Acta Derm Venereol 2012; 92: 132–137

INVESTIGATIVE REPORT

Preoperative Characterization of Basal Cell Carcinoma Comparing Tumour Thickness Measurement by Optical Coherence Tomography, 20-MHz Ultrasound and Histopathology

Torsten HINZ[1], Lin-Kristin EHLER[1], Thorsten HORNUNG[1], Harald VOTH[1], Ines FORTMEIER[2], Tanja MAIER[3], Tobias HÖLLER[4] and Monika-Hildegard SCHMID-WENDTNER[1]

[1]Department of Dermatology and Allergology, University of Bonn, Bonn, [2]W.O.M., World of Medicine AG, Berlin, [3]Department of Dermatology and Allergology and [4]Institute for Medical Biometry, Informatics and Epidemiology, University of Bonn, Bonn, Germany

Optical coherence tomography (OCT) is a new imaging method with promising results for several dermatological indications, including preoperative skin tumour characterization. While high-frequency ultrasound (HFUS) is frequently used for this purpose, overestimation of tumour thickness is a problem, due to subtumoral inflammatory infiltration that cannot be differentiated from tumour tissue. The aim of this single-centre study was to describe OCT features of basal cell carcinoma (BCC) and to determine vertical tumour thickness accurately, including a comparison with HFUS and histopathology. Tumour thickness values of 10 BCCs measured by OCT did not differ significantly from those measured by histopathology (median difference 0.12 mm). By contrast, the difference between HFUS and histopathology was greater (median difference 0.3 mm). A Pearson's correlation coefficient of 0.83 showed a stronger correlation of OCT in measuring tumour thickness compared with HFUS (0.59). Bland-Altman plots revealed a better agreement of OCT and histopathology concerning tumour thickness measurements. On the basis of this explorative study cohort, OCT was more exact than HFUS in preoperative tumour thickness estimation of BCCs compared with histopathological measurements. ***Key words: basal cell carcinoma; non-melanocytic skin lesion; optical coherence tomography; tumour thickness; ultrasound.***

(Accepted June 28, 2011.)

Acta Derm Venereol 2012; 92: 132–137.

Monika-H. Schmid-Wendtner, Department of Dermatology and Allergology, University of Bonn, Sigmund-Freud-Str. 25, DE-53127 Bonn, Germany. E-mail: Monika-Hildegard.Schmid-Wendtner@ukb.uni-bonn.de

Basal cell carcinoma (BCC) is the most prevalent skin cancer in the light-skinned population and is a frequent problem in daily dermatological practice (1, 2). Although surgical treatment is used mainly for nodular and deeper variants of BCC, especially located on the face, non-invasive treatment is increasingly used for patients with BCC who have superficial lesions, making the application of non-invasive diagnostic technologies highly relevant (3–5). Various diagnostic tools are available, including dermoscopy, fluorescence imaging, confocal microscopy, high-frequency ultrasound (HFUS), and optical coherence tomography (OCT) (6). Whereas the first ones of these tools can be used to improve clinical diagnostic accuracy, HFUS and OCT are most useful in the estimation of tumour size, which is used in planning surgical approaches as well as choosing thin lesions suitable for non-surgical management. For decades, HFUS has been a well-established technique for determining preoperative thickness of melanocytic and non-melanocytic skin tumours, and is used frequently, especially in European countries (7–12). For dermatological purposes, high-frequency scanners of 20–50 MHz are used to evaluate skin morphology. The penetration of a 20 MHz ultrasound transducer is approximately 3.8 mm, with an axial resolution of 39 μm and a lateral resolution of 210 μm, which does not approach the resolution of a light microscope. However, HFUS is helpful in detecting and describing the morphological and volumetric appearance of skin tumours *in vivo*. OCT, on the other hand, is a novel optical imaging technique that offers real-time imaging within micrometre resolution (13–16). It works in an analogous fashion to ultrasound imaging, except that it uses light rather than sound waves. Although OCT was only recently introduced in skin cancer imaging, first studies on melanoma as well as of non-melanoma skin cancer (NMSC) indicate promising results (17–20). Few studies have compared OCT, HFUS and histopathological tumour thickness measurements for BCC (21).

The aim of the current study was to compare the accuracy of OCT and HFUS measurements *in vivo*, and to correlate the results with the histopathological tumour thickness measured in patients with the clinical diagnosis of a BCC. In addition, morphological aspects of BCCs studied with OCT were assessed.

MATERIALS AND METHODS

Patients

From July to August 2010, 10 patients with the clinical presumptive diagnosis of a BCC were scanned by OCT and HFUS. The study population consists of 1 woman and 9 men with a

mean age (± standard deviation (SD)) of 73.8 ± 6.03 years (age range 62–80 years). After scanning of the tumours, excisions were performed, followed by histopathological examinations. The study followed the principles outlined in the Declaration of Helsinki. All patients gave written informed consent.

High-frequency ultrasound

A commercially available real-time high-resolution 20 MHz HFUS probe (taberna pro medicum, Lueneburg, Germany) was used with an axial resolution of 72 µm and maximum measurable depth of 8–10 mm. As a coupling agent water was needed between the skin surface and the probe. The linear probe was applied with minimal pressure perpendicular to the skin surface and moved over the skin to visualize the entire lesion. We compared the internal echogenicity of all lesions using standard ultrasound terminologies and criteria such as isoechoic, hypoechoic or hyperechoic compared with surrounding tissue, and additionally characterized the pattern of internal echoes as homogeneous or heterogeneous. In HFUS, non-melanocytic skin tumours generally appear as homogenous hypoechoic structures compared with the surrounding hyperechoic dermis. It is not possible to differentiate between skin tumours by means of HFUS. Lesion margins and the demarcation from normal skin were documented. The thickness was measured independently by 2 investigators (TH and MHSW) on a vertical axis perpendicular to the surface (from the middle of the so-called hyperechoic "entrance echo" to the deepest point of the lesion) using an electronic calliper.

Optical coherence tomography

OCT is a non-invasive, depth-resolved, non-destructive optical imaging method, that measures reflection of infrared radiation from the skin. For the current study, a Swept-Source-OCT-System (OCS1300SS, Thorlabs, Dachau/Munich) was used, based on frequency-domain technology. The laser radiation is focused on the surface of the tissue with an objective. The different structures of the tissue reflect different percentages of the radiation. The back-reflected radiation of all layers is collected by the objective and is redirected to the beam splitter, where the signal is superimposed with the signal of the reference arm. The combined signal is measured by a single-photodetector as a function of time. The swept laser source of the system used in this study has a centre wavelength of 1,325 nm, with a spectral bandwidth of 100 nm and a sweeping frequency of 16 kHz. The parameters of the system yield to a maximum theoretical imaging depth of 3 mm and an axial resolution of 12 µm in air. The real imaging depth in tissue is, due to scattering effects, lower than in air and varies around approximately 1 mm according to body site and type of lesion. The lateral resolution is 15 µm. A charge-coupled device (CCD)-camera provides a surface image of the measured region. The system has an aiming laser (660 nm) showing the scanning trace of the swept laser on the surface of the skin in order to improve the user's orientation. For all measurements acquired in this study an image size of 6 mm lateral (1024 pixels) and 2.26 mm axial (3 mm in air, 512 pixels) was used. Every lesion was measured by setting the handheld imaging probe onto the lesion. Then its position was corrected by monitoring the trace of the aiming laser and the real-time OCT image of the lesion until a good cross-sectional image of the lesion was displayed on the screen. After acquiring the OCT image the thickness of the lesion was measured independently by 2 investigators (TH and MHSW) using the software provided by the manufacturer of the OCT system. One horizontal measurement line was set to the upper margin of the lesion, the other was set to the lower margin. The software of the system provides the calculated distance between the 2 measurement lines. For getting correct measurements the refraction index was set to 1.33, which is a typical value for tissue.

Excision and histological examination

All skin tumours were removed with 3–5 mm margins, resulting in complete excisions, and processed for histopathological examination following the above-mentioned imaging procedures. Specimens were fixed in formaldehyde and stained routinely with haematoxylin and eosin. Histopathological diagnoses were made by an experienced dermatopathologist (LE) and the vertical thickness of the BCCs was measured using a micrometer on histology slides, with the vertical axis perpendicular to the skin surface. The dermatopathologist was blinded to the results of HFUS and OCT imaging.

Statistical analysis

The differences in mean tumour thickness measured by OCT and HFUS in reference to measurement by histopathology were illustrated by Bland-Altman plots. The correlation of tumour thickness in OCT, HFUS and histopathology was assessed by Pearson's correlation coefficient. Data were calculated with SPSS software (SPSS 17.0 for Windows; SPSS Inc., Chicago, IL, USA).

RESULTS

Features of tumours

Ten BCCs from 10 patients were identified for study inclusion, processed and excised as above. Two lesions were located on the trunk, 5 were located on the head, and 3 on the limbs. Histopathological examination

Table I. *Clinical and histopathological characteristics of 10 basal cell carcinomas (BCC), and vertical tumour thickness measurement data depicted by high-frequency ultrasound (HFUS), optical coherence tomography (OCT) and histopathology*

Tumour no.	Age, years/sex	Body site of lesion	Histopathological type	Vertical tumour thickness (mm)		
				HFUS	OCT	Histopathology
1	71/F	Chest	Superficial BCC	0.65	0.65	1.20
2	70/M	Upper arm	Superficial BCC	0.81	0.53	0.58
3	62/M	Cheek	Solid BCC	2.10	0.98	1.40
4	70/M	Nose	Superficial BCC	1.34	0.91	1.04
5	76/M	Lower leg	Superficial BCC	1.00	0.84	0.55
6	73/M	Chest	BCC (fibroepithelioma of Pinkus)	1.00	0.60	0.70
7	80/M	Forehead	Superficial BCC	0.64	0.17	0.30
8	80/M	Forehead	Solid BCC	1.50	0.64	0.73
9	79/M	Forehead	Solid BCC	1.00	0.95	1.50
10	79/M	Lower leg	Superficial BCC	0.30	0.20	0.15

revealed 6 superficial BCCs, 3 solid BCCs, and 1 fibroepithelioma of Pinkus. Details of the excised lesions are given in Table I.

High-frequency ultrasound

In HFUS, all BCCs presented solid homogenous hypoechoic lesions beneath a strong hyperechoic entrance echo. In many cases, the hypoechoic lesions could be distinguished well by a sharp border between the hypoechoic lesion and the surrounding hyperechoic dermis. Histological subclassification of BCCs could not be achieved with HFUS (Figs 1A). Measurements of vertical tumour thickness (represented by white double arrows in Figs 1A) could be performed in all cases (Table I). The mean tumour thickness of the 10 BCCs estimated by HFUS was 1.03 mm, compared with 0.82 measured by histopathology (Table II).

Optical coherence tomography

In OCT, BCCs presented as well-defined grey or dark areas with a more or less homogenous signal distribution. In some cases a white peripheral surrounding could be observed illustrating the tumour stroma. In addition, destruction of the normal architecture, resulting in break-up of the layering was also seen. Representative OCT images of 3 BCCs are shown in Figs 1B, demonstrating less-defined dermoepidermal borders and a disarrayed architecture. Vertical tumour measurements are summarized in Table I. The mean tumour thickness of all 10 BCCs measured by OCT was 0.65 mm ± 0.29 mm), which is very close to the mean tumour thickness of 0.82 ± 0.46 mm) finally measured by histopathology (Table II).

Comparison of the measurements

Taking the histopathological tumour thickness as "gold standard", OCT revealed more exact vertical tumour thickness measurements of BCCs compared with 20 MHz ultrasound (see the mean as well as the median values listed in Table II). Tumour thickness values measured by OCT did not differ significantly from those measured by histopathology (median difference 0.12 mm). In contrast, there was a clearly higher dif-

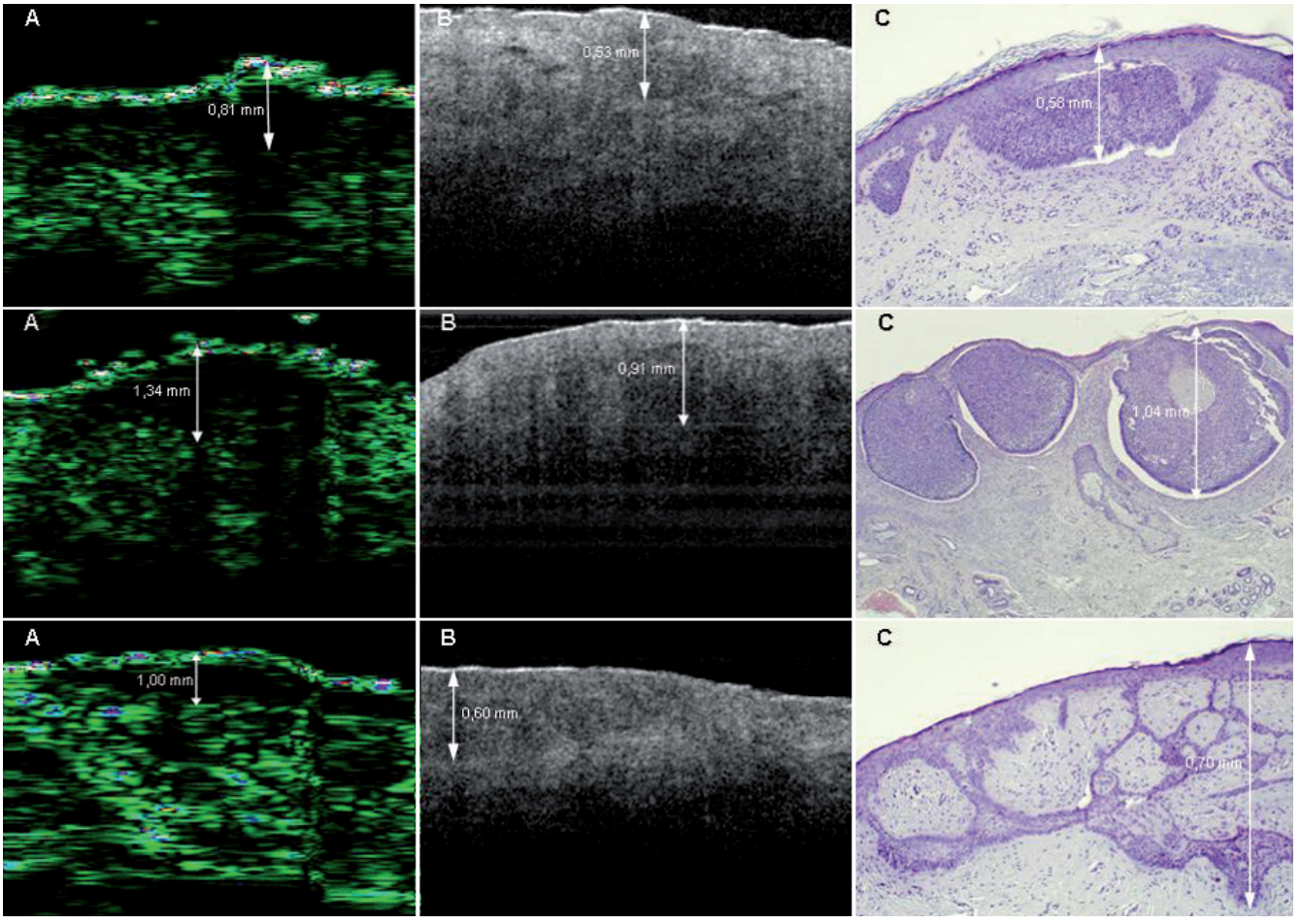

Fig. 1. Superficial basal cell carcinoma on the right upper arm of a 70-year-old man (case 2) (*top panel*); and the nose of a 70-year-old man (case 4) (*middle panel*). Basal cell carcinoma (fibroepithelioma of Pinkus) on the left chest of a 73-year-old man (case 6) (*lower panel*) (A) high-frequency ultrasound; (B) optical coherence tomography; and (C) histopathology. Vertical tumour thickness measurements (in mm) are marked by double arrows.

Table II. *Tumour thickness measurement parameters in mm, including mean ± standard deviation (SD), median, minimum and maximum values depicted for high-frequency ultrasound (HFUS), optical coherence tomography (OCT) and histopathology in 10 patients*

Tumour thickness measurements in BCCs	Mean ± SD (mm)	Median (mm)	Minimum (mm)	Maximum (mm)
HFUS	1.03 ± 0.51	1.00	0.30	2.10
OCT	0.65 ± 0.29	0.65	0.17	0.98
Histopathology	0.82 ± 0.46	0.72	0.15	1.50

Table III. *Pearson's correlation coefficients for high-frequency ultrasound (HFUS) and optical coherence tomography (OCT) tumour thickness measurements in relation to histopathological tumour thickness measurements*

Pearson's correlation	HFUS	OCT	Histopathology
HFUS	1.00	0.722	0.593
OCT	0.722	1.00	0.834
Histopathology	0.593	0.834	1.00

ference between HFUS and histopathology tumour thickness measurement (median difference 0.30 mm) with a tendency to overestimation using HFUS. The opposite was true for OCT imaging, which tended to underestimate tumour thickness. For comparison of tumour thickness, Pearson's correlation coefficients were calculated (Table III) and revealed a higher value for OCT (0.83) compared with 0.59 for HFUS. Bland-Altman plots for OCT and histopathology, as well as for HFUS and histopathology are shown in Fig. 2. OCT and histopathology revealed a better agreement concerning tumour thickness measurements compared with HFUS and histopathology. A direct comparison of tumour imaging by HFUS, OCT and histopathology is shown in Fig. 1.

DISCUSSION

Several studies focusing on non-invasive diagnosis and estimation of tumour margins in BCC by ultrasound have been published during the last decades (7, 8, 22–26). In the preoperative setting, especially, tumour thickness estimation had been shown to be useful (7, 22). In a comprehensive study, Desai et al. investigated 50 superficial and nodular BCCs at various locations using a 20 MHz ultrasound device (22). Clinical and ultrasonic tumour thickness measurements correlated well for width, depth and length of the investigated tumours. Forty-five out of 50 tumours had been assessed with clear margins by HFUS (22). Another study including 25 patients with 27 skin lesions suspicious for facial BCCs, revealed positive findings for the pre-surgical HFUS employing a special compact linear 15 MHz probe, designed for difficult anatomical areas such as the nose (23). The authors reported that HFUS enabled the additional detection of 2 subclinical satellite lesions, resulting in the correct estimation of tumour margins in 29 facial BCCs, which could be removed with tumour-free borders at the first surgery (23). A more critical view of HFUS was presented in a comprehensive study by Jambusaria-Pahalajani et al. (8), who enrolled 100 patients with NMSC (BCCs as well as SCCs) for preoperative HFUS before Mohs micrographic surgery. A sensitivity of 32%, a specificity of 88% and a positive predictive value of 47% was reported. The authors pointed out that tumours with subtle areas of extension, such as small foci of dermal invasion, are an especially serious problem for HFUS diagnostics.

OCT was recently introduced as a new imaging technique that might overcome the disadvantages of HFUS in tumour diagnostics (27). Olmedo and his group compared tumour thickness values of 20 BCCs measured by OCT with values raised by histopathology, and found an excellent correlation of tissue thickness up to a depth of approximately 1 mm (28). In contrast to HFUS, OCT offers the possibility to describe tumour morphology and to give hints about tumour typical architecture, although cellular morphology cannot be identified (17, 28–30). In the present study, it was possible to identify several morphological characteristics, such as break-up of layering and dark roundish tumour areas surrounded by a white core, corresponding to the histopathology of BCC islands with surrounding stroma

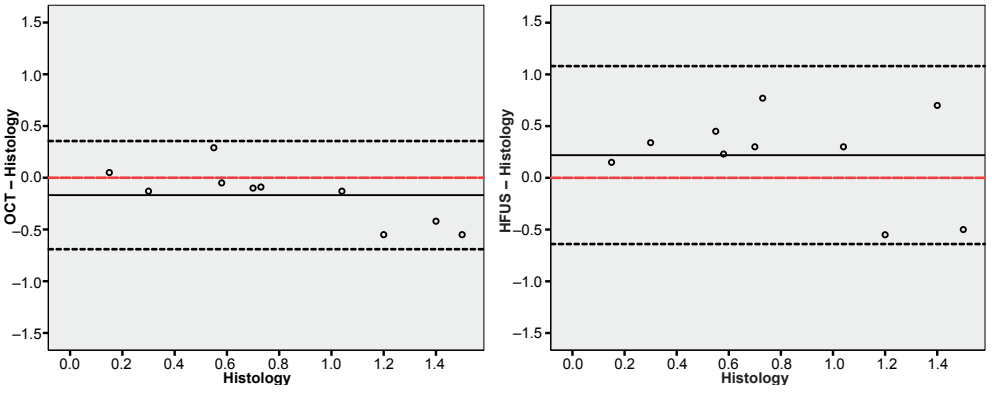

Fig. 2. Bland-Altman plots of the measurements of tumour thickness (in mm) by optical coherence tomography (OCT) and high-frequency ultrasound (HFUS) in relation to the measurements of histology. The mean difference (*black line*: OCT –0.17; HFUS: 0.22) and the 95% confidence intervals (CI) (*black dashed lines*) are also shown. Difference OCT: 95% CI –0.69 to 0.35; difference HFUS: 95% CI –0.64 to 1.08.

(28, 30). However, assessment of morphological aspects should be performed with caution because these aspects, in general, are more subjective, and the main focus of our investigation was on the estimation of clear-cut vertical tumour margins. In accordance with former investigations (19, 30, 31) a classification of BCCs in various subtypes by OCT means was not possible in our patient cohort.

Data concerning the direct comparison of HFUS, OCT and histopathology tumour thickness measurements in BCCs are rare. Perhaps the most comprehensive study in this field is the investigation by Mogensen et al. (21), who investigated the accuracy of OCT and HFUS for *in vivo* tumour thickness measurements of actinic keratoses and BCCs and compared their data with histopathological findings. According to the OCT device used, the vertical thickness of the lesions was limited to a depth of 2 mm. As in our study, OCT was revealed to be superior to HFUS regarding the accuracy of tumour thickness measurement. The authors felt that the better results obtained by OCT were explained by the better resolution of OCT and the better contrast of BCCs and actinic keratoses from back-scattered infrared radiation, compared with the contrast provided by the acoustic characteristics of the tissue (21). Just as Mogensen et al. (21) and Olmedo et al. (28) found, the advantage of OCT over HFUS was most pronounced for smaller BCCs (< 1 mm tumour thickness) in our patient collective. Unlike the previous studies, we did not observe any overestimation of BCCs by OCT. This may be explained in part by the OCT device used (which is not yet available for commercial use) and by the inclusion of all skin lesions clinically suspicious for BCC without exclusion of tumours exceeding the OCT limit of 1 mm. Known problems from HFUS, such as the additional measurment of a peripheral inflammation beneath the tumours could not be observed for OCT measurements in the present investigation.

Based on our own data on a small number of patients, we conclude that OCT might be a suitable tool for the non-invasive measurement of tumour thickness in BCCs, which is superior to HFUS, especially in thin tumours. It might also have the potential for the preoperative evaluation of other thin NMSC (tumour thickness < 1 mm). However, further studies are needed, including larger study populations and considering potential influencing factors, such as skin hydration and pigmentation to finally assess the value of OCT for *in vivo* imaging. Another limitation of our study besides the small study population size might be that the exact points of measurement by OCT and HFUS might not be congruent with the areas measured by histopathology. Here, further developments of OCT devices might help to enable the physician using aiming laser beams for exact marking of special areas within skin lesions in the future. Another factor that might influence the measurement of skin lesion thickness is tissue shrinkage after formalin fixation and embedding in paraffin. Salmhofer et al. investigated the influence of this phenomenon on melanocytic as well as epithelial lesions, comparing HFUS and histopathological tumour thickness measurements. They showed that the mean histological tumour thickness was only slightly lower than the mean thickness measured by HFUS, which they felt was due to primary expansion of tissue after excision, followed by shrinkage after formalin fixation (32). Besides the measurements of tumour thickness, morphological aspects will be an important issue in the future (33). Concerning this point, the recently published, so-called, speckle reduction technique (SR-OCT) might be of interest (30). In an experimental setting, SR-OCT lead to improved images of BCC lesions due to repeated scanning, by altering the distance between the probe and the skin surface (34). Improved imaging of BCCs is of great clinical importance, not only for preoperative estimation of tumour thickness and margins, but also for selection of patients with superficial tumours suitable for other therapeutic approaches, such as photodynamic therapy or 5-fluorouracil treatments (25, 26).

ACKNOWLEDGEMENTS

We thank Walter Burgdorf, MD, for critical review of the final manuscript as a native English speaker.

This study was supported by a grant from the German Cancer Aid (Program for the Development of Interdisciplinary Oncology Centers of Excellence in Germany), Bonn, Germany.

The authors declare no conflicts of interest.

REFERENCES

1. Neville JA, Welch E, Leffell DJ. Management of nonmelanoma skin cancer in 2007. Nat Clin Pract Oncol 2007; 4: 462–469.
2. Diepgen TL. Epidemiology of chronic UV-damage. J Dtsch Dermatol Ges 2005; 3: 32–35.
3. Tillman DK Jr, Carroll MT. A 36-month clinical experience of the effectiveness curettage and imiquimod 5% cream in the treatment of basal cell carcinoma. J Drugs Dermatol 2008; 7: 7–14.
4. Wagstaff AJ, Perry CM. Topical imiquimod: a review of its use in the management of anogenital warts, actinic keratoses, basal cell carcinoma and other skin lesions. Drugs 2007; 67: 2187–2210.
5. Surrenti T, De Angelis L, Di Cesare A, Fargnoli MC, Peris K. Efficacy of photodynamic therapy with methyl aminolevulinate in the treatment of superficial and nodular basal cell carcinoma: an open-label trial. Eur J Dermatol 2007; 17: 412–415.
6. Mogensen M, Jemec GB. Diagnosis of nonmelanoma skin cancer/keratinocyte carcinoma: a review of diagnostic accuracy of nonmelanoma skin cancer diagnostic tests and technologies. Dermatol Surg 2007; 33: 1158–1174.
7. Marmur ES, Berkowitz EZ, Fuchs BS, Singer GK, Yoo JY. Use of high-frequency, high-resolution ultrasound before Mohs surgery. Dermatol Surg 2010; 36: 841–847.
8. Jambusaria-Pahlajani A, Schmults CD, Miller CJ, Shin D, Williams J, Kurd SK, et al. Test characteristics of

high-resolution ultrasound in the preoperative assessment of margins of basal cell and squamous cell carcinoma in patients undergoing Mohs micrographic surgery. Dermatol Surg 2009; 35: 9–15.
9. Petrella LI, Valle HA, Issa PR, Martins CJ, Pereira WC, Machado JC. Study of cutaneous cell carcinomas ex vivo using ultrasound biomicroscopic images. Skin Res Technol 2010; 16: 422–424.
10. Machet L, Belot V, Naouri M, Boka M, Mourtada Y, Giraudeau B, et al. Preoperative Measurement of thickness of cutaneous melanoma using high-resolution 20 MHz ultrasound imaging: a monocenter prospective study and systematic review of the literature. Ultrasound Med Biol 2009; 35: 1411–1420.
11. Vilana R, Puig S, Sanchez M, Squarcia M, Lopez A, Castel T, Malvehy J. Preoperative assessment of cutaneous melanoma thickness using 10-MHz sonography. Am J Roentgenol 2009; 193: 639–643.
12. Bessoud B, Lassau N, Koscielny S, Longvert C, Avril MF, Duvillard P, et al. High-frequency sonography and color Doppler in the management of pigmented skin lesions. Ultrasound Med Biol 2003; 29: 875–879.
13. Huang D, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W, et al. Optical coherence tomography. Science 1991; 254: 1178–1181.
14. Fujimoto JG. Optical coherence tomography for ultrahigh resolution in vivo imaging. Nat Biotechnol 2003; 21: 1361–1367.
15. Welzel J, Lankenau E, Birngruber R, Engelhardt R. Optical coherence tomography of the human skin. J Am Acad Dermatol 1997; 37: 958–963.
16. Gladkova ND, Petrova GA, Nikulin NK, Radenska-Lopovok SG, Snopova LB, Chumakov YP, et al. In vivo optical coherence tomography imaging of human skin: norm and pathology. Skin Res Technol 2000; 6: 6–16.
17. Gambichler T, Orlikov A, Vasa R, Moussa G, Hoffmann K, Stücker M, et al. In vivo optical coherence tomography of basal cell carcinoma. J Dermatol Sci 2007; 45: 167–173.
18. Strasswimmer J, Pierce MC, Park BH, Neel V, de Boer JF. Polarization-sensitive optical coherence tomography of invasive basal cell carcinoma. J Biomed Opt 2004; 9: 292–298.
19. Gambichler T, Regeniter P, Bechara FG, Orlikov A, Vasa R, Moussa G, et al. Characterization of benign and malignant melanocytic skin lesions using optical coherence tomography in vivo. J Am Acad Dermatol 2007; 57: 629–637.
20. Wang T, Mallidi S, Qiu J, Ma LL, Paranjape AS, Sun J, et al. Comparison of pulsed photothermal radiometry, optical coherence tomography and ultrasound for melanoma thickness measurement in PDMS tissue phantoms. J Biophotonics 2011; 4: 335–344.
21. Mogensen M, Nürnberg BM, Forman JL, Thomsen JB, Thrane L, Jemec GB. In vivo thickness measurement of basal cell carcinoma and actinic keratosis with optical coherence tomography and 20-MHz ultrasound. Br J Dermatol 2009; 160: 1026–1033.
22. Desai TD, Desai AD, Horowitz DC, Kartono F, Wahl T. The use of high-frequency ultrasound in the evaluation of superficial and nodular basal cell carcinomas. Dermatol Surg 2007; 33: 1226–1227.
23. Bobadilla F, Wortsman X, Muñoz C, Segovia L, Espinoza M, Jemec GB. Presurgical high resolution ultrasound of facial basal cell carcinoma: correlation with histology. Cancer Imaging 2008; 8: 163–172.
24. Ruocco E, Argenziano G, Pellacani G, Seidenari S. Noninvasive imaging of skin tumors. Dermatol Surg 2004; 30: 301–310.
25. Moore JV, Allan E. Pulsed ultrasound measurements of depth and regression of basal cell carcinomas after photodynamic therapy: relationship to probability of 1-year local control. Br J Dermatol 2003; 149: 1035–1040.
26. Gupta AK, Turnbull DH, Foster FS, Harasiewicz KA, Shum DT, Prussick R, et al. High frequency 40-MHz ultrasound. A possible non-invasive method for the assessment of the boundary of basal cell carcinomas. Dermatol Surg 1996; 22: 131–136.
27. Gambichler T, Moussa G, Sand M, Sand D, Altmeyer P, Hoffmann K. Applications of optical coherence tomography in dermatology. J Dermatol Sci 2005; 40: 85–94.
28. Olmedo JM, Warschaw KE, Schmitt JM, Swanson DL. Correlation of thickness of basal cell carcinoma by optical coherence tomography in vivo and routine histologic findings: a pilot study. Dermatol Surg 2007; 33: 421–425.
29. Olmedo JM, Warschaw KE, Schmitt JM, Swanson DL. Optical coherence tomography fort he characterization of basal cell carcinoma in vivo: a pilot study. J Am Acad Dermatol 2006; 55: 408–412.
30. Bechara FG, Gambichler T, Stücker M, Orlikov A, Rotterdam S, Altmeyer P, Hoffmann K. Histomorphologic correlation with routine histology and optical coherence tomography. Skin Res Technol 2004; 10: 169–173.
31. Mogensen M, Joergensen TM, Nürnberg BM, Morsy HA, Thomsen JB, Thrane L, et al. Assessment of optical coherence tomography imaging in the diagnosis of non-melanoma skin cancer and benign lesions versus normal skin: observer-blinded evaluation by dermatologists and pathologists. Dermatol Surg 2009; 35: 965–972.
32. Salmhofer W, Rieger E, Soyer HP, Smolle J, Kerl H. Influence of skin tension and formalin fixation on sonographic measurement of tumor thickness. J Am Acad Dermatol 1996; 34: 34–39.
33. Khandwala M, Penmetsa BR, Dey S, Schofield JB, Jones CA, Podoleanu A. Imaging of periocular basal cell carcinoma using en face optical coherence tomography: a pilot study. Br J Ophthalmol 2010; 94: 1332–1336.
34. Mogensen M, Jørgensen TM, Thrane L, Nürnberg BM, Jemec GB. Improved quality of optical coherence tomography imaging of basal cell carcinomas using speckle reduction. Exp Dermatol 2010; 19: 293–295.