798

RESEARCH ARTICLE

The Assessment of Maxillofacial Soft Tissue and Intracranial Calcifications via Cone-beam Computed Tomography

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Abstract: *Background*: Cone-beam Computed Tomography (CBCT) scans obtained with larger field of view let us see various incidental findings, anatomical variations and pathologies, like intracranial and soft tissue calcifications.

Objective: The purpose of this retrospective study was to determine the prevalence of intracranial and soft tissue calcifications *via* CBCT.

Methods: Full volume (maxillofacial region) scans of 290 patients achieved for various reasons were investigated by blinded two dentomaxillofacial radiologists. Demographic data of the patients were saved. The findings were categorized and statistically analyzed with descriptive statistics, crosstabs and chi-square tests.

ARTICLEHISTORY

Received: December 04, 2016 Revised: March 24, 2017 Accepted: April 09, 2017 DOI: 10.2174/1573405613666170428160219

Results: Totally 290 patients aged between 24 and 81 years old (mean age \pm standard deviation: 49 \pm 14) consisting of 155 females (53.4%) and 135 males (46.6%) were examined in the study. The most common calcifications were pineal gland calcification (64.5%), followed by tonsillolith (34.1%), petroclinoid ligament calcification (33.4%), Intracranial Internal Carotid Artery Calcifications (IICAC) (18.3%), Extracranial Internal Carotid Artery Calcifications (EICAC) (8.3%) and the others (1.7%, equally sialolith, antrolith and choroid plexus calcification), respectively.

Conclusion: Tonsillolith, EICAC and IICAC showed an increase with age. EICAC was seen more in females, conversely petroclinoid ligament calcification was seen more in males. There was a statistically significant correlation between EICAC and IICAC.

Keywords: Soft tissue calcification, intracranial calcification, CBCT, dentomaxillofacial, patients, pineal gland.

1. INTRODUCTION

Cone-beam Computed Tomography (CBCT) was first used for angiography in 1982 and its use in dentistry was welcomed in late 1990s for maxillofacial hard tissue imaging [1-3]. The use of CBCT in dentistry increases day by day.

CBCT scans obtained with larger Field of View (FOV) let us see various incidental findings, anatomical variations and pathologies. The majority of these findings may be routine benign entities, but sometimes they may be an indicator of vital important diseases [4]. Also, several findings related with brain and intracranial region may be visible in maxillofacial and craniofacial CBCT images. Therefore, the clinicians have to examine all of the image sections not to miss the possible important findings [5]. However, along with the examination of images, dentomaxillofacial radiologists have to recognize the lesions and remark in the radiological report, because of their medicolegal responsibilities. Those pathologies may include the intracranial signs like intracranial calcifications [6].

The clinicians mostly focus on dentoalveolar structures and hard tissues on CBCT images during routine dental practice. Though, various calcifications in soft tissues and intracranial region may be viewed outside of the region of interest [1, 7]. These calcifications are generally considered as asymptomatic incidental findings and physiologic formations, but sometimes advance medical examination or consultation may be required [8]. Etiology of the intracranial calcifications may originate physiological, developmental, reactive or neoplastic pathologies [9].

In literature, a limited number of investigators have focused on soft tissue and intracranial calcifications on CBCT images. To the best of our knowledge, there are a few published articles regarding both intracranial and soft tissue calcifications on CBCT scans [1, 9, 10].

The purpose of this retrospective study was to determine the prevalence of intracranial and soft tissue calcifications *via* CBCT.

2. MATERIALS AND METHODS

Before starting the study, Ethical Approval was received from Gazi University Ethics Committee (19.06.2015-77082166-604.01.02, Ankara, Turkey). CBCT scans of 290 patients (155 females and 135 males) achieved for various reasons between January 2013 and December 2014 were included at Gazi University Faculty of Dentistry Department

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The Assessment of Maxillofacial Soft Tissue

of Dentomaxillofacial Radiology (Ankara, Turkey). CBCT images of the patients who had a history of maxillofacial trauma or operation and the images with any artifacts were excluded. Only full volume (20x17 cm) CBCT images were selected for the study.

CBCT images were obtained by ProMax 3D Mid (Planmeca Oy, Helsinki, Finland), using parameters of 90 kVp, 12 mA, total scanning time of 27.7 seconds and 0.4 mm voxel size. Scanning was performed by fixing the patient's jaw and head support apparatus while the patient was standing. Images were examined on 24-inch Philips medical monitor with NVDIA Quadro FX 380 graphics card and 1920×1080 pixel resolution by using Romexis 2.7.0. program (Planmeca Oy, Helsinki, Finland).

Demographic data of the patients were recorded. Tonsilloliths (Fig. 1), Extracranial Internal Carotid Artery Calcifications (EICAC) (Fig. 2), brain calcifications [pineal gland (Fig. 3) and choroid plexus calcifications (Fig. 4)], sialoliths (Fig. 5), antroliths (Fig. 6), petroclinoid ligament calcifications (Fig. 7) and Intracranial Internal Carotid Artery Calcifications (IICAC) (Fig. 8) were examined on the axial, coronal and sagital sections of CBCT images. All evaluations were carried out by blinded two dentomaxillofacial radiologists (MO and IP) in a quiet room with subdued ambient lighting, approximately 50 cm away from the screen.



Fig. (1). Axial CBCT image of a tonsillolith (arrow).



Fig. (2). Axial CBCT image of bilateral EICACs (arrows).



Fig. (3). Mid-sagital CBCT image of a pineal gland calcification (arrow).



Fig. (4). Axial CBCT image of bilateral choroid plexus calcifications (arrows).



Fig. (5). Coronal CBCT image of bilateral submandibular sialoliths (arrows).

For the data analysis; the patients were divided into three age groups: 24-40 years old (N=71, 24.5%), 41-50 years old (N=66, 22.8%) and 51-81 years old (N=153, 52.8%). Obtained data were statistically analyzed by using SPSS program version 21.0 (SPSS Inc., Chicago, USA). The findings were categorized and statistically analyzed with descriptive statistics, crosstabs and chi-square tests. Kappa coefficients were calculated for interobserver agreement. The correlations between the calcifications according to age and gender were analyzed with chi-square test.



Fig. (6). Coronal CBCT image of bilateral antroliths in the maxillary sinuses (arrows).



Fig. (7). Axial CBCT image of bilateral petroclinoid calcifications (arrows).

3. RESULTS

Totally 290 patients aged between 24 and 81 years old (mean age \pm standard deviation: 49 \pm 14), consisting of 155 females (53.4%) and 135 males (46.6%) were examined in the study.

Table 1. Interobserver agreement coefficients.



Fig. (8). Coronal CBCT image of bilateral IICACs (arrows).

Interobserver agreement coefficients were 0.59 and which was statistically significant (Table 1).

The possibility of tonsillolith and IICAC increased in older ages. For instance, tonsilloliths were more common in patients with over 51 of age (40.5%, N=62) than in under 40 of age (26.8%, N=19). The statistically significant correlations were found between the age and tonsilloliths and II-CAC. In a similar way, the frequencies of IICAC were 28.1% (N=43) and 2.8% (N=2) in the patients with over 51-age and under 40-age, respectively. Pineal gland calcification was detected in 64.5% (N=187) of the patients while choroid plexus calcification was seen only in 1.7% (N=5). Details are shown in Table **2**.

Statistically significant correlations were found between the gender and EICAC-petroclinoid ligament calcification. The presence of EICAC was higher in females (11.6%, N=18) than in males (4.4%, N=6). In contrast, the rate of petroclinoid ligament calcification in males was 45.2% (N=61), while 23.2% (N=36) in females. Details are shown in Table **3**.

Calcifications	Ν	Kappa Coefficient
Tonsillolith	290	.939*
EICAC	290	.875*
Pineal gland calc.	290	.591*
Choroid plexus calc.	290	.611
Sialolith	290	.764*
Antrolith	290	.887*
Petroclinoid ligament	290	.705*
IICAC	290	.851*

* Statistically significant correlation at the level of P<0.01.

Type of the Calcification	Presence of the Calcification		24-40 Years Old	41-50 Years Old	51-81 Years Old	Total	Chi-square
		N	52	48	91	191	
Type of the Calcification Prescription Tonsillolith - EICAC - Pineal gland calcification - Choroid plexus calcification - Sialolith - Petroclinoid ligament calcification - IICAC -	Not present		73.2	72.7	59.5	65.9	C 00*
		Ν	19	18	62	99	5.88
	Present	%	26.8	27.3	40.5	34.1	
	N. A. A.	Ν	68	60	138	266	
Type of the CalcificationPresence of the Calcification24-40 Years OTonsillolithNot presentN529073.2PresentN199426.8EICACNot presentN689695.8PresentN3964.2PresentN3964.2PresentN26969636.6969636.6969636.69798.69698.69636.69696.6969696.6969798.61.19698.61.19698.61.19698.61.19798.61.19698.61.19796.61.1961.196.69798.61.1961.196.69798.61.1961.196.69696.61.1961.196.69798.61.1961.196.69697.01.1961.196.69798.61.1961.196.69697.01.1961.196.69797.296.6961.196.6961.196.6<	Not present	%	95.8	90.9	90.2	91.7	2.06
	3	6	15	24	2.06		
	Presence of the CalcificationN Years Old41-50 Years Old31-51 Years OldNot presentN %524891%73.272.759.5PresentN %26.827.340.5Not presentN %26.827.340.5PresentN 	9.8	8.3				
	N. A. A.	Ν	26	21	51	98	
Pineal gland calcification	Not present	%	36.6	31.8	33.3	33.8	0.29
Pineal gland calcification	Durant	Ν	45	44	98	187	0.38
	Present	%	63.4	66.7	64.1	64.5	
	N-4	Ν	26	21	51	98	
	Not present	%	36.6	31.8	33.3	33.8	_
Choroid plexus calcification	D	Ν	0	1	4	5	a
	Present	%	0	1.5	2.6	1.7	
			70	63	152	285	
Sialalith	Not present	%	98.6	95.5	99.3	98.3	a
Statolith	Present	N	1	3	1	5	
		%	1.4	4.5	0.7	1.7	
	Not present		70	66	149	285	_
Antrolith			98.6	100.0	97.4	98.3	
Antionth	Prosont	N	1	0	4	5	a
	Present		1.4	0.0	2.6	1.7	
	Not present	Ν	47	40	106	193	
Potroalinoid ligament adoification	Not present	%	66.2	60.6	69.3	66.6	- 1.56
Petroclinoid ligament calcification	Decement	Ν	24	26	47	97	
	Tresent	%	33.8	39.4	30.7	33.4	
	Not present	Ν	69	58	110	237	
ИСАС	not present		97.2	87.9	71.9	81.7	- 22.93**
IICAC	Present		2	8	43	53	
			2.8	12.1	28.1	18.3	
Total		Ν	71	66	153	290	
		%	100,0	100.0	100.0	100.0	

Table 2. Statistical correlation between age groups and the calcifications and the crosstabs.

* P<0.10; ** P<0.01; a: No test was performed.

Table 3. Statistical correlation between genders and the calcifications and the crosstabs.

Type of the Calcification	Presence of the Calcification		Female	Male	Total	Chi-square	
Torsillelith	NT-44	N	106	85	191		
	Not present	%	68.4	63.0	65.9	0.04	
ronsmontn	_	Ν	49	50	99	0.94	
	Present	%	31.6	37.0	34.1		
		Ν	137	129	266		
FIGLO	Not present	%	88.4	95.6	91.7	4.00*	
EICAC	D	Ν	18	6	24	4.88*	
	Present	%	11.6	4.4	8.3		
	N	Ν	55	43	98		
	Not present	%	35.5	31.9	33.8	0.40	
Pineal gland calcification		Ν	98	89	187	0.43	
	Present	%	63.2	65.9	64.5		
	N	Ν	55	43	98		
	Not present	%	35.5	31.9	33.8		
Choroid plexus calcification	Present	Ν	2	3	5	a	
		%	1.3	2.2	1.7		
	N	Ν	152	133	285	а	
	Not present	%	98.1	98.5	98.3		
Sialolith	. .	Ν	3	2	5		
	Present	%	1.9	1.5	1.7	-	
	N	Ν	152	133	285		
	Not present	%	98.1	98.5	98.3		
Antrolith	D	Ν	3	2	5	а	
	Present	%	1.9	1.5	1.7		
	N. 4	Ν	119	74	193		
Petroclinoid ligament calcification	Not present	%	76.8	54.8	66.6	15.63**	
	_	Ν	36	61	97		
	Present	%	23.2	45.2	33.4		
ПСАС	N. 4	Ν	130	107	237	1.02	
	Not present	%	83.9	79.3	81.7		
	Durant	Ν	25	28	53	1.03	
	rresent	%	16.1	20.7	18.3		
Total		Ν	155	135	290		
		%	100.0%	100.0	100.0		

* P<0.10; ** P<0.01; a: No test was performed.

-	Tonsillolith	EICAC	Pineal Gland Calc.	Choroid Plexus Calc.	Sialolith	Antrolith	Petroclinoid Liga- ment Calcification
EICAC	.111	-	-	-	-	-	-
Pineal gland calc.	.064	.103	-	-	-	-	-
Choroid plexus calc.	.123	.118	.066	-	-	-	-
Sialolith	.016	.056	.011	.024	-	-	-
Antrolith	.072	.040	.034	.044	.018	-	-
Petroclinoid ligament calcification	.029	.001	.003	.019	.075	.075	-
IICAC	.021	.149*	.069	.100	.006	.074	.024

Table 4. Cramer's V coefficient of correlation between calcifications.

* P<0.05.

The correlations between the calcifications were investigated by Cramer's V test. Regarding the correlation of the calcifications, there was a statistically significant correlation between only EICAC and IICAC (Table 4).

4. DISCUSSION

Head and neck soft tissue calcifications may be pathological, age-related or idiopathic origin [4]. The pathological calcifications are rare, but it is necessary to differentiate the physiological and pathological calcifications [9]. Computed Tomography (CT) images allow better differentiation of the soft tissues due to the better contrast resolution and less image-noise and it is still the best imaging method for soft tissue calcifications in cranial region [11, 12].

Although CBCT has many advantages for the diagnosis of maxillofacial pathologies, distinction of the soft tissues cannot be defined via CBCT due to its insufficient contrast resolution [13]. CBCT is commonly used during clinical practice however, most of the physicians have not enough knowledge about image's interpretation [13]. The American Academy of Oral and Maxillofacial Radiology (AAOMR) and the European Academy of Dentomaxillofacial Radiology (EADMFR) defined that all CBCT images within the FOV must be examined carefully [5, 14]. It is very possible to see pathologies outside the dental arches while exploring CBCT images [1]. The consultation with a dentomaxillofacial radiologist is required if the practitioner hesitates in anyway during clinical practice [14]. The detection of soft tissue calcifications is generally based on their anatomic location, distribution and morphologic features on radiographic images [4]. Previous studies reported that carotid artery calcifications can be determined evenly by both CT and CBCT [15, 16]. In the literature, there are limited number of studies about the soft tissue and intracranial calcifications via CBCT [1, 4, 8-10, 17].

Tonsilloliths are calcified structures organizing from the tonsillar crypts' repeated inflammation bouts [2]. Although they are usually asymptomatic, large palatine tonsilloliths can cause throat irritation, pain, dysphagia, dysgeusia, halitosis, otalgia, and foreign body sensation during swallowing [18]. No treatment is required in most of the cases, but treatment procedures are suggested in the immunosuppressed patients due to the risk of aspiration pneumonia [4]. The prevalence of palatine tonsilloliths on CT images has been found to be 16 to 46.1% [19-23] and its prevalence has been reported as remarkably lower (4.9-10.1%) [1, 4, 10] on CBCT images. Several studies detected that tonsilloliths were more common in males than in females and also increased with age (approximately >40-50 years old) [18, 20, 22]. However, tonsilloliths have been found to be more common in females by some authors [19] and in younger individuals than 30 years old on cervical CT scans of trauma patients [23]. In this study, the prevalence of tonsilloliths was 34.1% on CBCT images. This finding was relatively in accordance with previous CT studies [19-23] and significantly higher than CBCT studies [4, 10]. Tonsilloliths were also observed to be more common in females and 50 years over individuals and these results were in accordance with previous reports [18, 20, 22]. Differences between the results of studies may be related with several factors such as soft tissue resolution of imaging method (CT or CBCT), slice thickness, study population and the evaluation criteria, etc.

Pineal gland calcification usually seen in older patients is a benign physiological lesion [1]. The lesion was seen in two-third of the adults [24]. Its radiographic manifestation appears as a single, well-demarcated, concentric radioopaque mass in the midline plane [9]. Pineal gland calcification might be an indicative of a neoplasm if it is bigger than 1 cm or seen in younger than 9-age [24]. The prevalence of the pineal gland calcification was found to be 72%, 71%, 68.5%, 67.7%, 64.3% and 37.4% on CT images [25-30]. It was found to be 4.76%, 14.7%, 19.2% and 28.2% on CBCT images, significantly lower than CT studies [1, 9, 10, 17]. The mean ages of the study samples in previous CBCT studies were substantially different (Table 5). In the present study, pineal gland calcifications were observed in 64.5% of the patients, higher than the previous CBCT studies, close to the previous CT reports [9, 10, 17, 26, 29]. The difference may arise from the higher mean age. No statistically significant differences were found between genders or the age groups, in contrast to previous reports [1, 26]. Pette, et al.'s CBCT study showed that brain pathologies occur 2.63 times more in women than in men [1]. In contrast with that study, in two CT studies, pineal gland calcification was found to be higher in males than in females [27, 28]. In addition, older

	This study	Sedghizadeh, <i>et al.</i> [9]	Price, <i>et al</i> . [4]	Allareddy, <i>et al.</i> [10]	Rheem, <i>et al.</i> [17]	Pette, <i>et al.</i> [1]	Damaskos Scand [39]
Tonsillolith	34.1	-	4.9	9.2	-	10.1	-
EICAC	8.3	-	1.5	(5.7)*	(2.0)*	5.7	31
Pineal gland	64.5	28.2	-	14.7	4.7	19.2	-
Choroid plexus	1.7	4.2	-	-	-	-	-
Sialolith	1.7	-	0.2	0.4	-	0.9	-
Antrolith	1.7	-	0.6	-	2.72	1.3	-
Petroclinoid liga- ment	33.4	8	-	-	-	0.31	-
IICAC	18.3	-	0.5	(5.7)*	(2.0)*	3.1	33.3
Mean age	49	52	49.3	?	28.1	63	60.2
N	290	500	272	1000	147	318	484

Table 5. Comparisons of the CBCT studies' soft tissue and intracranial calcifications' ratio in the literature.

*In these studies, the investigators did not divide the carotid artery calcifications as EICAC and IICAC.

age groups' ratio was found to be statistically significantly higher than younger age groups [1, 25-28, 31]. In this study, the pineal gland calcification was determined as the most prevalent lesion in agreement with the results of Daghighi, *et al.* [26].

Choroid plexus calcification was seen in 66.2%, 46%, 57.6% and 43.3% of the patients in CT studies [25, 26, 28, 30]. The frequency of the lesions was found to be higher in men than in women increasing with age [25, 26]. It was detected as 4.2% in a CBCT study [9]. In this study, choroid plexus calcifications were observed in 1.7% of the patients, in accordance with previous CBCT study [9].

Petroclinoid ligament calcification is a linear calcification, localized in postero-lateral side of clinoid processes [32]. According to the best of our knowledge, there are only a few reports in the literature about the incidence of the petroclinoid ligament calcification via CT and CBCT [1, 9, 33]. Petroclinoid ligament calcification has been detected in 31.8% and 34.1% in the right and left sides of the patients on CT images [33]. Also, it was more common in males when compared to females increasing with age [33]. Pette, et al. used CBCT images with 13 cm FOV and observed it in only 0.31% of the patients [1]. Its prevalence has been reported as 8% on whole brain CBCT images in another study [9]. In this study, we used the images in maxillofacial FOV (17 cm height), the prevalence of petroclinoid ligament was 33.4% and more common in females than in males. These results were in accordance with previous study performed on CT images. On the other hand, its prevalence was very higher than the results of previous CBCT studies and the difference may be related with the use of different FOV in CBCT scans.

Calcified carotid plaque is an important sign of ischemic cerebrovascular diseases [34]. It may increase the atherosclerotic load and the risk of morbidity and mortality [35]. Carotid artery calcifications may be confused by the other neck calcifications such as calcifications of thyroid cartilage and stylohyoid ligament, sialoliths and tonsilloliths. Also, the appearance and localization of the carotid artery calcifications may help to confirm the differential diagnosis [36]. It has been reported that CBCT would be useful imaging method for the carotid artery calcifications [1]. Threedimensional technology of CBCT let us to see the exact location of these calcifications which could be an indicator of the stroke or metabolic disease [4, 36-38]. On radiographs, carotid artery calcifications were seen as single or multiple rice grain appearances [39]. EICAC are localized in cervical soft tissue area, postero-lateral to the pharyngeal airway space while IICAC are placed in extended from the anterior to posterior clinoid process region [39, 40]. The patients with these calcifications should be referred for further examinations and treatments [4]. Atherosclerosis causes high mortality, so early diagnosis has critical prescription. It has been associated with several diseases such as diabetes, osteoporosis, coronary artery diseases and chronic renal failure, and often occurs in older ages (after 50 years of age). Internal carotid artery calcifications are seen in 2-4.5% of the over 50-year old population and this rate can be up to 22-37% in patients with hypertension, type 2 diabetes, smoking habit, hypercholesterolemia, cardiovascular disease, sleep apnea syndrome, metabolic syndrome, menopause and neck radiotherapy history [2]. Although most patients are initially asymptomatic, pathologies such as cutaneous gangrene, peripheral vascular disease and myositis may occur in these patients [2]. It is stated in the common decision of oral and medical radiologists in 2012 that extra or intracranial internal carotid artery calcifications in clinical practice should be regarded as "the visible part of the iceberg" and that these patients should be evaluated with medical consultation due to the risk of developing cerebral embolism (6, 8, 41, Macdonald 2012, Schulze 2013, Crouse 1987, Griniatsos 2009).

The prevalence of carotid artery calcifications was found to be 22.9% in a CT study [23]. IICAC was found in 82.2% of the patients, with the mean age of 69.6 by Bos, *et al.* [41]. Iwasa, *et al.* analyzed the intracranial calcifications in hemo-

The Assessment of Maxillofacial Soft Tissue

dialysis patients, IICAC was found in 62.1% of the hemodialysis patients while 18.6% in control group [42]. Most of the studies in the literature used panoramic radiographs for EICAC; it was seen in 0.43%-9.9% of the patients [43-46]. In CBCT studies, carotid artery calcifications were found as 2-5.7% of the samples [10, 17]. The investigations showed that these calcifications were higher in males than in females and the individuals with 50-years over [10, 23, 39]. In CBCT studies, the prevalence of EICAC was reported as 1.5%, 5.7% and 31%, while the prevalence of IICAC was found to be 0.5%, 3.1% and 33.3% [1, 4, 39]. Pette, et al. emphasized that the incidence of the vascular pathologies (like carotid artery calcifications) was 5 times more in patients with 65age over [1]. In the present study, EICAC was observed in 11.6% of females and 4.4% of males (overall: 8.3%), which was statistically significantly different. IICAC was observed in 16.1% of females and 20.7% of males (overall: 18.3%). The differences between the studies may be related with age of study samples and the use of FOV and also imaging method. The prevalence of both EICAC and IICAC increased with the age and was mostly observed in the patients with 50-years over. These results confirmed the results of the previous studies [1, 26]. However, the results regarding gender were different from Allareddy, et al.'s report [10]. Statistically significant correlation was found between EICAC and IICAC. This result was compatible with the previous CBCT study performed by Damaskos, et al. [8].

Sialoliths are the calcification of the salivary gland ducts [2]. These lesions may be symptomatic or asymptomatic depending on whether the salivary canal is completely blocked [47]. The submandibular glands are mostly affected, because their canals are longer and more tortuous [2]. Further tests or excision are suggested for the patients with sialoliths [4]. The prevalence of sialoliths was reported as 0.2%-0.9% in previous CBCT reports [1, 4, 10]. The calcifications located in maxillary sinus antrum are called antrolith. Antroliths were found in 0.6%-2.7% of the patients in previous studies [1, 4, 17]. In this study, we found the ratio of both sialoliths and antroliths to be 1.7% in accordance with previous reports [1, 4, 10, 17].

There are some limitations in our study. Due to a retrospective radiographic study of this study, we did not know the potential systemic diseases and complaints of the patients. Additionally, because of the absence of soft tissue window in CBCT, the calcifications were hardly localized and confirmation of the lesions was not made.

CONCLUSION

In this study, the distributions of soft tissue calcifications in maxillofacial region and intracranial calcifications on CBCT images were investigated. The most common calcifications were pineal gland calcification, followed by tonsillolith, petroclinoid ligament calcification, IICAC, EICAC and the others (equally sialolith, antrolith and choroid plexus calcification), respectively. Tonsillolith, EICAC and IICAC showed an increase with age. EICAC was seen more in females, conversely petroclinoid ligament calcification was seen more in males.

ETHICS APPROVAL AND CONSENT TO PARTICI-PATE

Ethical Approval was received from Gazi University Ethics Committee (19.06.2015-77082166-604.01.02, Ankara, Turkey).

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are base of this research.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

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