J Cutan Pathol 2015: 42: 253–257
doi: 10.1111/cup.12401
John Wiley & Sons. Printed in Singapore

Journal of
Cutaneous Pathology

Study of shrinkage of cutaneous surgical specimens

Background: The assessment of discrepancies between surgical and histopathological measurements of specimens is important in order to avoid repeat surgery and unnecessary follow-ups.
Objectives: The objective of this study was to quantify the degree, time and influential factors of shrinkage of cutaneous surgical specimens.
Methods: Data of 111 patients were gathered on age, sex, localization, diagnosis and specimen width and length before surgical excision (*in vivo*), at 5 min postsurgery (*ex vivo*) and after 24 h of fixation in 10% buffered formalin (*postfixation*).
Results: The length and width were significantly lower in the *postfixation* vs. *in vivo* specimens, with a mean shrinkage of 17.0% in the length ($p < 0.01$) and 9.5% in the width ($p < 0.01$). 81.8% and 92.3% of the total shrinkage in length and weight was observed between *in vivo* and *ex vivo* measurements. No significant differences were observed as a function of sex, age or diagnosis. A greater shrinkage in length between *in vivo* and *postfixation* was found in specimens from the trunk.
Limitations: The most of the skin samples were diseased.
Conclusion: The largest proportion of specimen shrinkage occurred within 5 min of its excision and the shrinkage was greater in specimens from the trunk.

Keywords: formalin, skin shrinkage, skin specimens, skin tumors, surgical margins

Blasco-Morente G, Garrido-Colmenero C, Pérez-López I, Carretero-García S, Martín-Castro A, Arias-Santiago S, Tercedor-Sánchez J. Study of shrinkage of cutaneous surgical specimens.
J Cutan Pathol 2015; 42: 253–257. © 2014 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

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Accepted for publication October 25, 2014

For many decades, skin tumors were treated with wide, deep and potentially disfiguring resections, until it became established that surgical margins could be reduced without compromising survival.[1] The minimization of adjusted tumor-free margins requires a precise surgical incision and a correct histopathological correlation. The assessment of discrepancies between surgical and histopathological measurements of specimens is important in order to avoid repeat surgery and unnecessary follow-ups, besides legal implications with respect to the surgical margins around malignant tumors.[2] Surgical specimens of various human tissues, including prostate, breast, brain, oral cavity, colorectal, lung and carotid artery,[3,4] are known to undergo shrinkage, which has been attributed to the retractile properties of the specimens themselves and the action of formalin.[1,4,5] However, there have been few studies on cutaneous surgical specimens, and

Table 1. Findings of studies on the shrinkage of cutaneous surgical specimens

			Total shrinkage (%)		Difference between measurements					
			Between *in vivo* and *postfixation*		Between *in vivo* and *ex vivo*		Between *ex vivo* and *postfixation*		Potentially associated factors	
Study	Year	n	Width	Length	Width	Length	Width	Length		Shrinkage
Golomb[6]	1991	199	20.7				–		Age	Lesser with higher age
Silverman[1]	1992	407	19.6				–		Age	Lesser with higher age
Gregory[3]	2003	54	20		22	$p < 0.05$	$p < 0.05$		Age	Lesser with higher age
									Localization	Lesser in head/neck and greater in limbs
									Diagnosis	Greater in benign tumors (Width)
Kerns[5]	2008	97	11.79	20.66		$p < 0.01$	No difference (dif)		Age	Lesser with higher age
									Localization	Greater in trunk than in head/neck
Dauendorffer[2]	2009	82	18	16		$p < 0.01$	No dif		Localization	Greater in limbs (Length)
Dumas[7]	2012	75	–			31%	–		Localization	Greater in upper limbs and neck Earlier in head, ear and periorbital area Lesser in lower limbs, back, nose and face
*	2014	111	9.5	17		$p < 0.01$	No dif	$p < 0.01$	Localization	Greater in trunk than in head/neck or limbs (Length)

*Present study; n: sample size; p: p-value.

inconsistent findings have been published on their amount of shrinkage and on the potential role of formalin fixation.[1–3,5–7] Results on the influence of factors such as sex, age, localization and diagnosis on the amount of shrinkage have also been controversial (Table 1). Therefore, the objective of this study was to quantify the degree of shrinkage of cutaneous surgical specimens, determine when it occurs and evaluate the role of potentially influential factors.

Material and methods

A cross-sectional, descriptive observational study was performed in patients who had undergone surgery in the Early-Discharge Dermatology Surgery Unit of the Virgen de las Nieves Hospital Complex (Granada, Spain) during a 3-month period. It included consecutive patients treated for basal cell carcinoma, squamous cell carcinoma, melanocytic tumor or other diagnoses by buttonhole surgery following relaxed skin tension lines. Patients undergoing repeat surgery were excluded from the study. Data were gathered on age, sex, localization, diagnosis and specimen width and length before surgical excision (*in vivo*), at 5 min postsurgery (*ex vivo*) and after 24 h of fixation in 10% buffered formalin (*postfixation*). Localizations were divided among head/neck, trunk (except areoles), limbs (except palms and soles) and other sites (palms, soles and areoles). The *in vivo* and *ex vivo* specimen measurements were made by a single surgeon (G.B.M.) using a standard millimeter ruler, the first immediately after the fine marking of surgical margins and before infiltration of local anesthesia with 2% mepivacaine, and the second at 5 min after the excision. A pathologist blinded to the previous results repeated the measurements after 24 h of immersion in 10% buffered formalin.

Statistical analysis

The difference between the *in vivo* and *postfixation* width and length measurements was considered as the total shrinkage; when differences were significant, comparisons were performed between *in vivo* and *ex vivo* and between *ex vivo* and *postfixation* measurements to determine the timing of the shrinkage. The Student's *t*-test for related comparisons was used for the global comparison of the 111 specimens, the Student's test for independent samples was employed to analyze the influence of sex and age, and analysis of variance (ANOVA) with Bonferroni's multiple

Table 2. Characteristics of the 111 patients

		n	%
Sex	Male	61	55
	Female	50	45
Age	Mean	61.77 (±21.73)	
	≤60 years	42	37.8
	>60 years	69	62.2
Localization	Head/neck	64	57.7
	Trunk	26	23.4
	Limbs	17	15.3
	Other	4	3.6
Diagnosis	Basal cell carcinoma	57	51.4
	Squamous cell carcinoma	16	14.4
	Melanocytic tumor	22	19.8
	Others	16	14.4

comparison was applied to analyze the influence of the diagnosis and tumor localization. Quantitative variables were expressed as means (cm), and categorical variables as percentages. $P \leq 0.05$ was considered significant, and SPSS 21.0 (IBM, Chicago, IL, USA) was used for the data analysis.

Results

Table 2 lists the characteristics of the 111 specimens from the 111 patients in the study; 61 (55%) were male and 50 (45%) female. The age ranged from 14 to 92 years, with a mean age of 61.77 years [standard deviation (SD) 21.73]; 42 (37.8%) patients were aged ≤60 years and 69 (62.2%) >60 years. The specimen was from the head/neck in 64 (57.7%) patients, the trunk in 26 (23.4%), limbs in 17 (15.3%) and other sites in 4 (3.6%, three on soles and one on areole). The diagnosis was basal cell carcinoma in 57 (51.4%) patients, squamous cell carcinoma in 16 (14.4%), melanocytic tumor (nevus or melanoma) in 22 (19.8%) and other diagnoses in 16 (14.4%; four infundibular cysts; four dermatofibromas, four seborrheic keratoses, two keloids, one lichenoid keratosis and one neurofibroma).

Global shrinkage of surgical specimens

The length and width were significantly lower in the *postfixation* vs *in vivo* specimens (Table 3), with a mean shrinkage of 17.0% in the length ($p < 0.01$) and 9.5% in the width ($p < 0.01$).

Differences in the length ($p < 0.01$) and width ($p < 0.01$) of specimens between the in *vivo* and *ex vivo* measurements were significant, and 81.8% and 92.3% of the total shrinkage in length and weight, respectively, was observed between these time points. There was also a significant reduction in the length ($p < 0.01$) but not the width ($p = 0.16$) between the *ex vivo* and *postfixation* measurements.

Factors potentially associated with shrinkage

No significant differences in overall mean shrinkage (difference in length or width between *in vivo* and *postfixation* measurements) were observed as a function of sex, age (>60 vs. ≤60 years), or diagnosis. No significant differences were found in the mean shrinkage in length as a function of the site or in the mean shrinkage in width between specimens from head/neck and limbs.

The degree of shrinkage in length from *in vivo* to *postfixation* significantly differed between specimens from the trunk and those from head/neck ($p < 0.01$) and limbs ($p = 0.02$) (Table 4). The mean shrinkage in length was 22.8% in trunk specimens vs. 14.9% in head/neck and 16.9% in limb specimens. The shrinkage in length from *in vivo* to *ex vivo* significantly differed between specimens from the trunk and those from head/neck ($p < 0.01$) and limbs ($p = 0.05$); it represented 75.4% of the total shrinkage in trunk specimens, 86.5% of that in head/neck specimens and 72.6% of that in limb specimens. The shrinkage in length from *ex vivo* to *postfixation* also significantly differed between trunk and head/neck specimens ($p < 0.01$) but not between trunk and limb specimens ($p = 0.39$).

Discussion

In this study of 111 cutaneous surgical specimens, a mean reduction in length of 17.0% and reduction in width of 9.5% were observed between their excision and the end of their fixation for 24 h with formalin, similar to previous reports in studies with smaller sample sizes (Table 1). This shrinkage was mainly observed between the *in vivo* and *ex vivo* measurements, which represented 81.8% of the total reduction in length and 92.3% of the reduction in width ($p < 0.01$), similar to the results reported by others studies.[2,5] However, differences in length alone were observed between *ex vivo* and *postfixation* measurements. This may be because of the continuity solution produced by the scalpel on the collagen and elastic fibers, which are relaxed in the direction of relaxed skin tension lines in their natural medium, explaining the greater shrinkage in length than width after an incision in this direction.[2,5] A role would also be

Table 3. Global comparison in mean measurements of the 111 surgical specimens pre-excision (*in vivo*), at 5 min post-excision (*ex vivo*), and after 24-h fixation in formaldehyde (*postfixation*)

Measurement of surgical specimen				Total shrinkage		Differences in mean measurements			
				From *in vivo* to *postfixation*		From *in vivo* to *ex vivo*		From *ex vivo* to *postfixation*	
	In vivo	*Ex vivo*	*Postfixation*	Difference	p-value	Difference	p-value	Difference	p-value
Width	1.37 (±0.60)	1.25 (±0.56)	1.24 (±0.54)	0.13 (±0.16)	**<0.01**	0.12 (±0.13)	**<0.01**	0.01 (±0.10)	0.16
Length	2.59 (±1.20)	2.23 (±1.03)	2.15 (±0.99)	0.44 (±0.35)	**<0.01**	0.36 (±0.27)	**<0.01**	0.08 (±0.16)	**<0.01**

Measurements expressed as means (cm); p-value obtained by Student t- test for related samples. Bold values are statistically significant.

Table 4. Comparison of surgical specimen measurements as a function of the localization: pre-excision (*in vivo*), 5 min post-excision (*ex vivo*), and after 24-h fixation in formaldehyde (*postfixation*)

		Measurements of the surgical specimen			Differences in total shrinkage		Differences among measurements			
					From *in vivo* to *postfixation*		From *in vivo* to *ex vivo*		From *ex vivo* to *postfixation*	
		In vivo	*Ex vivo*	*Postfixation*	Difference	p-value	Difference	p-value	Difference	p-value
Head/neck	Width	1.40 (±0.64)	1.27 (±0.60)	1.26 (±0.58)	0.15 (±0.16)	1.00				
Trunk		1.38 (±0.51)	1.27 (±0.47)	1.26 (±0.43)	0.12 (±0.17)					
						1.00				
Limbs		1.36 (±0.65)	1.25 (±0.59)	1.24 (±0.56)	0.12 (±0.16)					
					vs. Head/neck	1.00				
Head/neck	Length	2.49 (±1.23)	2.17 (±1.08)	2.12 (±1.05)	0.37 (±0.28)	**<0.01**	0.32 (±0.23)	**<0.01**	0.05 (±0.14)	**<0.01**
Trunk		3.03 (±1.26)	2.51 (±1.04)	2.34 (±0.98)	0.69 (±0.45)		0.52 (±0.34)		0.17 (±0.22)	
						0.02		**0.05**		0.39
Limbs		2.49 (±0.97)	2.17 (±0.90)	2.07 (±0.88)	0.42 (±0.24)		0.32 (±0.20)		0.10 (±0.10)	
					vs. Head/neck	1.00		1.00		0.75

Measurements are expressed as means (cm). *P*-values obtained by analysis of variance (ANOVA) with Bonferroni's multiple comparison test. Bold values are statistically significant.

played in shrinkage by vascular collapse, the loss of blood flow and tissue fluids through the cut surface, and the possible shrinkage of smooth muscle and endothelium because of the loss of nutritional supply.[8] The differences in length between *ex vivo* and *postfixation* dimensions may be explained by an effect similar to that of *rigor mortis*, which is maximal at 6 h and persists until 24 h, when the *postfixation* measurement were performed.[9,10] The effect of formalin on specimen shrinkage appears to be minor, as observed in other studies.[2,5]

Our results indicated that the shrinkage of specimens was not related to the sex, age or diagnosis of the patients. Previous studies have also found no gender differences in cutaneous specimen shrinkage,[1–3,5–7] but older age has been related to lesser shrinkage by some authors,[1,3,6] and one study reported greater shrinkage in specimens of benign vs. malignant tumors.[3]

We observed a greater mean length shrinkage in specimens removed from the trunk (22.8%) than in those from the head and neck (14.9%) or limbs (16.9%), which may be attributable to the greater width of the dermis, which contains most collagen and elastic fibers, on the trunk.[2] The difference in mean length shrinkage between trunk and head/neck specimens was significant between i*n vivo* and *ex vivo* and between *ex vivo* and *postfixation*, whereas the difference between trunk and limb specimens was only significant between *in vivo* and *ex vivo*. A greater shrinkage in specimens from the trunk vs. head/neck was previously reported,[5] while greater shrinkage was found in specimens from the limbs by some authors,[2,3] and in upper limbs and neck vs. lower limbs and back by others[7]

One study limitation is that most of the skin samples were diseased, which may have produced structural changes that affect shrinkage. Further studies are required in wider samples to allow the differentiation of all localizations, relevant diagnoses and age-groups for a more complete study of the influence of these factors.

In conclusion, the largest proportion of specimen shrinkage occurred within 5 min of its excision (i.e. removal from its natural support), and the shrinkage was greater in specimens from the trunk than from other areas. This information is useful for dermatologists and dermopathologists to resolve discrepancies in the clinical history.

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