterized by an initial phase producing a superficial extension with radial character (this phase lasts a few years and has a quite low risk of metastatic dissemination) and a vertical extension phase, when the melanoma penetrates the deep cutaneous layers (this phase has a high risk of distance metastasis).

The diagnosis of CMM in early stages could allow a complete recovery after the surgical treatment.

ABSTRACT

Cutaneous malignant melanoma (CMM) represents about 4% of cutaneous tumors and about 2% of malignant tumors, determining lately a quick increase of incidence compared to other neoplasm. It is a tumor with an important aggressiveness and it accounts for approximately 77% of cutaneous tumor deaths.

Objectives: *We intended to identify ultrasonographic specific features of CMM in a preliminary study. This could be a base for other ampler studies which establish the ultrasonography usefulness in diagnosis, pre-therapeutic balance and post-therapeutic observation of CMM.*

Method: *24 patients with CMM have been ultrasonographically evaluated in order to characterize the primary lesion and to detect the possible side determinations.*

Results: *The most frequently described ultrasonographic aspect of primary tumor was the hypoechogenic, inhomogeneous lesion, with irregular contour, with no vascular signal. The local recurrences have been described as hypoechogenic lesions, with irregular contour and exacerbated vascularization, somehow similar to CMM with a vertical growth pattern. In over 56% of cases, the ultrasonographic lymph nodes have an inhomogeneous structure, regular contour, low echogenity and vascular signal detectable in Doppler modulus.*

Conclusions: *The ultrasonography of tegument and nearby structures is useful in diagnosing CMM, by preoperatively evaluating the morphology and size of primary tumor, helping at determining the phase and the therapeutic line. As a complementary diagnosis method, this technique implies low costs and it has no harmful effects.*

Keywords: malignant melanoma, ultrasound, diagnosis

At the moment, the CMM diagnosis and stadialization depend on the excisional biopsy, that brings the information about thickness of the tumor (Breslow index), presence of ulceration, anatomic level of invasion (Clark index), growth phase, mitotic rate, presence of regression and lymphocytic infiltration, invasion of lymphatic and sanguine vessels. Some of these (presence of ulceration, Breslow and Clark indices) and moreover presence of lymph nodes metastases and at distance are the AJCC/UICC (American Joint Committee on Cancer / International Union Against Cancer) criteria for CMM stadialization.

Actual trend is to get information mainly by non-invasive means. Clinical examination, dermoscopy, routine laboratory tests, LDH and specific tumor markers dosage are limited according to the investigator and/or the given information. Dermoscopy, an "in vivo" microscopic method, has increased the accuracy of the CMM precocious diagnosis with percentages ranging between 5 and 30% more than the visual cutaneous examination [2]. However, dermoscopy cannot evaluate lesions with extension in depth beyond papillary dermis [3].

Lymphoscintigraphic techniques, useful for lymph nodes identification, are highly sensitive (sensitivity over 95%) but unspecific. Therefore, the use of a complementary imagistic method that can provide additional information about lymph nodes morphology and lesions beyond papillary dermis (complementary to dermoscopy) can be extremely useful. Photographic techniques, spectrophotometry, ultrasonography, laser Doppler perfusion imaging, confocal microscopy and nuclear magnetic resonance alow a better "administration" of tegumentary pathology, but these aren't yet standardized or included in diagnosis protocols [4].

According to the protocol used by the Romanian Dermatology Society (RDS) the diagnosis explorations include: dermoscopy and excisional biopsy with the determination of the histopathological microstadialization parameters (Clarck index, Breslow index) and the immunehistological analysis. Among imaging methods, are used: ultrasonography for lymph nodes and at distance metastases identification (just for CMM over "in situ" stage, with histopathological confirmation), thorax radiological examination (for tumors with Breslow thickness over 1 mm) and CT, RMN are optional examinations.

Given the actual position of ultrasonography (underestimate considered) in RDS protocol and the international studies concerning US utilization for diagnosis and stadialization CMM, we initiate this preliminary study with CMM patients. By identification of some ultrasonographic specific features of CMM lesion (primary and side determination: regional – "in transit" and lymph nodes metastases), this preliminary assessment could be a base for other ampler studies which establish the usefulness of US in CMM evaluation, as a non-invasive and relatively low cost imagistic method. ❑

METHOD

During May-November 2005 have been ultrasonographically evaluated 24 patients with melanic tumoral pathology: 17 women (70.83%) and 7 men (29.17%), with the age between 20 and 72 years (the average age: 47.28 for men and 49.35 for women).

The patients have been taken under observation, depending on the situation, at IOC and the Dermatology Clinic of Cluj-Napoca and they were sent to our department in order to ultrasonographically evaluate the primary tumor and the possible side determinations.

The ultrasonographic examination has been done by using two echipamentes: Toshiba Applio (with linear transducer of 7.5-11 MHz) and General electric GE Logiq 500 (with linear transducer of 7-11 MHz), both with Doppler facilities, and in some cases, ultrasound transmission means (Ultrasound gel pad Aquaflex).

The position of the patient during the examination varied depending on the location of the primary tumor and the lymph node drainage stations: dorsal decubitus with the upper limb in abduction and supination (axilla examination), the lower limb in adduction (inguinal area examination), with and without the counterlateral of cephalic extremity (examination of supraclavicular and laterocervical areas) or ventral decubitus (popliteus area examination).

The evaluation of primary melanic tumor and local recurrences included: highlighting the lesions, the extension in surface and depth (in "mm", the ratio with the muscular plan), the contour (regular or irregular), the echogenity (low or high – central, asymmetric or on the whole), the presence of vascularization, the type (arterial, venous or mixed), the location (central,

peripherical or mixed) and its character (organized or disorganized).

The ultrasonographic aspect of the primary lesion was correlated with the histopathologic aspect (Clark and Breslow index).

The evaluation of lymph node stations was focused on: identifying the ganglions, the number, size (in "mm"), contour (with or without, regular or irregular), echogenity (low or high – central, asymmetric or on the whole), the echostructure (homogenous, inhomogenous – asymmetric or on the whole), vascularization (by observing the same elements as for the primary lesion).

The US criteria of differential diagnosis of lymph nodes were taken into consideration, although they have only an approximate value. The parenchymal hypoechogenity, the disappearance of central echogenity and the interruption of capsular contour are parameters of gray-scale sonomorphologic analysis, characteristic to the malign condition of lymph nodes, with a high degree of non-specificity. Doppler criteria for the malign pattern of lymph nodes angioarchitecture are: central aberrant vessels, dislocated intranodular vessels, focal absence of vascular signal and subcapsular vessels. [5]

Moreover, each patient benefited from abdominal US evaluation in order to reveal possible visceral side determinations. ❑

RESULTS

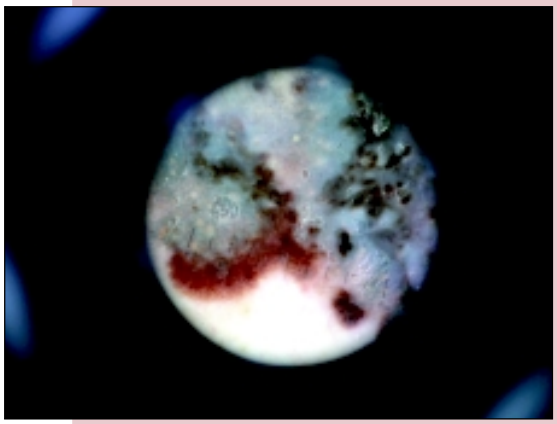
The 24 patients of the study have been evaluated in different phases of the disease. 7 patients had a primary tumor (clinically diagnosed), being pre-operatively evaluated. The other 17 patients, already operated on, with histopathologic diagnosis, had local recurrences found during the periodical postoperative control, clinically visible (2), distance metastasis (1) and/or clinically visible adenopathy (6). The rest of the patients (8) had no clinically visible adenopathy.

The most frequent location of the primary tumor was at the limbs (13 cases) and the other locations: the hind chest (5), fore abdomen (3), throat (2) and mucous membranes (1).

As for the 7 patients pre-operatively evaluated, 4 cases had a growth in surface and 3 cases had melanoma with vertical growth. The most frequent US aspect was the inhomogenous lesion (57.14%), with irregular contour (71.42%), low echogenity (85.71%), with no vascular signal (71.42%), with no extension in depth (85.71%), and no associated adenopathies (57.14%).

The most frequent aspects met when ultrasonographically examining the formations with the growth in surface pattern, were: homogenous echostructure (75%), low echogenity (75%), the absence of vascular signal at Doppler examination (100%) and the absence of lymph node extension (100%) and in depth (75%).

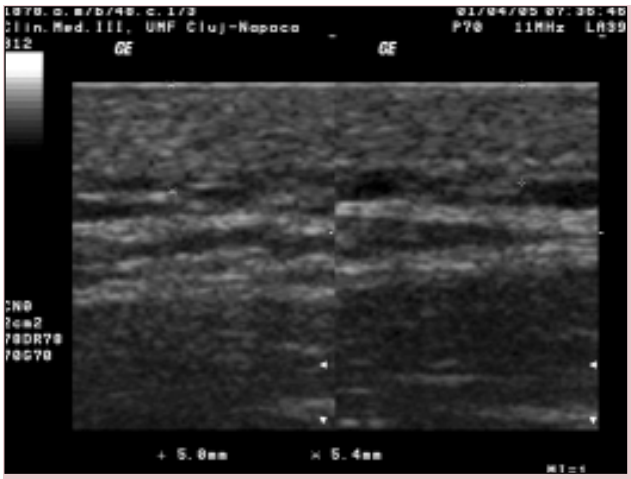
1.



2.

FIGURE I. Cutaneous malignant melanoma with superficial extension

1. macroscopic aspect
2. dermatoscopic aspect (collection of Prof.Dr. Rodica Cosgarea)



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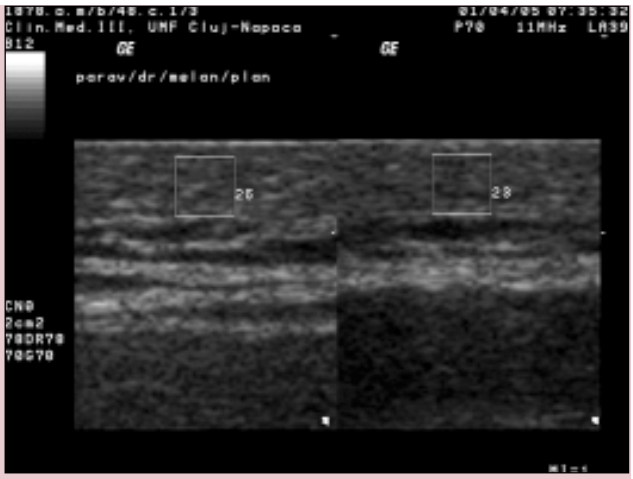
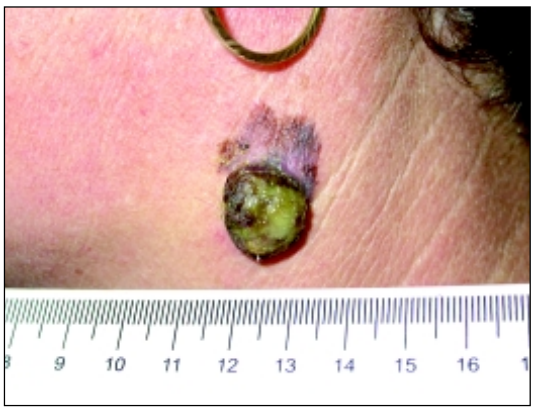


3 b)

3 c)

FIGURE I.
3. comparative echographic aspect between the normal tegument (on the left) and the melanic primary tumor (on the right)
a) minimum changes of tegument thickness
b) minimum differences of echogenity on gray-scale, detectable only through histogram
c) absence of vascular signal at Doppler examination

The formations with vertical growth pattern have been ultrasonographically described as hypo-echogenic lesions, with inhomogeneous echostructure and irregular contour. Among them, 66.6% had exacerbated vascularization and suspect regional lymph nodes, meaning metastasis.



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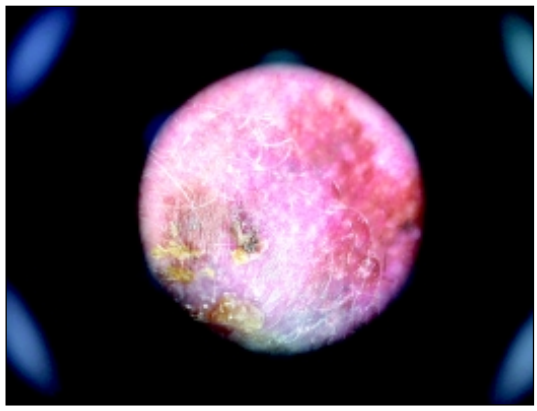

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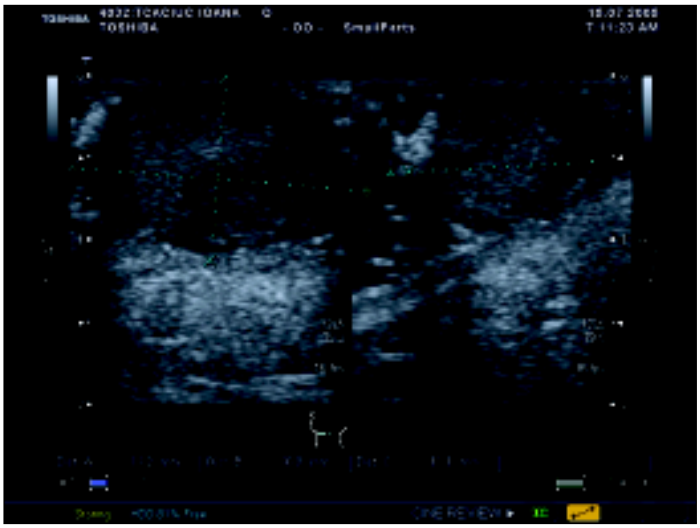
FIGURE II. Cutaneous malignant melanoma with vertical extension
1. macroscopic aspect
2. dermatoscopic aspect (collection of Prof.Dr. Rodica Cosgarea)

Regarding the histopathologic aspect of primary tumor, 3 of the 7 cases had Clark index >/=3 and Breslow index > 1 mm (eloquent for low risk of metastasis). From the ultrasonographic point of view, they have been described as lesions with low echogenity and irregular contour. In two cases, the tumor had an inhomogeneous structure and extension in depth, ultrasonically detectable (histopathologically certified).

Among the 24 patients, 16 had adenopathies and 8 had no changes of the regional or distance lymph node stations. The most frequent US aspect was: lymph node with low echogenity (68.75%); n=11), regular contour (56.25%); n=9), inhomogeneous structure (56.25%; n=9) and vascularization (62.50%).The particular aspect of cortical asymmetry was encountered in 12.50% (n=2).



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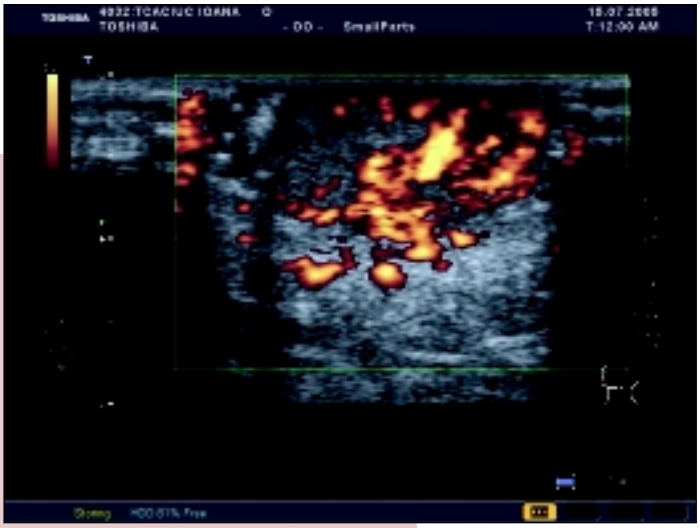

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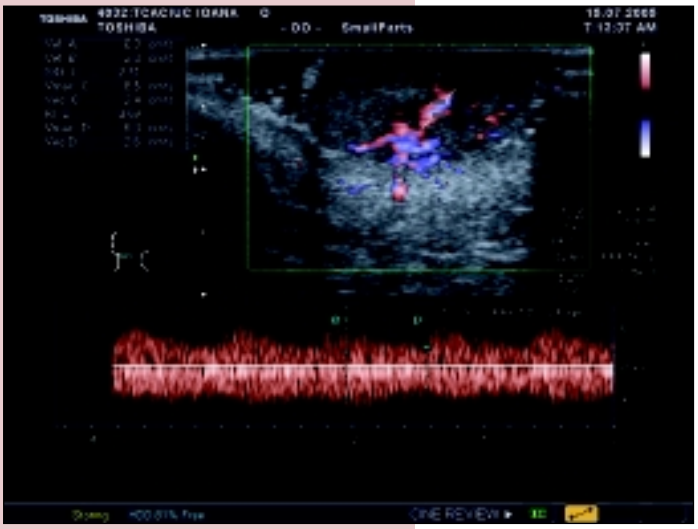
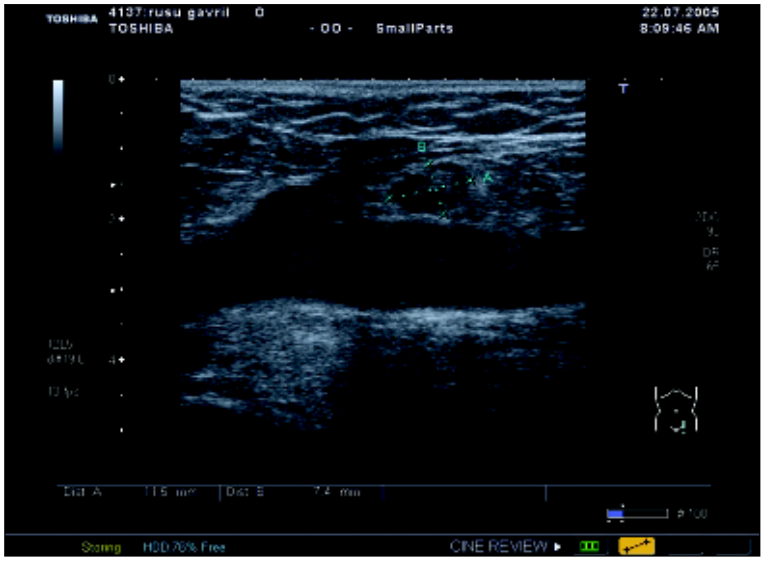


3 c)

FIGURE II.
3. echographic aspect
a) primary tumor size in 3 axis
b) vascularization aspect
c) the determination of vascular index in pulsed Doppler way shows arterial vascularization with low resistance



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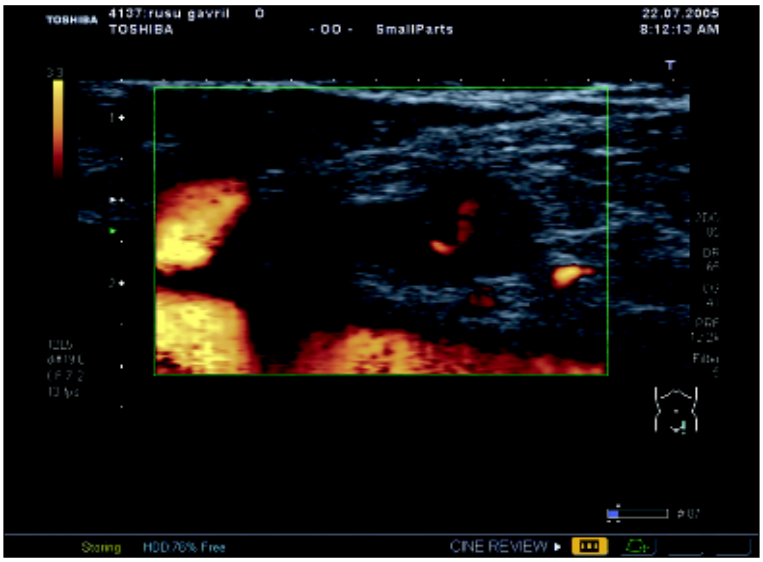

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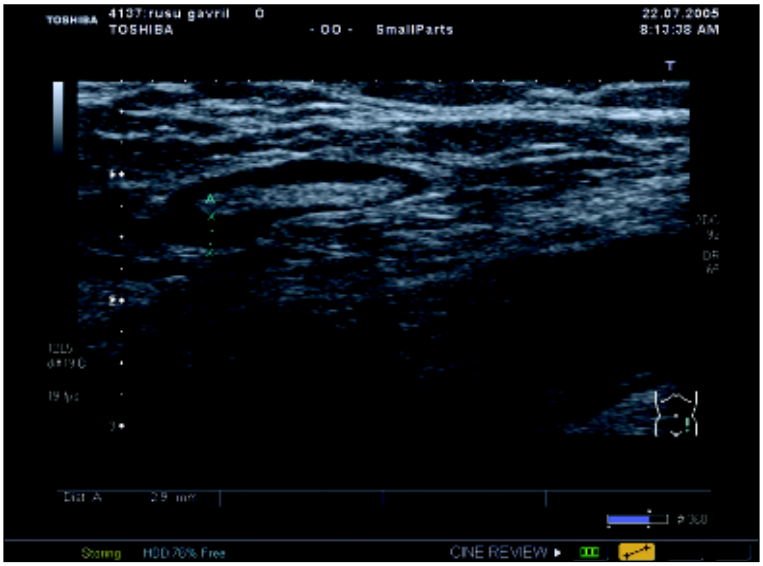


3

7 patients out of 16 with adenopathies, had the adenopathy at the first drainage station and the rest of the patients, at the second drainage station (n=5), at distance (n=2) or with multiple locations (n=2).

Regarding the number of affected stations, there was only one lymph node station involved in 50% (n=8), two stations in 37.50% (n=5) and more stations in 12.50% (n=2).

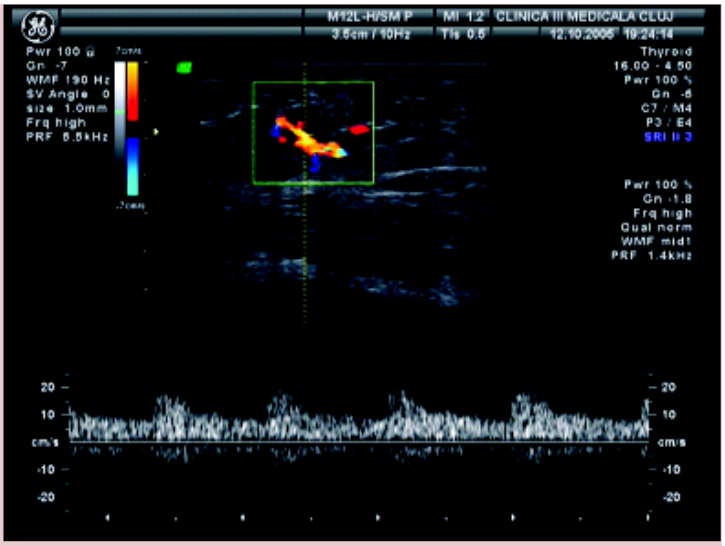
2 patients of the studied lot were evaluated for local recurrences and both of them had CMM of the extremities (lower limbs) with Clark index III and Breslow index > 1mm. They had almost the same US aspect: low echogenity, irregular contour, exacerbated vascularization of arterial type, centrally and peripherically located; the homogeneity was different (one of them had more inhomogeneous lesions) and also the extension in depth (one of them had surpassed muscular fascia and the other one had limit to the subcutaneous cell tissue).

FIGURE III. Right inguinal metastatic lymphadenopathies coming from MMC of right hallux, with characteristic US aspect of asymmetric expansion of the cortical
1. adenopathy on gray-scale
2. and Doppler way
3. nearby adenopathy on gray-scale

Only one patient had distance side determinations: hepatic, splenic, in the right temporal area (with extension in the bone structures), with ultrasonographic aspect as solid, hypoechogenic and well-vascularized lesions and also in the peritoneum and the abdominal wall. There were no inguinal lymph nodes, in the retroperitoneal area or on the iliac vessels tract. In this case, the primary location of CMM was on the right thigh. ❑

1.

2.



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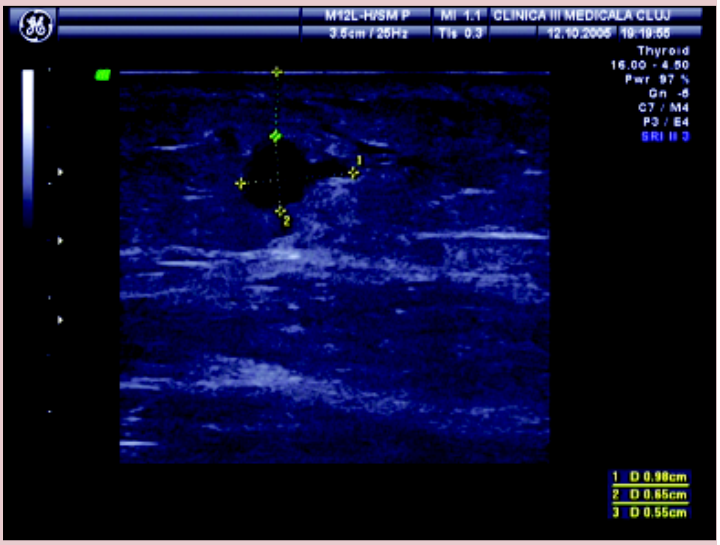

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FIGURE IV. Cutaneous malignant melanoma with local recurrences
1. postoperative scar of primary lesion
2. local recurrences. The tegument areas marked on, correspond to deep lesions echographically detected
3. echographic aspect of gray-scale (a) and color and pulsed Doppler (b) local recurrences

DISCUSSIONS

The tegument and subcutaneous tissue ultrasound has become an important non-invasive, exact and reproductive method in detecting focal lesions and describing their morphological aspect.

The ultrasound image of the tegument may be obtained in A mode (useful for thickness evaluation), B mode (allows vertical sections of scanned structures), C mode (generates horizontal images of the tegument surface) and the computer processing may generate three-dimensional images. [4, 6] The highest the frequency of used ultrasounds is, the better the image resolution will be. The resolution may be defined both as axial resolution (the discrimination capacity between two interfaces per-

NAME / AGE (years)	CLINIC (growth phase)	ECHOGRAFIC						HISTOPA-THOLOGIC
		echostructure	contour	echo-genity	vascularization	extension in depth	LN preop	
S.I. / 43	in surface	homogenous	irregular	grown	absent	non-penetrating, minimum changes of tegument thickness	Without	Clark II Breslow < 1 mm
O.M. / 49	in surface	inhomogeneous	regular	low	absent	non-penetrating, minimum changes of tegument thickness	Without	Clark III Breslow 0,8 mm
P.F. / 26	vertically	inhomogeneous	irregular	low	exacerbated	2mm, cellular sc. tissue	Without	Clark III Breslow 4 mm
T.I. / 55	vertically	inhomogeneous	irregular	low	exacerbated	non-penetrating	At least 9 malign ganglions	Clark IV Breslow <0,75 mm
R.G. / 72	vertically	inhomogeneous	irregular	low	absent	7mm, periosteum	1-2 malign ganglions	Clark III Breslow 3 mm
D.M. / 40	in surface	homogenous	irregular	low	absent	non-penetrating	Without	Clark III Breslow 1,5 mm
T.A. / 20	in surface	homogenous	regular	low	absent	non-penetrating, minimum changes of tegument thickness	At least 3 ggl with unspecific character	non-operated on

TABLE 1. Clinical – ultrasonographic and morphologic comparison of malignant melanoma in our study

pendicularly oriented on US propagation direction and it depends on US frequency) and lateral resolution (the discrimination capacity between two interfaces oriented in parallel on US propagation direction, depending on the width of the ultrasound fascicle) [4, 7, 8].

Most of the conventional equipments used for evaluating the intraabdominal organs operate with frequency up to 7.5 MHz providing an axial resolution not bigger than 0.3-0.5 mm [4,7]. Frequences of 20-25 MHz are used for tegument evaluation, offering an axial resolution of 50-80 mm and a lateral resolution of 200-300 mm; in this case, the derm and hypoderm may be easy differentiated but the epidermis may not be pointed out as a separate structure because it is very thin (excepting the palmar and plantar level) [4,9].

Despite the exact description of ultrasound cutaneous tumor [10], most studies describe the same pattern – hypo-echogenic-, both for benign and malign lesions. This technique has a high sensitivity in detecting tumoral lesions but a low specificity in characterizing them. [11] A previous study evaluating the cutaneous tumor has found out that the ultrasound pattern corresponds to the surgical and histopathologic aspect [11]. Harland and his collaborators have investigated 29 basal cell papillomas and 25 melanomas by using high resolution ultrasound (20 MHz B-scan imaging) and they found out that their ultrasound differentiation is possible but without obtaining the same result when differentiating the melanoma from the benign nevi [12]. Another study evaluating 71 cutaneous and subcutaneous nodules from 51 patients, described 4 nodules patterns based on color Doppler aspect and proved the fact that the sensitivity and specificity of hypervascularization in malign lesions is of 90%, respectively 100% and of hypovascularization in benign lesions of 100%, respectively 90%. In conclusion, the color Doppler method may increase the ultrasound specificity in evaluating cutaneous nodular lesions [13].

The new phasing system of CMM implies a compulsory pathological phasing of regional lymph nodes in all cases of CMM, especially those with an invasion > 1 mm in depth [14, 15,16]. This is the reason why the preoperative evaluation of tumor morphology and size, by using the ultrasound, may have a great value in phasing primary CMM and therapeutic line. Moreover, the therapeutic value of sentinel lymph nodes extirpation is already known – SLN (identified by lymphoscintigraphy), being recommended for primary tumors >1 mm. Researches on selective lymphadenectomy pointed out that in 20% of the cases the micrometastasis depends on the thickness and location of the tumor, on the age and sex of the patient [17, 18]. There were teams trying to ultrasonographically diagnose LNS. By using a linear transducer with

the frequency of 7.5 – 11 MHz, Kahle et al have shown SLN of 3-4 mm, with a characteristic pathological structural pattern (asymmetric expansion of the cortical), highlighting the ultrasound importance in diagnosing and observing CMM [15, 16].

Because of the inhomogeneous and insufficient number of lot members, our study does not have a statistic significance. Anyway, some correlations do exist between the ultrasonographic and histopathologic aspect, taking into consideration the prognosis of the cases.

The most frequent location of primary tumor was at the extremities (especially the lower limbs), an aspect also mentioned in the literature. [19]

The most frequently described ultrasound aspect of the primary tumor (hypoechogenic, inhomogenous lesion, with irregular contour, with no vascular signal and no associated lymphadenopathy) was encountered in over 57% of the cases. The vertical growth pattern (known as an "active" phase of CMM, with a high metastasis risk) was correlated in all situations with a hypoechogenic, inhomogenous aspect, with an irregular contour, and with exacerbated vascularization and associated regional lymphadenopathies in 66.66% of the cases. In opposition, the lesions with growth in surface pattern did not show any vascular signal detectable with color Doppler examination and power angio or regional adenopathies. In 75% of cases, there was a homogenous, hypoechogenic echostructure, with no extension in depth.

The local recurrences were described as hypoechogenic lesions, with an irregular contour and exacerbated vascularization, similar to CMM with vertical growth pattern.

The lymph nodes have in more than 56% of the cases an inhomogeneous echostructure, regular contour, low echogenity and vascular signal detectable in Doppler way.

In CMM diagnosis, the ultrasound is a simple method bringing useful information but also certain disadvantages. It cannot make a difference between a benign nevus and a CMM. On the other hand, the spectrophotometric analysis, with digital reconstruction of images, allows the representation of tegument structures, contributing to the differentiation between malignant melanoma and benign pigmented lesions [4]. In order to be evaluated, the epiderm requires high frequency ultrasounds (40-100 MHz) or an association between ultrasound and other imaging techniques, such as confocal microscopy. This offers the possibility of a better epidermis evaluation and a dermo-epidermis junction [4,20]. The ultrasound-related researches have pointed out the complementarity of the two methods and the utility of correlating the results in researches regarding the ageing, morphopathology and physiopathology of tegument (the effect of local medicines) [20]. MRI may also differentiate the horny layer, the epidermis and the derm in vivo [4].

All these techniques (and many others) cannot solve by themselves the problem of non-invasive diagnosis of CMM, they are expensive and some of them still under experiment. ❑

CONCLUSION

1. The ultrasound is a non-invasive, repeatable, with relative low price and satisfactory accuracy diagnostic method.
2. In pretherapeutical evaluation of the cutaneous malignant melanoma, ultrasound is useful in disease staging (by measuring primary lesion thickness, determining the safety limits) and for the evaluation of lymph nodes involvement and sometimes for identification of the sentinel lymph node.
3. In posttherapeutical evaluation of the cutaneous malignant melanoma, ultrasound may have a god performance for the identification of regional (in transit) metastases, lymph node metastases and metastases at distance from primary lesion.
4. The method accuracy may be increased by using higher frecquences and combining ultrasound with other imaging methods (confocal microscopy, spectrophotometric analysis).

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