Research Square

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Assessment of Jaw bone Invasion and Its Correlation with Worst Pattern of Invasion and Depth of Invasion in Oral Squamous Cell Carcinoma

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Abstract

Background:

Bone invasion is a major prognostic factor in oral squamous cell carcinoma (OSCC), which frequently signifies aggressive tumor behaviour with poor clinical outcomes. Histopathological parameters like depth of invasion (DOI) and worst pattern of invasion (WPOI) are established, but their combined relation to bone invasion has not been further evaluated.

Aim:

To evaluate jaw bone invasion in OSCC and to determine its correlation with DOI and WPOI.

Materials and Methods:

A prospective study was undertaken on 80 histopathologically confirmed cases of OSCC. Hematoxylin and eosin- stained sections were observed to determine bone invasion. DOI was measured as a continuous variable between the basement membrane of adjacent normal mucosa as a baseline and the deepest point of tumor infiltration. WPOI was evaluated and classified according to predetermined standards. Statistical analysis was done to establish the relationship between bone invasion and the parameters to be studied.

Results:

Bone invasion in 46 (57.5%) cases was observed. A significant association between bone invasion and WPOI (2 = 12.07, p = 0.016) was found with higher grades of WPOI showing higher levels of bone involvement. The mean DOI was significantly higher in cases with bone invasion (13.65 ± 4.83 mm) compared to those without (9.18 ± 3.33 mm) ($p < 0.001$). There was a weak and non-significant positive correlation between DOI and WPOI ($r = 0.19$, $p = 0.091$).

Conclusion

Jaw bone invasion in OSCC is significantly associated with DOI and WPOI. Combined evaluation of these histopathological parameters may enhance prognostic assessment and assist in better clinical management of patients.

Introduction

Oral squamous cell carcinoma constitutes 90 percent of all oral malignancies and is a major health problem globally given its high prevalence and high mortality rate [1, 2]. The prevalence of OSCC is very high, especially in developing countries, where risk factors like tobacco smoking, alcohol consumption, and chewing of areca nuts are highly prevalent [3]. Although various diagnostic methods and treatment approaches have been developed, the overall survival rate of OSCC has not significantly improved over the last decades, mainly because of late diagnosis and the nature of the disease being highly aggressive [4, 5].

One of the primary characteristics of malignancy and a defining factor in the clinical progression and prognosis of OSCC is tumor invasion [6]. The biological aggressiveness of tumor cells is expressed by their ability to infiltrate the surrounding tissues, such as muscles, nerves, and bone [7]. Among these, some of the specific clinical relevance include the invasion of the jaw bones which are associated with advanced tumor stage, higher morbidity, and the need to perform extensive surgical intervention [8]. The bone invasion normally results in functional impairment and grossly affects the quality of life of the affected individuals [9].

The process of bone invasion in OSCC is complex and dynamic, involving both the tumor cells and the bone microenvironment. The tumor cells also secrete diverse cytokines and signaling molecules which lead to osteoclast differentiation and activation leading to bone resorption [10]. One of the most important links in the process is the RANK/RANKL/OPG pathway as it regulates the activity of the osteoclasts and promotes bone destruction caused by tumor[11]. Additionally, matrix metalloproteinases (MMPs) and other proteolytic enzymes are also important in degradation of the extracellular matrix, and subsequent tumor invasion into the osseous structures [12]. These biological activities underline the viciousness of OSCC and its capacity to destroy tissue locally [13].

The gold standard for assessment of tumor characteristics and prognosis in OSCC is the histopathological analysis [14]. DOI has received substantial attention among the various parameters under study due to its strong association with nodal metastasis and survival rates [15, 16]. DOI can be defined as the vertical distance between the basement membrane of the adjacent normal mucosa and the deepest point of tumor infiltration [15]. Compared to the tumor thickness, DOI provides a more realistic presentation of the true extent of the tumor invasion [16]. Consequently, DOI has been incorporated into the American Joint Committee on Cancer (AJCC) staging system, which implies its clinical relevance [17]. It has been established in many studies that increasing DOI is associated with an increase in cervical lymph nodes metastasis and a poorer prognosis [18, 21]. With higher DOI, tumors are more likely to spread to the nearby anatomical structures such as bone thereby contributing to the disease progression [20, 21]. Further, DOI is an excellent parameter in the determination of treatment options, particularly at an early stage of OSCC [18].

Another important histopathological parameter is WPOI, which reveals the architectural pattern of tumor cells [22, 23]. WPOI is categorized into five various patterns, which are well defined pushing borders, highly infiltrative development with satellite tumor islands [22, 23]. Patterns 4 and 5 (high WPOI grades)

are reflective of aggressive tumor behaviour and have been associated with higher recurrence, metastasis and poorer survival rates [24, 25]. WPOI evaluation is an effective predictor of tumor invasiveness and is complementary to other prognostic markers [23, 24].

Though the interaction between DOI and WPOI with bone invasion has not been clearly explained, they have been studied as independent prognostic factors. The occurrence of bone invasion reflects progression to an advanced stage of local disease and significantly influences staging and treatment planning. [26, 27]. Research has suggested that tumors having higher DOI and higher WPOI grades are more likely to exhibit aggressive behaviour including invasion into adjacent osseous structures [28]. However, it is known that there are few studies that have evaluated the joint action of DOI and WPOI on bone invasion.

Besides these histopathological parameters, there is new evidence to indicate that the tumor microenvironment and molecular factors play a role in determining tumor invasion and progression [29, 30]. Tumor cell interactions with stromal elements and immune cells also play a role in the invasive potential of OSCC [29]. Tumor proliferation, angiogenesis, and immune response biomarkers have been explored with the possibility of predicting tumor behaviour and prognosis [30].

Considering the clinical importance of bone invasion and its correlation with tumor aggressiveness, it is necessary to comprehensively understand its relationship with critical histopathological parameters. A better evaluation of tumor behavior and enhance prognostic stratification might be achieved by evaluating the combined effect of DOI and WPOI on bone invasion [28].

Thus, the current research aims to evaluate the extent of jaw bone invasion in OSCC and how it correlates with the DOI and WPOI. By combining these parameters, the study will help to strengthen the knowledge about tumor biology and help to improve clinical management of patients with OSCC.

Methods

Study design

The purpose of the study was intended to be a prospective observational analytical study aimed at assessing the existence of jaw bone invasion and its interrelation with the histopathological parameters, i.e. DOI and WPOI, in patients diagnosed with OSCC. The prospective nature of the study enabled real-time data gathering and standardized evaluation of histopathological features, which reduces the amount of recall and selection bias. No therapeutic treatment was given. All observations were conducted on regularly processed biopsy and resected specimens.

Study setting

The research has been carried out in the Department of Oral Pathology and Microbiology, Sharad Pawar Dental College and Hospital, Datta Meghe Institute of Higher Education and Research, Wardha, Sawangi Meghe, a tertiary care teaching hospital with diagnostic and histopathological facilities. The institution caters to a large and diverse patient population, so that there are enough cases to analyze. The patients with a clinically suspicious appearance of oral lesions were referred for biopsy and then histopathological evaluation. All the qualified cases that were diagnosed within the study period of July 2025 till April 2026. The laboratory procedures, including tissue processing and slide preparation, had been performed in a standardized way to sustain consistency and dependability of observations.

Study population

A total of 80 patients diagnosed with oral lesions clinically were used as a study population and subsequently proved as OSCC on histopathological examination. The study recruited all patients who reported to the outpatient department, prospectively in the study period. To maintain consistency and eliminate possible confounding factors of previous treatment, only new, untreated cases were taken into consideration. The population of the study included diversified demographic profile with the variations in age, sex and anatomical location of lesion, thus reflecting the clinical spectrum of OSCC that is experienced in a typical practice. All the cases used in this study provided adequate tissues for histopathological evaluation and assessment of parameters such as bone invasion, DOI and WPOI. These parameters will be assessed in detail. All the participants were recruited in a consecutive manner to minimize selection bias and to guarantee representativeness of the study sample.

Inclusion criteria

1. Histopathologically proven cases of OSCC.
2. Newly diagnosed and previously untreated patients
3. Patients who are undergoing biopsy or surgical resection.
4. Adequate tissue such as invasive front to make histopathological analysis.
5. Written informed consent by patients.

Exclusion criteria

1. Recurrent OSCC cases
2. Patients who had previous treatment (surgery, chemotherapy or radiotherapy).
3. Specimens lacking adequate tissue for evaluation of invasion
4. Poorly maintained or autolyzed samples.
5. Missing clinical or histopathological data.

Histopathological examination

The tissue samples which were collected either by biopsy or by surgical resection were fixed in 10 percent neutral buffered formalin and processed in the usual manner. The tissue samples were embedded in paraffin, and thin sections measuring 4–5 µm were prepared using a microtome. The staining of the sections was performed using H&E and was subjected to light microscopy.

To confirm the diagnosis of OSCC, a histopathological investigation was performed. Morphological criteria, such as epithelial dysplasia, cellular atypia, keratinization, and invasion of underlying connective tissue were taken into consideration for diagnosis of OSCC. Special focus was given on tumor invasive front to evaluate DOI, WPOI and the presence of jawbone invasion.

All slides were independently evaluated by two experienced oral pathologists. A consensus diagnosis was reached by joint review in cases of discrepancy to ensure accuracy and reproducibility of the observations.

Measurement of depth of invasion (DOI)

With the help of the light microscope, DOI was measured as a continuous variable through a calibrated ocular micrometre. The greatest distance between the basement membrane of the adjacent normal mucosa and the deepest point of tumor infiltration was measured. In cases with ulceration or surface disruption, a reconstructed mucosal baseline was used as the reference point. All measurements were recorded in millimetres.

Depth of Invasion (DOI) classification

DOI (mm)	AJCC T-Category Implication	Interpretation
≤ 5 mm	T1 (if tumor size ≤ 2 cm)	Low risk
> 5–10 mm	T2 (if tumor size ≤ 4 cm)	Intermediate risk
> 10 mm	T3	High risk

Assessment of worst pattern of invasion (WPOI)

The WPOI was measured at the tumor invasive front and was categorized in terms of existing criteria in five patterns (15). Pattern 1–3 featured cohesive growth of tumors with well-defined borders, whereas patterns 4 and 5 were characterized by non-cohesive, infiltrative tumor growth with small tumor islands or satellite tumor cells. Patterns 4 and 5 were regarded as indicative of aggressive tumor behavior and therefore were included in analytical use.

Worst Pattern of Invasion (WPOI) classification

WPOI Type	Histopathological description
Type 1	Pushing, well-defined tumor borders
Type 2	Finger-like pushing invasion
Type 3	Large tumor islands (> 15 cells per island)
Type 4	Small tumor islands (≤ 15 cells per island), infiltrative pattern
Type 5	Tumor satellites ≥ 1 mm from the main tumor front

Evaluation of jaw bone invasion.

Jaw bone invasion was also evaluated histopathologically on H&E-stained sections and categorized as positive or negative based on the presence or absence of malignant epithelial cells infiltrating bone.

The assessment involved detection of tumor-bone interface, bone destruction evidence, and osteoclastic activity of bone including resorption lacunae. Gomori's trichrome stain was also used selectively to help improve visualization of collagen and bone matrix to aid in confirmation of tumor infiltration into the osseous structures.

All measurements were carried out at the invasive front of the tumor to provide effective assessment of bone involvement.

Statistical analysis

The association between categorical variables, bone invasion, categorized DOI and WPOI was evaluated using the Chi-square test. Fisher's exact test was performed where the cell count was less than 5.

Independent samples of t-test or one way analysis of variance (ANOVA) was used to compare continuous variables across groups depending on the number of groups and distribution of data. In instances where normality assumptions were not upheld, then respective non-parametric tests were conducted.

Pearson or Spearman correlation coefficient was used to determine the correlation between DOI and WPOI, depending on the nature and distribution of the data.

The logistic regression analysis was conducted to determine the independent predictors of bone invasion.

The p-value of less than 0.05 was taken to be statistically significant. Findings were represented in the form of tables and proper statistical output to interpret the results.

Results

A total of 80 cases of OSCC were included in the present study. The clinicopathological parameters, including bone invasion, DOI and WPOI, were evaluated and analyzed.

Distribution of Bone Invasion

Bone invasion was identified in 46 (57.5%) cases, while 34 (42.5%) cases did not show evidence of bone involvement (Table 1). This indicates that a substantial proportion of OSCC cases in the study cohort exhibited tumor infiltration into bone.

Table 1
Distribution of bone invasion in cases of oral squamous cell carcinoma

Bone invasion	n%
Present	46 (57.5%)
Absent	34 (42.5%)

Association Between Bone Invasion and WPOI

The relationship between bone invasion and WPOI was assessed using the chi-square test. A statistically significant association was observed ($\chi^2 = 12.07$, $p = 0.016$).

As shown in (Table 2) that tumors with lower WPOI grades (1 and 2) were mostly observed without bone involvement. In contrast, lesions with higher grades, particularly WPOI 4 and 5, showed a clear rise in the occurrence of bone invasion. It is noteworthy that bone invasion was identified in every case categorized as WPOI 5, suggesting a highly aggressive pattern of tumor.

Table 2
Association between bone invasion and worst pattern of invasion (WPOI) grades in oral squamous cell carcinoma

WPOI	Bone Invasion Absent n (%)	Bone Invasion Present n (%)	Total
1	2 (5.9%)	0 (0%)	2
2	4 (11.8%)	1 (2.2%)	5
3	11 (32.4%)	9 (19.6%)	20
4	17 (50.0%)	30 (65.2%)	47
5	0 (0%)	6 (13.0%)	6

This relationship is also evident in (Fig. 1), where the proportion of bone invasion increases progressively with higher WPOI grades.

Comparison of DOI based on bone Invasion.

The mean DOI in cases with bone invasion was 13.65 ± 4.83 mm, whereas cases without bone invasion had a much lower mean DOI of 9.18 ± 3.33 mm is shown in (Table 3).

Table 3
Comparison of depth of invasion (DOI) between cases with and without bone invasion in oral squamous cell carcinoma

Bone Invasion	Mean DOI (mm) ± SD	p-value
Absent	9.18 ± 3.33	
Present	13.65 ± 4.83	< 0.001

This difference was found to be highly significant ($p < 0.001$), according to the independent t-test, which was used to perform statistical analysis. As shown in (Fig. 2) that tumors which have deeper depth of invasion have a higher likelihood of involving bones.

Correlation Between DOI and WPOI

The correlation between DOI and WPOI was evaluated using Spearman's correlation coefficient as shown in (Table 4). A weak positive correlation was observed ($r = 0.19$); however, this association did not reach statistical significance ($p = 0.091$).

Table 4
Correlation between depth of invasion (DOI) and worst pattern of invasion (WPOI) in oral squamous cell carcinoma

Variables	Correlation Coefficient (r)	p-value
DOI vs WPOI	0.19	0.091

This suggests that although higher WPOI grades may be associated with increasing DOI, the relationship was not strong enough to be statistically confirmed within the present sample.

Discussion

OSCC remains a major global health issue because of its high occurrence in the population, aggressive nature, and poor survival prospects [1, 2]. Intrusion of tumor in surrounding structures, especially bone, indicates an advancing disease and is correlated with a higher morbidity and poorer prognosis [6, 8]. In the current research, the correlation between DOI, WPOI and jaw bone invasion was assessed to gain a better insight into the tumor aggressiveness.

Recent literature proved that there was a strong correlation between WPOI and bone invasion. Patterns 4 and 5 (patterns of non-cohesive and infiltrative growth pattern) were found to have a higher frequency of bone involvement. The architectural features of tumor cells at the invasive front are reflected in WPOI

and it has been generally accepted as an important prognostic parameter [21–23]. A previous study has reported that higher WPOI grades, higher the risk of local recurrence, nodal metastasis, and lower survival [24, 25]. These findings are consistent with the current findings which indicate that tumors with aggressive patterns of invasion are more likely to penetrate the adjacent structures.

It was also noted that the association between DOI and bone invasion was highly significant with cases which exhibited bone involvement having a higher mean DOI.DOI is the vertical extent of tumor infiltration and has been included in the AJCC staging system as it has a strong prognostic value [15, 17]. It has been demonstrated in a number of studies that an increase in DOI is correlated with increased risk of cervical lymph node metastasis and poor clinical outcome [18, 19, 20]. Moreover, a continued prognostic variable, which is continuous, has been proposed as an additional variable, which can allow more accurate determination of tumor aggressiveness [16]. The findings of the current research also support the significance of DOI as a good predictor of bone invasion in OSCC.

Surprisingly, the correlation between DOI and WPOI was observed to be weak and not significant. This implies that, though both parameters are independent variables, which are associated with bone invasion, they might be different kinds of tumor biology. DOI indicates the extent of tumor invasion, and WPOI indicates the pattern of invasion at the front of tumor. Other researchers have reported similar findings when assessing multiple histopathological prognostic factors and indicated that the parameters provide complementary rather than overlapping information [20, 28, 29].

The mechanism of bone invasion by OSCC involves complex interactions between the tumour and the bone microenvironment. Pathways activated by tumor derived factors comprises RANK/RANKL signaling causes bone resorption, leading to signaling which stimulates osteoclasts and tumor growth [10, 11]. Further, matrix metalloproteinases play a crucial role in the extracellular matrix degradation, allowing tumor cell invasion to the bony structures [12]. Such biological processes underlie the perceived relationship between aggressive tumor factors (e.g., elevated DOI and elevated WPOI) and bone invasion.

The results of the current research imply the significance of concomitant evaluation of histopathological parameters in OSCC. DOI can be used to obtain quantitative data on the depth of the tumor, whereas WPOI can be used to obtain qualitative data on the pattern of tumor invasion. Combination of these parameters could enhance prognostic stratification and help clinicians to plan treatment, especially in planning surgical resection of the patient.

Limitations

The current study has some limitations such as the small sample size and the single center nature of the study, which could limit the generalizability of the results. Also, there were no long-term follow-up data, so these parameters could not be correlated with survival outcomes.

Conclusion

Under the confines of the study, it can be concluded that both DOI and WPOI are significantly related to the invasion of the jaw bone in OSCC. These parameters can be used as valuable prognostic factors and can be used to predict the aggressiveness of tumors and to guide clinical therapy.

Abbreviations

OSCC
Oral squamous cell carcinoma
DOI
Depth of invasion
WPOI
Worst pattern of invasion
AJCC
American Joint Committee on Cancer
H&E
Hematoxylin and eosin
MMPs
Matrix metalloproteinases
RANKL
Receptor activator of nuclear factor kappa–B ligand
OPG
Osteoprotegerin
SD
Standard deviation
CI
Confidence interval
SPSS
Statistical Package for the Social Sciences

Declarations

Ethical approval and consent to participate:

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and all relevant guidelines and regulations. The institutional ethics committee approval has been granted from Datta Meghe Institute of Higher Education and Research (DU), Sawangi (Meghe), Wardha, IEC Ref.No.DMIHER(DU)/IEC/2025/626. Written informed consent was obtained from all participants prior to their inclusion in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to institutional policies but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

- **Sejal Basawnathe**: Conceptualization, data collection, histopathological analysis, manuscript drafting
- **Alka Hande, Swati Patil, Aayushi Pakhale, Husna Tehzeeb**: Study design, supervision, critical revision of manuscript

All authors have read and approved the final manuscript.

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Figures

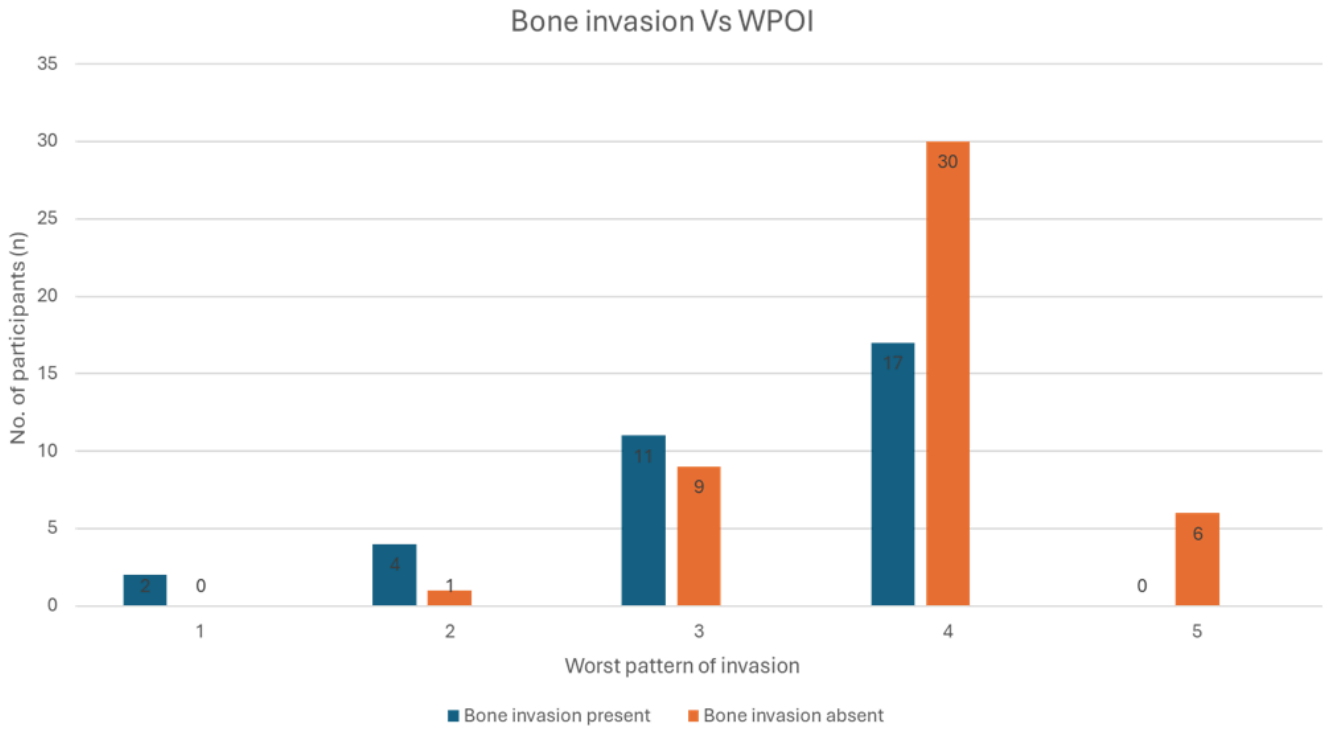


Figure 1

Bar chart illustrating the distribution of bone invasion among different WPOI grades in oral squamous cell carcinoma.

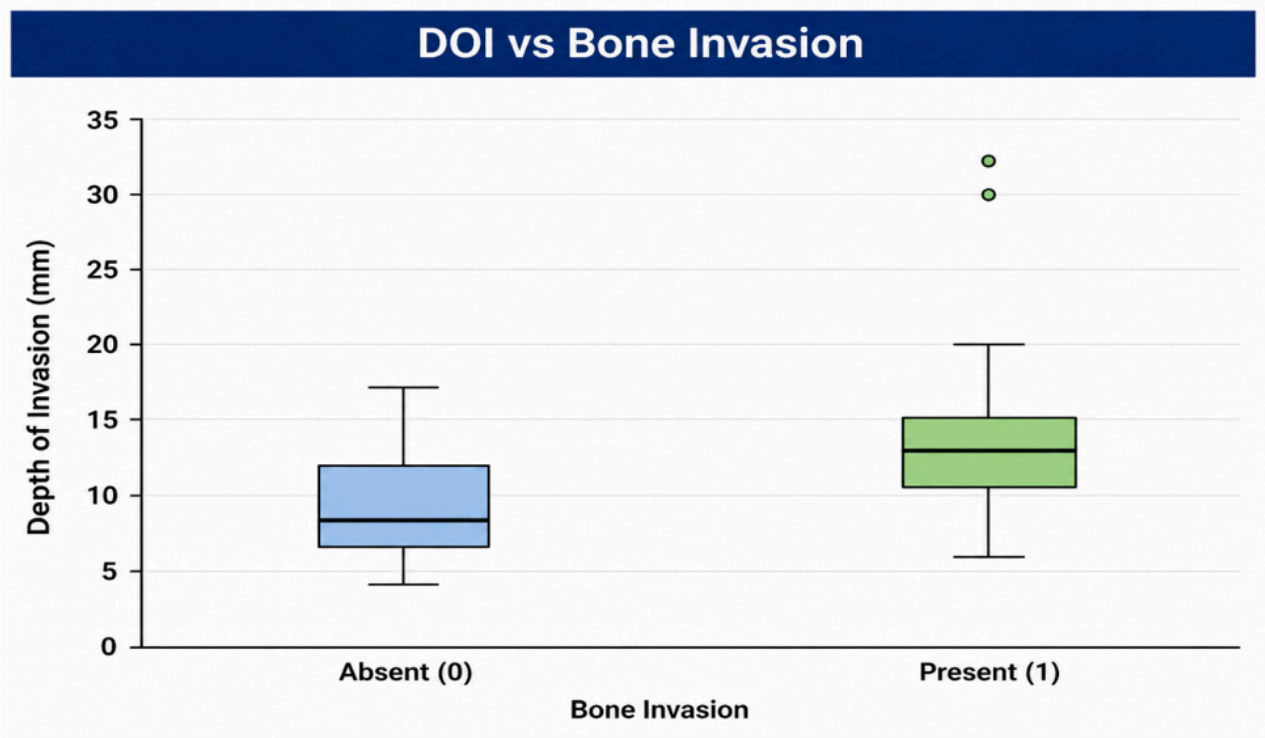


Figure 2

Boxplot showing a higher median DOI and broader dispersion across cases where bone has been invaded, as well as the existence of outliers representing deeply invasive tumors.