



# Rat models of osteonecrosis of the jaw

## Un update



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# The progress of the periodontal syndrome in the rice rat

## II. The effects of a diphosphonate on the periodontium



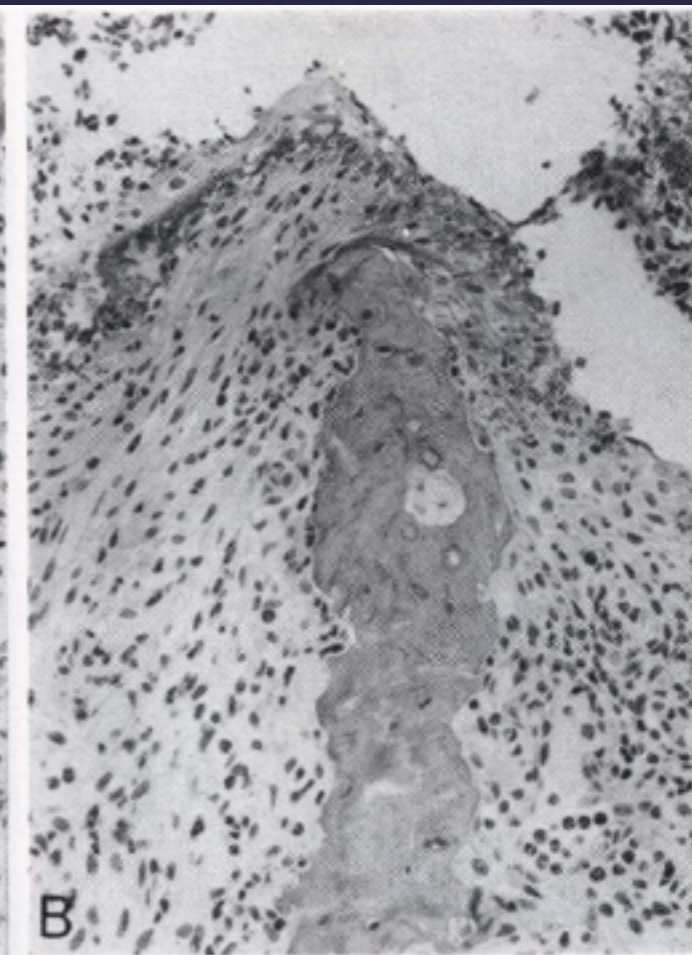
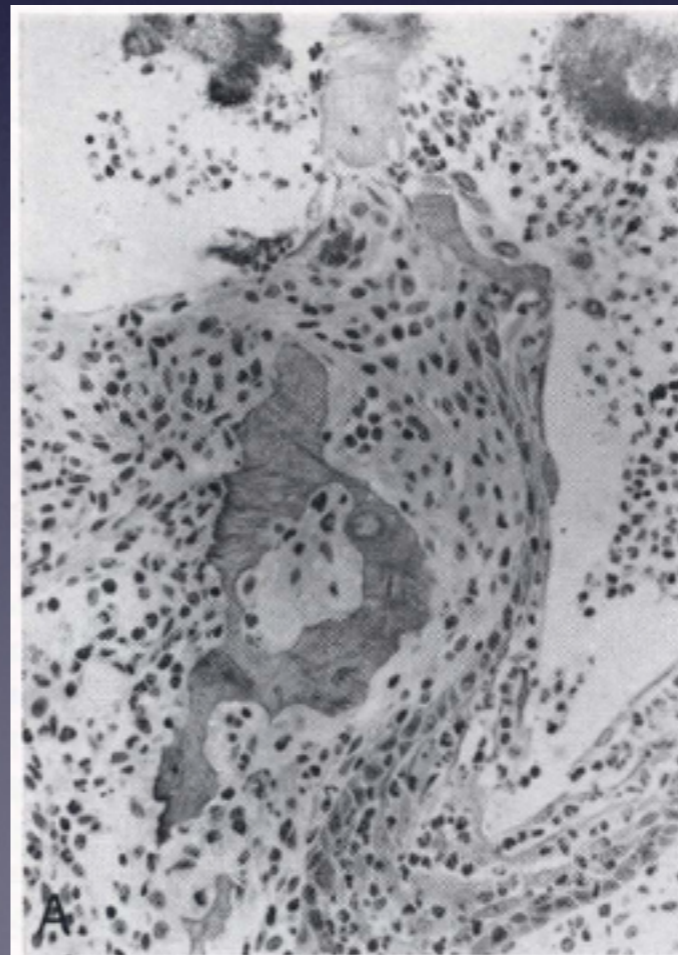
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University of Utah College of Medicine, Division of Radiobiology,  
Department of Pharmacology, Salt Lake City, Utah, U.S.A.



0.1 mg/kg/day of drug (Figs. 2A, B). In diseased animals treated with high doses of  $\text{Cl}_2\text{MDP}$ , trabeculae of alveolar bone were observed protruding into the oral cavity or well into the oral epithelium (Figs. 2C, D, 3A, B). This bone was devoid of typical

there was a greater amount of bone present in these animals. In some cases, some portions of alveolar crestal bone exposed to the oral cavity were devoid of bone cells and thus, might be considered as devitalized. In other samples, osteoblasts and osteocytes were present in this exposed bone.





# RAT MODELS

## Advantages

easy to manage with  
cost  
huge experience

## Disadvantages

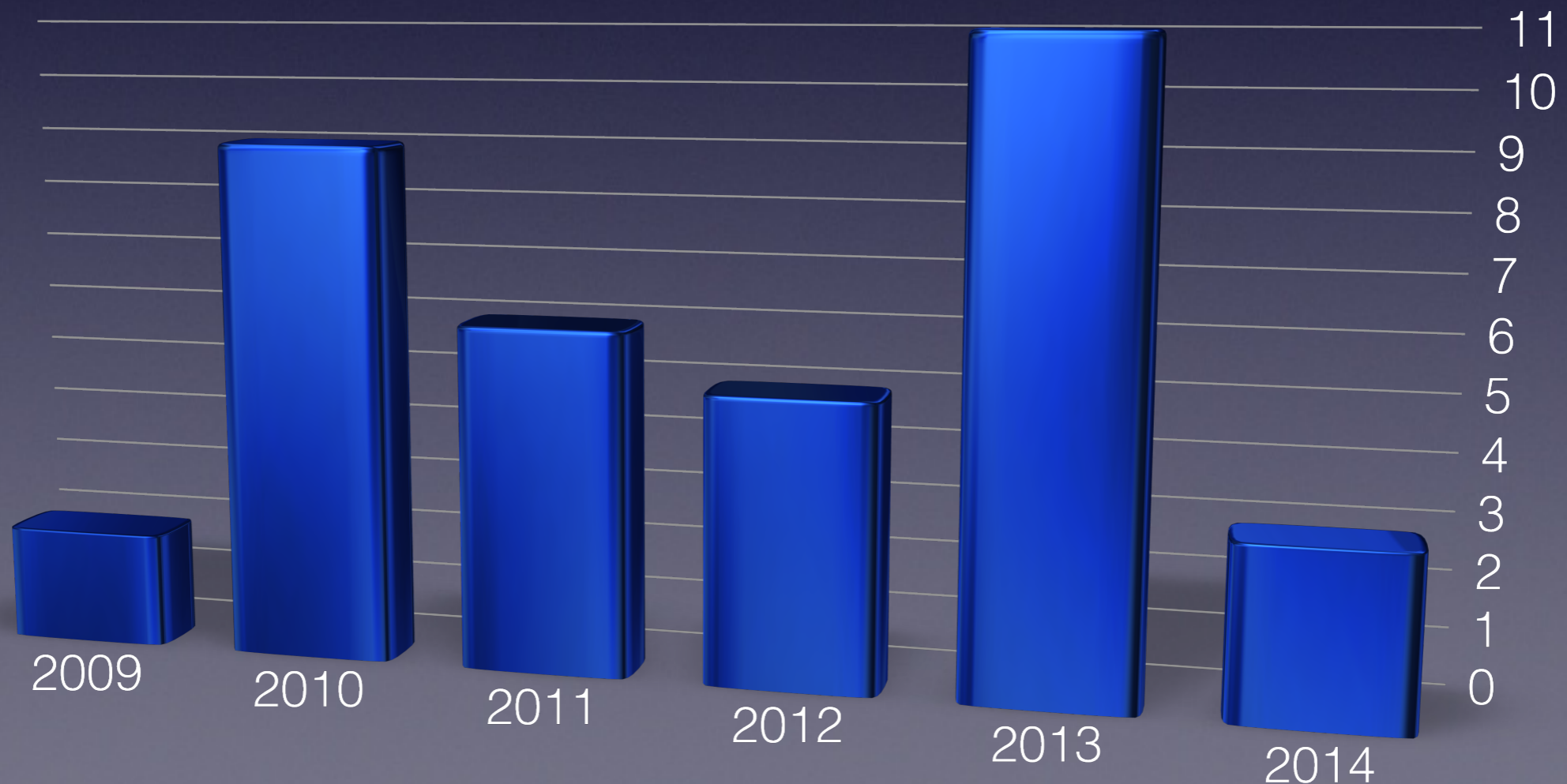
anatomy  
no intracortical remodeling  
higher regeneration capacity  
biologic differences

# Aim and inclusion criteria

*to critically review the recent literature on BRONJ in rat models  
retrieving all the relevant articles from MEDLINE/Pubmed  
database and by hand-searching in bibliographies*

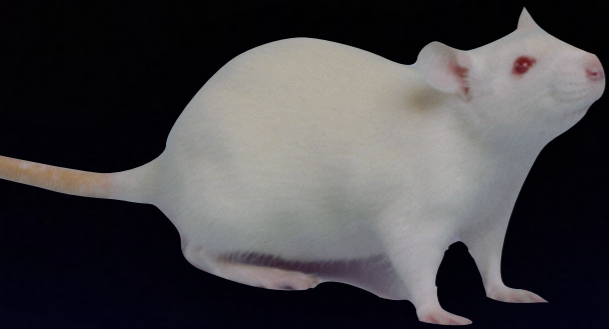
## RESULTS

36 articles selected



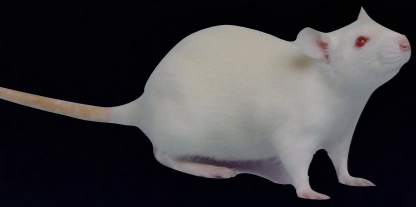


# RAT SPECIES



Wistar	Sprague-Dawley		Rice Rat	Holtzman
Ali-Erdem (2011)	Abtahy (2012)	Kim (2011)	Aguirre (2012)	Conte Neto (2012)
Barba-Recreo (2013)	Abtahy (2013)	Kuroshima (2013)		Conte Neto (2013)
Biasotto (2010)	Abtahy (2013)	Kuroshima (2014)		
Bigi (2010)	Aghaloo (2011)	Lopez Jornet (2010)		
Cankaya (2011)	Aguirre (2010)	Lopez Jornet (2011)		
Hikita (2009)	Basi (2011)	Marino (2012)		
Maahs (2010)	Cankaya (2013)	Senel (2010)		
Okamoto (2013)	Dayisolu (2013)	Sonis (2009)		
Soraya (2014)	Dayisolu (2014)	Xiong (2010)		
Tsurushima (2013)	Ersan (2014)	Yamashita (2011)		
Vasconcelos (2012)	Guevarra (2013)			
Yamamoto-Silva (2013)	Hokugo (2010)			

# BISPHOSPHONATE



Alendronate	Zoledronate		Olpadronate	Pamidronate	Clodronate
Abtahi (2012)	Aghloo (2011)	Guevarra (2013)	Bigi (2010)	Lopez-Jornet (2010)	Vasconcelos (2012)
Aguirre (2012)	Aguirre (2012)	Hokugo (2010)		Lopez-Jornet (2011)	
Abtahi (2013)	Ali-Erdem (2011)	Kuroshima (2014)		Senel (2010)	
Conte Neto (2013)	Barba-Recreo (2013)	Maahs (2010)			
Hikita (2009)	Basi (2011)	Marino (2012)			
Kim (2011)	Biasotto (2010)	Okamoto (2012)			
Kuroshima (2013)	Cankaya (2011)	Senel (2010)			
Maahs (2010)	Cankaya (2013)	Sonis (2009)			
Soraya (2013)	Dayisoylu (2013)	Tsurushima (2013)			
Xiong (2010)	Dayisoylu (2014)	Vasconcelos (2012)			
Yamamoto (2013)	Ersan (2014)	Yamashita (2013)			

# LOCAL RISK FACTORS



Tooth Extraction		Dental Implant	Bone drilled defetct	Bacterial lyophilized	Mucosal wound	Periodontal Disease	Periapical Infection
Abtahi (2012)	Dayisoylu (2014)	Abthai (2013)	Biasotto (2010)	Tsurushima (2013)	Vasconcelos (2012)	Aghaloo (2011)	Xiong (2010)
Abtahi (2013)	Ersan (2014)	Kim (2011)			Yamashita (2011)	Aguirre (2012)	
Aguirre (2010)	Guevarra (2013)				Abtahi (2012)		
Abtahi (2013)	Hikita (2009)						
Ali-Erdem (2011)	Hokugo (2010)						
Barba-Recreo (2013)	Kim (2011)						
Basi (2011)	Kuroshima (2013)						
Biasotto (2010)	Kuroshima (2014)						
Cankaya (2011)	Lopez-Jornet (2010)						
Conte Neto (2012)	Lopez-Jornet (2011)						
Conte Neto (2013)	Maahs (2010)						
Dayisoylu (2013)	Marino (2012)						
Soraya (2013)	Sonis (2009)						
Yamamoto (2013)							



# SYSTEMIC RISCK FACTORS



Dexamethasone	Vit D deficiency	Diabetes
Abtahi (2012)	Hokugo (2010)	Soraya (2013)
Abtahi (2013)		
Abtahi (2013)		
Ali-Erdem (2011)		
Cankaya (2011)		
Kuroshima (2013)		
Lopez-Jornet (2010)		
Lopez-Jornet (2011)		
Sonis (2009)		
Soraya (2013)		

# PREVENTIVE FACTORS



Peri-operative antibiotics	Teriparatide	Mucoperiosteal coverage	Sodium bicarbonate
Lopez-Jornet (2011)	Dayisoylu (2013)	Abtahi (2013)	Dayisoylu (2014)
	Ersan (2014)		
	Kuroshima (2013)		

# EXPERIMENTAL PROTOCOLS



rat



bisphosphonate



local risk  
factor



systemic risk  
factor



preventive  
measures

# EXPERIMENTAL PROTOCOLS



rat



bisphosphonate



local risk  
factor



systemic risk  
factor



preventive  
measures



Bigi  
(2010)

Senel  
(2010)

Okamoto  
(2012)

Cankaya  
(2013)

# EXPERIMENTAL PROTOCOLS



rat



bisphosphonate



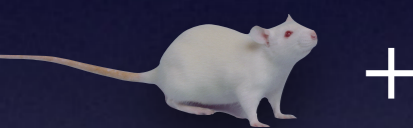
local risk factor



systemic risk factor



preventive measures



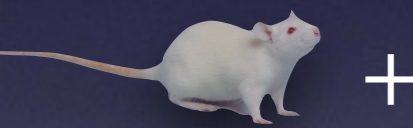
+



Aghaloo  
(2011)

Barba-Recreo  
(2013)

Kuroshima  
(2014)



+



+



Aguirre  
(2012)

Basi  
(2011)

Maahs  
(2010)

Xiong  
(2010)

Aguirre  
(2010)

Biasotto  
(2010)

Marino  
(2010)

Yamamoto  
(2013)

Conte Neto  
(2013)

Guevarra  
(2013)

Tsurushima  
(2013)

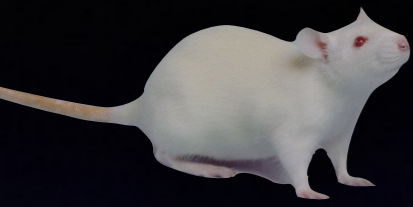
Yamashita  
(2010)

Hikita  
(2009)

Kim  
(2011)

Vasconcelos  
(2012)

# EXPERIMENTAL PROTOCOLS



rat



bisphosphonate



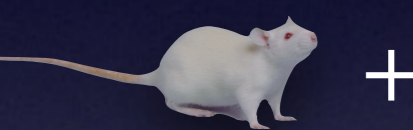
local risk factor



systemic risk factor



preventive measures



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Sonis  
(2009)

Hokugo  
(2010)

Lopez-Jornet  
(2010)

Cankaya  
(2011)

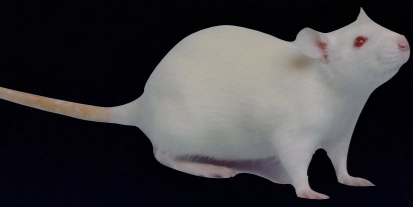
Ali-Erdem  
(2011)

Abtahi  
(2012)

Abtahi  
(2013)

Soraya  
(2013)

# EXPERIMENTAL PROTOCOLS



rat



bisphosphonate



local risk factor



systemic risk factor



preventive measures

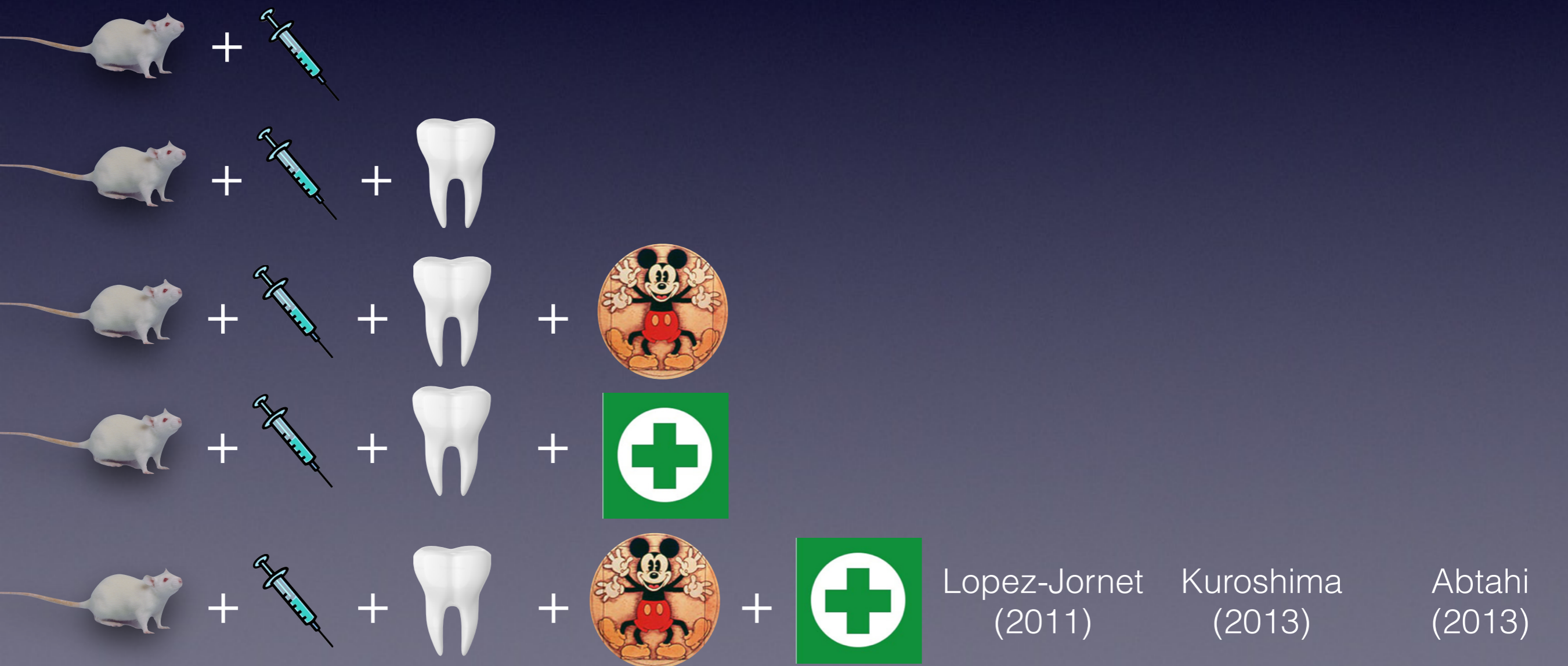


Dayisoylu  
(2013)

Dayisoylu  
(2014)

Ersan  
(2014)

# EXPERIMENTAL PROTOCOLS







Macro

Rx

Micro

Molecular

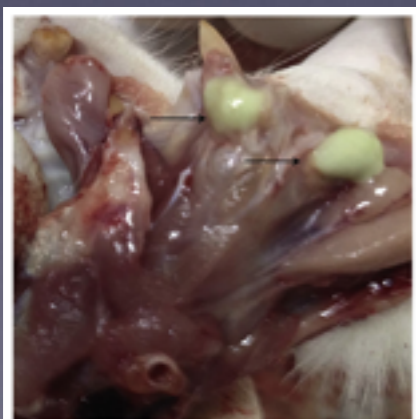
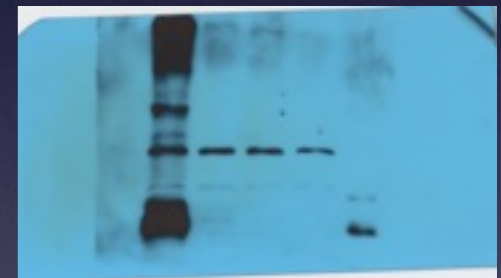
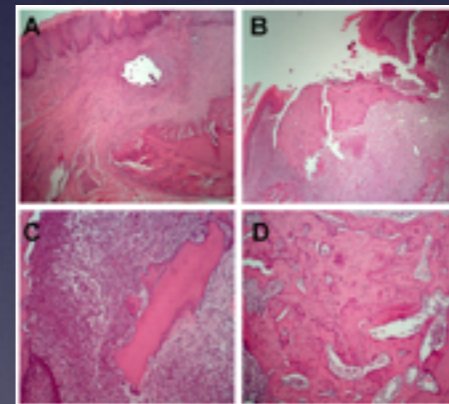
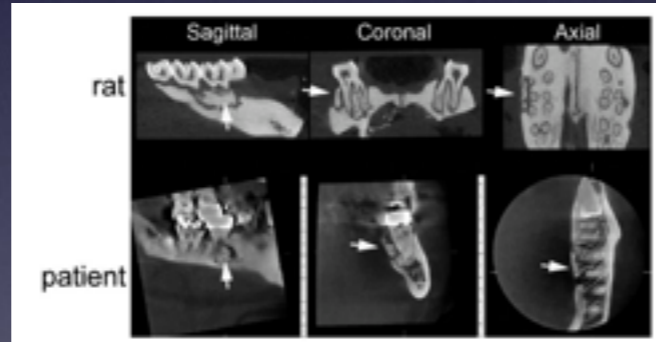
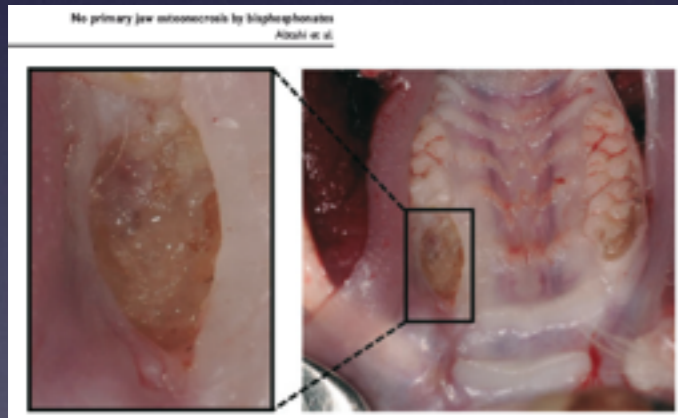


Fig. 2. Macroscopic view of the specimens in group III. Note the gross necrosis and pus formation (black arrow).

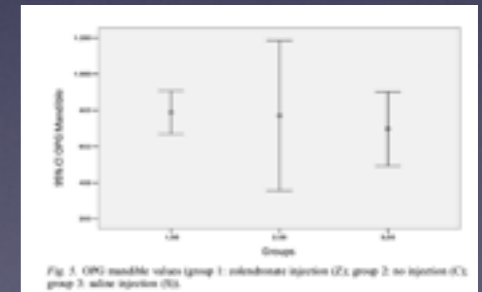
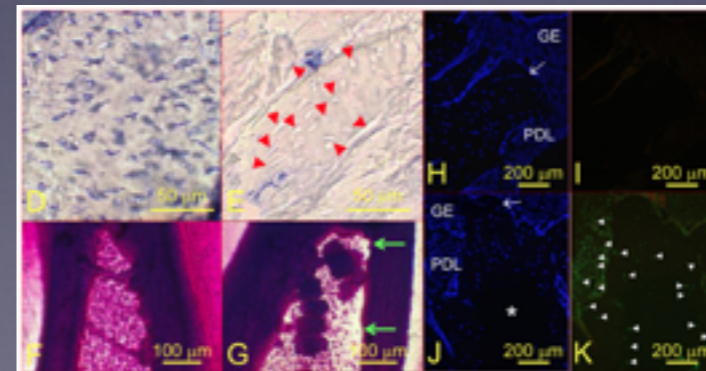
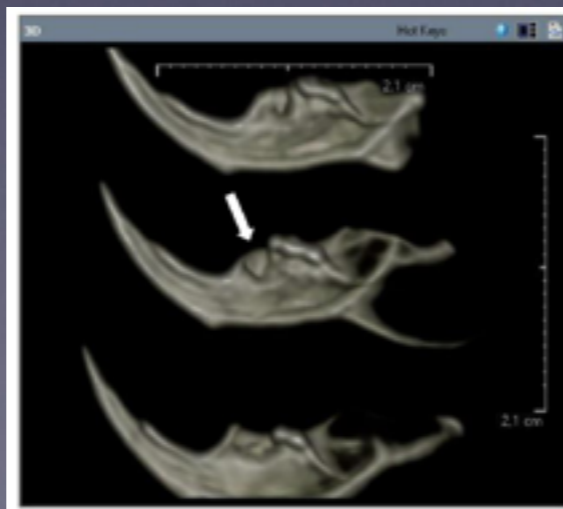


Fig. 3. OPG mandible values (group 1: infested rat (Rx), group 2: no infection (Cx), group 3: saline injection (S)).

# Conclusions /1

- ▶ a local risk factor is necessary to have macroscopic evidence of BRONJ
- ▶ the reported incidence of BRONJ ranges from 0 to 100% depending on different factors

# Conclusions /2

- ▶ BRONJ in rats, like in humans, is mainly associated with high potency amino BP combined with dento-alveolar surgical procedures and/or other predisposing factors, in particular corticosteroids
- ▶ some preventive strategies tested gave promising results