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RESEARCH

The hidden gap: impact of specimen shrinkage on melanoma surgical margins and histological evaluation

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Abstract

Background Understanding the shrinkage phenomenon after wide local excision of melanoma is critical for precise surgical planning and accurate histopathologic evaluation. However, the extent of shrinkage and its influencing factors are not fully established.

Methods The present study is a retrospective analysis of 329 patients who underwent wide local excision for melanoma between 2018 and 2022 at our institution. Melanoma characteristics, anatomical location, patient age, and gender were collected to investigate correlations with specimen shrinkage from in vivo to ex vivo. Statistical analyses included ANOVA and various post-hoc tests to identify significant differences.

Results Significant differences in specimen shrinkage percentages were found based on patient age and melanoma location. Younger patients exhibited greater shrinkage, likely due to higher skin elasticity. Additionally, certain body sites, such as the back, demonstrated higher rates of shrinkage compared to other areas.

Conclusions These findings highlight that melanoma specimen shrinkage is influenced by both age and anatomical site, underscoring the importance of accounting for this phenomenon during surgical planning and in guidelines. Standardizing the definition of excision margins as in vivo measurements is essential to ensure adequate oncologic clearance.

Level of Evidence: Level III, risk/prognostic study

Keywords Melanoma · Wide Local Excision · Shrinkage · Melanoma guidelines · Surgical Margins

Introduction

Melanoma is a malignant tumor originating from melanocytes of the skin and mucous membranes or, more rarely, from extracutaneous sites such as the eyes, meninges, inner ear, etc. Any suspected melanoma should be excised, with a 1 to 2 mm of healthy tissue margin (excisional biopsy) in accordance with current surgical guidelines [1–4].

Incisional biopsy is discouraged [5, 6] and complete, primary excision of suspicious lesions should aim to preserve the architecture of the lesion to ease the histopathologic diagnosis and give proper assessment of tumor thickness and ulceration [7].

Subsequently, wide local excision surgery is performed to achieve local control of the tumor. Surgical standards call for *en-bloc* resection of the scar resulted from the first surgery, including the surrounding healthy skin and subcutaneous tissue, down to the muscle fascia [8]. Excision margins should be determined according to the Breslow thickness of the primary lesion as follows:

- Melanoma In Situ (MIS): 0.5–1 cm starting from the outer margin of the scar.
- Breslow thickness ≤ 1 mm: 1 cm starting from the outer margin of the scar.
- Breslow thickness 1–2 mm: 1–2 cm starting from the outer margin of the scar.
- Breslow thickness > 2 mm: 2 cm starting from the outer margin of the scar.

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Sentinel node biopsy is also indicated for melanoma with Breslow thickness more than 0.8 mm or thinner than 0.8 mm with high-risk features like ulceration.

As for other surgical resection of skin and subcutaneous tissue, the surgical specimen undergoes shrinkage in the transition from in-vivo to ex-vivo [9] immediately after wide local excision, resulting in a quantitative difference between the margins given by the plastic surgeon and those found at histology [10–13]. Therefore, the presence of shrinkage phenomenon could have an important impact on the correct medical-surgical treatment of the patient and legal consequences for the surgeon, who should always adhere to updated guidelines [1–4].

The objectives of our statistical analysis were to confirm the presence and quantify the extent of the shrinkage phenomenon, as well as to identify the factors that influence it.

Materials and methods

A total number of 329 patients who underwent post-diagnosis wide local excision (WLE) surgery for cutaneous melanoma, between 2018 and 2022, was included in the study. Inclusion criteria for patient selection were a WLE of at least 1 cm margin from the previous melanoma scar, or a WLE surgery associated with sentinel lymph node removal. All patients included in this study were white caucasians. The histology report of each patient was carefully revised. The following information were extracted from the histological reports: gender, age, melanoma location, size (in cm) of the cutaneous ellipse, Breslow thickness (in mm).

Patients were divided into three groups according to sex, age and excision site (see Table 1).

To quantify the shrinkage phenomenon, the "healthy tissue margin" of post-operative ex-vivo skin ellipse was compared with the one reported by the surgeon in patients' operative notes. The ex-vivo skin ellipse "healthy tissue margin" measure was derived by the histological reports using the following mathematical formula "x = Ellipse width – Scar width/2" where x was the distance between the scar and the edge of the ellipse, measured at the width axis of the ex-vivo specimen (Figs. 1 and 2).

To assess if any shrinkage occurred, the x value (in cm) was subtracted from the "healthy tissue margin's" value y (in cm) given by the plastic surgeon (1–2 cm) at each side of the scar when performing the WLE, so that "*Shrinkage* $= x - y, y \in \{1, 2\}$cm".

Another measure to consider was the scar width: at our institution in histological reports, scar width is indicated only when widened. Otherwise, for a normal linear-surgical scar, the given thickness was considered negligible. In these cases, the value of 0.3 cm was used for the calculation. This measure was considered to be the average width value of a scar as reported in the literature (2.7 ± 1.19 mm).

Table 1 Clinical characteristics of the sample

Group		Patients	(*N*°)
Sex			
	Male	86	
	Female	105	
Age			
Location	0 − 49	62	
	50 − 100	129	
	Head	13	
	Trunk	38	
	Upper Limb	23	
	Lower Limb	57	
	Back	54	
	Genitals	6	

Statistical analysis

The Analysis of Variance (ANOVA) was used to define whether a statistically significant difference existed between the averages of the groups which were not directly comparable due to different sample sizes.

Firstly, the presence of any outliers in the data, which could have affected all subsequent tests, was checked. After excluding the outliers, remaining values were subjected to the Shapiro-Wilk normality test or the Kolmogorov-Smirnov test to assess the normal distribution of the considered values, and to the Levene's homogeneity of variance test to prove samples equal variance.

Finally, the ANOVA test was performed and followed by the Games-Howell and Tuckey post-hoc tests to compare the groups in pairs and determine which subgroup characteristic was most influential on the shrinkage phenomenon.

The Statistical Package for the Social Sciences (SPSS) program provided by IBM under academic license was used to perform the tests.

Results

The shrinkage phenomenon was observed in 191 patients, 58% of the study population. The size of the cutaneous ellipse changed from in-vivo to ex-vivo, registering a shrinkage of about 28% on average. Statistical results are summarized in Table 2.

Sex The Kolmogorov-Smirnov test found the absence of a normal distribution ($p < 0.05$) for the sub- groups "Males" ($n = 79$) and "Females" ($n = 98$). In contrast, Levene's test of homogeneity of variances gave a positive result ($p > 0.05$), while the ANOVA test found the absence of statistical

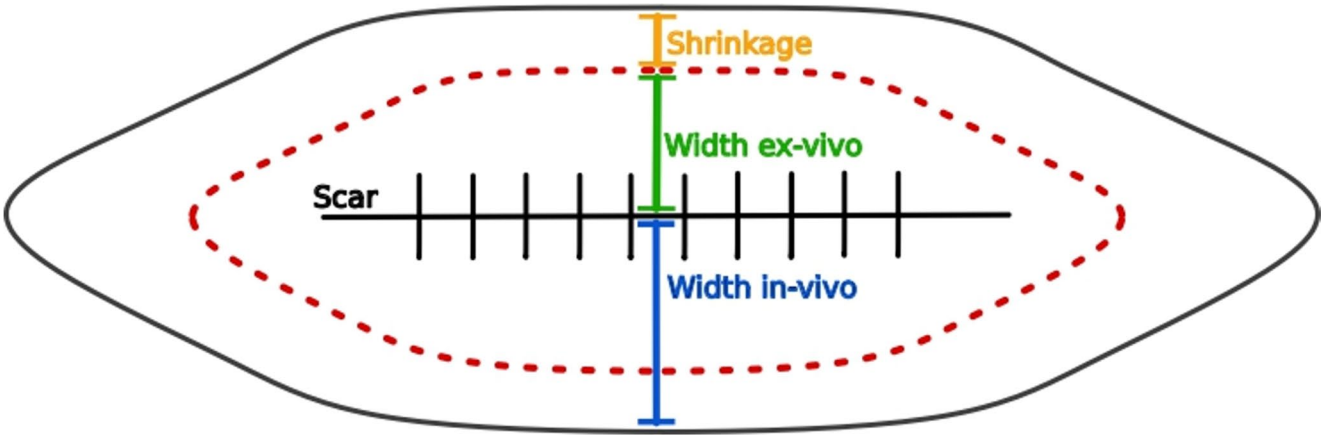

Fig. 1 Schematic representation of an in-vivo (black) and ex-vivo (red) skin ellipse, with in-vivo (blue), ex-vivo (green), and shrinkage (orange) widths highlighted

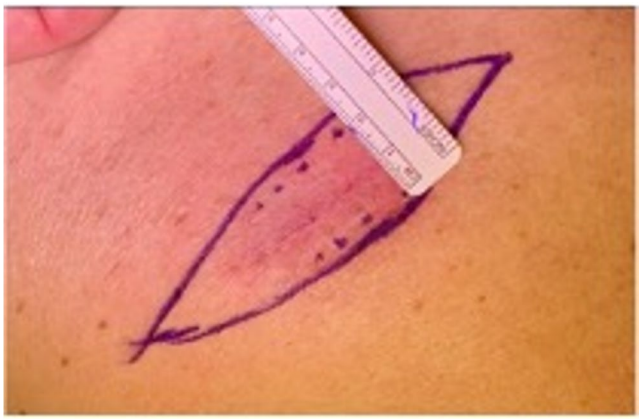

Fig. 2 the in-vivo ellipse drawn on the patient

Table 2 Results of the statistical analysis

Group		Shapiro-Wilk or Kolmogorov-Smirnov	LeveneANOVA
Sex			$p=0.388 p=0.542$
	Male	$p<0.001$	
	Female	$p<0.001$	
Age			$p=0.018 p=0.003$
Location	0−49	$p=0.004$	$p<0.001 p<0.001$
	50−100	$p<0.001$	
	Head	$p=0.486$	
	Trunk	$p=0.063$	
	Upper Limb	$p=0.016$	
	Lower Limb	$p<0.001$	
	Back	$p<0.001$	
	Genitals	$p=0.683$	

significance in the difference between the means of the two subgroups ($p>0.05$).

Age The Kolmogorov-Smirnov test found no normal distribution ($p<0.05$) for the age subgroups "0–49" ($n=58$) and "50–100" ($n=116$). The Levene test of homogeneity of variances also returned a negative result ($p<0.05$). The ANOVA test found the presence of statistical significance in the difference between the means of the two subgroups ($p<0.05$), specifically shrinkage of the subgroup "0–49" presented a mean of 27.8% and a variance of 16.8%, while that of subgroup "50–100" presented a mean of 21.14% and a variance of 12.43%.

Location To verify the normal distribution of the data, the Shapiro-Wilk test was performed for all subgroups considered, except for the "Lower Limb" subgroup where the Kolmogorov-Smirnov test was used. These tests showed that the samples belonging to the subgroups "Head", "Trunk" and "Genitals" were normally distributed ($p>0.05$), while for the remaining subgroups there was no normal distribution ($p<0.05$).

One-way ANOVA was performed to determine whether the percentage of shrinkage correlated with melanoma location which was different in the various subgroups identified: "Head" ($n=12$), "Trunk" ($n=33$), "Upper Limb" ($n=22$), "Back" ($n=49$), "Genitals" ($n=4$) and "Lower Limb" ($n=55$), whereby it was found that the difference in shrinkage percentage in the identified subgroups was statistically significant.

The Games-Howell post-hoc analysis was performed since the Levene test of homogeneity of variances showed inhomogeneity in the variances. This analysis showed a

statistically significant ($p < 0.05$) increase of 19.8% ± 5.4% (mean ± variance) in the shrinkage rate for melanomas located on the "Back", compared with those located on the "Head"; and a statistically significant ($p < 0.05$) increase of 8.14% ± 2.66% for melanomas located on the "Back", compared with those located on the "Lower Limb". Also, there was an increase in the shrinkage percentage for melanomas located on the "Back" of 14.6% ± 3.4% compared with those located on the "Genitals", which could be considered statistically significant ($p = 0.058$). In contrast, all other differences between the various locations were found to be statistically non-significant ($p > 0.05$).

Discussion

In recent years numerous authors have analyzed the phenomenon of skin ellipse shrinkage and the factors influencing it.

Alves Wainstein, et al. [10], studied the shrinkage of the surgical specimen at three different time points, in-vivo, ex-vivo and in-vitro, assessing any impacting factors as well as formalin fixation, age, sex and location of the lesion. Their study reported a mean ellipse width retraction of 26.80% during the transition from in-vivo to in-vitro, also concluding that age, sex and location of the lesion had an impact on this phenomenon.

Notwithstanding, in the study proposed by Moret et al. [14] no statistically significant correlation between these factors and skin shrinkage was found.

De Waal et al. [11], statistical analysis revealed a mean shrinkage of 9% in width, consistent with the results obtained by Monk et al. [15] (8.59%) and Blasco-Morente et al. [9] (9.5%).

Larger mean shrinkage values of 11.79% and 18% were found by Kerns et al. [16] and Dauendorffer et al. [17] respectively. In these studies, it was also observed that location was the most impacting factor on the shrinkage phenomenon. The impact of the age in the shrinkage phenomenon was also found consistent by Kerns et al. [16]. Conversely, in the study proposed by Silverman et al. [13], the age was found to be the only factor influencing the shrinkage phenomenon.

In the present study, no statistically significant correlation between sex and shrinkage was observed, whereas significant differences were found for age, as greater shrinkage was observed in the younger population (0–49 years) than in the older one (50–100 years).

Regarding anatomical location, however, a statistically significant correlation was found by comparing certain areas of the body, such as: "Back"- "Head", "Back"- "Genitals", and "Back"- "Lower Limb".

In consideration of the observations obtained in this study, correlation between shrinkage and age could be explained with the decrease of skin elasticity and collagen fibers in older age [18]. Furthermore, correlation between shrinkage and certain areas of the body could be explained by differences in skin elasticity and collagen fibers present [18].

Our findings underscore the practical implications of the shrinkage phenomenon following wide local excision for melanoma, highlighting how the measured histologic margins may substantially underestimate the in vivo margins planned during surgery. This discrepancy is clinically significant, as most international guidelines recommend excision margins in absolute distances without explicitly clarifying that these refer to in vivo measurements. Only, the NCCN guidelines for cutaneous melanoma explicitly define excision margins as in vivo distances, acknowledging the impact of tissue contraction after excision and formalin fixation [2]. Given our evidence that both patient age and tumor location influence the degree of specimen shrinkage, standardizing the definition of surgical margins as in vivo is critical to ensure appropriate oncologic clearance and avoid under-treatment. Our data support advocating for clearer recommendations across all melanoma guidelines to define excision margins in terms of in vivo planning, thereby accounting for the predictable, yet variable, tissue shrinkage that occurs post-excision.

Conclusions

WLE surgery for melanoma treatment may be conditioned by skin shrinkage phenomenon thereby causing the size of the ellipse to change from in-vivo to ex-vivo. As a result, the width and length of surgical margins assessed in the operating room are no longer the same as those found in the pathology laboratory. Therefore, better clarification is needed in the current guidelines to specify whether clear skin margins should be "at surgery" or "at histology". These clarifications could prevent unnecessary surgery especially in sensitive areas like the face, as well as medico-legal repercussions for not strictly following melanoma treatment guidelines.

Further research with larger, prospective cohorts is needed to strengthen the statistical reliability of our findings. Additionally, future studies could investigate potential correlations between the shrinkage phenomenon and other variables not assessed in our analysis, such as body mass index (BMI), Fitzpatrick skin phototype, and ethnicity.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval Our institution's Research Ethics Committee has confirmed that no ethical approval was required for this retrospective study. This study was conducted in line with the principles of the Declaration of Helsinki.

Patient consent For this type of study, formal consent was not required. All data were anonymized prior to analysis in accordance with institutional and national research ethics standards.

Competing interests The authors declare no competing interests.

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