

# Comparison of the recurrence rate of 3 treatment modalities for Bowen disease in an aging city

## A retrospective multivariate analysis

Young Woong Mo, MD<sup>a,b</sup>, Dong Lark Lee, MD, PhD<sup>b,\*</sup>

### Abstract

A wide range of therapeutic options are available for the treatment of Bowen disease. However, few studies have been conducted on wide excision using various resurfacing methods. The objectives of this study were:

- 1) to analyze statistically epidemiologic characteristics, demographics, and treatment modalities by anatomical sites; and
- 2) to determine the efficacy of wide excision with respect to recurrence.

One hundred forty-eight lesions were studied. All lesions were histopathologically confirmed as Bowen disease. Lesions were classified by anatomical site and treatment modality and their dimensions were measured. Punch biopsy was reperformed when a treated lesion was considered to have possibly recurred. Recurrence rates were then compared. Preoperative and intraoperative photos and follow-up images were also taken.

The most common site of Bowen disease was the head and neck region. Wide excision was found to provide good outcomes with minimal tumor recurrence. Recurrence after cryotherapy occurred relatively quickly (mean 0.2 years, median 0.2 years) while recurrence after wide excision occurred at a mean 2.5 years. Treatment modality was significantly associated with recurrence ( $P < .05$ ).

The optimal treatment for Bowen disease has not been determined. Wide excision provided lower recurrence than other treatment modalities. Providers should be aware of the multiple treatment options available and select the method most appropriate for each patient. The limitations of our study are that it was retrospectively designed and conducted at a single institution.

**Abbreviations:** 5-FU = 5-fluorouracil, FTSG = full-thickness skin graft, PDT = photodynamic therapy, SCC = squamous cell carcinoma, STSG = split-thickness skin graft.

**Keywords:** Bowen disease, carbon dioxide laser, cryotherapy, excision

### 1. Introduction

Bowen disease is defined as a form of intraepidermal squamous cell carcinoma (SCC) that does not invade the dermal layer. The

disease is characterized by persistent, non-elevated, red, scaly, or crusted plaque and has some potential to develop into an invasive malignancy. Progressive growth is usual but spontaneous partial regression occasionally occurs.<sup>[1,2]</sup> Fewer than 5% of lesions evolve into invasive SCC, but if the disease progresses to invasive cancer, one-third of lesions may metastasize.<sup>[3]</sup> It has also been reported that at least 42% of Bowen disease patients develop precancerous or cancerous lesions on skin or mucosa in the long-term,<sup>[4]</sup> which is why Bowen disease must be treated as early as possible.

A wide range of therapeutic options are available for the treatment of Bowen disease, such as cryotherapy, topical 5-fluorouracil (5-FU), curettage and electrodesiccation, excision, topical imiquimod, laser ablation, radiation, and photodynamic therapy (PDT).<sup>[1,2,4,5]</sup> However, topical cryotherapy and topical 5-FU have been disappointingly associated with high recurrence rates.<sup>[5]</sup> Surgical excision is useful, particularly for small lesions in poor healing sites, perineal lesions, and digital lesions.<sup>[1]</sup> Multiple studies have demonstrated an initial cure rate of 54% to 100% by PDT with variable long-term efficacy. Truchuelo et al reported a 76% clearance rate after 2 methyl-aminolevulinic acid photodynamic therapy sessions.<sup>[5]</sup> Little is known of the effectiveness or recurrence rate of carbon dioxide (CO<sub>2</sub>) laser ablation. Low-risk premalignant lesions can usually be adequately treated conservatively, but risk of recurrence after appropriate conservative treatment is greater than that after surgical excision.<sup>[1,2,5]</sup>

Comparisons of the relative effectiveness of different therapies and regimens are difficult because published studies have not fully controlled for factors such as lesion site and size

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The study was approved by the Institutional Review Board of Dongguk University Hospital (IRB No. IRB; approval # 110757-201905-HR-05-02) and performed in accordance with the principles of the Declaration of Helsinki.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available; consent for figures.

<sup>a</sup> Department of Plastic and Reconstructive Surgery, Dongguk University Graduate School of Medicine, 30, Pildong-ro 1-gil, Jung-gu, Seoul, <sup>b</sup> Department of Plastic and Reconstructive Surgery, College of Medicine, Dongguk University, 87 Dongdae-ro, Gyeongju, Republic of Korea.

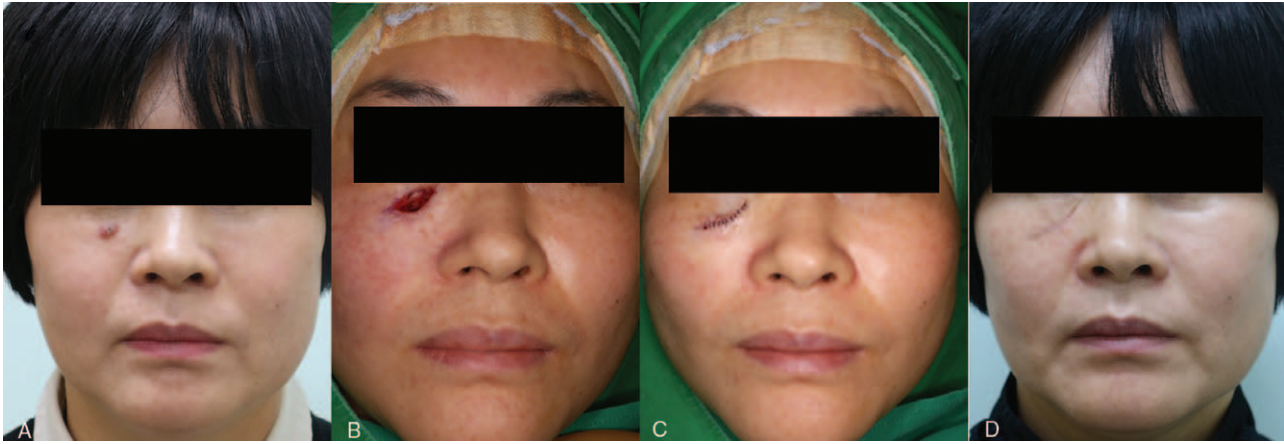
\* Correspondence: Dong Lark Lee, Department of Plastic and Reconstructive Surgery, College of Medicine, Dongguk University, 87 Dongdae-ro, Gyeongju 38067, Republic of Korea (e-mail: drleedr@gmail.com).

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**Figure 1.** Conventional elliptical excision on the right lid-cheek. A, A  $0.5 \times 0.9 \text{ cm}^2$  sized rapidly growing Bowen disease tumor on a right lid-cheek. B–C, After conventional elliptical excision, the defect was closed using a primary simple interrupted suture. D, A curvilinear scar remained on the right lid-cheek at 3 weeks postoperatively.

and because centers use different regimens.<sup>[1]</sup> Several attempts have been made to compare the efficacies and recurrence rates of different treatment methods. However, no statistical study has been performed with adjustment for various parameters, tumor size and location, and different surgical treatment modalities.

The objectives of this study were;

- 1) to analyze statistically epidemiologic characteristics, demographics, and treatment modalities by anatomical sites; and
- 2) to determine the efficacy of wide excision with local flap coverage or skin graft for the treatment of Bowen disease as compared with cryotherapy or laser ablation.

Given the background stated above, we conducted this retrospective study to identify factors that influence the outcomes of treatments for Bowen disease. We compared the long-term effectiveness of CO<sub>2</sub> laser ablation and cryosurgery with that of

surgical excision and investigated the relationship between clinical factors and responses to respective treatments.

## 2. Methods

### 2.1. Study method

Patients were retrospectively selected using histological data. Patient, tumor, and treatment characteristics were obtained from medical records with pre- and post-operative clinical photos. The parameters studied included; age, gender, anatomic location, tumor size (longest and shortest lesion axes based on the assumption of an elliptical shape) at time of biopsy, previous treatment of the tumor, treatment modality employed, defect size and tumor closure length (if treated surgically), and recurrence after treatment. All lesions were examined by plastic surgeons 1, 2, 3, 6, 12, and 24 months after first examination.



**Figure 2.** Wide excisions with a local flap (advancement). A, A 75-year-old woman visited our outpatient department with three Bowen disease tumors (all were histopathologically confirmed) on her right cheek (preoperative clinical photo). B, Wide excision with local flap coverage was performed. After undermining, both flaps were advanced and sutured. C, Clinical photograph of the hypertrophic phase taken at 1 month postoperatively. D, No complications, such as contour deformation, margin irregularity, or recurrence, were evident at 6 months postoperatively, though mild melanocyte migration was observed.



**Figure 3.** Wide excisions with local flap (V-Y advancement). A–C, A  $1.2 \times 1.5 \text{ cm}^2$  sized Bowen disease tumor on a right lid-cheek. After wide excision, the defect was resurfaced using a V-Y advancement ipsilateral cheek flap. D–F, The defect was closed using a V-Y advancement flap based on underlying nasalis.

During follow-up, clinical appearance of recurrence at previously treated sites was assessed by clinicians and punch biopsy was performed on all suspicious lesions. Recurrence was defined as new proliferation at the site of the original tumor with histopathological confirmation by a pathologist.

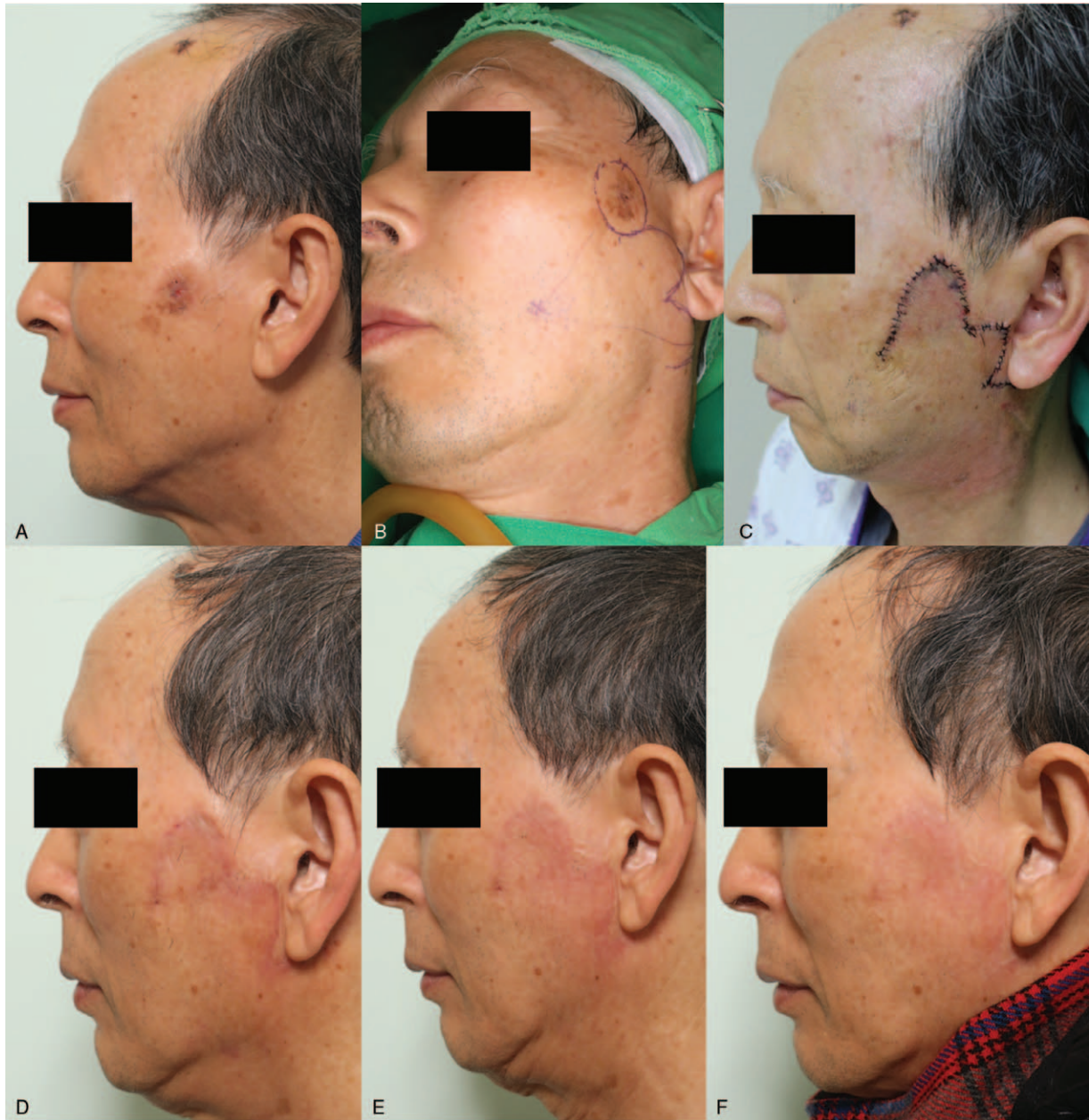
## 2.2. Subjects

One hundred thirty-seven patients (148 lesions) that visited our outpatient department over the 8-year period from 2010 to 2017 were recruited. All were diagnosed to have Bowen disease by punch biopsy, requested treatment consultation at our department of

plastic and reconstructive surgery, and all were treated by plastic surgeons. Patients were retrospectively selected using histological data. The exclusion criteria were:

- 1) Bowen disease affecting mucous membranes, or lesions near invasive skin cancer.
- 2) Treatment for Bowen disease during the 6 months prior to presentation.
- 3) Tumors associated with human papilloma virus.
- 4) A severe scar history (e.g., hypertrophic scars or keloids).

Patient, tumor, and treatment characteristics were obtained from medical records with pre- and post-operative clinical



**Figure 4.** Wide excisions with a local flap (transposition). A, A 71-year-old man visited our outpatient department with a histopathologically confirmed Bowen disease tumor on his left cheek. B–C, After wide excision of the tumor, the defect was resurfaced with a geometric bilobed flap (a type of transposition flap). Adequate undermining, proper flap thickness, and counter-clockwise flap rotation resulted in no skin tension or venous congestion. D–F, Clinical photos taken at 1, 2, and 6 months postoperatively. The wound matured with time and the scar faded.

photos. This study was approved by the Institutional Review Board of our hospital (IRB approval # 110757-201905-HR-05-02), and was performed in accordance with the principles of the Declaration of Helsinki. Patient photographic consent, authorization, and release forms were obtained from all patients.

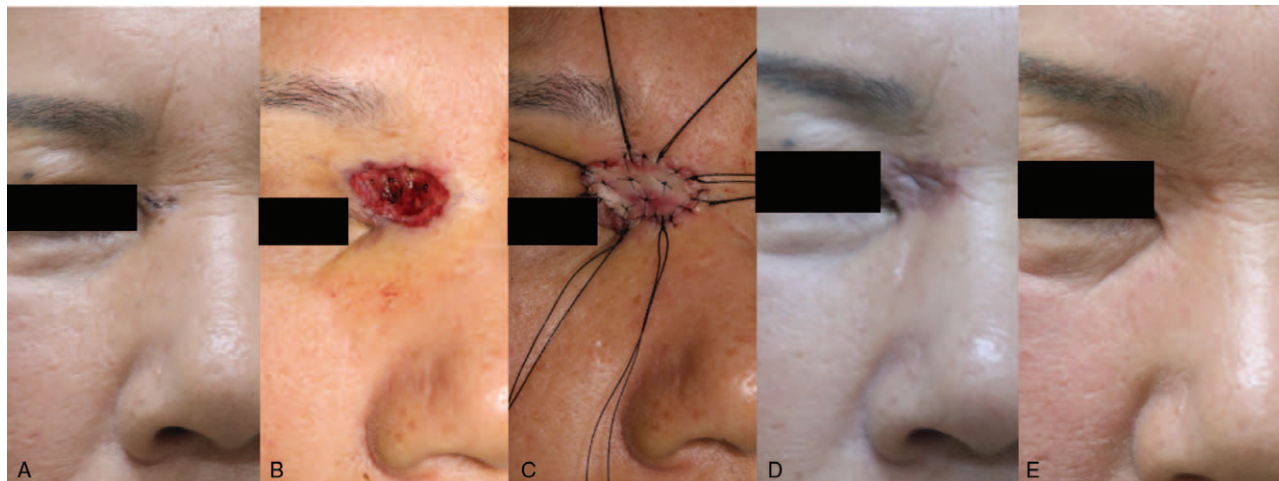
### 2.3. Treatment modalities

Cryotherapy was performed in a single session with the margin of 3 mm using the open spray technique. Mean time taken and number of freeze–thaw cycles (FTC) were 15 to 30 seconds and 1 cycle respectively.

Laser ablation was performed in 3 sessions over 3 weeks using the MULTIXEL (Daeshin Enterprise, Seoul, South Korea) multi-function fractional CO<sub>2</sub> laser system. The laser was set at Super Pulse Mode with a repeat time of 5 to 30 ms. No margin was considered, the focus was on laser ablation and visual confirmation that lesions had been completely ablated. Photographs taken before and immediately after surgery were evaluated.

The surgical methods adopted were;

- 1) Elliptical excision (Fig. 1),
- 2) Wide excision with local flap coverage (V-Y advancement, advancement, transposition) (Figs. 2–4),



**Figure 5.** Bowen disease. Wide excision with a full-thickness skin graft (FTSG). A, Photograph showing a Bowen disease tumor on right medial canthal area. B, A small subcutaneous defect remained after wide excision of the lesion. C, The defect was resurfaced with full-thickness postauricular skin graft. D, One-month postoperative photo. E, At 1 year postoperatively, the recipient site scar had matured substantially. FTSG = Full-thickness skin graft.

### 3) Wide excision with skin graft (full-thickness skin graft, split-thickness skin graft) (Figs. 5 and 6).

Wide excision was defined as complete tumor excision with a 5 mm margin.

#### 2.4. Statistical analysis

To analyze the effects of age, gender, tumor size, and treatment modality on recurrence in the non-operative group, we used logistic regression analysis because the dependent variable was discrete (i.e., recurrence vs no-recurrence).

The data were collated in MS Excel and analyzed using SPSS Statistics Software for Windows version 22.0 (IBM Corp., Armonk, NY). Results are presented as means  $\pm$  SDs, and statistical significance was accepted for  $P$  values of  $< .05$ .

The statistical validity of this study was certified, reviewed, and proofread by statisticians in the department of statistics at a national university.

### 3. Results

Mean age of the 137 patients was  $75.0 \pm 11.2$  years (range, 25–105 years) and 50 (36.5%) were men. The number of Bowen disease tumors was 148 (9 patients had multiple tumors). Sixty cases were right-sided, 58 were left-sided, and 30 involved single lesions.

Patient demographics and tumor distributions are summarized in Table 1. The most common site of Bowen disease was the head and neck region (94/148, 63.5%). Classification of lesion distributions by anatomic location revealed the cheek was the most commonly involved site in the head and neck region in women (38/72, 52.8%).

Treatment methods are summarized in Table 2. The most frequently used method was surgical excision (75/148, 50.6%). Surgical excision was subdivided into elliptical excision (25/148, 16.9%), wide excision with local flap coverage (transposition: 5/148, 3.4%; V-Y advancement: 7/148, 4.7%; advancement 28/148, 18.9%), and wide excision with skin graft (FTSG: 8/148, 5.4%; STSG: 2/148, 1.4%).

Mean tumor sizes by anatomical location and treatment modality are summarized in Table 3. Mean tumor size was largest in the genital region ( $6.67 \pm 6.10 \text{ cm}^2$ ) and by treatment modality, was largest in the wide excision group ( $2.15 \pm 3.44 \text{ cm}^2$ ).

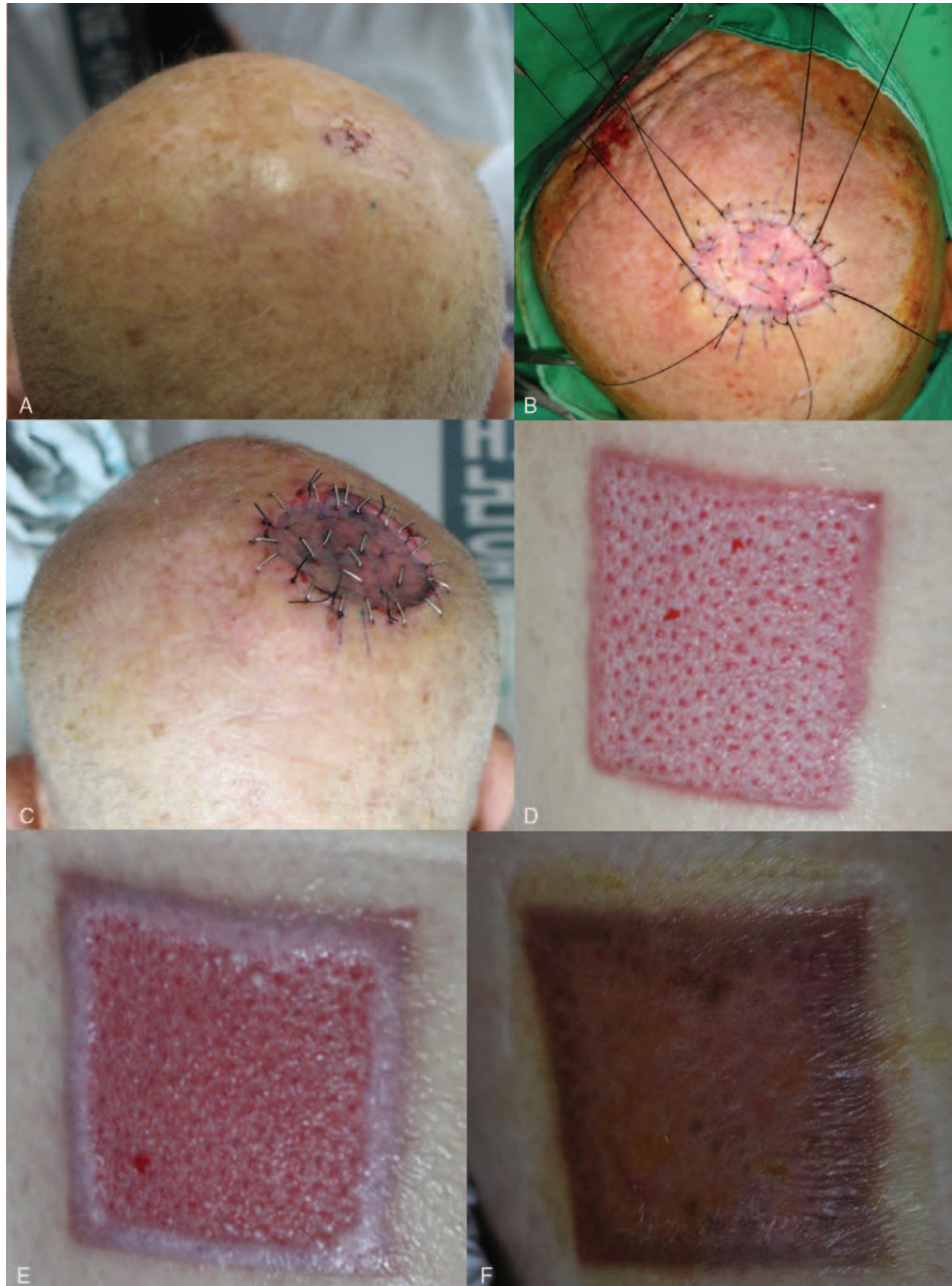
Recurrence rates of each modality and estimated recurrence period values are detailed in Table 4. Recurrence after cryotherapy occurred relatively quickly (mean 0.2 years, median 0.2 years) while recurrence after wide excision occurred at 2.5 years. Upstaging rates were documented, and 35.3% (6/17) of relapsed lesions in the cryotherapy group turned out to be SCC. SCC was not detected in relapsed patients' lesions in the laser ablation and surgical excision groups.

Logistic regression analysis was used to analyze the effects of independent variables on recurrence. All 148 lesions were included in the analysis. The Hosmer and Lemeshow test returned a Chi-square value of 9.132, a degree of freedom of 8, and  $P$  value of .331, which confirmed the validity of the current study. Regression analysis showed that  $P$  value = .013 ( $< .05$ ) only in treatment modality variable.

### 4. Discussion

In this retrospective study, Bowen disease was found to be widely distributed in all body regions (Table 1). The most commonly involved site was the head and neck (94/148, 63.5%) followed by upper and lower extremities (35/148, 23.6%). In 14 of the 19 lower extremity cases (73.7%) lesions were located at or distal to knees (ankle, foot, or lower leg), and in 12 of 16 upper extremity cases (75.0%) were located distal to elbows (finger, forearm, hand, or wrist), which is consistent with anatomical locations of chronic and predominant sun exposure. This is important because ultraviolet radiation is considered to play a role in the pathogenesis of Bowen disease.<sup>[6,7]</sup> In terms of head and neck involvement, cheeks were involved more than three times as often in females (9 lesions in males and 38 in females), which concurs with the results of other studies.<sup>[8,9]</sup>

It has been suggested that tumors of the cheek exhibit a female predominance because tumors have a predilection for superficial



**Figure 6.** Wide excisions with a split-thickness skin graft (STSG). A, A 78-year-old man visited our outpatient department with a histopathologically confirmed  $\sim 2.0 \times 2.0 \text{ cm}^2$  sized Bowen disease tumor on his occiput. B–C, After wide excision of the tumor, the defect was resurfaced with a split-thickness (10/1000 in) skin graft harvested from his left thigh using an air dermatome. D–F, Clinical photos of left thigh donor site at 1, 3, and 5 weeks postoperatively. The donor site defect was resurfaced by secondary intention using a simple foam dressing. Epithelialization initiated at the defect margin and the wound was completely epithelialized at about 5 weeks postoperatively. STSG = Split-thickness skin graft.

vellus as compared with terminal hairs, based on the assumption that vellus hair is more vulnerable to ultraviolet damage.<sup>[9]</sup>

Patients had a mean age of  $75.0 \pm 11.2$  years (range 25–105 years), which is much older than those previously reported.<sup>[7–11]</sup> We suggest 2 explanations for this result:

- 1) Gyeongju is an agricultural region with a high and growing percentage of elderly people; and
- 2) unlike other studies, which were conducted in the 1990s,<sup>[7,9–11]</sup> our samples were collected in the 2010s, and during these 2

decades awareness of skin tumors and hospital accessibility increased among the elderly.

The most frequently adopted treatment modality was surgical excision (75/148, 50.7%), followed by cryotherapy (43/148, 29.1%). The principle of cryotherapy is that several repeated cycles of alternating rapid and slow cooling lead to more damage than procedures based on a single rapid or slow cooling treatment.<sup>[6]</sup> Cryotherapy provides a quick, cost-effective means of managing Bowen disease, but has a relatively high recurrence

**Table 1**  
**Demographics and tumor distribution. Patient demographics and distribution of Bowen disease tumors.**

Patients, <i>n</i>	137
Gender, <i>n</i> (%)	
Male	50 (36.5)
Female	87 (63.5)
Age, years, <i>mean value</i> ± <i>SD</i>	75.0±11.2
Range	25-105
Bowen disease tumors, <i>n</i>	148
Mean number of Bowen disease tumors per patient, <i>n</i>	1.08
Patients with multiple Bowen disease tumors, <i>n</i> (%)	9 (6.6)
Mean number of Bowen disease tumors for patients with multiple tumors, <i>n</i>	2.22
Location of Bowen disease tumors, <i>n</i> (%)	
Breast, abdomen, trunk	17 (11.5)
Genital region	2 (1.4)
Head & neck	94 (63.5)
Upper extremity	16 (10.8)
Lower extremity	19 (12.8)
Treatment modality, <i>n</i> (%)	
Surgical excision	75 (50.7)
Laser ablation	30 (20.2)
Cryotherapy	43 (29.1)
Recurrence, <i>n</i> (%)	
Yes	29 (19.6)
No	119 (80.4)

SD, Standard deviation

rate of 6–21%.<sup>[12,13]</sup> In the present study, the recurrence rate of cryotherapy was 39.5% (17/43), which was considerably higher than previously reported rates. We believe this was due to lack of a strict protocol. It has been previously reported the results of cryotherapy are clinician dependent.<sup>[6]</sup>

We employed a CO<sub>2</sub> laser in a destructive manner to treat Bowen disease as it provides a bloodless surgical field, and thus, good visualization and less tissue injury. Thirty lesions were treated in this manner and most were located in the head and neck (19 cases) or upper extremity (6 cases; 4 on hands) regions. Eight of these 30 lesions (26.7%) recurred, which is relatively high as compared with rates reported in other studies (6.8%–12%). In the 4 cases with hand involvement, no recurrence occurred, which suggests recurrence may be partially due to follicular involvement in Bowen disease and explains the better success rate of relatively hairless volar side hand lesions treated with laser therapy.<sup>[14]</sup>

**Table 2**  
**Treatment modalities.**

Treatment	Frequency, <i>n</i> (%)
Cryotherapy	43 (29.1)
Laser ablation	30 (20.3)
Surgical excision	75 (50.6)
Elliptical excision	25 (16.9)
Wide excision + Local flap (transposition)	5 (3.4)
Wide excision + Local flap (V-Y advancement)	7 (4.7)
Wide excision + Local flap (advancement)	28 (18.9)
Wide excision + FTSG	8 (5.4)
Wide excision + STSG	2 (1.4)
Total	148 (100.0)

FTSG=full-thickness skin graft, STSG=split-thickness skin graft.

**Table 3**  
**Tumor sizes. Tumor size by anatomical location.**

Tumor size, cm <sup>2</sup> , <i>mean value</i> ± <i>SD</i>	
Breast, abdomen, trunk	3.9±4.6
Genital region	6.7±6.1
Head & neck	0.8±1.0
Upper extremity	2.4±3.4
Lower extremity	1.4±1.5
Total (by anatomical location)	1.5±2.5
Tumor size (by treatment modalities), cm <sup>2</sup> , <i>mean value</i> ± <i>SD</i>	
Cryotherapy	0.8±1.2
Laser ablation	1.3±2.4
Conventional elliptical excision	1.5±1.5
Wide excision (local flap coverage±skin graft)	2.2±3.4
Total (by treatment modalities)	1.5±2.5

SD, Standard deviation

Surgical excision was the most frequently used modality in the present study. Surgical excision was subdivided into 3 categories:

- 1) Conventional elliptical excision (Fig. 1),
- 2) Wide excision with local flap coverage (Figs. 2–4), and
- 3) Wide excision with skin graft (Figs. 5 and 6).

Simple elliptical excision is commonly used and offers diagnostic confirmation, but relatively few studies support its efficacy.<sup>[6]</sup> In the present study, the recurrence rate of conventional excision was 12% (3/25). The largest study on this topic reported a clinical recurrence rate of 19.4% (29/155), but over an unspecified time.<sup>[15]</sup> Serial vertical sections of entire excisional specimen require an excessive number of sections to be examined. Step sections, representative vertical sections taken at 2 to 4 mm intervals as in the breadloaf method (Fig. 7), are customarily obtained when excisional specimens are sent to a pathology laboratory. However, this method leaves marginal areas between sections that are not microscopically visualized and only allows examination of <1% of tumor margin, which is why this method fails to identify residual tumor between sampled areas. Furthermore, failure to detect subclinical microscopic tumor foci is often responsible for recurrence despite ‘clear’ margins on pathology reports.<sup>[16]</sup>

Wide excision with local flap coverage or skin graft resulted in recurrence in one of 50 cases (2%; 40 of these cases were treated using a local flap and 10 cases with a skin graft). Somewhat surprisingly, surgical scars were aesthetically satisfactory at long-term follow-up (3–12 months). After wide excision, defect resurfacing procedures were determined based on tumor sizes and locations, patient age, and surgeon’s preference. Safety margins were 5 mm in all cases. Westers-Attema et al compared complete excision rates for different safety margins. In their 5 mm group (n = 54), 51 lesions (94.4%) were excised completely, and in the <5 mm group (n = 17), 15 tumors (88.2%) were completely excised. The authors recommended that a safety margin of 5 mm should be used in Bowen disease to achieve high complete excision rates.<sup>[17]</sup>

Estimated recurrence periods (Table 4) showed that the more invasive the modality, the longer the estimated time to recurrence. Mean estimated recurrence times of cryotherapy, laser ablation, conventional elliptical excision, and wide excision were 0.2, 0.5, 1.3, and 2.5 years, respectively, and corresponding median values were 0.2, 0.4, 1.2, and 2.5, respectively. Log Rank, Breslow, and

**Table 4**  
**Recurrences. Recurrences by treatment modalities.**

	Treatment Modality	Recurrence (%)	OR	Estimated recurrence period (yr) <sup>‡</sup>		
				Mean (95% C.I.)	Median (95% C.I.)	
Conservative treatment	Cryotherapy	17/43 (39.5)	1.0	0.2 (0.1–0.3)	0.2	
Surgical excision	Laser ablation	8/30 (26.7)	1.2	0.5 (0.3–0.7)	0.4 (0.2–0.6)	
	Elliptical excision	3/25 (12.0)	1.5	1.3 (1.1–1.5)	1.2	
	Wide excision with local flap coverage	Wide excision + Local flap (V-Y advancement)	0/7	44.8		
		Wide excision + Local flap (advancement)	1/28	1/40 (2.5)	8.6	2.5 (2.5–2.5)
		Wide excision + Local flap (transposition)	0/5	24.1		
		Wide excision with skin graft	Wide excision + FTSG*	0/8	0/10 (0)	0.2
Total	–	Wide excision + STSG <sup>†</sup>	0/2	–	0.1	
	–	–	29/148 (19.6)	–	0.5 (0.3–0.7)	0.3 (0.1–0.5)

Log Rank (Mantel-Cox): Chi square = 23.760, *P* value < .001.

Breslow (Generalized Wilcoxon): Chi square = 16.050, *P* value = .001.

Tarone-Ware: Chi square = 19.553, *P* value < .001.

OR = odds ratio.

\* FTSG = full-thickness skin graft.

† STSG = split-thickness skin graft.

‡ Estimated recurrence period is calculated by Kaplan-Meier survival analysis.

Tarone-Ware tests showed all modality-associated recurrence times were significantly different (all *P* values ≤ .001).

The rate of upstaging observed in relapsed patients proved interesting. Only 35.3% (6/17) relapses in the cryotherapy group turned out to be SCC, and no upstaging occurred among relapsed patients in the surgical excision groups (elliptical excision, wide excision with local flap coverage group, or wide excision with skin graft). These results are meaningful since a recent study showed that up to 10% of SCC/SCC in situ (Bowen disease) cases were upstaged after definitive excision.<sup>[18]</sup> This means that Bowen disease can confidently be treated non-invasively and that the risk of leaving an invasive component behind is low. Only one patient recurred in the surgical excision group, which obviously prevented statistical analysis.

Logistic regression analysis indicated that the current study provided a suitable model. The Hosmer and Lemeshow test produced a *P* value of .331, which meant the null hypothesis could not be dismissed. However, Cox & Snell and Nagelkerke *R*<sup>2</sup> values were 0.183 and 0.291, respectively. These values assess overall suitability of the study model used, in other words, values indicate the degree of explainability of this model.

About 29.1% of variation in the dependent variable (recurrence) was explained by the logistic regression model. Thus, only treatment modality was found to have statistical significance (*P* = .013).

We originally believed tumor size would affect recurrence, but contrary to expectation, tumor size had no significant effect (*P* = .104). Only treatment modality was found to affect recurrence by multivariate regression analysis.

The present study was limited by its retrospective, single institution design and by the assumption that all tumors were elliptical, which possibly compromised the accuracy of analysis.

The optimal treatment for Bowen disease has not been determined. UK guidelines state no single treatment modality is superior in all clinical situations and that all therapeutic options have failure and recurrence rates in the range 5% to 10%.<sup>[17]</sup> In

the present study, treatment modality, rather than other factors such as tumor size or patient age or gender, was found to significantly influence tumor recurrence.

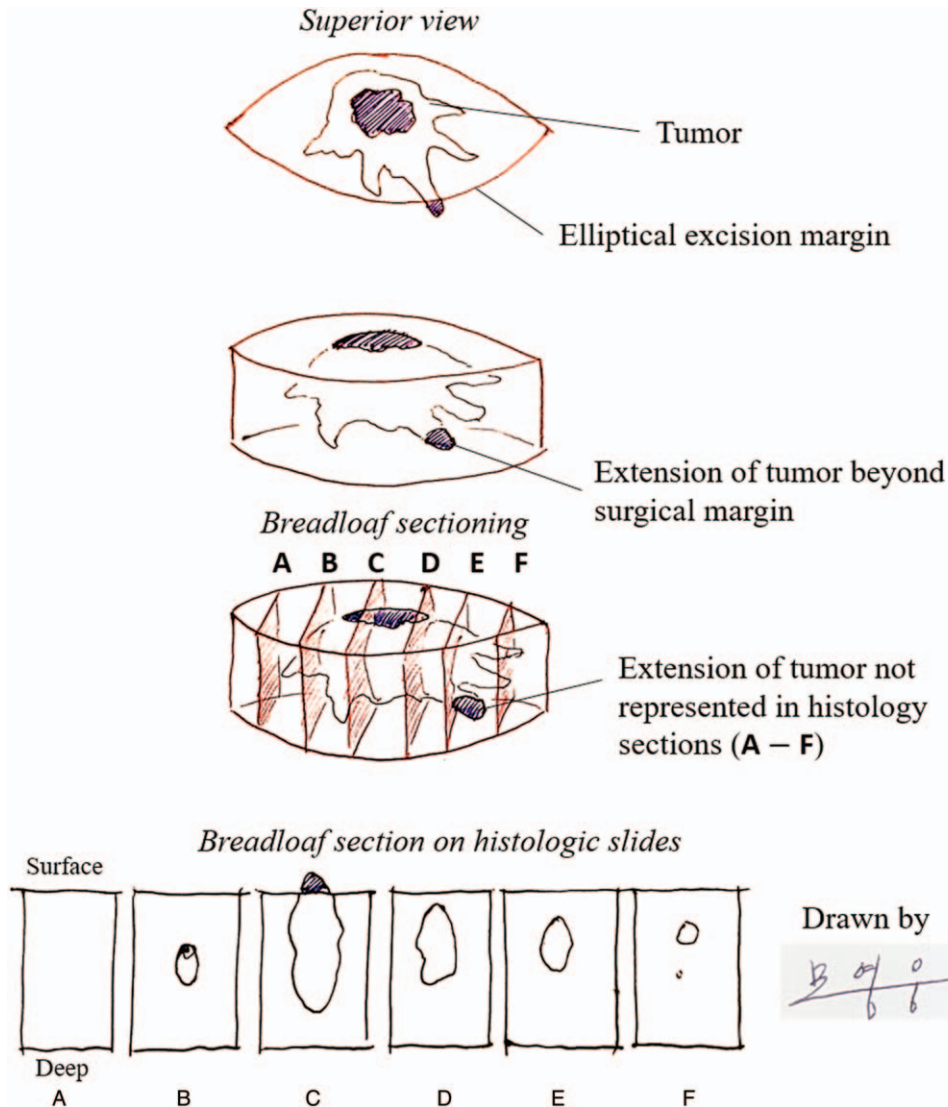
The safety margins used for wide excision different from country to country, and no definitive comparative trial has been conducted on the topic, although a small number of studies have attempted to define optimal safety margins.<sup>[17]</sup> In the United States, a 4 to 6 mm margin is advised for low risk SCC and Bowen disease.<sup>[19]</sup> The French guideline recommends a minimal margin, but does not specify what this margin should be,<sup>[20]</sup> and in the Netherlands low risk SCC is excised with a 5 mm safety margin, but margins for Bowen disease are not specified.<sup>[21]</sup> Guidelines issued in other countries do not specify safety margins for Bowen disease.<sup>[19,20,22]</sup>

Selection of the most appropriate therapy is achieved by considering three key factors, that is, tumor size, tumor location, and likely tumor characteristics based on clinical, and when available, pathological assessments,<sup>[1]</sup> though immune state, patient age, treatment cost, patient preference, and clinician's preference may also play important roles.

Based on our results, we recommend wide excision with a resection margin of at least 5mm. Resurfacing may be conducted using a local flap or a skin graft depending on tumor location and surgeon's preference. Various types of local flaps provided excellent aesthetic outcomes and coverages depended on anatomic location, in addition, surgical scars were less obvious than expected. However, if a tumor is extensive, multifocal, located at a body site associated with poor wound healing, or when a surgical approach is contraindicated for some other reason, non-surgical modalities such as laser ablation, PDT, or imiquimod cream are recommended despite their relatively high recurrence rates. However, we do not recommend cryotherapy because of its high recurrence rate and poor patient compliance.

In order to select a treatment that is most appropriate for individual patients, it is important that providers be aware of the multiple treatment options available and take into consideration





**Figure 7.** Limitation of the breadloaf biopsy sampling method when examining the margins of conventional elliptical excisions.<sup>[16]</sup> In this example, excisional tip breadloaf sections A and F were clear of tumor, but sections B, C, D, and E demonstrated tumor. Furthermore, extension to the peripheral margin was not detected in any section, and thus, the excision was technically clear on margins. However, this margin assessment was inaccurate. Extension of tumor to the surgical margin between sections D and E was missed<sup>[16]</sup>.

other factors such as recurrence rate, procedural invasiveness, and cosmesis.

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**Author contributions**

Study concept and design: Mo YW. Data acquisition: Mo YW. Data analysis and interpretation: Mo YW, Lee DL. Drafting of the manuscript: Mo YW. Critical revision of the manuscript for important intellectual content: Lee DL. Statistical analysis: Mo YW, Lee DL. Study supervision: Lee DL. Approval of final manuscript: all authors.

Young Woong Mo orcid: 0000-0002-4180-3139.

Dong Lark Lee orcid: 0000-0003-1279-5245.

**Corrections**

When the article was first published, the legends for figures 2 and 3 were reversed. They have now been fixed.

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