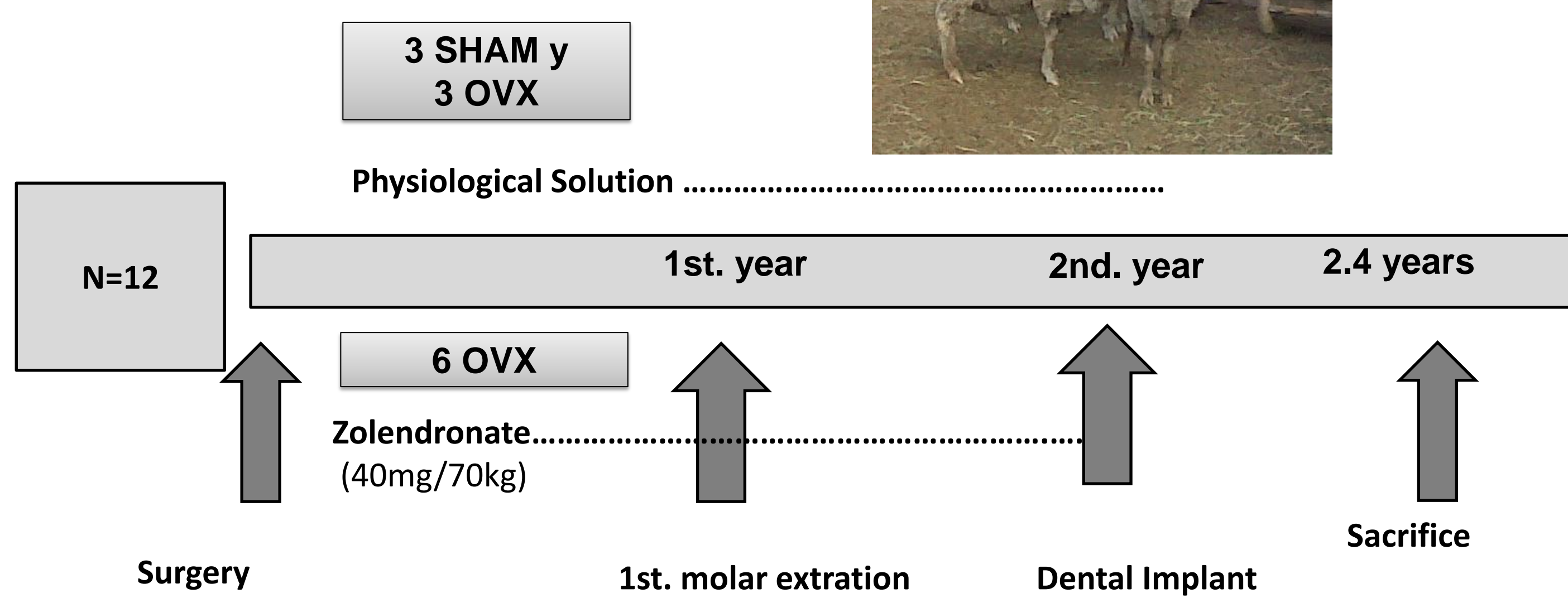


**Introduction:** ONJ has emerged as a complication of bisphosphonate (BPs) treatment. The most powerful induce a strong reduction in bone remodeling after several years of treatment. Female ewes could be a useful experimental model because, besides endocrine similarities, it is possible to do oral cavity interventions.

**Objective:** to evaluate: 1) the effect of high doses of ZOL (equivalent to cancer treatment) on bone remodeling and maxillary bone mass in OVX ewes; 2) the possible development of ONJBPs after dental interventions.

## Materials and methods:

Experimental design:



## Animals and experimental design:

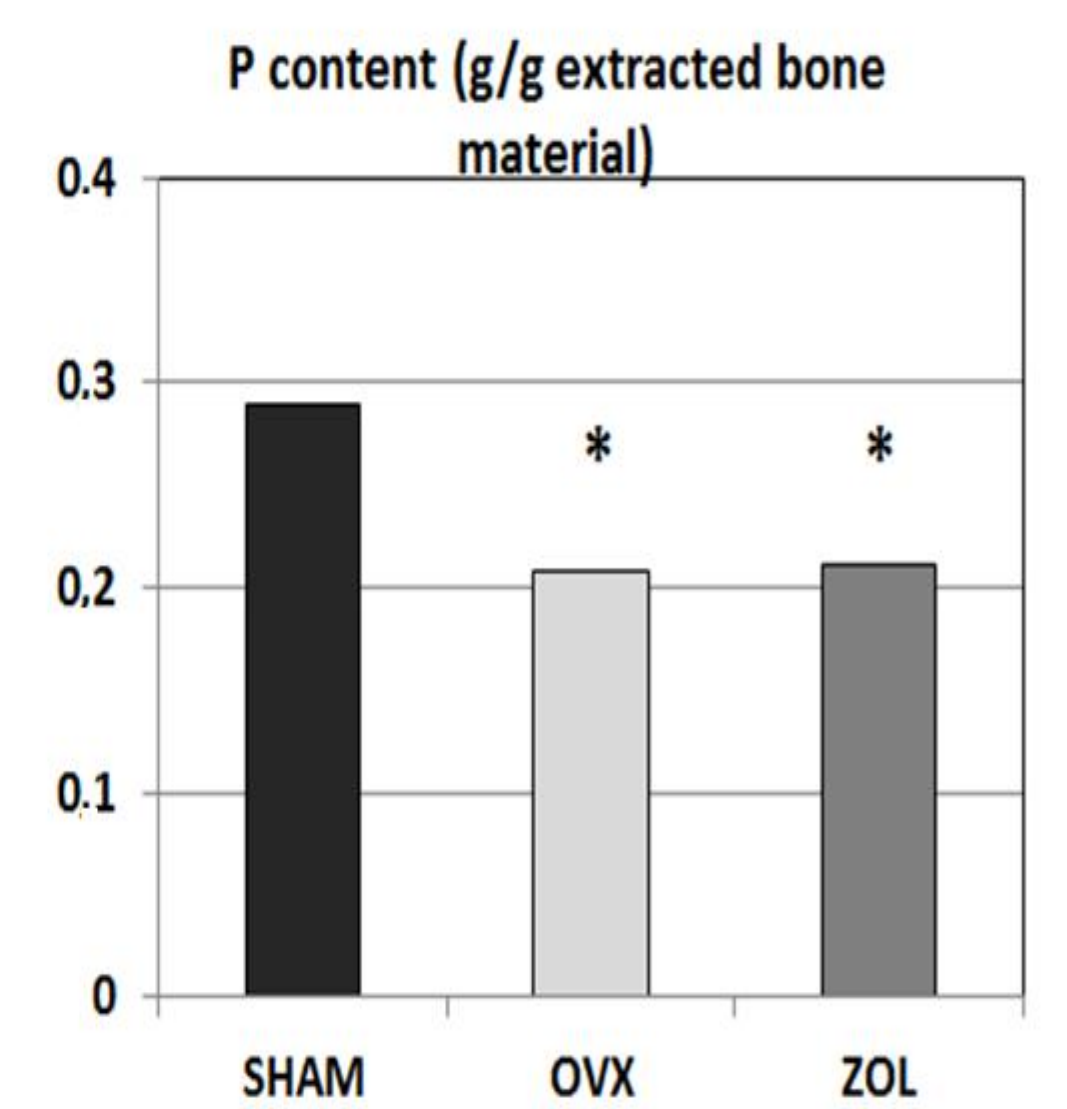
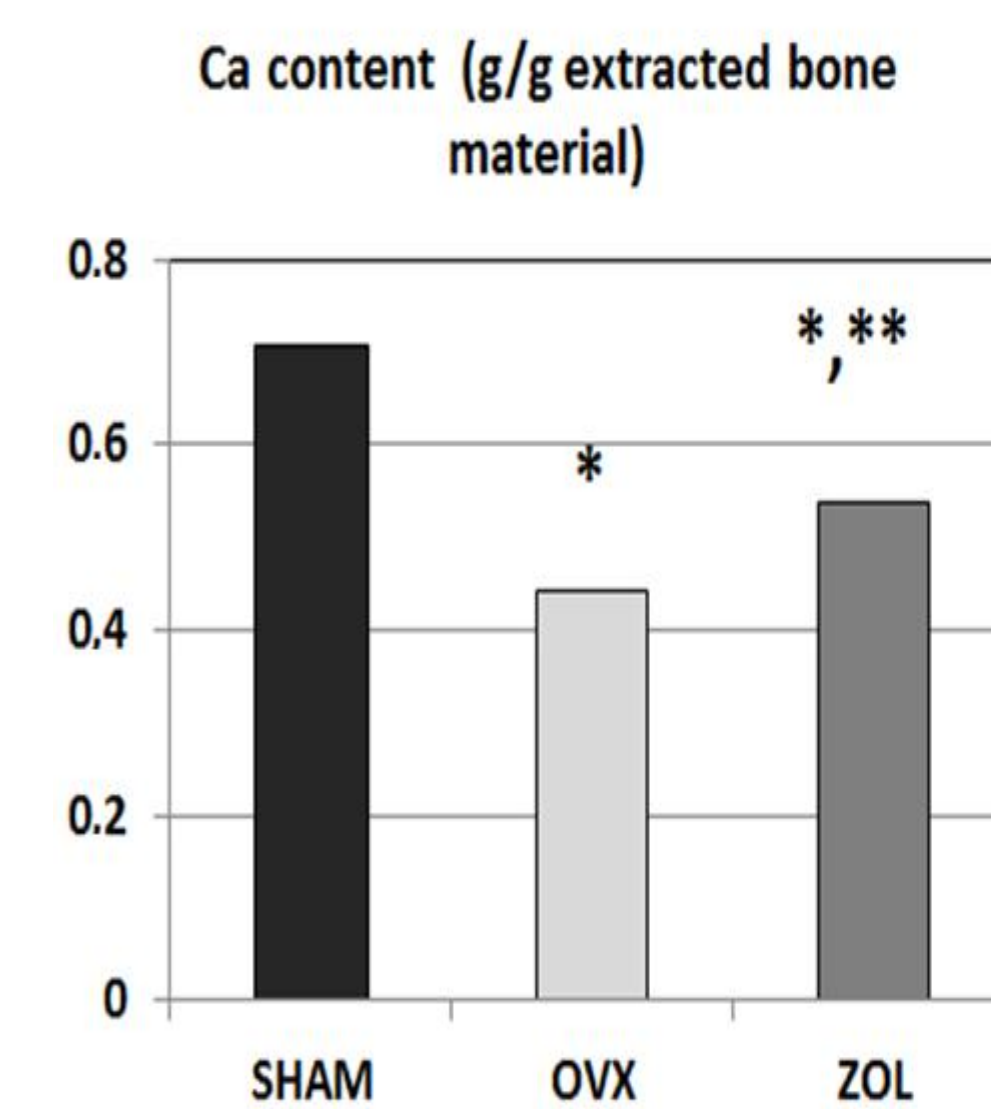
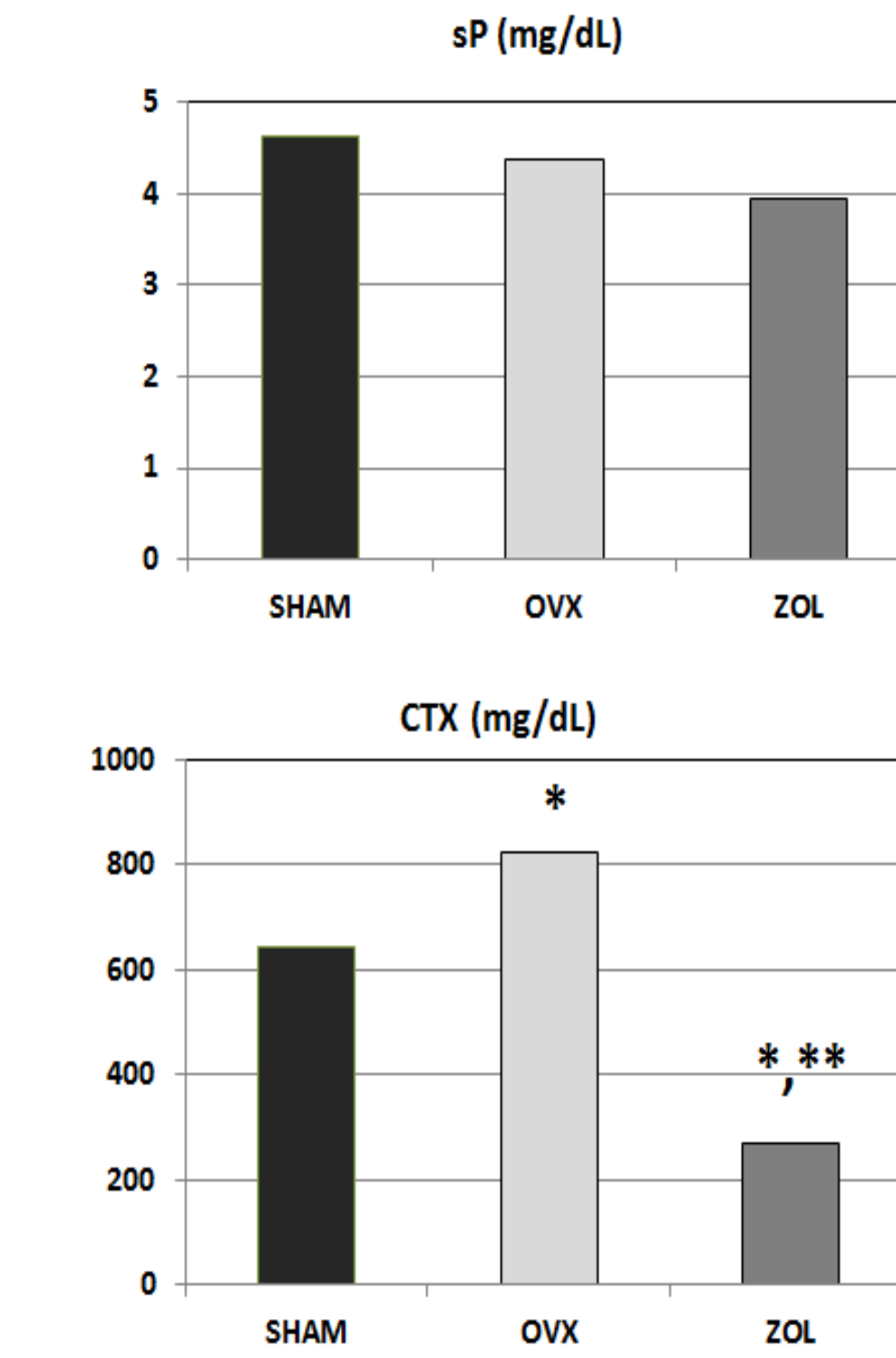
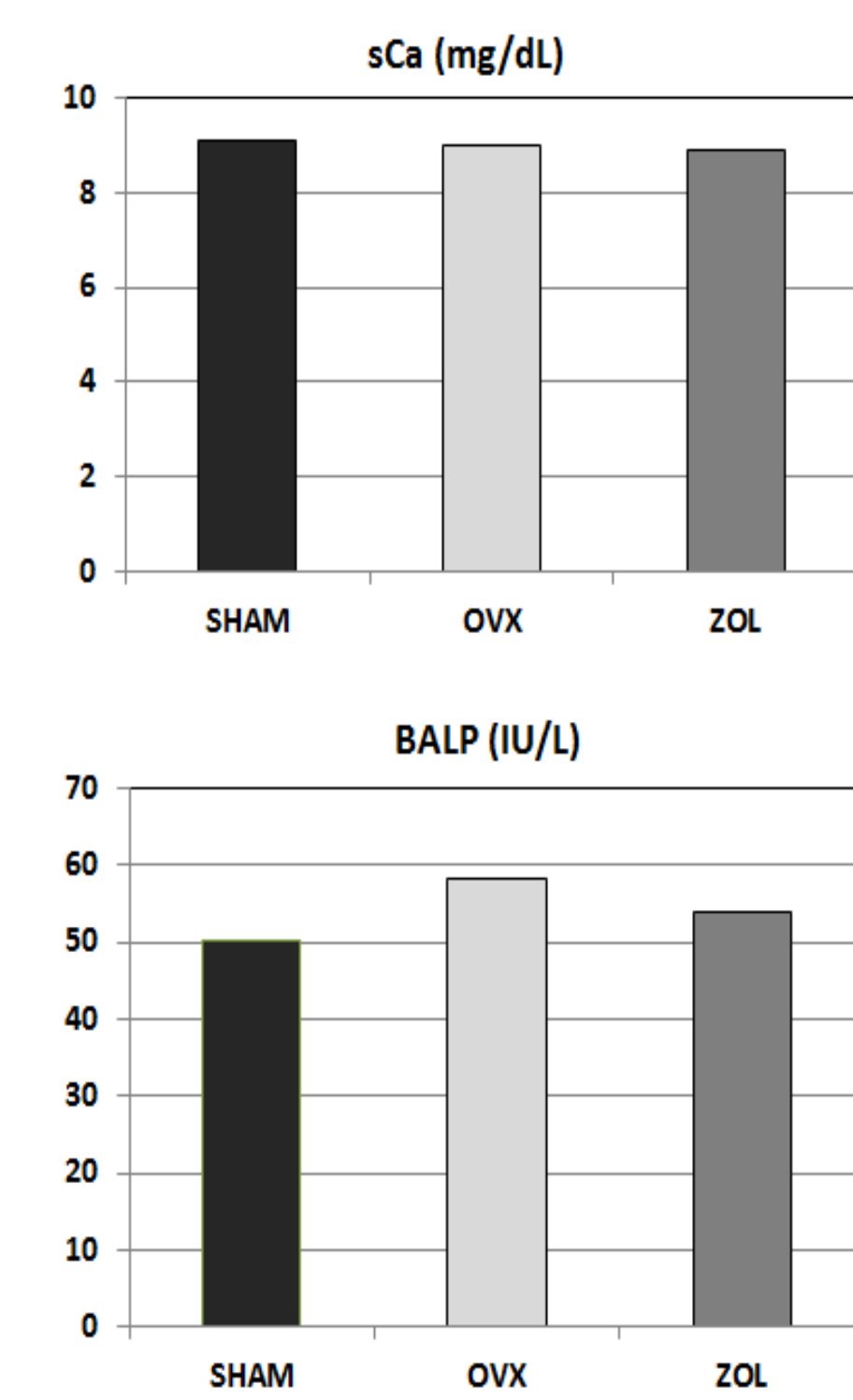
Adult female Corriedale ewes (35-45 kg body weight) Baseline (T<sub>0</sub>): They were bilateral OVX or SHAM operated and divided to receive 4mg ZOL /month (n=6) or physiological solution (3 OVX and 3 SHAM). After 1 year (T=12) : the first molar was extracted At the 2<sup>nd</sup>. year (T=24): a dental implant was done and a bone defect was done contra-laterally . After 4 additional months (the end of the study)(T=28): ewes were sacrificed.

## Determinations:

Blood was drawn during all these interventions and serum Calcium (Ca) , phosphorus (P), crosslaps (CTX) and bone alkaline phosphatase (BALP) were evaluated. At T=24 Ca and P content was evaluated in the extracted mandible material which was created to place the implant. At T=28 left hemimandible bone mineral content (BMC) was evaluated *ex vivo*.

## Results:

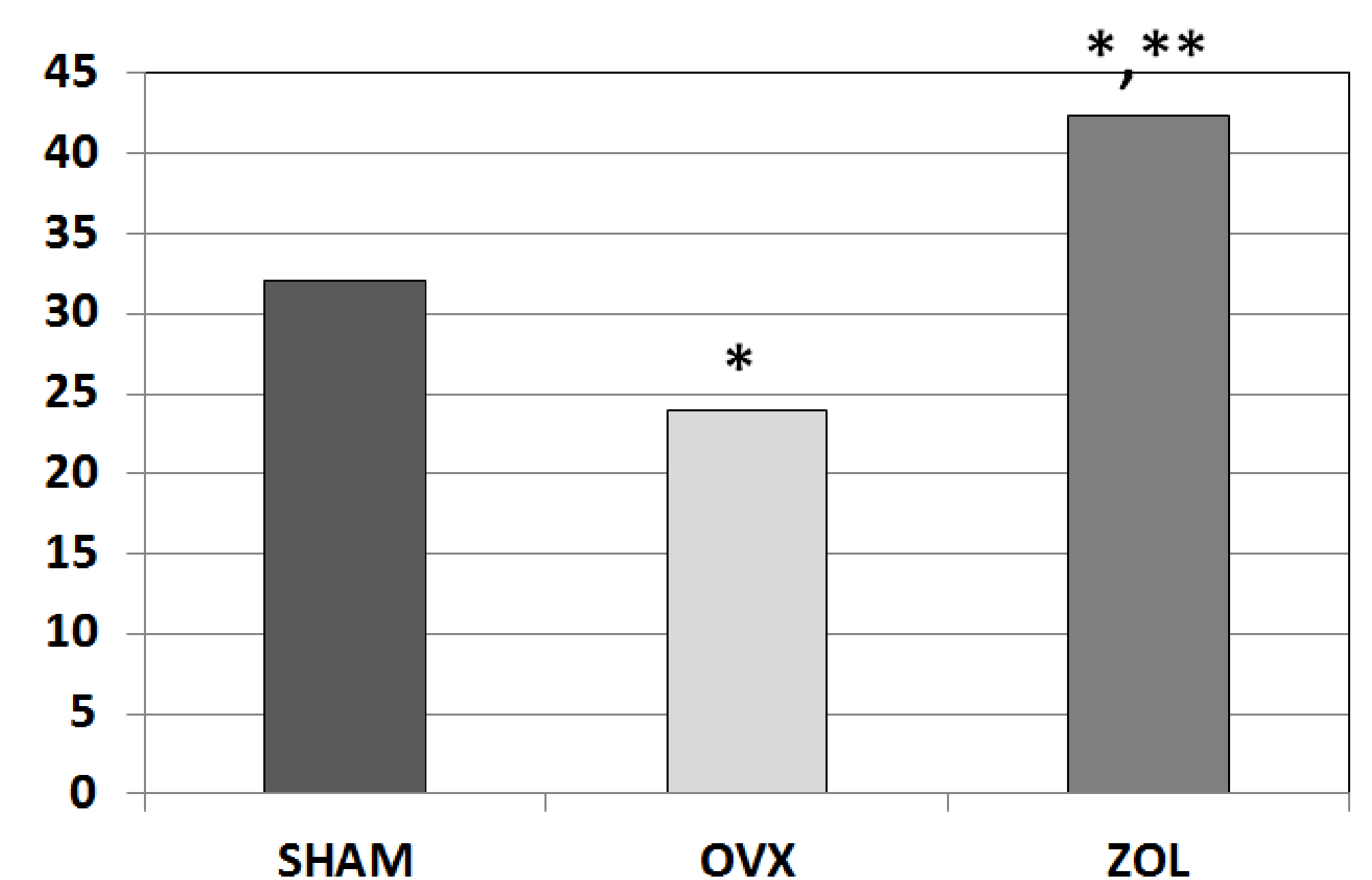
	SHAM	OVX+FS	OVX+ZOL
Baseline Body Weight (Kg)	33±2	36±4	35±2
Final Body Weight (Kg)	35±6	36±5	37±4
Left hemimandible weight (g)	87±7	84±3	107±20*,**
Cyanotic mucous (1st. year)	-	-/+	++
Actynomices culture (1st year)	+	++	+++
Survival	100%	100%	77%
Dental implant conservation	ALL	ALL	NONE
Maxillary Necrosis (Actynomices)	NON	NON	YES (2/6)



(\*) p<0.01: vs. SHAM; (\*\*) p<0.01: vs. OVX

(\*) p<0.01: vs. SHAM; (\*\*) p<0.01: vs. OVX

Hemimandible BMC (g/cm<sup>2</sup>) at the end of the study



(\*) p<0.01: vs. SHAM; (\*\*) p<0.01: vs. OVX



SHAM/OVX



ZOL



OSTEONECROSIS

**Conclusion:** Under our experimental conditions, the group of ewes treated with high doses of ZOL showed a marked decrease in bone resorption that induced an increase in mandible BMC. ONJ by Actynomices were observed in two ewes under this treatment.

Implants (ODONTIT IMPLANT SYSTEMS) were kindly provided by Odontit S.

Part of doctoral thesis of Dent. R. Davison Grants: Rio Negro National University, PICTO-2010-0181 and CONICET.