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# Trends in the number of patients with cutaneous melanoma and their Breslow thicknesses between 2000 and 2018: A tertiary hospital-based study in İstanbul

## *2000-2018 yılları arasındaki kutanöz melanomlu hastaların sayılarında ve Breslow kalınlıklarındaki değişimler: İstanbul'da üçüncü basamak bazlı bir çalışma*

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### Abstract

**Background and Design:** The global incidence of cutaneous melanoma is increasing. Breslow thickness has been reported to have decreased in recent years, in contrast to this increase. This study aims to determine annual changes in the number of diagnosed cutaneous melanoma cases and their Breslow thicknesses in our hospital.
**Materials and Methods:** Pathology reports from cutaneous melanoma patients admitted to our hospital's dermatology clinic between 2000 and 2018 were reviewed retrospectively.
**Results:** The study included 210 cases, 122 (58.1%) of which were male and 88 (41.9%) of which were female. The mean age of the cases was 61.08±17.07. The year and the number of cases seen each year had a statistically significant positive correlation ($p=0.003$; $\rho=0.640$). The number of reported cases has risen over time. The year had a statistically significant negative correlation with case Breslow thicknesses ($p<0.001$; $\rho=-0.292$). The cases' Breslow thickness decreased over time.
**Conclusion:** Our study found that as the incidence of cutaneous melanoma has increased, the Breslow thickness of cases diagnosed in recent years has decreased. These findings suggest that awareness of cutaneous melanoma has increased over time in the population served by our hospital, and the diagnostic methods and algorithms used by physicians have aided in earlier detection of the disease. However, there are still a significant number of thick cutaneous melanoma lesions, implying that more emphasis should be placed on awareness-raising activities, disease screening programs, and in-service training to detect these lesions earlier.
**Keywords:** Breslow thickness, cutaneous melanoma, early diagnosis

### Öz

**Amaç:** Kutanöz melanom insidansı genel olarak dünya çapında artmaktadır. Bu artışın aksine son yıllarda Breslow kalınlığının azaldığı bildirilmiştir. Bu çalışmada hastanemizde tanı almış kutanöz melanom olgularının sayılarındaki ve Breslow kalınlıklarındaki yıllık değişimlerin belirlenmesi amaçlanmıştır.
**Gereç ve Yöntem:** Hastanemiz dermatoloji kliniğine 2000-2018 yılları arasında başvuran kutanöz melanom hastalarının patoloji raporları geriye dönük olarak değerlendirildi.
**Bulgular:** Çalışmaya alınan 210 olgunun 122'si (%58,1) erkek, 88'i (%41,9) kadındı. Olguların yaş ortalaması 61,08±17,07 idi. Yıl ile her yıl görülen olgu sayısı arasında istatistiksel olarak anlamlı pozitif korelasyon bulduk ($p=0,003$; $\rho=0,640$). Yıllar geçtikçe olgu sayısı arttı. Yıl ile Breslow olgu kalınlıkları arasında istatistiksel olarak anlamlı negatif korelasyon vardı ($p<0,001$; $\rho=-0,292$). Yıllar geçtikçe, olguların Breslow kalınlığı azaldı.
**Sonuç:** Çalışmamız, son yıllarda tanı konulan olgularda kutanöz melanom sıklığının artmasıyla birlikte Breslow kalınlığının azaldığını göstermiştir. Bu bulgular dolaylı olarak hastanemizin hitap ettiği popülasyonda kutanöz melanom farkındalığının arttığını ve hekimlerin kullandığı tanı yöntemleri ve algoritmaların hastalığın daha erken tanınmasına yardımcı olduğunu göstermektedir. Bununla birlikte, farkındalık artırma

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aktivitelerine, hastalık tarama programlarına ve bu lezyonları daha erken tanımak için hizmet içi eğitime vurgu yapılması gerektiğini düşündüren önemli sayıda kalın kutanöz melanom lezyonu halen bulunmaktadır.
**Anahtar Kelimeler:** Breslow kalınlığı, kutanöz melanom, erken tanı

## Introduction

Cutaneous melanoma is a deadly malignant tumor that develops from melanocytes. Vertical tumor thickness, or Breslow thickness, is the foundation for cutaneous melanoma and remains the most important prognostic factor today[1,2]. For melanoma, Breslow thickness is measured millimetrically from the upper border of the granular layer of the epidermis or the ulcer base to the deepest point reached by the tumor, if an ulcer is present, using an ocular micrometer. Breslow thickness is the primary determinant of category T in the staging system based on the criteria of tumor, lymph node, and metastasis regulated by the American Joint Committee on Cancer[3]. Category T is used to determine melanoma status, prognosis estimates, minimal excision margin recommendations, whether to recommend sentinel lymph node biopsy, and the frequency and extent of follow-up examinations[1,4]. Early diagnosis and appropriate excision result in a cure rate of >90% in patients with low-risk melanoma (i.e., Breslow <1 mm). The incidence of melanoma has rapidly increased in recent years, and estimates indicate that this will continue[5]. It is one of the fastest-growing cancer types worldwide[6,7]. Despite the increase in incidence, several centers have reported a reduction in average tumor thickness. The incidence and Breslow thickness distributions are critical parameters for understanding melanoma trends and prevention strategies[8]. With the help of screening strategies in recent years, the majority of detected melanomas are diagnosed when they are in the I-IIB stages[7]. Consequently, while the increase in incidence is concerning, overall survival durations are increasing globally in tandem with this increase in incidence because disease detection rates have also increased. Only a few studies have been conducted in Türkiye to assess the general incidence of melanoma, and no studies have been conducted to assess the change in Breslow thickness over time. The main purpose of this study was to determine the change in the number of cutaneous melanoma lesions and their Breslow thicknesses diagnosed in our hospital between 2000 and 2018.

## Materials and Methods

Patients admitted to the dermatology clinic of the hospital in İstanbul between January 1, 2000, and December 30, 2018, with cutaneous melanoma were included in our study.

The study included reports of patients over the age of 18 years, diagnosed with melanoma with excisional biopsy, and first excisional biopsy reports of melanoma patients with multiple skin biopsies. Patients under the age of 18 years, patients diagnosed with melanoma via a punch or incisional biopsy, and patients diagnosed with melanoma following examination of biopsy samples sent from another center to our hospital's pathology clinic for consultation were excluded from the study.

The pathology reports for the patients were obtained from the pathology department's digital and printed report archive. Age, gender, year of diagnosis, type of melanoma, Breslow thickness, and lesion localization were collected.

Ethical approval was obtained from the University of Health Sciences Türkiye, Haydarpaşa Numune Training and Research Hospital Local Ethics Committee (approval number: 771/07/2018).

### Statistical Analysis

The SPSS Statistics 22 (IBM SPSS, Türkiye) program was used to evaluate the pathological data for the statistical analysis. The normal distribution of the parameters was evaluated using the Shapiro-Wilk test. To compare the qualitative data, descriptive statistical methods [mean, standard deviation, median, interquartile range (IQR), and range] and Pearson's correlation were used to examine the relationships between parameters with normal distributions. Spearman's correlation ρ was used to examine the relationships between parameters that did not follow a normal distribution. The Kruskal-Wallis test was used to compare the parameters of more than two groups, and the Mann-Whitney U test with Bonferroni adjustment was used for binary comparisons of these groups. The significance was determined using a p-value of <0.05.

## Results

The study included 210 cases, with 122 (58.1%) males and 88 (41.9%) females. The age of the patients ranged between 23 and 95 years. The mean age of the patients was 61.08±17.07, and the median age was 61 (IQR: 72).

There were 41 (19.5%) lesions on the head and regions, 34 (16.2%) on the upper extremities, 56 (26.7%) on the trunk, 60 (28.6%) on the lower extremities, and 19 (9%) in other anatomical regions (Table 1).

Superficial spreading melanoma was found in 72 (34.3%) of all melanoma patients, followed by nodular melanoma in 64 (30.5%), acral lentiginous melanoma in 41 (19.5%), lentigo maligna melanoma in 17 (8.1%), verrucous melanoma in 2 (1%), subungual melanoma in 2 (1%), subungual desmoplastic melanoma in 1 (0.5%), and

**Table 1. Number of lesions and mean and median values for Breslow thickness according to localization**

| | n (%) | Mean ± SD | Median (IQR) |
|---|---|---|---|
| Head/neck | 41 (19.5%) | 3.87±4.42 | 2.8 (6.5) |
| Upper limb | 34 (16.2%) | 3.10±2.68 | 3 (3.25) |
| Trunk | 56 (26.7%) | 5.46±9.49 | 3.25 (3.74) |
| Lower limb | 60 (28.6%) | 7.84±9.45 | 5 (6.08) |
| Other | 19 (9%) | 3.29±3.92 | 2 (5) |

SD: Standard deviation, IQR: Interquartile range

tumorogenic melanoma in 1 (0.5%). Ten cases (4.8%) had no melanoma type reported.

Male patients had a median Breslow thickness of 3.51 mm (IQR: 4.96), and the female patients had a median Breslow thickness of 3.25 mm (IQR: 6.80). In terms of Breslow thickness, there was no statistical difference between the two groups (Mann-Whitney U test, p=0.524).

There was no statistically significant relationship between Breslow thickness and age (Spearman's correlation ρ=0.019, p=0.783).

The Breslow thicknesses of the lesions according to localization are summarized in Table 2. In terms of the Breslow thickness of the lesions, there was a statistically significant difference between these groups (Kruskal-Wallis test, p<0.001). When the groups were compared, it was discovered that the difference between the groups was caused by the localization of the lower extremities. The median Breslow thickness of melanoma lesions in the lower limb was significantly greater than the median Breslow thickness of melanoma lesions in all other localizations. The number of cases by year and the mean and median values of the Breslow thicknesses are shown in Table 3.

In our study, there was a statistically significant positive correlation between the year and the number of cases seen each year (Pearson's correlation p=0.003; ρ=0.640). The number of reported cases has risen over time (Figure 1).

There was a statistically significant negative correlation between the year and the Breslow thicknesses of cases seen each year (Spearman's correlation ρ=-0.292, p<0.001). The Breslow thickness of the cases had decreased over time (Figure 2).

When the years were divided into four distinct periods, 34 (16.2%) of the cases were diagnosed between 2000 and 2004, 39 (18.6%) between 2005 and 2009, 80 (38.1%) between 2010 and 2014, and 57 (27.1%) between 2015 and 2018. Breslow thicknesses of cases reported during these four time periods were classified as 0 to ≤1, >1 to ≤2, >2 to 4, and >4 mm (Table 4). Although the incidence of thin melanomas has increased over time, a significant number of thick melanoma cases have been observed (Table 3 and Figure 3). While there was a positive significant correlation between the number of

**Table 2. Statistical comparison of the Breslow thicknesses of lesions according to localization**

| | Head/neck | Upper limb | Trunk | Lower limb | Other |
|---|---|---|---|---|---|
| Head/neck | - | p=0.760 | p=0.217 | **p=0.002** | p=0.865 |
| Upper limb | p=0.760 | - | p=0.286 | **p<0.001** | p=0.563 |
| Trunk | p=0.217 | 0.286 | - | **p=0.004** | p=0.168 |
| Lower limb | **p=0.002** | **p<0.001** | **p=0.004** | **-** | **p=0.004** |
| Other | p=0.865 | p=0.653 | p=0.168 | **p=0.004** | - |

Note. The groups were compared with each other using the Mann-Whitney U test. A result was accepted as statistically significant if the p-value was <0.01 with Bonferroni correction

**Table 3. Number of cases and Breslow thicknesses by year**

| Year | Number of cases | Breslow thickness min.-max. (mm) | Breslow thickness mean ± SD (mm) | Breslow thickness median IQR (mm) |
|---|---|---|---|---|
| 2000 | 4 | 4-50 | 17.00±22.18 | 7 (36) |
| 2001 | 10 | 0.75-12 | 5.22±3.92 | 5 (7.35) |
| 2002 | 8 | 2-9 | 4.81±2.87 | 3.5 (5.63) |
| 2003 | 7 | 0-15 | 5.92±5.43 | 4 (9.5) |
| 2004 | 5 | 3-6 | 5.14±1.32 | 6 (2.15) |
| 2005 | 8 | 1-11 | 5.87±3.39 | 5.5 (6) |
| 2006 | 5 | 1-51 | 13.8±20.99 | 4 (27.5) |
| 2007 | 7 | 2-6 | 4.14±1.57 | 5 (3) |
| 2008 | 6 | 0.3-40 | 11.38±14.74 | 7 (17.43) |
| 2009 | 13 | 0.3-43 | 7.21±11.71 | 3.62 (8.5) |
| 2010 | 18 | 0-30 | 5.87±7.90 | 2.8 (7.01) |
| 2011 | 15 | 0-20 | 4.39±5.34 | 3 (4.89) |
| 2012 | 16 | 0-9 | 3.87±2.89 | 3.2 (4.35) |
| 2013 | 13 | 1.4-10 | 4.53±2.77 | 4 (3.85) |
| 2014 | 18 | 0-45 | 6.26±10.12 | 3.9 (5.8) |
| 2015 | 23 | 0-14 | 3.08±3.63 | 2.2 (3.25) |
| 2016 | 13 | 0-4.8 | 0.84±1.34 | 0.3 (1.29) |
| 2017 | 11 | 0-8 | 3.09±3.17 | 1.4 (6.7) |
| 2018 | 10 | 0-15 | 4.95±5.34 | 3.45 (10.04) |
| Total | 210 | - | - | - |

min.: Minimum, max.: Maximum, SD: Standard deviation, IQR: Interquartile range

patients with 0 to ≤1 (Spearman's correlation ρ=0.640, p=0.003) and >1 to ≤2 mm (p=0.015; p=0.549) Breslow thicknesses over the years, no statistically significant positive or negative correlation was found between the number of cases with >2 to ≤4 (Pearson's correlation p=0.655; ρ=0.110) and >4 mm (p=0.188; ρ=0.316). Breslow thicknesses have increased over time.

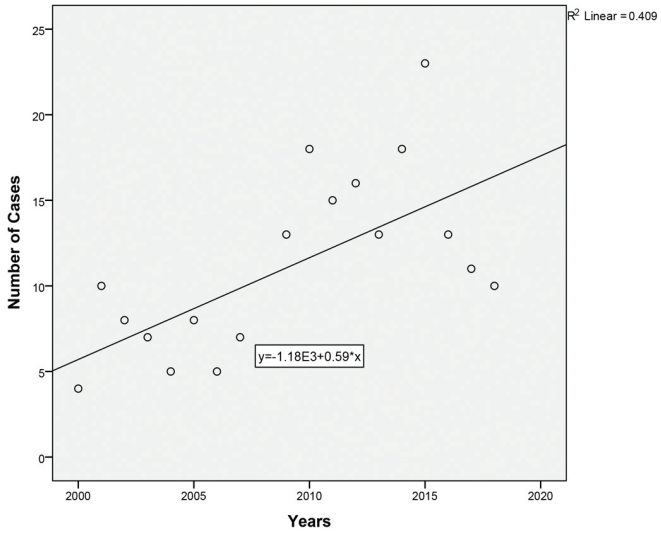


**Figure 1.** Correlation curve showing the relationship between the number of cases and year

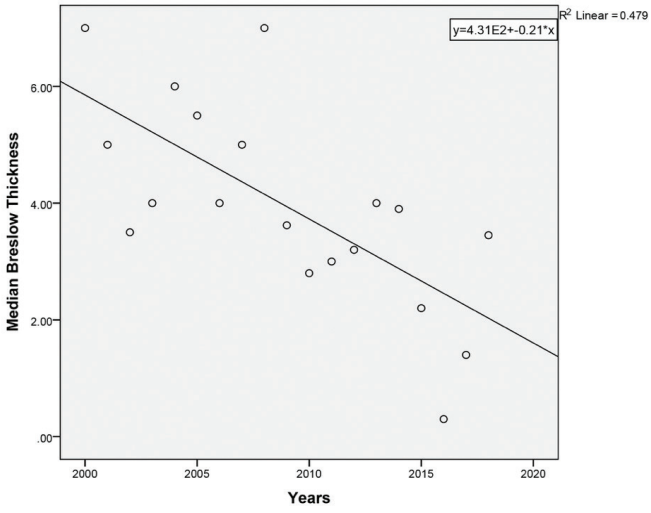


**Figure 2.** Correlation curve showing the relationship between the median Breslow thickness and year

## Discussion

Although cutaneous melanoma accounts for 1% of all skin cancers, it is the leading cause of death from skin cancer[9,10]. The incidence of cutaneous melanoma is increasing worldwide[8]. This increase can be attributed to increased ultraviolet (UV) exposure, ozone layer thinning, an increase in the number of vacations in sunny areas, and an increase in artificial UV exposure (i.e., solariums). Thin melanomas are becoming more common. This is more likely due to the fact that melanoma awareness studies are conducted in broad communication environments, such as visual media and the internet, and physicians conduct regular monitoring of nevi with both hand and computerized dermoscopy[11].

According to different studies conducted in Türkiye, the average age of melanoma patients from ranges between 51.6 and 57.7 years[2,9,12,13]. In other countries, the average age is 54 in Canada and 65.5 in Hong Kong; melanoma most commonly occurs in the fifth and sixth decades of life[14,15]. In our study, the average age was 61.08 years, which is consistent with the literature.

Melanoma is more common in men than in women across all age groups. This difference has been attributed to sex hormones, such as estrogen, a greater emphasis on UV protection, and more frequent doctor examinations[16,17]. In our study, there were more male cases than female cases, which is consistent with the literature.

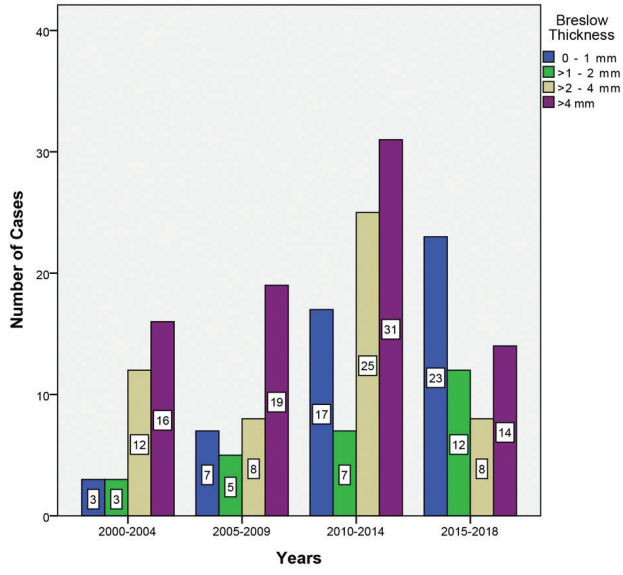


**Figure 3.** Distribution of cases seen according to year divided by separate periods for categorized Breslow thickness. Cases of thin melanoma were proportionally higher than others from 2015 to 2018

**Table 4. Categorized Breslow thicknesses according to years divided by separate periods**

| | 0 to ≤1 mm, n (%) | >1 to ≤2 mm, n (%) | >2 to ≤4 mm, n (%) | >4 mm, n (%) | Total, n (%) |
|---|---|---|---|---|---|
| 2000-2004 | 3 (8.8) | 3 (8.8) | 12 (35.3) | 16 (47.1) | 34 (100) |
| 2005-2009 | 7 (17.9) | 5 (12.8) | 8 (20.5) | 19 (48.7) | 39 (100) |
| 2010-2014 | 17 (21.3) | 7 (8.8) | 25 (31.3) | 31 (38.8) | 80 (100) |
| 2015-2018 | 23 (40.4) | 12 (21.1) | 8 (14.0) | 14 (24.6) | 57 (100 |
| Total | 50 (23.8) | 27 (12.9) | 53 (25.2) | 80 (38.1) | 210 (100) |

The most commonly observed localization of melanoma varies in the literature. In a study of 227 patients, Baykal et al.[9] found that melanoma was most commonly found in both genders on the head and neck regions (34.78%), lower extremities (28.02%), trunk (23.67%), and other locations. According to Abali et al.[12], the lower extremities were the most common site of melanoma (30.5%). The trunk and, particularly, the back were the most common melanoma localizations in Kruijf et al.'s[5] work in the Netherlands and Rubegni et al.'s[18] work in Italy. In our study, the most common lesion locations were the trunk, lower extremities, head and neck, and upper extremities.

In terms of melanoma type, superficial spreading melanoma is the most common type reported in Turkish studies[9,12,13]. This is followed by nodular melanoma, acral lentiginous melanoma, and lentigo maligna melanoma in decreasing order of frequency[12,13]. The melanoma types in our study were compatible with this sequence. Similarly, in a Turkish study, lentigo maligna melanoma was ranked second, acral lentiginous melanoma was ranked third, and nodular melanoma was ranked fourth[9]. In an Italian study[19], superficial spreading melanoma was ranked first, whereas in a Korean series[20], acral lentiginous melanoma was the most common type of melanoma. This suggests that the prevalence of melanoma types may vary geographically and racially.

Although Breslow described the Breslow thickness as the vertical thickness of a tumor for the first time in 1970, it is still the strongest prognostic factor for melanoma today[21,22]. In the fight against melanoma, it is critical to increase patient awareness of the disease to consult a doctor in the early period of the disease when the Breslow thickness is thin and recognition of lesions by physicians in the early period of disease. The frequency of melanomas seen over time, clinical and demographic features of the disease, the effect of these features on Breslow thickness, and changes in Breslow thicknesses over time have been investigated in some retrospective studies. The reported change in Breslow thicknesses over time can be an indirect indicator of the success of training, diagnostic methods, and algorithms.

Stefansson et al.[11] investigated changes in Breslow thickness in Iceland between 1980 and 2009 using Breslow thickness and demographic data. They discovered that melanomas <1.0 mm in size were diagnosed more frequently in all ages and in both genders; however, thin melanomas were diagnosed more frequently in young women than in men. The incidence of thick melanomas (>4 mm) did not increase during this time period[11].

The study by Ambrosini-Spaltro et al.[8] evaluated the incidence of melanoma and Breslow thickness in South Tyrol and the Alpine mountainous region of northern Italy between 1998 and 2012. The highest Breslow value was found, particularly in elderly male patients. Breslow thickness increased for thin melanomas from 8.39 to 16.18 mm and for thick melanomas from 4.30 to 6.70 mm[8].

Minini et al.[23] conducted a study in Switzerland involving 8,469 melanoma patients between 1980 and 2010 and found that the incidence of melanoma increased in both genders, with thin melanomas increasing in both genders.

Sacchetto et al.[24] studied the trend of thin, thick, and in situ melanomas in 415,000 lesions in 18 cancer centers across European countries between 1995 and 2012. They found that invasive melanoma increased by 4% in men and 3% in women as the average annual percentages changed, while in situ melanoma increased by 7.7% in men and 6.2% in women. While the detection of thin melanomas increased gradually over time, the detection of thick melanomas increased more slowly, but they were detected less often than thin melanomas. Despite an increase in detected *in situ* and thin melanomas, they found that invasive melanoma mortality has continued to increase in Norway, Iceland (only in elderly patients), the Netherlands, and Slovenia.

In a cohort study by Hollestein et al.[25] involving 45,919 patients in the Netherlands between 1989 and 2008, the annual incidence of melanoma increased by 4.1%, and the incidence rates were greatest for thin (≤1.0 mm) and thick melanomas (>4 mm). Our findings show that over while the number of melanomas has increased significantly in Türkiye over the last 18 years, Breslow thickness has decreased significantly. When we categorized Breslow thickness, we found a significant increase in the number of cases with Breslow thicknesses of 0 to ≤1 and >1 to ≤2 mm, while the increase in the number of cases with Breslow thicknesses of >2 to ≤4 and >4 mm was not statistically significant. There was no significant relationship between age and gender and Breslow thickness.

The incidence of melanoma was reported to have rapidly increased in recent years in a study conducted by Kruijff et al.[5] in the Netherlands: 5.4% in an elderly patient group (≥65 yr) and 3.9% in young people. They also found that while Breslow thicknesses had decreased significantly for all localizations, this was particularly true for the head and neck in young patients and the trunk in elderly patients. Rubegni et al.[18] conducted a study in which anatomical regions were classified as either anterior or posterior, and it was suggested that lesions in the anterior region were more easily recognized and thus diagnosed earlier, while lesions in the posterior region were diagnosed later. However, in their studies, interestingly, the decrease in Breslow thickness was most frequently detected on the head, posterior part of the upper extremities, posterior part of the lower extremities, and the back[18].

### Study Limitations

In our study, Breslow thickness was thicker in the lower extremities than in other anatomical regions. We believe that this was due to more sun exposure and the difficulty of finding lesions located between the legs, back of the feet, soles of the feet, and the heel, which may have been easier to overlook.

## Conclusion

Our findings show that the incidence of melanoma is gradually increasing, but there has been a significant decrease in Breslow thickness in cases diagnosed in recent years. This could be an indirect indication that the methods and algorithms used to fight melanoma have been quite successful in terms of early diagnosis, information dissemination, screening, and social awareness of the disease. However, because there are still a significant number of cases of thick melanoma, it is too early to declare that we have successfully combated this disease. At this stage, further investigation of the causes of late diagnoses of thick melanoma is prominent in the fight against this disease, with the goal of decreasing the frequency of its occurrence and taking appropriate measures.

### Ethics

**Ethics Committee Approval:** Ethical approval was obtained from the University of Health Sciences Türkiye, Haydarpaşa Numune Training

and Research Hospital Local Ethics Committee (approval number: 771/07/2018).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally and internally peer-reviewed.

**Authorship Contributions**

Concept: Ş.Y., F.G., Design: Ş.Y., F.G., Data Collection or Processing: Z.T.K., P.G., Analysis or Interpretation: Z.T.K., Ş.Y., P.G., F.G., Literature Search: Z.T.K., Writing: Z.T.K., Ş.Y., F.G.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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