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ORIGINAL ARTICLE

# Usefulness of Dermatoscopy for the Preoperative Assessment of the Histopathologic Aggressiveness of Basal Cell Carcinoma

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**Background:** Limited information is available regarding dermatoscopic differences between non-aggressive and aggressive types of basal cell carcinoma (BCC). **Objective:** To investigate dermatoscopic differences between non-aggressive and aggressive types. **Methods:** We evaluated 145 histopathologically confirmed BCCs from 141 patients. Histopathologic types and aggressiveness from 4 mm punch biopsy and their dermatoscopic findings were evaluated. We assessed the statistical significance of dermatoscopic differences between non-aggressive and aggressive types. To objectively predict aggressiveness, we created a "dermatoscopic index of BCC aggressiveness" in which 1 point was added and subtracted for each dermatoscopic finding significantly higher in aggressive and non-aggressive types, respectively. **Results:** Large blue-gray ovoid nests were found more frequently in non-aggressive type than aggressive one (85/105 [80.9%] vs. 21/40 [52.5%], $p=0.001$). Compared to non-aggressive type, aggressive type had more multiple blue-gray globules (29/40 [72.5%] vs. 57/105 [54.3%], $p=0.046$), arborizing telangiectasia (29/40 [72.5%] vs. 48/105 [45.7%], $p=0.004$), and concentric structure (11/40 [27.5%] vs. 12/105 [11.4%], $p=0.018$). Regarding dermatoscopic index, cases of aggressive type with a score of 1 were most common (n=18, 45.0%), followed by a score of 2 (n=14, 35.0%). Limited number of aggressive type of BCCs and the effect of width on the determination of histopathologic aggressiveness. **Conclusion:** Aggressive type BCCs more often exhibited multiple blue-gray globules, arborizing telangiectasia, and concentric structure, while the non-aggressive type exhibited large blue-gray ovoid nests more frequently. Score exceeding 2 on the dermoscopic index can be screening criteria for aggressiveness. These dermatoscopic features and dermoscopic index could be useful for assessing aggressiveness of BCCs before surgery. **(Ann Dermatol 27(6) 682~687, 2015)**

**-Keywords-**
Basal cell carcinoma, Dermatoscopy, Histopathologic aggressiveness

## INTRODUCTION

The prevalence of basal cell carcinoma (BCC) is increasing; it is the most common skin cancer worldwide including Korea[1,2]. The clinicopathologic subtypes of BCCs can be classified as non-aggressive including nodular, adenoid, and superficial subtypes, as well as aggressive including micronodular, infiltrative, and morpheaform subtypes[3,4]. Compared to the non-aggressive type, the aggressive type requires more cautious treatment and closer follow-up because of the greater likelihood of incomplete excision and recurrence[5-8].

Dermatoscopy is a very useful diagnostic tool for various skin disorders including BCC. Classic dermatoscopic structures of BCC include maple leaf-like areas, spoke-wheel

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areas, large blue-gray ovoid nests, multiple blue-gray globules, arborizing telangiectasia, and ulceration[9]. Although many studies reported the dermatoscopic patterns of BCC, no study has evaluated the dermatoscopic differences between the non-aggressive and aggressive types of BCC or assessed the histopathologic aggressiveness of BCC preoperatively by dermatoscopy[10-13]. Therefore, this retrospective histopathologic and dermatoscopic analysis of 145 BCCs including 105 and 40 non-aggressive and aggressive types respectively, evaluated the dermatoscopic differences between the non-aggressive and aggressive types of BCC.

## MATERIALS AND METHODS

### Patient selection and imaging equipment

This study included 141 patients with 145 primary BCCs histologically confirmed by 4 mm punch biopsy at the Dermatologic Clinic of Pusan National University Hospital between January 2006 and April 2012 (IRB No. PNUHIRB E-2015052). We excluded BCC specimens obtained by the shave technique and those that appeared to have mixed histopathologic subtypes. The patients' mean age was 69 years (range, 36～91 years). The majority of lesions were located on the head and face (n=131, 90.3%) followed by the trunk (n=8, 5.5%) and extremities (n=6, 4.1%).
Clinical photographs were taken with Canon EOS 50D digital single lens reflex cameras (Canon, Tokyo, Japan). For dermatoscopic images, Dermlite II PRO HR equipment (3 Gen, San Juan Capistrano, CA, USA) was used and dermatoscopic photographs were taken with a DSC-W290 (Sony, Tokyo, Japan).

### Histopathologic classification and dermatoscopic criteria of basal cell carcinoma

All samples taken using 4 mm punch biopsy were classified histologically according to Lang and Maize[3] and Sexton et al.[4] as non-aggressive including nodular, adenoid, or superficial subtypes or aggressive includingmicronodular, infiltrative, or morpheaform subtypes. There were 105 non-aggressive lesions including nodular (n=85, 80.9%), adenoid (n=11, 10.5%), and superficial subtypes (n=9, 8.6%). Meanwhile, there were 40 aggressive lesions including micronodular (n=28, 70.0%), infiltrative (n=10, 25.0%), and morpheaform subtypes (n=2, 5.0%).
We analyzed the following dermatoscopic features of BCC according to the criteria of Menzies et al.[9] and Altamura et al.[10]: (1) classic BCC patterns including large blue-gray ovoid nests, multiple blue-gray globules, maple leaf-like areas, spoke-wheel areas, arborizing telangiectasia, and ulceration and (2) non-classic BCC patterns including short fine superficial telangiectasia, multiple small erosions, concentric structures, and multiple in-focus blue-gray dots. We also analyzed dermatoscopic features not classifiable into the above categories but found in various skin lesions including BCCs in previous reports[13-16]. We named these patterns 'other BCC patterns' which included non-arborizing vessels, brown-black dots, blue-white veil, and pigment network. The dermatoscopic features of BCC were assessed by two dermatologists who were experienced with dermatoscopy.

### Dermatoscopic index of basal cell carcinoma aggressiveness

To objectively predict the aggressiveness of BCC, we established an index in which 1 point was added or subtracted for each dermatoscopic findings that was significantly more common in the aggressive and non-aggressive types, respectively.

### Statistical analysis

The $\chi^2$ test was performed to analyze the differences in the dermatoscopic patterns between non-aggressive and aggressive types. PASW Statistics ver. 18.0 for Windows (IBM Co., Armonk, NY, USA) was used for statistical analysis. The level of significance was set at $p<0.05$.

## RESULTS

### Differences in dermatoscopic features between non-aggressive and aggressive types of basal cell carcinoma

In non-aggressive type, the most common pattern was large blue-gray ovoid nests (85/105, 80.9%) followed by ulceration (65/105, 61.9%), multiple blue-gray globules (57/105, 54.3%), arborizing telangiectasia (48/105, 45.7%), and blue-white veil (43/105, 40.9%) (Fig. 1). Meanwhile, aggressive type exhibited multiple blue-gray globules and arborizing telangiectasia most frequently (29/40, 72.5%; 29/40, 72.5%; respectively), followed by ulceration (25/40, 62.5%), large blue-gray ovoid nests (21/40, 52.5%), multiple blue-gray dots (13/40, 32.5%), blue-white veil (10/40, 25.0%), and short fine superficial telangiectasia (9/40, 22.5%) (Fig. 2). Comparing the dermatoscopic differences with respect to aggressiveness revealed significant differences in several patterns. Large blue-gray ovoid nests were more frequent (85/105 [80.9%] vs. 21/40 [52.5%], $p=0.001$) in non-aggressive type. Meanwhile, multiple blue-gray globules (29/40 [72.5%] vs. 57/105 [54.3%], $p=0.046$), arborizing telangiectasia (29/40 [72.5%] vs. 48/105 [45.7%], $p=0.004$), and concentric structure (11/40 [27.5%] vs. 12/105 [11.4%], $p=0.018$) were significantly more common in aggressive

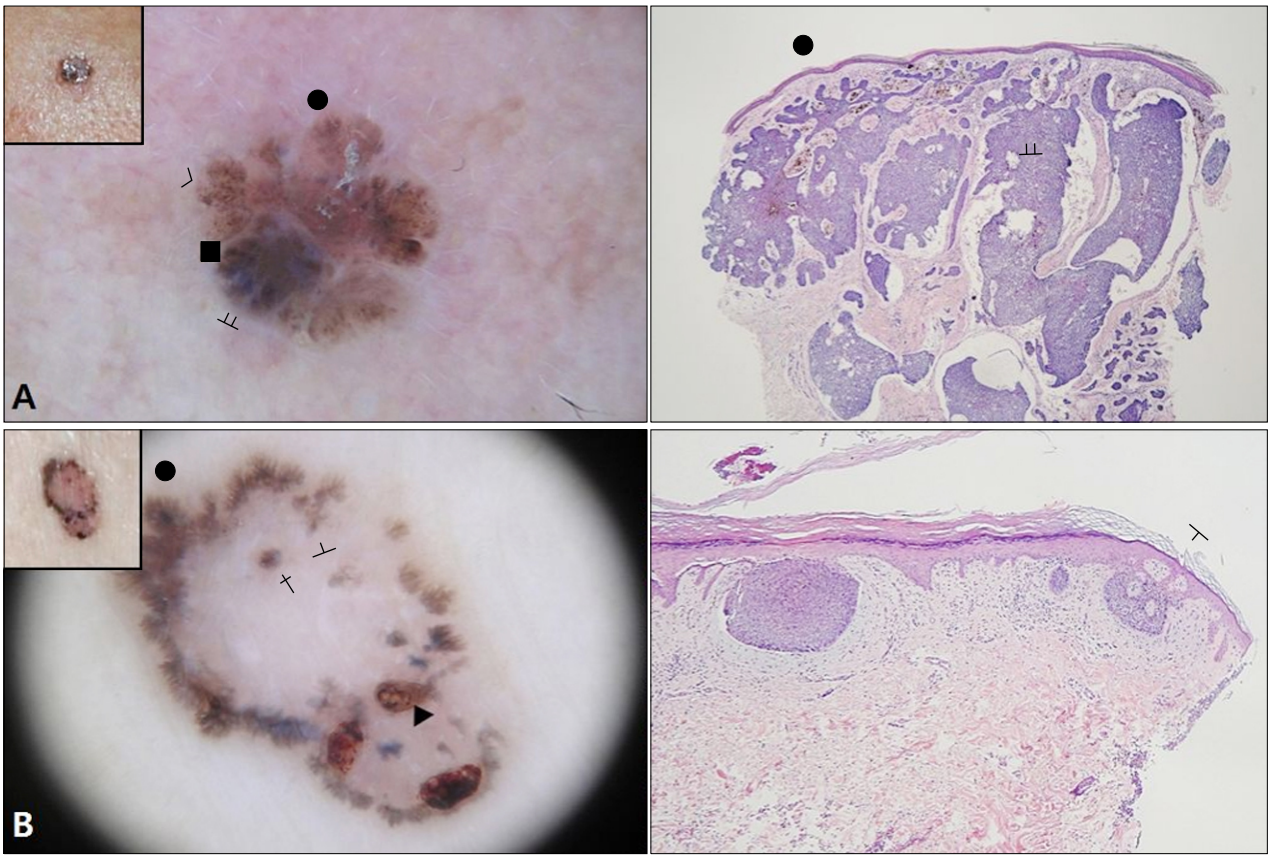


**Fig. 1.** Non-aggressive types of basal cell carcinoma. (A) Nodular type, (B) superficial type. Left column: dermatoscopic findings (inset, clinical photo). Right column: histologic findings (H&E, ×40). ⫫: large blue-gray ovoid nests, ■: multiple blue-gray globules, ●: maple leaf-like areas, ⊥: spoke-wheel areas, ▲: ulceration, †: concentric structure, >: brown-black dots.

type (Table 1).

### Dermatoscopic index of basal cell carcinoma aggressiveness

According to the dermatoscopic index of BCC aggressiveness, the dermatoscopic findings of multiple blue-gray globules, arborizing telangiectasia, and concentric structure were scored +1, while large blue-gray ovoid nests were scored −1. Among aggressive type, BCCs with a score of +1 were most common (n=18, 45.0%), followed by a score of +2 (n=14, 35.0%). Among non-aggressive type, BCCs with a score of 0 were most common (n=46, 43.8%), followed by a score of +1 (n=35, 33.3%). The sensitivity, specificity, positive predictive value and negative predictive values of this index are shown in Table 2.

## DISCUSSION

Although BCC has low mortality and metastasis rates, it can be locally invasive and destructive. The aggressive histologic type of BCC includes micronodular, infiltrative, and morpheaform subtypes[5-8]. Aggressive BCC is not rare: its incidence ranges from 2.5% to 44%[7]. In the present study, 27.6% of BCCs (40/145) were the aggressive type. The aggressive type of BCC is challenging to treat because of its local invasive behavior, increased subclinical extension, and tendency to recur[5-7]. Thus, aggressive type of BCC requires more cautious treatment and closer follow-up than non-aggressive type. Therefore, the ability to predict the aggressiveness of BCC on the basis of dermatoscopic features would improve disease management. Although the classic and non-classic dermatoscopic patterns of have been established by Menzies et al.[9] and Altamura et al.[10] respectively, no study has used dermatoscopy to assess the histologic aggressiveness of BCC.

In the present study, all BCC lesions exhibited at least 1 of classic BCC patterns except for 1 case of non-aggressive type BCCs. The prevalence of large blue-gray ovoid nests (73.1% vs. 47.1%) and ulceration (62.1% vs. 22.5%) were much higher in the present study than the study of Altamura et al.[10] These differences may be because of the different distribution of histologic subtypes between two

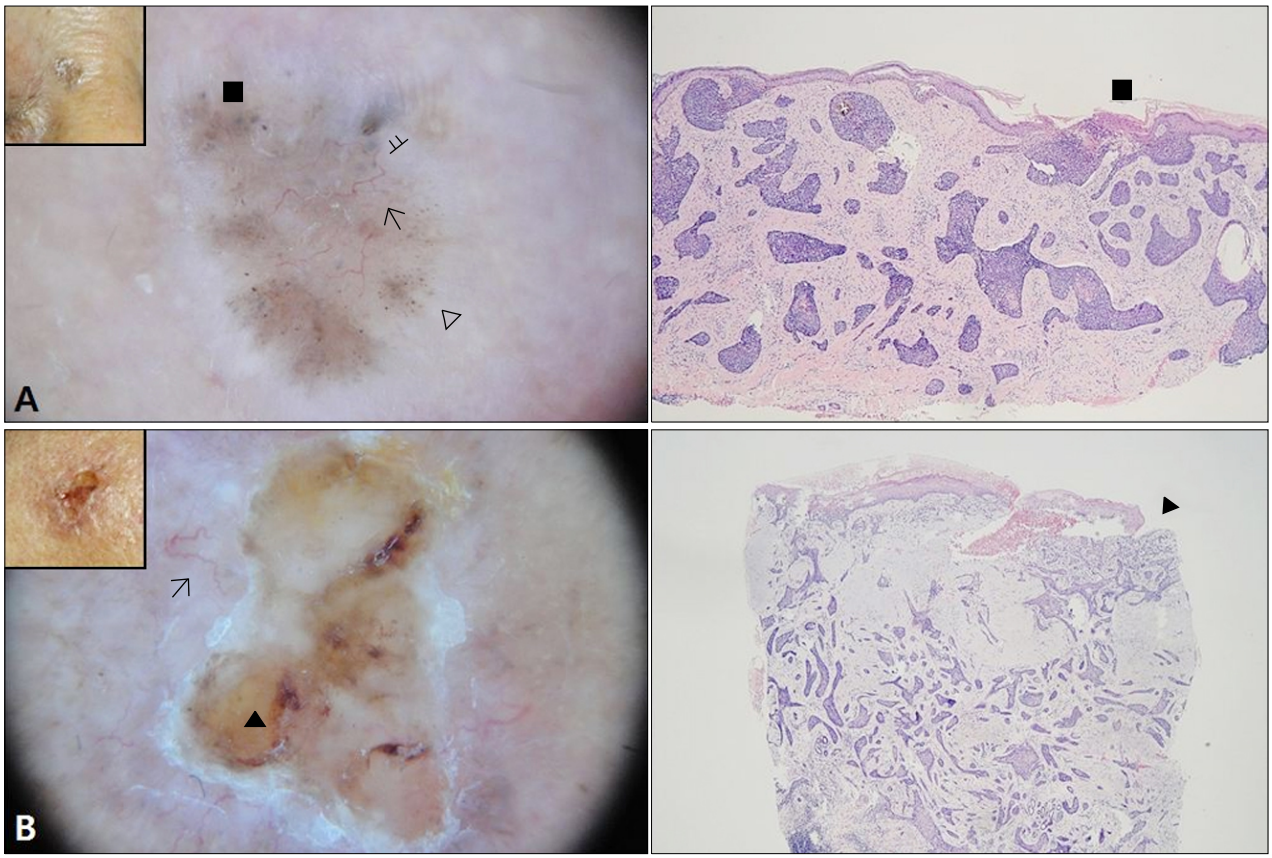


**Fig. 2.** Aggressive types of basal cell carcinoma. (A) Micronodular type, (B) infiltrative type. Left column: dermatoscopic findings (inset, clinical photo). Right column: histologic findings (H&E, ×40). ■: large blue-gray ovoid nests, ■: multiple blue-gray globules, ➔: arborizing telangiectasia, ▲: ulceration, △: multiple blue-gray dots.

**Table 1.** Comparision of classic, nonclassic and other basal cell carcinoma dermatoscopic patterns between non-aggressive and aggressive types*

| Variable | Non-aggressive type (n=105) | Aggressive type (n=40) | Total (n=145) | *p*-value* | Kappa coefficient (κ) |
|---|---|---|---|---|---|
| Classic | | | | | |
| Large blue-gray ovoid nests | 85 (80.9) | 21 (52.5) | 106 (73.1) | 0.001 | 0.774 |
| Multiple blue-gray globules | 57 (54.3) | 29 (72.5) | 86 (59.3) | 0.046 | 0.928 |
| Maple leaf-like areas | 22 (20.9) | 6 (15.0) | 28 (19.3) | 0.417 | |
| Spoke wheel areas | 9 (8.6) | 3 (7.5) | 12 (8.3) | 0.834 | |
| Arborizing telangiectasia | 48 (45.7) | 29 (72.5) | 77 (53.1) | 0.004 | 0.834 |
| Ulceration | 65 (61.9) | 25 (62.5) | 90 (62.1) | 0.947 | |
| Nonclassic | | | | | |
| Short fine superficial telangiectasia | 33 (31.4) | 9 (22.5) | 42 (29.0) | 0.289 | |
| Multiple small erosions | 13 (12.4) | 3 (7.5) | 16 (11.0) | 0.557 | |
| Concentric structure | 12 (11.4) | 11 (27.5) | 23 (15.9) | 0.018 | 0.868 |
| Multiple blue-gray dots | 28 (26.7) | 13 (32.5) | 41 (28.3) | 0.486 | |
| Other | | | | | |
| Non-arborizing vessels | 2 (1.9) | 3 (7.5) | 5 (3.4) | 0.129 | |
| Brown-black dots | 3 (2.8) | 4 (10.0) | 7 (4.8) | 0.092 | |
| Blue-white veil | 43 (40.9) | 10 (25.0) | 53 (36.6) | 0.075 | |
| Pigment network | 2 (1.9) | 1 (2.5) | 3 (2.1) | 0.822 | |

Values are presented as number (%). *$\chi^2$ test, $p<0.05$.

**Table 2.** Sensitivity, specificity, and positive and negative predictive values of the dermoscopic index of BCC aggressiveness

| Aggressivenss dermoscopic index of BCC (score) | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|---|---|---|---|---|
| ≥0 | 0.98 (39/40) | 0.16 (17/105) | 0.31 (39/127) | 0.94 (17/18) |
| ≥1 | 0.83 (33/40) | 0.60 (63/105) | 0.44 (33/75) | 0.90 (63/70) |
| ≥2 | 0.375 (15/40) | 0.93 (98/105) | 0.68 (15/22) | 0.80 (98/123) |
| ≥3 | 0.025 (1/40) | 1.00 (105/105) | 1.00 (1/1) | 0.73 (105/144) |

BCC: basal cell carcinoma.

studies. Compared to classic BCC patterns except for maple leaf-like areas and spoke wheel areas, all non-classic BCC patterns were less common, with short fine superficial telangiectasia (42/145, 29.0%) being the most common pattern. Among 'other patterns', blue-white veil was found in 36.6% of BCC lesions (53/145), while others were found in less than 5%. Blue-white veil is considered to be specific to melanoma, but Altamura et al.[10] report finding it in 17.3% and 61.8% of pigmented and heavily pigmented BCCs , respectively; accordingly, they suggest the heavily pigmented variant could be difficult to differentiate from melanocytic nevi or melanomas. In the present study, blue-white veil was observed in 43.5% of nodular BCCs (37/85) and 54.5% of adenoid BCCs (6/11) (data not shown).

To our knowledge, no study has investigated the dermatoscopic features with respect to various histologic subtypes of BCC. Although we wanted to perform such an analysis, we opted not to, because the discordance rate of BCC histologic subtype between biopsy and an excision specimens ranged from 18% to 38%[17-19]. This high discordance rate could be due to differences in width and/or depth between biopsy and excision samples. We could not calculate the discordance rate in this study, because all the specimens were excised by Mohs micrographic surgery, making them inappropriate and ambiguous for histological classification. Instead, only 4 mm punch biopsy specimens were included. The width of these specimens is unsatisfactory. However, their depth makes them sufficient for assessing aggressiveness, because the length of the punch blade is approximately 8 mm and the mean depth of aggressive BCCs was less than 3 mm (micronodula, 2.01 mm; infiltrative, 1.82 mm) in the study of Welsch et al.[17].

Large blue-gray ovoid nests represent the melanin-containing cell nests in papillary or reticular dermis; the histopathological counterparts of these features are superficial and nodular types[12]. Multiple blue-gray globules, which reflect the melanin-containing cell aggregates within the dermis, are more commonly present in the micronodular and superficial subtypes[12]. In the present study, compared to non-aggressive type, aggressive type exhibited multiple blue-gray globules more commonly , and large blue-gray ovoid nests less commonly with statistical significance. These results may be attributable to BCC subtype distributions in the present study; that is, nodular type was the most common subtype in non-aggressive type and micronodular type in aggressive type in this study.

Aggressive type more frequently exhibited non-arborizing vessels (3/40 [7.5%] vs. 2/105 [1.9%], $p=0.129$) and arborizing telangiectasia (29/40 [72.5%] vs. 48/105 [45.7%], $p=0.004$) than non-aggressive type. Microvessel density is reported to be helpful for determining tumor aggressiveness in BCC[12]. Newell et al.[20] used videocapillaroscopy and immunohistochemistry to quantify the microvasculature of BCC, and demonstrated that angiogenesis is significantly greater in BCC than actinic keratosis; this suggests angiogenesis is a precondition for the growth for invasive tumors. In the present study, angiogenesis represented by various vascular patterns, which may suggest a more aggressive histologic pattern, and the higher prevalence of arborizing and non-arborizing vascular patterns in aggressive BCCs support this hypothesis.

Concentric structure were significantly more common in aggressive BCCs (11/40, 27.5%) than non-aggressive BCCs (12/105, 11.4%) ($p=0.018$). The histologic characteristics of micronodular BCC, which is the most common type of aggressive BCC, are uniform small nests of neoplastic basal cells extending throughout the dermis and small tumor nests occasionally connected to the epidermis that may resemble concentric structures on dermatoscopy.

In addition, we established the 'dermoscopic index of BCC aggressiveness' on the basis of the significant differences between aggressive and non-aggressive types. Regarding the sensitivity, specificity, and positive and negative predictive values of this index, the most valid and reliable index score was score +2 which enables the estimation of the aggressiveness of BCC lesions. Hence, dermoscopic index of BCC aggressiveness score exceeding +2 can be used as a criterion of high aggressiveness of BCC lesions.

The main limitation of our study is the small sample size of aggressive type of BCC. Furthermore, biopsy width may

have affected the determination of histopathologic aggressiveness, although although its effect is likely minimal. In summary, multiple blue-gray globules, arborizing telangiectasia, and concentric structures are significantly more common in aggressive type BCC, while large blue-gray ovoid nests are more common in the non-aggressive type BCC. These dermatoscopic features and the dermoscopic index of aggressiveness BCC may aid the assessment of the aggressiveness for BCC before skin biopsy or excision as well as treatment selection. The result of this study demonstrate dermatoscopy not only serves as a diagnostic tool but also as an assessment tool of the aggressiveness of BCC.

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