Project Deliverable

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Title:
D4.2 Completed testing and comparison of the various CBCT and MSCT with the phantom models for segmentation, linear and diagnostic accuracy *in vitro*

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PU	Public	X
PP	Restricted to other programme participants (including the Commission)	
RE	Restricted to a group defined by the consortium (including the Commission)	
CO	Confidential, only for members of the consortium (including the Commission)	

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Abstract:

This deliverable describes the methodology and results of the *in vitro* section using human jaw bones of WP4.
The approach was twofold: on the one hand, software-driven analyses were done to compare the segmentation accuracy of several Cone Beam CT (CBCT) devices in an automated way. On the other hand, observer studies were performed for diagnostic accuracy testing of root and bone lesions.
For segmentation accuracy, CBCT images were compared to clinical and/or gold standards using surface registering as well as structural descriptions of the internal bone structure. These standards were multislice CT (MSCT) and microCT (µCT). Preliminary results could be obtained describing the optimal settings to obtain high segmentation accuracy for specific devices.
For diagnostic accuracy, observers were asked to assess images of several devices and detect, locate and describe lesions on roots (resorption) or bone tissue. Again, a comparison of the devices could be made.
The deliverable ends with a note on ongoing research (within project) and future research to be performed.

Table of Contents

1. The Context

1.1: SEDENTEXCT Aims and objectives

The aim of this project is the acquisition of the key information necessary for sound and scientifically based clinical use of dental Cone Beam Computed Tomography (CBCT). In order that safety and efficacy are assured and enhanced in the ‘real world’, the parallel aim is to use the information to develop evidence-based guidelines dealing with justification, optimisation and referral criteria and to provide a means of dissemination and training for users of CBCT. The objectives and methodology of the collaborative project are:

1. To develop evidence-based guidelines on use of CBCT in dentistry, including referral criteria, quality assurance guidelines and optimisation strategies. Guideline development will use systematic review and established methodology, involving stakeholder input.

2. To determine the level of patient dose in dental CBCT, paying special attention to paediatric dosimetry, and personnel dose.

3. To perform diagnostic accuracy studies for CBCT for key clinical applications in dentistry by use of *in vitro* and clinical studies.

4. To develop a quality assurance programme, including a tool/tools for quality assurance work (including a marketable quality assurance phantom) and to define exposure protocols for specific clinical applications.

5. To measure cost-effectiveness of important clinical uses of CBCT compared with traditional methods.

6. To conduct valorisation, including dissemination and training, activities via an ‘open access’ website.

At all points, stakeholder involvement will be intrinsic to study design.

1.2: Work package 4 (WP4) objectives

- To determine *in vitro* the segmentation, linear and/or diagnostic accuracy of various CBCT scanners versus MSCT (WP4.1)
- To assess the diagnostic accuracy of CBCT in an animal model (WP4.2)
- To determine the diagnostic accuracy of various CBCT scanners for specified clinical applications (WP4.3)

1.3: Deliverable D4.2

Deliverable D4.2 (Completed testing and comparison of the various CBCT and MSCT with the phantom models for segmentation, linear and diagnostic accuracy *in vitro*) describes several outcomes, coming from WP4.1. It includes all *in vitro* studies except the animal model. It aims for segmentation accuracy, based on scanning different skulls with several devices and comparing it to a gold standard. Next to that, *in vitro* diagnostic accuracy is assessed for bone lesions and root lesions. From this deliverable, at least 5 publications are envisaged.

2. The Methodology

2.1 Segmentation accuracy

To simulate and evaluate various settings, we collected maxillary as well as mandibular bone, dry and including soft tissues, dentate as well as edentulous.
The first step was scanning the materials. For the CBCT, the samples were scanned at standard clinical settings of the devices, which sometimes meant several scans to be taken per device. An overview of the scans is given in the table below:

	Maxilla A **Soft tissue**	**Maxilla B** **Soft tissue**	**Mandible A** **Soft tissue**	**Mandible B** **Soft tissue**	**Mandible C** **Dry**	**Mandible D** **Dry Fragments**
Accuitomo	X	x	X	X	X	
Galileos	X	X	X	X	X	
i-CAT	X	X	X	X		
Kodak 9000		X	X	X	X	
Picasso		X	X	X	X	
Promax		X	X	X	X	
Scanora 3D	X	X	X	X	X	X
Somatom (MSCT)		X	X	X	X	
Skyscan (µCT)	X	X	X	X		X

CBCT scans were always compared to a reference standard: the gold standard µCT and/or the clinical standard (up to now) MSCT.
The images were analysed from 2 points of view: segmentation accuracy using the surface and segmentation accuracy using the internal bone structure (trabecular bone). For surface analysis, µCT and MSCT images were both used as a reference.

Surface
The reconstructed volumes of the scans were exported as DICOM-images to be segmented using Simplant Pro® by Materialise Dental NV (Haasrode, Belgium). The created jaw bone models were internally filled resulting in a 3D surface model using Mimics® and 3-Matic® by Materialise NV. The last was also used for comparative calculations. The differences in dimension were visualised in a histogram using a standardized range from -2mm to +2mm: expansion in red, shrinkage in blue;, approximately corresponding surfaces in green (Figure 1). These same colours were projected on the jaw models. The percentage of surface exceeding -1mm to +1mm range was used to evaluate the reproducibility (Figure 2).
The following samples were used for surface analysis: Maxilla B, Mandible A, Mandible B and Mandible C.

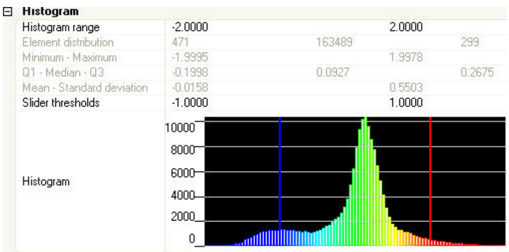


Figure 1: Example of histogram analysis: clear peak around 0-value. Red means enlargement, bleu shrinkage compared to the reference standard.

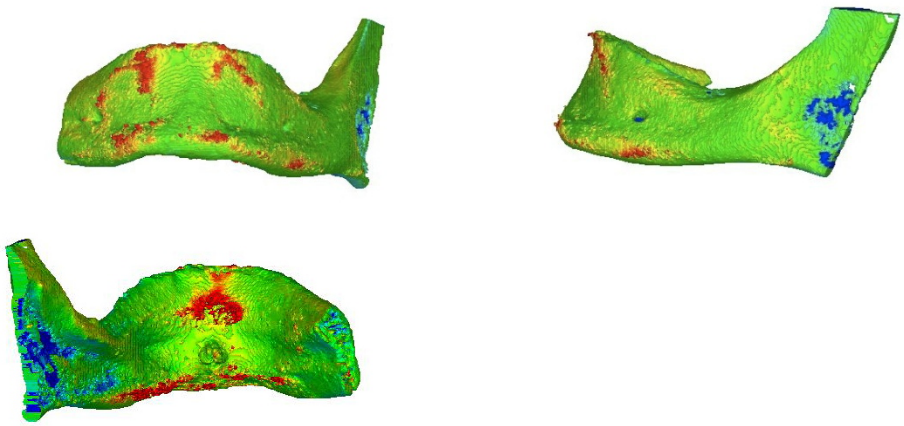


Figure 2: Frontal and lateral view of the distance calculation using images of Sirona Galileos 3D to match MSCT images. In the frontal region, we can see an enlargement, at the ramus part of the cortical surface is missing.

Trabecular bone

Description of the internal structure was made in analogy to histological analysis. The advantage of using µCT instead of histology was time, cost and the fact that the description can be done in a non-destructive way, keeping the samples available for further scanning if necessary (new devices, repeated scans). In this part of the study, several unexpected events slowed down the imaging procedure as well as the analysis. Therefore, the segmentation accuracy of the trabecular bone structures is still ongoing (cfr. Remarks).

2.2 Diagnostic accuracy *in vitro*

A separate description for the diagnostic accuracy studies is granted, because of the different research-approach. For diagnostic accuracy *in vitro*, observer studies were performed. Both bone lesions and root lesions were simulated and investigated.

Root lesions

A paediatric skull with early mixed dentition was obtained from the Department of Anatomy, Hasselt University, Belgium with ethical approval. This skull had an impacted maxillary left canine and therefore allowed a reliable simulation of this clinical situation. Simulated root resorption cavities were created in 8 extracted human maxillary left lateral incisors by the sequential use of ISO 0.16 mm diameter round burs in the distopalatal root surface. Cavities of varying depths were drilled in the middle or apical thirds of each tooth root according to 3 set-ups: slight (0.15, 0.20 and 0.25 mm), moderate (0.60 and 1.00 mm), and severe (1.50, 2.00, and 3.00 mm) resorption. The lateral incisors, 2 intact teeth, were repositioned individually in the alveolus of the paediatric skull with approximal contacts to the impacted maxillary left canine.
Six sets of CBCT images were obtained by using the Scanora 3D® (Soredex, Finland), Accuitomo® (J. Morita, Japan), Galileos® (Sirona, Germany), Kodak 9000® (IMTEC/Kodak dental System, USA), ProMax® (Planmeca, Finland) and Picasso® (EWoo Technology, Korea) for each tooth setup.

Six observers (postgraduate students in orthodontics as well as postgraduate research students in the oral imaging center) examined the sets of images for the presence of resorption cavities. The observers needed to assess the image quality, canine location, contact between canine and lateral incisors, severity (if present) of lateral incisor resorption and the location of the resorption.

Bone lesions

An *in vitro* model was used to simulate the bone lesions. A human dry edentulous cadaver skull was used for this study, after ethical approval was obtained from the commission of medical ethics of the University Hospitals, K.U.Leuven. The mandible was cut into five blocks. To establish a gold standard, simulated defects of known width and depth were prepared with an ISO 0.16 mm diameter round bur. Defects were created using a vertical milling machine. In every section, experimental lesions of various types were made with a round bur. Holes were drilled into each sections with a depth of 150 µm, 175 µm, 200 µm, 250 µm and 300 µm. The lesions were created in the trabecular bone, the cortical bone and in the cortico-trabecular area.
Six sets of CBCT images were obtained by using the Scanora 3D® (Soredex, Finland), Accuitomo® (J. Morita, Japan), Galileos® (Sirona, Germany), Kodak 9000® (IMTEC/Kodak dental System, USA), ProMax® (Planmeca, Finland) and Picasso® (EWoo Technology, Korea).
Six observers (5 dentists & 1 student), evaluated all digital images. The images from the different CBCT systems were analyzed and performed with at least a one week interval between each session. The observers were asked to make rankings on the presence or absence of lesions at three sites (cortex, trabecular bone and in the cortico-trabecular area) on a 5-point probability scale. The lesions seen in the CBCT were pointed out on schematic images showing the bone blocks separately.

3. The Results

3.1 Segmentation accuracy

Surface

Based on the histogram analysis for each CBCT imaging parameter, the optimal parameter for scanning was determined. Based on these parameter comparisons, all devices could be compared, using their optimal settings. In Appendix 1, results for all scanners are assembled.

Optimal settings when comparing the surface to the surface determined with MSCT were:

- Sirona Galileos 3D: 85kV 21mA (14s scanning time)
- Soredex Scanora 3D: 85kV 10mA (20s scanning time)
- Kodak 9000 3D: All settings gave comparable results
- Morita Veraviewepocs 3D: 75kV 4mA (17.5s scanning time)
- Picasso Trio: 75kV 5mA (20s scanning time)
- Morita 3D Accuitomo: 70kV 4mA (17.5s scanning time)

Internal structure

The results for this study are not yet consolidated (cfr. Remarks).

3.2 Diagnostic accuracy *in vitro*

Root lesions

The observer study was done for two devices. The rest of the observer studies is currently ongoing (cfr. Remarks).

The percentages of correct assessment for all samples (including no resorption samples) with respect to resorption, degree of resorption, location of resorption, contact relationship, canine position are shown below.

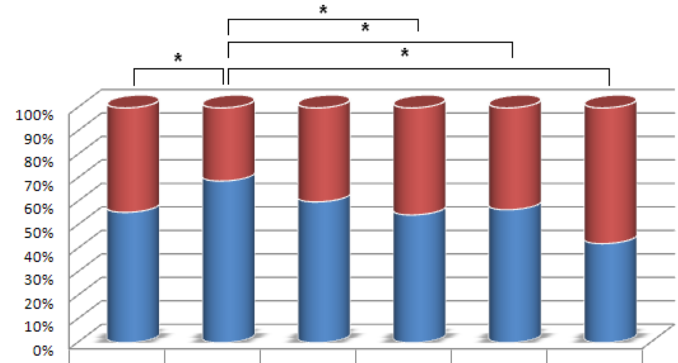
Assessment	Accuitomo	Scanora 3D
Presence of resorption	91%	90%
Degree of resorption	40%	41%
Location of resorption	60%	61%
Contact relationship	73%	84%
Canine position	69%	65%
Agreement	19%	28%

The sensitivity was 95% for Accuitomo CBCT and 94% for Scanora CBCT, and the specificity was 75% for both CBCT methods.

The differences in correct detection of root resorption for all resorption sizes (including teeth without resorption) was not significantly different between the Accuitomo and Scanora CBCT systems. Significant differences were found between both CBCT systems for correct classification of degree of resorption in the categories of slight and severe resorption. A significant Spearman correlation were observed between the agreement rate for the location of resorption and cavity size (p=0.01) when using the Accuitomo CBCT (Spearman rho=0.83). In addition, a significant relationship was found between agreement and size (p=0.02) for the Scanora CBCT (Spearman rho=0.78).

Bone lesions

This section first addressed the overall visibility of lesions, independent of their size and was therefore an evaluation of the CBCT systems. The scores collected from the observers were visualized in a graph (Figure 3) including frequency table (wrong-correct). A correct lesion identification and localisation was scored as 1 (correct); a false answer as 0 (wrong).



	Accuitomo	Scanora	Galileos	Kodak	Promax	Picasso
Wrong	40	28	36	41	39	52
Correct	50	62	54	49	51	38

Figure 3: Lesion detection and localisation for each device (* indicates significant difference $p < 0.05$)

The graph demonstrated a more correct detection of the bone lesions with the Scanora-images. Wilcoxon Matched Pairs Test was performed between the different scores for the detection of the simulated bone lesions. The Scanora had a significant ($p \leq 0.05$) higher detection level compared with all the other CBCTs except for the Galileos, where no significant difference was found.

The second question addressed the visibility of the bone lesions according to their size. In five different slices, holes were drilled with a different depth. The scores of the observers were collected. Wilcoxon Matched Pairs Test was performed to compare the detection of bone lesions of different sizes. The diagnostic accuracy was significantly higher for bone lesions with depth of 250µ and 300µ.

As a third analysis, the visibility of bone lesions of different sizes for the different CBCT devices was evaluated separately. Results are shown in Appendix 2. For the different CBCT systems, minimal detection threshold ranged from 175 µm to 250 µm. More specific, for the Scanora 3D® the threshold was 175 µm. For ProMax 3D®, Kodak 9000®3D, Picasso® and 3D Accuitomo® it was 250 µm.

The fourth question addressed the detection of the bone lesions in the different regions: trabecular, cortico-trabecular and cotircal area. The detection of the bone lesions in cortical area was significantly better than the detection in trabecular bone and in the cotrico-trabecular area. Detection of the cortico-trabecular lesions was not significantly different compared to the detection of the trabecular lesions. Of the defects that perforated the cortex 72,2% were detected, the score dropped to 52,2% for the trabecular region and dropped even to 44,4% for the defects in the cortico-trabecular area.

4. Conclusions

4.1 Segmentation accuracy

Surface
From this study, we could define the most convenient parameter settings to obtain optimal segmentation accuracy (cfr. Results). Moreover, we defined Picasso-based model to be best fitting the MSCT (clinical reference) images. Further comparative analysis will be done using µCT as a gold standard.

Trabecular bone
To be analysed (cfr. Remarks)

4.2 Diagnostic accuracy *in vitro*

Root lesions
The results of this *in vitro* study suggest that the CBCT technique could be a reliable diagnostic tool for detecting canine impaction and associated lateral incisor root resorption. Lesions as small as 0.20 mm could be easily diagnosed. The thin slices and 3D information might increase the detection rate. The need for additional conventional panoramic radiographs is unnecessary, thus additional X-ray exposure of the patient may be avoided. In addition, the radiation dose of CBCT is significantly lower as compared to conventional CT, and the typical overlap of dental structures on panoramic radiography was not observed.
Since much work is needed to demonstrate the added value of CBCT in routine orthodontic cases of root resorption, similar comparative studies will be performed on patients with canine impaction to demonstrate the canine location and determine whether the accuracy of CBCT remains high. Further studies including randomized controlled prospective studies should also be performed to determine the clinical relevance and clinical threshold for symptomatic resorption.
We did not yet make a device-based comparison on accuracy. The observer studies for the remaining devices is ongoing (cfr. Remark).

Bone lesions
A number of defects remained undiagnosed in the CBCT images. This number differed depending on the CBCT scanners and on the size of the lesions. False negative defects were more frequently reported than false positive defects for CBCT radiographs. The result of this study shows that none of the created bone lesions could be identified on the intraoral radiographs. For the settings used in the current study, Scanora 3D® performed best, making the identification of lesions sized 175µm possible.
Further research should address less well-defined lesions, e.g. created using acid. This type of lesions might simulate better clinical reality. Furthermore, a combination of the current approach and the approach used in the animal study (D4.1; peri-apical bone lesions) could be addressed in the future.

5. Deliverable remarks

As mentioned in several locations, not all analyses were performed within WP4.1 (associated with D4.2).

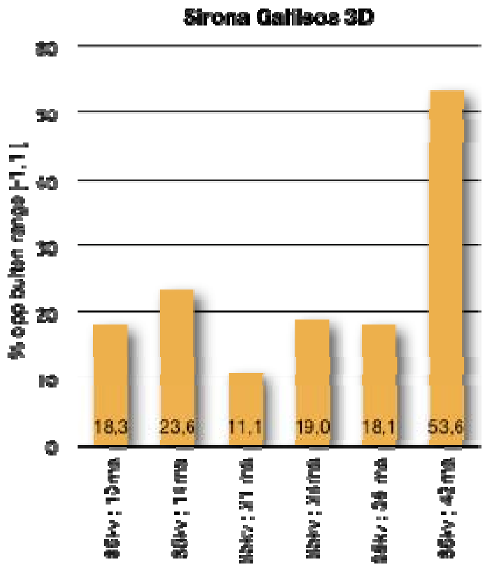
First of all, it needs saying that all scans were performed and therefore, all study material was collected to date.

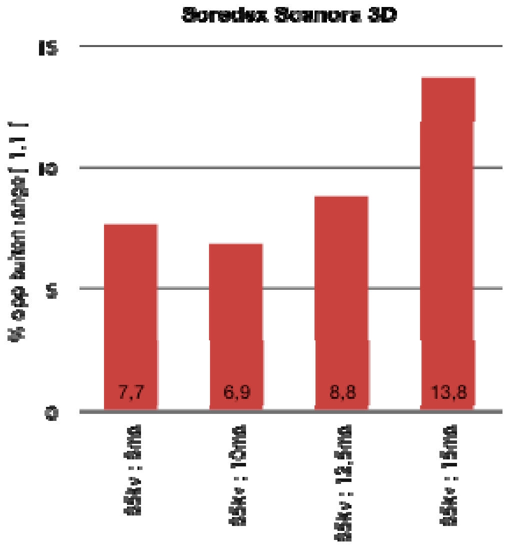
The analyses are done for most sub-divisions, but still running for others. The reason for this are the practical problems arising during µCT scanning. We contacted Skyscan (Kontich, Belgium) directly, to have access to the latest µCT-model. The major advantage of having access to this was the larger field of view. However, since the model was new, there were several sessions necessary, not only to optimise scan settings, but also to optimise reconstruction algorithms, which were still being developed at the time of our cooperation. Apart from that, since the scanning of one jaw took several hours (up to 5), there was a permanent risk of movement artefacts, making repeated scans necessary at several occasions. Third, the presence of soft tissue made the µCT scans even more challenging, since these tissues were shrinking due to the scanning process. Last, our contact person at the company, and the expert for this specific type of scans and the reconstruction process thereof fell sick. This caused a substantial delay in the scanning procedures.

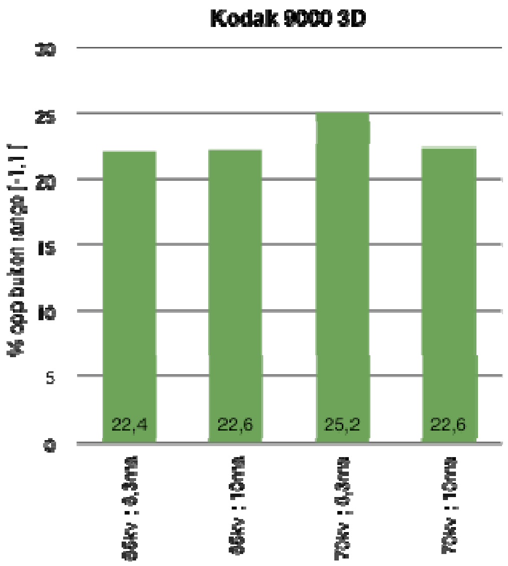
However, we feel confident these issues will not compromise the delivery of the actual report of the in vitro section of WP4, to be delivered at month 28.

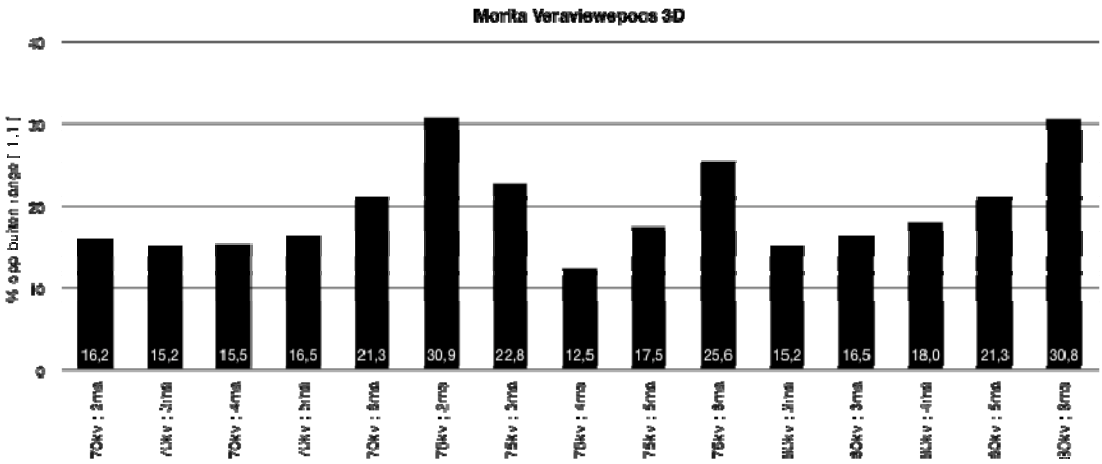
Appendix 1

Results for segmentation accuracy for all scanners and parameters. A clear bar showing the least deviation from the reference (bar showing ‘optimal setting’) is usually visible.





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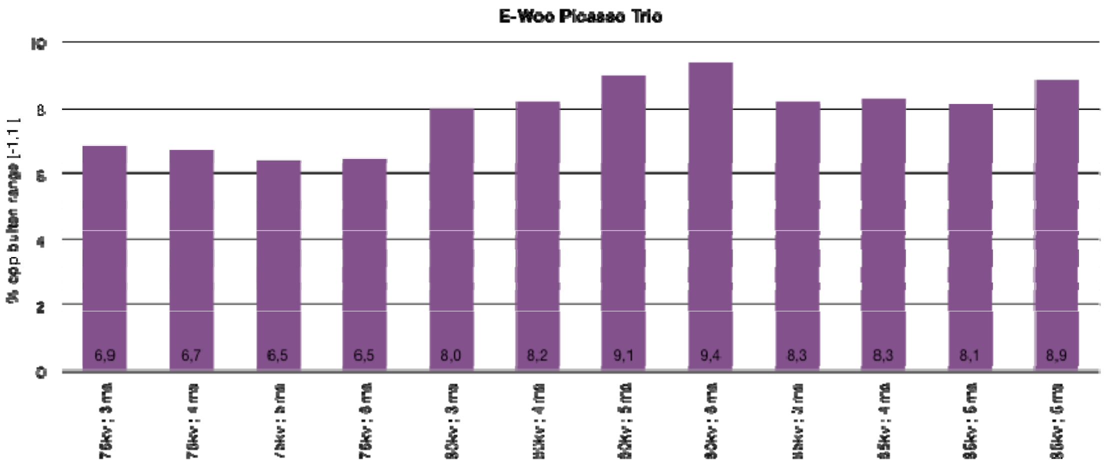
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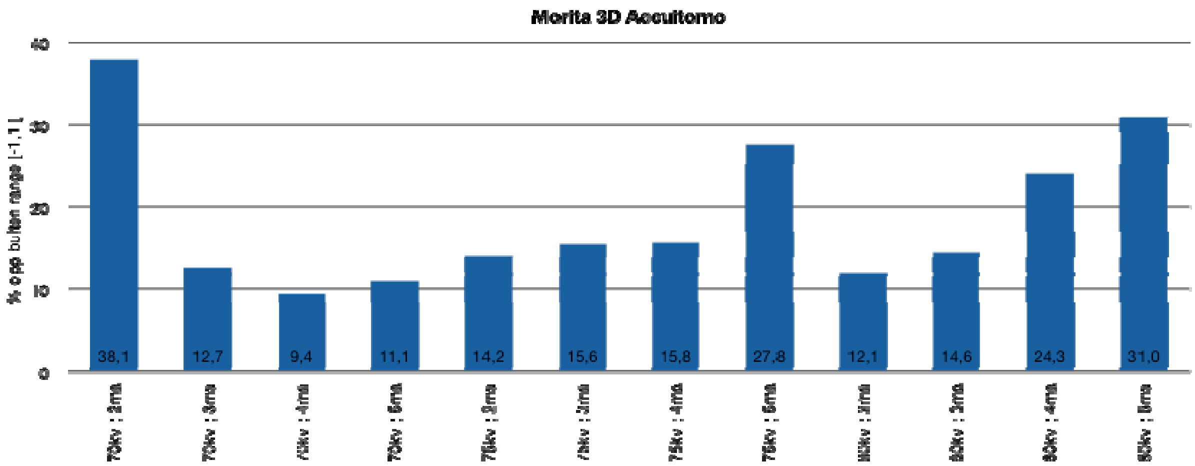
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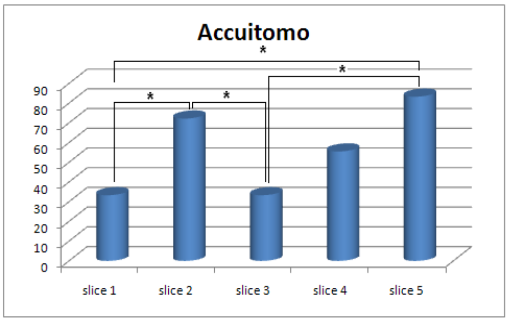
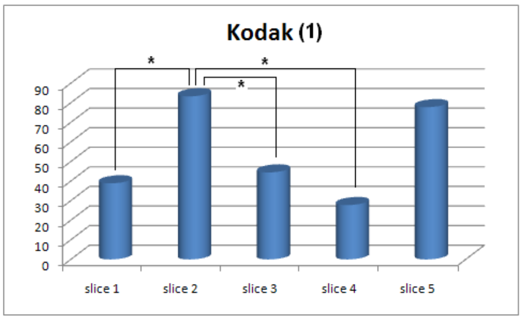
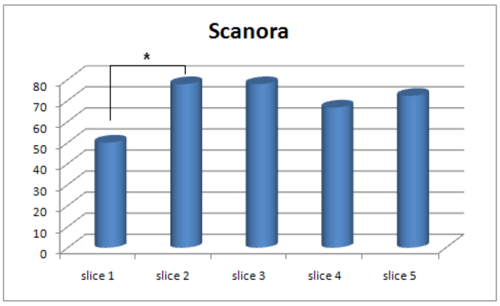
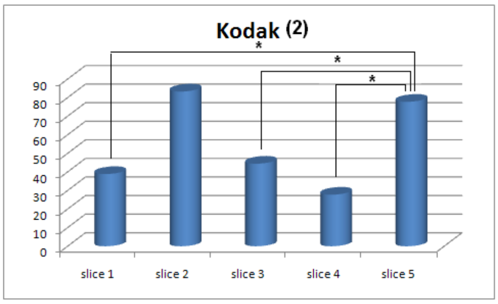
Appendix 2

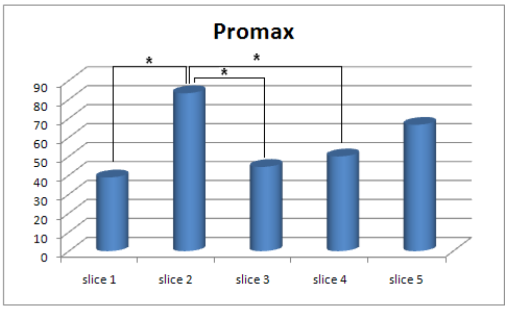
Detection of bone lesions for the different CBCT and bone blocks

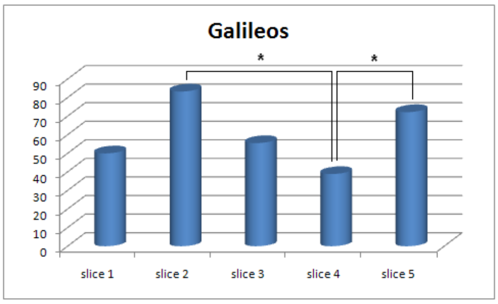


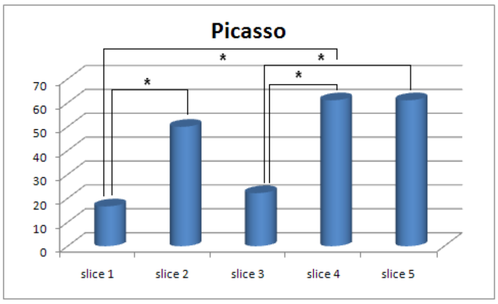












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