New Bone Fluorescence Detection System: Quantitative Analysis of Spectrophotometric Variations Between Necrotic and Vital Bones

Ilaria Giovannacci, DDS, MSc, PhD,[*†] *Achille Tarsitano, MD, FEBOMS,*[‡§] *Diana D'Alpaos, MD,*[‖] *Giuseppe Pedrazzi,*[¶#] *Aurora Andrea Venuti, DDS,*[**] *Roberta Iaria, DDS,*[††] *and Paolo Vescovi, DDS MSc, PhD*[*‡‡]

Background: Osteonecrosis of the jaw (ONJ) management remains challenging due to the lack of standardized surgical margin criteria. Bone autofluorescence (AF) has shown potential to distinguish necrotic from vital bone tissue intraoperatively.

Purpose: The study aimed to measure the association between bone AF intensity and histopathologic diagnosis to explore the potential of a new spectrophotometric method for real-time assessment of bone vitality.

Study Design, Setting, and Sample: This was a prospective, multicentric, cross-sectional ex vivo study including 40 subjects treated for ONJ at 2 Italian university hospitals between 2023 and 2024. Exclusion criteria were age <18 years and inability to provide informed consent.

Predictor Variable: The predictor variable was bone AF intensity coded as vital (CTRL) or necrotic (ONJ).

Outcome Variable: The primary outcome variable was histologic tissue diagnosis coded as vital or necrotic. The secondary outcome was to assess whether systemic or pharmacological variables could influence the spectrophotometric measurements.

Covariates: Covariates included clinical history, pharmacologic treatments, and ONJ characteristics.

*Adjunct Professor, Oral Medicine and Oral Surgery Laser Unit, University Center of Dentistry, Department of Medicine and Surgery, University of Parma, Parma, Italy.

†Adjunct Professor, Uni-Camillus-Saint Camillus International University of Health Sciences, Rome, Italy.

‡Full Professor, Oral and Maxillofacial Surgery Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy.

§Full Professor, Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, Bologna, Italy.

‖Oral and Maxillofacial Surgery Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy.

¶Associate Professor, Department of Medicine and Surgery, Unit of Neuroscience, Plesso Biotecnologico Integrato, University of Parma, Parma, Italy.

#Associate Professor, Interdepartmental Center of Robust Statistics (Ro.S.A.), University of Parma, Parma, Italy.

**Resident, Oral Medicine and Oral Surgery Laser Unit, University Center of Dentistry, Department of Medicine and Surgery, University of Parma, Parma, Italy.

††PhD student (Molecular Medicine UniPr), Oral Medicine and Oral Surgery Laser Unit, University Center of Dentistry, Department of Medicine and Surgery, University of Parma, Parma, Italy.

‡‡Spec. Oral Surgery, Full Professor, Oral Medicine and Oral Surgery Laser Unit, University Center of Dentistry, Department of Medicine and Surgery, University of Parma, Parma, Italy.

Conflict of Interest: None of the authors have any relevant financial relationship(s) with a commercial interest.

Address correspondence and reprint requests to Dr Venuti, Oral Medicine and Oral Laser Surgery Unit, Department of Medicine and Surgery, University of Parma, Via Gramsci 14, 43125 Parma, Italy; e-mail: auroraandrea.venuti@unipr.it

Received September 15 2025

Accepted November 20 2025

0278-2391/25/00937-1

https://doi.org/10.1016/j.joms.2025.11.014

Analyses: Descriptive statistics were computed for all variables. Normality was assessed with the Shapiro–Wilk test, and group differences were analyzed using parametric and nonparametric tests. A mixed-effects modeling framework was applied to account for repeated measures, including a linear mixed-effects model for fluorescence ratios and a mixed-effects logistic regression to assess the association between AF and histology; diagnostic accuracy was derived from model-based probability thresholds.

Results: The sample included 33 females (82.5%) and seven males (17.5%) with a mean age of 68.4 ± 11.9 years. A total of 294 spectral points were analyzed (147 necrotic, 147 vital). The mean photon count at 500 nm for the areas with ONJ was 7,886 ± 4,452, while the mean photon count at 500 nm for the healthy areas was 33,825 ± 10,791. The mean loss of fluorescence intensity (LoFI) ratio was 5.2 ± 2.4.

Fluorescence did not differ by oncologic status ($P = .8$) but was significantly reduced in patients treated with new antiresorptive drugs ($P = .004$).

Conclusions and Relevance: Quantitative bone AF was directly correlated with histopathologic vitality. This objective, real-time method may improve the precision of surgical margin identification in ONJ management.

J Oral Maxillofac Surg 84:578-591, 2026

The American Association of Oral and Maxillofacial Surgeons updated its Position Paper in 2022 highlighting that medication-related osteonecrosis of the jaw (MRONJ) should be distinguished from other forms of osteonecrosis of the jaws (ONJ) and thus identified early by history and clinical exam.[1] The last Italian update of 2020 defined MRONJ as bone necrosis occurring in patients exposed to bone-modifying agents (BMAs) and/or antiangiogenic agents (AAs), with no history of radiation therapy to the jaws or primary or metastatic malignancy involving the jaws.[2] Osteoradionecrosis (ORN), on the other hand, should be suspected in patients with a history of radiotherapy to the jaws.[3]

In both conditions, the treatment strategies range from conservative to surgical.[4,5] In the last years, innovative treatment modalities have been studied as an alternative to invasive treatment, such as hyperbaric oxygen (HBO) therapy, ozone therapy (OT), and low-level laser therapy (LLLT) showing good results, although large-scale evidence remains limited.[6,7]

The main issue regarding MRONJ treatment is recurrence, which appears to be influenced by the duration of pharmacologic therapy, the presence of bacterial infection within necrotic areas, and the treatment modality adopted.[8,9] Xiaobo Dai et al state that the persistence of residual necrotic tissue contributes significantly to recurrence rates, which is estimated in the literature to be between 11 and 39% for MRONJ.[7,10-12]

Similarly, ORN carries a risk of recurrence, related to the severity of the initial disease and the surgical approach employed.[13]

The expert panel of the Italian Scientific Societies of Maxillofacial Surgery (SICMF) and Oral Pathology and Medicine (SIPMO) recognizes that among the factors that could negatively influence the result of surgery is "the lack of a common strategy to define the surgical bone margins".[14] Resection margins should ideally extend beyond the borders of necrotic bone into areas of vital, bleeding bone. However, their delineation currently relies on preoperative radiographic imaging and clinical bone characteristics. Both indicators have significant limitations and are highly dependent on interpretation and subjectivity.[15,16]

In recent years, increasing interest has focused on fluorescence-guided bone surgery, with or without fluorescent tetracycline labeling, as a promising technique to improve the intraoperative identification of surgical margins and increase the precision of necrotic bone removal.[14,16-19]

However, current fluorescence-based methods rely on qualitative visual assessment, which remains subjective. To maximize the potential of bone autofluorescence (AF), it is necessary to develop a tool that evaluates the degree of fluorescence emitted numerically, to give an objective quantification of spectral emission through photon count, not subject to interpretation.

The purpose of this study is to measure the association between bone AF intensity and histopathologic diagnosis to explore the potential of a new spectrophotometric method for real-time assessment of bone vitality.

Based on this premise, the working hypothesis is that necrotic bone tissue exhibits statistically significant lower fluorescence intensity compared to vital bone, and that this difference can be objectively quantified through spectrophotometric photon counting. Accordingly, the specific aims of the study are: 1) to

measure the fluorescence emission spectra of vital and necrotic bone using a novel spectrophotometric system, 2) to compare fluorescence intensity values with histopathologic findings in order to evaluate diagnostic accuracy, and 3) to explore potential influences of clinical and pharmacological variables on fluorescence intensity measurements.

Materials and Methods

STUDY DESIGN AND SAMPLE

The study was a prospective, multi-centric, preclinical *ex vivo* study. It was approved by the local ethical committees of two participating centers: the promoting center was the Azienda Ospedaliero-Universitaria di Parma (AVEN ethical committee: study number: 739/2022/TESS/AOUPR AFBONE), and the affiliated center is IRCCS Azienda Ospedaliero Universitaria di Bologna, Policlinico Sant'Orsola (AVEC ethical committee: study number: 331/2023/Sper/AOUBo). The research was conducted according to the Helsinki Declaration. All patients signed informed consent to the use of their data for research purposes.

The study population was composed of patients surgically treated for osteonecrosis of the jaw between 2023 and 2024 at the 2 hospitals. To be included in the study, patients had to be older than 18 years, be able to provide informed consent, and present with a diagnosis of osteonecrosis of the jaws requiring surgical therapy.

Patients were excluded if they were under 18 years of age or unable to provide informed consent.

STUDY VARIABLES

The primary predictor variable was bone AF photon count at 500 nm, corresponding to the emission peak of collagen-related fluorophores in vital bone. AF emission intensity was quantitatively measured using a fiber optic spectrophotometric system which emits a violet light with a wavelength in the range of 400-430 nm.

For each bone specimen, the mean photon count at 500 nm was recorded.

During spectral acquisition, measurement sites were clinically classified as CTRL (control group) (clinically healthy bone) or ONJ (clinically necrotic bone) to distinguish between the 2 types of regions within each patient.

The primary outcome variable was the histopathological diagnosis of bone tissue, categorized as vital or necrotic. Histological evaluation was performed on all bone fragments obtained from both clinically healthy and necrotic areas.

Vital bone was defined by the presence of viable osteocytes within well-organized lacunae and a preserved trabecular and collagen matrix. Necrotic bone was characterized by empty osteocytic lacunae, disorganized trabeculae, and extensive degradation of the collagen network.

For each necrotic site (checked histologically), the number of photons emitted at 500 nm was calculated and compared with the number of photons emitted at 500 nm by the marginal control bone (checked histologically as vital bone).

The ratio between the 2 measurements is called LoFI (loss of fluorescence intensity) and represents an objective measure for assessing objectively the degree of necrosis produced by a loss of AF in that patient.

Assuming a LoFI equal to 1 would mean that necrotic bone and healthy bone have the same fluorescence intensity (null hypothesis).

Secondary outcome was to investigate whether systemic or pharmacological anamnestic variables could influence the spectrophotometric measurements. More specifically, since MRONJ is generally caused by the intake of bisphosphonates or new antiresorptive drugs, we investigated whether fluorescence intensity varies differently following the use of these different molecules.

Covariates included clinical and pharmacological characteristics potentially influencing AF intensity: age, sex, smoking habit, diabetes, autoimmune and oncological diseases, and pharmacological therapies. In particular, the exposure to oral anticoagulants, corticosteroid therapy, bisphosphonates, or other antiresorptive and anti-neoangiogenic drugs was recorded. Information about necrosis was also recorded: localization, stage at diagnosis (the American Association of Oral and Maxillofacial Surgeons staging), and any trigger event.[2]

POWER AND SAMPLE SIZE ANALYSIS

For osteonecrosis of the jaws, preliminary data (unpublished) suggested an average auto-fluorescence ratio (CTRL/ONJ) exceeding 2.5, corresponding to a large effect size (Cohen's d), well above 1. Using a conservative estimate of d = 1 and assuming a two-tailed test with a statistical significance level of $\alpha = 0.05$ (5%) and statistical power $(1 - \beta) = 0.95$ (95%), the minimum required sample size, calculated with G*Power v. 3.1.9.7 (retrieved from: https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower), was 16 participants. To account for potential dropouts, a minimum of 20 subjects was considered appropriate for enrollment.

DATA COLLECTION METHODS

Spectrophotometric Setup

The spectrophotometric setup was composed of the following items (Fig 1): an LED source (LLS,

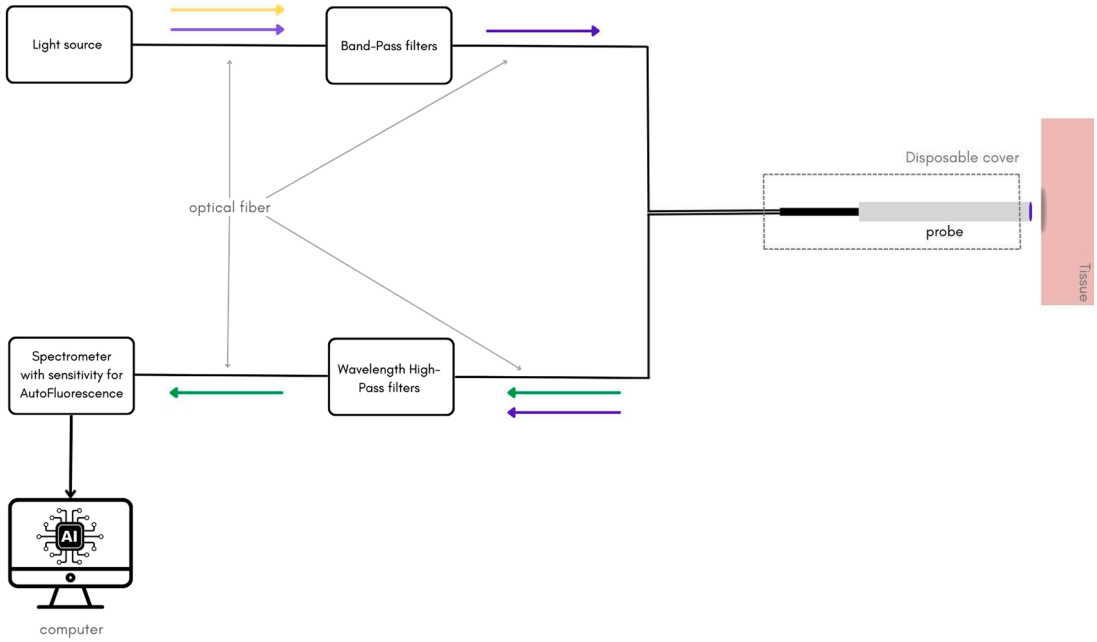

FIGURE 1. Schematic composition of the spectrophotometric setup.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

Ocean Optics, Dunedin, FL, USA), which emits a violet light with a wavelength in the range of 400-430 nm, the one that has proven to be the most suitable for the inducement of AF in human tissues; 2 dichroic filters (Thorlabs, Newton, NJ, USA) and filter holders (*Mightex*), which permit to delate all the unwanted wavelengths from excitation light and the collected emission light; a bifurcated optical fiber probe (Ocean Optics), which is necessary for tissue irradiation and collecting the emission light from the tissue; a spectrophotometer (*Flame*, (Ocean Optics), whose function is to measure the spectrum of the collected emission light in the visible range above the excitation wavelengths; and a personal computer (*Linux operating system*), used to control the spectrophotometer.

A specific software application (SW) was also developed in C language and integrated into the spectrophotometer setup (HW). The software acquires the AF spectra of the specimen, processes the acquired spectra, saves the processed spectra into a database (DB), and generates a unique code for each sample. The International Organization for Standardization date-time format yyyymmdd_hhmmss is used to

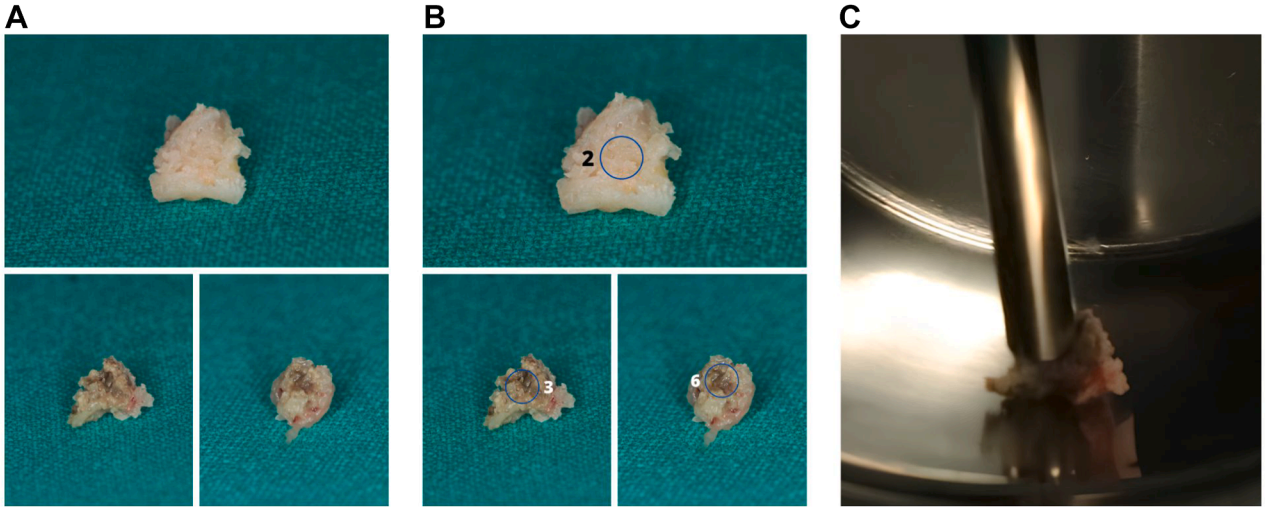

FIGURE 2. Frame of the analyzed sample with localization of the area to be scanned (*A*); graphic marking of the precise point that will be scanned (*B*); scanning of the area (*C*).

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

generate a unique identifier (ID) for each sample, to ensure anonymity, to perform a postprocessing analysis of the spectra that are saved in the DB, and to plot the results of the postprocessing analysis.

Study Protocol

After surgical excision, the fluorescence of each ex vivo bone specimen was evaluated using the spectrophotometer setup.

Each sample was washed to remove blood residues that could alter fluorescence.[20]

All sampled surfaces were photographed to precisely document the locations where the fluorescence examination was performed (Fig 2). These images ensure accurate localization of the sampling sites, allowing for a precise correlation between the analyzed areas and the obtained results (Fig 3A,B).

The sampled areas were irradiated with the optical fiber emitting in the 400-430 nm range (Fig 3C). The emitted light was recorded by the same optical fiber and was filtered to remove the reflected excitation light and selectively isolate the AF emission. The AF emission is measured by spectrophotometer and processed by the software. For each analyzed area, the SW produces a graph with the emitted fluorescence spectrum, which can be visualized both in absolute modality and normalized to 500 nm modality to better appreciate the variations in shape (Fig 3D-F).

The obtained spectrum was correlated with the histopathological aspect to establish a correlation between AF alteration and histopathological alteration (Fig 3E-G).

The same procedure is then performed on the bone at the resection margin considered clinically healthy.

The piece of bone at the margin is separated from the clinically necrotic portion, and both spectrophotometric and histopathological examinations were performed.

Figure 4 shows step-by-step the technique and shows where the fluorescence spectrophotometric analysis fits in and how it helps to standardize the choice of resection margins.

After raising the full-thickness mucosal flap, the necrotic bone sequestration was removed (Fig 4C,D). The bone specimen was cleaned and irradiated with the setup's optical fiber at several precisely marked points (Fig 4E). Interestingly, the necrotic bone sample exhibits a red fluorescence so intense that it can be seen without bandpass filters, and this is the fluorescence from the porphyrins in the bacterial load (Fig 4F).

The obtained spectrum shows a curve typical of necrotic bone, and the SW provides a measure of the photon count (ie, a quantitative measurement of AF) (Fig 4G). The photon count at 500 nm was 2,500; additionally, spectral graphs revealed additional peaks at 630-650 and 700 nm, indicating the presence of porphyrins.

At this point, further bone was removed using instruments that allow for great surgical precision, such as Piezosurgery and the Er:YAG laser[21] (Fig 4H,I). A small sample of residual bone was now removed and irradiated again with the optical fiber (Fig 4J): the obtained spectrum has a linear curve,

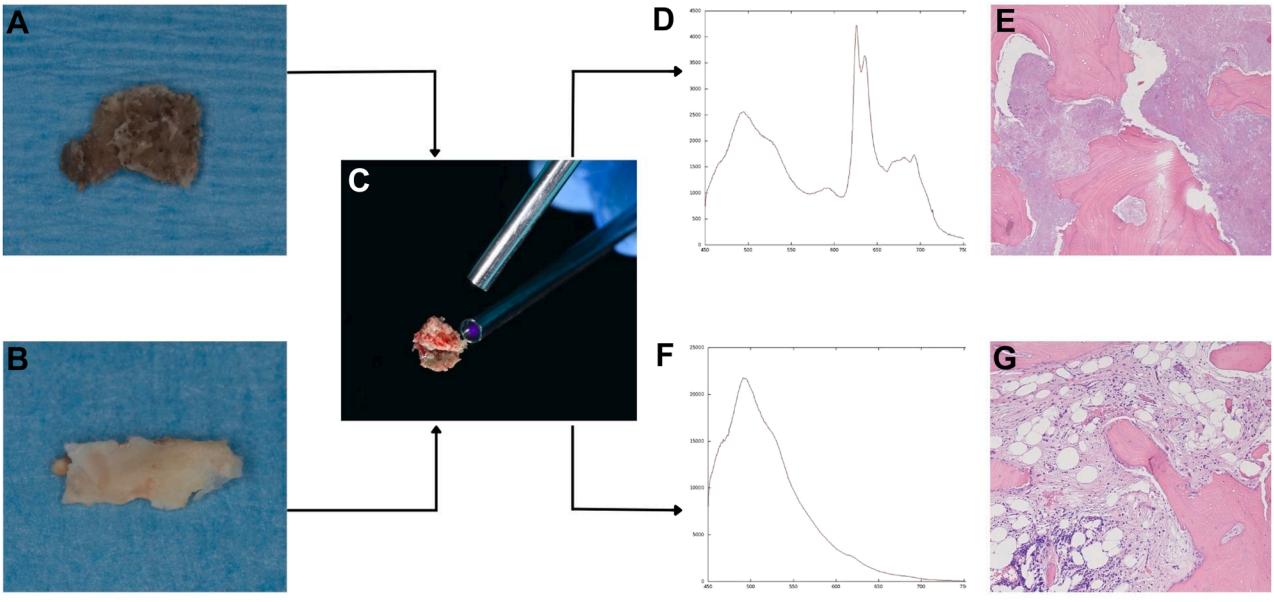

FIGURE 3. Diagram showing the workflow: the necrotic sample is irradiated with the probe, the same probe collects and measures the emitted fluorescence, producing a graph, subsequently the data are correlated with the histopathological analysis of the precise irradiated point (A-C-D-E). The same workflow is applied to the healthy marginal resection specimen (B-C-F-G).

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

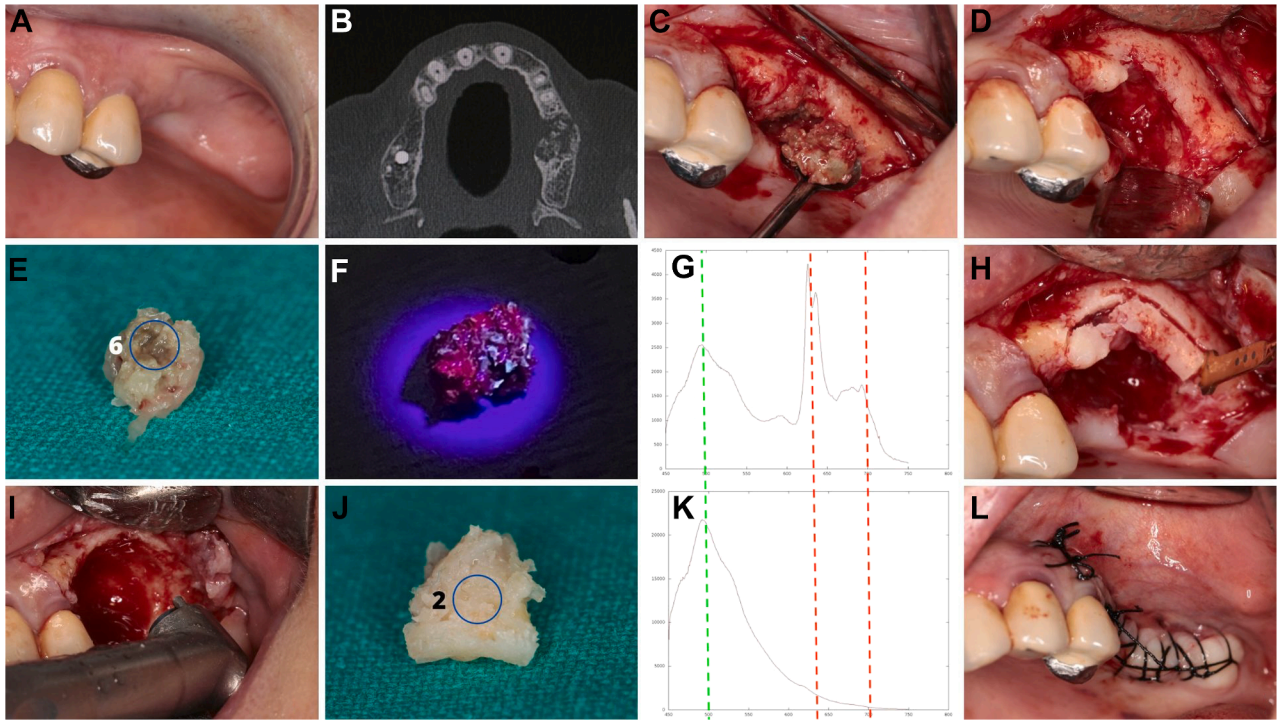

FIGURE 4. Explanatory representation of the technique using a clinical case. Case of unexposed stage II ONJ with extensive area involving the maxillary bone (*A, B*). The necrotic bone sequestrum is removed (*C, D*), the necrotic bone is irradiated, and the fluorescence emission spectrum is visualized (*E-G*). Further bone is selectively removed, with extremely precise technologies such as piezosurgery (*H*) or Erbium laser (*I*). Now, a sample of clinically healthy bone is removed and analyzed using setup (*J, K*). Once a spectrum with intensity and shape compatible with healthy bone is obtained, the margins are considered definitive, and suturing is performed (*L*). In panels g and k, a green dashed line at 500 nm highlights the collagen-associated emission peak, while 2 red dashed lines indicate the porphyrin emission range between 630-650 and 700 nm.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

and the photon count at 500 nm has now risen to 22,000 (Fig 4K). The healthy/diseased ratio is approximately 8.8, meaning that the residual bone has average fluorescence intensity eight times greater than fluorescence intensity of the diseased bone. At this point, the procedure can be completed, and the flap closed with sutures (Fig 4L).

DATA ANALYSES

Data analysis was performed using IBM SPSS Statistics for Windows (version 29, IBM Corp., Armonk, NY) and the open-source statistical system Jamovi v .2.7.6 (The jamovi project (2025)). Measures of central tendency, dispersion, and shape were calculated for all the variables in the data set. Summaries included arithmetic mean, median, SD, interquartile range, minimum, maximum, asymmetry, kurtosis, the relevant standard errors, and 95% CIs. Normality of the data was tested by the Shapiro–Wilk test. Categorical data were reported in frequency tables and expressed as absolute, relative, cumulated frequencies, and percentages. Univariate comparisons between continuous variables were performed using both parametric test (Student's *t* test, analysis of variance and nonparametric test (Mann-Whitney's *U* test, Kruskal-Wallis test).

Statistical significance was set at $P < .05$.

Since multiple fluorescence spectra were collected from both vital and necrotic areas of the same subject, independence between observations could not be assumed. Therefore, a mixed-effects modeling framework was adopted to account for within-subject correlation.

A linear mixed-effects regression (LME) was used to evaluate the within-patient variability of the fluorescence ratio (LoFI= CTRL/ONJ), including a random intercept for patient ID to account for repeated measures. The fixed effect tested whether the mean LoFI significantly exceeded 1, corresponding to higher fluorescence intensity in vital bone.

A mixed-effects logistic regression model was applied to assess the association between AF intensity and histopathologic diagnosis (vital vs necrotic bone). Tissue type (0 = vital, 1 = necrotic) was the outcome variable, AF photon count was the fixed effect, and patient ID was the random intercept.

A decision threshold for AF was derived from the logistic model at a predicted probability of necrosis equal to 0.5, from which sensitivity, specificity, and overall diagnostic accuracy were calculated. CIs

were estimated by clustered (patient-level) resampling.

The within-patient contrast between tissue types was summarized by the CTRL/ONJ ratio and log-transformed and analyzed using a one-sample *t* test; geometric mean ratios and 95% CIs were obtained by back-transforming log-scale estimates.

Results

DESCRIPTIVE SAMPLE ANALYSIS

A total of 40 subjects were enrolled, 33 females (82.5%) and seven males (17.5%). The mean age was 68.4 ± 11.9 years (minimum: 40 years; maximum: 91 years). Twenty-five patients out of 40 (62.5%) were nonsmokers, nine were smokers (22.5%), and five were ex-smokers (12.5%). Only three out of 40 (7.5%) patients were affected with an autoimmune disease, four out of 40 (10%) were taking corticosteroid drugs, and nine out of 40 (22.5%) taken oral anticoagulant drugs.

Thirty-two out of 40 patients (80%) were affected by oncological disease, 21 had taken bisphosphonates (52.2%), 17 had taken new antiresorptive drugs (42.5%), and in two of these cases (5%), the patients had taken both bisphosphonates and monoclonal antibodies.

Regarding the characteristics of ONJ, Table 1 summarizes the etiology of the necrosis, the localization, the stage at the time of diagnosis, and the presence of a trigger event.

All bone specimens submitted for histologic examination confirmed the clinical and spectrophotometric assessments, showing complete concordance between autofluorescence-based evaluation and histopathologic diagnosis of necrotic and vital bones. However, 7.5% of samples (n = 3) were histologically classified as "vital bone with sclerotic changes consistent with prior bisphosphonate therapy".

Table 1. DISTRIBUTION OF PRIMARY DISEASE, LOCALIZATION, CLINICAL STAGE, AND PRESENCE OF TRIGGER EVENTS IN THE STUDY POPULATION. THE MAJORITY OF CASES WERE ASSOCIATED WITH BONE METASTASIS (62%), MOST FREQUENTLY FROM BREAST CANCER (40%). LESIONS WERE PREDOMINANTLY LOCALIZED IN THE MANDIBLE (73%), AND MOST PATIENTS PRESENTED AT STAGE II (65%). A TRIGGER EVENT WAS IDENTIFIED IN 32% OF CASES, MOST COMMONLY TOOTH EXTRACTION (61%)

Primary Disease, Localization, Stage, and Trigger Event	No	%
Primary disease		
Bone metastasis	25	62%
Breast cancer	16	64%
Kidney cancer	4	16%
Lung cancer	1	4%
Prostate cancer	2	8%
Stomach cancer	1	4%
Breast + lung cancer	1	4%
Multiple myeloma	4	10%
Head and neck cancer	3	7%
OSCC tongue	2	67%
Parotid gland cancer	1	33%
Osteoporosis	5	13%
Osteoperosis	2	5%
Unknown	1	3%
Localization		
Maxillary	11	27%
Mandibular	29	73%
Stage		
I	5	12%
II	26	65%
III	9	23%
Presence of trigger event		
No	27	68%
yes	13	32%
Extraction	8	61%
Perimplantitis	3	23%
Periodontitis	1	8%
Dentures	1	8%

SPECTRAL ANALYSIS OF FLUORESCENCE INTENSITY

The total number of spectral points analyzed was 294: 147 points corresponded to necrotic areas and 147 points corresponded to vital areas.

The mean photon count at 500 nm for the areas with ONJ was 7,886 ± 4,452, while the mean photon count at 500 nm for CTRL was 33,825 ± 10,791 (Table 2).

The comparison between the photon count in the ONJ group and the control group was statistically significant in both parametric and nonparametric tests ($P < .001$) (Table 2 and Fig 5).

Figure 6 shows the data from the 2 groups paired with each control. The downward trend is evident

Table 2. ANALYSIS OF 294 SPECTRA (ONJ VS CTRL) SHOWS A MARKED DIFFERENCE IN MEAN PHOTON COUNTS AT 500 NM. BOTH PARAMETRIC AND NONPARAMETRIC TESTS CONFIRM A HIGHLY SIGNIFICANT DIFFERENCE BETWEEN NECROTIC AND HEALTHY AREAS ($P < .001$)

	n	Mean ± SD	Median [IQR]	*P* Value
ONJ	147	7,886 ± 4,452	6,217 [5,444]	<.001*
CTRL	147	33,825 ± 10,791	33,680 [7,638]	<.001†

Note. $H_a\ \mu_{\text{Measure 1 - Measure 2}} \neq 0$.
* Paired samples *t* test: [1]Student's t, [2]Wilcoxon W.
† Paired samples *t* test: [1]Student's t, [2]Wilcoxon W.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

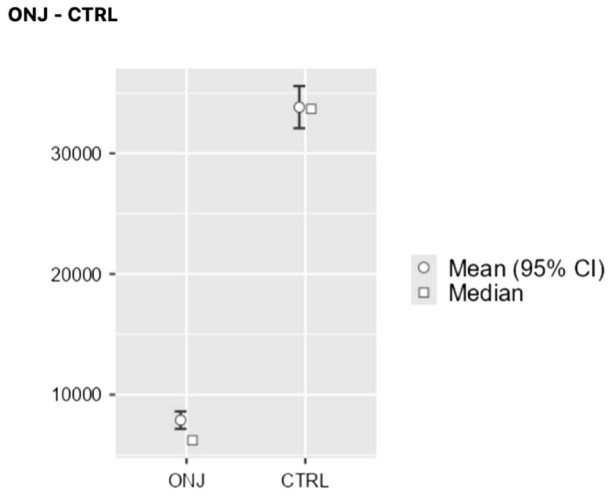

FIGURE 5. Bar plot with mean and median values: Comparison of fluorescence photon counts between ONJ and control (CTRL) groups. Both mean values (±95% CI) and medians are shown, highlighting the markedly lower fluorescence signal in necrotic bone compared with healthy bone.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

toward the ONJ group for each of the pairs (the average trend is in bold).

Figure 7 shows the distribution of photon counts in the 2 groups. The graph clearly shows that the 2 distributions have an almost negligible overlap.

LOSS OF FLUORESCENCE INTENSITY (LoFI) EVALUATION

The *ratio* of fluorescence intensity at 500 nm between the healthy areas and diseased areas is on

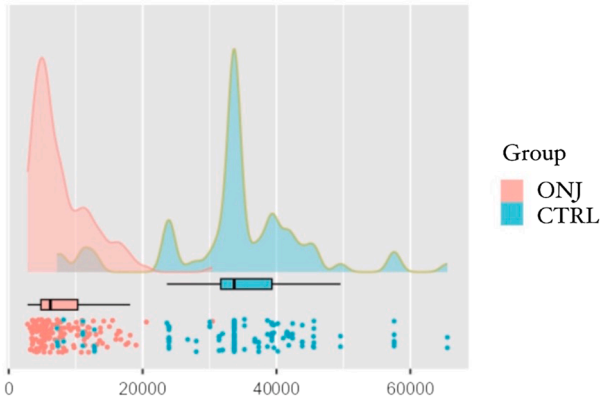

FIGURE 7. Density distribution, boxplots, and individual data points of photon counts in CTRL and ONJ groups. The 2 distributions show minimal overlap, indicating a clear separation between healthy and necrotic bone fluorescence.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

average 5.23 (Table 3). This means that, on average, healthy bone shows fluorescence more than five times greater than the diseased area. Similarly, if the ratio between diseased and healthy areas is considered, the result is 0.25. Both parametric and nonparametric statistical tests resulted extremely statistically significant ($P < .001$).

The analysis of LoFI using a linear mixed-effects model confirmed that all patient-level mean ratios were significantly above the reference value of 1, indicating consistently higher fluorescence in vital bone. Figure 8 illustrates the mean LoFI values for each patient, with the red dashed line representing the null hypothesis (LoFI = 1). All individual means (blue

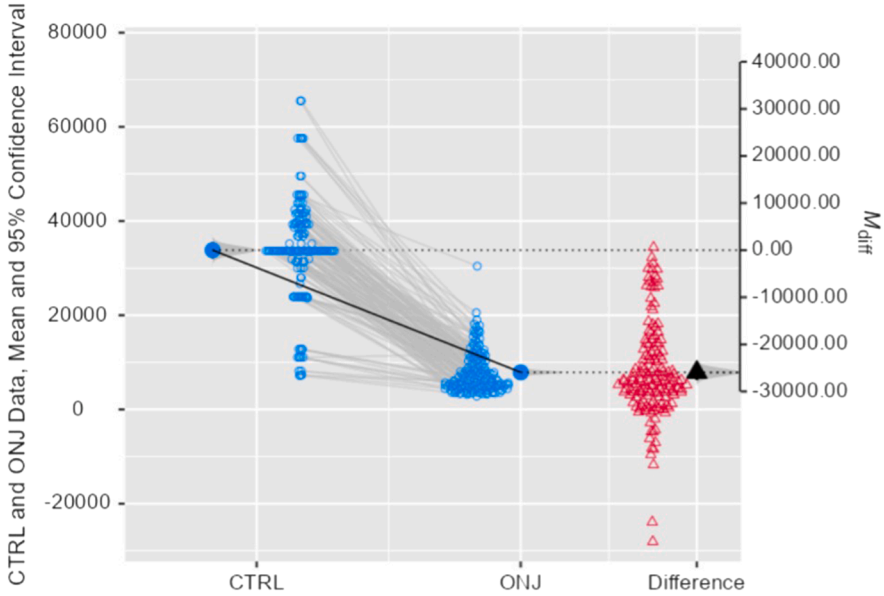

FIGURE 6. Paired analysis of photon counts in CTRL and ONJ groups for each sample, with the mean difference represented on the right. The consistent reduction in photon counts in ONJ samples confirms the statistically significant fluorescence loss.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

Table 3. DESCRIPTIVE STATISTICS AND ONE-SAMPLE TESTS FOR ONJ/CTRL AND CTRL/ONJ PHOTON COUNT RATIOS. BOTH RATIOS SIGNIFICANTLY DIFFERED FROM THE NULL HYPOTHESIS VALUE OF 1 ($P < .001$, FOR BOTH STUDENT'S *T* TEST AND WILCOXON W)

Ratio	n	Missing	Mean ± SD	Median [IQR]	*P* Value
ONJ/CTRL	146	5	0.257 ± 0.157	0.209 [0.198]	<.001*
					<.001†
CTRL/ONJ	146	5	5,232 ± 2.717	4,772 [4.081]	<.001*
					<.001†

Note. H_a μ ≠ 1.
* One samples *t* test: [1]Student's t, [2]Wilcoxon W.
† One samples *t* test: [1]Student's t, [2]Wilcoxon W.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

columns) were clearly above this line. Statistical testing confirmed a highly significant difference relative to 1 ($P < .001$).

ASSOCIATION BETWEEN AF INTENSITY AND HISTOLOGIC DIAGNOSIS

The mixed-effects logistic regression showed a clear inverse association between fluorescence intensity and tissue necrosis. As AF values increased, the probability of necrosis significantly decreased. The fixed-effect estimates were $\beta_0 = 3.99 \pm 0.41$ and $\beta_1 = -2.55 \pm 0.29$ (AF scaled by 10,000).

The corresponding odds ratio for necrosis was 0.08 (95% CI: 0.04-0.14), indicating that each 10,000-unit increase in AF reduced the likelihood of necrosis by about 92% ($P < .001$) (Table 4).

The fluorescence value corresponding to a predicted probability of necrosis of 0.5 was approximately 15,650 AF units (95% CI: 11,000-20,300). Using this threshold, the model achieved a sensitivity of 97.5%, a specificity of 87.5%, and an overall diagnostic accuracy of 92.5%.

Across all patients, fluorescence values were consistently higher in vital bone than in necrotic bone. The geometric mean ratio CTRL/ONJ was 4.53 (95% CI: 3.86-5.31), with a highly significant log-ratio test ($t = 19.1$, $df = 39$, $P \approx 2.2 \times 10^{-21}$). All patients showed ratios greater than 1, and 95% exceeded 3.4, confirming a marked and consistent fluorescence contrast between the 2 tissue types.

ANALYSIS OF FLUORESCENCE INTENSITY AS A FUNCTION OF OTHER DESCRIPTIVE VARIABLES

None of the general anamnestic and pharmacological variables (age, gender, smoking, diabetes, autoimmune, and corticosteroid and anticoagulant therapies) resulted statistically significant.

However, the most interesting variables to analyze with respect to the variation in fluorescence are the presence of oncological diseases and the medications taken that are related to the development of ONJ (ie bisphosphonates and other antiresorptive drugs).

Regarding the presence or absence of oncological diseases, no statistically significant variations were found with correlation to fluorescence alteration.

The mean LoFI ratio was 4.8 ± 2.39 in the cancer patient group and 6.3 ± 2.6 in the noncancer patient group. The difference was not statistically significant ($P = .8$) (Fig 9E, Table 5).

Subsequently, the possible influence of medications on fluorescence alteration was investigated.

In particular, the analysis was focused on those medications associated with the development of MRONJ, such as bisphosphonates and other antiresorptive and anti-neoangiogenic drugs.

Table 4. PAIRED COMPARISON OF AUTOFLUORESCENCE PHOTON COUNTS (500 NM) BETWEEN NECROTIC AND VITAL BONES, WITH *P* VALUES ADJUSTED FOR WITHIN-PATIENT CLUSTERING

	n	Mean ± SD	Median [IQR]	95% CI	*P* Value (Adjusted*)
Necrotic	40	7,886 ± 4,452	6,850 [4,120-10,200]	—	
Vital	40	33,825 ± 10791	31,500 [25,200-41,000]	—	<.001

* *P* value adjusted for multiple observations per subject (mixed-effects model).

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

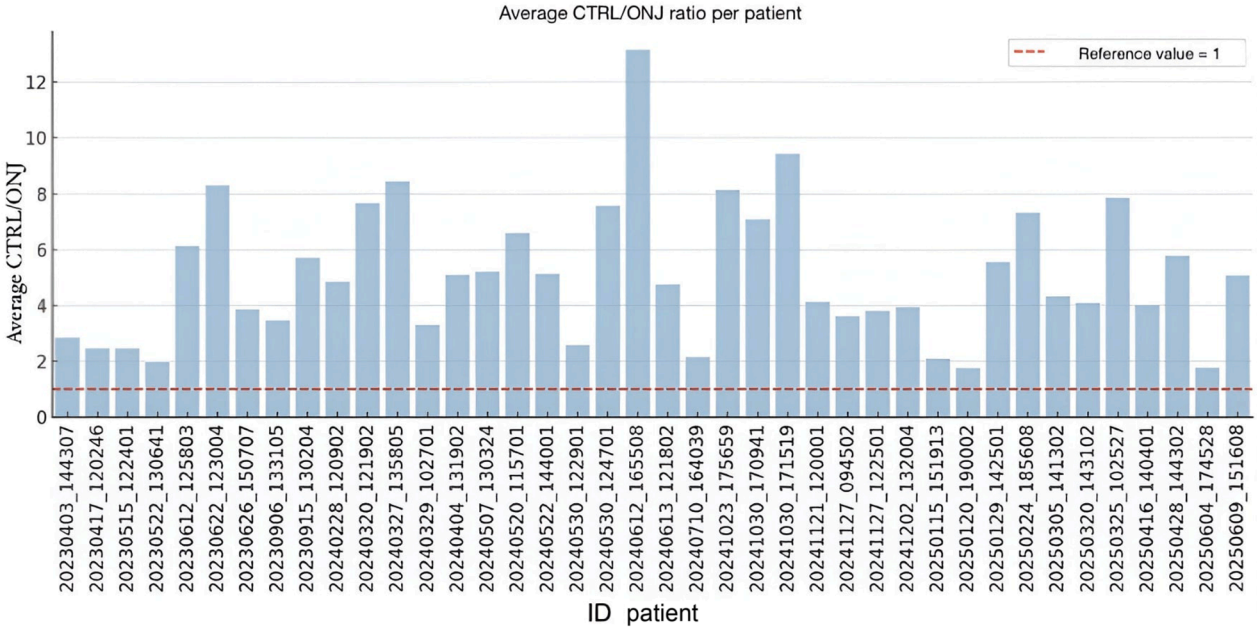

FIGURE 8. Mean fluorescence intensity ratios (CTRL/ONJ) calculated for each patient. All values are consistently above the reference line (LoFI = 1), indicating significantly higher fluorescence in healthy bone compared with necrotic bone.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

Statistical analysis exploring the influence of bisphosphonates and other antiresorptive and antineoangiogenic drugs on CTRL/ONJ fluorescence ratio (LoFI) shows that other antiresorptives have a statistically significant impact ($P = .004$).

The graph shown in Figure 10 shows that how the LoFI varies as a function of the intake of the investigated drugs.

The LoFI when taking both drugs is lowest (3.2: which means healthy bone fluorescence is 3 times greater than necrotic bone). This is followed by a LoFI of 4.1 if only the new antiresorptive drugs are taken, a LoFI of 5.6 if only bisphosphonates are taken, and a LoFI of 7.1 if neither bisphosphonates nor new antiresorptive drugs are taken.

This higher ratio of 7.1 in the case of no drug (neither bisphosphonates nor new antiresorptives) is justified not by a greater loss of fluorescence but by a higher starting value of healthy bone.

Specifically, the mean photon count in the control group was approximately 32,000 for both bisphosphonate (32,736 ± 13,115) and new antiresorptive therapy (32,047 ± 17,195). For those not taking any drugs, it was 41,515 ± 14,367. Looking instead at the photon

Table 5. DESCRIPTIVE STATISTICS FOR CTRL AND ONJ MEAN PHOTON COUNTS AND FOR THE CTRL/ONJ RATIO, STRATIFIED BY GROUP STATUS (NO VS YES). BETWEEN-GROUP COMPARISONS WERE PERFORMED ONLY FOR THE CTRL/ONJ RATIO USING INDEPENDENT SAMPLES *T* TESTS, WHICH SHOWED NO SIGNIFICANT DIFFERENCES ($P > .6$)

Mean Photon Counts	Group	N	Mean ± SD	Median [IQR]	*P*-value
CTRL mean photon counts	NO	8	34,364.2 ± 13,307.2	32,807.5 [5,560]	-
	YES	32	33,427.5 ± 12,475.8	33,680.1 [12,857]	-
ONJ mean photon counts	NO	8	6,172.7 ± 3,737.3	5,349.5 [1,491.5]	-
	YES	32	7,619.8 ± 3,112.8	7,336 [4,294]	-
CTRL/ONJ ratio mean photon counts	NO	8	6.32 ± 2.6	6.89 [3.74]	.812*
	YES	32	4.78 ± 2.39	4.22 [2.53]	.666†

Note. H_a $\mu_{NO} \neq \mu_{YES}$.
*Independent samples *t* test: [1]Student's t, [2]Mann-Whitney *U*.
†Independent samples *t* test: [1]Student's t, [2]Mann-Whitney *U*.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

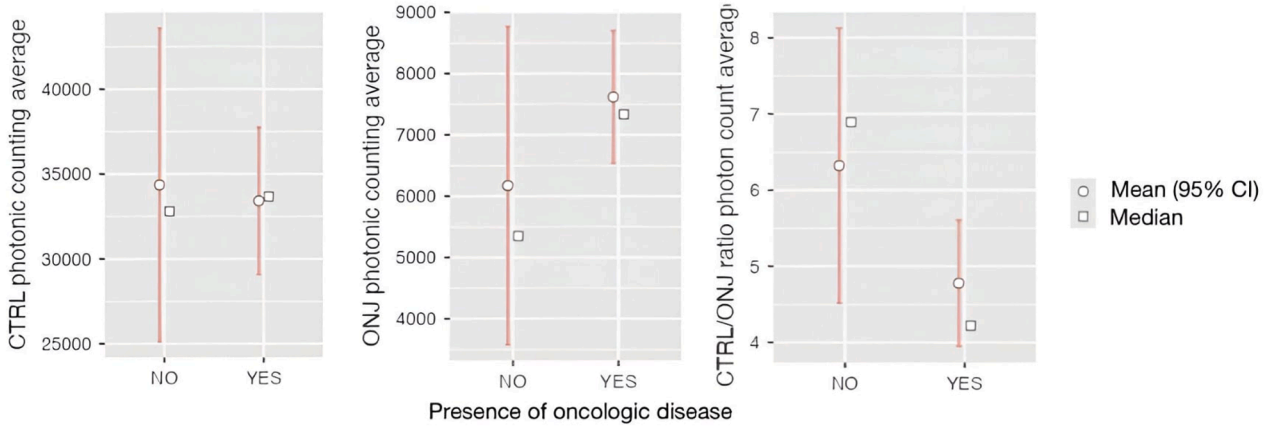

FIGURE 9. Photon counting averages in CTRL and ONJ groups, stratified by oncologic disease (left: CTRL, middle: ONJ, right: CTRL/ONJ ratio). Patients with oncologic disease showed a lower CTRL/ONJ ratio compared to nononcologic patients, suggesting an effect of cancer status on photon emission profiles. Data are shown as mean ± 95% CI (circles with error bars) and medians (squares).

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

count values in the necrotic areas, the mean values resulted higher in case of taking new antiresorptive drugs (9,621.9 ± 5,125.7 vs 6,292.3 ± 2,493.1).

Discussion

The purpose of this study was to determine the efficacy of a novel spectrophotometric system for quantitative assessment of bone AF, with the aim of providing an objective and reproducible method for distinguishing vital from necrotic bone tissue.

Validation of this tool would enable its intraoperative use for identifying surgical resection margins in osteonecrosis of the jaws. This represents a significant advancement in real-time delineation of surgical margins as it overcomes the limitations of qualitative evaluation of imaging.

Surgical treatment, in combination with medical therapy, has been shown to provide improved clinical outcomes in ONJ.[22-26]

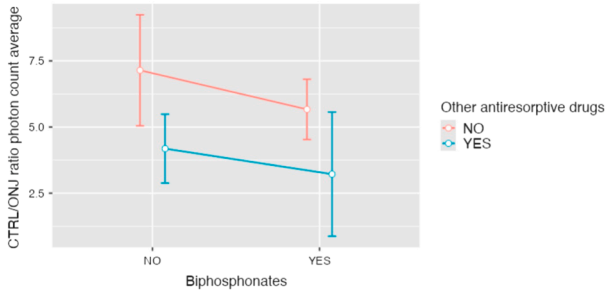

FIGURE 10. CTRL/ONJ photon count ratio according to bisphosphonate treatment and concomitant use of other antiresorptive drugs.

Giovannacci et al. Spectrophotometric Autofluorescence Assessment in Jaw Osteonecrosis. J Oral Maxillofac Surg 2026.

Er:YAG laser-assisted surgery has shown some advantages over conventional surgical techniques. These advantages are due to tissue biomodulation, bactericidal actions, and the creation of a more favorable surface for tissue adhesion through microcavities. Furthermore, Er:YAG laser-assisted surgery allows precise and minimally invasive bone vaporization, which is essential to remove all necrotic bones while at the same time preserving most bone volume possible according to the extent of the disease.[19,21]

As long as surgery needs to be as conservative as possible and ONJ has a certain recurrence rate (up to 45% when no direct closure of surgical site is performed[27]), it results essential to find and test a method for clearly identifying safe surgical margins.

In addition to the surgeon's clinical experience, the preoperative radiographic examinations are available as a guide. Computed tomography remains the gold standard for bone imaging, but it often has difficulty distinguishing healthy bone from necrotic areas in regions with extensive fibrosis, reduced vascularity, or irregular bone architecture.[28] In particular, it tends to overestimate the extent of the alteration, as it visualizes areas altered by antiresorptive drugs, but not necrotic areas.

Conventional intraoperative indicators of bone vitality, such as vascularization, texture, and color, do not always correlated with true bone vitality.[16,17]

To overcome these limitations, real-time technologies for accurately identifying the margins of necrotic tissue could revolutionize surgical outcomes, minimizing recurrence and the need for secondary interventions, and ensuring curative yet conservative interventions, resulting in a better quality of life.

For several years, fluorescence-based techniques, such as those employing the VELscope system (LED

Dental, White Rock, BC, Canada), have demonstrated the clinical potential of bone AF to differentiate necrotic from vital tissue during ONJ surgery.[16-19]

The VELscope device emits blue-violet light (400-460 nm), which excites the natural AF of vital bone. Under this illumination, healthy bone appears bright green, whereas necrotic bone remains dark, enabling clear distinction between viable and nonviable tissues.

A systematic review published by Dipalma et al investigated the efficacy of AF-guided MRONJ resection surgery.[29] From their analysis, the authors highlighted the strong ability of the VELscope system to provide physicians with real-time, high-contrast images, thus revolutionizing the management of MRONJ.

This efficacy is also confirmed by a large case series published by the authors in which fluorescence of 56 bone samples is histopathologically correlated. This study showed that 100% of the hypo-fluorescent samples were necrotic bone, and 86% of the hyper-fluorescent samples were vital bone.[30]

However, this system relies on a qualitative visual assessment that remains dependent on the operator's perception.

The spectrophotometric system tested in this study addresses this limitation by providing numerical fluorescence data and allowing precise, reproducible quantification of AF in real time. It consisted of an optical fiber capable of emitting a wavelength perfectly suitable to stimulate the fluorophores of bone tissue, a fiber capable of collecting the emitted fluorescence, filtering it, and passing it to a spectrophotometer that measures the emission spectrum of the tested tissue. In this way, the information that emerges from the spectrophotometer measurements, processed by a specific SW, comes out in a numerical, irrefutable way and does not need to be submitted to the surgeon's impression.

The same setup was used to measure the intensity of fluorescence emitted by the dermis in nonmelanoma skin cancer, and it proved to be perfectly able to distinguish the measurement of AF intensity in diseased areas compared to healthy skin (difference between healthy skin/diseased skin: 4).[31]

The primary endpoint was to evaluate the effectiveness of this system to measure fluorescence intensity in quantitatively way. The null hypothesis was that pathological bone and surrounding healthy bone showed the same level of fluorescence (LoFI ratio of 1). The present study largely refutes the null hypothesis and demonstrates that on average, surrounding healthy tissue emits a fluorescence intensity five times higher than necrotic tissue. This result could be explained by principle that healthy and normally structured bone tissue contains natural fluorophores, mainly collagen, which emits fluorescence when excited by specific wavelengths. In the presence of necrosis, the degradation of collagen leads to a marked loss or absence of fluorescence.

In addition to collagen-related AF, spectral analysis of several necrotic points revealed distinct emission peaks at 630-650 and 700 nm (Fig 3D and Fig 4G). These wavelengths correspond to the emission of porphyrins, which are bacterial metabolism products and fluorophores that emit in the red spectrum. This emission in the red range could contribute to perceiving the color of porphyrins as red or orange, depending on the concentration and observation conditions.

Kim et al reported similar findings using a quantitative light-induced fluorescence (QLF) system (QLF-D Biluminator; Inspektor Research Systems BV, Amsterdam, Netherlands), which employed a violet-blue LED light at 405 nm and a pink filter to emphasize the 630-640 nm band.[32] Their study identified 3 fluorescence patterns, nonred, hypo-red, and hyper-red, corresponding to different degrees of bacterial involvement.

Histology confirmed that hyper-red fluorescent areas were associated with *Actinomyces* colony and osteolysis, supporting the link between red fluorescence and infection.

The secondary endpoints of the study were to evaluate any variations in fluorescence intensity as a function of other variables. The most important consideration is that in any case, the fluorescence intensity between healthy and necrotic bones is statistically significantly different.

The only statistically significant variable resulting from multivariate analysis was the assumption of antiresorptive drugs (not bisphosphonates) and antineoangiogenic medications. Other general variables (such as age, sex, and smoking), pathologies (such as diabetes, autoimmune, and oncological diseases), and drugs (corticosteroids, anticoagulants) don't seem to have an impact on the variation in fluorescence.

Analyzing the mean photon count of healthy (nonnecrotic) control bone was found to have comparable values both in the group of patients taking bisphosphonates and in the group of patients taking the new antiresorptive/antineoangiogenic drugs. However, the group of patients not taking either of these drugs appeared to have a photon count in their healthy bone that was on average 10,000 photons higher than that of those taking the drugs.

Future studies analyzing the fluorescence of a large series of normally structured and vital bones (even in patients not affected by ONJ) will be needed to verify whether this difference exists and is not a coincidence.

Furthermore, analyzing the average photon count of the necrotic samples, it is evident that if the new antiresorptive/anti-neoangiogenic drugs are taken,

necrotic areas have higher values than those taking bisphosphonates or neither. From our data, it appears that patients taking bisphosphonates have lower fluorescence intensity values than those taking other drugs.

This result will need to be investigated with further studies that consider all pharmacological variables such as dosage, route of administration, and number of doses taken.

Similarly, for necrosis caused by radiotherapy, it would be necessary to investigate any variations in fluorescence intensity as a function of irradiation dose, exposure time, and other specific variables.

In general, regardless of the influence of drugs or not, the important demonstrated endpoint is that in any case, the difference between necrotic and vital bones is statistically significantly detectable using this spectrophotometric examination.

One limitation of the study is that a small subset of samples (7.5%) was histologically classified as vital bone with sclerotic changes consistent with prior bisphosphonate therapy. These specimens exhibited unexpectedly high fluorescence intensity, attributable to the dense mineralization and compact microarchitecture characteristic of osteosclerotic bone. Osteosclerosis involves morphological thickening of trabeculae, reduction of medullary spaces, and increased osteoblastic activity, often accompanied by aberrant mineral deposition.[33] These changes are not only structural but also biochemical, leading to the accumulation of autofluorescent molecules within the bone matrix, such as cross-linked collagen and advanced glycation end products (AGEs).[34] This biochemical profile contributes to the increased fluorescence signal observed during spectrophotometric analysis.

Importantly, despite these sclerotic changes, these specimens were confirmed histologically as vital bone and photon counts of the surrounding necrotic bone, yielding significantly different results.

This study represents the first phase of a larger research project whose aim is to use the spectrophotometer intraoperatively to guide the surgeon in choosing resection margins.

In this study, we validated the setup under controlled ex vivo conditions. The next step will be to test the device in vivo during surgical procedures, with the aim of confirming its diagnostic accuracy and evaluating its usability in real time.

Further studies will need to be carried out to confirm these data and carefully analyze the potential variables influencing the photon count.

References

1. Ruggiero SL, Dodson TB, Aghaloo T, Carlson ER, Ward BB, Kademani D. American Association of oral and maxillofacial surgeons' position paper on medication-related osteonecrosis of the jaws-2022 update. J Oral Maxillofac Surg 80:920–943, 2022
2. Campisi G, Mauceri R, Bertoldo F, et al. Medication-Related Osteonecrosis of Jaws (MRONJ) prevention and diagnosis: Italian consensus update 2020. Int J Environ Res Public Health 17:1–15, 2020
3. Zadik Y, Ganor Y, Rimon O, Bersudski E, Meirovitz A. Assessment of jaw osteonecrosis diagnostic criteria in cancer patients with a history of radiation therapy and exposure to bone-modifying agents. Radiother Oncol 156:275–280, 2021
4. Vescovi P, Manfredi M, Merigo E, et al. Surgical approach with Er:YAG laser on Osteonecrosis of the Jaws (ONJ) in patients under bisphosphonate therapy. Lasers Med Sci 25:101–113, 2010
5. On SW, Cho SW, Byun SH, Yang BE. Various therapeutic methods for the treatment of Medication-Related Osteonecrosis of the Jaw (MRONJ) and their limitations: A narrative review on new molecular and cellular therapeutic approaches. Antioxidants (Basel) 10:680, 2021
6. Pourzarandian A, Watanabe H, Aoki A, et al. Histological and TEM examination of early stages of bone healing after Er:YAG laser irradiation. Photomed Laser Surg 22:342–350, 2004
7. Dai X, Yang B, Zhou L, et al. Label-free rapid diagnosis of jaw osteonecrosis via the intersection of Raman spectroscopy and deep learning. Bone 197:117510, 2025
8. Mücke T, Koschinski J, Deppe H, et al. Outcome of treatment and parameters influencing recurrence in patients with bisphosphonate-related osteonecrosis of the jaws. J Craniomaxillofac Surg 44:1694–1699, 2016
9. Wichelmann TA, Ahdi HS, Pandravada S, Ehrenpreis ED. A Summary of the rare reports of osteonecrosis of the jaw associated with tumor necrosis-α inhibitors in the United States Food and Drug Administration's adverse event reporting system database. J Oral Maxillofac Surg 81:1311–1318, 2023
10. El-Rabbany M, Duchnay M, Raziee HR, et al. Interventions for preventing osteoradionecrosis of the jaws in adults receiving head and neck radiotherapy. Cochrane Database Syst Rev 12: CD011559, 2019
11. Beth-Tasdogan NH, Mayer B, Hussein H, Zolk O, Peter JU. Interventions for managing medication-related osteonecrosis of the jaw. Cochrane Database Syst Rev 7:CD012432, 2022
12. Varoni EM, Lombardi N, Villa G, Pispero A, Sardella A, Lodi G. Conservative management of Medication-Related Osteonecrosis of the Jaws (MRONJ): A retrospective cohort study. Antibiotics (Basel) 10:195, 2021
13. Treister NS, Brennan MT, Sollecito TP, et al. Exposed bone in patients with head and neck cancer treated with radiation therapy: An analysis of the Observational Study of Dental Outcomes in Head and Neck Cancer Patients (OraRad). Cancer 128:487–496, 2022
14. Bedogni A, Mauceri R, Fusco V, et al. Italian position paper (SIPMO-SICMF) on Medication-Related Osteonecrosis of the Jaw (MRONJ). Oral Dis 30:3679–3709, 2024
15. Khan AA, Morrison A, Hanley DA, et al. Diagnosis and management of osteonecrosis of the jaw: A systematic review and international consensus. J Bone Miner Res 30:3–23, 2015
16. Giovannacci I, Meleti M, Corradi D, Vescovi P. Clinical differences in autofluorescence between viable and nonvital bone: A case report with histopathologic evaluation performed on medication-related osteonecrosis of the jaws. J Oral Maxillofac Surg 75:1216–1222, 2017
17. Ristow O, Pautke C. Auto-fluorescence of the bone and its use for delineation of bone necrosis. Int J Oral Maxillofac Surg 43: 1391–1393, 2014
18. Ristow O, Otto S, Geiß C, et al. Comparison of auto-fluorescence and tetracycline fluorescence for guided bone surgery of medication-related osteonecrosis of the jaw: A randomized controlled feasibility study. Int J Oral Maxillofac Surg 46:157–166, 2016
19. Vescovi P, Giovannacci I, Otto S, et al. Medication-related osteonecrosis of the jaw: An autofluorescence-guided surgical approach performed with Er:YAG laser. Photomed Laser Surg 33:437–442, 2015
20. Franzen S, Boxer S. On the origin of heme absorption band shifts and associated protein structural relaxation in myoglobin following flash photolysis. J Biol Chem 272:9655–9660, 1997
21. Vescovi P, De Francesco P, Giovannacci I, Leão JC, Barone A. Piezoelectric surgery, Er:YAG laser surgery and Nd:YAG laser

photobiomodulation: A combined approach to treat Medication-Related Osteonecrosis of the Jaws (MRONJ). Dent J (Basel) 12: 261, 2024
22. Kim HY, Lee SJ, Kim SM, et al. Extensive surgical procedures result in better treatment outcomes for bisphosphonate-related osteonecrosis of the jaw in patients with osteoporosis. J Oral Maxillofac Surg 75:1404–1413, 2017
23. Di Fede O, Canepa F, Panzarella V, et al. The treatment of Medication-Related Osteonecrosis of the Jaw (MRONJ): A systematic review with a pooled analysis of only surgery versus combined protocols. Int J Environ Res Public Health 18:8432, 2021
24. Fliefel R, Tröltzsch M, Kühnisch J, Ehrenfeld M, Otto S. Treatment strategies and outcomes of Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ) with characterization of patients: A systematic review. Int J Oral Maxillofac Surg 44: 568–585, 2015
25. Vescovi P, Merigo E, Meleti M, Manfredi M, Fornaini C, Nammour S. Clinical study surgical approach and laser applications in BRONJ osteoporotic and cancer patients. J Osteoporos 2012:585434, 2012
26. Camolesi GC, Ortega KL, Medina JB, et al. Therapeutic alternatives in the management of osteoradionecrosis of the jaws: Systematic review. Med Oral Patol Oral Cir Bucal 26:e195–e207, 2021
27. Kang MH, Lee DK, Kim CW, Song IS, Jun SH. Clinical characteristics and recurrence-related factors of medication-related osteonecrosis of the jaw. J Korean Assoc Oral Maxillofac Surg 44:225–231, 2018
28. Chronopoulos A, Zarra T, Ehrenfeld M, Otto S. Osteoradionecrosis of the jaws: Definition,epidemiology, staging and clinical and radiological findings. A concise review. Int Dent J 68:22–30, 2018
29. Dipalma G, Inchingolo AD, Piras F, et al. Efficacy of guided autofluorescence laser therapy in MRONJ: A systematic review. Eur Rev Med Pharmacol Sci 27:11817–11831, 2023
30. Giovannacci I, Venuti AA, Corcione L, Nammour S, Vescovi P. Autofluorescence-guided surgery in the management of osteonecrosis of the jaw: Correlation between bone autofluorescence and histopathological findings in 56 samples. Life (Basel) 15:686, 2025
31. Giovannacci I, Meleti M, Garbarino F, et al. Correlation between autofluorescence intensity and histopathological features in non-melanoma skin cancer: An ex vivo study. Cancers (Basel) 13:3974, 2021
32. Kim Y, Jung HI, Kim YK, Ku JK. Histologic analysis of osteonecrosis of the jaw according to the different aspects on quantitative light-induced fluorescence images. Photodiagnosis Photodyn Ther 34:102212, 2021
33. Blaquière RM, Guyer PB, Buchanan RB, Gallagher PJ. Sclerotic bone deposits in multiple myeloma. Br J Radiol 55:591–593, 1982
34. Vaidya R, Rezaee T, Edwards T, et al. Accumulation of fluorescent advanced glycation end products and carboxymethyl-lysine in human cortical and trabecular bone. Bone Rep 17:101634, 2022