Fractal Dimension of the Deep Margin of Tongue Carcinoma: A Prognostic Tool?

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INTRODUCTION

Medicine and biology use fractal geometry to characterize complex irregular structures, mostly vascular networks [13], imprecisely described by standard mathematical methods [14]. It has been suggested that fractal geometry, already applied in quantitative cytological studies [1] and melanoma morphometric evaluation [3], could be useful in oncology [5]. A 1994 study demonstrated a quantitative difference between normal and degenerative neoplastic mucosa of the floor of mouth [9].

Our study aim was to assess fractal analysis as a prognostic tool and as discriminant between aggressive and non-aggressive tongue carcinomas. Our study-definition of aggressive tumour is a tumour that recurs during follow-up.

METHODS

The study population encompassed 33 men and 15 women who had undergone T1 or T2 squamous cell carcinoma (UICC staging) excision with or without lymph node dissection. Surgery was the initial treatment; no prior therapy had altered the histological appearance of the tumour. Mean follow-up was 35 months (range: 12-132).

Clinical elements analysed were patients' age and sex, TNM staging, and tumoural macroscopic appearance (ulcerated, infiltrating or exophytic).

Surgical specimens were analysed for macroscopic appearance, anatomical location and margin status. Correlation for margin status between intra-operative frozen section diagnosis and final histopathological report was also assessed. Independently, a pathologist analysed possible histological prognostic factors affecting the survival rate: tumour size; histological staging; fractal dimension of the tumour deep margin; muscle, perineural, and vascular invasion.

Patients were grouped as: A - no initial lymph node metastasis; no recurrence (n=20); B - no initial lymph node metastasis; recurrence (n=21); C - lymph node metastasis initially present; recurrence (n=7). All groups were compared with control group D: cadaver specimens without tongue disorder (n=15). The Kaplan-Meier log-rank test provided statistical analysis.

RESULTS

For group A, D=1.44±0.09; for group B, D=1.42±0.01; for group C, D=1.44±0.03; and for group D, D=1.08±0.04. While no statistical difference exists between groups A, B and C, a difference exists between these three groups and group D.

Predictors for overall survival rate (univariate statistical analysis) were: patients' age (p<0.001); tumour size (p<0.0001); tumour-free margins identified by frozen section (p=0.0009) and in the final histopathological report (p=0.0002); and tumour macroscopic appearance (ulcerated tumours proved unfavourable in outcome) (p=0.008).

Tumour macroscopic appearance, patients' sex and tumour location (p>0.05) did not influence the disease-free interval. The latter correlated with tumour size (p<0.0001); patients' age (p<0.0003); tumour-free margins identified by frozen section (p=0.02) and in the final histopathological report (p=0.04); and initial lymph node status (p=0.004).

Survival rate without recurrence was statistically correlated with tumour size (p=0.007); patients' age (p=0.004); tumour macroscopic appearance (p=0.007); lymph node status (p=0.02); and margin status in the final
histopathological report (p=0.04).

Although muscle invasion depth was significantly correlated with overall survival rate (p=0.01), it cannot be used as predictor for locoregional recurrence (p=0.11). Vascular invasion significantly influenced the disease-free interval (p=0.004) but not the overall survival rate (p=0.06). Tumour thickness above 5 mm significantly reduced the overall survival rate (p=0.03) but not the disease-free interval (p=0.12). Perineural invasion alone had no statistical value for overall survival rate (p=0.32) or recurrence-free survival rate (p=0.27).

DISCUSSION
Histopathology lacks objective and quantitative evaluation methods. With various degrees of success, pathologists attempt new methods derived from fundamental sciences, e.g., mathematics. They aim to determine whether tissue is normal or pathological and to assign a prognostic index to the specimen. To this end, quantitative evaluation methods were developed, e.g., histomorphometric analyses (nuclear area, diameter, perimeter; vascular density) [11].

Although standard quantitative methods are based on classical Euclidean geometry, fractal geometry is now largely accepted as more valid for investigating and quantifying complex natural structures. Histopathological studies have investigated fractal analysis and confirm the applicability of the method [5]. Several studies demonstrate and quantify the complexity or roughness differences between normal and abnormal cells or tissues [6, 9]. This does not provide the pathologist with new information. Should fractal analysis yield original or additional data, it could prove a relevant prognostic tool. This was the aim of our study, based on patients with primary tongue tumour compared in terms of curability and recurrence.

Several standard clinical and histological factors were analysed. Our results agree with other authors’ conclusions: fractal dimension alone does not provide relevant information for diagnostic purposes or prognostic evaluation. Thus, currently, fractal analysis is not a useful morphometric discriminant: other data must be included [6]. Nevertheless, the practical use of fractal analysis, i.e., objective measurements of natural structures and phenomena, should be further assessed with other carcinomas and larger populations.

CONCLUSIONS
Although fractal analysis is clearly one of the best, if not the best, quantitative methods currently available, it is of limited practical use in histopathology because other data must be included in the diagnostic and prognostic analysis.

Our results suggest that fractal dimension bears no relationship with recurrence outcome or survival rate, further corroborating the evidence that fractal dimension is not a relevant prognostic or diagnostic tool. Nevertheless, fractal analysis provides objective structural measurements and relevancy should be further assessed.

REFERENCES

Figure 1:
(a) Tongue carcinoma section (magnification x40). Relatively smooth deep margin.
(b) While maintaining visual control on the original histological specimen, the pathologist isolates the same deep margin from the rest of the picture.

Figure 2:
(a) Different tongue carcinoma (magnification x40). Deep margin more irregular than that of Fig 1.
(b) Deep margin is isolated.