Tumor check through teledermatology: a critical appraisal

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Original article:
Kroemer S, Frühauf J, Campbell T, Massone C, Schwantzer G, Soyer H, Hofmann-Wellenhof R. Mobile teledermatology for skin tumour screening: diagnostic accuracy of clinical and dermoscopic image tele-evaluation using cellular phones. Br J Dermatol. 2011;164(5):973-979.

SUMMARY

Aim: The original article aimed to evaluate the diagnostic accuracy of clinical and dermoscopic image tele-evaluation for mobile skin tumor screening

Setting and population: The tumors examined in the study were selected prospectively from an outpatient clinic in Graz, Austria in a duration of 3 months. They are from men or women with benign and/or malignant skin tumors of either melanocytic or non-melanocytic origin. A total of 104 tumors from 80 patients using a mobile phone camera were gathered. The lesions were from the head and neck area, trunk, legs and feet and genital area.

Study examination: A board-certified dermatologist with clinical expertise in teledermatology and dermoscopy reviewed the clinical and dermoscopic pictures with clinical information separately. The results from the review of the pictures were compared with those obtained by face-to-face examination and the gold standard face-to-face examination plus histopathology.

Outcome: Tumors were classified under four categories: benign non-melanocytic, benign melanocytic, malignant non-melanocytic and malignant melanocytic. The table **(Table 1)** below shows the final diagnoses of the skin tumors examined per category.

Results: Among these 104 lesions, 25 (24%) benign non-melanocytic, 15 (14%) benign melanocytic, 58 (56%) malignant non-melanocytic and six (6%) malignant melanocytic lesions were identified. Clinical and dermoscopic tele-evaluations showed high sensitivity and specificity. For malignant non-melanocytic tumors, sensitivity for both clinical and dermoscopic lesions is 97%; specificity for clinical and dermoscopic lesions are 91% and 94%, respectively. For classifying malignant melanocytic lesions, sensitivity for both clinical and dermoscopic lesions is 100% while specificity is 98% and 97%, respectively.

Conclusions: Clinical image tele-evaluation might be the method of choice for mobile tumor screening. Both clinical image tele-evaluation and teledermoscopy achieved excellent and equally high concordance rates with the gold standard.

Key words: tumors, teledermatology, critical appraisal

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Table 1. Final diagnosis of the skin tumors assessed using the gold standard classified into 4 categories

Benign non-melanocytic	Benign melanocytic	Malignant non-melanocytic	Malignant melanocytic
• Seborrhoeic keratosis • Soft tissue tumor (epidermal cyst, hypertrophic scar, nevus sebaceous, etc.) • Angioma • Solar lentigo • Virus-induced tumor (verruca, molluscum contagiosum) • Trichilemmoma • Tophi • Excoriated prurigo • Others	• Nevus	• Basal cell carcinoma • Actinic keratosis • Squamous cell carcinoma • Bowen disease	• Lentigo maligna • In situ melanoma • Metastasis of malignant melanoma • Melanoma

Acronyms and definitions

FTF: face to face consultation

VTC: video teleconferencing. A technique where patients and dermatologists engage in a live or real-time electronic consultation and lesions in question are presented live through video as well.

SAF: store and forward. A technique where clinical (or dermoscopic) images are first taken by the patient through a cellular phone camera, automatically stored, and later forwarded to an assessor, usually the dermatologist.

Mobile examination: a teledermatology technique where a photo (either clinical or dermoscopic) is sent to a dermatologist for assessment

PPV: positive predictive value or predictive value of a positive test. In this report, when a dermatologist states through mobile examination that a test is malignant, how probable is it that it is so?

NPV: negative predictive value or predictive value of a negative test

Comment

What is already known about this topic?

Smartphones are part of our daily lives. In contrast to the sole communication function of older cellular phones, smartphones now may function like a computer with access to the Internet and may be linked to multiple dermatology assessment and monitoring apps.1 Because of the wide use of smartphones anywhere in the world, it is a useful platform for teledermatology.

Teledermatology is the practice of providing skin care at a distance using telecommunications technologies.[1] The three modalities for teledermatology are store-and-forward (SAF), real-time video teleconferencing (VTC), and hybrid. SAF is more efficient for physicians from different time zones as data in the form of clinical information and quality pictures are sent asynchronously. However, because some data in the medical history may be incomplete, multiple or repeated consultations are sometimes required. VTC may definitely save time for both the physician and the patient as questions and concerns may immediately be addressed but this requires significant bandwidth to achieve a clear audio and

video transmission. A hybrid has both the time-saving qualities of a VTC and also the quality images of SAF. This however, is still not ideal for physicians working from another time zone or those without access to good Internet connection.[1,2]

The diagnostic accuracy of SAF has been reported to be high when compared against histopathology. A study by Massone et al confirmed that teledermatology is excellent for triaging skin cancers as its diagnostic accuracy was 94% with very high sensitivity and specificity at 100% and 95.8%, respectively.[3] In terms of patient satisfaction, the content and style of healthcare providers' communication was reported to be similar via both teledermatology and face to face consultation. The categories accessed were small talk, clinical assessment, psychosocial issues, patient education, patient compliance, patient treatment, and administrative issues.[4]

The use of a dermatoscope in clinical practice has been increasing because of its added value for increasing diagnostic accuracy especially of skin tumors. Dermoscopy for experienced examiners increases the accuracy of melanoma by 49% versus unaided eye visualization.[1,5] Additionally, smartphone dermoscopy attachments have been developed which may help with the efficiency of data transfer electronically. Although a few studies report that teledermoscopy has no advantage over SAF clinical mobile examination especially for untrained users, it may still be beneficial to use for expert dermatologists. [1]

Strength of the research

This study tested clinical mobile examination and dermoscopic mobile examination against face to face consultation and the gold standard face to face with histopathologic analysis of a skin tumor. The analysis for each is done separately. In doing so, the strength of each type of mobile examination is assessed and compared individually with the gold standard.

The study also specified that the review and assessment for the mobile examination (clinical and dermoscopy pictures) were done by a board certified dermatologist with clinical expertise in teledermatology and dermoscopy. This is particularly important as spot-on clinical dermatologic diagnosis is guided by a developed clinical eye and that dermoscopy is examiner-dependent.

Validity

The reference standard is defined as what is accepted by the scientific community as the yardstick with which the performance of the test is measured. For skin tumors, the ideal diagnostic would be to perform a histopathological assessment to be correlated clinically. In the study, the reference standard is histopathology and face to face examination – the ideal set-up to diagnose skin tumors. The index test, on the other hand, is a mobile examination by an experienced dermatologist. The reference standard was also interpreted independently from the index test.

Statistical Analysis

This section will mathematically compute for the usefulness of mobile examination in a given situation. Non-melanocytic and melanocytic tumors will be analyzed separately as the clinical appearance and behavior of these skin tumors differ. The computation for the predictive strength of both the clinical mobile examination and dermoscopic mobile examination will be presented below.

Non-melanocytic tumors

Clinical mobile examination

Computing from the constructed table below (Table 2), the sensitivity and specificity are 97% and 91%, respectively, for a dermatologist performing a clinical mobile examination on skin tumors. The predictive value of a positive and a negative test is 93% and 95%, respectively. When the dermatologist commits that a non-melanocytic lesion is malignant, it is 93% probable that it is truly malignant. But when the same dermatologist commits that a lesion is nonmalignant (benign), the probability that it is benign is 95%. Performing clinical teledermatology on non-melanocytic lesions provided high measures of accuracy (sensitivity and specificity) and predictive values.

Table 2. Proportion of non-melanocytic tumors reviewed through clinical mobile examination

Test Result: Clinical mobile examination	Reference Standard		
	Benign melanocytic	Malignant non-melanocytic	Malignant melanocytic
Test Positive	56	4	60
Test Negative	2	42	44
Column Total	58	46	104

From the computed measures of accuracy above, the likelihood ratio may now be estimated. Because the positive likelihood ratio is the ratio between the true positive rate versus the false positive rate, a computed higher value is ideal for an index test. The computed positive likelihood ratio is 10.8. If clinical teledermatology calls it malignant, the likelihood that a non-melanocytic lesion is truly malignant is 10.8 times than it is not. On the other hand, the negative likelihood ratio (ratio of true negative rate versus false positive rate) is only 0.03, an excellent value because it is very low. If the expert dermatologist calls a lesion non-malignant or benign, the likelihood that it is malignant is only 0.03 times than it is benign.

A subjective pre-test probability estimates the likelihood of the disease based on the clinician's experience, confidence level, clinical eye, epidemiology of the disease and other external factors. The value changes from one clinician to another. If set at 60%, this means that before asking an expert dermatologist to examine the clinical photo, the probability that a lesion is a malignant non-melanocytic skin tumor is only 60% for a clinician. Assuming a 60% pre-test probability, using the positive and likelihood ratio of the index test computed above, the post-test probability may now be estimated using a nomogram **(Figure 1 and 2)**. Post-test probability is the new calculated likelihood of the disease after the expert dermatologist commits to a diagnosis.

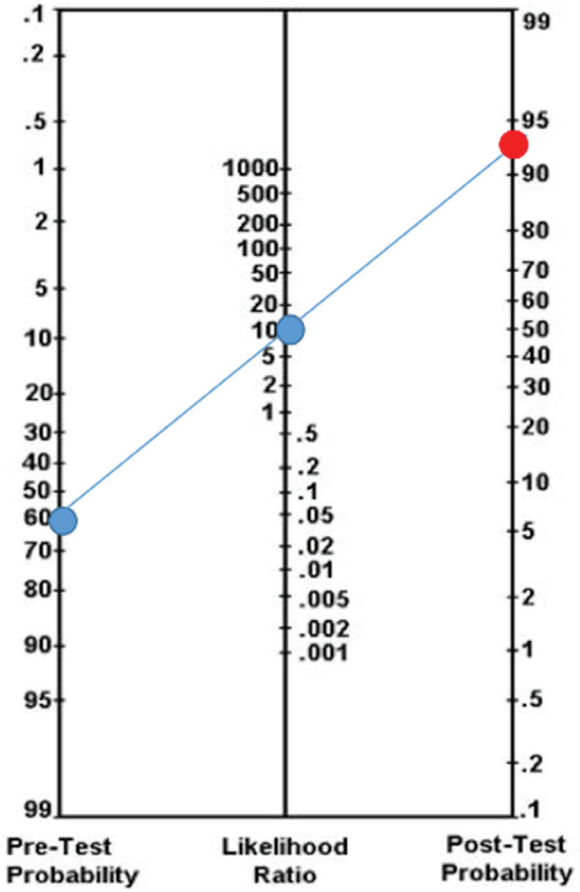

Figure 1. Positive likelihood ratio of 10.8. From pre-test probability of 60%, when the expert dermatologist calls a non-melanocytic lesion **malignant** from clinical pictures, the likelihood that it is really malignant becomes a very high 94.2% from 60%.

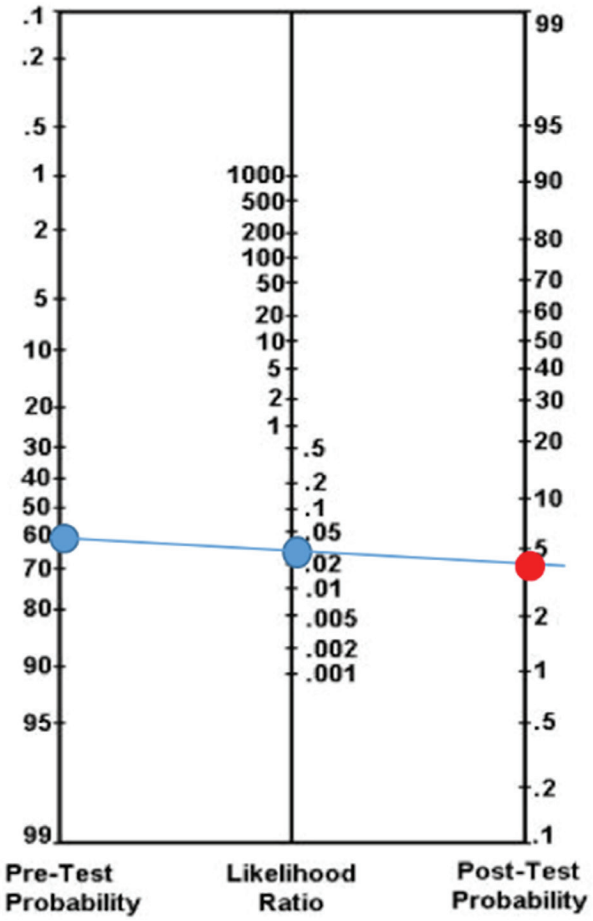

Figure 2.
Negative likelihood ratio of 0.03. From a pre-test probability of 60%, when the expert dermatologist assesses a non-melanocytic lesion as **benign**, the likelihood that it is malignant becomes very low 4.7% from 60%.

Dermoscopic mobile examination

Computing from another table derived from the article **(Table 3)**, for dermoscopic mobile examination in non-melanocytic skin tumors, the sensitivity and specificity are 97% and 94%, respectively. The predictive value of a positive and a negative test is 95% and 96%, respectively. Of all the lesions that were diagnosed malignant by teledermoscopy, 95% are really malignant non-melanocytic. In contrast to that, 96% of the lesions that were diagnosed benign by the expert dermatologist is truly benign non-melanocytic via dermoscopic examination.

Test Result: Teledermoscopy	**Reference Standard: FTF and biopsy**		
	Disease Present	**Disease Absent**	**Row Total**
Test Positive	56	3	59
Test Negative	2	43	45
Column Total	58	46	104

Table 3. Proportion of non-melanocytic tumors reviewed through dermoscopic mobile examination

Following a similar computation as above, the positive likelihood ratio is 16.2 and the negative likelihood ratio is 0.03. To explain, when an expert dermatologist diagnoses a non-melanocytic skin tumor malignant through dermoscopic pictures, the tumor is 16 times more likely that it is malignant than benign. In the same way, when the dermatologist commits that it is benign by reviewing dermoscopic pictures alone, the tumor is now only 0.03 times likely that it is malignant than it is benign. Setting the pre-test probability at 60% again, the post-test probability of a positive test is now 96% **(Figure 3)** and of a negative test is 4.6% **(Figure 4)**.

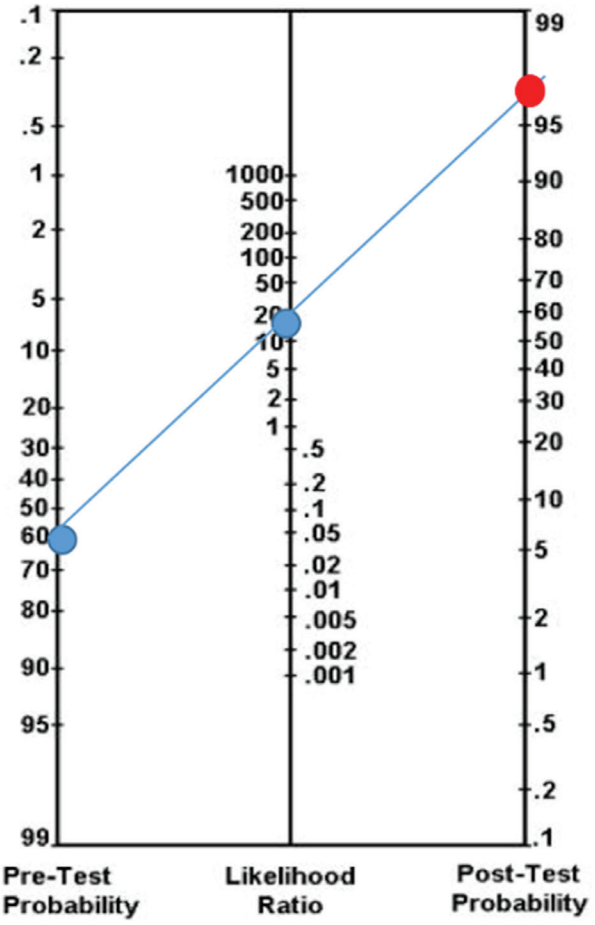

Figure 3. Positive likelihood ratio of 16.2. The likelihood that a skin tumor is **malignant** non-melanocytic increases from 60% to 96% when an expert dermatologist calls the tumor so.

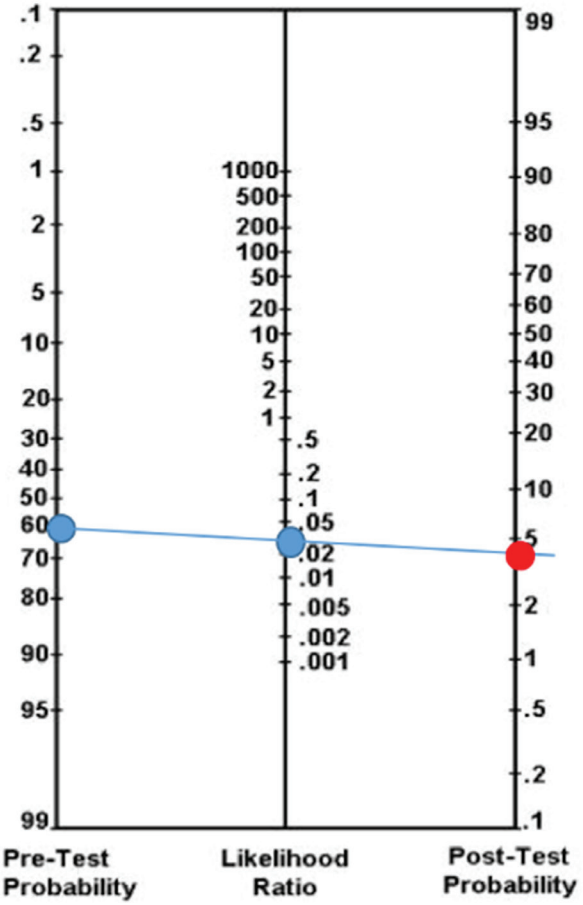

Figure 4. Negative likelihood ratio of 0.03. When the expert dermatologist calls a non-melanocytic lesion **benign** from dermoscopic pictures, the likelihood that it is really malignant drops to a very low 4.6% from 60%.

Melanocytic tumors

Clinical mobile examination

Although malignant melanocytic skin tumors like melanoma appear and behave differently from malignant non-melanocytic tumors like basal cell carcinoma, the use of mobile examination to screen and help diagnose them cannot be discounted. Computing from the table **(Table 4)** below, the sensitivity of diagnosing melanocytic lesions through clinical mobile examination is 100% while the specificity is 98%. The predictive value of a positive test is only 75% but the predictive value of a negative test is 100%. This means that out of all the skin tumors assessed by the dermatologist to be malignant melanocytic through clinical pictures, only 75% of them are truly so while 100% of all the tumors that were diagnosed benign teledermatologically are really benign melanocytic tumors.

Table 4. Proportion of melanocytic tumors reviewed through clinical mobile examination

Test Result: Clinical mobile examination	Reference Standard: FTF and biopsy		
	Disease Present	Disease Absent	Row Total
Test Positive	6	2	8
Test Negative	0	96	96
Column Total	6	98	104

The computed positive likelihood ratio is 50. This means that when the dermatologist diagnoses a tumor as malignant melanocytic through teledermatology, the skin tumor is 50 times more likely that it is malignant than it is not. However, since the sensitivity of detecting a malignant melanocytic lesion is already 100%, the negative likelihood ratio will come out 0 and cannot be computed. Given the values of the study, the likelihood that a melanocytic skin lesion is malignant is so much less likely to occur when the expert dermatologist states it to be benign. A pre-test probability of 60% converts to a post-test probability of 98.7% **(Figure 5)** with a high positive likelihood ratio of 50. When an expert dermatologist commits that a skin tumor is malignant melanocytic, the likelihood that it is truly malignant becomes 98.7% from a pre-test probability of 60%.

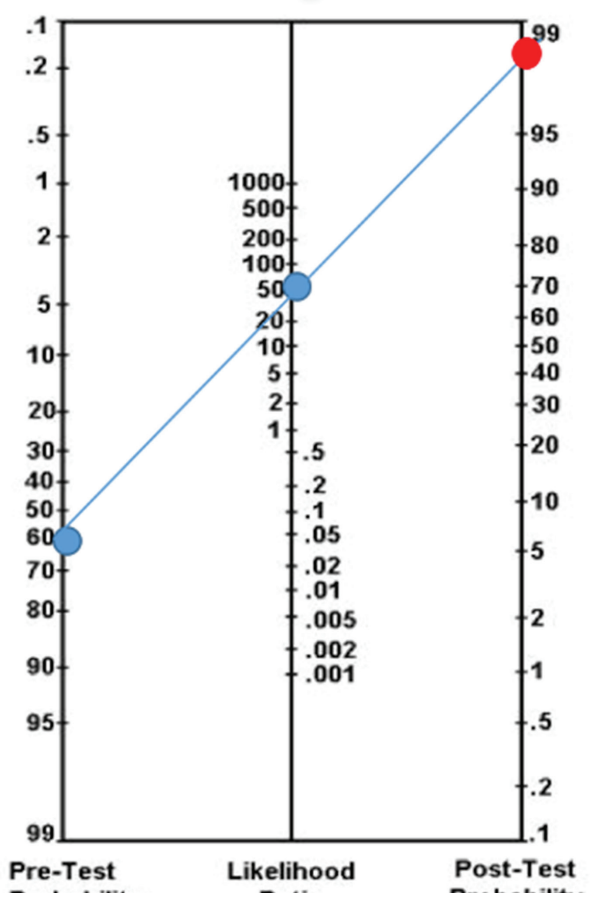

Figure 5. Positive likelihood ratio of 50. The likelihood of a malignant melanocytic tumor increases from 60% to 98.7% when the dermatologist diagnosis it as such through teledermatology.

Dermoscopic mobile examination

Ideally, melanocytic tumors should also be assessed dermoscopically also. In a teledermatology set-up, the usefulness of teledermoscopy may also be assessed. Computing from the table below **(Table 5)**, the sensitivity of teledermoscopy in diagnosing malignant melanocytic tumors is 100% with a specificity of 97%. The predictive value of a positive test is 67%. Sixty-seven percent of the tumors that were diagnosed through teledermoscopy by the dermatologist were truly malignant melanocytic tumors. The predictive value of a negative test is 100% which means that all the lesions that were classified as benign melanocytic teledermoscopically are truly so.

Table 5. Proportion of melanocytic tumors reviewed through dermoscopic mobile examination

Test Result: Teledermoscopy	Reference Standard: FTF and biopsy		
	Disease Present	Disease Absent	Row Total
Test Positive	6	3	9
Test Negative	0	95	95
Column Total	6	98	104

The computed positive likelihood ratio is 33.3. When the dermatologist calls a lesion malignant melanocytic, the likelihood that it truly is malignant is 33.3 times compared to the likelihood that is benign. As with the previous test, a perfect sensitivity does not allow for a computation of a negative likelihood ratio. Basing from the data of the study, the likelihood of a lesion to be a malignant melanocytic tumor is extremely small when the dermatologist calls it benign via teledermoscopy. A pre-test probability of 60% becomes a post-test probability of 98% with a high likelihood ratio of 33.3.

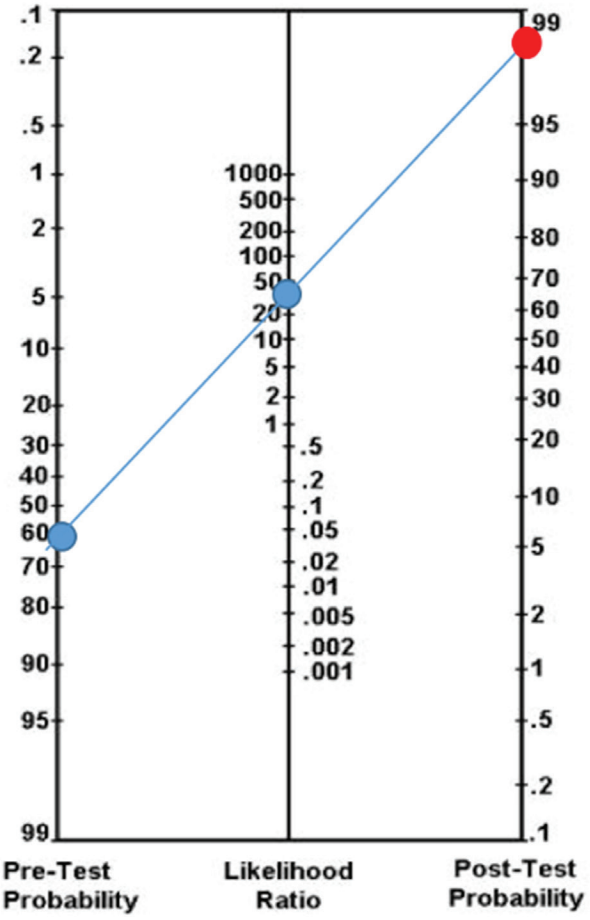

Figure 6. Positive likelihood ratio of 33.3. From pre-test probability of 60%, when the expert dermatologist calls a tumor **malignant** melanocytic from dermoscopic pictures alone, the likelihood that it is really malignant becomes a very high 98% from 60%.

The diagnostic and treatment thresholds, like the pre-test probability, are also subjective values. These should be based on various factors intrinsic to the disease, including its nature and behavior as well as reported prognosis. The diagnostic threshold is the probability of the disease in that below which, we should just reassure the patient and not test further. The therapeutic threshold is the probability of the disease in which above it, we should stop diagnostics and start treatment. In this case, if the probability of the disease is scored between the treatment and diagnostic thresholds, the clinician should continue to perform laboratory tests or diagnostics like dermoscopy, histopathology, stains, or immunofluorescence until reaching the treatment threshold when topical therapy or surgery should be advised.

Sample situations

Case 1. A dermoscopic photo of a suspicious pigmented nevus is sent through teledermatology and the set pre-test probability (personally set by the clinician) for this to be a malignant melanocytic tumor is 60%. Hypothetically, the diagnostic threshold is set at a low 10% and the treatment threshold at a high 90%. Using the values computed above, if an expert dermatologist calls this a melanoma (malignant melanocytic) from teledermoscopy, the likelihood that it is truly a malignant melanocytic tumor becomes 98% **(Figure 6)**. The jump from 60% to 98% **(Figure 7)** crossed the therapeutic threshold at 90% which may mean that the patient may come in for management already. The clinician may choose to forego additional diagnostics and start treatment.

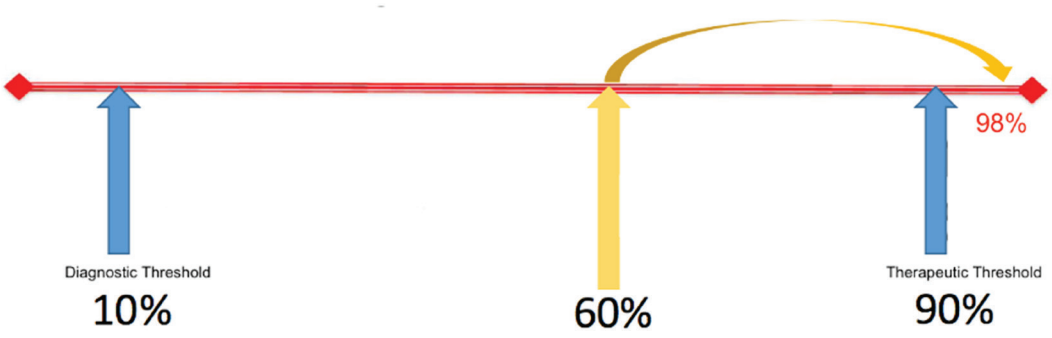

Figure 7. The likelihood of the skin tumor to be malignant became 98% from 60% after the expert dermatologist assessed it to be a melanoma via dermoscopic pictures.

Case 2. With a clinician's pre-test probability for non-melanocytic tumors set at 60% and diagnostic and therapeutic thresholds for this set at 10% and 80%, respectively, when a clinical photo of a brownish papule is sent for assessment and the expert dermatologist diagnoses it as excoriated prurigo (benign non-melanocytic), the likelihood of the lesion to be malignant drops from 60% to 4.6% **(Figure 4)**. Since the drop crossed the diagnostic threshold of 10% **(Figure 8)**, the clinician may reassure the patient and opt not to biopsy the skin lesion anymore.

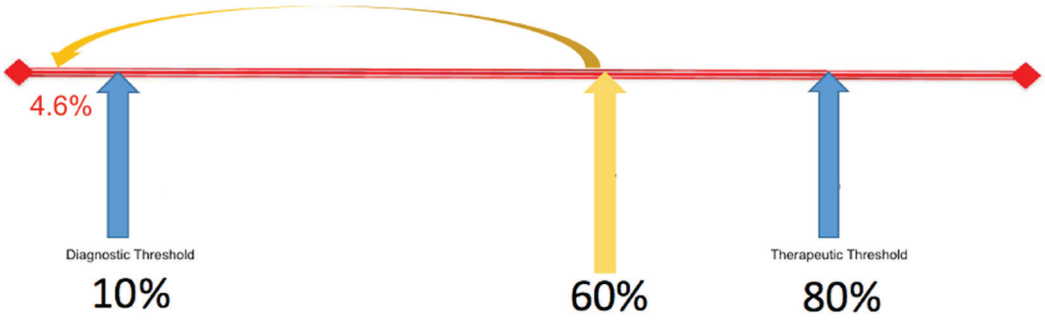

Figure 8. The likelihood of the skin tumor to be malignant non-melanocytic is now only 4.6% from 60% after the expert dermatologist commits that the lesion is only an excoriated prurigo from clinical pictures.

Other issues

Teledermatology and teledermoscopy are heavily reliant on technology. Teledermatology is made better by the continuing technological developments that make cellular phones more powerful. On the other end of the spectrum, some cellular phones, although able to send photos, are limited by the camera specifications. These include pixels, autofocus, flash or zoom features. Despite sending well-lit photograph from different angles on a neutral background, there are still innate camera characteristics that are not adjustable and contribute to a blurred photo.

Another issue that may hinder an accurate assessment of skin tumors is the variation of clinical presentation across ethnicities. For instance, only 6% of Caucasians present with pigmented basal cell carcinoma while 50% of this non-melanocytic skin tumor is seen in Asians.[6] The typical clinical presentation of basal cell carcinoma in Caucasians is a translucent nodule with ulcers and telangiectasia while in people of color, this usually presents as a pigmented lesion with a pearly appearance.[7]

Overall assessment

Mobile examination or teledermatology done by an expert dermatologist is a useful tool to assess skin tumors. Both clinical and dermoscopic mobile examination of melanocytic and non-melanocytic skin tumors showed excellent measures of accuracy against the gold standard which is face to face consultation with histopathological assessment.

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