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Landscape Fragmentation as a Risk Factor for Buruli Ulcer Disease in Ghana

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Abstract. Land cover and its change have been linked to Buruli ulcer (BU), a rapidly emerging tropical disease. However, it is unknown whether landscape structure affects the disease prevalence. To examine the association between landscape pattern and BU presence, we obtained land cover information for 20 villages in southwestern Ghana from high resolution satellite images, and analyzed the landscape pattern surrounding each village. Eight landscape metrics indicated that landscape patterns between BU case and reference villages were different ($P < 0.05$) at the broad spatial extent examined (4 km). The logistic regression models showed that landscape fragmentation and diversity indices were positively associated with BU presence in a village. Specifically, for each increase in patch density and edge density by 100 units, the likelihood of BU presence in a village increased 2.51 (95% confidence interval [CI] = 1.36–4.61) and 4.18 (95% CI = 1.63–10.76) times, respectively. The results suggest that increased landscape fragmentation may pose a risk to the emergence of BU.

INTRODUCTION

Landscape disturbances alter ecosystem patterns and processes, and are increasingly recognized to have cascading effects on ecosystem functions at local to global scales.[1] Specifically, human-driven land cover changes that cause habitat loss and fragmentation have been associated with the outbreak and transmission of multiple infectious diseases.[2,3] For example, in the Amazon rainforest, deforestation was associated with increased malaria prevalence due to an increase in suitable habitat of the malaria vector, *Anopheles darlingi*.[4] The construction of dams in Senegal was found to be responsible for the rise of the outbreaks of schistosomiasis due to increases in water habitat beneficial to the vector (snails) and parasite transmission.[5] In the northeastern United States, Lyme disease risk is associated with forest fragmentation, largely through resultant modification of trophic interactions that favor vector transmission.[6] These studies highlight an increased understanding of landscape patterns and disease risk, but to date few studies have evaluated the usefulness of pattern metrics on Buruli ulcer (BU) prevalence,[7] despite the fact the changes in land use have been previously reported in association with the disease.[8–10] Understanding how landscape patterns influence human disease could aid the development of landscape-level management plans to reduce disease risk.

BU is a skin infection caused by *Mycobacterium ulcerans*, and has emerged in over 30 countries worldwide and become the third most common disease caused by Mycobacteria, after tuberculosis and leprosy.[11] Though its transmission mode is still unclear, it is generally recognized to be associated with aquatic habitats[11] and aquatic biting insects[12] as well as nonbiting aquatic invertebrates[11] although results are equivocal.[13] Other landscape disturbances, such as deforestation and agriculture, have also been linked to BU prevalence. In Benin, the dynamics of BU disease were correlated with human alterations to landscapes and natural land cover.[9] Recently, in Ghana, Wu and others[10] documented positive relationships between BU prevalence and differences in mining and agriculture between endemic and nonendemic regions. However, it is still unclear whether these changes in habitat loss were indicative of changes in fragmentation and landscape structure, which may have differential effects on ecosystem processes[14] that influence disease emergence.

Ghana is one of the most prevalent countries of BU disease, second only to Cote d'Ivoire.[15] Rapid land cover change has taken place in Ghana in recent decades. For example, forest area has decreased roughly 2% per year since the 1990s,[16] while agriculture has grown very rapidly and expanded at an annual rate of 5.5%.[17] In addition, across Ghana, gold mining has increased sharply in recent decades. From 2004 to 2009, overall gold production in Ghana increased from 2.6% to 3.8% of global production,[18] which poses risks to environmental and human health.[19]

In this study, we explore whether landscape patterns can be used as an indicator of BU disease, given its importance as a rapidly emerging tropical disease. Specifically, two questions are answered: 1) do landscape metrics for landscape fragmentation and diversity differ between BU case and reference villages and 2) to what degree is BU presence at a village level associated with landscape metrics surrounding villages? We hypothesized that BU case villages would have higher levels of fragmentation and that the correlation would be positive at broader spatial extents (e.g., 4 km away from village center) if landscape heterogeneity increased.

METHODS

Study area. Our study area included 20 villages in southwestern Ghana, which were located in three study regions (Figure 1). We selected two study regions (hereafter called Subin and Ayanfuri) in a BU endemic area where BU cases were clustered.[10] A reference region (Kedadwen) was also included, where BU has not been reported. These three regions were selected after the discussion with a diverse team of experts during an interdisciplinary workshop in 2008 and then were confirmed by a field visit. The key characteristics of these study areas, such as climate, the type of vegetation and land cover, and geology, are similar or comparable (Supplemental Table 1). The area of each study area is near 580 km^2. Six villages from Subin region (V1–V6) and five villages from Ayanfuri region (V7–V11) were selected as the BU case

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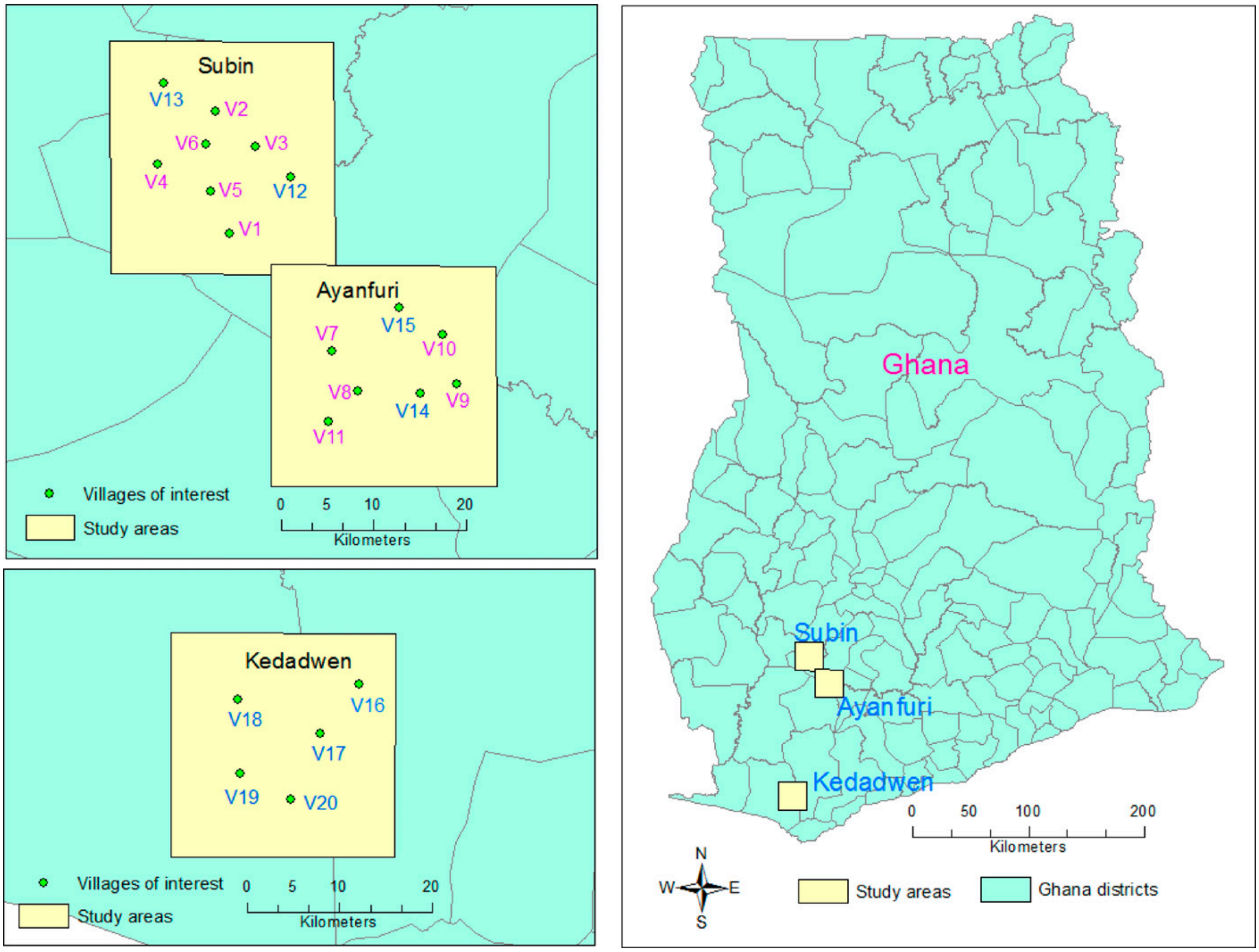

FIGURE 1. The study areas (Subin, Ayanfuri, and Kedadwen) and village center locations in southwestern Ghana used for landscape metric analysis.

villages. Five villages from Kedadwen region (V16–V20) were selected as the reference villages. In addition, two villages in which BU cases have not been reported were selected from the Subin (V12 and V13) and Ayanfuri regions (V14 and V15), respectively, as reference villages. These villages were roughly randomly selected after the distance between villages and the number of villages in these areas was taken into account. In total, 11 villages with BU cases and nine villages without BU cases were used.

BU disease data. Hospital-based BU data were collected between 2007 and 2010. When patients with skin infections visited hospitals and clinics, they were examined by experienced doctors based on the symptoms of the infection. These cases were confirmed by clinical diagnosis rather than laboratory testing of pathogens because of technical difficulties. Once a case was confirmed, the age, gender, residence, and other information were recorded. Therefore, the village in which a patient is living was identified.

Land cover and landscape pattern analysis. RapidEye satellite imagery with a spatial resolution of 5 m acquired in January 2012 was used to obtain land over information in the study areas. The images were classified into six types of land cover classes (urban, mining area, water, grassland, forest, and agriculture) using supervised classification with a maximum likelihood algorithm[10] (Supplemental Figure 1). The ground truth information in the study areas was initially collected based on participatory mapping activities in these communities. Besides the participatory maps, highly resolved (resolution ≤ 5 m) QuickBird images, Google Earth maps, as well as experts' opinion, were used as the reference for land cover classification.[10] The classification was carried out with ENVI class software (Exelis Inc., McLean, VA). To analyze landscape patterns surrounding each village, buffers with radii of 1, 2, and 4 km surrounding each village center were created and clipped from classified satellite imagery using ArcGIS 10.1 (ERSI, Redlands, CA). To examine the relationship between landscape-level metrics and BU at each of the three buffer distances a total of 8 metrics were selected: patch density (PD), edge density (ED), mean in Euclidean nearest neighbor distance (ENN_MN), standard deviation in Euclidean nearest neighbor distance (ENN_SD), Shannon's diversity index (SHDI), Simpson's diversity index (SIDI), Shannon's evenness index (SHEI), and Simpson's evenness index (SIEI). These metrics were selected because they provide complementary influences of land fragmentation and diversity along several key metrics.[20] The explanation and formulae of calculation of these metrics can be found elsewhere.[21] FRAGSTATS v.4.2 (Amherst, MA) was used for all metrics calculations.[21]

Statistical analysis. To test for the difference in individual landscape metric between BU case and reference villages (question 1), we used one-way analysis of variance (ANOVA). Multivariate analysis of variance (MANOVA) was conducted to test the overall difference in landscape patterns between two groups of villages. Before conducting ANOVA and MANOVA, we validated some assumptions for these analyses, including normality, homogeneity of variances and covariances, linearity, and outliers of dependent variables. Because some variables were highly correlated (Pearson $r > 0.9$, $P < 0.01$), we only put one of these highly correlated variables in the model for MANOVA. Therefore, three dependent variables, ED, ENN_SD, and SHDI were included in MANOVA. To reduce type I error, we adjusted multiple comparisons with a Bonferroni correction. The same methods were used to test the difference in land cover components between two groups of villages. The relationship between land cover classes was examined with Pearson correlation analysis. To examine BU presence in villages as a function of landscape metrics, buffer radius, and land cover (question 2), we used logistic regression models. The dependent variable was BU presence in a village, which followed a binomial distribution. Specifically, if a village had BU cases, the value was set to one, otherwise, the value was set to zero. First, univariate logistic regression models were used to examine the association between BU presence and an individual variable. Then multivariable logistic regression models were used to examine the association between BU risk and the multiple variables simultaneously. Before carrying out multivariable logistic regression, the collinearity between independent variables (landscape metrics) was examined by Pearson correlation analysis and variance inflation factors (VIF). If the collinearity was identified (e.g., $r > 0.6$, $P < 0.01$, or VIF > 5), only one of these correlated variables was put into the model. The fit of model was evaluated using Akaike's Information (AIC) as the criterion, which assumes the model is better fitted if the value of AIC is smaller.[10] The association between the likelihood of BU presence in a village and landscape metrics was assessed by an odds ratio and 95% confidence intervals, calculated from the logistic regression models. Since the ranges of the metrics are different in magnitude (e.g., PD ranged from 332 to 1,278, while SIDI ranged from 0.39 to 0.74), the effects of the increase by one unit in these metrics are not comparable. To address this issue, we normalized the metrics to obtain a reasonable scale,[22] for example, $SIDI_{new} = SIDI \times 10$. In addition, to evaluate how sensitive the models to the reference village selection, univariable logistic regression models were used to examine the association between the presence of BU and landscape metrics in BU endemic areas that included nine BU case villages and four reference villages.

RESULTS

In total, 73 cases were confirmed in 11 villages between 2007 and 2010. Among these cases, 40 cases were male and 33 cases were female, 34% of total cases were young people (0–19), 44% were adults (20–60), and 22% were older people (60 and above). The highest number of cases was reported in Dunkwa (33 cases), followed by Ayanfuri, Subin, and Nkonya (14, nine, and five cases, respectively). Pokukrom, Nkotumso, and Nyinawusu reported four cases in each village. The remaining villages only reported one or two cases (Supplemental Figure 2).

Land cover components between BU case villages and reference villages were significantly different (Figure 2 and Supplemental Table 2). At 4 km, except the percentage of agricultural area, the percentages of other five types of land cover classes were significantly different between BU cases villages and references villages ($P < 0.01$). The differences in land cover components between two groups of villages at 2 km were similar as those observed at 4 km, except the differences in the percentages of urban, mining, and forest areas were significant at the level of 0.05, instead of 0.01. However, at 1 km, the differences in land cover components between two groups of villages were only significant for the percentages of water area ($P < 0.05$) and grassland ($P < 0.01$). In the BU case villages, the percentage of agriculture was the dominant land cover class at all buffer distances, followed by grassland, forest, urban, water, and mining. As the buffer distance increased, the percentages of agricultural area and forest increased, while the percentages of urban area and grassland decreased. In the reference villages, the predominant land cover classes differed significantly with buffer distance. Agriculture was the predominant land cover class at 1 and 2 km, while forest became the predominant land cover class at 4 km. Pearson correlation analysis of the percentages of land cover classes at 4 km indicated that strong positive correlations ($P < 0.01$) existed between water, grassland, and mining areas, while negative correlations existed between forest and urban, and between forest and agriculture (Supplemental Table 3).

Landscape patterns were significantly different between BU case villages and reference villages at the radii of 4 and 2 km, but not significant at the radius of 1 km. At 4 km, PD, ED, ENN_MN, and ENN_SD were different between BU case and reference villages ($P < 0.05$). SHDI, SHEI, SIDI, and SIEI also differed between BU case and reference villages ($P < 0.01$). At 2 km, only SHDI, SHEI, SIDI, and SIEI were significantly different, while no metrics were significantly different between BU case villages and reference villages at 1 km (Table 1 and Supplemental Table 4).

Univariate logistic regression showed PD, ED, and four diversity indices (SHDI, SHEI, SIDI, and SIEI) were positively associated with BU across all villages (Supplemental Table 5). The similar associations were obtained when only villages in endemic areas were included in the models (Supplemental Table 6). In the multivariable logistic regression model, the above metrics had significantly positive associations with the presence of BU after controlling buffer radius and the percentage of forest area. Specifically, model results indicated that an increase in PD and ED by 100 units were associated with the increases in likelihood of BU presence in a village by 2.51 and 4.18 times, respectively. When diversity indices increased by 0.1 units, the likelihood increased 2.50–10.92 times (Table 2).

DISCUSSION

We compared land cover and landscape patterns in BU-endemic areas with nonendemic areas and examined the

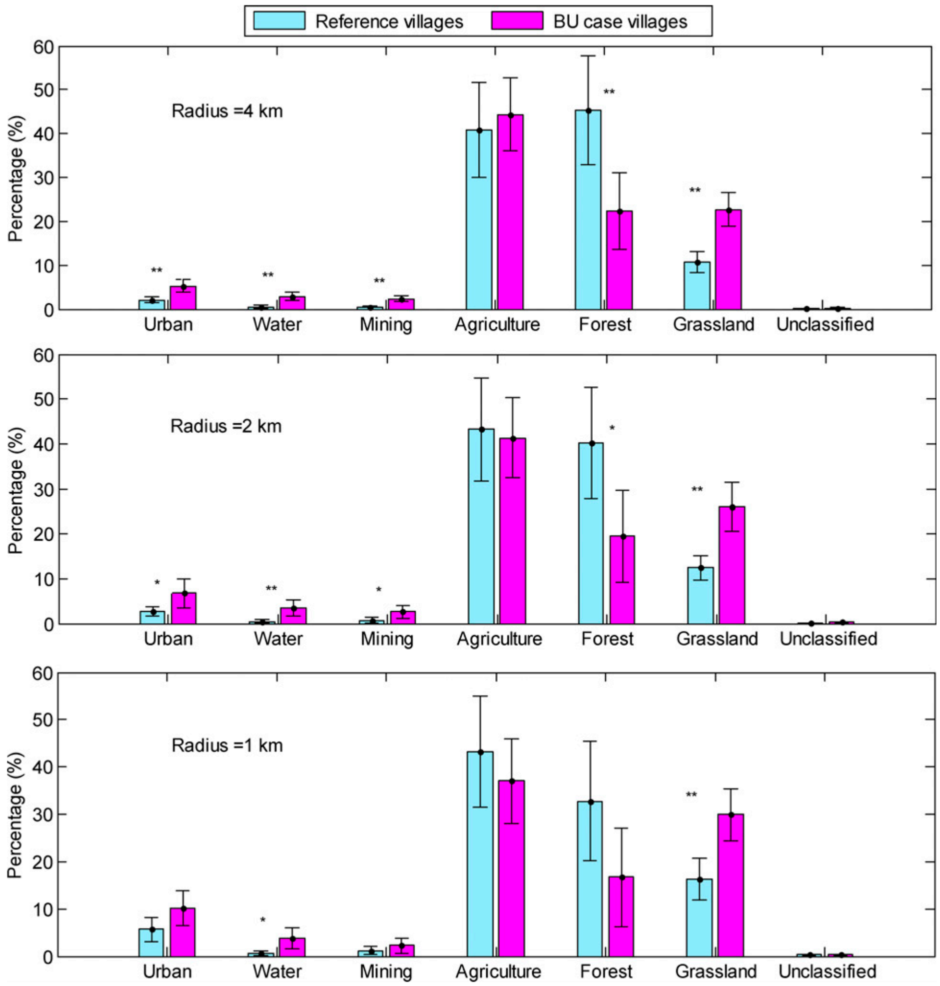

FIGURE 2. Comparison of land cover classes in villages with Buruli ulcer (BU) and without BU (the error represents 95% confidence interval). ** $P < 0.01$, * $P < 0.05$.

association between landscape pattern and BU using high resolution satellite images at multiple spatial extents. Our results indicate that increases in land cover fragmentation and landscape diversity were associated with the presence of BU disease in a village in Ghana. The finding is consistent with recent studies highlighting the close relationship between human health and landscape changes due to disturbance.[1,10,23] Although the relationship between land cover and BU disease has been examined in several studies,[9–11] the comparison of fine-scale landscape patterns and associated metrics between endemic and nonendemic areas has rarely been presented.[7]

It is increasingly recognized that landscape structure plays an important role in disease transmission.[24–26] In terrestrial systems, environmental changes driven by human activities affect the form, size, and connectivity of patches in a landscape, leading to habitat fragmentation, which is considered as a health risk because it may alter the density, abundance,

TABLE 1
Comparison of landscape pattern metrics in BU case villages and reference villages with one-way ANOVA at different spatial scales

		4 km (N = 20)		2 km (N = 20)		1 km (N = 20)	
Variable	Mean ± SD (N = 60)	F value	P	F value	P	F value	P
PD	683 + 259	4.515	0.048	2.260	0.150	0.690	0.417
ED	588 + 139	6.112	0.024	2.810	0.111	0.640	0.436
ENN_MN	24.38 + 2.88	5.150	0.036	0.580	0.455	0.180	0.677
ENN_SD	30 + 8	6.540	0.020	0.610	0.443	0.070	0.797
SHDI	1.20 + 0.21	18.820	< 0.001	7.520	0.013	3.470	0.079
SHEI	0.62 + 0.11	19.460	< 0.001	7.430	0.014	3.000	0.100
SIDI	0.62 + 0.08	8.720	0.009	6.130	0.024	3.520	0.077
SIEI	0.73 + 0.10	8.850	0.008	6.370	0.021	3.400	0.082

ANOVA = analysis of variance; BU = Buruli ulcer; ED = edge density; ENN_MN = mean in Euclidean nearest neighbor distance; ENN_SD = standard deviation in Euclidean nearest neighbor distance; MANOVA = multivariate analysis of variance; PD = patch density; SHDI = Shannon's diversity index; SHEI = Shannon's evenness index; SIDI = Simpson's diversity index; SIEI = Simpson's evenness index; SD = standard deviation. Full names of metrics are described in the text. MANOVA test indicates the overall difference in landscape pattern between BU case village and reference villages is significant at the radii of 4 km (F = 5.83, P = 0.007) and 2 km (F = 3.43, P = 0.042), but not significant at the radius of 1 km (F = 2.14, P = 0.135).

TABLE 2

Multivariable logistic regression analysis of the association between BU risk and landscape metrics in southwestern Ghana

Model ID	Variables	β	OR Point estimate	OR 95% CI		P	AIC
1	PD_{new}	0.92	2.51	1.36	4.61	0.003	54.32
	Forest	−0.12	0.89	0.83	0.95	< 0.001	
	Buffer radius	0.63	1.88	0.95	3.72	0.070	
2	ED_{new}	1.43	4.18	1.63	10.76	0.003	56.62
	Forest	−0.10	0.90	0.86	0.95	< 0.001	
	Buffer radius	0.59	1.80	0.93	3.49	0.083	
3	$SHDI_{new}$	0.91	2.50	1.52	4.09	< 0.001	52.12
	Forest	−0.08	0.93	0.89	0.97	0.001	
	Buffer radius	0.35	1.42	0.77	2.63	0.264	
4	$SHEI_{new}$	1.81	6.13	2.28	16.49	< 0.001	52.27
	Forest	−0.08	0.93	0.88	0.97	0.001	
	Buffer radius	0.37	1.45	0.78	2.69	0.240	
5	$SIDI_{new}$	2.39	10.92	2.84	41.98	0.001	52.30
	Forest	−0.09	0.91	0.87	0.96	< 0.001	
	Buffer radius	0.38	1.46	0.79	2.68	0.226	
6	$SIEI_{new}$	2.09	8.10	2.48	26.44	0.001	52.07
	Forest	−0.09	0.91	0.87	0.96	< 0.001	
	Buffer radius	0.39	1.48	0.80	2.74	0.207	

AIC = Akaike's information criterion; BU = Buruli ulcer; CI = confidence interval; ED = edge density; OR = odds ratio; PD = patch density; SHDI = Shannon's diversity index; SHEI = Shannon's evenness index; SIDI = Simpson's diversity index; SIEI = Simpson's evenness index. PD_{new} = PD/100; ED_{new} = ED/100; $SHDI_{new}$ = SHDI × 10; $SHEI_{new}$ = SHEI × 10; $SIDI_{new}$ = SIDI × 10; $SIEI_{new}$ = SIEI × 10. Each model has three independent variables, including buffer radius, the percentage of forest area and a landscape metric.

and geographic distribution of hosts, vectors, and pathogens involved in disease transmission and change the ecology of microorganisms,[27] as has been shown for Lyme disease in the northeastern United States.[25] As another example, habitat fragmentation was associated with the increase in hantavirus hosts, potentially increasing the potential for an outbreak of hantavirus infection in Panama.[27] Our results reveal that several landscape pattern metrics, for example, PD, ED, SHDI, and SIDI, were significantly different between BU case villages and reference villages, and two landscape fragmentation indices, PD and ED, were significantly and positively associated with BU presence in a village.

There are two primary reasons that fragmentation may be associated with BU. First, landscape fragmentation increases the probability that vectors in the preferred habitat encounter habitat edges, which results in a higher chance of the vectors moving into other habitats, facilitating disease transmission.[26] Second, the increase in landscape fragmentation may enhance human exposure to the disease, as evidenced by the effect of forest fragmentation on Lyme disease.[24] Specifically, the high resolution satellite images revealed that many mining activities existed in the endemic areas, contributing to landscape fragmentation[24]; given the large number of people working and living near mining communities or small scale farms, the landscape structure of these environments may contribute to increased exposure to the bacterium that causes the disease. Both of these ideas will require further research.

Scale is an unavoidable issue in ecology because it influences the results of landscape pattern analysis.[28] In this study, we analyzed landscape pattern around each village at three spatial extents (radii at 1, 2, and 4 km), which were also used in other studies to analyze landscape context.[26] In a study on the relationship between BU and landscape metrics in Benin, radii from 0.8 to 2 km were used,[7] which were also included as radii in this study. Our results indicated that eight metrics were significantly different between BU case villages and reference villages at the distance of 4 km, four metrics were significantly different at the distance of 2 km, while none were significantly different at the distance of 1 km, suggesting the importance of landscape heterogeneity and context at broader spatial extents, consistent with the result from a previous study.[29] Collectively, the MANOVA suggested results were different at 4 and 2 km but not significant at 1 km. Both mean and standard deviation of landscape metrics declined with increasing radii, indicating that the difference was not caused by changes in variance with scale (Supplemental Table 3). Moreover, the landscape metrics are calculated at patch, class, or landscape levels, not for individual pixels, constraining the influence of increased sampling units with scale. Finally, the multivariate regression indicated a greater influence of landscape metrics and land cover than distance, per se.

Ultimately, understanding the effects of landscape structure on disease transmission can help to predict and control disease outbreaks. To date, the use of land cover and landscape pattern metrics as predictors for BU presence or risks has been explored.[7,9,30] However, studies on the relationship between landscape diversity and BU disease are still rare. Brou and others[8] reported that landscape diversity was related to BU in Cote d'Ivoire. They found that the BU risk zones were located at irrigated rice field cultures areas, banana fields, and areas close to dams used for irrigation. However, their study did not measure any landscape diversity index and quantify the relationship between BU and the landscape diversity index. Campbell and others[7] examined three landscape metrics with BU risks but did not find positive associations, which could be explained by several reasons. First, Campbell and others examined the landscape at relatively small scales (radii ranged from 0.8 to 2 km). Our study showed that stronger associations were observed at 4 km. Second, Campbell and others used Landsat ETM + imagery with the spatial resolution of 30 m, which is relatively coarse and not favorable for landscape pattern analysis. In addition, Campbell and others only chose a limited set of metrics (three). Our study used higher resolution imagery, broader spatial extents, and a broader set of metrics, and revealed positive associations between BU with several landscape fragmentation and diversity metrics.

In this study, we used metrics to quantify landscape diversity for each village and found that they were significantly different between BU case villages and reference villages at the 4 km extent. The results suggested that landscape context could be used to predict BU presence at the village level. It follows that these metrics can be used to prioritize the location of conservation and health treatment activities, independent of the availability of disease data, which is often limited and uncertain in rural areas.

It should be cautioned that the BU cases used in this study were collected from hospitals and clinics only. Therefore, patients who did not visit hospitals or clinics were not recorded in our dataset. In addition, BU cases were confirmed through symptoms but not laboratory tests. It cannot completely rule out false-positive patients. As a result, our BU cases might be either underestimated or overestimated.

In summary, our analyses demonstrated the connection between land cover disturbance and BU disease in southwestern Ghana. Specifically, we found that there were significant differences in landscape pattern metrics between BU case villages and reference villages, suggesting that the increased fragmentation and diversity of landscape structure may be potential risk factors for the emergence of BU disease. Understanding these connections may provide insights to reduce the risk of BU disease in Ghana, and other areas experiencing rapid land cover change and provide a metric for prioritizing conservation and health activities in data-poor regions.

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