

DESIGN OF AN OSTEONECROSIS EXPERIMENTAL MODEL IN RATS. A HISTOMORPHOMETRIC STUDY

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INTRODUCTION

Medication-related osteonecrosis of the jaw (MRONJ) is a non-resolving lesion developing in the maxillary bones, that persists for more than 8 weeks. It is common in patients receiving antiresorptive and oncologic medications such as bisphosphonates, denosumab and antiangiogenic drugs. So far, there is no effective treatment for its resolution.

OBJECTIVE

The aim of this work was to develop and characterize an experimental model of mandibular osteonecrosis in rats, triggered by injection of zoledronic acid (ZA) and tooth-extraction, in order to evaluate the effects of melatonin as a therapeutic agent in future studies

METHODOLOGY

- ✓ 8 Female wistar rats: 6 animals received a weekly injection of 50µg/kg bw of zoledronic acid : ZA Group, for 60 days.
- ✓ Control Group (CT, n=2) received saline solution.
- ✓ On day 30 after starting treatment, extraction of the first lower molars, were done. (Figure 1).
- ✓ After euthanasia mandibles were dissected, photographed, radiographed (Figure 2 & 3) and histologically processed.
- ✓ Bucco-lingual sections at level of the mesial alveolus stained with hematoxylin/eosin.
- ✓ Histopathological analysis was performed and histomorphometry was carried out (Figure 4) , taking 10 fields in the post-extraction alveolar bone (PAB) and 10 fields in the cortical basal bone (CBB) to determine osteonecrosis foci (bone áreas with empty osteocytic-lacunae). Data were statistically analyzed (T-Student's test)

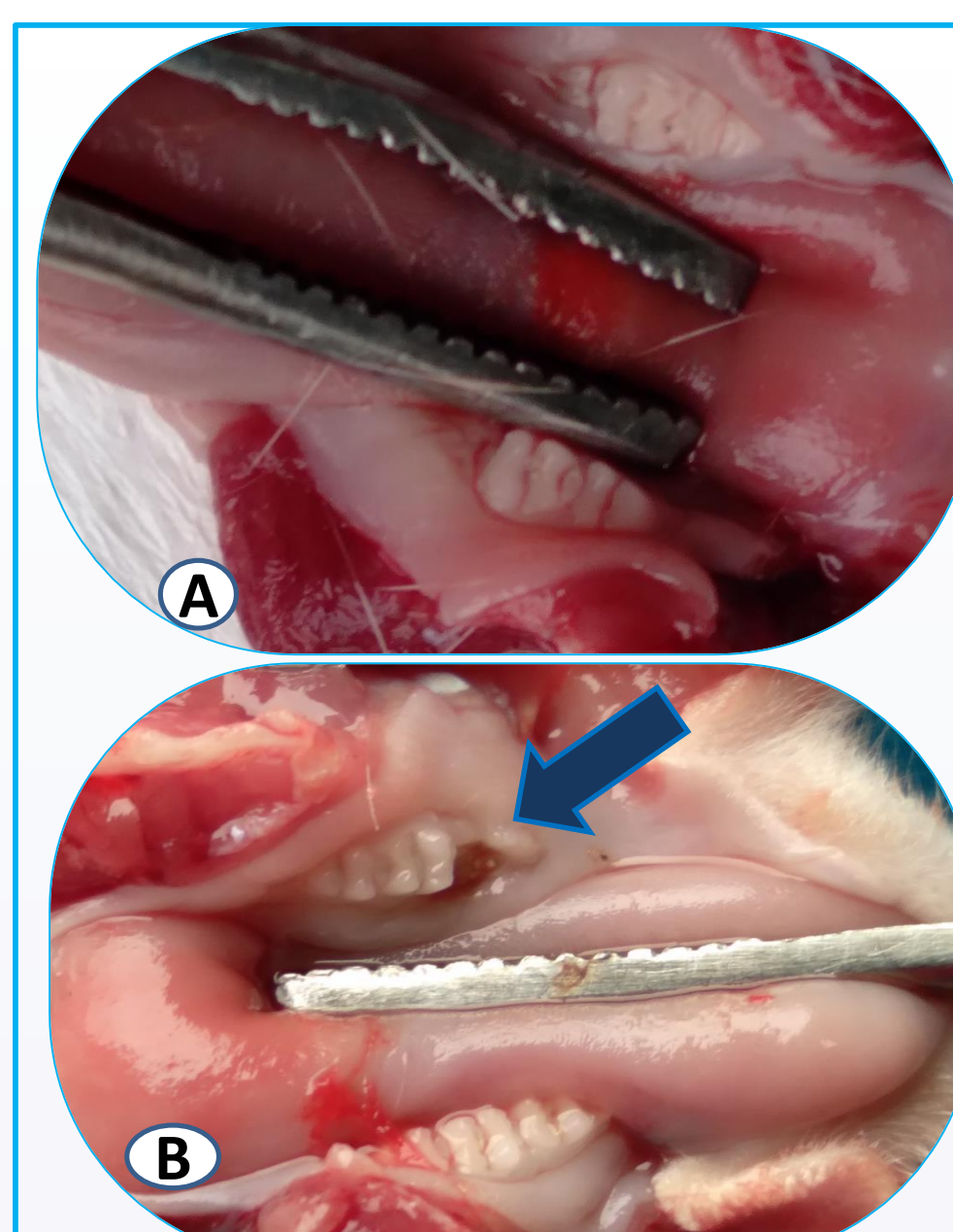
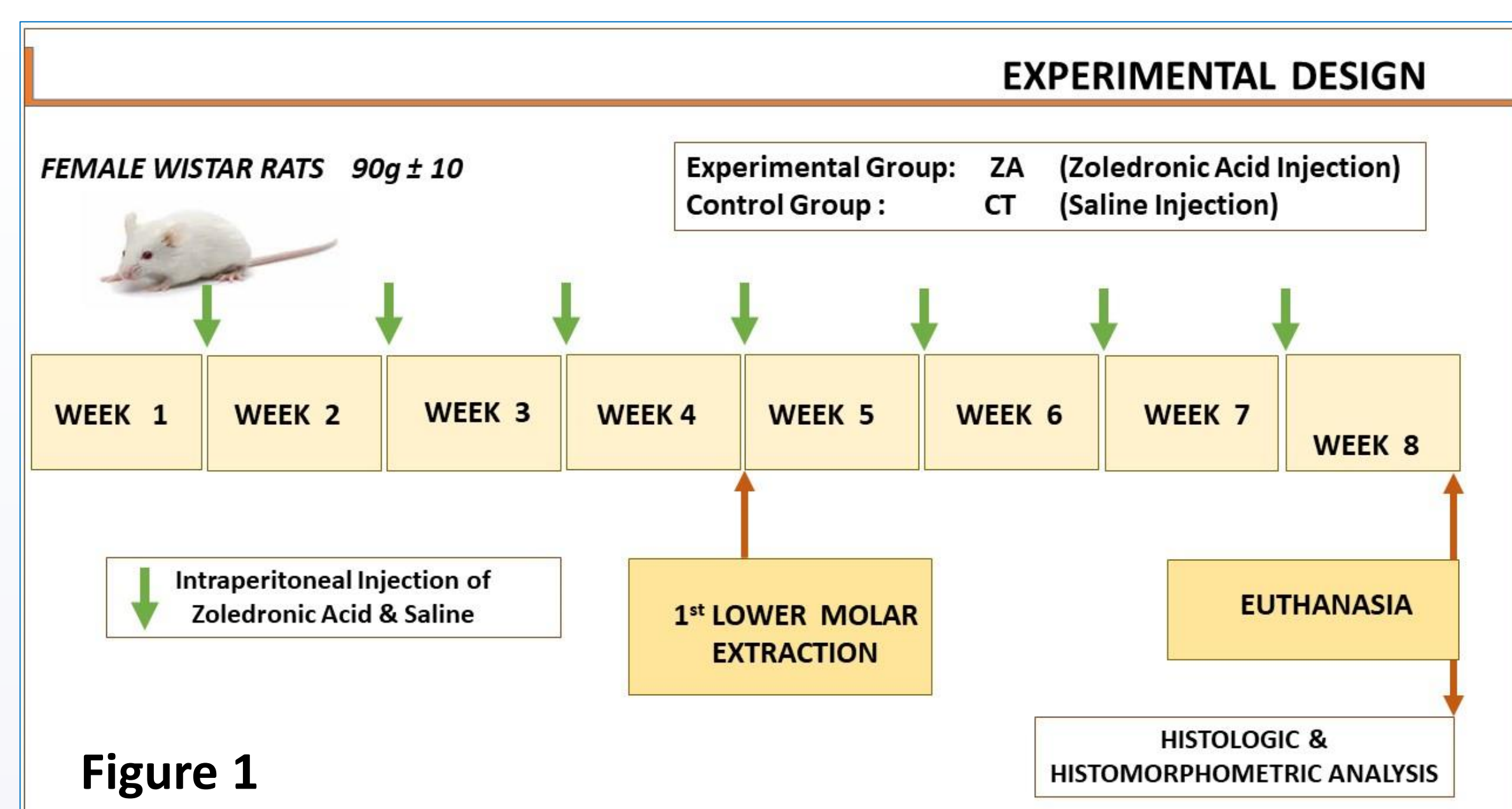


Figure 2: Macroscopic view of biopsies: In A, a CT case with normal healing of de alveoli. In B a mucosal lesion with exposed bone (blue arrow).

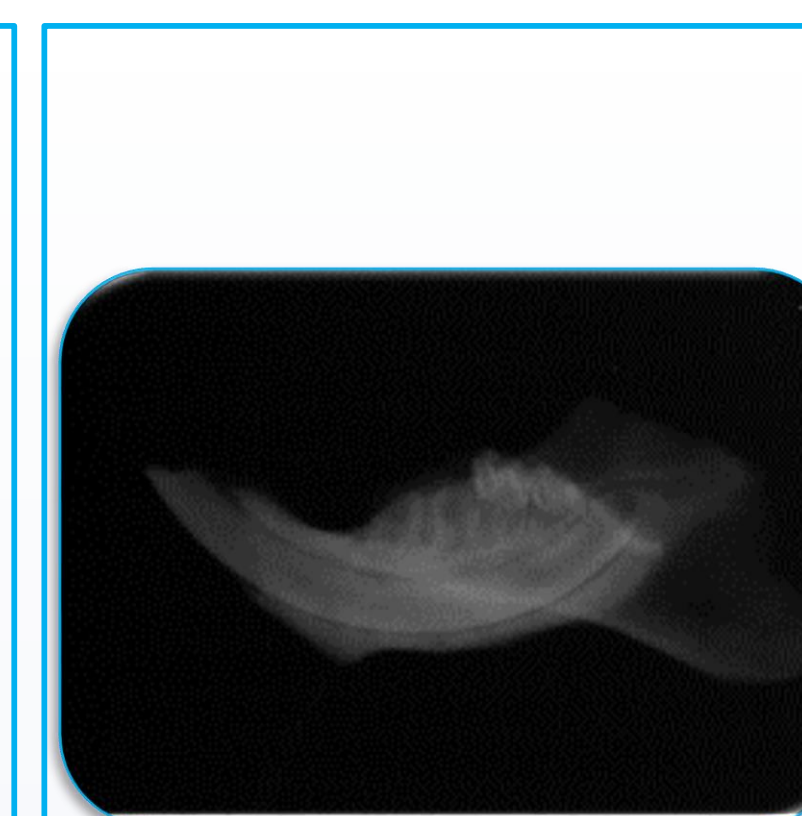


Figure 3: X-ray captured by a Sirona XIOS Plus Sensor (AZ Group).



Figure 4: Histomorphometric measures by Image Pro-Plus.

RESULTS

- ✓ Histological analysis (Fig.5-8) showed that PAB in the ZA group presented thickened trabeculae, reduced marrow-spaces and irregular bone formation, with a mosaic pattern. This was not observed in CT

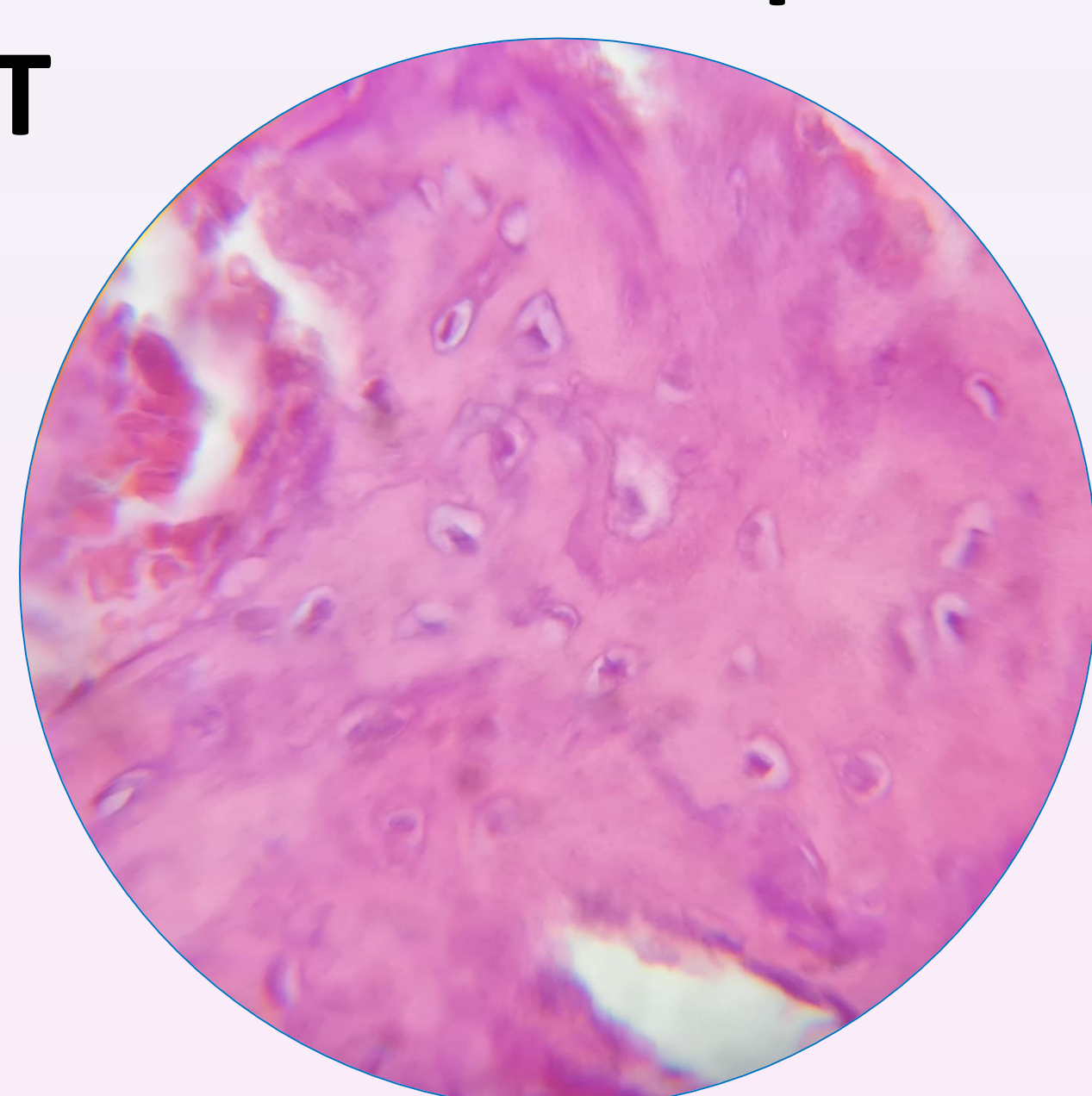


FIGURE 5: POST-EXTRACTION ALVEOLAR BONE IN CT GROUP

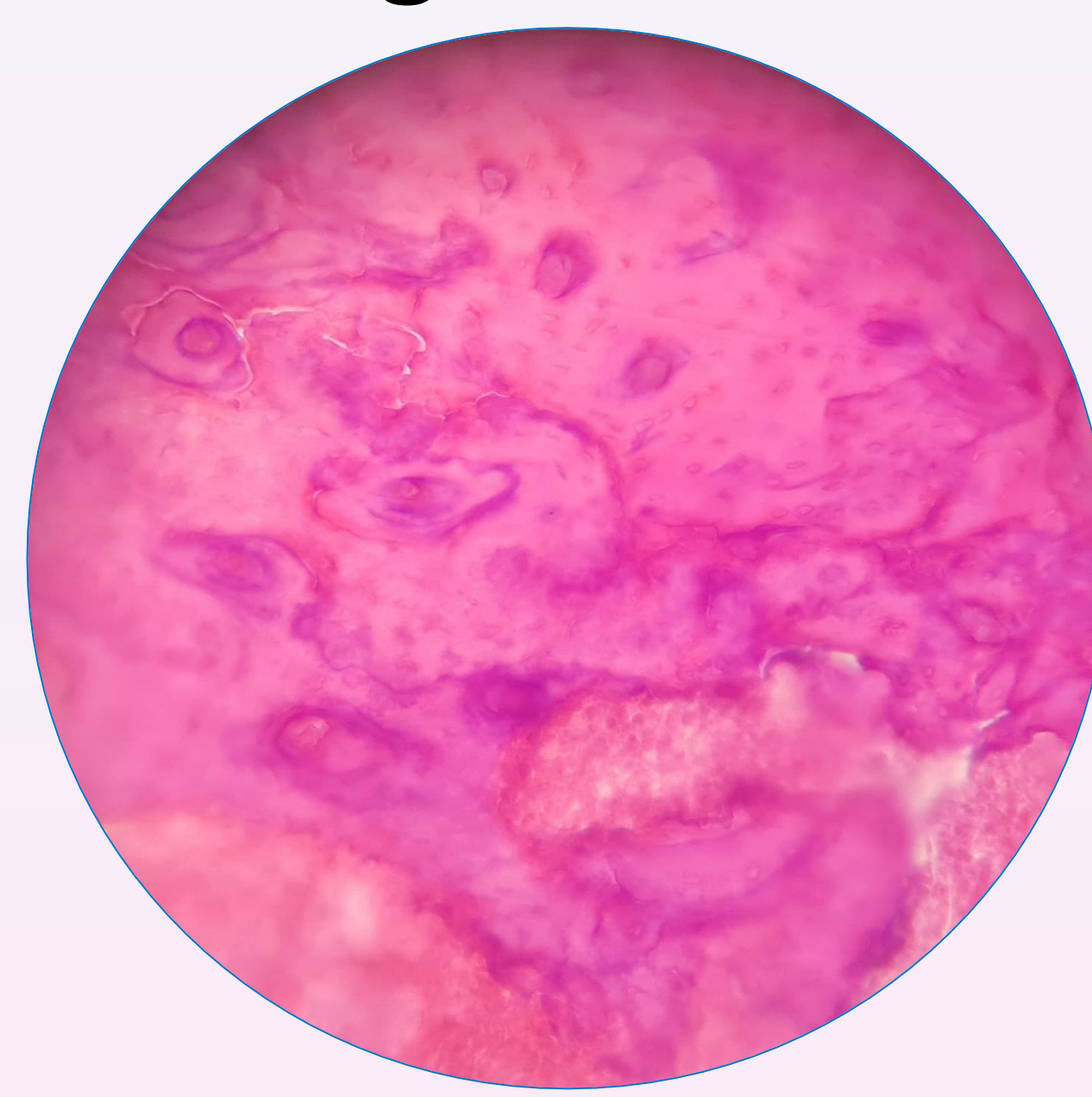


FIGURE 6: POST-EXTRACTION ALVEOLAR BONE IN ZA GROUP

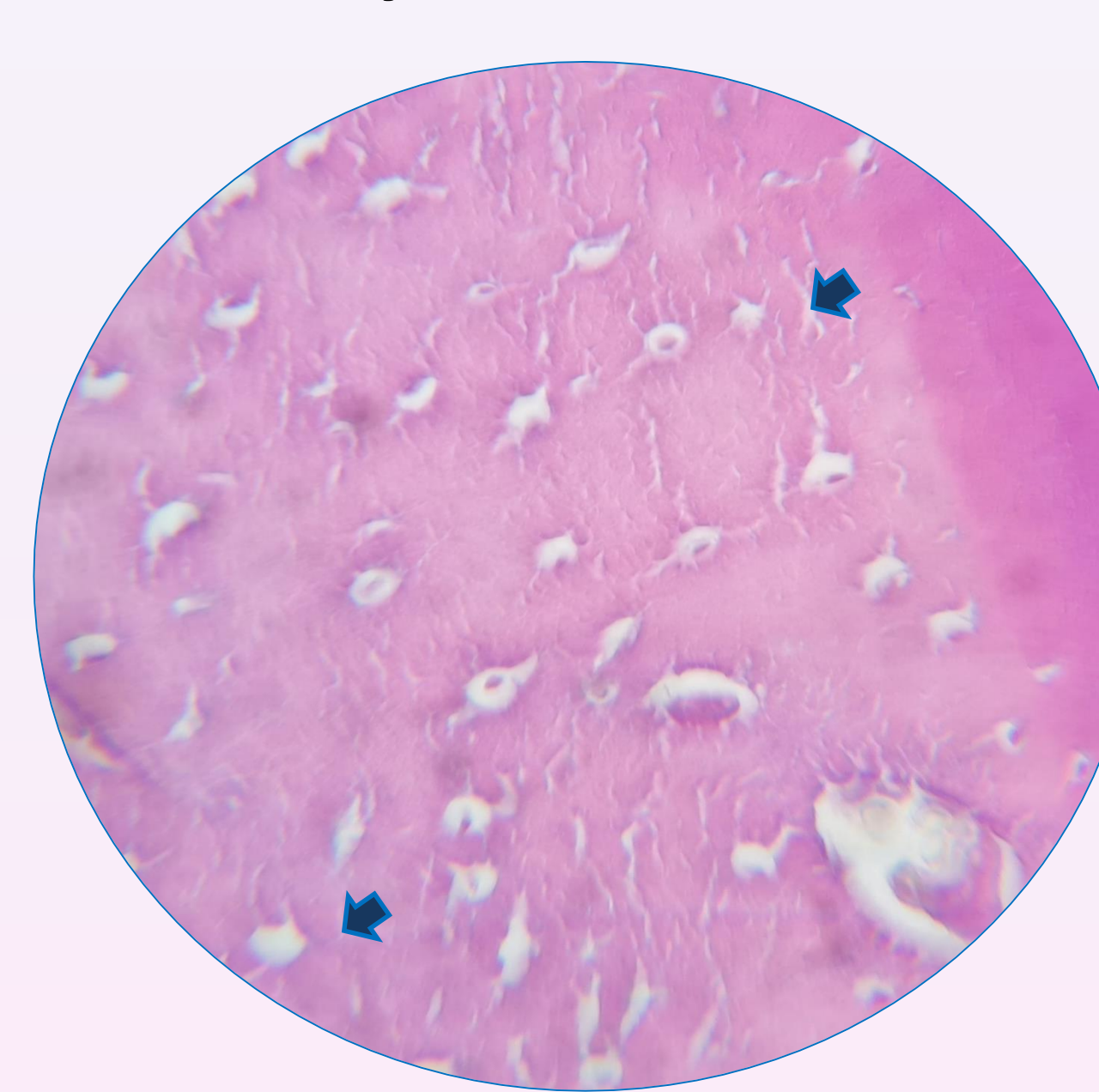


FIGURE 7: CORTICAL BASAL BONE IN ZA GROUP (H/E x 40)

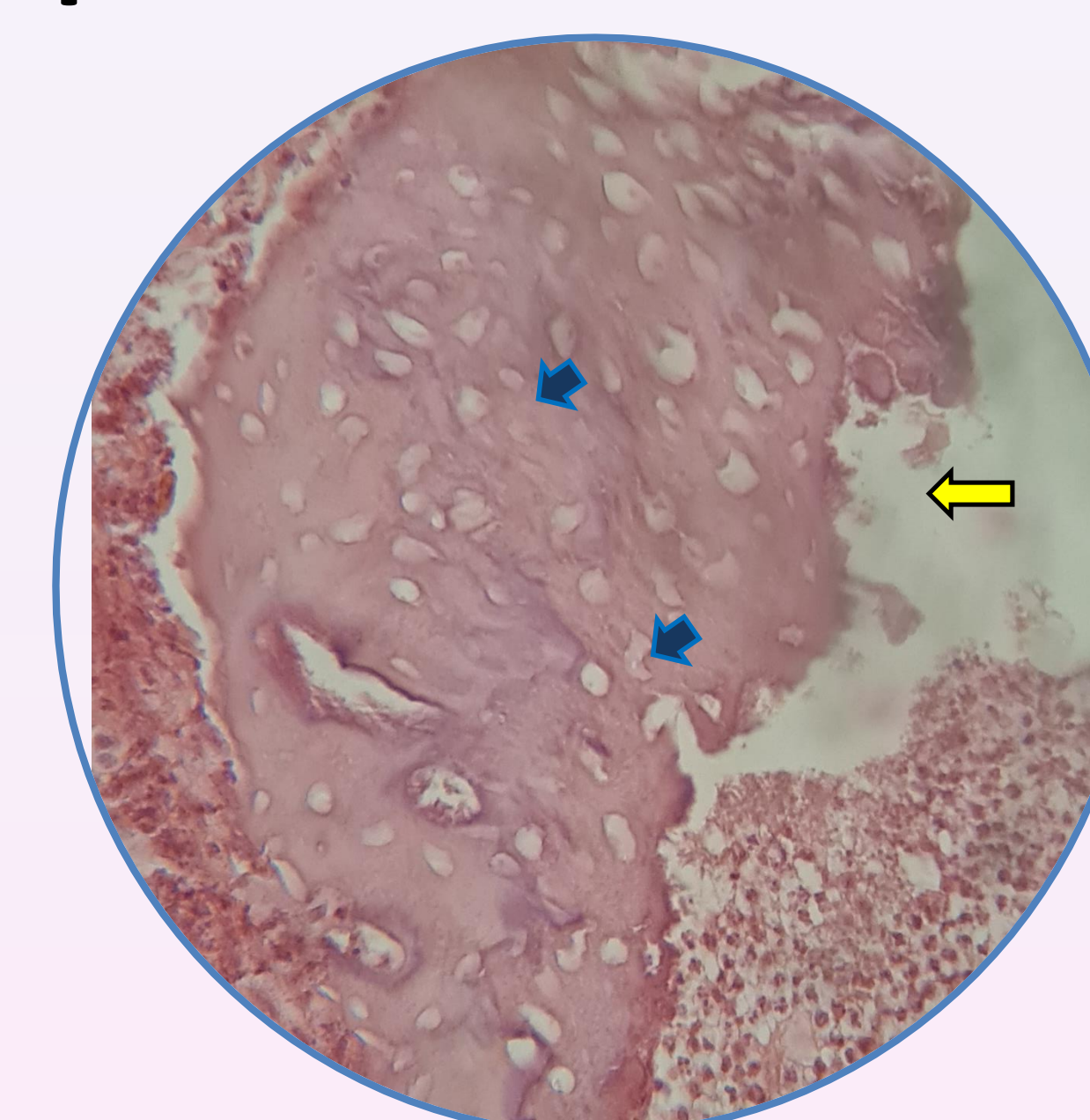


FIGURE 8: FOCI OF OSTEONECROSIS (↑) IN POST EXTRACTION ALVEOLAR BONE OF ZA GROUP. EOL (↑) (H/E x 40)

- ✓ Histomorphometry of PAB of ZA group, clearly indicated a significant decrease in the number of osteocytic lacunae (OL), and an increased percentage of empty OL (% EOL), related to CBB-ZA and CT, (Table 1).

	ZA Group		CT Group
	PBA zone	CBB zone	
NUMBER OF OSTEOCITIC LACUNAE (OL)	83 ± 19*	178 ± 22	232 ± 11
PERCENTAGE OF EMPTY OSTEOCITIC LACUNAE (%EOL)	23.77 % ± 8,32 %*	3.97 % ± 072 %	0.23 % ± 0.1 %

TABLE 1: OL and EOL values, expressed as median ± standard deviation.

CONCLUSIONS

This findings suggest that ZA can lead a delay in the repair, and bone-architecture changes. This osteonecrosis experimental model could be valid for the studying of new therapeutic options, such as the application of melatonin, in further studies.



REFERENCES & Authors' Contacts