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● *Original Contribution*

AUTOMATIC DIFFERENTIAL DIAGNOSIS OF MELANOCYTIC SKIN TUMORS USING ULTRASOUND DATA

Kristina Andrėkutė,* Gintarė Linkevičiūtė,[†] Renaldas Raišutis,* Skaidra Valiukevičienė,[†] and Jurgita Makštienė[‡]

*Ultrasound Institute, Kaunas University of Technology, Kaunas, Lithuania; [†]Department of Skin and Venereal Diseases, Lithuanian University of Health Sciences, Kaunas, Lithuania; and [‡]Department of Pathology, Lithuanian University of Health Sciences, Kaunas, Lithuania

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Abstract—We describe a novel automatic diagnostic system based on quantitative analysis of ultrasound data for differential diagnosis of melanocytic skin tumors. The proposed method has been tested on 160 ultrasound data sets (80 of malignant melanoma and 80 of benign melanocytic nevi). Acoustical, textural and shape features have been evaluated for each segmented lesion. Using parameters selected according to Mahalanobis distance and linear support vector machine classifier, we are able to differentiate malignant melanoma from benign melanocytic skin tumors with 82.4% accuracy (sensitivity = 85.8%, specificity = 79.6%). The results indicate that high-frequency ultrasound has the potential to be used for differential diagnosis of melanocytic skin tumors and to provide supplementary information on lesion penetration depth. The proposed system can be used as an additional tool for clinical decision support to improve the early-stage detection of malignant melanoma. (E-mail: kristina.andrekute@ktu.lt or kristina.andrekute@gmail.com) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Malignant melanoma, Automatic diagnosis, Spectral analysis, Tissue characterization, Radiofrequency signal, Ultrasound.**

INTRODUCTION

Malignant melanoma (MM) is a less common but highly metastatic skin tumor having a poor prognosis and high resistance to treatment. The prevalence of MM is rising worldwide (Garbe and Leiter 2009). Its rate of incidence is <10–20 per 100,000 in Europe and 20–30 per 100,000 in the United States (Garbe et al. 2012). Melanomas account for 90% of deaths associated with cutaneous tumors (Garbe et al. 2012). Early MM detection (≤1 mm in thickness) is crucial for patient survival and promising treatment results. The 5-y survival rate if caught at an early stage is 95% (Hauschild and Christophers 2001). Regular skin screening is the basis for early detection of MM. However, melanocytic nevi (MNs), being benign skin lesions, can bear a strong resemblance to MM when observed with an unaided eye.

Histologic evaluation is the "gold standard" of MM diagnosis. Complete excision of the lesion is required for the histologic procedure if an MM is suspected. If diagnosis is confirmed, re-excision should be performed with margins of 1–2 cm (Garbe et al. 2012). Therefore, *in vivo* differentiation between benign and malignant melanocytic skin tumors (MSTs) is one of the most important issues in clinical dermatology.

Accuracy in the diagnosis of MM depends on the experience of a dermatologist (Morton and Mackie 1998). The accuracy achieved with the unaided eye is only slightly higher than 60%. Dermatoscopy can increase the accuracy by 10–27% (Kittler et al. 2002). Unfortunately, dermatoscopic images do not provide information on thickness, which is important for the prognosis of MM and surgery planning. Ultrasound methods are non-invasive and harmless and provide information about the tissues in real time. High-frequency (>20 MHz) ultrasound has been used since 1979 in dermatology for screening and skin tumor thickness evaluation (Alexander and Miller 1979). However, there have been only a few works related to the possibility of using

Address correspondence to: Kristina Andrėkutė, Ultrasound Institute at Kaunas University of Technology, K. Baršausko str. 59, Kaunas LT- 51423, Lithuania. E-mail: kristina.andrekute@ktu.lt or kristina.andrekute@gmail.com

ultrasonography in MM characterization and differentiation from MNs so far (Edwards et al. 1989; Harland et al. 2000; Rallan et al. 2007; Samimi et al. 2010).

Harland et al. (2000) evaluated the possibility of classification using B-scan images of seborrheic keratosis, melanocytic nevi and melanoma. They reported <30% specificity for differentiation of melanoma from MNs, assuming the threshold for the test must be set at 100% sensitivity (Harland et al. 2000). The authors remarked that MNs are mainly hypo-echoic with many small echoes, are symmetric and usually are well delimited from the adjacent dermis (Harland et al. 2000). Also they found that MMs are homogeneous and hypo-echoic, more frequently compared with MNs, and MMs frequently differ in shape from MNs (Harland et al. 2000). Rallan et al. (2007) proposed using 3-D high-frequency ultrasound reflex transmission imaging for discrimination between the pigmented skin lesions. Surface heterogeneity has been the most important discriminator between MMs and benign pigmented lesions. The study revealed that MMs are more attenuating than other MNs and have a higher surface heterogeneity and lower intra-lesion heterogeneity (Rallan et al. 2007).

Ultrasonography can be used as a non-invasive diagnostic tool for discrimination between blue melanocytic nevi and cutaneous metastases of MMs (Samimi et al. 2010) and between hemangioma and MM (Dybiec et al. 2015). Samimi et al. (2010) reported 70.8% sensitivity and 94.0% specificity of ultrasound diagnosis. In all these studies the sonographic features were semi-quantitative, and the results were observer dependent.

The accuracy of MM diagnosis also can be improved using quantitative parameters and automatic classification algorithms (computer-aided diagnosis [CAD]), which are widely used for dermatoscopic images. CAD based on ultrasound images has been successfully used for breast, prostate, liver, kidney and other lesions (Chen et al. 2002; Machado et al. 2006; Schmitz et al. 1999). Most tissue characterization and segmentation algorithms are based on conventional ultrasound images (envelope-detected log compressed signals), because only B-scan images are available on most of the commercial medical ultrasound systems (Chen et al. 2002; Noble 2010; Schmitz et al. 1999). The radiofrequency (RF) ultrasound signal can provide more information on the size, density and spatial distribution of scatterers (Liu et al. 2004, 2007, 2009; Lizzi et al. 1996, 2003; Schmitz et al. 1999).

Schmitz et al. (1999) have analyzed RF and demodulated ultrasound signals with the aim of extracting the tissue characterization parameters of the prostate and representing them as color-coded images with estimated probabilities of malignancy. They investigated different classifiers as well and found only minor differences in their performance.

Liu et al. (2004, 2007, 2009) proposed using 2-D spectrum parameters for tissue characterization at the sub-resolution level. They reported that 2-D spectrum analysis provides axial and lateral information on tissue microstructure (Liu et al. 2007). They also reported that 2-D spectrum properties are suitable for prostate and ocular tumor characterization and have the potential to be informative for differential diagnosis (Liu et al. 2004, 2007, 2009).

In our previous work (Andrekute et al. 2016), we proposed an automated method based on ultrasound raw data time–frequency analysis for early-stage (≤1 mm in thickness) MST segmentation and thickness evaluation. The purpose of this study was to evaluate the potential of differential diagnosis of MST using quantitative ultrasound and develop an algorithm for automatic differentiation of MMs from MNs using ultrasound data. Acoustical, textural and shape parameters were used for MST characterization in this study. To our knowledge, this is the first approach to automated differentiation of malignant melanoma from melanocytic nevi based on the use of ultrasound data.

The article is organized as follows. The methods section covers the clinical study design and ultrasound tissue characterization features, describes the feature selection method and introduces the support vector machine classifier for differential diagnosis of MSTs. The receiver operating characteristic curves of the proposed classification system are provided in the results section. The discussion and conclusions are the final sections.

METHODS

Patients

In this study, we involved 120 (78 women and 42 men) patients of 18 to 89 y of age with clinically suspicious MST. Histologic examinations had indicated that there had been 48 melanomas (25 superficial spreading, 1 lentigo maligna, 5 acral lentiginous, 2 nodular melanoma, 2 spindle cells, 3 *in situ* and 11 unidentified morphologic types) and 71 MNs, of which 35 were dysplastic melanocytic nevi. Histologic thickness of MSTs varied from 0.25 to 2.5 mm. Data had been collected at the Department of Skin and Venereal Diseases of the Lithuanian University of Health Sciences. The study was approved by the regional ethics committee (No. P2-BE-2-25/2009). All data were collected with the approval of the institutional review board after patients provided informed consent, in accordance with the Declaration of Helsinki protocols.