

Available online at www.sciencedirect.com

journal homepage: <http://www.elsevier.com/locate/medici>

Original Research Article

Preoperative assessment of skin tumor thickness and structure using 14-MHz ultrasound

Vesta Kučinskienė^{a,*}, Daiva Samulėnienė^a, Aistė Gineikienė^a, Renaldas Raišutis^b, Rymantas Kažys^b, Skaidra Valiukevičienė^a

^a Department of Skin and Venereal Diseases, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

^b Ultrasound Institute, Kaunas University of Technology, Kaunas, Lithuania

ARTICLE INFO

Article history:

Received 27 November 2012

Accepted 3 June 2014

Available online 13 August 2014

Keywords:

Ultrasound

Skin tumor thickness

Melanocytic skin tumors

Basal cell carcinoma

ABSTRACT

Objective: The aim of this study was to compare the relationship between skin tumor thickness and homogeneity and to evaluate the accuracy of 14-MHz ultrasound while measuring the thickness of different skin tumors.

Material and methods: The ultrasonographic and histological analysis of 72 skin tumors was performed. Preoperative vertical tumor thickness (T) and structure of 12 melanomas, 34 melanocytic nevi and 26 basal cell carcinomas was assessed by 14-MHz ultrasonography. After the tumors were excised the vertical thickness measurement (Breslow index, pT) was performed by pathologist. According to the histological thickness all skin tumors were divided to thin (≤ 1 mm) and thick (> 1 mm). The accuracy of the 14-MHz ultrasound measurements and correlation between the ultrasonographic and histological tumor thickness were estimated. **Results:** Homogeneous structure was assessed for all thin (≤ 1 mm) and the majority (81.3%) of thick (> 1 mm) melanocytic skin tumors. Nonhomogeneous structure was estimated in thin and thick basal cell carcinomas, accordingly 42.9% and 31.9%. Measurements of T and pT correlated moderately in thick (> 1 mm) tumors ($r = 0.694$), while in thin (≤ 1 mm) tumors correlation was low ($r = 0.336$). Moderate correlation between ultrasonographic and histological thickness was computed for melanocytic skin tumors as well as for basal cell carcinomas ($r = 0.564$ and $r = 0.690$).

Conclusions: Medium frequency ultrasound is not a reliable tool for the precise measurement of thin (≤ 1 mm) skin tumors. Ultrasonography using a 14-MHz frequency transducer enables more precisely to measure the thickness of basal cell carcinoma than melanocytic skin tumors. The 14-MHz ultrasound is support tool to suggest the morphologic type of skin tumor.

© 2014 Lithuanian University of Health Sciences. Production and hosting by Elsevier Urban & Partner Sp. z o.o. All rights reserved.

* Corresponding author at: Department of Skin and Venereal Diseases, Medical Academy, Lithuanian University of Health Sciences, Eivenių 2, 50009 Kaunas, Lithuania.

E-mail address: kvesta@delfi.lt (V. Kučinskienė).

Peer review under the responsibility of the Lithuanian University of Health Sciences.



<http://dx.doi.org/10.1016/j.medici.2014.08.002>

1010-660X/© 2014 Lithuanian University of Health Sciences. Production and hosting by Elsevier Urban & Partner Sp. z o.o. All rights reserved.

1. Introduction

Ultrasound is a noninvasive technique that provides complementary information to the clinical examination of various skin lesions, especially skin tumors. Ultrasonographic assessment of skin tumor margins, thickness, echo pattern and its location may aid the diagnosis, plan the treatment or detect subclinical recurrence of the tumor after treatment.

The prediction of surgical margins of skin melanoma and performance of sentinel lymph node biopsy are based on the tumor thickness assessed according to Breslow [1–3]. Excisional biopsy with histological analysis is the best way to determine the precise tumor thickness. However, it may damage the lymphatic vessels, altering the pattern of tumor drainage, particularly in anatomic regions with ambiguous lymphatic circulation (e.g., neck and trunk) [4–6].

Basal cell carcinomas (BCCs) are more accurately identified and measured ultrasonographically, often yielding the larger measurements than those obtained at clinical examination which can be particularly important at locations with a higher risk of recurrences, mainly face [7–9]. According to the 7th edition of the American Joint Committee on Cancer Classification (AJCC), the thickness more than 2 mm of BCC has been included as one of the high-risk factors for tumor staging [10]. Ultrasound allows the surgical planning of BCC to be adapted by identifying the extent of the tumor. It can also help to monitor the early detection of recurrence of BCC [11–13].

In previous studies investigators have evaluated good accuracy of the ultrasonography with higher than 20-MHz scanners to determine the margins and thickness of BCC and skin melanoma [4,5,8,14]. Assessment of skin melanoma thickness using transducers of 100-MHz frequency has better agreement with histology compared to 20-MHz ultrasonography. There is the tendency of 20-MHz device to overestimate tumor thickness because of several factors, e.g. tumor regression, lymphocytic infiltration [15]. However, in case of 100-MHz ultrasonography, the ultrasonic penetration depth is limited to 1.5 mm [5]. In the recent years technologic advances have improved the quality of the more commonly available ultrasonic scanners having frequency close to 15 MHz, allowing axial and lateral resolutions of 0.1 mm in superficial planes at those frequencies [16]. There are reported data showing higher agreement between ultrasonically and histologically determined thickness in thicker (>2 mm) skin melanomas and lower in thinner (1–2 mm) skin melanomas while using a 14-MHz ultrasound transducer [17]. Other investigators give a high accuracy of 10-MHz ultrasound measurements when evaluating skin melanomas of >1 mm thickness [18]. The thickness of BCC can be accurately estimated when using a 7–15-MHz ultrasound transducer [7]. Higher frequency ultrasonography can show nonhomogeneously scattered internal echoes in basal cell carcinoma and homogeneous reflex pattern in melanoma [11,19]. There is insufficient information about the effectiveness of 14-MHz ultrasound when estimating the homogeneity of skin tumors.

According to these controversial results we designed a study to evaluate the accuracy of 14-MHz ultrasound for the preoperative assessment of the thickness and structure of melanocytic skin tumors and BCC.

2. Material and methods

A total of 72 patients (26 men and 46 women) with clinically and dermatoscopically identified melanocytic tumors and BCCs in various locations before the excision were included in the study. The study was carried out from January 2010 through 2011. The tumor structure and thickness were evaluated ultrasonographically before surgical treatment. The maximum tumor thickness (T) measurements were made in B-scan from the lower edge of the entry echo to the inferior boundary of the echo-poor region representing the tumor (Figs. 1 and 2). Vertical tumor thickness of 34 melanocytic nevi, 12 melanoma and 26 basal cell carcinoma was preoperatively assessed using a 14-MHz Toshiba Xario XG ultrasonic scanner (Tokyo, Japan). All skin tumors were surgically excised and processed for routine histopathology. The vertical distance from the uppermost level of the stratum granulosum in the epidermis to the lowest point of the tumor (Breslow index, pT) was recorded in mm. The pathologist who measured the tumor thickness did not know the thickness of the lesion estimated by ultrasonography. According to the histological thickness (pT) all skin tumors were divided to thin (≤ 1 mm) and thick (>1 mm). Melanocytic skin tumors (melanocytic nevi and melanoma) were analyzed together in one group. Distribution of internal echoes (homogeneous or nonhomogeneous) was assessed in skin tumors according to the morphological analysis of an ultrasonographic structure by Altmeyer and Hoffman [19]. Analyses were conducted using SPSS statistical software (version 13.0, SPSS for Windows). The descriptive summary statistics and techniques include frequencies, means, standard deviations, standard errors and graphs. The nonparametric Wilcoxon test, Spearman correlation coefficient, and chi-square test (χ^2) were used for statistical analysis. The data were given as mean values and 95% confidence interval (95% CI) as deemed appropriate. Sensitivity, specificity, and accuracy of the 14-MHz ultrasonography method were calculated when using standard descriptions and formulas for these values given under Table 2.

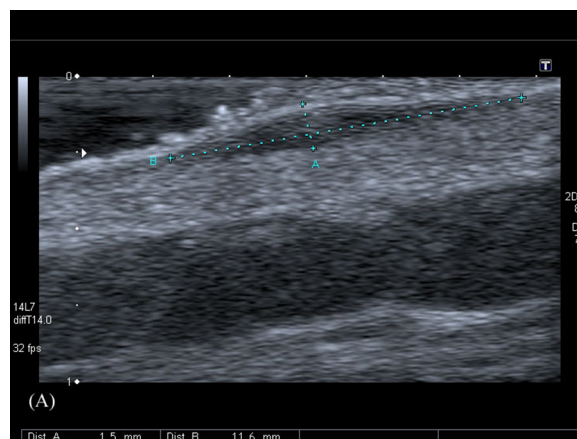


Fig. 1 – 14-MHz ultrasound image of skin melanoma ($T = 1.5$ mm).

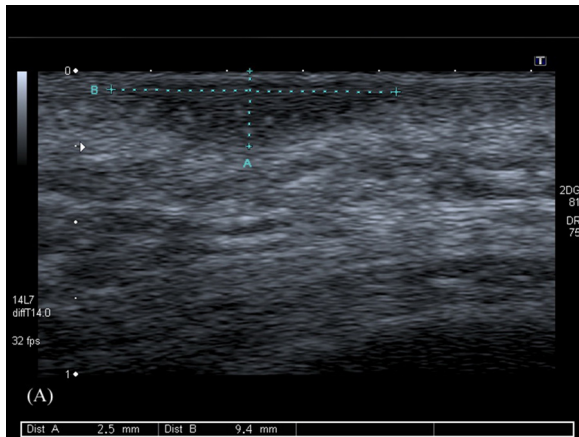


Fig. 2 – 14-MHz ultrasound image of basal cell carcinoma (T = 2.5 mm).

3. Results

The mean age of 72 patients enrolled in this study was 49.29 years (range, 18–80 years). The locations of the investigated 72 skin tumors are presented in Table 1. Most cases of melanocytic nevi were located on trunk, while skin melanoma on the trunk or lower extremities, and BCC on the head, the face, or the trunk, correspondingly.

Histologically there was estimated the thickness of ≤ 1 mm in 37 lesions and > 1 mm in 35 tumors. The 14-MHz ultrasound measurements of skin tumors showed a sensitivity of 79.3%, a specificity of 67.4%, NPV of 82.25%, PPV of 62.2%, and accuracy of 72% (Table 2). When estimating by 14-MHz frequency ultrasonic transducer 12/72 skin tumors had

Table 1 – Location of skin tumors assessed by 14-MHz ultrasonography.

Location	Melanocytic nevi	Melanoma	Basal cell carcinoma
Head and face	3	2	10
Trunk	24	4	9
Upper extremities	2	2	2
Lower extremities	5	4	2
Other	0	0	3
Total	34	12	26

Values are numbers.

nonhomogeneous structure and 60/72 homogeneous structure. Homogeneous structure was assessed for all thin (≤ 1 mm) and the majority (81.3%) of thick (> 1 mm) melanocytic skin tumors. Nonhomogeneous structure was estimated in thin (≤ 1 mm) and thick (> 1 mm) basal cell carcinomas, accordingly 42.9% and 31.9%.

The mean thickness of thin (≤ 1 mm) tumors using a 14-MHz frequency ultrasonic transducer was 0.71 mm (95% CI, 0.65–0.78) compared to 1.14 mm (95% CI, 0.86–1.43) determined by histometry. The ultrasonographic mean thickness of thick (> 1 mm) tumors was 2.07 mm (95% CI, 1.76–2.37) compared to 2.5 mm (95% CI, 1.95–3.05) determined histologically. The comparison of T and pT measurements showed a low correlation of 0.336 in thin (≤ 1 mm) skin tumors and a moderate correlation of 0.694 in thick (> 1 mm) lesions (Table 3). The thickness measured by a 14-MHz ultrasonic transducer had a good correlation for basal cell carcinoma ($r = 0.690$), although a lower accuracy ($r = 0.564$) for melanocytic tumors (Table 4). Ultrasonographic measurements correlated well with the histological data in thick (> 1 mm) melanocytic skin tumors and basal cell carcinoma ($r = 0.783$

Table 2 – Thickness of skin tumors measured using 14-MHz ultrasonography versus histological measurements.

Ultrasound measurements	Histological measurements		All	Prognostic value
Melanocytic tumors	pT	pT		
	≤ 1 mm	> 1 mm		
≤ 1 mm	19 (a)	11 (b)	30	63.3% (PPV)
> 1 mm	4 (c)	12 (d)	16	75% (NPV)
All	23	23	46	
Basal cell carcinoma	pT	pT		
	≤ 1 mm	> 1 mm		
≤ 1 mm	4 (a)	3 (b)	7	57.14% (PPV)
> 1 mm	2 (c)	17 (d)	19	89.47% (NPV)
All	6	20	26	
Skin tumors of both types	pT	pT		
	≤ 1 mm	> 1 mm		
≤ 1 mm	23 (a)	14 (b)	37	62.2% (PPV)
> 1 mm	6 (c)	29 (d)	35	82.25% (NPV)
All	29	43	72	

pT, histological thickness; PPV, positive predictive value; NPP, negative predictive value.

For melanocytic tumors: sensitivity $a/(a+c) = 19/(19+4) = 82.6\%$, specificity $d/(d+b) = 12/(12+11) = 52\%$, NPV $d/(c+d) = 12/(4+12) = 63.3\%$, PPV $a/(a+b) = 19/(19+11) = 75\%$, accuracy $(a+d)/(a+b+c+d) = 31/46 = 67\%$.

For basal cell carcinomas: sensitivity $a/(a+c) = 4/(4+2) = 66.7\%$, specificity $d/(d+b) = 17/(17+3) = 85\%$, NPV $d/(c+d) = 17/(2+17) = 89.47\%$, PPV $a/(a+b) = 4/(4+3) = 57.14\%$, accuracy $(a+d)/(a+b+c+d) = 21/26 = 80\%$.

For skin tumors of both types: sensitivity $a/(a+c) = 23/(23+6) = 79.3\%$, specificity $d/(d+b) = 29/(29+14) = 67.4\%$, NPV $d/(c+d) = 29/(6+29) = 82.85\%$, PPV $a/(a+b) = 23/(23+14) = 62.2\%$; accuracy $(a+d)/(a+b+c+d) = 52/72 = 72\%$.

Table 3 – Correlation between the histological and ultrasonographic estimation of thin and thick skin tumors using a 14-MHz frequency transducer.

Thickness (pT) of skin tumors	Number	Mean ultrasonographic tumor thickness (mm) (95% CI)	Mean histometric tumor thickness (mm) (95% CI)	Spearman correlation coefficient (r)
Thin (≤1 mm)	37	0.71 (0.65–0.78)	1.14 (0.86–1.43)	0.336
Thick (>1 mm)	35	2.07 (1.76–2.37)	2.50 (1.95–305)	0.694

pT, histological thickness in mm.

Table 4 – Correlation between the histological and ultrasonographic estimation of melanocytic tumors and basal cell carcinomas using a 14-MHz frequency transducer.

Skin tumors	Number	Mean ultrasonographic tumor thickness (mm) (95% CI)	Mean histometric tumor thickness (mm) (95% CI)	Spearman correlation coefficient (r)
Melanocytic tumor	46	1.19 (0.93–1.45)	1.81 (1.31–2.31)	0.564
Basal cell carcinoma	26	1.68 (1.31–2.06)	1.79 (1.43–2.15)	0.690

Table 5 – 14-MHz ultrasonography thickness agreement with histology in thin and thick melanocytic tumors and basal cell carcinomas pT, histological thickness in mm.

Skin tumors (pT)	Number	Mean ultrasonographic tumor thickness (mm) (95% CI)	Mean histometric tumor thickness (mm) (95% CI)	Spearman correlation coefficient (r)
Melanocytic skin tumor (≤1 mm)	30	0.70 (0.63–0.76)	1.14 (0.80–1.48)	0.417
Basal cell carcinoma (≤1 mm)	7	0.79 (0.56–1.01)	1.16 (0.56–1.75)	0.860
Melanocytic skin tumor (>1 mm)	16	2.13 (1.64–2.61)	3.06 (1.96–4.17)	0.783
Basal cell carcinoma (>1 mm)	19	2.02 (1.60–2.44)	2.03 (1.61–2.45)	0.720

Table 6 – Ultrasonographic and histological thickness of skin tumors according to their structure estimated using a 14-MHz frequency transducer.

Skin tumors	Number	Mean ultrasonographic tumor thickness (mm) (95% CI)	Mean histometric tumor thickness (mm) (95% CI)	Spearman correlation coefficient (r)
Homogenic structure	60	1.28 (1.05–1.52)	1.74 (1.37–2.10)	0.580
Nonhomogenic structure	12	1.82 (1.25–2.38)	2.14 (1.16–3.13)	0.717

and $r = 0.720$, respectively). While thin (≤ 1 mm) melanocytic tumors showed a weak ultrasonographic and histological correlation ($r = 0.417$), correspondingly in thin (≤ 1 mm) basal cell carcinomas it was insignificant ($P = 0.860$) (Table 5). The correlation between T and pT in skin tumors of nonhomogeneous structure was stronger ($r = 0.717$) than in those of homogeneous structure ($r = 0.580$) (Table 6). A strong correlation of T and pT was obtained in nonhomogeneous basal cell carcinomas ($r = 0.760$), while the groups of homogeneous basal cell carcinoma and homogeneous melanocytic skin tumors had a moderate correlation ($r = 0.603$ and $r = 0.567$, accordingly). There were only a few cases of nonhomogeneous melanocytic skin tumors (Table 7).

4. Discussion

The ultrasound of 100-MHz frequency allows detailed visualization of the upper skin layers especially the horny layer and small structures in it while 20-MHz ultrasound is valuable to

discriminate between the viable epidermis and papillary dermis and tumor cell nets especially in BCC [20]. Due to higher frequencies ultrasound provides higher resolution but sacrifices tissue penetration so the ultrasonic transducers from 7.5 up to 12–15 MHz are commonly used in clinical practice to estimate the skin tumor thickness [5,14,17,21]. When the tumors extend beyond the dermis-subcutis border, the demarcation may become difficult because apart from connective tissue septae, the subcutaneous fatty tissue is also hypoechogenic. In most studies for evaluation of skin lesions the investigators have used an ultrasonic transducer of 20 MHz [22–33]. In the current study we have investigated the possibility of using a 14-MHz ultrasonic transducer for measuring skin tumor thickness before the surgical excision. Our results have shown the ability of a 14-MHz ultrasonic transducer to distinguish thick tumors better than thin though in the studies of Vilana et al. and Music et al. the 10-MHz and 12–15-MHz ultrasonic transducers can reliably discriminate between thin (≤ 1 mm) and thick (> 1 mm) skin melanocytic tumors [18,34]. Several factors could influence our results. A

Table 7 – Ultrasonographic and histological thickness of melanocytic tumors and basal cell carcinomas according to their structure estimated using a 14-MHz frequency transducer.

Skin tumors	Number	Mean ultrasonographic tumor thickness (mm) (95% CI)	Mean histometric tumor thickness (mm) (95% CI)	Spearman correlation coefficient (r)
Homogenic melanocytic tumor	43	1.14 (0.88–1.41)	1.72 (1.23–2.20)	0.567
Non-homogenic melanocytic tumor	3	1.93 (0.00–3.86)	3.13 (0.00–10.34)	NA
Homogenic basal cell carcinoma	17	1.64 (1.15–2.12)	1.78 (1.30–2.27)	0.603
Non-homogenic basal cell carcinoma	9	1.78 (1.04–2.52)	1.81 (1.16–2.46)	0.760
NA, not applicable.				

larger sample size normally should lead to a better estimate of accuracy as in the study it was found to be worthless when measuring thin skin tumors. In our study the anatomic localization of skin tumors was different and most of the skin tumors were located on a head, face and trunk. Ultrasonographic determined tumor thickness may exceed the measurement of histological sections partly due to the shrinkage of tissue processed for histology or probe pressure during the ultrasound scanning. A similar situation occurs while scanning a recurrent BCC because of the scar formation caused by a previous cutaneous surgery [8,14,35]. In our study when analyzing skin tumors according to the different morphology higher correlation was estimated between the histological and ultrasonographic thickness in basal cell carcinomas than in melanocytic tumors. Bobadilla et al. proved the strong correlation between the 7–15-MHz ultrasound depth measurements and histological measurements when estimating 25 facial basal cell carcinomas [7]. In the other studies the clinical dimensions (without histology) and ultrasonographic measurements of basal cell carcinomas were compared and the stress was put on lateral measurements of basal cell carcinomas but not thickness [8,9].

Considering melanocytic skin tumors, there was an estimated higher correlation between the histological and 14-MHz ultrasonographic examination in thick (>1 mm) melanocytic tumors compared to thin (≤1 mm). Gamblicher et al. observed the lower accuracy for ultrasonographic measurements of melanocytic skin lesions with a tumor thickness smaller than 1 mm using 20-MHz ultrasound while Lassau et al. determined the strong correlation between the thickness assessed by 20-MHz ultrasound and histology in 27 thin (≤1 mm) melanomas [5,36].

An inflammatory infiltrate or melanocytic nevus structures underlying tumor is an important source of overestimation. The inflammatory process weakens viable tissue causing the decreased echogenicity than of normal skin, contributing to the increased size of a skin tumor [27,35,36]. Similarly to the other studies [18], the melanocytic skin tumors were mainly visualized as homogeneous (hypoechoic) structures within the hyperechoic dermis. BCCs were evaluated more heterogenic tumors (showed a mixed echogenicity). When comparing the BCCs of different homogeneity there was identified better correlation between 14-MHz ultrasonographic and histological thickness in nonhomogeneous BCCs.

Our study had several limitations. We did not assess the reproducibility of the ultrasonographic (T) and histological (pT) measurements (intraobserver variability). Skin tumors were of different localization, and the low number of basal cell

carcinomas did not support the estimation of significant correlation between ultrasonographic and histological thickness in that group. Despite that, the study attempted to compare histological and 14-MHz ultrasonographic thickness of skin tumors and made no assessment as to how this might affect the treatment of skin tumors.

5. Conclusions

We conclude that 14-MHz ultrasound is not a reliable tool for the precise measurement of thin (≤1 mm) skin tumors thickness and it enables more precisely to measure the thickness of BCCs than melanocytic skin tumors. 14-MHz ultrasound is a support tool in diagnosing skin tumors as structure of thin (≤1 mm) skin tumors could suggest the morphologic type of tumor. The homogeneous structure is specific for melanocytic skin tumors, while homogeneous and nonhomogeneous structure is characteristic for BCCs.

Conflict of interest

The authors state no conflict of interest.

Acknowledgments

This work was partially sponsored by the Agency for International Science and Technology Development Programs in Lithuania under the Eurostars project SKINMONITOR “Diagnosis of Skin Cancer Based on Information and Communication Technologies Tools.”

We thank histopathologist Gintaras Sabaliauskas from the Department of Pathology, Lithuanian University of Health Sciences, for the contribution.

REFERENCES

- [1] Hautschild A, Christophers E. Sentinel node biopsy in melanoma. *Virchows Arch* 2001;438:99–106.
- [2] Breslow A. Thickness cross-sectional areas and depth of invasion in the prognosis of cutaneous melanoma. *Ann Surg* 1970;172:902–8.
- [3] Kaikaris V, Valiukeviciene S, Rimdeika R, Gollnick H, Ulrich J. Sentinel lymph node biopsy in melanoma patients:

- methods, indications, and clinical significance. *Medicina* 2003;39:621-30 [Kaunas].
- [4] Hayashi K, Koga H, Uhara H, Saida T. High-frequency 30-MHz sonography in preoperative assessment of tumor thickness of primary melanoma: usefulness in determination of surgical margin and indication for sentinel lymph node biopsy. *Int J Clin Oncol* 2009;14:426-30.
- [5] Gambichler T, Moussa G, Bahrenberg K, Vogt M, Ermert H, Weyhe D, et al. Preoperative ultrasonic assessment of thin melanocytic skin lesions using a 100-MHz ultrasound transducer: a comparative study. *Dermatol Surg* 2007;33:818-24.
- [6] Pellacani G, Seidenari S. Preoperative melanoma thickness determination by 20-MHz sonography and digital videomicroscopy in combination. *Arch Dermatol* 2003;139(3):293-8.
- [7] Bobadilla F, Wortsman X, Muñoz C, Segovia L, Espinoza M, Jemec GB. Pre-surgical high resolution ultrasound of facial basal cell carcinoma: correlation with histology. *Cancer Imaging* 2008;8:163-72.
- [8] Desai TD, Desai AD, Horowitz DC, Kartono F, Wahl T. The use of high-frequency ultrasound in the evaluation of superficial and nodular basal cell carcinomas. *Dermatol Surg* 2007;10:1220-7.
- [9] Lassau N, Spatz A, Avril MF, Tardivon A, Margulis A, Mammelle G, et al. Value of high-frequency US for preoperative assessment of skin tumors. *Radiographics* 1997;17:1559-65.
- [10] Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. 7th ed. *AJCC cancer staging manual*, vol. 29, 7th ed. New York, NY: Springer; 2010. p. 301.
- [11] Machet L, Ossant F, Bleuzen A, Grégoire JM, Machet MC, Vaillant L. High-resolution ultrasonography: utility in diagnosis, treatment, and monitoring dermatologic diseases. *J Radiol* 2006;87:1946-61.
- [12] Madan V, Loncaster JA, Allan D, Lear JT, Sheridan L, Leach C, et al. Nodular basal cell carcinoma in Gorlin's syndrome treated with systemic photodynamic therapy and interstitial optical fiber diffuser laser. *J Am Acad Dermatol* 2006;55:86-9.
- [13] Allan E, Pye DA, Levine EL, Moore JV. Non-invasive pulsed ultrasound quantification of the resolution of basal cell carcinomas after photodynamic therapy. *Lasers Med Sci* 2002;17:230-7.
- [14] Guitera P, Li LX, Crotty K, Fitzgerald P, Mellenbergh R, Pellacani G, et al. Melanoma histological Breslow thickness predicted by 75-MHz ultrasonography. *Br J Dermatol* 2008;159:364-9.
- [15] Tacke J, Haagen G, Hornstein OP, Huettinger G, Kiesewetter F, Schell H, et al. Clinical relevance of sonometry-derived tumour thickness in malignant melanoma – a statistical analysis. *Br J Dermatol* 1995;132:209-14.
- [16] Raisutis R, Jasiuniene E, Jasaitiene D, Valiukeviciene S. Investigation of human skin using pulse-echo ultrasonic technique: review and development. *Ultragarasas (Ultrasound)* 2010;1:37-41.
- [17] Kaikaris V, Samsanavicius D, Maslauskas K, Rimdeika R, Valiukeviciene S, Makstiene J, et al. Measurement of melanoma thickness – comparison of two methods: ultrasound versus morphology. *J Plast Reconstr Aesthet Surg* 2011;64(6):796-802.
- [18] Vilana R, Puig S, Sanchez M, Squarcia M, Lopez A, Castel T, et al. Preoperative assessment of cutaneous melanoma thickness using 10-MHz sonography. *Am J Roentgenol* 2009;193:639-43.
- [19] Altmeyer P, Hoffmann K, Stucker M, Goertz S, El Gammal S. General phenomena of ultrasound in dermatology. In: Altmeyer P, el Gammal S, Hoffmann K, editors. *Ultrasound in dermatology*. New York, NY: Springer; 1992. p. 55-65.
- [20] El Gammal S, El Gammal C, Kaspar K, Pieck C, Altmeyer P, Vogt M, et al. Sonography of the skin at 100 MHz enables in vivo visualization of stratum corneum and viable epidermis in palmar skin and psoriatic plaques. *J Invest Dermatol* 1999;113(5):8.
- [21] Dill-Müller D, Maschke J. Ultrasonography in dermatology. *J Dtsch Dermatol Ges* 2007;5:689-707.
- [22] Reali UM, Santucci M, Paoli G, Chiarugi C. The use of high resolution ultrasound in preoperative evaluation of cutaneous malignant melanoma thickness. *Tumori* 1989;75:452-5.
- [23] Gassenmaier G, Kiesewetter F, Schell H, Zinner M. Value of high resolution ultrasound in determination of vertical tumor thickness in malignant melanoma of the skin. *Hautarzt* 1990;41:360-4.
- [24] Hoffmann K, Jung J, el Gammal S, Altmeyer P. Malignant melanoma in 20-MHz B scan sonography. *Dermatology* 1992;185:49-55.
- [25] Fornage BD, McGavran MH, Duvic M, Waldron CA. Imaging of the skin with 20-MHz US. *Radiology* 1993;189:69-76.
- [26] Partsch B, Binder M, Püspök-Schwarz M, Wolff K, Pehamberger H. Limitations of high frequency ultrasound in determining the invasiveness of cutaneous malignant melanoma. *Melanoma Res* 1996;6:395-8.
- [27] Krahn G, Gottlober P, Sander C, Peter RU. Dermatoscopy and high frequency sonography: two useful non-invasive methods to increase preoperative diagnostic accuracy in pigmented skin lesions. *Pigment Cell Res* 1998;11:151-4.
- [28] Solivetti FM, Thorel MF, Di Luca Sidozzi A, Bucher S, Donati P, Panichelli V. Role of high-definition and high frequency ultrasonography in determining tumor thickness in cutaneous malignant melanoma. *Radiol Med* 1998;96:558-61.
- [29] Hoffmann K, Happe M, Schüller S, Stücker M, Wiesner M, Gottlöber P, et al. Ranking of 20 MHz sonography of malignant melanoma and pigmented lesions in routine diagnosis. *Ultraschall Med* 1999;20:104-9.
- [30] Ulrich J, Peterreit S, Gollnick H. Preoperative sonographic diagnosis of melanoma – comparison of 7.5- and 20-MHz sonography. *Ultraschall Med* 1999;20:197-200.
- [31] Serrone L, Solivetti FM, Thorel MF, Eibenschutz L, Donati P, Catricalà C. High frequency ultrasound in the preoperative staging of primary melanoma: a statistical analysis. *Melanoma Res* 2002;12:287-90.
- [32] Pellacani G, Seidenari S. Preoperative melanoma thickness determination by 20-MHz sonography and digital videomicroscopy in combination. *Arch Dermatol* 2003;139:93-298.
- [33] Machet L, Belot V, Naouri M, Boka M, Mourtada Y, Giraudeau B, et al. Preoperative measurement of thickness of cutaneous melanoma using high-resolution 20 MHz ultrasound imaging: a monocenter prospective study and systematic review of the literature. *Ultrasound Med Biol* 2009;35:411-1420.
- [34] Music MM, Hertl K, Kadivec M, Pavlović MD, Hocevar M. Pre-operative ultrasound with a 12-15 MHz linear probe reliably differentiates between melanoma thicker and thinner than 1 mm. *J Eur Acad Dermatol Venereol* 2010;24:1105-8.
- [35] Jasaitiene D, Valiukeviciene S, Linkeviciute G, Raisutis R, Jasiuniene E, Kazys R. Principles of high frequency ultrasonography for investigation of skin pathology. *J Eur Acad Dermatol Venereol* 2011;25(4):375-82.
- [36] Lassau N, Koscielny S, Avril MF, Margulis A, Duvillard P, De Baere T, et al. Prognostic value of angiogenesis evaluated with high-frequency and color Doppler sonography for preoperative assessment of melanomas. *Am J Roentgenol* 2002;78:1547-51.