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ANATOMIC FACTORS RELATED TO BISPHOSPHONATE OSTEONECROSIS A RETROSPECTIVE BRONJ* STUDY AT THE UNIVERSITY DEPARTMENT OF STOMATOLOGY OF SANTA MARIA HOSPITAL – LISBON – PORTUGAL



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INTRODUCTION

BISPHOSPHONATES

**Synthetic drugs, similar in structure to pyrophosphate,
with a potent inhibitory action of bone resorption mediated by osteoclasts,
while taking an important inhibitory activity of angiogenesis**

LANDMARKS

1996 – Beginning of the prescription of the bisphosphonates in the treatment of osteoporosis and bone metabolism disorders related with cancer.

2003 – Marx and Migliorati reported the first cases of bisphosphonate related osteonecrosis of the jaws (BRONJ)*.

2008 – Mariotti; Felgueiras; **2010** (Robert) - There is an increasing prevalence of BRONJ (risk of 1% – 10% intravenously; 0.00007% – 0.04% orally administered), putting new issues on the procedures of dental extractions and the possibility of a window of intervention, based on clinical evidence.

STATE OF KNOWLEDGE

- **Dose-dependent reduction of bone resorption**
- **Inhibition of recruitment and promotion of apoptosis of osteoclasts**
- **Osteoblastic activity stimulation**
- **Decreasing the formation of capillary tubes, with reduction of blood vessels (avascular osteonecrosis)**
- **Occurrence in the jaws**
- **Spontaneous phenomena, although often triggered or aggravated by traumatic factors, which includes dental extractions procedures.**

CONDITIONING ANATOMIC FACTORS

- **Increased blood supply and more rapid bone remodeling related to periodontal vasculature observed in the jaws, affecting higher local drug concentration.**
- **Thin mucous coating for bone.**
- **Local predisposition to operative trauma.**

OBJECTIVES

To know:

- What is the local distribution of the BRONJ.
- If there are anatomical associated or determinant factors.
- If there are other bones involved.

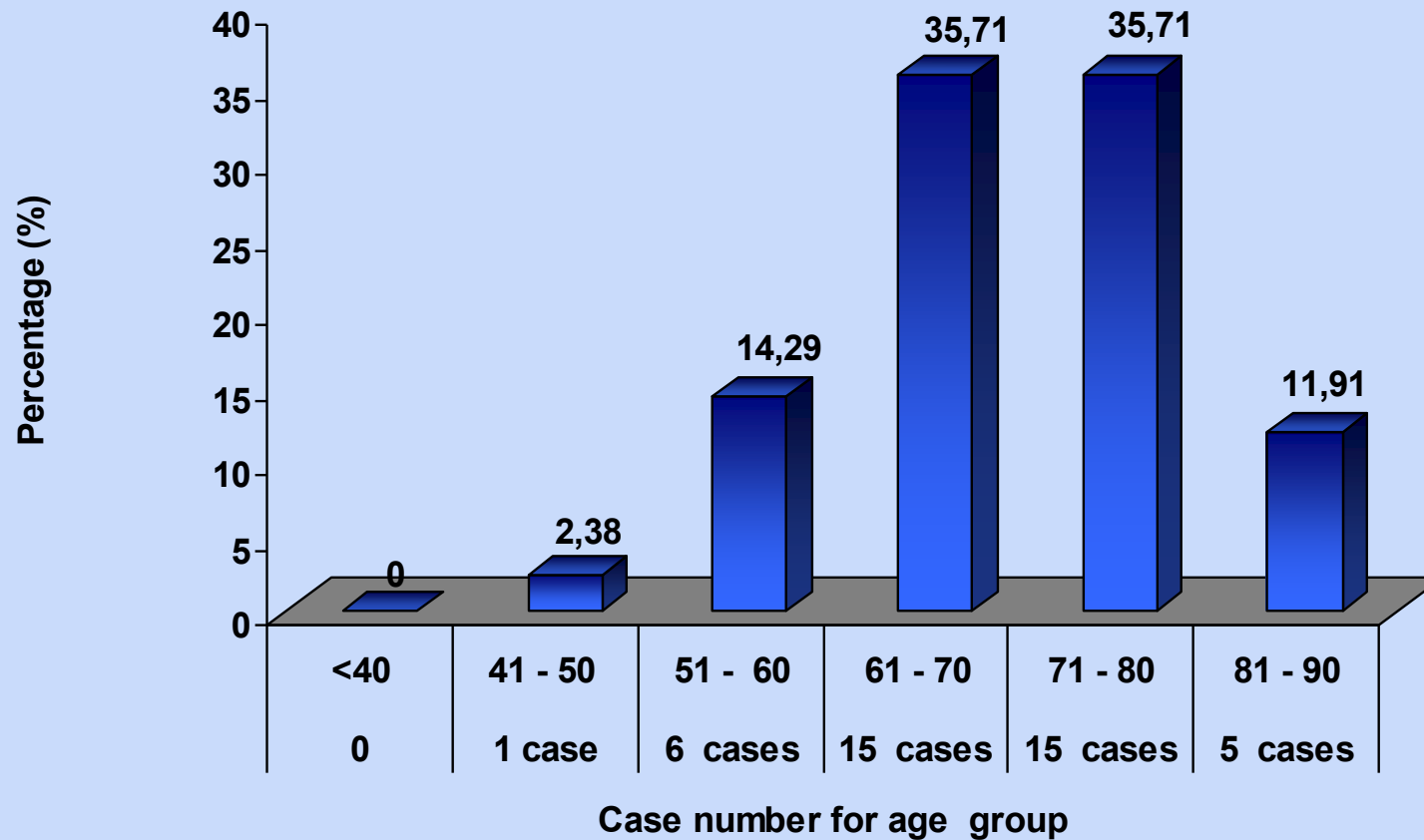
To contribute with new data for the establishment of the prevalence of the disease in Portugal.

MATERIAL AND METHODS

A RETROSPECTIVE STUDY

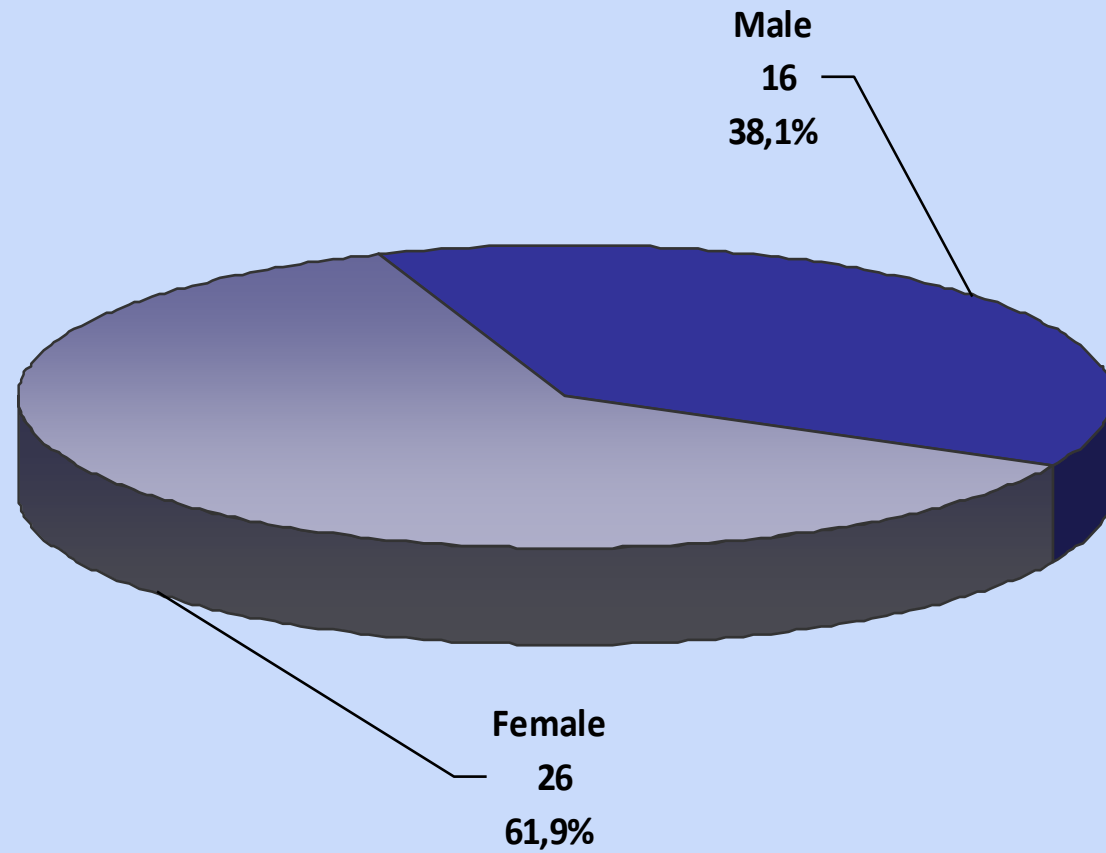
- **42 cases** treated at the Oral Surgery Unit and Oral Oncology Consultation of the University Department of Stomatology of Santa Maria Hospital – Lisbon – Portugal.
- The period of 1st January 2004, to April 30rd 2011.

DISTRIBUTION OF TREATED POPULATION BY AGE GROUPS



Total = 42 cases

POPULATION DISTRIBUTION BY GENDER



Total = 42 cases

DATA COLLECTION SHEET

FICHA DE RECOLHA DE DADOS SOBRE OSTEONECROSE DOS MAXILARES POR BISFOSFONATOS DO SERVIÇO DE ESTOMATOLOGIA DO CENTRO HOSPITALAR DE LISBOA-NORTE

Relação com trauma cirúrgico:

Sim () ; Não () ; Outro () Qual? _____ ; Extracções : Sim () - N° efectuado _____ ; Não ()

Relação a trauma protésico: Sim () – Onde? _____ ; Não ()

Aparecimento espontâneo Sim () – Onde? _____ ; Não ()

Titulação do CTX sérico _____

Evidências Imagiológicas:

TC _____

Ortopantomografia _____

Outros Exames Imagiológicos _____

Factores relevantes associados:

Higiene Oral: Boa () ; Má () ; Tabaco () ; Álcool ()

Doenças associadas:

Diabetes () ; Insuficiência Renal () ; Hipertensão () ;

Imunossupressão () - Quimioterapia associada () – Corticoterapia ()

Nome do Médico _____ Data ____/____/____

COLLECTED RELEVANT DATA

- **Underlying disease**
- **Type of bisphosphonate and route and time of administration**
- **Anatomical location (by sextant) and associated factors**
- **Imaging (panoramic radiography and CT) and analytical (serum CTX, when performed)**

STATISTICAL ANALYSIS

SPSS

$p < 0.05$ considered significant

RESULTS

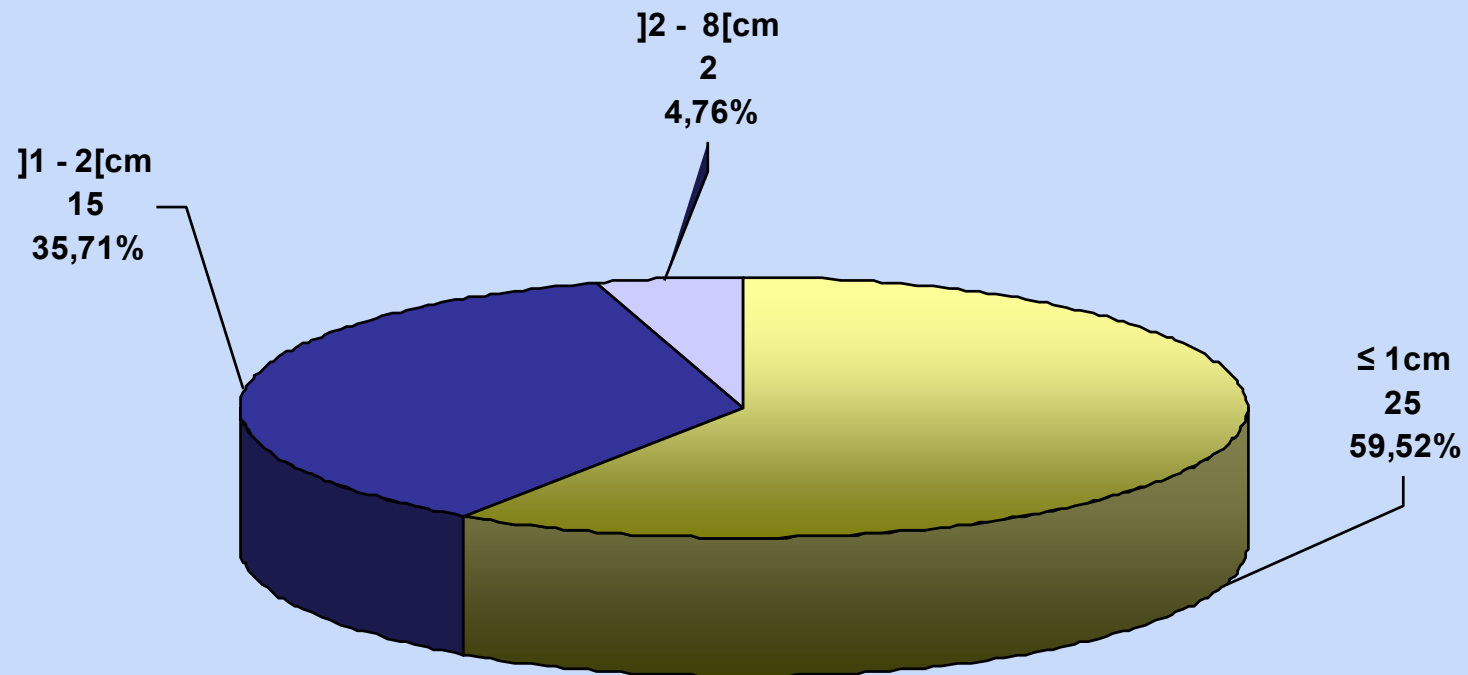
MACROSCOPIC APPEARANCE OF OUTSIDE CLASSIC LESION

- Rounded
- Larger diameter varying size between 2mm and 80 mm.
- Yellow greyish appearance
- Secondarily infected

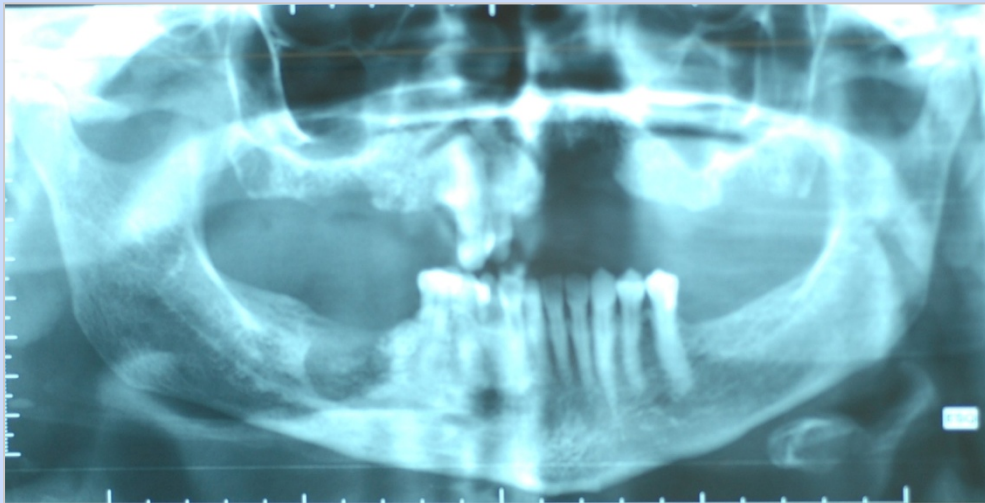


SIZE OF THE LESIONS FOUND

(number of cases)

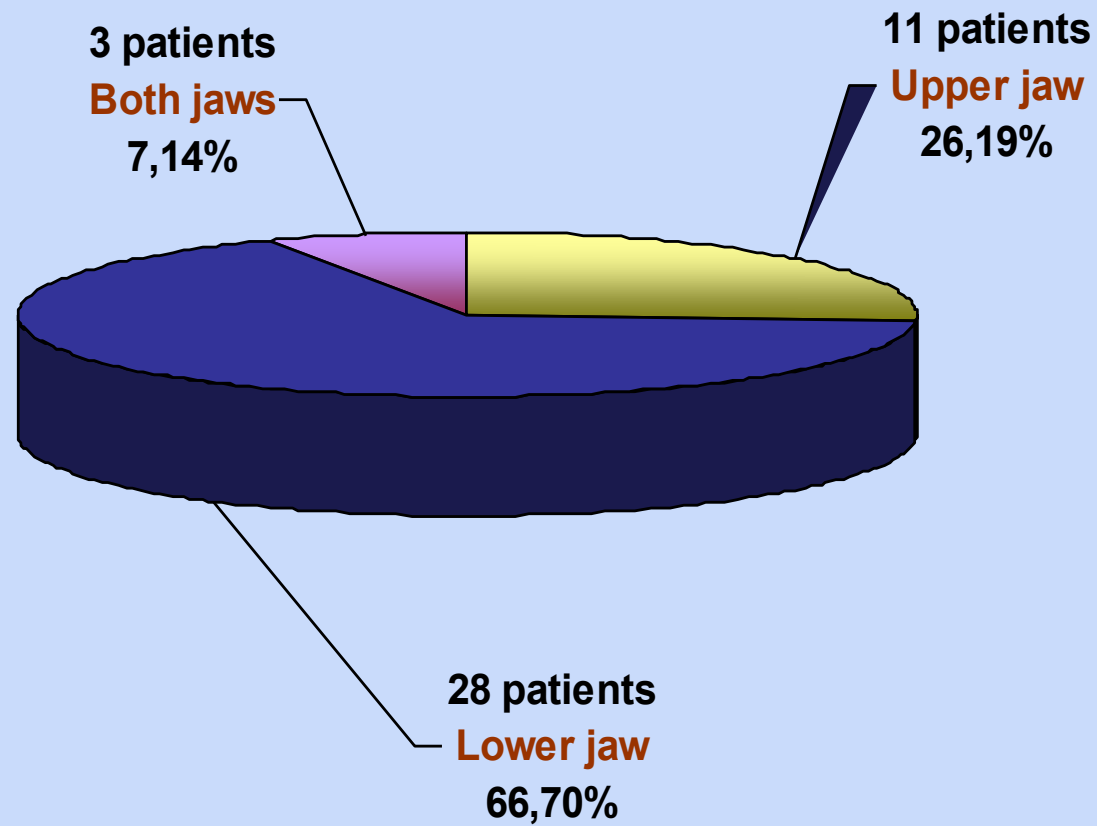


EVOLUTIVE PHENOMENA

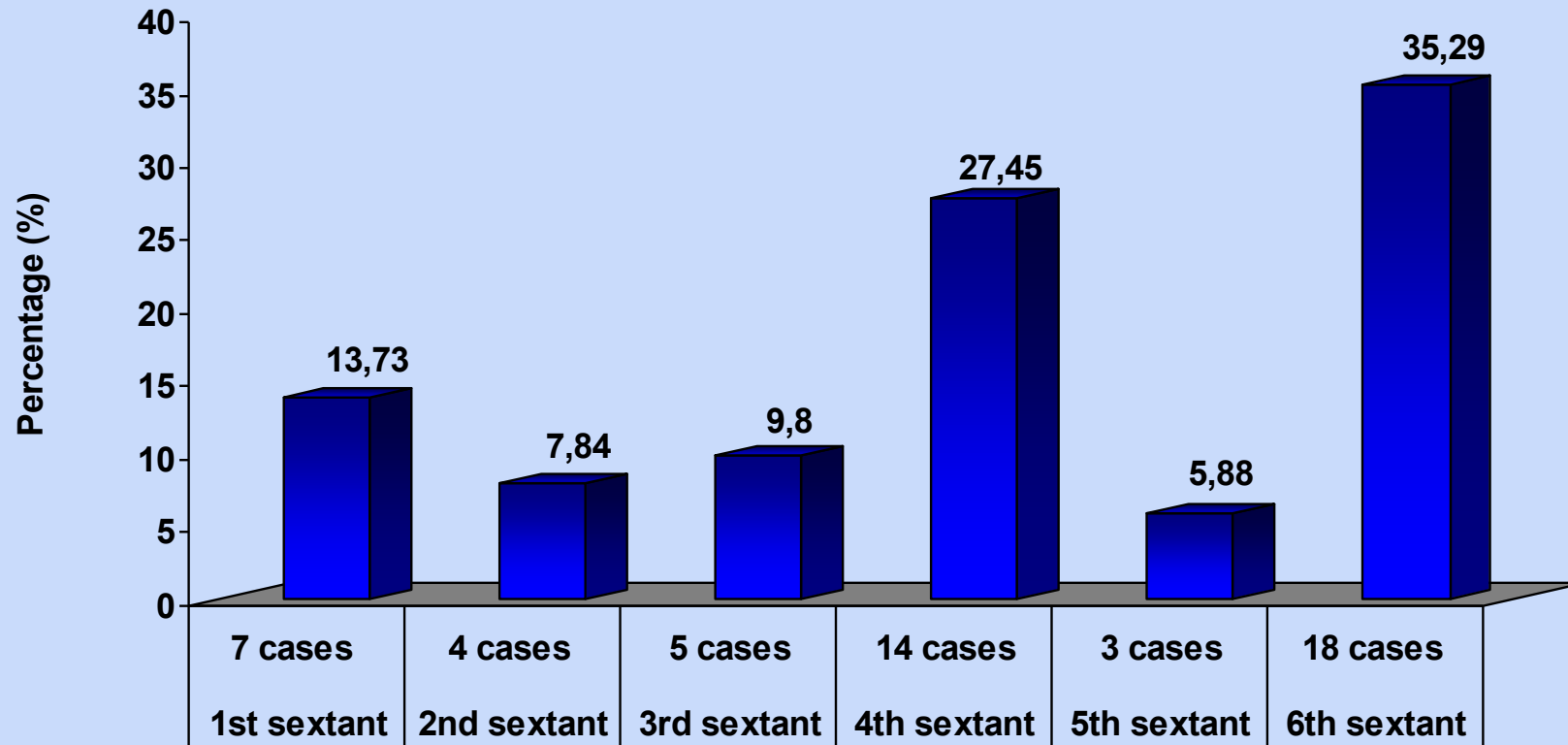


- 88,1% with pain (37 patients)

ANATOMICAL LOCATIONS

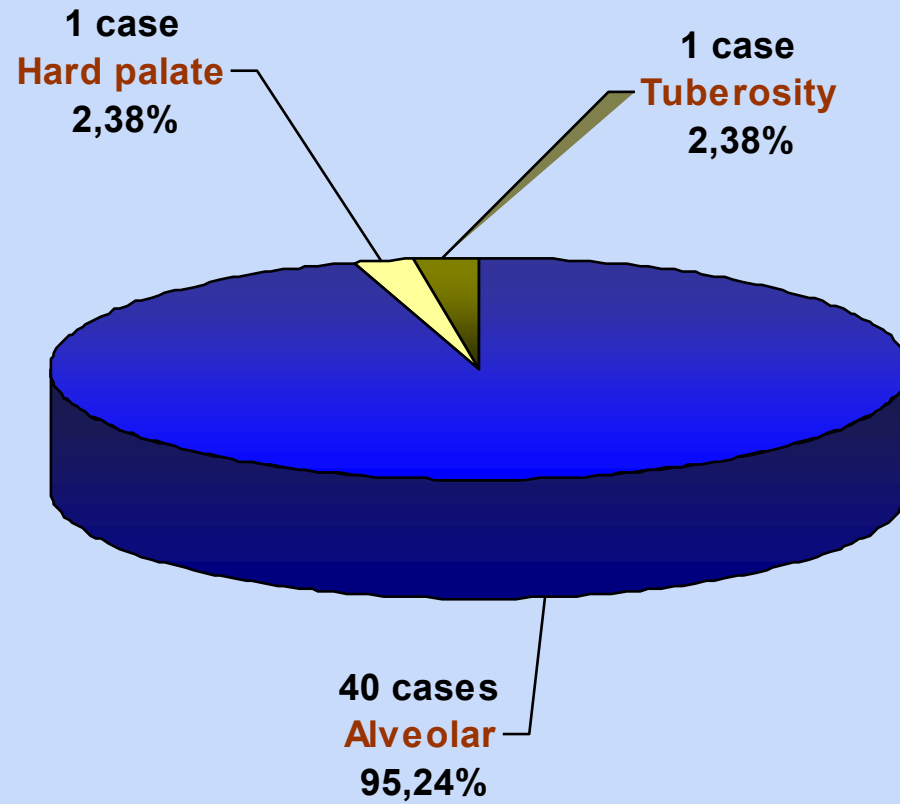


INVOLVED SEXTANTS

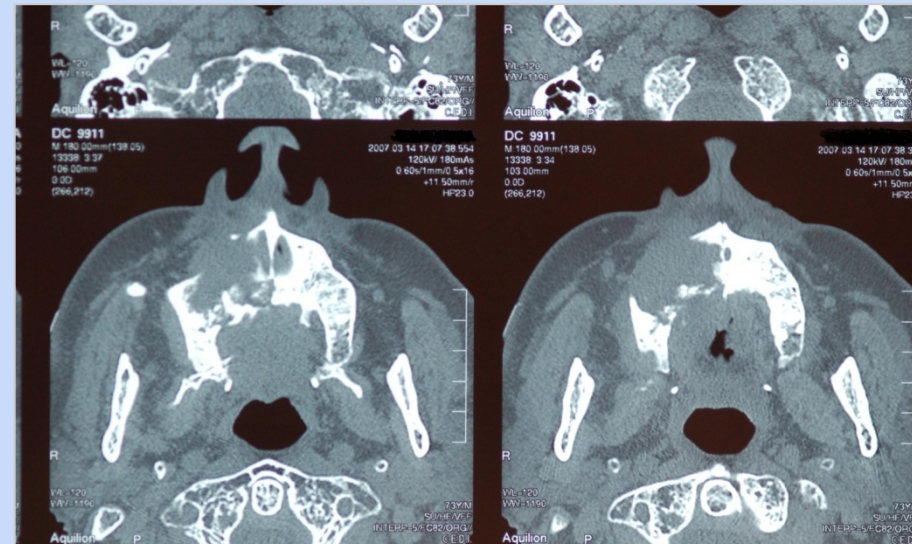
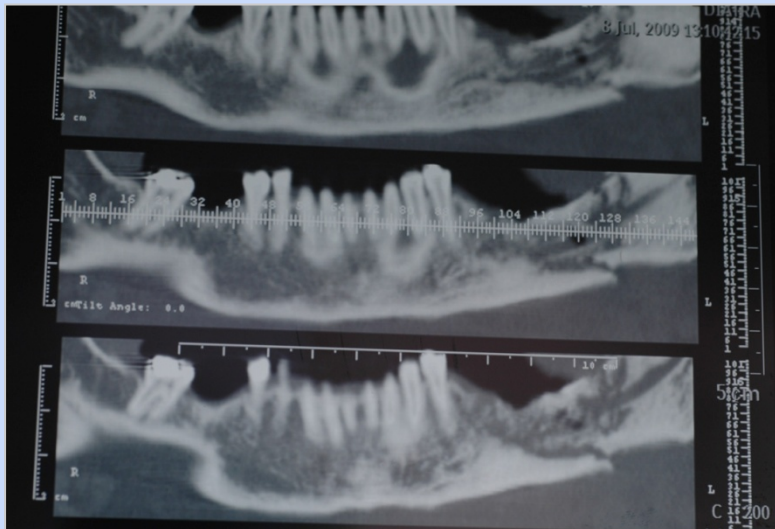


Total = 42 patients

DISTRIBUTION IN THE JAWS



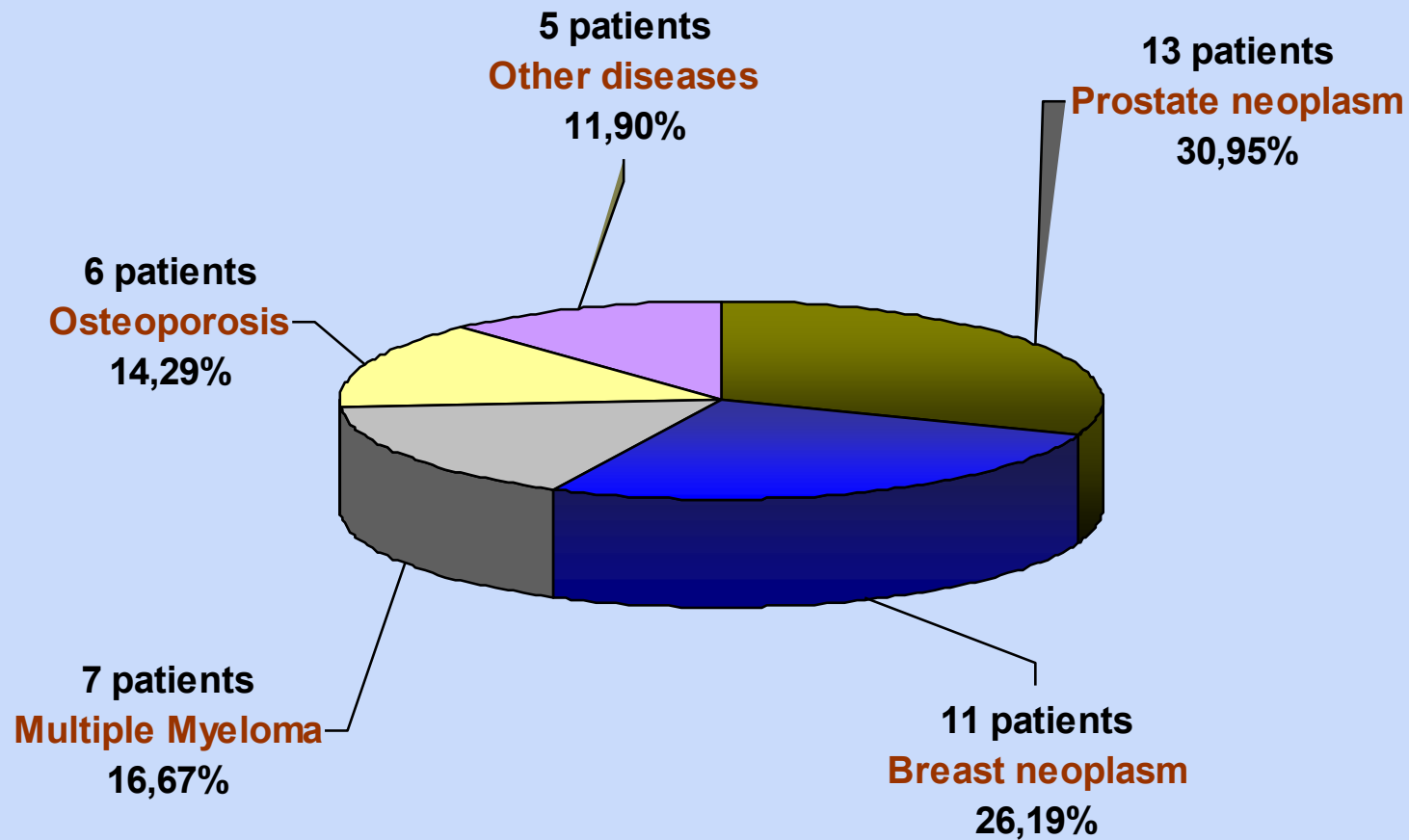
DEMONSTRATIVE EXAMPLES PHOTOS/TC



CLINICAL INVOLVEMENT OF THE BONE

Bone involved	Number of cases	Percentage (%)
Basal bone	8	19.05%
Lingual wall	10	23.8%
Buccal wall	5	11.9%
Both walls	2	4.76%
Mylohyoid ridge	2	4.76%

UNDERLYING DISEASES

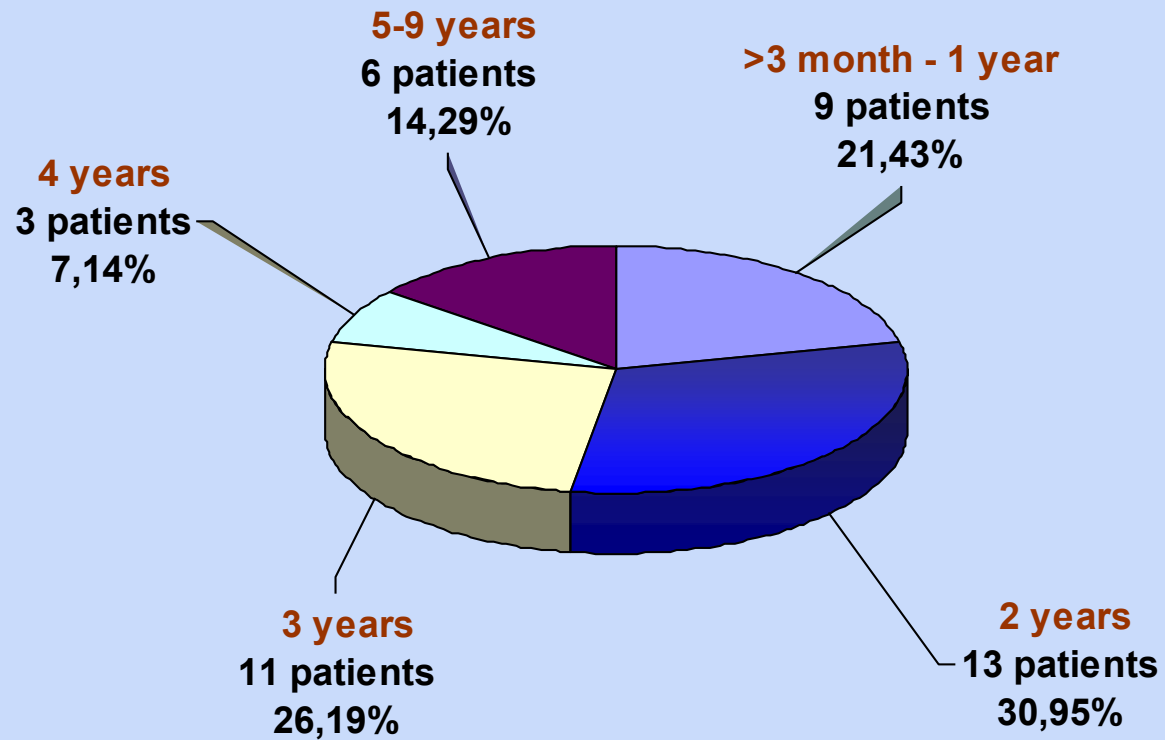


Total = 42 cases

TYPE OF BISPHOSPHONATE AND ROUTE OF ADMINISTRATION

Type of bisphosphonate	Route of administration	Number of cases	Percentage (%)
Zoledronate	Intravenously	32	76.19%
Alendronate	Orally	8	19.05 %
Ibandronate	Orally	1	2.38 %
Association of oral administration of Alendronate and Ibandronate		1	2.38%

TIME COMPLETED MEDICATION



Total = 42 patients

RELATIONSHIP OR NOT WITH TRAUMA

Trauma	Number of patients	Percentage (%)
Surgical trauma	32	76.19%
Dental direct trauma	1	2.38%
Prosthetic trauma	1	2.38%
Inflammatory relationship	2	4.76%
Spontaneous occurrence	6	14.29%

DISCUSSION

COMPARATIVE TABLE OF LOCAL DISTRIBUTION OF BRONJ WITH OTHER RESEARCHERS

Investigators	Total number of cases	Percentage distribution (number of patients)		
		Upper jaw	Lower jaw	Both jaws
Marx (2003)	36	14% (---)	80% (---)	6% (---)
Ruggiero et al. (2004)	63	37% (23)	62% (39)	1% (1)
Marcin et al. (2010)	34	35.29% (12)	64.71% (22)	11.77% (4)
Furtado et al. (2011)	42	26.19% (11)	66.7% (28)	7.14% (3)

COMPARATIVE TABLE OF CORRELATED FACTORS WITH OTHER RESEARCHERS

Author	Total number of cases	Percentage (number of patients)				
		Cases of trauma			Inflammatory episode	Spontaneous occurrence
		Surgical	Dental direct trauma	Prosthetic		
Marx (2003)	36	78% (---)	---	---	---	22% (---)
Ruggiero et al (2004)	63	86% (54)	---	---	---	14% (9)
Marcin et al (2010)	34	91.18% (31)			---	8.82% (3)
Furtado et al (2011)	42	76.19% (32)	2.38% (1)	2.38% (1)	4.76% (2)	14.29% (6)

- **A slow bone turnover in the basal bone of the jaw, justifies its lower occurrence (19.05%).**
- **There is a window period of 90 days (100%).**

Increased blood supply and more rapid bone remodeling related to periodontal vasculature observed in alveolar bone, affecting higher local drug concentration, may explain the high prevalence in this area (95.24%).

CONCLUSIONS

- 1.** BRONJ is a relevant anatomoclinical entity, not only by the incidence (42 new cases in this study), but also by associated severity and discomfort (pain in 81.1% of patients).
- 2.** Affects differently the various areas of the jaws, either in an isolated manner or with multiple lesions in different locations, involving only one or both jaws.
- 3.** There is a higher prevalence of lesions in the lower jaw (66.7%), when compared with the upper jaw (26.19%).
- 4.** The prevalence is significantly higher in alveolar bone (95.24%).
- 5.** The area of molars and premolars is the most affected (highest value at 6th sextant = 35.29%).



CONCLUSIONS

- 6.** Sites of surgical trauma, dental direct or prosthetic trauma , and recent inflammatory episode, are more predisposed to the occurrence of osteonecrosis.
- 7.** In all cases, the injury onset occurred after a medication period of 90 days, up, spontaneously in 14.29% of patients.
- 8.** Preventive measures must be implemented, avoiding trauma and using the window of intervention .
- 9.** The jaws are the unique place of the occurrence of the disease in our cases.



THANK YOU !