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SHORT COMMUNICATION

Counting Actinic Keratosis – Is Photographic Assessment a Reliable Alternative to Physical Examination in Clinical Trials?

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Actinic keratoses (AKs) occur as a consequence of long-term sun exposure (1). The clinical significance of AKs is mainly related to the malignant potential of a small proportion (1, 2), but the lesions are also cosmetically disfiguring, painful and occasionally bleed (3). Existing and new therapies used for treatment of AKs rely on clinical counting as a means of measuring treatment end-point in clinical trials (4, 5). Similarly, large epidemiological studies that evaluate AK burden often rely on clinical counting of AKs rather than histopathology due to the associated aethical and practical challenges of the latter (6).

There are known difficulties with AK counting such as non-uniform morphology and the subjective nature of the clinical diagnosis (7). In order to improve the reliability of AK counting, published studies have focused on various important factors, which include defining the diameter of individual AKs being counted (8, 9), defining the total body surface area affected by AKs (8, 9) and segmenting body sites for counting AKs (10).

There is now high-resolution digital photography available and, although it has been successful as an adjunct for naevus surveillance, its utility in assessment of AK prevalence is yet to be evaluated (1). The present study aims to compare the inter-observer agreement between trained observers for AK counts based on photographs compared with clinical AK counts.

MATERIALS AND METHODS

A total of 6 people with varied degrees of actinic damage were recruited from the dermatology and renal outpatient departments at the Princess Alexandra Hospital in Brisbane, Australia. Three of the study participants were immunocompetent; the other 3 were immunosuppressed solid organ transplant recipients.

At the outset, a counting consensus workshop was held to establish clear definitions and protocols for both the clinical and photographic AK counts.

An AK was defined as an erythematous lesion measuring 2–10 mm in diameter with a fine or thick scale. AKs on the face, dorsal forearms and hands of each patient were counted. Contiguous AKs > 10–≤ 20 mm in diameter were counted as 2 AKs and those > 20–≤ 30 mm in size were counted as 3 AKs, and this principle was maintained for all measurements.

Clinical AK counting was carried out in 2 sessions by 4 dermatologically trained clinicians with 6 months or more of dermatological experience and a senior consultant dermatologist with over 25 years of experience, whose counts served as practical reference standard. All 5 observers independently performed clinical counts and the sizes of AKs were accurately measured using a standard ruler.

A professional photographer assisted with training the observers to optimize images for AK counting in the consensus workshop. Digital photographs were taken using Canon digital SLR (EOS 550D, Tokyo, Japan) equipped with a telephoto lens (EF-S 60 mm F/2.8 macro, Canon, Tokyo, Japan). Two 400s soft boxes equipped with light stands and full-length white screens were used in the background to ensure high quality photography. Images of the face were taken front-on and forearms and hands were taken with the subjects facing the screen with thumbs pointed superiorly. A ruler was also used in the same plane as the photographs for measurement of AK lesions. JPEG images were used for the photographic counting with a resolution of 350 dpi and dimensions of 3,456 × 5,184 pixels. Counting was performed using a computer monitor with a resolution of 1,680 × 1,050 in a fixed room with good lighting. The observers repeated counting from the same photographic images, 2 weeks later.

All observers annotated all visible AK directly onto the corresponding digital images on the computer screen using a standard setting in the paintbrush program. They were instructed to label each AK by drawing an outline to completely enclose the lesion without overlapping with other lesion markings.

Image processing was performed in Matlab (Version R2012b, The Mathworks Inc., Natick, Ma., USA). Digitally marked annotations were extracted from each image; with each fully enclosed clinician label counted as a single distinct lesion.

Agreement of AK counts was measured using interclass and intraclass correlation coefficients (ICC). The values > 0.75 were considered to indicate excellent agreement, and between 0.40 and 0.75 as fair to good agreement and < 0.40 as poor agreement (11).

Absolute agreement and significant differences across observers and within each observer for the mean AK counts of clinical and photographic data were also examined using a mixed effect model; with study participants as a random effect and body site and operator as fixed effects. Differences between the 3 sampling situations were compared for each observer using a paired sample *t*-test. All data were analysed using the SPSS (version 19).

RESULTS

The majority (84%) of study participants were male and their mean age was 60 years (SD 15). The ICC for agreement across 5 observers for the photographic AK counts was 0.63 (95% CI 0.48–0.78) compared with 0.79 (95% CI 0.68–0.88) for clinical counts (Count 1). The ICC for agreement between photographic AK counts and clinical counts ranged from 0.66 (95% CI 0.48–0.81) to 0.84 (95% CI 0.73–0.91) across the 5 observers (Table I). The interclass correlation coefficient for agreement

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Table I. *Intraobserver agreement for total clinical and photographic actinic keratosis (AK) counts for the 4 trained clinicians and the senior observer*

	Senior	1	2	3	4
AK[a]	0.79	0.66	0.84	0.77	0.81
	(0.65–0.88)	(0.48–0.81)	(0.73–0.91)	(0.63–0.87)	(0.69–0.90)
Photographic AK[b]	0.90	0.93	0.99	0.86	0.93

Values are given as intraclass correlation coefficient (95% confidence interval).
[a]Clinical and photographic count 1 and 2. [b]Count 1 versus 2.

between AK counts based on the same photographs but counted on 2 separate occasions ranged from 0.86 to 0.99 (Table I).

In regard to absolute agreement, statistically significant differences between observers were noted in the mean AK counts for each of the photographic AK counts ($p = 0.015$ and 0.017, respectively) and clinical AK counts ($p = 0.031$) (Table II).

DISCUSSION

We found that photographic counts showed fair to good agreement across the observers while clinical AK counts showed excellent agreement across observers. Repeated photographic counts were also found to have excellent intraobserver agreement. Despite this the magnitude of the mean AK counts for the 6 study participants varied widely and significantly among observers, not only for the two separate photographic counts but also for the clinical AK counts. Our results also showed lack of clinician consensus about the precise magnitude of AK counts. Thus based on our assessments in this small series of patients, photographic AK counting seems not to be a reliable alternative method to clinical AK counting.

Interobserver agreement for clinical AK counting in our study was comparable to results from other studies (9, 11). However, we found the differences in absolute mean AK counts between observers on clinical examination to be substantial, confirming the results of many previous studies (8–13), and we found similar variability in mean AK counts of observers examining photographs of affected skin.

This study is novel for its examination of the objective quantification of AK burden using high-resolution digital photography. We have shown that it is feasible, though accuracy is no better than, and reliability appears inferior to, clinical assessment. As technological advancements occur, three-dimensional photography will largely supersede two-dimensional photographs in clinical practice, and more robust image capturing techniques should improve the accuracy of photographic counting (14). At present however, it seems that traditional clinical counting methods provide superior results compared to photographic counting methods.

Table II. *Absolute agreement: observer mean actinic keratosis (AK) counts for clinical and photographic AK counting methods for the 4 trained clinicians and the senior observer**

	Senior	1	2	3	4	SD	*p*-value
Clinical count	17.1[a,b]	13.9	15.9[a]	23.9**	17.9	11.2	0.031
Photographic count 1	15.5[b]	14.8	10.9[b]	24.3**	14.6	13.6	0.015
Photographic count 2	18.7[a]	16.7	9.6[c]**	25.9	15.6	16.4	0.017

*Overall difference is indicated by the *p*-value and individual differences from the practical reference standard are indicated by **.
[a,b,c]Differences between the 3 sampling situations have been compared for each operator using a *t*-test and significant differences are indicated by combinations of a,b,c means within columns with a letter in common are not significantly different ($p > 0.05$).

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