Verification of a formula for determination of preexcision surgical margins from fixed-tissue melanoma specimens

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Background: Recently our group reported on the shrinkage of 199 malignant melanoma surgical-excision specimens. In that report, a multivariate analysis revealed that the age of the patient was the only factor that significantly affected the percentage shrinkage of a surgical specimen. In addition, a formula was presented that extrapolates the actual surgical margins (in vivo) from the (contracted) fixed-tissue pathology report measurement and the reported in vivo lesion diameter.
Objective: The goals of this study are to verify that shrinkage of surgical specimens is approximately 20% and that the margin formula can be successfully applied to a different group of patients.
Methods: Four hundred seven patients with malignant melanoma were prospectively enrolled to measure preexcision (outlined with ink) surgical margins, fixed-tissue (contracted) surgical margins, and overall specimen shrinkage.
Results: It is verified that overall shrinkage of cutaneous surgical specimens is approximately 20%. Surgical specimens from patients younger than 50 years of age have approximately 25% shrinkage. Those specimens from patients 50 to 59 years of age have approximately 20% shrinkage and those from patients 60 years of age or older have about 15% shrinkage. The surgical margins predicted by the margin formula were within ±3.5 mm of the actual measured surgical margin 86.5% of the time.
Conclusion: The actual surgical margins (in vivo) of a malignant melanoma can be reasonably estimated from the fixed-tissue pathology measurement via the margin formula. The shrinkage of a surgical specimen is 15% to 25% depending on the patient's age.
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For many decades the accepted method of treatment of all primary malignant melanomas (MMs) was "wide and deep surgical excision." Fortunately, in the past two decades it has been learned that this type of potentially disfiguring surgery is unnecessary for thin melanomas (≤1.0 mm Breslow thickness).[1-12] In addition, whereas in the past a 5 cm margin was the standard treatment of MM more than 1 mm thick,[13] the practice now is to remove no more than 3 cm margins for these tumors.[5, 6, 8, 11] These changes in practice have evolved from the results of several prospective and retrospective studies on the relation between surgical margins and survival rates of patients treated surgically for stage I MM.[1-3, 5, 7, 14] Two of the referenced prospective studies were published as interim reports and are still in progress.[2, 12] In addition, another prospective study is in progress (Intergroup Melanoma Committee of the National Cancer Institute). The ultimate goal of these types of studies is to delineate the minimum margins necessary to treat MMs of all thickness ranges without decreasing survival.

One problem with the conclusions of several of the retrospective margin studies is that the "surgical

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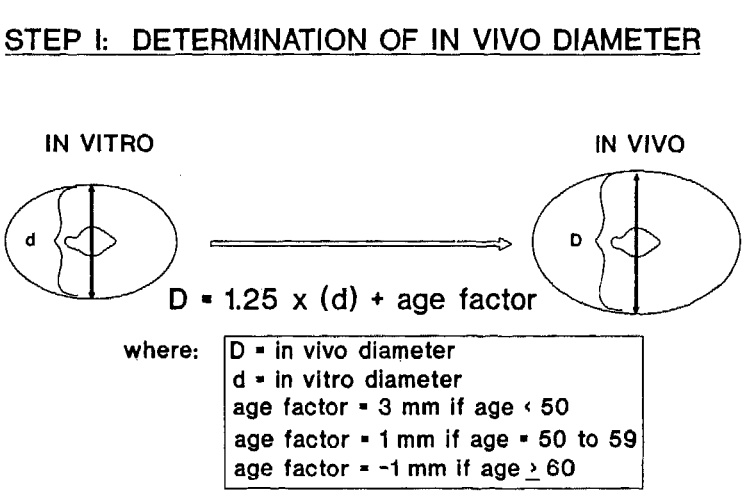

Fig. 1. A two-step formula (old formula) for the determination of the width of the in vivo surgical margins.

margins" were measured from the fixed-tissue specimens.[1, 5-7] Although these registries meticulously documented up to 300 parameters related to the patient/lesion history, family history, treatment modality, and histologic characteristics of the MM, they did not record the preexcision (in vivo) surgical margin measurements. The fixed tissue is a recoiled, contracted specimen and does not reflect the actual size of the in vivo specimen accurately. In fact, it underestimates the true specimen size and surgical margins by as much as 29%, according to Elder et al.[3]

We recently quantitated the amount of tissue shrinkage that occurs from excision to tissue fixation on a group of 199 MMs operated on by one of us (F. M. G.).[15] We learned that the average specimen shrinks about 20% from excision to fixation, but the amount of shrinkage is dependent on the age of the patient. Those patients younger than 50 years of age had the most shrinkage, whereas those older than 60 years of age had the least shrinkage.

With this information we derived a formula that allows one to calculate the in vivo preexcision surgical margins from the fixed tissue measurements if the size of the in vivo lesion is known.[15] This formula worked well for the specimens from which it was derived. The purpose of the present study is to verify the accuracy of the formula by applying it to a different group of patients than those used in the initial study.

METHODS AND RESULTS

Since 1982, one of us (F. M. G.) has been meticulously documenting the size of surgical specimens

Table I. Shrinkage of the surgical specimens

	Original study ($N = 199$)	This study ($N = 407$)
Mean pre-excision specimen size (in vivo) (mm)*	32.3	41.9
Mean fixed tissue specimen size (in vitro) (mm)*	25.5	32.5
Overall mean % shrinkage: (all age groups)†	20.7	19.6
Percentage shrinkage: age up to 49 yr	24.9	23.7
Percentage shrinkage: age 50-59 yr	20.9	18.6
Percentage shrinkage: age 60 yr or greater	15.5	15.7

*Minimum diameter.
†The mean percentage shrinkage was determined by calculating the percentage shrinkage for each specimen and taking the mean of these calculated shrinkages.

before excision (in vivo) and immediately after excision. Precise cutaneous measurements of the following were obtained with a millimeter ruler at the time of the operation on relaxed skin: (1) the minimum and maximum diameters of the entire surgical specimen to be excised, (2) the minimum and maximum diameters of the lesion or of the linear excisional biopsy scar to be excised, and (3) the preexcision minimum and maximum surgical margins. In each case a fixed-tissue measurement was done by a pathologist or a pathology technician.

Previously, 199 specimens that were excised and had measurements for in vivo (preexcision) specimen diameter, postexcision (but before formalin fixation) specimen diameter, and fixed-tissue (after formalin fixation) specimen diameter (all measured by F. M. G.) were reported.[15] These data were entered into a multivariate analysis. Only the patient's age and the in vivo diameter of the surgical specimen were found to independently influence the amount of shrinkage. The anatomic site from which the specimen was excised, whether or not an excisional biopsy was done, and the sex of the patient did not significantly affect tissue shrinkage after the patient's age was accounted for. On the basis of the measurements of the 199 specimens, a formula was derived to calculate the actual excisional margins (in vivo) knowing the in vivo lesion diameter and the pathology specimen diameter.

This equation permits calculation of the in vivo specimen diameter and the in vivo surgical margins with a two-step process (Fig. 1). The formula was previously found to predict the measured margin 92.4% of the time within ±3.5 mm.

In the present report the formula is tested on a new group of 407 MM surgical specimens not used in deriving the above formula. In this study the mean age of the patients was 52 years (range 14 to 86 years). Of the 407 excisions 271 were of intact lesions and 136 were of linear scars resulting from previous excisional biopsies.

In the original study, the formula derived was the one that best fit the data for the 199 specimens. One unsettling aspect of the formula was the inclusion of a constant (+3 mm, +1 mm, or −1 mm) depending on the patient's age. Although this formula with a constant provided the best method to approximate tissue shrinkage for the original 199 patients, we were concerned that it may not work as precisely on a different group of MMs with larger or smaller specimens. Later in this section we propose a shrinkage formula that circumvents the use of a constant and therefore may have more universal application (henceforth: original formula = old formula; new formula = formula to be proposed).

Because with multivariate analysis the patients in each age group were found to have a different percentage of shrinkage, a more teleologic approach (than the use of an age-factor constant) is to calculate the mean percentage shrinkage for each age group and use that percentage for each age group to calculate the in vivo specimen size from the fixed-tissue specimen (instead of via step one in the original formula). Table I demonstrates the overall mean percentage shrinkage and the mean percentage shrinkage by patient age group for the specimens previously reported and for the verification specimens. The overall shrinkage in the original 199 specimens was 20.7% versus 19.6% in this group of 407 specimens. Likewise, the specimen shrinkage in each of the three patient age groups has remained fairly uniform (Table I). The new formula utilizes the mean-percentage shrinkage, by age group, found in the previously reported 199 specimens. For patients younger than 50 years of age approximately 25% shrinkage occurred; for patients between 50 and 59 years of age approximately 20% shrinkage occurred; and for patients older than 60 years of age approximately 15% shrinkage occurred. So, for example, a 100 mm large specimen on a 35-year-old

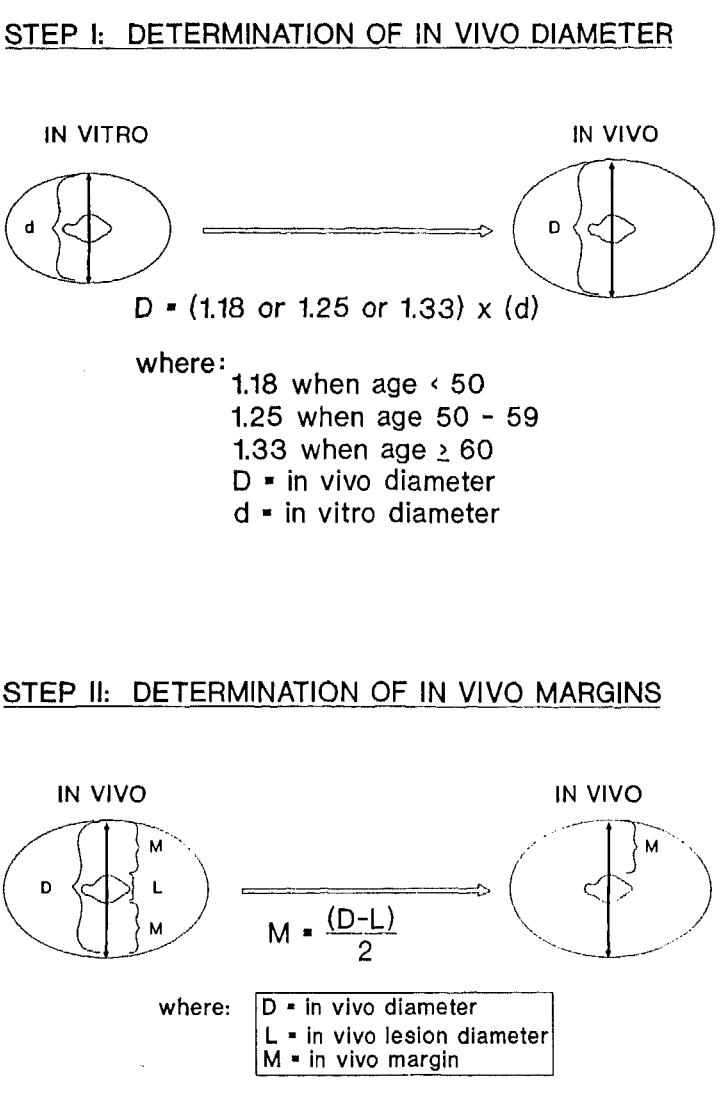

Fig. 2. A two-step formula (new formula) for the determination of the width of the in vivo surgical margins.

person would shrink 25% to 75 mm. Simple algebra reveals that 25% shrinkage translates to approximately a 1.33% "reexpansion factor." Likewise, 20% shrinkage translates to approximately a 1.25% "reexpansion factor," and finally 15% shrinkage translates to approximately a 1.18% "reexpansion factor."

The new formula is as follows:

Step 1: D = (1.33 or 1.25 or 1.18) × d
(1.33 for age <50)
(1.25 for age 50 to 59)
(1.18 for age ≥60)

Step 2: M = (D - L)/2

where D = in vivo specimen diameter in millimeters, d = in vitro specimen diameter in millimeters, M = calculated in vivo surgical margin, L = actual measured in vivo lesion diameter. The new formula is depicted in Fig. 2.

Table II contrasts the calculated surgical margin with the old and new formulas against the actual measured surgical margin in the 184 cases with accurate in vivo margin measurements from the first study and for the 339 cases with accurate in vivo margin measurements in this verification study. It is shown that both formulas accurately calculate the in vivo margins in the original and verification patients.

DISCUSSION

The results of this verification study show that the shrinkage of human tissue after surgical excision is quantifiable. This present study confirms the finding in our previous study that overall tissue shrinkage is

Table II. Accuracy of calculated preexcision surgical margins versus the true measured margins

Calculation method used	Original patients ($N = 184$)	Verification patients ($N = 339$)
Old formula*	92.4% of cases within ±3.5 mm	84.4% of cases within ±3.5 mm
New formula†	90.8% of cases within ±3.5 mm	86.5% of cases within ±3.5 mm

*Old formula: Step 1: D = 1.25 × (d) + Age Factor; Step 2: M = (D − L)/2 where D = in vivo specimen diameter in millimeters, d = in vitro specimen diameter in millimeters, M = calculated in vivo surgical margin, L = actual measured in vivo lesion diameter. Age factor +3 for patients <50 years old; +1 for patients between 50 and 59 years old; and −1 for patients 60 years old or older.

†New formula: Step 1: D = (1.33 or 1.25 or 1.18) × d, (1.33 for age <50), (1.25 for age 50 to 59), (1.18 for age ≥60); Step 2: M = (D − L)/2 where D = in vivo specimen diameter in millimeters, d = in vitro specimen diameter in millimeters, M = calculated in vivo surgical margin, and L = actual measured in vivo lesion diameter.

approximately 20% (Table I). However, despite a mean overall shrinkage of 20% in both studies there is variation between patients. Some of this variation is explained by the multivariate analysis in our previous study that showed the patient's age to be an independent predictor of shrinkage. In fact, as Table I demonstrates, the present study found that patients younger than 50 years of age have about 25% specimen shrinkage; patients between 50 and 59 years of age have about 20% shrinkage, and those 60 years old or older have about 15% shrinkage.

Besides specimen shrinkage being quantifiable, it is also shown that preexcision surgical margins can be calculated reasonably well when pathologists' fixed-tissue measurements are used. When the old formula was used on the 339 specimens in this study with accurate recorded margin measurements, it worked well in most instances. In fact, 84.4% of the cases had a calculated margin within ±3.5 mm of the actual measured margin. This is in contrast to the 92.4% concordance in the specimens from which the old formula was derived. It is not surprising that a formula that is derived from a specific group of patients would work better on that group of patients than on a different group of patients.

The new formula was within 3.5 mm of the actual measured margin 90.8% of the time for the original patients studied. For the patients in the verification study it was 86.5% of the time within 3.5 mm of the measured margin. In fact, for the patients in the verification study the new formula was slightly more precise than the old formula (Table II).

As discussed previously, the old formula contains a constant that was derived from a group of patients with an average specimen size of 32.3 mm. In the verification study, with an average specimen size about 30% larger than in the original study, the old formula is not as accurate in calculating margins as in the original 199 patients from which it was derived. In fact, as one might expect, the new formula, which utilizes a more logical approach (a shrinkage-percentage factor), calculates margins more accurately than the old formula for the patients in the verification study.

In some large registries (e.g., the New York University Melanoma Cooperative Group) a fixed-tissue margin is reported.[16] In this instance the size of the in vivo lesion does not need to be known; simply the measured in vitro margin needs to be multiplied by either 1.33, 1.25, or 1.18 depending on the patient's age. For example, a reported 8 mm fixed-tissue margin in a 55-year-old person would translate to a 1 cm in vivo surgical margin (8 mm × 1.25 = 10 mm or 1 cm).

Surgical specimen shrinkage appears to be reasonably consistent within age groups. In the future, if pathologists would report in vitro minimum fixed-tissue surgical margin measurements, the in vivo margin measurements could be calculated readily without knowledge of the lesion size in vivo. Frequently, in vivo lesion size is either not available or not measured precisely. Thus in vivo preexcisional margins could be easily calculated with knowledge only of the fixed-tissue margin measurements. In fact, if our shrinkage-percentage findings are duplicated by other groups, calculated in vivo surgical margin measurements could be included as part of the routine pathology report of excised MM.

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