PLASTIC AND RECONSTRUCTIVE SURGERY

Royal Australasian College of Surgeons

Skin tumour specimen shrinkage with excision and formalin fixation—how much and why: a prospective study and discussion of the literature

John de Waal
Plastic Surgery North Shore, Auckland, New Zealand

Key words
formalin, margins of excision, resection margin, skin shrinkage, surgical margins.

Correspondence
Dr John de Waal, Plastic Surgery North Shore, 181Shakepeare Rd, Milford, Auckland 0620, New Zealand.
Email: jdewaal@xtra.co.nz

J. de Waal MBChB, FRACS.

Accepted for publication 17 July 2021.

doi: 10.1111/ans.17109

Abstract

Background: Surgical skin specimens are known to undergo significant shrinkage when excised and processed. The degree of shrinkage is important for medical care, research and third-party assessment. Studies to date have shown variable degrees of shrinkage. Most have included multiple and sometimes unspecified variables—different surgeons, varied sites, ill-defined excision patterns and/or multiple pathologies. This study tries to exclude many of these variables to try to ascertain a more accurate predictor of shrinkage with a single surgeon, lower limb only site using a controlled excision pattern and restricted pathology cohort.
Method: 100 previously untreated malignant BCC's and SCC's on the lower limb were excised and measurements made of the resulting wound and the specimen removed. Measurements were subsequently made after pathologic processing and statistically compared.
Results: With excision of lower limb skin tumours the surgical defect enlarges significantly (15%) and the specimen shrinks significantly (20%) in both length (12%) and width (9%). The specimen shrinks a further 11%—again shrinking in length (8%) and width (2.6%) with formalin processing. The pathology specimen is 28.6% smaller than the specimen marked for excision. Anatomical site contributes to the degree of shrinkage. The pathologic specimen is only 75% of the suture repaired wound length.
Conclusions: Skin specimens shrink significantly both with excision and processing. Most shrinkage (70%) takes place with excision while the remaining 30% with processing. The shrinkage takes place disproportionately in the normal tissue component of the specimen. Age, anatomical location, and pathology appear to play a part.

Introduction

Accurate assessment of tissue shrinkage has implications for individual patient treatment, medical research and third-party assessments.

The provision of appropriate patient treatment means surgically procuring sufficient margin to prevent recurrence while sacrificing as little tissue as possible.[1] The margin in turn helps one to assess future risk and so make decisions as to whether further excision, follow-up, or discharge is appropriate.[1,2] An over-estimate of shrinkage may lead one to under-estimate risk while under-assessment of shrinkage may lead to over-excision.[1]

Medical research requires an accurate measure so studies of in vivo/clinical margins can be compared with studies based on margins of fixed pathology specimens.[3]

Third Party Assessments raise the spectre of both legal implications of appropriate malignant tumour margin resection and down-coding of surgical codes due to discrepancies in surgical and pathology reports.[4,5] Currently in New Zealand the largest private medical insurer compensates surgeons for skin tumour removal on the basis of the length of the repaired wound.

Overarching this debate is the debate between clinical and histological margins. Some studies of skin tumour removal have shown no significant difference in clinical and histological margins.[6] The most recent guidelines on management of cutaneous melanoma by a working group of the American Academy of Dermatology advises reporting only on positive and negative margins and discourages routine reporting of histological margins in mm by pathologists as it is feared that such reporting could lead to confusion and unnecessary additional wide excisions as treatment is based on clinical

margins.[7] This is in spite of important studies showing a clear correlation between histologic margins and recurrence[8] and poor correlation between surgical and histological margins.[9] As Sevray[10] has noted 'the guidelines for the surgical excision of skin cancer recommend a clinical margin before excision …. Nevertheless, the evaluation of the sufficiency of the margins is based on histological measurement'.

While a number of studies have been made of surgical margins and tissue shrinkage in skin specimens to date they have on the whole been multi-surgeon, retrospective studies involving multiple skin tumour types, including benign, in situ and malignant types and involve multiple locations, without clearly stating excision shape (i.e. simple elliptical, curvilinear, circular, tension line orientation, depth, etc.).

This study attempts to preclude as many variables as possible so as to optimise the validity of the results and calculate normal tissue shrinkage in a single anatomical zone and assess this in comparison to preceding studies to try and ascertain how much difference these variables may make.

Method

This is a prospective, single surgeon study of 100 primary malignant skin tumours (BCC or SCC only and specifically excluding in situ pathology) from 97 different patients collected over a 4-year period. All were taken from the lower limb, excised under local anaesthetic by simple ellipse, and subjected to traditional formalin fixation. Excisions were all directed with their long axis down the length of the limb and in depth to, but not including, deep fascia. Surgical measurements were made using a mm ruler to the closest mm and only excisions longer than 3 cm in length were included to minimise relative size measurement errors. No tumours had been subject to previous surgery including biopsy. No tumours were included if a scar from other surgery or injury was sited within 5 cm of the tumour excision margins. All wounds were directly closed in 2 simple layers. Specimens that were shown subsequently on histology, not to be a BCC or SCC were excluded. In this series all had clear histologic margins.

Measurements pre-excision were performed prior to local anaesthetic infiltration. Post excision measurements of the wound defect were prior to any diathermy (Hudson-Peacock showed a 14% size difference post diathermy[11]). Surgical measurements were taken by the operating surgeon. Pathologic measurements were taken directly from the pathology report.

Overall measurements were then subjected to paired *t*-tests to look for significant differences at each stage of processing.

Subgroup analysis were done via independent group *t*-tests.

Results

Table 1 summarises the overall average length, width changes in mm and percentage changes at each stage of processing, together with their respective *P*-value significance.

There was a significant change in length and in width from in vivo to the fixed pathology specimen with mean shrinkage of approx. 20% and 10% respectively.

The change in length and width of the specimen was significant at both stages—length reduced 12% with excision and a further 8% with fixation. The reduction in width was 9% with excision and further 2.6% with fixation.

The surgical wound shrank statistically in length (2%) and expanded significantly in width (17%).

The length of the repaired surgical wound was approx. 130% of the pathology specimen length.

Sex, age and pathology made no statistical difference (see Table 2 which summarises the subgroup analysis). Location (comparing calf with pretibial excisions) had a statistical effect on width, but not length shrinkage.

Discussion

Wound expansion with excision

Surgical skin wounds expand in size from their surgically marked size with specimen excision. Hudson-Peacock[11] 20%, Gregory[5] 25%.

If one uses the classic πab formula for the area of an ellipse then in this study it is closer to 15%. The length itself changed little but did notably shrink a statistically significant approx. 2%, while the width widened by 17%.

Table 1 Average measurements and changes in 100 patients

	Surg Def*	SD-IV	In vivo	IV-EV	Ex vivo	EV-PF	Post fix	SL-PF	Sut Lgth†	Total IV-PF
Ave L mm	67.71		68.92		60.51		55.47		71.59	
L%chg		1.76		−12.2		−8.33		29		−19.52
P val Lchg		0.000		0.000		0.000		0.000		
Ave W mm	25.44		21.71		19.77		19.26			
W%ch		17.18		−8.96		−2.56				−11.29
P val Wchg		0.000		0.000		0.036				
Area %chg		+15		20		10.7				28.6

t-test *P* values relate to the length (L) and width (W) change (chg) in mm between each stage of processing. Negative values for W and L %change imply tissue shrinkage.

Area change is a calculated value using the Πab formula for an ellipse.

*Surg Def, Surgical defect, that is, the skin/soft tissue defect left on specimen removal).

†Sut Lgth, Sutured length, that is, length of the repaired wound).

Table 2 Summary of subgroup analysis

		Number	*P*-value* (length change)
Sex	M	50	0.75
	F	50	
Age	Ave 77	Range 52–98	0.85†
Location	Thigh	4	
	Pretibia	48	
	Calf	37	0.08‡ (0.014 width)
	Ankle/foot	11	
Pathology	BCC	27	0.45
	SCC	73	

*P values for change from in-vivo to post fixation only.

†P values comparing 70 years. and under with over 70 years.

‡P value for comparison of pretibial and calf area only. Note no significant difference in length but a significant difference in width from in-vivo to post fixation.

Since the work of Langer in 1861 we have known skin wounds open in a preferred direction and recent work[12] showing that collagen and elastic fibres form a mesh like network in which both type of fibres follow the same orientation provides a solid anatomical basis for this.

Most expansion of the wound takes place in the width of the defect—one would surmise largely due to intrinsic elastic tissue recoil. The overall lesser expansion compared to previous studies may be due to this study being limited to lower limb lesions—apart from true intrinsic anatomical site differences the dimensions of a torso wound in the chest or upper back can change significantly with patient positioning alone, for example, arms across chest, extended or by side—and measurements might therefore indicate more or less wound expansion accordingly. Positional factors have been precluded from this study by limiting excisions to the lower limb, excising using a longitudinal ellipse and operating on the limb in an extended position.

In contrast to the situation of Langer's lines however we have the added compounding factor of pathology. More sclerotic and more invasive tumours may restrain or even contract adjacent tissue. With excision this restraint is released. Both Hudson Peacock and Gregory however had high proportions of benign lesions. It may have been expected then that this factor would minimise the expansion recoil.

Overall specimen shrinkage with processing

Surgical skin specimens undergo significant shrinkage when excised and processed (Table 3).

Previous studies have shown overall specimen shrinkage of 22% in Gregory,[5] 29% in Sevray[10] and 31% in Hudson-Peacock.[11] This study shows an overall average specimen shrinkage of approx. 28.6% (based on Πab using Table 1 averages). Shrinkage has been explained by both vascular collapse and dehydration[13] and loss of continuity of elastic and collagen fibres along skin tension lines,[4,14] The tension line theory would be consistent with several studies (see Table 3) showing that shrinkage is more in length than width—the length of the specimen appears to shrink approx. 20% (16–22%) and the width 15% (9.5–21%). In this study the length shrank 20% and the width 11%.

Golomb[3] in a small subsample showed no significant shrinkage difference related to orientation relative to Langer's lines. Dauendorffer,[4] Silverman[15] and Hudson-Peacock[11] showed more width than length shrinkage—suggesting then that tension line direction does not account for the differential shrinkage.

Interestingly Dauendorffer, Silverman, and Golomb, who showed the greatest width shrinkage relative to length operated primarily or exclusively on melanoma or benign melanocytic lesion. While Hudson-Peacock showed no overall effect in wound shape when all the planned and actual wound ratios were compared, he performed circular and elliptic excisions (and his elliptical lesion removal was more oval than true ellipses judging by his average specimen size—20 × 15 mm). These observations again raise the question—does pathology itself play a part?

Shrinkage with excision

Most (50–100%) of the shrinkage occurs with excision and prior to fixation. Dauendorrfer[4]100%, Kerns[14] 100%, Golomb[3] 94.2% of total shrinkage, Blasco-Morente[2] 100% of width and 82% of length shrinkage, Davis[1] 80.4% of total, Hudson-Peacock[11] 72% by area, Gregory[5] 50%). This has been explained by Kerns[14] as due to 'intrinsic contractile properties'.

The additional 0–50% of the shrinkage in these studies occurs with fixation. Kerns however showed an approx. 4% length and

Table 3 Previous significant papers looking at skin specimen shrinkage

Paper	Case no.	Type	Site	%Area shrink	%Length shrink	%Width shrink
Sevray M 2020[10]	104	Skin tumours Benign and 78% Malignant	All		17	15
Friedman 2019[9]	252	Malignant (post biopsy) (54% melanoma)	All		NM	14
Blasco-Morente 2015[2]	111	>65% Malignant BCC/SCC			17	9.5
Davis 2010[1]	20	Clinically Malignant	All		21.5	13.1
Blasdale 2010[18]	42	BCC's	TorsoH&N		14	NM
Dauendorffer 2009[4]	82	83% Benign 77% melanocytic	All		16	18
Kerns et al. 2008[14]	97	'mostly' Malignant Tumours excluding infiltrative, sclerotic, nodular	All	16	21	12
Gregory 2003[5]	54	54% Benign +18% melanoma	All	22	22	20
Hudson-Peacock 1995[11]	93	32%Benign+68% Malignant BCC/SCC	All	31	15	20
Silverman 1992[15]	407	Melanoma	All			19.6
Golomb 1991[3]	199	Melanoma	All			20.7

Note: NM, not measured.

width increase with formalin which has been explained as a possible 'rehydration' effect.

Sevray[10] was the only study showing duration of fixation (i.e. time in formalin) to be an independently significant variable. None was shown by Davis.

These findings have led Kerns to state 'the majority of cutaneous shrinkage post excision is because of intrinsic contractile properties of the tissue itself and not due to fixation in formalin' and Dauendorffer[4] to state 'formalin fixation is not the culprit'.

In this study there was an overall approx. 30% shrinkage—20% with excision (i.e. 70% of the total shrinkage occurred with excision) and an additional 11% shrinkage (i.e. accounting for 30% of the shrinkage) with formalin fixation. Significant length and width shrinkage occurred at both stages. Notably however the shrinkage in width with fixation was relatively small (2.6%) when compared to the other percentage changes.

It raises the question—why overall does the shrinkage effect with fixation seem more pronounced in length than width? Does the significant group of studies that go against this trend and show fairly consistent changes in both length and width do so because of their excision patterns as above and/or their pathology? Does formalin disproportionally effect 'normal' tissue?

Tissue pathology and shrinkage

Normal and 'benign' tissue shrinks more than malignant tissue. Excision and processing in lip SCC specimens showed a shrinkage rate at the surgical margin of up to 41% to 47% but the tumour itself showing no significant shrinkage.[16] In oesophageal tumours the upper and lower margins shrunk approx. 68% and 60% respectively with excision and formalin while the tumour shrink approx. 10%.[17]

In skin Hudson-Peacock[11] estimates a 32% shrinkage in benign tumours and 25% in malignant, Gregory[5] 25% shrinkage in benign and 20% in malignant. Sevray[10] though showing no difference in shrinkage with pathology type does show overall specimen shrinkage of 29% but only 21% retraction in the tumour.

Blasdale[18] reported an 11% width shrinkage for tumour tissue in BCC's versus 19% for the tumour free edge. Additionally it should be noted that Blasdale analyses only BCC's, 80% of which are nodular and 93% of the specimens are in the head and neck. On both counts then Blasdale's shrinkage would be expected to be, and indeed is, at the lower end when compared to other studies.

In contrast Dauendorrfer[4] showed an in vivo to ex vivo width shrinkage significantly more important in malignant tumours ($P = 0.02$). The series showing the largest width shrinkages are largely either exclusively melanoma patients as in the cases of Golomb[3] and Silverman[15] or largely benign pathologies as with Dauendorffer who has 83% benign lesions in his series. Gregory has a combination—72% benign or melanoma pathologies (though also specifically identifies more width shrinkage in benign than malignant lesions).

Two mechanisms are postulated as to why these studies show large width shrinkages or similar width to length shrinkages—the amount of pathology in the tissue and the type of pathology. As regards pathology in the tissue there are three variables identified. (a)Different margin widths are required by different pathologies, for example, margins varying from 1–2 mm for BCC's to 10–20 mm for pigmented lesions. (b)Prior biopsy—All the melanoma series had significant numbers of scars from biopsies and possibly even excisional biopsies and so it is postulated that large parts of the specimens will essentially be 'margin' and hence made up of 'normal' tissue (and possibly in situ changes). (c)Excision 'shape'—The variety of excisions—circular, oval, 'pointed' elliptical, makes comparison of length and width measurements difficult due to the varying margin of normal tissue in different axes. Hudson-Peacock, the seeming exception to the 'melanoma' postulate had 32% benign pathologies but 61% BCC's. The series however has mostly small excisions (ave. 20×15 mm) which were tumour plus margin type excisions, that is, oval in shape. This may also go part of the way to explaining why this study along with 'melanoma' studies have length and width shrinkage measurements that are similar. There is a lot more normal tissue in the length of a standard surgical ellipse than in width especially in a standard BCC/SCC excision and hence there is little 'normal' tissue width to shrink. The increase in length shrinkage, may simply be due to the relative abundance of normal tissue relative to pathology—rather than related to skin tension lines as some have suggested. This may be why Blasco-Morente,[2] has noted that with fixation further significant reduction was only in length and not width—There is then plenty of normal tissue length to shrink with both excision and fixation. As pathologic tissue does not shrink as much and the width margin of normal tissue is small, the width only notably shrinks with excision.

As regards the pathology type—Different shrinkage of tumour tissue itself dependent on the specific pathology. Kerns noted that 'as solar elastosis increased, shrinkage decreased'.[14] It may well be that superficial melanoma tissue for example shrinks more than do sclerotic BCC's. Likewise, however, a benign fibrohistiocytoma might be expected to contract as little as an invasive tumour, that is, shrinkage may be more inversely related to degree of dermal sclerosis than pathology per se.

Most studies suffer from relatively small numbers from multiple sites. This study showed no difference with pathology type but this study is very selective with only primary excisions of two invasive skin tumours types, BCC and SCC, considered.

Anatomic site and shrinkage

Anatomic Location appears to be significant. This study was limited to lower leg lesions. It showed no statistical difference in length ($P = 0.08$) by location between the calf and pretibial area. It did however show a statistical difference in width change ($P = 0.014$) between those two sites reinforcing the idea that location is an important variable. It is theorised that this difference is related to the increased deep tissue tethering in the pretibial area as opposed to the calf where the soft tissues have to accommodate some exercise induced muscle enlargement.

Prior studies that show a difference tend to show the least shrinkage in the head and neck. Dauendorffer[4] showed significantly more limb specimen length shrinkage than other sites while more shrinkage was seen in the trunk by Kerns[14] (5% more than head/neck)

and Blasco-Morente[2] (22.8% in trunk specimen length vs. 16.9% in limb, 14.9% in head and neck). Gregory[5] showed a shrinkage difference in both limb (22%) and trunk (25%) as opposed to head and neck (14%). This is also consistent with Gardner[19] who looked at MOH's processed specimens (16.3% for trunk and extremities vs. 10.2% for head and neck). Sevray[10] showed greatest retraction in the upper limb only. Golomb,[3] Hudson-Peacock[11] and Friedman[9] however showed no difference between sites. Greater trunk shrinkage has been attributed by Dauendorffer[4] to a thicker dermis with more collagen and elastic fibres.

This is consistent with basic science studies which tend to suggest that facial skin is less elastic than limbs or torso.[20]

If and how much, simple positional issues, particularly in trunk excisions, may have contributed to apparent skin specimen shrinkage, does not appear to have been considered.

Age and tissue shrinkage

Golomb,[3] Silverman,[15] Gregory[5] and Kerns[14] all showed younger age to be associated with more shrinkage. Golomb[3] showed significant shrinkage with two clear cut-off points—those less than 50 showing the greatest shrinkage and those greater than 60 showing significantly less. This was validated later by Silverman[3] who showed similar width shrinkages of approx. 20% (but significantly 25% for under 50yo, 20% for 50–59yo and 15% for over 60yo) and again by Gregory[5] who showed significantly greater shrinkage in under 60s (26%) as opposed to those over (19%). Gardner[19] endorses the significance of age 60 in MOH's processed surgical skin excisions and argues this relates to both loss of elastic tissue with age especially after the seventh decade but further exaggerated by photodamage[14] and loss of collagen / tensile strength with age.

Kerns also shows age to be significant—shrinkage decreasing by 0.3% per year of increasing age. Hudson-Peacock,[11] while showing no significant specimen shrinkage difference with age, did show a significant age related expansion in the wound itself, produced with excision in the limb and trunk (from 55% expansion in a 20 yr. old to 16% in a 90 yr. old) though not the head and neck.

Other studies[2,4,9,10,18] show no change with age.

This study also showed no change but notes that the average age was 77 (youngest 52, and only 2 persons under 60), so probably falls outside the range previously described as significant in the aforementioned studies. It would however imply that the shrinkage calculated in this study would be anticipated to be at the lower end of the range.

Miscellaneous shrinkage factors

Sex shows no evidence of statistical significance in the studies in which it has been considered[2,3,4,5,10,11] It is not found to be a significant variable in this study.

Prior excision as a variable was specifically excluded from this study. It was not a statistically significant variable in Golomb's study.[3]

Pathology specimen and defect repair

The other variable this study did assess was the issue of 'objective' measurement difference between the pathology specimen length and the sutured defect (using a standard surgical ellipse). An increase of 29% added to the pathology specimen length gave the suture repair length. This is consistent with the paper Gregory[5] who suggested a remuneration correction factor of 1.28.

Conclusion

Studies to date are unanimous that specimens shrink and this shrinkage occurs preferentially with excision rather than fixation.

This study further reinforces this finding. It gives added credence to the idea that anatomical site plays a significant part. The data from other studies tend to also suggest age as an important variable but the elderly sample of this study means this cannot be meaningfully assessed.

Past this however the data is not easily read at face value—multiple surgeons, sites, excision patterns and pathologies mean sample sizes are small and variables often not accounted for. This current study has attempted to quantify skin shrinkage by removing some of these variables and by comparison with prior studies help to clarify apparently contradictory results.

It consequently postulates post excision shrinkage takes place primarily in normal skin. It is largely related to intrinsic contractile properties of normal skin. Formalin also plays a part in normal skin shrinkage but not as much in pathologic tissue.

This raises a further question—if normal tissue shrinks more than the pathologic tissues then is the shrinkage of the pathologic part of the specimen pathology dependent. Do in situ specimens shrink more and sclerotic or invasive pathology less? That is, is the degree of shrinkage inversely proportional to the degree of pathology in the specimen.

It is clear that these questions regarding pathology and the effects of age and site in particular need further work.

Going forward it is suggested studies should specify surgical site more specifically, clarify the pathology type and load (the amount of normal as opposed to pathologic tissue) in the specimen including excision margins and state the excision pattern used.

Acknowledgements

Monika Jones, Data Analyst, Education Development and Research, RACS for direction on statistical analysis. Dalice A. Sim PhD, BioStatistician, University of Otago, for checking the statistics.

Conflict of interest

No financial support was received. No conflict of interest is known. This paper or its data has not been submitted to any other journal for publication or consideration.

References

1. Davis MM, Barry. Surgical versus pathological excision margins—an excision too far. *Eur J Plast Surg*. 2010;**33**:117–20. https://doi.org/10.1007/s00238-009-0384-x.
2. Blasco-Morente G, Garrido-Colmenero C, Perez-Lopez I, et al. Study of shrinkage of cutaneous surgical specimens. *J Cutan Pathol*. 2015;**42**:253–7. https://doi.org/10.1111/cup.12401.
3. Golomb FM, Doyle JP, Grin CM, et al. Determination of preexcision surgical margins of melanomas from fixed-tissue specimens. *Plast Reconstr Surg*. 1991;**88**:804–9. https://doi.org/10.1097/00006534-199111000-00010.
4. Dauendorffer JN, Bastuji-Garin S, Guero S, et al. Shrinkage of skin excision specimens: formalin fixation is not the culprit. *Br J Dermatol*. 2009;**160**:810–4. https://doi.org/10.1111/j.1365-2133.2008.08994.x.
5. Gregory N, Mulvaney M, Pattison T, et al. Shrinkage of skin excision specimens and downcoding. *Arch Dermatol*. 2003;**139**:542–3. https://doi.org/10.1001/archderm.139.4.542.
6. Yao SZ, Nelson K, Fahmy FS. Correlation between operative and histological excision margins for cutaneous squamous cell carcinomas. *J Plast Reconstr Aesthet Surg*. 2014;**67**:e63–4. https://doi.org/10.1016/j.bjps.2013.09.007.
7. Swetter SM, Tsao H, Bichakjian CK, et al. Guidelines of care for the management of primary cutaneous melanoma. *J Am Acad Dermatol*. 2019;**80**:208–50. https://doi.org/10.1016/j.jaad.2018.08.055.
8. MacKenzie Ross AD, Haydu LE, Quinn MJ, et al. The association between excision margins and local recurrence in 11,290 thin (T1) primary cutaneous melanomas: a case-control study. *Ann Surg Oncol*. 2016;**23**:1082–9. https://doi.org/10.1245/s10434-015-4942-0.
9. Friedman EB, Dodds TJ, Lo S, et al. Correlation between surgical and histologic margins in melanoma wide excision specimens. *Ann Surg Oncol*. 2019;**26**:25–32. https://doi.org/10.1245/s10434-018-6858-y.
10. Sevray M, Brenaut E, Grangier Y, et al. Retraction of cutaneous specimens: tumours and margins after surgical excision. *J Clin Pathol*. 2020;**73**:42–6. https://doi.org/10.1136/jclinpath-2019-205988.
11. Hudson-Peacock MJ, Matthews JN, Lawrence CM. Relation between size of skin excision, wound, and specimen. *J Am Acad Dermatol*. 1995;**32**:1010–5. https://doi.org/10.1016/0190-9622(95)91341-6.
12. Ueda M, Saito S, Murata T, et al. Combined multiphoton imaging and biaxial tissue extension for quantitative analysis of geometric fiber organization in human reticular dermis. *Sci Rep*. 2019;**9**:10644. https://doi.org/10.1038/s41598-019-47213-5.
13. Potter GK, Re: Kerns MJJ, Darst MA, Olsen TG, Fenster M, Hall P, et al. Shrinkage of cutaneous specimens: formalin or other factors involved? *J Cutan Pathol*. 2009;**36**:1030. https://doi.org/10.1111/j.1600-0560.2009.01268.x.
14. Kerns MJ, Darst MA, Olsen TG, et al. Shrinkage of cutaneous specimens: formalin or other factors involved? *J Cutan Pathol*. 2008;**35**:1093–6. https://doi.org/10.1111/j.1600-0560.2007.00943.x.
15. Silverman MK, Golomb FM, Kopf AW, et al. Verification of a formula for determination of preexcision surgical margins from fixed-tissue melanoma specimens. *J Am Acad Dermatol*. 1992;**27**:214–9. https://doi.org/10.1016/0190-9622(92)70173-d.
16. Egemen O, Bingöl D, Orman Ç, et al. Quantification of the surgical margin shrinkage in lip cancer: determining the relation between the surgical and histopathologic margins. *J Craniofac Surg*. 2014;**25**:2152–5. https://doi.org/10.1097/scs.0000000000001150.
17. Siu KF, Cheung HC, Wong J. Shrinkage of the esophagus after resection for carcinoma. *Ann Surg*. 1986;**203**:173–6. https://doi.org/10.1097/00000658-198602000-00011.
18. Blasdale C, Charlton FG, Weatherhead SC, et al. Effect of tissue shrinkage on histological tumour-free margin after excision of basal cell carcinoma. *Br J Dermatol*. 2010;**162**:607–10. https://doi.org/10.1111/j.1365-2133.2009.09577.x.
19. Gardner ES, Sumner WT, Cook JL. Predictable tissue shrinkage during frozen section histopathologic processing for Mohs micrographic surgery. *Dermatol Surg*. 2001;**27**:813–8. https://doi.org/10.1046/j.1524-4725.2001.01017.x.
20. Ryu HS, Joo YH, Kim SO, et al. Influence of age and regional differences on skin elasticity as measured by the Cutometer. *Skin Res Technol*. 2008;**14**:354–8. https://doi.org/10.1111/j.1600-0846.2008.00302.x.