**Differentiation of Benign and Malignant Skin Lesions with Color and Power Doppler Ultrasonography**

**Abstract**
Aim: The aim of this study was to prospectively evaluate the usefulness of color Doppler ultrasonography, power Doppler ultrasonography, and gray scale ultrasonography in differentiating benign and malignant skin lesions. Material and Method: Patients were histopathologically divided into two groups as benign and malignant skin tumors. The dimensions of the lesion, the contour characteristics, existence of pagoda echo, levels of invasion, the internal echogenicities and vascular patterns were investigated. We analysed velocity waveforms and determined peak systolic velocity, end-diastolic velocity, resistive index, and pulsatility index. Results: Eighty patients (35 female, 45 male) with populo-nodular lesions on the surface of the cutaneous and subcutaneous tissues were prospectively enrolled in this study. A significant difference was noted between malignant and benign skin lesion groups as for color and power doppler ultrasonographic findings such as blood flow analysis and as for the gray scale ultrasonographic findings such as irregular contour, pagoda echo and hypocoechogenic echogenicity. Blood flow was observed in 33 patients. The existence of the flow was mostly observed in 92.2% of the malignant skin lesions and in 33.3% of the benign lesions. The analysis of peak systolic velocity, end-diastolic velocity, resistive index, and pulsatility index between the study groups did not reveal a significant difference (p>0.005). Discussion: Doppler ultrasound is a non-invasive and powerful technique for the differentiation of benign and malignant skin lesions.

**Keywords**
Skin Tumors; Color Doppler Ultrasonography; Gray Scale Ultrasonography; Power Doppler Ultrasonography
Introduction
Ultrasonography (US) is a valuable diagnostic imaging method widely used in medicine. During the last three decades, this non-invasive skin imaging method has been extended to dermatology [1]. Diagnostic process in dermatology usually depends on clinical assessment, dermoscopic and histopathologic examinations [2]. US can be helpful in the assessment of cutaneous pathologies. Some important qualitative and quantitative features of skin, such as thickness, roughness, texture, vascularity, diameter, and volume of the lesions can be evaluated more objectively [3,4]. Furthermore, US is able to give reliable information about the exact position of a tumor, surrounding anatomical structures, its echo pattern as well as the distance from the skin surface.

The use of gray scale ultrasonography (GSUS) scanning is not as widespread, although promising results have been reported from specialized diagnostic units, especially for the assessment of peripheral lymph nodes and soft tissue tumors [5-7]. Color Doppler ultrasonography (CDUS) was performed to analyze vascularity of the skin lesions. GSUS combined with CDUS has the advantage of providing a rapid, relatively inexpensive, and non-invasive assessment of lesion morphology and vascularity [8].

The main technical limitation of CDUS is the inability to show very slow flow or tiny tumor vessels. Power Doppler ultrasonography (PDUS) has improved the sensitivity of the Doppler technique by enabling the detection of low-amplitude blood flow. The prominent feature of PDUS is the lack of angle dependence. As noise has low amplitude, it can be filtered out, allowing the gain to be increased [8].

The aim of this study was to prospectively evaluate the usefulness of GSUS, CDUS, and PDUS in differentiating benign and malignant skin lesions.

Material and Method
Study Design: Eighty patients (35 female, 45 male) with focal, popular, and nodular skin lesions were prospectively enrolled in this study. After skin lesions had been assessed clinically, they were evaluated with GSUS, CDUS and PDUS. The ultrasonographic examinations were performed by the same radiologist using a Toshiba PowerVision 6000 (Toshiba Medical System, Rome, Italy). Biopsy was performed to all lesions. They were histopathologically divided into two different groups as benign skin tumors (BST) and malignant skin tumors (MST).

Ethical Committee approval was obtained from Ethical Committee of Cumhuriyet University and the study protocol conformed to the Declaration of Helsinki. All patients were informed about the purpose and the method of the study.

Outcome Measures: After skin lesions had been assessed clinically, they were evaluated with GSUS, CDUS and PDUS. First, the lesion was evaluated through GSUS. The morphological parameters were studied with a frequency of 7.5 and 15 MHz GSUS. Linear transducer was raised up to 12 MHz and the depth was adjusted to 5 cm. The dimensions of the lesion, the contour characteristics, existence of pagoda echo, invasion of skin layers, and the internal echogenicities were investigated. Following GSUS, CDUS was performed. In the cases in which vascularization was not clearly determined, or in order to show the vascular continuity better, PDUS was performed.

CDUS is mainly based on the mean frequency shift of the Doppler signal and has an invaluable role in non-invasive imaging of major vessels and the intraparenchymal vasculature of most organs. PDUS has recently gained attention as an additional color flow imaging technique that overcomes some of the limitations of CDUS which include angle dependence and difficulty in separating background noise from true flow in slow-flow states [9].

According to the vascular pattern detected on PDUS, the lesions were classified as having peripheral, central, or mixed-type vascularity, similar to a categorization reported for breast tumors [10]. Vascularity observed only at the periphery of the lesion was called "peripheral." For those only showing central vascularity the term "central" pattern was adopted. Both peripheral, central vascularization, and peripheral vessels branching and penetrating through the lesion, was accepted as a "mixed" pattern.

Results Eighty patients (35 female, 45 male) were enrolled in this study. The average age of the patients was 36.50±2.15 (range: 0.5-79) years.

Of the 66 patients with BST, 39 (59.0%) were male and 27 (40.9%) were female. Of the BST group, 23 were nevus, 10 were lipom, 9 were epidermal cyst, 7 were sebace cyst, 5 were hemangiom, 5 were dermatofibrom, 3 were keratoacanthoma, 2 were pyogenic granuloma, solitary angiookeratoma and 1 was syringoma.

Of the 14 patients with MST, 6 (42.9%) were male and 8 (57.1%) were female. Of the MST group, 6 were basal cell carcinoma (BCC), 3 were squamous cell carcinoma (SCC), 3 were malignant melanoma, one was intraepidermal malignant eccrine poroma and one was mycosis fungoides.

Differences between the groups regarding sex is statistically insignificant (χ²=1.26; p>0.05). The mean age of patients according to their diagnosis was 30.07±2.19 for patients with BST, 60.00±4.23 for patients with MST. The difference between the groups regarding their age was statistically significant (KW=60.00±4.23 for patients with BST, 30.07±2.19 for patients with MST, the difference between the groups regarding their age was statistically significant (KW=108 | Journal of Clinical and Analytical Medicine
Blood flow was observed in 33 patients. The existence of the flow was mostly observed in the MST group [13 of 14 patients (92.2%)]. The flow was observed only in the 20 of 66 benign lesions (33.3%) (Table 1).

Study groups were compared according to the spectral wave analysis of blood flow (pulsatility index, resistive index, peak systolic velocity, and end diastolic velocity). The difference between the study groups was not significant (p>0.05). When diagnostic groups were compared concerning the “hypoechoic echogenicity” finding, the difference between BST and MST groups was statistically significant (t=2.20; p<0.05).

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The choice of the frequency depended on the lesion depth, size and site. The 12 MHz linear probe was used to assess superficial and subcutaneous lesion such as tumors, assessing their relationship to the adjacent tissue including nerves and vessels to provide crucial preoperative information. Meanwhile, the 7.5 MHz linear probe was used to assess the lesions which were larger and/or located in deeper area. Color Doppler and power Doppler methods were performed to analyze vasculature of the skin lesions.

Sonographic features that can assist in the differential diagnosis between benign and malignant skin lesions have been widely discussed in literature [1-4]. Nevertheless, these morphologic criteria alone are insufficient in lesion characterization and assessment. Some authors have now focused on tumor microvasculature analysis. Since work by Srisvastava et al. was published in 1989, several studies have focused on analysis of tumor microvasculature [13]. It has been shown in animal models that Doppler mode (color or power Doppler) allows microvessel detection with a threshold of 100 μm. A high correlation with histological and immunohistochemical specimens in terms of vascular density has been reported [14,15]. Detection of microvessels in a skin lesion increases the conspicuity for malignancy, but reports in the literature are still variable in that microvessel detection has shown a good specificity for malignancy (90%–100%) but sensitivity has been in the 34%–100% range [16]. These variations could be related to the natural history of angiogenesis in tumors and also to the advances in ultrasound.

Giovagnorio et al. divided skin-underskin nodules into four groups concerning vascularization; Type 1: Avascular, Type 2: Hypovascular having only one vascular pole, Type 3: Hypervascular having multiple peripheral pole (Figure 1) and Type 4: Hypervascular nodules including internal vascular structures [1]. In our study, the lesions were classified as having peripheral, central, or mixed-type vascularity, similar to a categorization reported for breast tumors [10].

Cysts: Cysts of different histological origin defined as vacuum filled with fluid are depicted as round to oval shaped hypoechoic to echo-free structures, with the phenomenon of a distinct dorsal echo enhancement and lateral shadowing [5,4,16,17]. They show well-defined borders to the adjacent tissue. In our study, 68.8% of the cystic lesions were observed anechoic, 31.2% heterogeneous. While 75% of the cases were with regular contour, lobule contour was seen in 25%. Irregular contour was not seen in cystic lesions. Also, in our cases, which are cystic skin lesions,
the depth was clearer than in other diagnostic groups. When CDUS and PDUS were applied to the lesions, it was determined that there was blood flow in the 37.5% of the cases and the type of flow was peripheral in 83.3% and mixed in 16.7%. That cystic lesions having flow are not anechoic, that lesions are hypoechoic-weighted heterogeneous echo pattern and that the diagnosis of infected and complicated cyst suggests that the cyst must be complicated for some reason (infection, bleeding and so on). It should be emphasized that Vp and Vd values were lower and RI and PI values were higher in cystic lesions than in lesions defined to be malignant.

Dermatofibromas: Dermatofibromas generally present with hypoechoic ecocgenity and they are all corium-settled [3,4]. In our study, the mentioned lesion was also hypoechoic. The flow pattern was not observed in CDUS and PDUS.

Lipomas: Lipomas are subcutaneous nodules consisting of adipose tissue, often elastic, and can be compressed during physical examination. Lipomas were defined to be echoluent or hypoechoic structures including poor internal echo and can rarely be seen echoic due to fibroitic component [3,4,18]. In this study, 75% of the lipomas were observed as hypoechoic, 25% as hypoechoic structures having echogenic components. That the pathology results of these lesions, in the appearance of heterogeneous are fibrolipom or infected lipom made us think that the cause of the echogenicity are due to other components. Almost all lipomas were regular contours. Some of the lesions reached the subcutaneous tissue and included corium. In 25% of our cases, flow pattern was determined by CDUS and PDUS. The characteristic of this flow-pattern was peripheral.

Hemangiomas: In all hemangiomas observed in our study, hypoechoic and heterogeneous occurrence due to internal septas and cavitations were observed in GSUS. In all lesions, a well-defined lobule contour was observed with clearly distinguished limits. Both internal and peripheral flow-pattern was also observed in CDUS and PDUS. Lesions with such appearances were fit to the type 4 pattern in the characteristics of hypervascular nodules including internal vascular structures of Giovagnoria et al [16]. High speed flow with low PI and RI was observed which fits to the characteristics of a malign structure. And therefore, we concluded that hemangiomas should be separated from other benign lesions due to flow-pattern. In such a lesion, the clinician’s physical examination becomes very important.

Nevus: In our study, all type of the nevus was observed in hypoechoic structure. Most of them were in regular contours. In CDUS and PDUS, flow pattern was not observed in any of the lesions.

Pyogenic granulomas: Also in our study, two pyogenic granulomas were observed. In GSUS, lesions were observed with regular contour, lying to subcutaneous layer, and isoechoic on the dermal layers. In one of the pyogenic granulomas, pagoda echo was also observed. In CDUS and PDUS, the lesions showed internal and peripheral vascularization, and fit to type 4 pattern of Giovagnoria et al. [16]. Giovagnoria had observed type 4 pattern only in malign lesions, and never in benign tumoral lesions. In our study, CDUS and PDUS are consisted with type 4 pattern in both cases with pyogenic granulomas.

BCC: In our study, all BCC lesions were in the appearance of hypoechoic or hypoechoic-weighted heterogeneous echogenity in GSUS. 50% of these lesions were irregularly contoured, 34% had regular contours and in 16% lobular nature with regular contours was observed. The pagoda echo in GSUS was observed in nearly 66.6% of the cases. In our study, we determined flow pattern with CDUS and PDUS in all cases with BCC. The peripheral flow pattern was observed in most of the lesions which was in accord with the type 2 and type 3 patterns of Giovagnoria et al. [19]. In our study, type 2 hypervascular pattern was observed, while it was usually not observed in malign lesions in the literature. Vp and Vd values were low except one case and spectral analysis values did not show a statistically significant difference with other malign lesions.

The most important characteristics of BST was that 61.5% of them were regular contoured, 32.7% were lobular (yet regular contoured), and that contour irregularity was observed in only 5.8%. This was the main difference of BST from MST in our study.

Mycosis fungoides: In one case with mycosis fungoides, flow pattern was not observed in CDUS and PDUS in our study. Malign melanomas: Malign melanomas are typically well-defined hypoechoic lesions with smooth or lobulated contours, mild to moderate heterogeneity, and increased acoustic through-transmission. Internal flow is revealed by color Doppler sonography [2,3]. In our study, it is observed that malign melano- mas lesions have irregular lobule contours and in hypoechoic or hypoechoic-weighted heterogeneous nature. In CDUS and PDUS, internal and peripheral flow was observed (Figure 2). RI values were found to be low.

SCC: Irregular contours and inhomogeneous hypoechoic patterns were observed in SCC lesions [1,3]. In our study, SCC lesions were hypoechoic with certain irregularity in the contours. In CDUS and PDUS, both internal and peripheral flow patterns were observed. Higher flow velocities were observed in spectral analysis in both cases. Patients with SCC have higher Vp and Vd and lower RI and PI in comparison with other benign and malign lesions. In three of our cases with SCC, type 3 and type 4 vascular pattern was observed.

Hypoechoic structure was observed in 32.7% and hypoechoic-weighted heterogenic structure was observed in 26.9% of the patients with BST and totally 59.6% of the BST were in hypoechoic pattern. We determined flow pattern in the 33.3% of the cases in CDUS and PDUS applied to the BST group. This is statistically signifi-
cant in comparison with the 92.9% flow rate determined in MST group in our study. In BST group, peripheral or mix flow pattern were observed in all cases. As for the MST group, internal vascularization alone was observed in the 30.7% of the cases.

Table 2: Spectral analysis values of cases in the study groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>PI</th>
<th>RI</th>
<th>Vd (cm/sec)</th>
<th>Vp (cm/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign skin tumors (n=66)</td>
<td>0.53±0.03</td>
<td>0.94±0.09</td>
<td>15.41±2.51</td>
<td>7.58±1.49</td>
</tr>
<tr>
<td>Malign skin tumors (n=14)</td>
<td>0.49±0.03</td>
<td>0.85±0.10</td>
<td>19.30±4.90</td>
<td>9.61±2.37</td>
</tr>
<tr>
<td>Total (n=80)</td>
<td>KW=1.01</td>
<td>KW=0.57</td>
<td>KW=4.66</td>
<td>KW=3.88</td>
</tr>
</tbody>
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Pl=Pulsatility index; RI=Resistive index; Vd=End-diastolic velocity; Vp=Peak systolic velocity.

Table 2. Spectral analysis values of cases in the study groups.

Conclusion

A significant difference was noted between malignant and benign skin lesion groups as for color and power Doppler ultrasoundographic findings such as tumor microvasculature analysis and as for the gray scale ultrasoundographic findings such as regular contour, irregular contour, pagoda echo and hypoechoic echogenicity. The application of US in cutaneous and subcutaneous tissues has a great benefit. US is a low-cost, non-invasive and powerful technique for the evaluation of malignant and benign skin lesions.

References