Original Contribution

PREOPERATIVE MEASUREMENT OF THICKNESS OF CUTANEOUS MELANOMA USING HIGH-RESOLUTION 20 MHZ ULTRASOUND IMAGING: A MONOCENTER PROSPECTIVE STUDY AND SYSTEMATIC REVIEW OF THE LITERATURE

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Abstract—Histologic measurement of the thickness of melanoma is a major prognostic factor and governs the size of the surgical excision (1 cm for melanomas less than 1 mm thick, 2 cm for melanomas thicker than 2 mm and 3 cm beyond 4 mm). To determine whether high-resolution ultrasound can be used to predict surgical margins and, thus, to operate on patients in a single procedure avoiding further re-excision, we performed a systematic review of studies published from January 1987 to June 2007 and a prospective study. The systematic review selected 14 studies comparing histologic and ultrasound measurements and showing correlation coefficients generally greater than 0.9. Data available from 7 of the 14 studies (total 869 patients) showed predictive values of adequate margins in at least 72% of lesions using preoperative measurement of ultrasound thickness. The prospective study included 31 patients referred with a primary melanoma from March 2005 to March 2007. Ultrasound measurement of thickness was possible except for thin melanomas (<0.4 mm) in areas with marked photoaging, in the plantar zone, and in the case of very thick melanomas exceeding the explored depth (7.6 mm). The average thickness was 1.96 mm measured by ultrasound (SD: 2.15) and 1.95 mm by histology (SD: 2.62) and the Bland and Altman graph showed moderate agreement between ultrasound and histology. Limits of agreement were estimated at –1.4 and +1.1, corresponding to relative limits of agreement of –40 to +80%. Ultrasound predicted appropriate margins (1, 2 or 3 cm wide according to sonometric thickness) in 26 of the 31 subjects (84%, 95% CI 66–95). Preoperative high-resolution ultrasound is a noninvasive examination that can help in choosing appropriate surgical margins and should reduce the need of partial or excisional biopsy before surgery, and the need for further re-excision. (E-mail: machet@univ-tours.fr) © 2009 World Federation for Ultrasound in Medicine & Biology.

Key Words: Skin, Melanoma, Ultrasound, Breslow thickness, Pathology, Surgical margins, Agreement.

INTRODUCTION

The maximum thickness of a melanoma is a major factor prognostic of metastatic dissemination and governs the size of surgical margins. The National Institutes of Health (NIH) consensus recommends a 5 mm margin for all in situ melanomas but this can be inadequate in a large percentage of cases, especially lesions occurring on the head and neck or hands and feet (Cook 2003). According to both French and British Consensus reports (Négrier et al. 2005; Roberts et al. 2002), a margin of 0.5 cm is necessary for in situ melanomas except on the face and a margin of 1 cm is necessary for tumors of 1 mm thickness or less and for in situ melanomas on the face. Although the impact on overall survival has not been demonstrated, wider resections are recommended for melanomas thicker than 1 mm to decrease the risks of local recurrence (Lens et al. 2002). Thus, the recommended margins are 1 to 2 cm for tumors between 1.01 and 2 mm, 2 cm for tumors between 2.01 and 4 mm and 3 cm for tumors thicker than 4 mm (Négrier et al. 2005; Roberts et al. 2002). According to these recommendations, when a pigmented lesion is suspected of being a melanoma on clinical examination, excisional biopsy is usually recommended with a margin of
2–3 mm. If the histologic examination confirms the diagnosis of melanoma, surgical removal is then carried out with margins depending on the maximum thickness measured with a micrometer on the histology slide (Breslow et al. 1970).

Noninvasive preoperative measurement of the maximum depth of a melanoma would be valuable, permitting choice of appropriate surgical margins. The traditional ultrasound equipment used for medical imaging operating at 7.5 MHz does not allow sufficiently precise measurement because the resolution is inadequate (Ulrich et al. 1999). As several studies have previously shown that ultrasound examination using 20 MHz allowed preoperative assessment of melanoma thickness that correlated well with histologic measurement (Hoffmann et al. 1992, 1999; Dummer et al. 1995; Tacke et al. 1995; Lassau et al. 1999; Serrone et al. 2002), our main aim was to check whether the use of 20 MHz ultrasound imaging made it possible to measure melanoma thickness in a sufficiently precise way to choose the appropriate surgical margin. We, therefore, carried out a prospective study comparing histologic and ultrasound thicknesses in a consecutive series of subjects referred with primary cutaneous melanoma not previously removed surgically and we performed a systematic review of the literature to analyze the causes of error and to determine the impact of preoperative ultrasound imaging on the surgical management of melanoma.

**METHODS**

**Subject selection criteria**

From March 2005 to March 2007, all the patients referred to our department for suspected cutaneous melanoma that had not been removed surgically were offered cutaneous ultrasound imaging before surgical removal. The study was approved by the local ethics committee.

The inclusion criteria included suspected primary cutaneous melanoma following clinical and dermatoscopic examination or proven melanoma following partial biopsy providing the pathology diagnosis of in situ or invasive cutaneous melanoma also allowing ultrasound imaging of the remaining lesion. All histologic subtypes of melanoma were eligible for inclusion, including those that were ulcerated or regressive. Subjects with lesions whose histologic examination later showed that it was not a primary cutaneous melanoma or cutaneous metastasis of melanoma were excluded, as were patients referred after having melanomas completely removed by excisional biopsy, mucosal melanoma and patients with pigmented lesions which were not clinically suggestive of melanoma.

**Ultrasound imaging**

Real-time high-resolution 20 MHz ultrasound imaging equipment (Dermcup 2020; Atys Médica, Soucieu en Jarrest, France) was used with an axial resolution of 80 μm and lateral resolution of 250 μm and maximum measurable depth of 7.6 mm (Berson et al. 1999; Machet et al. 2006).

A standard echographic gel was used as coupling agent between the skin surface and the probe. Minimal pressure was applied to preserve the thickness and echogenicity of the lesion. The linear probe was held manually, maintained perpendicular to the skin surface and moved over the skin surface to provide acquisition of 10 images per second and screening of the entire lesion. Four examiners participated in the study; two of them had little experience (2 days) of ultrasound examination. Examinations were performed by a single examiner for any given lesion, which was scanned in at least two perpendicular directions (transverse and sagittal). We compared the internal echogenicity of all lesions using standard ultrasound terminologies and criteria for isoechoic, hypoechoic or hyperechoic. We also characterized the pattern of internal echoes using standard ultrasound terminology and criteria as homogeneous and heterogeneous. The limits of the lesion and the demarcation from normal skin were studied. It was possible both to store a sequence of images, and to visualize them on the screen. Second, the thickness was measured on a vertical axis perpendicular to the surface, from the skin surface to the deepest point of the lesion, using an electronic caliper. At least three sonometric thicknesses were measured for each lesion and the greatest depth was used for comparison with the greatest depth measured on the histology slide (Breslow thickness). No intra- or interobserver variability study was carried out.

**Excision and pathology study**

The lesions were removed either with a margin according to the sonographic thickness when the clinical diagnosis was unambiguous or partial biopsy had confirmed the diagnosis or with a few millimeters margin when the diagnosis was not certain or when the surgeon did not want to remove with wide margins without histologic confirmation of melanoma (Fig. 1). Then, excision lesions were fixed in formaldehyde and processed routinely. Immunohistochemical study was performed with PS-100 and HMB-45 (Dako France SAS, Trappes, France) when the diagnosis of melanoma needed to be confirmed with PS-100 or HMB-45 staining or to better appreciate dermal invasion in melanoma arising on melanocytic nevus. The histology report was standardized and included Breslow thickness, Clark level, ulceration, regression, peritumoral infiltrate, vascular invasion and rate of mitosis. As superficial dermal elastosis is associated with a superficial hypoechoic band localized in the
upper dermis, the presence of elastosis was noted as absent, moderate or marked. Breslow thickness was measured at initial diagnosis by a pathologist who was blinded to the ultrasound thickness measurement. This measurement was performed with a micrometer on a histology slide, with the vertical axis perpendicular to the skin surface. The maximum value indicates the Breslow thickness (Breslow 1970). All pathology slides were re-examined by a pathologist who was blinded to the previously measured Breslow thickness and the sonometric thickness. In the case of marked discordance (>1 mm) between histometric and sonometric measurements, new slides were requested by the dermatologist. This second series of measurements was used for the interobserver histometric agreement study.

**Statistics**

Thickness measurements of each lesion were compared on the basis of the Breslow thickness values of the initial pathology report. Agreement between sonographic and histometric measurements was assessed by fitting the Bland and Altman graph (Bland and Altman 1986). Such a graph plots individual differences between two measurements vs. individual mean of these two measurements. It allows assessing whether a systematic bias exist, whether measurement errors increases with means (which then suggests applying a log-transformation of data prior analysing them) and which finally allows to assess the “limits of agreements” which have to be compared with clinically important difference (i.e., in case limits of agreement are smaller than clinically important differences, the two methods can be used interchangeably). We also estimated a weighted Kappa coefficient. Agreement between both histometric measurements was also assessed by the Bland and Altman graph.

**Systematic review**

A systematic review was carried out on PubMed from January 1987 to 30 June 2007 to allow comparison with previous studies using the following key words:

Fig. 1. Synopsis of study. Sonographic thickness was measured in all patients and surgery was planned as a single intervention without biopsy in 15 cases and with partial biopsy in nine cases. Two patients with metastatic disease had limited resection. Five patients had a few millimeters in sano resection and further re-excision. Excessive ° means that in two patients planned margins were overestimated from sonographic thickness but were correct on Breslow thickness because of a large in situ lateral component in facial melanoma. Insufficient * means that sonographic thickness was concordant with Breslow thickness but margins were insufficient because of a wide in situ lateral component in vulvar melanoma. Finally, 20/24 patients (83%, 95% CI 63–95) were operated on in single interventions with appropriate margins and appropriate margins were predicted by ultrasound thickness for 26/31 patients (84%, 95% CI 66–95).
melanoma, ultrasound, preoperative and thickness in the last 20 years. Studies mentioning at least the correlation coefficient and using high-frequency (20 MHz and above) were selected. From these studies, we calculated the numbers of subjects for whom surgical margins had been adequately predicted by preoperative ultrasound imaging, when available.

RESULTS

Subjects

Two hundred seven new patients with melanoma were referred in this 2-year period. However 176 lesions had been excised before referral. Thirty-one lesions from 31 subjects (10 women, 21 men, mean age 64 years, range 35–85 years) were included. Thirteen lesions were on the trunk, two on the upper limbs, eight on the lower limbs, seven on the face and one in the genital area. Two lesions from two subjects were excluded, corresponding to dysplastic nevus after histologic examination.

Ultrasound imaging

All 31 lesions were examined and measured by one of the four examiners. Twenty-eight melanomas were visualized with ultrasound; all were hypoechoic with a homogeneous structure overall and generally well-delimited from normal skin (Fig. 2). However, we were not able to characterize the lesion from surrounding normal skin in three cases and, in two cases, the maximum depth of the lesion was beyond the maximum depth explored by the device (7.6 mm).

Pathology

The characteristics of histologic types of melanoma and locations are shown in Table 1. Histologic thickness measurements generally showed good interobserver agreement for all the 31 lesions except for a lesion \( > 10 \) cm wide on the arm with an initial Breslow thickness measurement of 3.8 mm and remeasurement of 6.5 mm on new slides, making a difference of 2.7 mm. For the other lesions, the differences ranged from –0.34 to +0.20 mm. The mean

<table>
<thead>
<tr>
<th>Subjects</th>
<th>( N = 31 )</th>
</tr>
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<tr>
<td>Female</td>
<td>10</td>
</tr>
<tr>
<td>Male</td>
<td>21</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean 64</th>
<th>Range 35–85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trunk</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Limbs</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Genitalia</td>
<td>1</td>
<td></td>
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</tbody>
</table>

<table>
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<tr>
<th>Histologic subtypes</th>
<th>SSM 16</th>
<th>LMM 7</th>
<th>ALM 4</th>
<th>NMM 1</th>
<th>Unclassified 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histologic features</td>
<td>Inflammatory infiltrate 17</td>
<td>Elastosis 7</td>
<td>None 7</td>
<td>Breslow thickness (mm) Mean 1.96 SD 2.15</td>
<td>Ultrasound thickness (mm) Mean 1.95 SD 2.62</td>
</tr>
</tbody>
</table>

![Fig. 2. Ultrasound imaging of two melanoma lesions. Lesions were generally hypoechoic and well demarcated from the dermis.](image-url)
difference between histometric thicknesses was –0.11 mm and the limits of agreement were estimated at –1.09 and +0.85 mm. After removing the discordant case re-examined on new slides, the mean difference between histometric thicknesses was –0.03 mm and the limits of agreement were estimated at –0.30 and +0.23 mm (Fig. 3).

Ultrasound thickness vs. histologic thickness

In four cases, the measurements were identical. Ultrasound over-estimated melanoma thickness in 17 cases and under-estimated it in 10 cases. The mean difference between ultrasound thickness and histologic thickness was +0.01 mm and the limits of agreement were estimated at –1.85 and +1.87 mm. After removing the two subjects with melanomas thicker than 7.6 mm, resulting in a systematic underestimation of thickness measured with ultrasound, the mean difference between ultrasound and histometric measurements was +0.16 mm and the limits of agreement were estimated at –1.36 and +1.67 mm. In 18 cases, the absolute difference was lower than 0.31 mm. The Bland and Altman graph was fitted for raw data (i.e., without any transformation) (Fig. 4). Because there appears to have a relationship between measurement difference and measurement mean (i.e., the measurement difference increases as the mean increases), a log-transformation was applied before re-plotting the Bland and Altman graph, as usually done (Bland and Altman 1996) (Fig. 5). The latter graph showed no systematic bias between the two methods. Limits of agreement were estimated at –1.4 and +1.8, which corresponds to relative limits of agreement of –40% to +80%.

Analysis of main differences between sonographic and histometric measurements in our series

When marked difference between ultrasound and histologic thickness was evidenced, the histologic slides were reviewed with the pathologist in order to understand the discrepancies. Two very thick melanomas (Breslow thickness 8.7 and 10 mm) were beyond the maximum depth explored by the device (7.6 mm). In another case located on the elbow, the ultrasound measurement was 4 mm. On histologic examination, the lesion was ulcerated and displayed marked signs of regression, with inflammatory infiltrate and fibrosis, and the Breslow thickness was 6.2 mm. One 10 cm-wide melanoma measured 5.6 mm on ultrasound compared with 3.8 mm for Breslow thickness but the histologic measurement on the second examination revealed a Breslow thickness of 6.5 mm.

Two thin facial melanomas with Breslow thickness of 0.4 and 1 mm measured 1.7 and 2.7 mm on ultrasound (difference 1.3 and 1.7), respectively. They both displayed marked dermal elastosis and marked inflammatory infiltrate was present in one. An in situ melanoma located in the plantar area was erroneously measured at 1.55 mm, partly because the thick stratum corneum resulted in a very large entry echo and a thick hypoechoic band seen beneath the stratum corneum and partly because there was marked dermal fibrosis with an inflammatory infiltrate.
Peritumoral reactions such as inflammatory infiltrate, fibrosis, neovascularization and elastosis in the surrounding dermis are believed to overestimate thickness when measured with ultrasound since all of these dermal modifications appear as hypoechoic. However, after removing the two lesions thicker than 7.6 mm, we compared the mean difference between ultrasound and histometric measurements of lesions with marked inflammatory infiltrate, regression, fibrosis or dermal elastosis with lesions, which displayed none of these histologic features. The mean difference was $1.18 \text{ mm SD 0.87}$ ($n=23$) vs. $1.10 \text{ mm SD 0.23}$ ($n=6$).

Recent cicatricial areas, which were hypoechoic, were not easily distinguishable from the surrounding melanoma. Partial biopsy was performed before ultrasound examination in six cases, Breslow thickness being measured in four cases. The examiner who performed the ultrasound examination was not blinded to the Breslow thicknesses in two cases. Agreement between ultrasound and histometric measurements was good in five cases (differences ranging from $-0.21$ to $+0.25$) and poor ($+1.7$) in one case.

**Surgical margins**

Ultrasound measurement alone was able to predict appropriate surgical margins in 23/31 melanoma lesions [74%, 95% CI 55–88] (Table 2). The weighted Kappa score was estimated at 0.71 [95% CI 0.54–0.88]. Surgical excision was planned according to ultrasound thickness in 29 cases (six of which had had partial biopsy before ultrasound and three after), the two remaining lesions were intentionally removed with insufficient margins despite the ultrasound thicknesses because of multiple loco-regional metastases in one subject and visceral metastases in the other. Of the 29 remaining lesions, 24 were removed surgically according to sonographic thickness and three with margins greater than might have been necessary because of overestimation of sonographic thickness. However, in two of these three subjects, this was not detrimental since the margins proved finally to be appropriate to the *in situ* lateral component of the tumor after histologic examination. Five lesions were removed with margins of a few millimeters and then proposed for re-excision with appropriate margins. One subject with a Breslow thickness of 0.2 mm refused. Four of these five subjects could have been operated on with appropriate margins according to preoperative sonographic measurements.

**Systematic review**

The literature review identified 18 studies focusing on correlation between sonometric and histometric thickness in melanoma subjects from 1987 to June 2007 using 20 MHz ultrasound apparatus. All studies selected reported a linear correlation between sonographic and histometric measurements (Table 3). Correlation coefficients ranged from 0.88 to 0.97 (median 0.95, mean 0.94, SD 0.02). To allow comparison of our study with the literature findings, the thickness measured by ultrasound was plotted in relation to Breslow thickness (Fig. 6) and the Pearson correlation coefficient was calculated (0.94), although we acknowledge that the use of this coefficient is in fact inappropriate to demonstrate agreement of measurements with two methods (Lee et al. 1989; Kraemer and Feinstein 1981). Two studies were not selected because they reported measurements of melanoma and nevus thickness for the whole group (Hoffman et al. 1992; Gambichler et al. 2007).

From seven of these studies with a total of 1611 melanoma lesions, it was possible to determine the number of lesions that were adequately classified according to histologic subgroups (Table 4).

**DISCUSSION**

The systematic review showed a strong correlation between sonometric and histometric thickness of melanoma lesions in the 14 studies selected. However, the methodology used was based on the calculation of the correlation coefficient. As previously reported (Tacke et al. 1995; Pellacani et al. 2003; Gambichler et al. 2007), we used the Bland and Altman graph, which is more appropriate to demonstrate agreement of measurements of tumor thickness with the two techniques. Despite a correlation
coefficient of 0.94 in our series and generally greater than 0.9 in the published studies, marked differences between the two techniques were evidenced in our series. The design of our study was very practical, with several examiners, some of whom were not experienced in ultrasound examination and included subjects with large and thick melanomas. It is, thus, not very surprising that the Bland and Altman graph showed evidence of greater differences between sonometric and histometric measurements than in other studies (Tacke 1995; Pellacani 2003; Gambichler 2007). These differences raised concerns about the accuracy of ultrasound measurement for predicting adequate surgical margins since limits of agreement were estimated at –1.4 and 1.8. Nevertheless, in our series it was possible to predict appropriate margins in 84% of the subjects [95% CI 66–95] according to the French and British Consensus reports. This was confirmed by the systematic review which identified 14 studies, of which seven (total 869 subjects) showed predictive values of adequate margins in at least 72% of the lesions using preoperative ultrasound thickness measurement (Table 4).

Causes of errors in measuring thickness

The main aim of the study was to assess the practical value of preoperative measurement of thickness when choosing surgical margins. In this consecutive series of 31 subjects, nine of whom had partial biopsy and, after excluding two subjects with metastases who were operated on with minimal margins, at least 20/24 subjects who were operated on according to sonographic thickness had appropriate margins in the initial intervention without need for re-excision. Of the five lesions excised with minimal margins, four could have been removed appropriately according to sonographic thickness. However, overestimation of thickness (average 0.16 mm in this series after excluding the two melanomas of thickness 7.6 mm) may have caused problems for the surgeon, particularly when he had to chose between 1, 2 or 3 cm margins for lesions with thicknesses measured close to recommended limits of surgical groups (i.e., close to 1 mm, to 2 mm and to 4 mm). This was not often the case in our series but may explain some of the “misclassifications”. For example, which margin should be chosen when a melanoma measures 2 mm (two cases) or 4 mm (one case) on ultrasound? When the location is not difficult, and if the patient agrees, a wider margin is preferable. In other cases, definite margins can be chosen after limited resection and measurement of Breslow thickness. The main problem we encountered was location on plantar and facial sites. In one case, we were unable to visualize a thin plantar melanoma correctly with ultrasound (Breslow 0.8 mm), in another case we overestimated an in situ plantar melanoma, resulting in excessive surgical margins and finally correctly measured a thick melanoma (6.4 mm with ultrasound, Breslow thickness 6.6 mm). Another problem was with lesions on the face. The melanomas were generally thin and associated with actinic damage resulting in a subepidermal hypoechoic band.
and thicknesses were mostly overestimated (4/6) with ultrasound (range 1.023 to 1.169). One was underestimated (−0.25) and the other was identical. Serrone et al. (2002) reported that sonographic measurement was poorly correlated with histologic measurement for melanomas up to 0.75 mm in thickness and was responsible for misclassification in 38% of these cases. This is in fact not a real problem in Europe since the recommended surgical margin for in situ melanoma of the face is 1 cm, i.e., the same as for melanomas of Breslow thickness less than 1 mm. However, the recommended margins for in situ facial melanoma remain 5 mm in the United States, although some authors have recommended wider margins because of high rates of incomplete excision and further recurrence with standard 5 mm margins (Bricca et al. 2005, Jejurikar et al. 2007; McKenna et al. 2006). For our cases, because of wide in situ lateral extension of the facial melanomas, overestimation was not detrimental to subjects and surgical margins were not excessive. This explains why only 21 lesions were well classified in histometric groups preoperatively (Table 2). If we add the melanomas of the face that required a 1 cm margin, 23 (74%) lesions were well classified.

Can initial wide excision following sonographic measurement of thickness affect sentinel lymph node biopsy (SLNB)?

SLNB is not recommended as standard treatment for melanoma patients in France or the United Kingdom but is routinely performed in patients with melanoma thickness > 1 mm in other countries, including the United States. The migration of the tracer and identification of the first node may theoretically be disturbed if a narrow or (even more so) a wide excision has been performed prior to SLNB. In a series of 104 patients who underwent wide excision prior to SLNB, the incidence of positive nodes, number of positive nodes and the outcome after follow-up of 51 months were similar to those of 1291 patients who had SLNB just before wide excision of melanoma (Gannon et al. 2006). This series included patients with lesions located on the trunk and near the median line. Thus, wide excision prior to SLNB does not appear to be detrimental and can be performed, except in patients requiring complex flap reconstruction because no study has demonstrated correct identification of the sentinel node in this particular setting. Moreover, measuring melanoma thickness with ultrasound may help in planning SLNB and wide excision in a single operation (Gambichler et al. 2007).

Can ultrasound help to distinguish melanoma from atypical nevi?

Sonographic measurement of melanoma arising on a pre-existing nevus, especially when the nevus is thicker than the melanoma, may overestimate thickness (Hoffmann et al. 1999). This occurred in only one subject in our series but the nevus was as thick as the melanoma and there was no disagreement (0.05 mm) between the measurements. In this case, as in two other excluded subjects with dysplastic nevus and no melanoma, it was not possible to differentiate between a benign melanocytic nevus and melanoma with ultrasound imaging. Although we agree with some studies, which have demonstrated that ultrasound imaging may help to differentiate benign pigmented lesions such as seborrheic keratosis pigmented basal cell carcinoma or dermal nevus from melanoma

Table 4. Prediction of adequate surgical margins by ultrasound thickness in the literature

<table>
<thead>
<tr>
<th>First author (year of publication)</th>
<th>Number of lesions</th>
<th>Histometric groups (mm)</th>
<th>Number of well classified lesions</th>
<th>PV %, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gassenmaier (1990)</td>
<td>73</td>
<td>19 20 24 63</td>
<td></td>
<td>86, 76-93</td>
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<tr>
<td>Dummer (1995)</td>
<td>332</td>
<td>106 73 77 256</td>
<td></td>
<td>77, 74-80</td>
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<tr>
<td>Ulrich (1999)</td>
<td>108</td>
<td>38 22 21 92</td>
<td></td>
<td>85, 77-91</td>
</tr>
<tr>
<td>Serrone (2002)</td>
<td>150</td>
<td>52 35 26 114</td>
<td></td>
<td>76, 68-83</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td><strong>410</strong></td>
<td><strong>133 95 70 316</strong></td>
<td></td>
<td><strong>77, 72-81</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Histometric groups (mm)</th>
<th>&lt;1</th>
<th>&gt;1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krähn (1998)</td>
<td>39</td>
<td>27 7 34</td>
</tr>
<tr>
<td>Pellacani (2003)</td>
<td>88</td>
<td>51 27 78</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td><strong>127</strong></td>
<td><strong>78 34 112</strong></td>
</tr>
</tbody>
</table>

PV: predictive value.
Note that the histometric subgroups were different from actual recommendations (<1 mm, 1.01 to 2 mm, 2.01 to 4 mm, > 4.01 mm).
(Rallan et al. 2006, 2007), we do not believe from our experience that 20 MHz ultrasound imaging can yet help a trained dermatologist to distinguish atypical nevi from thin melanomas, which is the main problem.

**How can diagnostic accuracy be improved?**

By increasing transducer frequency and as it increases axial resolution, technological advances can be expected to improve the accuracy of sonometric measurement of melanomas thinner than 1 mm. In a recent study comparing 20 and 100 MHz ultrasound imaging of 37 subjects with 37 melanocytic nevi and 13 melanomas, Bland and Altman graphs showed greater accuracy of measurement of sonometric thickness using a 100 MHz probe (Gambichler et al. 2007). In this series, 95% limits of agreement were better even with the 20 MHz probe than in our own series. However, there were fewer subjects, and subjects with melanoma larger than 1 cm, thicker than 1 mm and with histologic signs of ulceration or regression were excluded, thus, limiting potential errors. On the other hand, increasing frequency results in reducing the ability to measure thick melanoma.

Combining ultrasound with Doppler may help to distinguish melanomas from other pigmented skin lesions. Abnormal vascularization was evidenced in one third of melanomas and was absent from all pigmented nevi (100% specificity, 34% sensitivity, 100% positive predictive value) in a study by Bessoud et al. (2003). Moreover, the use of contrast agents may increase the sensitivity of the method (Lassau et al. 2001) but this has not been specifically demonstrated with primary cutaneous melanomas. However, this is not routinely available and the clinical dilemma of distinguishing thin melanomas from atypical nevi remains a frequent problem. It can be hoped that ultrasound techniques would help in distinguishing benign atypical pigmented lesions from true melanomas (Rallan et al. 2007). The dilemma is currently solved by using dermoscopy (Braun et al. 2005) or histology. Dermoscopy combined with computer-assisted diagnostic imaging methods (Perrinaud et al. 2007) or confocal microscopy is also used in referral centres (Pellacani et al. 2007). These techniques need experienced examiners and, although they can estimate the depth of a pigmented lesion, they cannot really measure them on a vertical axis. However, the combination of videomicroscopy with sonographic measurement of thickness has been demonstrated to improve the accuracy of predicting appropriate margins in a series of 88 patients with melanoma (Pellacani et al. 2003).

**CONCLUSION**

High-resolution ultrasound imaging offers the advantage of real-time examination of the entire lesion in a few minutes to determine echoic appearance and maximum depth of a pigmented lesion and to help in the differential diagnosis between pigmented basal cell carcinoma or seborrhoeic keratoses and melanoma. However, it adds little to clinical examination to distinguish an atypical benign pigmented nevus from true melanoma. Ultrasound cannot replace biopsy when it is necessary and we emphasize the difficulties of measuring melanoma thickness with ultrasound in the planar area, *i.e.*, the only cause of excessive margins in our series. However, our prospective study and the systematic review demonstrate that ultrasound imaging helps in determining surgical margins without biopsy or diagnostic excision in most cases. We believe that high-resolution ultrasound imaging is a valuable and noninvasive tool that can be used in preoperative assessment of cutaneous melanomas, permitting better choice of surgical margins in a single operation. It can even be combined with SLNB (Gambichler et al. 2007), thus, decreasing the number of reinterventions and may, therefore, prove to be a time- and cost-saving procedure. Moreover, accurate preoperative measurement of melanoma thickness could make it possible for part of the primary melanoma not to be routinely processed for histologic examination but used for research to provide greater understanding of the mechanisms of metastatic progression.

**REFERENCES**


